NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology consultation: SEM Scanner 200 for preventing pressure ulcers

Supporting documentation – Committee papers

The enclosed documents were considered by the NICE medical technologies advisory committee (MTAC) when making their draft recommendations:

1. **EAC assessment report** – an independent report produced by an external assessment centre who have reviewed and critiqued the available evidence.
2. **Assessment report overview** – an overview produced by the NICE technical lead which highlights the key issues and uncertainties in the company's submission and assessment report.
3. **Scope of evaluation** – the framework for assessing the technology, taking into account how it works, its comparator(s), the relevant patient population(s), and its effect on clinical and system outcomes. The scope is based on the sponsor's case for adoption.
4. **Adoption scoping report** – produced by the adoption team at NICE to provide a summary of levers and barriers to adoption of the technology within the NHS in England.
5. **Sponsor submission of evidence** – the evidence submitted to NICE by the notifying company.
6. **Expert questionnaires** – expert commentary gathered by the NICE team on the technology.
7. **EAC correspondence log** – a log of all correspondence between the external assessment centre (EAC) and the company and/or experts during the course of the development of the assessment report.
8. **Company fact check comments** – the manufacturer's response following a factual accuracy check of the assessment report.

Please use the above links and bookmarks included in this PDF file to navigate to each of the above documents.

Document cover sheet

Assessment report: SEM Scanner

EAC team:

Project Lead(s): Jamie Erskine, Tom Macmillan

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Version number	Brief description of changes	Author/reviewer (e.g. J Smith)	Date (DD/MM/YY)	Date sent to NICE (if applicable)
1.0	First draft to NICE	A Chalkidou J Erskine M Kartha T Macmillan M Pennington	18/11/2019	18/11/2019
1.1	Amended draft to NICE	J Erskine T Macmillan M Pennington	25/11/2019	25/11/2019
1.2	Final draft to NICE	T Macmillan M Pennington	28/11/2019	28/11/2019

1.3	Amended draft to NICE	M Pennington T Macmillan	13/01/2019	13/01/2019
1.4	Final draft to NICE	M Pennington	20/01/2019	20/01/2019
1.5	Amended following company fact check	J Erskine T Macmillan	05/02/2020	05/02/2020

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technologies guidance

MT445 SEM Scanner 200 for pressure ulcer prevention

External Assessment Centre report

Produced by: King's Technology Evaluation Centre

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Date completed: 05/02/2020

Contains confidential information: Yes

Number of attached appendices: 1

Purpose of the assessment report

The purpose of this External Assessment Centre (EAC) report is to review and critically evaluate the company's clinical and economic evidence presented in the submission to support their case for adoption in the NHS. The report may also include additional analysis of the submitted evidence or new clinical and/or economic evidence. NICE has commissioned this work and provided the template for the report. The report forms part of the papers considered by the Medical Technologies Advisory Committee when it is making decisions about the guidance.

Declared interests of the authors

None.

Acknowledgements

Fawad Hussain is a Consultant Dermatologist and Skin Cancer Lead at Barking, Havering and Redbridge University Hospitals NHS Trust, no conflict declared.

Michael Clark is the Commercial Director of the Welsh Wound Innovation Centre; Professor Clark has worked in consultancy to several wound management companies but not to the manufacturer of SEM Scanner. WWIC has worked on NICE funded research.

Samantha Holloway is a Programme Director of Wound Healing and Tissue Repair at the Cardiff University School of Medicine, no conflicts declared.

Responsibility for report

The views expressed in this report are those of the authors and not those of NICE. Any errors are the responsibility of the authors.

Instructions for the EAC:

The assessment report is an important component of the information available to the Medical Technologies Advisory Committee (MTAC) when developing its provisional and, following consultation, final recommendations on the technology.

The template should be completed with reference to NICE's Medical Technologies Evaluation Programme methods guide. The headings and prompt questions in the template provide a consistent structure for the assessment of the company's submission. But the assessment, format and presentation may be adapted by the EAC to maximise the clarity of the report.

Any [redacted] information in the submission document should be underlined and highlighted in turquoise.

Any [redacted] information in the submission document should be underlined and highlighted in yellow.

If either type of confidential information is quoted or described in the assessment report, it must be underlined and highlighted as in the original. This allows the automated removal of this information and makes subsequent editing quicker and more reliable. It is very important to ensure removal of confidential information before public consultation. It is the assessment centre's responsibility to ensure all confidential information in the assessment report is underlined and highlighted in the appropriate colours.

All grey text in this template should be removed before submitting the final version to NICE.

Table of contents to be removed by NICE before including in the MTAC pack and publishing on the website.

Contents

Abbreviations

Term	Definition
BWAT	Bates-Jensen Wound Assessment Tool
CI	Confidence interval
DTI	Deep Tissue Injury
EAC	External Assessment Centre
FDA	Food & Drug Administration
HAPU	Hospital acquired pressure ulcer
ICER	Incremental cost effectiveness ratio
MAUDE	Manufacturer and User Facility Device Experience
MHRA	Medicines & Healthcare products Regulatory Agency
MTEP	Medical Technologies Evaluation Programme
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NICE CG	NICE clinical guideline
NICE MIB	NICE Medical Innovation Briefing
NICE MTG	NICE medical technology guidance
NICE QS	NICE quality standard
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSA	Probabilistic sensitivity analysis
PU	Pressure Ulcer
PURP	Pressure Ulcer Reduction Programme
RCT	Randomised controlled trial
SD	Standard deviation
sDTI	Suspected Deep Tissue Injury
SEM	Sub-epidermal moisture
STA	Standard tissue assessment
vs	Versus
VSA	Visual skin assessment

Executive summary

The included evidence for SEM Scanner comprises 2 before-after comparative studies (Raizman et al 2018, Hancock & Lawrance 2019) and 5 prospective observational single-arm studies (Gefen & Gershon 2018, O'Brien et al 2018, Okonkwo et al 2017, 2018, O'Keefe & McLusky 2019). A number of the studies are published as conference abstracts although the company provided pre-publication full-text versions and an unpublished report to provide additional detail on various aspects of the studies. All of the studies were funded by the company.

Due to the lack of high quality studies (there were no RCTs), no meta-analysis was carried out. The primary outcome in the two comparative studies was the incidence of PUs in two separate phases, in which patients were treated with and without the use of SEM Scanner. Both studies showed a reduction in the incidence of PUs and the EAC calculated odds ratios, both of which were statistically significant (OR 0.06, p=0.0005, in Raizman et al 2018; OR 0.43, p=0.0023, in Hancock & Lawrance 2019). The two comparative studies did not report any other outcomes listed in the scope. Three of the non-comparative studies investigated the diagnostic accuracy of SEM Scanner, though the usefulness of these studies is limited. The studies measure the performance of the SEM Scanner alongside Skin and Tissue Assessment (STA), which is the reference standard. This gives a measure of agreement between the tests rather than a true measure of diagnostic accuracy, however,the EAC notes that the IFU states the device is not to be used for diagnosing or detecting PUs. Three of the studies investigated the time to PU detection relative to visual assessment and found SEM Scanner to be 3-4.7 days quicker.

The EAC made substantial revisions to the company's cost model and found that SEM Scanner is not cost saving when used as an adjunct technology to VSA. The only relevant economic evidence comprised one unpublished study co-authored by the CEO of the company with Deloitte. In the company's model, cost savings are driven by a reduction in the incidence of stage II-IV PUs, which can require costly medical interventions such as reconstructive surgery. However, the evidence does

not support the reduction in PU incidence that the company claim is due to SEM Scanner. The EAC also took into account the effect of increasing rounding from every 6 hours to every 4 hours, taken from the trial by Defloor et al (2005). The EAC subjected this parameter, and others, to sensitivity analyses, which confirmed the findings were robust.

The EAC modelled SEM Scanner as a replacement for VSA and found that the device is cost saving in this scenario due to increased specificity compared to VSA. This finding was robust to sensitivity analyses of all parameters except for specificity – SEM Scanner became cost incurring when specificity fell to 51%. The EAC notes that the standalone use of the device is not supported by the IFU and is not seen in any of the published evidence.

There are a number of methodological shortcomings to the available evidence, which makes it difficult to draw meaningful conclusions with any confidence. The EAC believes the existing evidence base does not support the case for adoption. The EAC recommends that future researchers should focus on designing comparative studies that are able to show the causal relationship between SEM Scanner readings and PU incidence and can therefore be used to determine the efficacy of the device.

1 Decision problem

The company clarified two points in the scope, which the EAC accepts as valid (see Table *1*).

Table 1 Decision problem from final scope

	Scope issued by NICE	Company's proposed variation from scope (if applicable)
Population	People at risk of developing pressure ulcers or with existing pressure ulcers.	As discussed, the SEM Scanner can only be used on intact skin in adults.
Intervention	SEM Scanner used as an adjunct to standard NHS clinical practice.	Enter text.
Comparator(s)	Standard NHS clinical practice for patients considered 'at risk' or 'at high risk' of pressure ulcers. This may involve a combination of: • Standard risk assessment using visual, tactile and biomarker tools • Frequent repositioning (at least 6 times hourly in people considered to be at risk and 4 times hourly in people considered to be at high risk) • Pressure redistribution using devices such as high-specification foam mattress or pressure redistributing cushions	Enter text.

Outcomes	The outcome measures to consider include: Intermediate/diagnostic outcomes • Diagnostic accuracy • Time to test result • Number of inconclusive results (including occasions where it is not possible to take 3 readings) • Impact on clinical management decisions Clinical effectiveness • Incidence of pressure ulcers • Incidence of skin breakdown at the heel and sacrum • Stage of pressure ulcer developed (stage I – IV, unstageable) • Device related adverse events • Rate of infection • Quality of life, and associated outcomes e.g. pain and discomfort, patient mobility, patient/carer satisfaction, patient depression and anxiety Systematic impact • Rate of complications avoided from pressure ulcer prevention e.g. infection, abscess, septicaemia, bone infections, meningitis • Length of hospital stay as a result of pressure ulcers, including ICU and conventional ward bed days • Costs of treating pressure ulcers and their complications e.g. nursing, hospital, surgical and treatment costs Additional outcomes to those relevant to the benefits claimed by the company: • Patient compliance with and the use of pressure ulcer prevention strategies • Ease of use of product, including training requirements	As discussed this refers to sensitivity and specificity

Cost analysis	Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and a combination of devices are needed.	Enter text.
Subgroups to be considered	People at high risk of developing pressure ulcers such as those with mobility issues, those with comorbidities affecting cognition and communication, people with spinal injury, those in residential homes and those with darker skin.	Enter text.

2 Overview of the technology

SEM Scanner is designed to assess patients who are at risk of developing pressure ulcers (PUs) by measuring the biocapacitance of tissue to detect the presence of fluid in the sub-epidermal tissues. The innovative aspect of the device is that it uses the biomarker of sub-epidermal moisture (SEM) to detect the presence of PUs before they become apparent through clinical signs such as rubor (reddening of the skin) or calor (warming of the skin). The instructions for use (IFU) and NPUAP/EPUAP/PPPIA Global Clinical Practice 2014 Guidelines highlight the fact that the standard of care, visual skin assessment (VSA), only detects the presence of PUs once they are visible at the skin level. SEM Scanner is designed to be used as an adjunct to the standard of care for assessing patients' anatomies for PU risk, and the IFU states that it is for use in the heels and sacrum of patients who are already at increased risk of developing PUs.

Damage to underlying tissue leads to inflammation, causing increased dilation and permeability of the surrounding blood vessels. This can lead to fluid building up in a layer under the skin, known as sub-epidermal moisture (SEM). SEM Scanner is a handheld, battery-powered device that uses a sensor comprising two concentric coplanar electrodes and an integrated pressure sensor to measure bioelectric impedance. These measurements are used to quantify SEM. An integrated display unit displays the SEM reading, a unit-less measurement ranging from 0.9-3.9. Once at least three readings have been taken, the device displays a delta value between the highest and lowest value. According to the IFU, a delta of ≥0.6 indicates an increased risk of the patient's anatomy developing a PU, while a delta of <0.6 indicates the patient's anatomy is at lower risk of developing a PU. The instructions also state that this delta value should not be used alone to make decisions and must be used in conjunction with standard of care and clinical judgement.

The device has been CE marked as a class IIa medical device since 2013.

The company submission mentions a new version of the device, the Provizio™ SEM Scanner, which integrates readings into the electronic patient record and includes a barcode reader. Although there is no published evidence for this version of the device, the EAC expects that evidence will be generalisable between the versions due to the similar mechanism by which they work. The company assert that unpublished research comparing this new version with the current one in tissue phantoms has been performed.

3 Clinical context

Pressure ulcers (PUs)[1] are caused by impaired blood supply to skin and underlying tissues under prolonged pressure. They typically occur in patients confined to a bed or a chair by their illness. According to NICE CG179, "they are more likely to occur in people who are seriously ill, have a neurological condition, impaired mobility, impaired nutrition, or poor posture or a deformity. Also, the use of equipment such as seating or beds, which are not specifically designed to provide pressure relief, can cause pressure ulcers."

The NHS Improvement report 'Pressure ulcers: revised definition and measurement' (June 2018) defines a PU as "localised damage to the skin and/or underlying tissue, usually over a bony prominence (or related to a medical or other device), resulting from sustained pressure (including pressure associated with shear). The damage can be present as intact skin or an open ulcer and may be painful".

PUs are sub-categorised by severity, defined in the EPUAP/NPUAP/PPPIA 2014 guidelines in Table 2. One clinical expert suggested that there might be scope for an additional PU category to be added to future guidelines that describes pre-stage I damage that is not visibly apparent but which will progress to higher stages if no intervention occurs. Clinical experts confirmed that there is no existing consensus on the optimal risk assessment scale to be used for PUs. NICE CG179 posits a simple 'at risk' and 'at high risk'

[1] Pressure ulcers are sometimes referred to in the literature as pressure injuries (PIs), pressure sores, bedsores and, rarely, decubitus ulcers. In this assessment report, the term "pressure ulcer" (PU) will be used throughout, except where studies have reported specifically on hospital acquired pressure ulcers (HAPUs).

categorisation, which combines “clinical judgement and/or a validated risk assessment tool”. Examples of risk assessment tools include the Braden, Norton, Waterlow and Cubbin-Jackson scales. Another example is the Bates-Jensen Wound Assessment Tool (BWAT). The Braden-Q scale is specifically for children. The scales apply a scoring system to different domains and define risk categories to the cumulative total. The Waterlow scale, used by one clinical expert, is given as an example in Figure 1. Another clinical expert described the use of the Braden scale to assess PU risk in in-patients, which occurs on admission and then weekly, or if new damage or changes in skin integrity is identified. NICE QS89 recommends that a risk assessment be carried out within 6 hours of admission in patients treated in hospital or care homes with nursing. In a Cochrane systematic review including two studies, Moore & Patton (2019) found that neither the Braden nor the Waterlow risk assessment tools made any significant difference to PU incidence rates, when compared to clinical judgement alone.

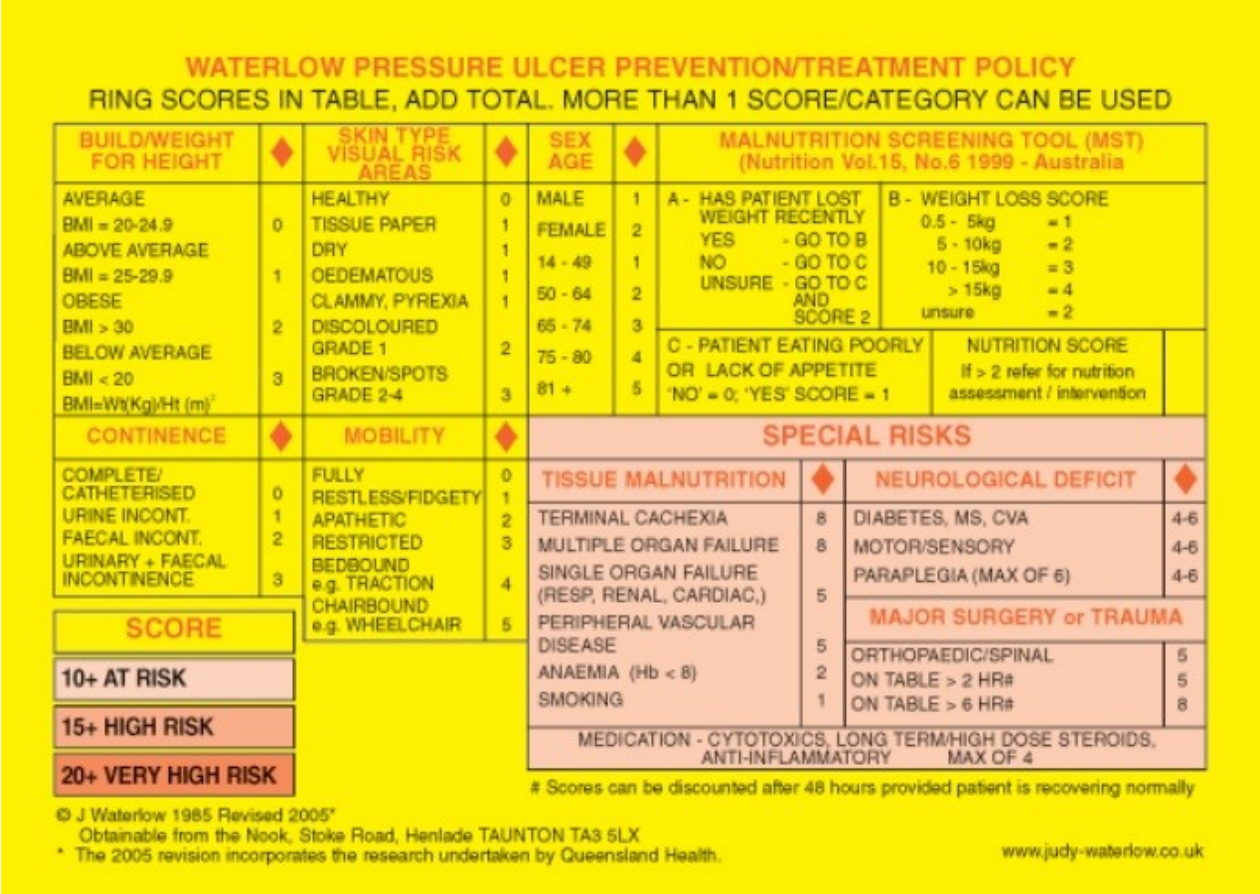
Table 2 International NPUAP/EPUAP Pressure Ulcer Classification System

Category/Stage I: Nonblanchable Erythema	Intact skin with non-blanchable redness of a localized area usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its colour may differ from the surrounding area. The area may be painful, firm, soft, warmer or cooler as compared to adjacent tissue. Category/Stage I may be difficult to detect in individuals with dark skin tones. May indicate “at risk” individuals (a heralding sign of risk).

Category/Stage II: Partial Thickness Skin Loss	Partial thickness loss of dermis presenting as a shallow open ulcer with a red pink wound bed, without slough. May also present as an intact or open/ruptured serum-filled blister. Presents as a shiny or dry shallow ulcer without slough or bruising.* This Category/Stage should not be used to describe skin tears, tape burns, perineal dermatitis, maceration or excoriation. **Bruising indicates suspected deep tissue injury.*
Category/Stage III: Full Thickness Skin Loss	Full thickness tissue loss. Subcutaneous fat may be visible, but bone, tendon or muscle are not exposed. Slough may be present but does not obscure the depth of tissue loss. May include undermining and tunnelling. The depth of a Category/Stage III pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput and malleolus do not have subcutaneous tissue and Category/Stage III ulcers can be shallow. In contrast, areas of significant adiposity can develop extremely deep Category/Stage III

	pressure ulcers. Bone/tendon is not visible or directly palpable.
Category/Stage IV: Full Thickness Tissue Loss	Full thickness tissue loss with exposed bone, tendon or muscle. Slough or eschar may be present on some parts of the wound bed. Often include undermining and tunnelling. The depth of a Category/Stage IV pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput and malleolus do not have subcutaneous tissue and these ulcers can be shallow. Category/Stage IV ulcers can extend into muscle and/or supporting structures (e.g., fascia, tendon or joint capsule) making osteomyelitis possible. Exposed bone/tendon is visible or directly palpable.
Unstageable: Depth Unknown	Full thickness tissue loss in which the base of the ulcer is covered by slough (yellow, tan, grey, green or brown) and/or eschar (tan, brown or black) in the wound bed. Until enough slough and/or eschar is removed to expose the base of the wound, the true depth, and therefore Category/Stage, cannot be determined. Stable (dry, adherent, intact without erythema or fluctuance) eschar

	on the heels serves as 'the body's natural (biological) cover' and should not be removed.
Suspected Deep Tissue Injury: Depth Unknown	Purple or maroon localized area of discoloured intact skin or blood-filled blister due to damage of underlying soft tissue from pressure and/or shear. The area may be preceded by tissue that is painful, firm, mushy, boggy, warmer or cooler as compared to adjacent tissue. Deep tissue injury may be difficult to detect in individuals with dark skin tones. Evolution may include a thin blister over a dark wound bed. The wound may further evolve and become covered by thin eschar. Evolution may be rapid exposing additional layers of tissue even with optimal treatment.



WATERLOW PRESSURE ULCER PREVENTION/TREATMENT POLICY

RING SCORES IN TABLE, ADD TOTAL. MORE THAN 1 SCORE/CATEGORY CAN BE USED

BUILD/WEIGHT FOR HEIGHT		SKIN TYPE VISUAL RISK AREAS		SEX AGE		MALNUTRITION SCREENING TOOL (MST) (Nutrition Vol.15, No.6 1999 - Australia
AVERAGE		HEALTHY	0	MALE	1	A - HAS PATIENT LOST WEIGHT RECENTLY YES - GO TO B NO - GO TO C UNSURE - GO TO C AND SCORE 2
BMI = 20-24.9	0	TISSUE PAPER	1	FEMALE	2	B - WEIGHT LOSS SCORE 0.5 - 5kg = 1 5 - 10kg = 2 10 - 15kg = 3 > 15kg = 4 unsure = 2
ABOVE AVERAGE		DRY	1	14 - 49	1	
BMI = 25-29.9	1	OEDEMATOUS	1	50 - 64	2	
OBESE		CLAMMY, PYREXIA	1	65 - 74	3	
BMI > 30	2	DISCOLOURED GRADE 1	2	75 - 80	4	C - PATIENT EATING POORLY OR LACK OF APPETITE 'NO' = 0; 'YES' SCORE = 1
BELOW AVERAGE				81 +	5	NUTRITION SCORE If > 2 refer for nutrition assessment / intervention
BMI < 20	3	BROKEN/SPOTS GRADE 2-4	3			
BMI=Wt(Kg)/Ht (m)^2						

CONTINENCE		MOBILITY	
COMPLETE/ CATHETERISED	0	FULLY	0
URINE INCONT.	1	RESTLESS/FIDGETY	1
FAECAL INCONT.	2	APATHETIC	2
URINARY + FAECAL INCONTINENCE	3	RESTRICTED	3
		BEDBOUND e.g. TRACTION	4
		CHAIRBOUND e.g. WHEELCHAIR	5

SPECIAL RISKS

TISSUE MALNUTRITION		NEUROLOGICAL DEFICIT	
TERMINAL CACHEXIA	8	DIABETES, MS, CVA	4-6
MULTIPLE ORGAN FAILURE	8	MOTOR/SENSORY	4-6
SINGLE ORGAN FAILURE (RESP, RENAL, CARDIAC,)	5	PARAPLEGIA (MAX OF 6)	4-6
PERIPHERAL VASCULAR DISEASE	5	MAJOR SURGERY or TRAUMA	
ANAEMIA (Hb < 8)	2	ORTHOPAEDIC/SPINAL	5
SMOKING	1	ON TABLE > 2 HR#	5
		ON TABLE > 6 HR#	8

MEDICATION - CYTOTOXICS, LONG TERM/HIGH DOSE STEROIDS, ANTI-INFLAMMATORY MAX OF 4

SCORE
10+ AT RISK
15+ HIGH RISK
20+ VERY HIGH RISK

Scores can be discounted after 48 hours provided patient is recovering normally

Obtainable from the Nook, Stoke Road, Henlade TAUNTON TA3 5LX

* The 2005 revision incorporates the research undertaken by Queensland Health.

www.judy-waterlow.co.uk

Figure 1 Waterlow Score Card (http://www.judy-waterlow.co.uk/downloads/Waterlow%20Score%20Card-front.pdf)

The company describes the introduction of the SEM Scanner in patients who are 'at risk' or 'at high risk' (tsee figure 2) of developing PUs (according to the NICE CG179 criteria). SEM Scanner is to be used on the heels and sacrum of patients:

1. Upon admission
2. During the patient's stay
3. At discharge

The frequency with which patients are scanned during the patient's stay is not defined by the company, who assert that this varies according to the kind of care setting. For example, in acute settings, scanning is recommended to be

undertaken daily (or at change of condition), whereas it would be every 3 days in “community/step-down facilities” (or at change of condition).

The 2019 update for the EPUAP guidelines (available in a quick reference guide) recommends considering the use of a sub-epidermal moisture/edema measurement device as an adjunct to SoC (rated as “no specific recommendation” in all patients, but as “weak positive recommendation; probably do it” in patients with darkly pigmented skin).

The IFU contains detailed instructions on how the device be used at different points. Notably, for the sacrum, 6 readings are required around the gluteal cleft and sacral bone, while 4 readings are required around each heel. Clinical experts highlighted the ischial tuberosities, femoral trochanters and occiput as other anatomical locations that are important to check for signs of PUs. At time of writing, the IFU does not contain any instructions for taking SEM readings from locations other than the heel and sacrum, although the company plan to expand this in the future.

The care pathway, and SEM Scanner’s position within it, is outlined in Burns et al (unpublished) and this shows that for patients deemed ‘at risk’ (CG179 risk assessment) a positive result from SEM Scanner (i.e. delta ≥0.6) results in the patient moving to the ‘high risk’ pathway (see Figure 2). The differences between the ‘at risk’ and the ‘high risk’ pathway is that rounding occurs every 6 or 4 hours, respectively (CG179). Additionally, with SEM Scanner in the pathway, SEM Scanner assessment occurs daily in the anatomical location (heel or sacrum) found to be at risk and weekly in the other location, whether it is at risk or not. For suspected heel PUs, heeling offloading is also added to the pathway following a positive result. It is notable that in some of the published studies (Okonkwo et al 2018) the device is used on the heels and sacrum of patients who already have visible reddening of the skin and would therefore, already have been identified as being at risk of developing a PU by the standard of care alone. The EAC considers the care pathway to be adequately described by the company. However, it should be noted that when the SEM Scanner is added to the care pathway, the change to the pathway (compared to following the existing standard of care) is limited.

The literature contains references to various other devices that have been used to objectively measure PU risk. (Swisher et al 2015; Uchiyama and Ohta et al 2007; Borzdynski et al 2016; Park and Lee 2019; Ching et al 2011; Liao et al 2015; Oliveira et al 2017; Kim et al 2018; Park et al 2018; Bates-Jensen et al 2007) However, with the exception of the Delfin Moisture Meter (Bates-Jensen et al 2007; Guihan et al 2012), SEM Scanner is the only CE-marked device of its kind available in the UK.

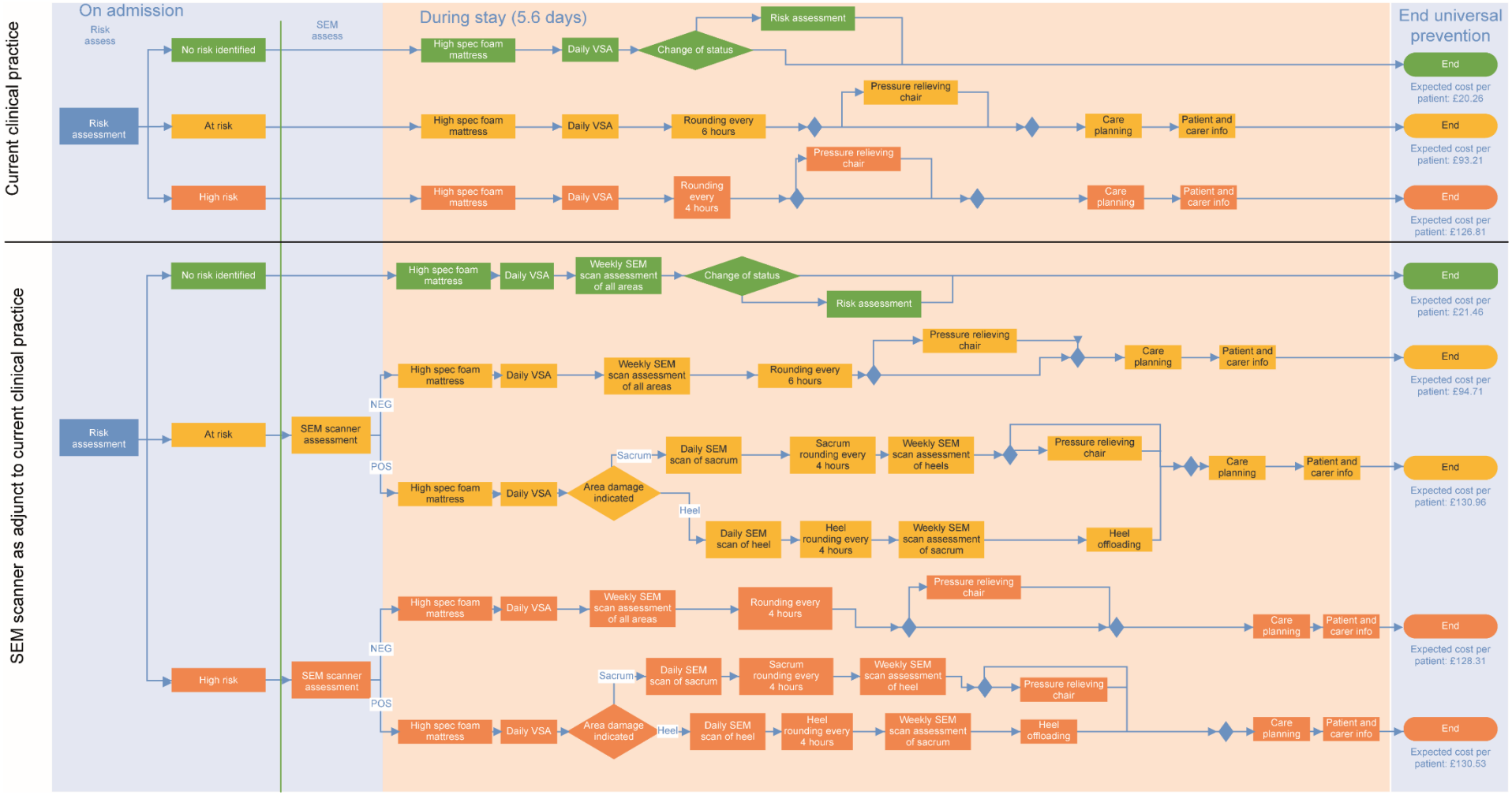


Figure 2 Modelled clinical pathways for prevention and management of hospital-acquired pressure ulcers in the UK from Burns (unpublished)

Special considerations, including issues related to equality

The company's submission highlights the potential for SEM Scanner to identify PUs in patients with dark skin, for whom visual skin assessment may not be as effective. In this case, the device has the potential to remedy potential equality issues in the existing care pathway. However, one clinical expert stated risk assessment does not differ between patients with lighter and darker skin tones.

The EAC did not identify any further equality issues.

4 Clinical evidence selection

4.1 *Evidence search strategy and study selection*

The company's search strategy was limited in both the search terms used (for example, the name of the device was not searched) and in the databases searched (only PubMed was used for published literature search). Therefore, the EAC performed its own searches, details of which are found in the Appendix A, along with a PRISMA flow diagram. Animal studies and certain publication types (such as editorials or letters) were excluded using a filter in some databases. No date limits were applied. 569 records were retrieved by the searches, plus 5 references from the company submission and 7 from NICE's Medical Innovation Briefing MIB182 "SEM Scanner for pressure ulcer prevention".

Following, deduplication in EndNote X7.8, two reviewers performed an initial sift of 379 records by checking titles and abstracts. Following the initial sift, 43 records remained, and the full-text documents were obtained and checked for relevance. Studies were selected as per the PICO table in the scope. The EAC excluded any studies published as abstracts that were subsequently published as a full-text article and any studies reporting a reanalysis of a population already included in a previously published study, except where

unique outcomes relevant to the scope were reported. The final selection comprised 7 studies.

4.2 *Included and excluded studies*

Table 3 Studies selected by the EAC as the evidence base

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAC comments

Raizman et al (2018) Canada	Prospective before-and-after study Full-text publication Partly funded by company SEM Scanner Standard care ●	**Phase 1:** 89 participants (55% female, 60% incontinent), assessed 5 times per week. Medical/stroke unit. Data gathered from 4 April-4 May 2016 (SEM Scanner readings taken but not used) **Phase 2:** 195 participants (55% female, >90% incontinent, Braden Mobility sub-score ≤3), scanned 3-5 times per week in ACU, 3 times in first 7 days in emergency room admissions. Alternative care unit (n=29) and emergency room	12 (13.5%) phase 1 participants developed a PU. 4 Stage I's, 6 Stage II's, 1 Stage III, and 1 deep tissue injury. 2 (1%) phase 2 participants developed a PU (1 in ACU, 1 in emergency room admissions). 1 Stage I and 1 Stage II. ●	The two phases were in different hospital units and although the baseline demographics were similar between the groups, the authors state that phase 2 patients were overall at a higher risk for developing PUs. The standard care protocol is not adequately reported. There are references to daily nursing checks, but it is not clear if this is usual practice or specific to this study. No power calculation is reported for the sample size. The EAC calculates that for effect size reported, the study would require 86 patients per cohort to be powered at an

		hospital admissions (n=166). Data gathered from 4 May-30 September 2016		alpha of 0.05 and a beta (power) of 90%. Although SEM Scanner readings were not used in phase 1, the readings were not blinded to clinicians. Staff had not been instructed in how to interpret the delta: the authors claim this avoided the Hawthorne effect. Braden scale used as standard of care. SEM Scanner was used as per IFU – a trainer was available throughout the study to assist clinicians in the use and interpretation of SEM Scanner.

Gefen et al (2018) USA	Prospective single-arm observational study. Full-text publication Funded by company SEM Scanner VSA Ultrasound ●	15 patients (66% female, mean age 74-years, 11 Caucasian, 4 black/African American) Post-acute care setting. Group 1: at risk (n=7) Group 2: stage I (n=3 Group 3: sDTI (suspected deep tissue injury) by VSA (n=3) Group 4: not at risk (n=2) (Braden score <13 for groups 2 and 3) ●	There was consistent agreement between SEM and US in group 3, but not always with VSA. All patients in group 1 (n=7) had SEM deltas of ≥0.6 of whom 1 developed sDTI. This patient's SEM reading was abnormal from day 1, while VSA indicated sDTI on day 3 and US on day 4. ●	Investigators defined an abnormal reading as a delta of ≥0.6 for at least 2 consecutive days. Ultrasounds assessed by radiology specialist (presence of hypoechoic lesion used to determine PU) – the EAC notes that this comparator is outside of the scope. However, VSA is part of the usual standard of care described in the commonly used risk assessment scales (such as Waterlow and Braden).

<table>
<tr>
<td>O’Brien et al (2018)

Ireland</td>
<td>Prospective single-arm observational study.

Full-text publication

Funded by company

SEM Scanner</td>
<td>47 patients (61.5% female, mean age 74.7-years), Norton score of ≤18 (medium, high or very high risk of PU).

Medical-surgical unit.

Data gathered in a 4-week period.</td>
<td>Diagnostic outcomes (VSA used as reference standard):

<table>
<tr><th>SEM Scanner</th><th>PU confirmed</th><th>No PU</th></tr>
<tr><td>Positive</td><td>21</td><td>20</td></tr>
<tr><td>Negative</td><td>0</td><td>100</td></tr>
</table>

Sensitivity was 100%, specificity 83.33%.

VSA detected PUs after a mean 5.5 days, SEM Scanner 2.1 days.

Overall correlation between VSA and SEM Scanner was moderate (r =0.47, p=0.001).</td>
<td>Nursing staff were blinded to SEM Scanner readings and the readings did not inform subsequent care.

Norton scale and VSA used as standard practice. SEM Scanner used separately with a cut off >0.5 for 3 or more days (a more stringent cut off than the IFU describes due to the requirement for the cut off to have been met for 3 or more days).</td>
</tr>
</table>

<table>
<tr>
<td>Okonkwo et al (2017)[2] USA and UK</td>
<td>Prospective observational study.

Conference abstract (plus unpublished full-text)

Funded by company

SEM Scanner

●</td>
<td>182[3] patients (46.7% male, mean age 76-years, 66.5% Caucasian, 24.2% Asian, 4.4% Black/African American), primarily from USA sites (77.8% USA, 9 sites vs. 22.2% UK, 3 sites).

Settings (12 sites – 9 USA, 3 UK) included acute hospital and nursing homes.

Braden scale <15 or Waterlow scale ≥10 or Norton scale ≤18

●</td>
<td>Diagnostic outcomes (VSA used as reference standard):

<table>
<tr><th>SEM Scanner</th><th>PU confirmed</th><th>No PU</th></tr>
<tr><td>Positive</td><td>42</td><td>257</td></tr>
<tr><td>Negative</td><td>6</td><td>124</td></tr>
</table>

Sensitivity was 87.5%, specificity 32.55%.

The 42 true positives detected by SEM Scanner were detected an average of 4.7 days (± 2.4 days) earlier than VSA.</td>
<td>The cut-off was defined as >0.5 in two or more readings out of three consecutive readings at an anatomical site. This aligns with the IFU for heel PUs but not for sacrum PUs.

The reference standard is VSA, which means this study does not measure the diagnostic accuracy of SEM Scanner versus VSA, and is rather a measure of agreement between the tests. This method also means that all non-visible PUs with SEM Scanner readings of >0.5 are treated as false positives.</td>
</tr>
</table>

			●	All sites used Braden (n=166), except one, which used Waterlow (n=16).

[2] Referred to as SEM200-008 in the company submission.
[3] 182 in intention-to-treat (ITT) analysis; 170 per protocol

Okonkwo et al (2018)[4] USA	Prospective observational study. Conference abstract (plus unpublished full-text) Funded by company SEM Scanner ●	175 patients in total 125 patients with confirmed PUs (66 sacral, 59 heel; stage I or stage II with blister intact. 56% female, mean age 82.7-83.6-years), recruited from a care home. 50 unaffected patients (50% female, mean age 66.8-years, 39 Caucasian, 9 Black/African American), recruited from a physician's office. All patients assessed with VSA and risk assessment with Braden scale before SEM Scanner readings taken.	**Patients with PUs (n=125):** 122 patients assessed with 126 PUs (3 patients excluded). **Unaffected patients (n=50):** Mean SEM Scanner readings ranged from 2.3-2.5 in the sacrum and from 1.7-2.0 in the heel. Variance between values was "well below" 0.6. Significant variability was calculated due to presence of callouses (p=0.0002) and race (p=0.003). Diagnostic outcomes for heel and sacrum combined	The affected cohort (n=125) all had PUs that had visible reddening and would therefore be identified by VSA alone. Therefore, this study only shows agreement between VSA and SEM Scanner, rather than clinical effectiveness. Gluteal cleft readings were not taken for sacral PUs (contrary to IFU). This study is exploratory and uses a ±0.5 bound, rather than the standard ≥0.6 threshold. As this varies from the true usage of the device as directed by the IFU,the comparability of this evidence to clinical practice is limited.

<table>
<tr>
<td></td>
<td></td>
<td></td>
<td>(calculated by EAC using confirmed PU status as reference standard):

<table>
<tr><th>SEM Scanner</th><th>PU confirmed</th><th>No PU</th></tr>
<tr><td>Positive</td><td>109</td><td>12</td></tr>
<tr><td>Negative</td><td>17</td><td>88</td></tr>
</table>

Sensitivity was 86.51%, specificity 88%.</td>
<td>The two different cohorts were recruited from different care settings (unaffected subjects from office setting, affected from care home).</td>
</tr>
</table>

[4] Referred to as SEM200-003 and SEM200-004 in the company submission.

Hancock & Lawrance (2019)[5] UK	Prospective before-and-after study. Conference abstract (plus unpublished supplementary information) Funded by company SEM Scanner ●	1478 patients in PURP period vs. 12,128 patients in historical control 15 acute care (AC) facilities, 1 hospice care (HC) facility. Waterlow scale >10 or patients admitted to PURP ward (1 site used Braden scale). Stage I PUs and suspected DTIs are not reported. ●	**AC:** Overall, HAPU rate reduced from 2.17% (263/12128) to 0.95% (14/1478). 79% of centres reported 0 HAPUs (hospital acquired pressure ulcer) during the PURP period. The risk of developing a PU in the PURP period was 23% of the historical cohort (95% CI: 8.2-64.7%, p=0.0105). Clinical decision-making was impacted in 52% of cases.	The study is reported in two separate conference abstracts and an unpublished report of supplementary information, with key information, such as the number of patients, differing between the documents. The study only reports stage II-IV PUs, which is unlike any other included study and makes it impossible to compare these outcomes to the only other comparative study (Raizman et al, 2018). The cut-off delta is reported as >0.6 in the abstract, though this is corrected to ≥0.6 in the

[5] Referred to as the PURP study in the company submission.

			56% of SEM readings were >0.6, of which 46% had no visible redness. 63% of patient received additional interventions. **HC:** 47% reduction in HAPUs compared to historical data. 	unpublished supplementary report. It is difficult to interpret the results from the small amount of information given, particularly on the methodologies/protocols used and demographic data on the participants. There is no information on the standard of care used in the historical control cohort. The inclusion criteria are not uniform across the different sites. The authors report that 2 of the sites found that the Hawthorne effect was not present, although there is no

				information about how this was deduced.

O'Keefe & McLuskey (2019) Ireland	Prospective single-arm observational study. SEM Scanner Conference abstract Funded by company ●	32 patients. Combined orthopaedic/plastic surgery ward Waterlow Score ≥10 Data collected during 12 week study period ●	72% (n=23) had a positive SEM reading (i.e. indicating damage), of whom 5 also had no visible redness. These patients received interventions they would not otherwise have under standard of care alone. 53% (n=17) had visible redness. No patients developed a PU during the study period (compared to a historical rate of 12.2%). ●	This abstract is only available on the company's website and is not found on the conference website – the abstract states that it was "submitted and accepted to the Tissue Viability Society, 2019", but it is not listed on the programme. Delta of ≥0.6 recorded on two separate occasions within 48 hours of each other. 3 consecutive readings were taken at the sacrum, heels (as well as the hips and ischial tuberosities: these are outside the scope). There is no demographic information given and there is no detail given on the historical

				rate of PUs. The authors claim SEM Scanner reduced the rate of PUs, though it is unclear how based on this study.

Table 4 Studies included by company and excluded by the EAC

Study name and location	**Design and intervention(s)**	**Participants**	**Outcomes**	**EAC comments** Provide EAC rationale for exclusion and refer to company's opinion, if relevant. Give reasons for disagreement.

Smith (2019) UK	Prospective single-arm observational study. Full-text publication Funded by company SEM Scanner ●	35 patients (9% aged 65–75-years, 74% were aged >75-years. 51% female) Medical-surgical ward. Waterlow scale used (24% at risk, 24% high risk and 52% very high risk) Data gathered over a 2-month period. ●	92% of patients had SEM deltas >0.5 on admission, and all patients had a reading of >0.5 at some point during the study. None of the cohort developed a new PU. 28% of SEM readings were ≤0.5, indicating no risk for PU, which contradicted the Waterlow scores that indicated all patients were at risk. ●	**Included by company, excluded by EAC** The outcomes do not match the scope and do not contribute to the decision problem. The data are also included in Hancock & Lawrance (2019). NHS setting. SEM delta of >0.5 was used (it does not mention the frequency). Authors note that although the delta indicates pre-existing damage, the seriousness of the damage cannot be determined. SEM Scanner readings and Waterlow Scores are not directly comparable as SEM Scanner is anatomy specific while Waterlow scores are based on whole body assessment.

Moore et al (2018) UK	Prospective single-arm observational study. Full-text publication Funded by company SEM Scanner ●	59 patients Orthopaedic trauma ward 8-week evaluation period (September-October 2017) ●	58 patients had “deviated” SEM reading, of whom 42% had no visible signs of redness. All 58 patients had “deviated” readings on admission. No HAPUs were reported during the study period. Historically, there were 27 PUs in one year (median 2 per month) – neither the total number of patients nor the percentage of PU is reported. A survey of the clinical team showed 86% of staff felt they had seen a benefit throughout the evaluation period.	**Included by company, excluded by EAC** The outcomes do not match the scope and do not contribute to the decision problem. The study is reported as part of a meeting report, with key demographic information omitted and very little detail on the methodology of the study. NHS setting. The protocol (delta, frequency) for SEM Scanner use is not reported. Possible overlap with part of the population in Okonkwo et al (2017) (Study 008): the setting and the investigator mentioned (Northumbria NHS Trust, and Milne, J.) are the same.

				
Gershon et al (2014) USA	Prospective observational study. Conference abstract (plus unpublished full-text) Funded by company SEM Scanner 	This study is an earlier version of Okonkwo et al (2018) and therefore constitutes an overlapping study population. 	SEM Scanner readings were significantly different at the centres and peripheries of sacral wounds, when compared to sacral readings of patients without PUs. 	**Included by company, excluded by EAC** The outcomes do not match the scope and do not contribute to the decision problem. The population is also included in a more complete form in Okonkwo et al (2018).

Clendenin et al (2015) USA	Prospective observational study SEM Scanner Funded by company	31 healthy adults (≥18 years)	Agreement between operators: mean differences ranged from -0.01 to 0.11. Inter-operator and inter-device reliability exceeded 0.80 at all anatomical sites assessed	**Included by company, excluded by EAC** The population and outcomes do not match the scope and do not contribute to the decision problem.
Peko Cohen et al (2019) Israel	Lab-based pilot study SEM Scanner	Phantoms of the human skull and heel	SEM Scanner can detect fluid content changes that are as small as 1 mL	**Included by company, excluded by EAC** The population and outcomes do not match the scope and do not contribute to the decision problem.

5 Clinical evidence review

5.1 *Overview of methodologies of all included studies*

The EAC included 7 studies reported in 3 full text publications and 4 abstracts. None of the included studies were randomised and most studies are single-arm observational studies. The overall evidence base is weak with the only reliable comparative evidence coming from a before-after observational study by Raizman et al (2018), which compared two cohorts treated in different settings at different times, with and without the use of SEM Scanner to risk assess patients. Hancock & Lawrance (2019) also carried out a before-after study design but the methodology and other information are poorly reported, and this study is not considered reliable. Neither of the comparative studies performed a power calculation. The EAC calculates that for the effect size reported by Raizman et al, the study would require 86 patients per cohort to be powered at an alpha of 0.05 and a beta (power) of 90%. The other included studies are prospective single-arm observational studies.

The populations included in the studies are moderately homogeneous, with the mean age in most studies being close to 75 years and females making up 55% of cohorts. However, despite baseline characteristics being similar between the studies it is difficult to be certain that patients were at the same levels of risk for developing PUs. One important element of heterogeneity between the two comparative studies is the inclusion of stage I PUs: Raizman et al (2018) included stage I PUs, while Hancock & Lawrance (2019) did not, which may explain the difference in baseline PU rates. Different risk scales have been used in the studies to quantify and stage the risk of developing PUs in the included populations but as previously discussed (see section 3), there is no consensus on which scale is optimal. The majority of patients were deemed ‘at risk’ by different scales used and therefore SEM Scanner was used as per the IFU (“patients who are at increased risk for pressure ulcers”). The settings of the studies include care homes, acute care facilities, surgical wards and a stroke unit.

The company included several studies that are published as abstracts or conference posters, although the company also provided unpublished full-text versions for Okonkwo et al (2017 and 2018) and an unpublished report with further information on Hancock & Lawrance (2019). These studies are referred to in this assessment report by the abstract reference, although information from the full-text versions has been used where it was deemed reliable by the EAC[6].

The settings for the studies are Canada, the USA, Ireland and the UK. Two of the included studies included NHS patients (Okonkwo et al, 2017 and Hancock & Lawrence, 2019).

5.2 *Critical appraisal of studies and review of company's critical appraisal*

The methodological quality of the included studies was very weak and there is very little comparative research involving SEM Scanner. The EAC carried out methodological quality assessments for observational studies, the details of which are in Appendix B. The study by Raizman et al (2018) employed a before-after design, in which two cohorts were treated with and without the use of SEM Scanner. However, there are several sources of potential bias in this study. The two cohorts were from different hospital settings (phase 1 was from the medical/stroke unit, while phase 2 was from a mixture of emergency room admissions and an alternative care unit). The baseline patient characteristics were similar between the two phases although the care pathways may not be equivalent in the different care settings. One strength of the study is that SEM Scanner readings were taken in both phases, but they were not used in phase 1, which implies a consistency of care that reduces the risk of selection bias. However, the SEM readings were not blinded to clinicians (although they were not informed how to interpret them during phase 1). The study does not report on how the SEM readings were used in

[6] For example, the full-text document provided by the company for Okonkwo et al (2017) - which is referred to as the "008 study" - is in a pre-review stage and contains a number of comments querying different aspects of the study, including the reporting of key figures.

the experimental phase and it does not report on how the readings might have been used in the control phase to influence care.

Hancock & Lawrance (2019), in a multi-centre before-after study, reported the incidence of HAPUs from periods without and with the use of the SEM Scanner ("pre-PURP" and "PURP" phases). The abstract contains very little methodological information about the study and much of the information has been taken from an unpublished supplementary document, although there are still significant gaps in the reporting of demographic information and details about the pre-PURP control phase. The most important missing information is the length of the study period: in the PURP phase, data was collected for 1.25-6 months, with substantial variation between the different centres. It is implied that the data collection period was as long as 12 months in the pre-PURP phase, although this is not adequately reported per centre. The study is also unusual in that stage I PUs and sDTIs were not included in the results; only stage II-IV PUs were reported. O'Keefe & McLuskey (2019), in a conference abstract, compared PU incidence between a cohort treated with SEM Scanner and an undefined historical control. As there is no reported information on the historical control cohort, the EAC has categorised this study as a single-arm observational study.

Other studies included by the company reported diagnostic outcomes (Okonkwo et al 2017, Okonkwo et al 2018, O'Brien et al 2018), the time taken for SEM Scanner to produce a result (Gefen & Gershon 2018, O'Brien et al 2018, Okonkwo et al 2017), or the agreement between SEM Scanner and other methods for assessing PU risk (O'Brien et al 2018). These studies were all single-arm in design and do not contribute meaningfully to the decision problem.

The EAC notes that there were some differences between the studies in how SEM Scanner was used. For example, Gefen & Gershon (2018) defined an abnormal reading as a delta of ≥0.6 for at least 2 consecutive days, whereas O'Brien et al (2018) required 3 consecutive days. Okonkwo et al (2017) reported using SEM Scanner as described in the IFU for the heels but diverged from the IFU for the sacrum. Similarly, in Okonkwo et al (2018)

gluteal cleft readings were not taken for sacral PUs, which is contrary to the IFU. O'Keefe & McLuskey (2019) used a delta of ≥0.6 recorded on two separate occasions within 48 hours of each other. The differences between the studies may influence the outcomes of the studies by making the criteria for a 'positive' SEM result either more stringent or more relaxed depending on how the studies have deviated from the IFU.

All included studies were funded by the company.

5.3 *Results from the evidence base*

The key outcomes of each included study have been summarised in Table 5 and the important points are further explored below.

Table 5 Summary outcomes

Study name and location	PU/HAPU reduction vs. standard of care	Time to PU detection	Sensitivity (VSA ref standard)	Specificity (VSA ref standard)	Correlation between SEM and VSA
Raizman et al (2018) Canada	13.5% vs. 1% (favouring SEM Scanner)	NR	NR	NR	NR

Study name and location	PU/HAPU reduction vs. standard of care	Time to PU detection	Sensitivity (VSA ref standard)	Specificity (VSA ref standard)	Correlation between SEM and VSA
Gefen & Gershon (2018) USA	NR	SEM Scanner: 1 day Ultrasound: 3 days VSA: 4 days	NR	NR	NR
O'Brien et al (2018) Ireland	NR	SEM Scanner: 2.1 days VSA: 5.5 days	100%	83.33%	r =0.47, p=0.001
Okonkwo et al (2017) USA and UK	NR	SEM Scanner detected PUs 4.7 days (± 2.4 days) earlier than VSA	87.5%	32.55%	NR

Study name and location	PU/HAPU reduction vs. standard of care	Time to PU detection	Sensitivity (VSA ref standard)	Specificity (VSA ref standard)	Correlation between SEM and VSA
Okonkwo et al (2018) USA	NR	NR	86.51% (PUs were confirmed present or not present at baseline)	88% (PUs were confirmed present or not present at baseline)	NR
Hancock & Lawrance (2019) UK	0.95% vs. 2.17% (favouring SEM Scanner).	NR	NR	NR	NR

Study name and location	PU/HAPU reduction vs. standard of care	Time to PU detection	Sensitivity (VSA ref standard)	Specificity (VSA ref standard)	Correlation between SEM and VSA
O'Keefe & McLuskey (2019) Ireland	0% vs. 12.2% (favouring SEM Scanner – the comparator is an unspecified historical control cohort)	NR	NR	NR	NR

NR – not reported; PU – pressure ulcer; HAPU – hospital acquired pressure ulcer; VSA – visual skin assessment; CI – confidence interval

Raizman et al (2018) showed that the introduction of SEM Scanner led to a significant reduction in PU incidence (1% vs. 13.5%, odds ratio 0.06 [95% CI: 0.01-0.30], p=0.0005[7]), although the study has several methodological shortcomings (see section 5.2 above). Hancock & Lawrance (2019) also reported a significant reduction of HAPU incidence with the introduction of SEM Scanner (0.95% vs. 2.17%, odds ratio 0.43 [95% CI: 0.25-0.74], p=0.0023[8]), although the reporting of this study is inadequate (see above).

Other studies included by the company focus on the diagnostic performance of SEM Scanner, notably Okonkwo et al (2017) in which sensitivity and specificity of SEM Scanner are reported, using VSA as the reference standard. The EAC considers this evidence irrelevant to the decision problem

[7] Calculated by the EAC.
[8] Calculated by the EAC.

because the device is designed to be used as an adjunct to the standard of care (VSA), not as a replacement for it. Using VSA as the reference standard means that SEM Scanner can be shown, at best, to match the sensitivity/specificity of VSA and in most of the reported studies, it does not. One clinical expert noted that if SEM Scanner was able to detect cases of no tissue damage, cost and staff time could be saved by avoiding putting in place detailed preventative interventions. This suggests that clinical utility of SEM Scanner would be to rule out PUs, by identifying patients at low risk. The low specificity (32.55%) reported by Okonkwo et al (2017) suggests that SEM Scanner may not be a reliable tool for ruling out PUs. The company claims that the focus of the Okonkwo et al (2017) study was on sensitivity, rather than specificity, because the notion of a true positive (visible pressure damage) could be objectively determined in their study. The company correctly argues that the use of VSA as the reference standard has the potential to "falsely" reduce the specificity of SEM Scanner. However, the EAC has identified no diagnostic accuracy studies that used a more appropriate reference standard. The EAC has treated outcomes from the Okonkwo et al (2018) study as diagnostic outcomes – in this study there were two cohorts (patients who had PUs confirmed at baseline, and patients without PUs), so it is possible to properly categorise true positives and true negatives. In this study, the EAC calculated sensitivity of 86.51% and specificity of 88%.

O'Brien et al (2018) reported the level of correlation between SEM Scanner and VSA, (overall moderate: r =0.47, p=0.001). Agreement ranged from r=0.65 for the sacrum to r=0.23 for the left heel. The EAC regards this estimation of correlation to be of limited use and another statistical test (for example Bland-Altman analysis) would have been preferable. The company also highlights the variation in SEM readings between heels and sacrum, with reference to Okonkwo et al (2018), which reported higher variability in average SEM readings at the heels compared with the sacrum (in patients without PUs).

Three studies reported the speed with which SEM Scanner could identify PU risk when compared to VSA. Gefen et al (2018), O'Brien et al (2018) and Okonkwo et al (2017) found that SEM Scanner results identified PU risk an average of 3 days, 3.5 days and 4.7 days quicker than VSA, respectively. The company claims that this gives "a window of 5 days earlier awareness of increased risk" that enables "anatomically specific interventions". However, none of these studies investigated the subsequent use of further interventions, so the clinical utility of the device cannot be ascertained from these studies.

6 Adverse events

The company reported no adverse events during clinical studies in over 270 patients. The EAC performed a search of the FDA website ("Bruin" or "SEM Scanner") and found no adverse events listed. The EAC's search of the MHRA drug and device alerts found one reference to SEM Scanner (MHRA reference: 2019/009/012/701/005 – see Appendix C for attachment), an Urgent Field Safety Notice, which details the failure of some units to switch on due to cracking in the flexible cable supplying the 'Action Button'. Out of a total of 23 units in clinical practice, there have been 2 confirmed failures and 3 suspected failures yet to be confirmed. The risk to patients is deemed "negligible" and advice to users is to return the device to the manufacturer.

One clinical expert highlighted the potential for contact allergic dermatitis or contact irritant dermatitis, though the device is made with non-cytotoxic materials. The same expert noted that if the device is used in a diagnostic capacity, false negatives could lead to worse outcomes in patients.

7 Evidence synthesis and meta-analysis

Due to the lack of high quality studies, no meta-analysis has been carried out.

8 Interpretation of the clinical evidence

The EAC considered the evidence to be generalisable to the NHS population. Two of the included studies included patients from the UK and the widespread use of the EPUAP/NPUAP/PPPIA 2014 guideline implies that evidence from other countries (Canada, the USA and Ireland) is relevant to the NHS.

The strongest evidence in favour of SEM Scanner comes from the prospective before-after observational study by Raizman et al (2018), which showed a significant reduction in PU incidence when SEM Scanner was introduced. This study provides an estimate of the baseline rate of PUs of 13.5% (from a medical/stroke unit in Canada). The authors did not report a breakdown of PU incidence by setting but did report the incidence of different stages (stage I 33%, stage II 50%, stage III 8%, stage IV 0%, unstageable/DTI 8%). SEM Scanner was used in the control phase (phase 1) and although clinicians were not blinded to the SEM Scanner readings, they had not been instructed in how to interpret them. The EAC considers that this presents a small risk of selection bias, which is outweighed by the advantages of having consistency of care between the two cohorts. However, in phase 2, SEM Scanner was used in a different care setting (patients who had been admitted via the emergency room, plus patients from an alternative care unit). Therefore, consistency of care was not maintained in any case. The authors reported baseline demographics and found the two cohorts were mostly well matched, with a slightly higher baseline risk of PUs in phase 2, where PU incidence was reduced to 1%. The EAC calculated an odds ratio of 0.06 (p=0.0005), but it is notable that the authors of the study did not report any adjusted analyses for the differences in the two cohorts. The EAC considers that this result, while being the most clinically useful outcome of all the included studies, is not entirely reliable.

Hancock & Lawrance (2019) report a baseline rate of PUs of 2.17% (range: 0.9%-16.1%), calculated from 12,128 patients from 15 different centres. This study had a wide range of settings (see Figure 3), but crucially only stage II-IV PUs were reported, whereas Raizman et al (2018) also included stage I PUs.

This may explain the large difference between the baseline rates reported. Hancock & Lawrance (2019) did not report demographic information about either the control cohort (pre-PURP phase) or the SEM Scanner cohort (PURP phase). There is no information about the standard of care used in the pre-PURP phase, so it is difficult to draw any reliable conclusions about the clinical effectiveness of SEM Scanner relative to, for example, VSA. The authors reported that in one centre, the clinical care of 40% of patients (n=58) was changed as a result of SEM Scanner, but there is no information regarding how care differed or the reasons for the changes. In the PURP phase, PU incidence declined to 0.95% (14 of 1478 patients). In 10 of the 15 centres, PU incidence declined to zero, compared to 0 centres in the pre-PURP phase. The EAC calculated an odds ratio of 0.43 (p=0.0023), but the limitations of this publication mean this figure cannot be considered reliable.

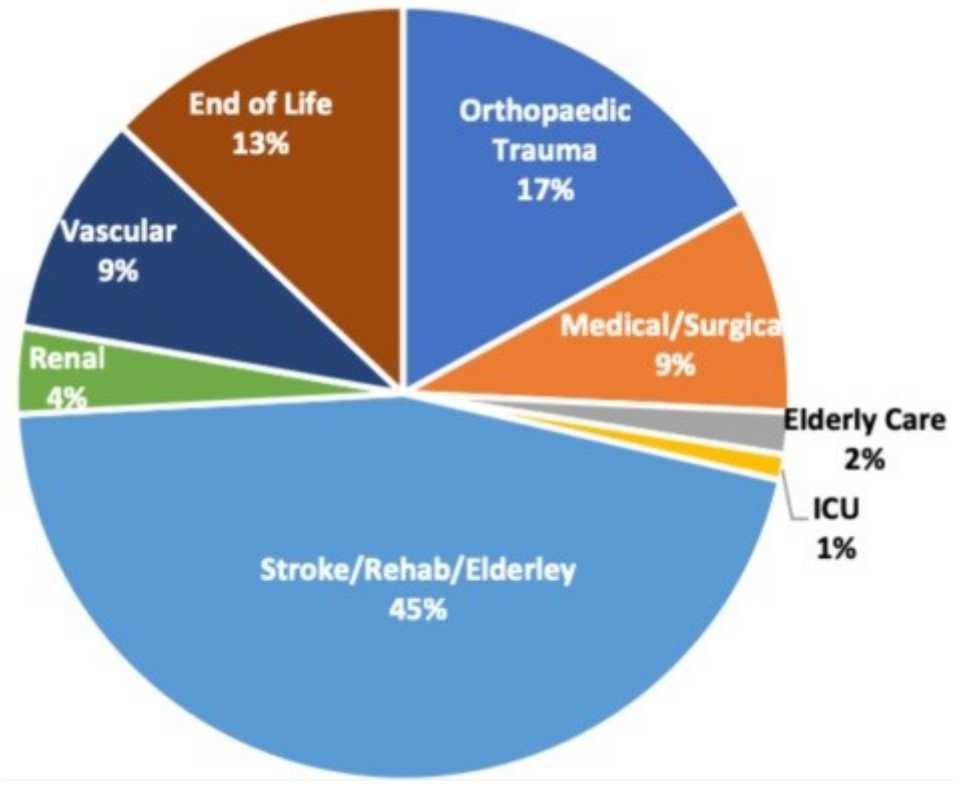


Figure 3 Patient care settings, from Hancock & Lawrance (2019)

The studies reporting diagnostic outcomes (Okonkwo et al 2017, O'Brien et al 2018) did so using VSA as the reference standard. As discussed in section

5.2, this is a flawed approach for two important reasons. Firstly, SEM Scanner is intended to be used as an adjunct to standard practice. Using this as the reference standard does not deliver a clinically useful measure of diagnostic accuracy. Secondly, as the company mentioned in the submission, the use of VSA as a reference standard may underestimate the specificity of SEM Scanner because non-visible damage, which may be correctly identified by SEM Scanner, would be counted as a false positive. The company suggests that this may explain the low specificity of SEM Scanner in this study (32.55%). The EAC used the figures from Okonkwo et al (2018) and calculated sensitivity/specificity, with the PU status of patients already confirmed at baseline (the study included two cohorts of patients confirmed with and without PUs). Sensitivity was 86.51% and specificity 88%. Theoretically, this result would be a better reflection of the diagnostic accuracy of SEM Scanner. However, this result is unreliable due to the fact patients were selected specifically due to their PU status (and therefore not representative of usual clinical environment)..

The EAC notes that the IFU for the device states: “WARNING: This device is not intended to be used for detecting or diagnosis of pressure ulcers.” The EAC considers the evidence on diagnostic outcomes reported by Okonkwo et al and O’Brien et al should be treated as measures of agreement between SEM Scanner and VSA. O’Brien et al also reported the correlation of results between SEM Scanner and VSA, although the clinical utility of this outcome is questionable given the intended use for SEM Scanner is alongside VSA, not as a replacement.

All 3 studies reporting the time to PU detection (Gefen et al 2018, O’Brien et al 2018 and Okonkwo et al 2017) found that SEM Scanner identified PU risk faster than VSA (between 3 and 4.7 days quicker). Unfortunately, none of these studies reported how this faster identification influenced ongoing patient care. None of the studies reported long-term outcomes, such as patient morbidity or length of hospital stay, so it is difficult to draw meaningful conclusions about this outcome (see section 12 on future research).

8.1 *Integration into the NHS*

The patients in the included studies were selected from settings appropriate to the likely use of the device in the NHS.

Adoption of SEM Scanner will require some changes to the pathway in that it is designed to be used regularly in addition to the current standard of care. For example, a positive result from SEM Scanner at admission then means that SEM Scanner should be used daily on the location of the positive result (heel or sacrum) and weekly on the other location. The company estimates that scanning a patient using SEM Scanner takes approximately 5 minutes and this would be in addition to, rather than replacing the usual standard of care, VSA. The time it takes for the device to fully switch on and become ready for use is approximately 45 seconds according to the IFU. Additionally, users must ensure it is completely dry before it is used (at least 2 minutes) and properly cleaned and disinfected after use (approximately 1 minute 45 seconds). One clinical expert highlighted the possibility that the presence of oedema could impair the accuracy of SEM Scanner, meaning the device should be contraindicated in these patients. The company claim that the delta calculation accounts for the spatial variation of oedema, however.

The company outlines the training requirements in the implementation section of the submission (see Figure 4 and Figure 5). This describes several meetings with the ward manager (30-45 minutes), key training partners (30 minutes) and ward lead (30 minutes x5), as well as weekly training sessions for the first 4 weeks following implementation. The company highlights the fact that no new staff, additional equipment or intervention equipment is required in order to implement SEM Scanner into the care pathway.

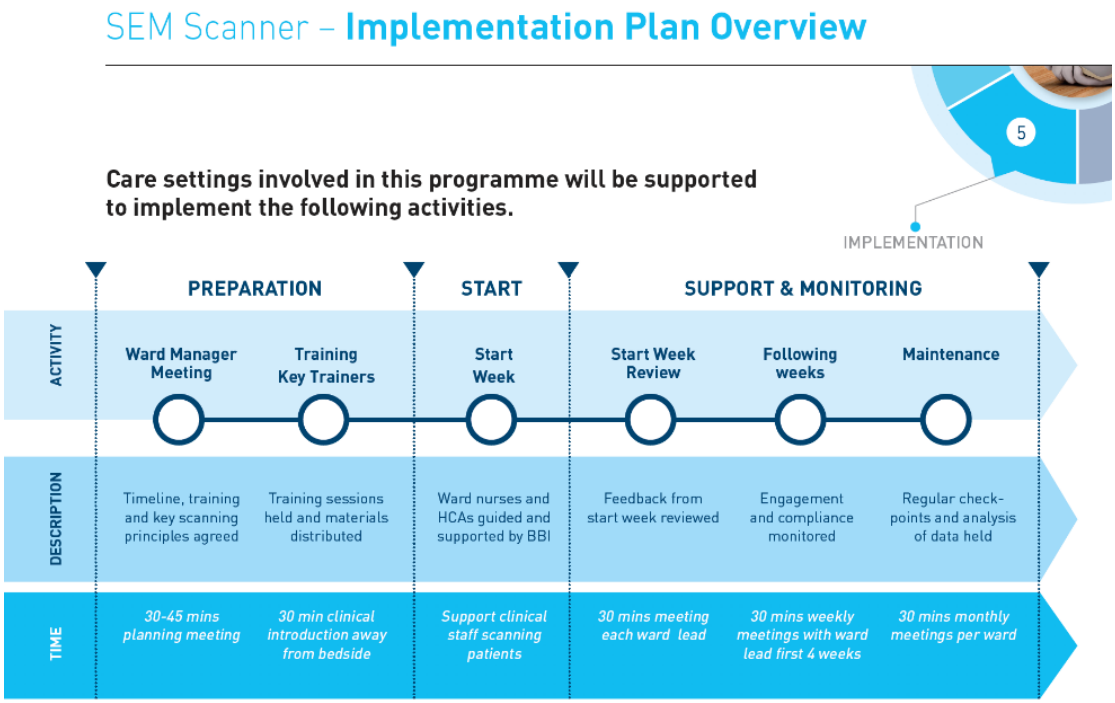


Figure 4 Implementation Plan Overview from company submission

Ward/Unit implementation plan

Activity	Content	Responsibility
Planning process	• Outline Implementation process • Identify key trainers • Set pre-implementation training dates and scanning start date • Confirm documentation to be used and PU pathway guidance	Project Lead Clinical Manager
Training	• Clinical Introduction – programme outline, ensure understanding of SEM • 'Hands on' practical session, how to scan correctly • SEM Implementation folder – outline content • Ensure understand PU pathway documentation	Clinical Manager Key Trainers
Week 1	• Work with Key Trainers only – observing, supporting good scanning technique • Complete Verification document and sign off • Observe key trainers teaching other staff, ensuring good practice upheld • Ensure compliance with pathway documentation and recording	Clinical Manager Key Trainers
Week 2	• Key Trainers – feedback, discuss experience, make any necessary updates • Clinical Manager – discuss the weeks findings, feedback from staff • Data Collection – reaffirm importance of good data, staff compliance	Clinical Manager Key Trainers
Week 3/4	• Assess adoption – plan time to overcome any training/compliance issues • Reduce support twice weekly dependent on confidence levels • Maintain weekly contact to review adoption progress	Clinical Manager Key Trainers
Maintenance	• Monthly meetings with Clinical Manager to review progress • Quarterly reviews with Project Lead, Clinical Manager, TVN – track progress on PU reduction	Project Lead Clinical Manager Matron/TVN

Figure 5 Implementation Plan from company submission

8.2 *Ongoing studies*

The EAC ran searches of several clinical trials registries and did not find any results for ongoing studies involving SEM Scanner. As mentioned above, some of the studies published as abstracts are expected to be published as full-text journal articles, though the company has submitted pre-publication versions to the EAC already.

The company listed 3 studies that are ongoing (details in Appendix D).

9 Economic evidence

9.1 *Published economic evidence*

Search strategy and selection

A search for economic evidence was carried out on PUBMED by the company using search words “Pressure Ulcers AND Costs AND economics AND United Kingdom”. These search terms are very specific and risk missing relevant literature and the EAC believes economic evidence should not be limited to the UK. Further, only economic evidence related to SEM Scanner is relevant for this assessment. Therefore, the EAC thinks the search could have been filtered more precisely by intervention. Ten studies were identified by the company as being relevant to the decision problem. The EAC reviewed the included studies and found that only one unpublished study (Burns et al, unpublished) could be included as economic evidence. This study reported the cost-effectiveness of SEM Scanner as an adjunct to standard of care (SoC) compared with SoC alone. The EAC conducted its own search (see Appendix A) to confirm no relevant papers had been missed out. Following the application of cost and economic filters, the EAC searches retrieved 44 abstracts related to economic evidence. After reviewing these abstracts, the EAC confirmed that no economic evidence in addition to the unpublished study submitted by the company was available.

No specific inclusion and exclusion criteria were applied for study selection. However, it is likely that the highly specific search terms will have excluded studies not undertaken in the UK. From the search strategy reported, studies related to incontinence-associated dermatitis, diabetic foot ulcer, venous leg ulcer were excluded. The EAC included all studies that presented economic results reported for the technology.

The company included ten studies. Three studies were abstracts and presented clinical results (Gershon et al 2014, Okonkwo et al 2017, and Hancock & Lawrance 2019). Five studies (Dealey et al 2012, Bennett et al 2004, Castelli et al 2015, Guest et al 2015, Guest et al 2018) reported on the

cost of pressure ulcers. One of these studies (Castelli et al 2015), and a further study (Hauck et al 2017) are retrospective analyses of hospital episode data on pressure ulcers. One unpublished study (Burns et al, unpublished) used a decision analytic model and cost-utility methodology to assess the cost-effectiveness of SEM Scanner. This was the only study included by the EAC as economic evidence for this assessment.

Published economic evidence review

The EAC considered only one unpublished study to provide an evaluation of the cost impact of SEM Scanner. The unpublished manuscript (Burns et al, unpublished) used a decision model to evaluate the cost-utility of SEM Scanner. The analysis compared the clinical pathway specified by the NICE clinical guideline (NICE CG179) with a clinical pathway that included assessment with the SEM Scanner in addition to visual assessment to diagnose early stage PUs. Costs and quality adjusted life years (QALYs) were analysed over one year for hospitalised patients at risk of developing a PU. Costs included purchase of SEM Scanner and training, preventive care and the costs of treating PUs. Health-state utility values were taken from the literature.

The analysis uses a decision tree model. In the branch representing the current SoC, risk assessment is based on visual inspection. In the intervention branch, risk assessment includes daily SEM Scanner measurements on the sacrum and heel as an adjunct to current SoC. The study assumes that 1.8% of patients receiving SoC progress to PUs of stage II or worse. The sensitivity of visual assessment is estimated at 60%. This figure has been previously reported but no citation is provided in the study. The sensitivity and specificity of SEM Scanner - 87.4% and 33.0%, respectively - were derived from Okonkwo et al (2017).

The analysis estimates the impact on nursing costs of increased assessment time arising from the use of SEM Scanner and detection of patients at risk of pressure ulcers, leading to increased repositioning frequency. The impact of SEM Scanner on the costs of PUs was estimated by assuming the inclusion

of the SEM Scanner in the clinical pathway leads to a 68% reduction in PUs. The parameter is derived from a before-after comparison of the incidence of stage II-IV PUs only following the introduction of PU prevention programme that included the use of SEM Scanners (Hancock & Lawrance, 2019).

The study reported expected cost-savings following the introduction of the SEM Scanner of £464,347 in the first year, or £9,300 per 100 patients at risk. The QALY gain was estimated at 0.046 per 100 patients at risk. Over a 1-year time horizon, the SoC plus SEM Scanner was a dominant option compared with SoC alone. In probabilistic sensitivity analysis, the authors reported SEM Scanner dominated SoC in 89% of simulations, and SEM Scanner was cost-effective in 90% of simulations compared to SoC, at a willingness-to-pay threshold of £20,000/QALY.

The company used the suggested tables to summarise each study's location, intervention and comparators, patient population, costs, outcomes, and sensitivity analysis for the included 8 studies. Further, the company also completed critical appraisal for each economic study included. In the opinion of the EAC, the critical appraisal for each of the included studies has been appropriately performed. Standard methods of economic evaluation (cost utility) were used in the included study, and the results reported that SEM Scanner was a dominant option compared with current clinical practice.

Results from the economic evidence

The company has included evidence generally on the cost and hospital episodes of pressure ulcers in UK. The EAC included only the unpublished manuscript reporting the economic evaluation of SEM Scanner (Burns et al), which showed that SEM Scanner used as an adjunct to current clinical pathway was cost-effective. The company concludes that this evidence supports the adoption of SEM Scanner. The EAC agrees that the manuscript does provide evidence to support the assertion that SEM Scanner is cost saving. However, the EAC has concerns regarding the estimate of effectiveness of SEM Scanner in reducing PUs that was not highlighted in the company's review. Specifically, the EAC regards the 68% reduction in PUs,

sourced from Hancock & Lawrance (2019), to be entirely consistent with estimates of the effectiveness of other PU reduction programmes, which did not include SEM Scanner (Mallah et al. 2015; Crawford et al. 2014). Hence, it is unclear to what extent SEM Scanner contributed to the observed reduction and to what extent the reduction arose from improvements in general vigilance and prophylaxis. Additionally, the study by Hancock & Lawrance (2019) included only stage II-IV PUs and did not report a breakdown by PU stage. The EAC notes that the relative proportions of different stage PUs would influence the overall cost of treatment, due to the greater cost of treating high stage PUs.

9.2 *Company de novo cost analysis*

Economic model structure

Patients included in the model are those “at risk” of developing pressure ulcers in acute care and long-term care facilities, including nursing homes. This is in line with the scope. The technology is SEM Scanner 200 used as an adjunct to standard NHS clinical practice and is compared to the standard NHS clinical practice pathway as described in the NICE pressure ulcer clinical guideline (CG 179, 2014) (Figure 6). This is also in line with the scope.

The company has used a decision tree based on the pathway described in CG179 and applied a one-year time horizon. The EAC regards the use of the CG 179 pathway to develop the decision tree over a one-year time horizon to be reasonable. Patients are assessed for risk and categorised as “low risk”, “at risk” and “high risk”. Low risk patients are excluded from the analysis. The decision tree assesses the cost of preventive measures for PUs. It is not used to assess the impact of SEM Scanner on the costs of treating PUs. Resource use for preventive care is derived assuming patients follow the recommended clinical pathway for ulcer prevention in the SoC arm, and initial assessment and daily visual assessment is complemented by assessment with SEM Scanner in the SEM Scanner arm. Patients ‘at risk’ of receiving a positive diagnosis for PU, either using the SEM Scanner or by visual assessment, are

re-categorised as high risk. Patients ‘at risk’ are repositioned every 6 hours and patients at high risk are repositioned every 4 hours. In addition, patients diagnosed with a stage I PU on the heel receive heel offloading care. Figure 7 and Figure 8 present these pathways. Using utility estimates, a cost-utility analysis reporting ICERs is submitted. Considering the remit of the NICE Medical Technology Evaluation Programme (MTEP), the EAC reviewed the parameters that were used to estimate only the costs and resultant cost savings of the technology.

The model structure is not used to estimate the impact of SEM Scanner on the cost of treating patients with PUs. Instead, an assumption is made that the introduction of SEM Scanner results in a reduction in the incidence of PUs of 68%. The EAC considers the model structure to be adequate to estimate the additional costs of preventive care arising from the deployment of SEM Scanner. However, the EAC notes that no cost has been included for a nutritional assessment; such an assessment forms part of the recommended treatment pathway for patients with a pressure ulcer. The EAC considers the model to be inadequate to estimate the impact of SEM Scanner on the costs of treating PUs.

The company’s model mirrors the approach of the unpublished economic analysis that the EAC included as relevant evidence in its estimation of the impact of SEM Scanner on PU treatment costs (Burns et al, unpublished). Both assume that the introduction of SEM Scanner will lead to a 68.9% reduction in the incidence of PUs requiring treatment, based on data before and after the introduction of a PU reduction programme, which included the use of SEM Scanner. As noted earlier, the EAC has concerns regarding this approach. Specifically, the EAC believes the incidence of PUs will be impacted both by detection and by improved attention to preventive measures (mainly rounding), and that both will have contributed to the observed reduction of PUs of 68.9% in the study cited by the company. The EAC notes that reductions of similar magnitudes to the study cited by the company have been observed in other reports on the impact of PU reduction programmes that did not include SEM Scanner (Mallah et al 2015; Crawford et al 2014).

The EAC takes the view that a significant proportion of the reduction of 68% in the incidence of PUs in the study cited by the company is attributable to improved attention to general care and preventive measures. Hence an assumption of a 68.9% reduction in the incidence and hence the costs of treating PUs following the introduction of SEM Scanner is an overestimate. The magnitude of this overestimation is difficult to specify but the existing literature would indicate it may be large. The EAC notes the lack of evidence in the area to populate a more sophisticated model of the impact of SEM Scanner on PU detection and treatment costs. However, the EAC considers a model that isolates the impact of SEM Scanner on detection of patients at risk of a stage II+ PU from the impact of subsequent treatment to be beneficial in assessing the likely impact of SEM Scanner on PU treatment costs from the available evidence on its diagnostic performance.

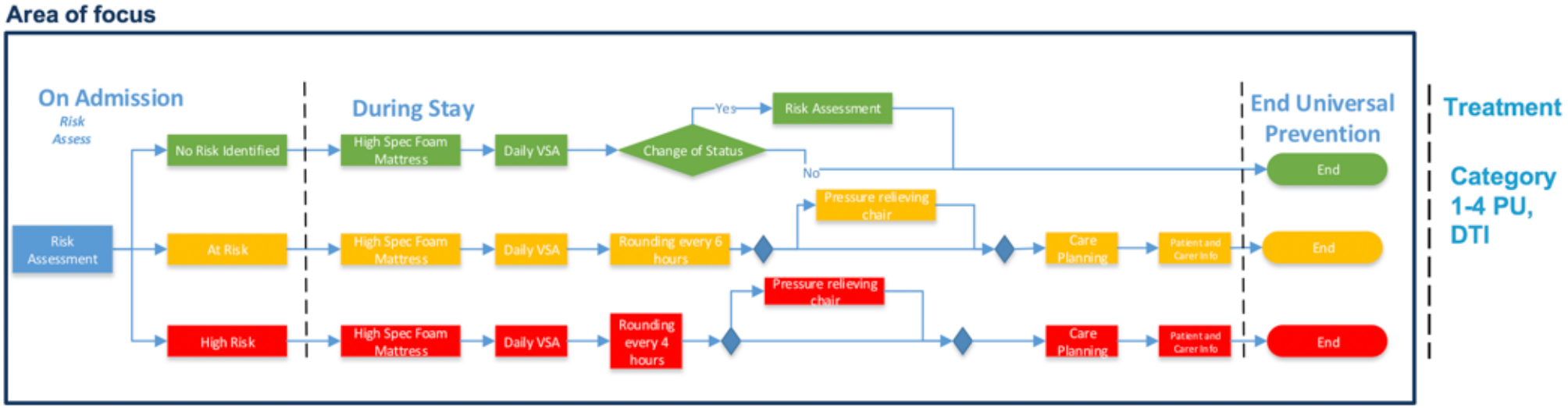


Figure 6 Current standard of care (NICE CG179)

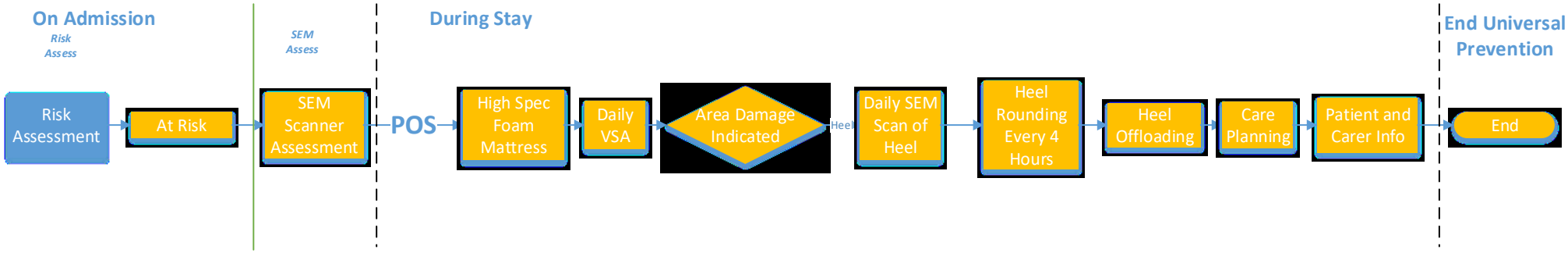


Figure 7 Current standard of care and SEM Scanner "positive"

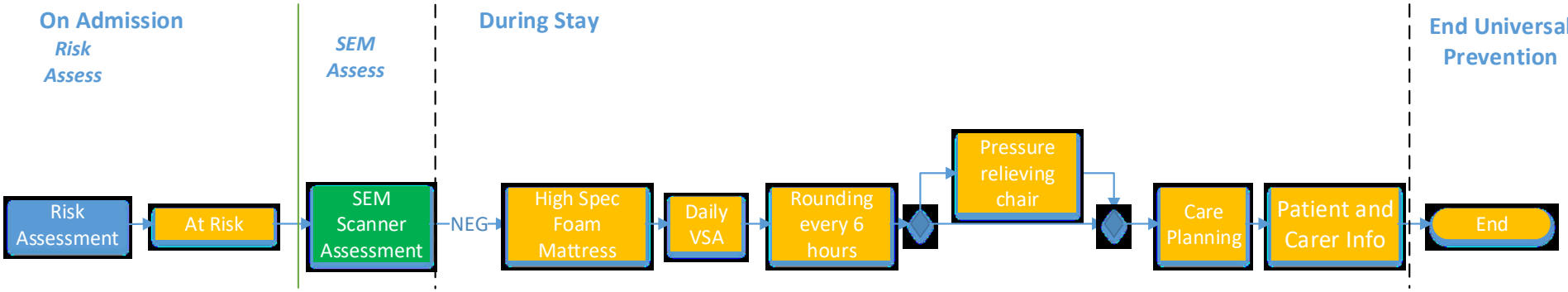


Figure 8 Current standard of care and SEM Scanner "negative"

The EAC built its own model to assess the impact of SEM Scanner on the costs of PUs in acute care wards. The model is a simple decision tree, which assesses the likelihood that a patient is diagnosed with a stage I PU and the likelihood that the PU heals or progresses to a more serious PU. The structure of the model and the predicted costs for care including the use of SEM Scanner are shown in Figure 9 below. The model assumes that diagnosis of a stage I PU triggers a change in repositioning from every 6 hours to every 4 hours, an assessment of nutritional status and location specific care. This change in care increases costs of care and increases the likelihood that the stage I PU will heal.

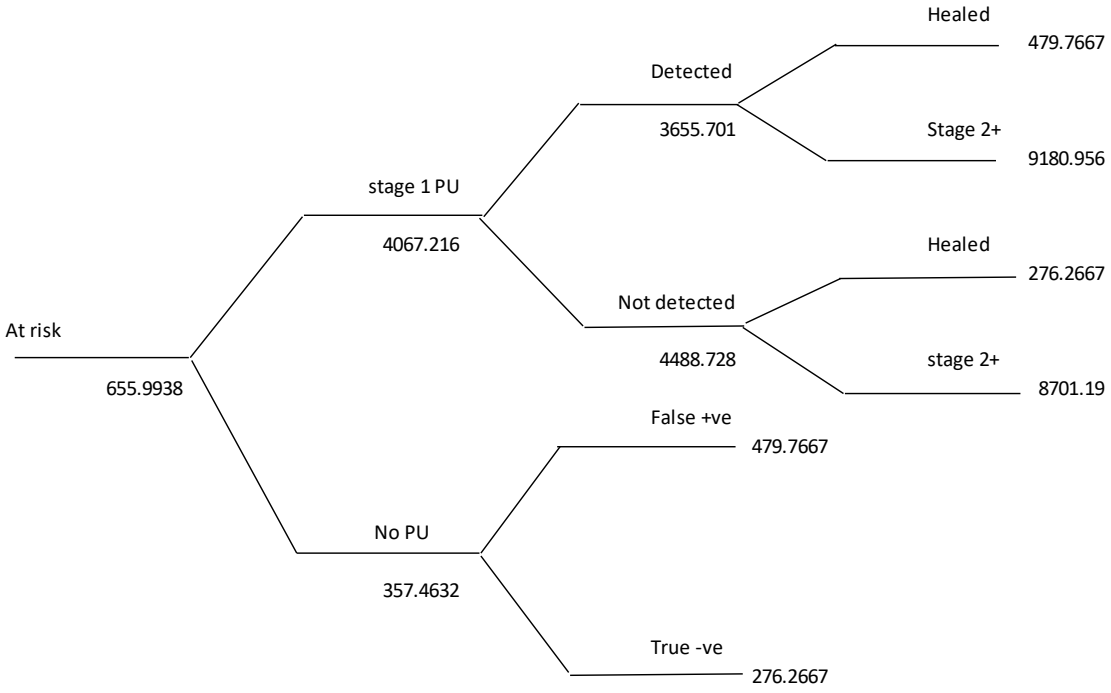


Figure 9 Decision tree built by the EAC with costs calculated for care including SEM Scanner

Clinical parameters and variables

- The company's submission considers a patient population of 12,182 based on an assumption of 10 wards with 21 beds each, a mean length of stay of 5.6 days and a bed occupancy rate of 89%. Of these patients, 4995 (41%) are assumed to be at risk of developing a PU. The proportion of patients at risk is taken from Vanderwee et al (2007). The EAC regards this as an acceptable source.

- The model assumes a PU incidence rate of 1.637% under SoC taken from a poster (Hancock & Lawrance 2019). With the introduction of SEM Scanner, the incidence of PUs is assumed to fall to 0.509% (a 68% reduction). The assumption of a 68% reduction is based on the results of a PU reduction programme that includes the introduction of SEM Scanner. The EAC notes that other PU reduction programmes have achieved this magnitude of effectiveness without the introduction of SEM Scanner (Mallah et al 2015; Crawford et al 2014). The model assumes that the reduction in PU incidence observed following the introduction of a PU reduction programme including the use of SEM Scanner is entirely attributable to the device. Given the numerous methodological shortcomings of this study (explored above), the EAC considers this assumption to be highly unlikely.

- The model assumes that 67% of observed PUs are stage II, 24% are stage III, and 9% are stage IV. This cited source for this distribution in the accompanying model is NHS safety thermometer (March 2017) which the EAC thinks is reasonable.

- Estimates of sensitivity (87.5%) and specificity (33%) of SEM Scanner and VSA combined are derived from Okonkwo et al (2017). Estimates of sensitivity (50.6%) and specificity (60.1%) for visual assessment are reported to be taken from the literature (Garcia-Fernandez et al 2014). The EAC notes that the data is from Pancorbo-Hildalgo et al (2006).

- The model estimates that 50.45% of the at-risk cohort are diagnosed to be at high risk (and hence repositioned every four hours) under SoC; in the arm including SEM Scanner 68% of patients are assumed to be high risk. The EAC is unable to determine how the parameter of 50.45% for SoC was estimated. The value of 68% for SEM Scanner is taken from Okonkwo et al (2017).

Table 6 Clinical parameters used in the company's model and any changes made by the EAC

Variable	Company value	Source	EAC value	EAC comment
Total number of beds	210	Unpublished company data assuming 10 wards of 21 beds each	same	Data accepted
Bed occupancy rate	89%	NHS England 2018	same	Appropriate source
Bed/nurse ratio	1 per 5 beds	Unpublished company data	same	Data accepted
Average length of stay	5.6 days	Health and Social Care Information Centre 2013	same	Appropriate source
Number of nurses	147	Calculated from data on length of stay and nurse to bed ratio assuming 3 shifts per day and 14% surplus staff	same	Data accepted
Proportion of patients at risk	41%	Vanderwee et al. 2007	same	Appropriate source
At risk population	4995	Calculated from data on number of beds, length of stay, proportion at risk and occupancy rate	same	Data accepted

Sensitivity of SEM Scanner	87.5%	Okonkwo et al 2017	same	The EAC accepts this estimate but notes concerns regarding the estimation of sensitivity and specificity
Specificity of SEM Scanner	33%	Okonkwo et al 2017	same	As above
Sensitivity of VSA	50.6%	Pancorbo-Hildalgo 2006	Same	Data accepted
Specificity of VSA	60.1%	Pancorbo-Hildalgo 2006	Same	Data accepted
Incidence of PU (all stages)	Not used		4.03%	Clark & Watts 1994
Incidence of PU in at risk patients	4.09%	Hancock & Lawrance 2019	8.05%	Calculation for at risk group assuming a diagnostic OR of 6.5 for initial risk assessment and incidence across all groups of 4.03%
Impact of SEM Scanner on stage II+ PU incidence	68.9%	Hancock & Lawrance 2019	Not used	The EAC believes the data used to estimate this parameter is insufficiently robust
Proportion of undetected stage I PU healing	Not used		0.5	Estimate derived from Halfens et al (2001) which showed 22% of PU healed and 22% deteriorated over time.
Relative risk of ulcer healing after detection and high risk management/ treatment			0.73	Defloor et al (2005)

Resource identification, measurement and valuation

- A band 5 nurse is costed at £18 per hour, sourced from the NICE costing statement for pressure ulcers published in 2014. This is based on mid-point Agenda for Change pay scales 2013–14. The EAC believe that this estimate is outdated and recommend the recent estimate of £37/hour for band 5 nurse (Curtis & Burns 2018). The latter estimate includes relevant overhead costs.

- The submission estimates an additional cost of £60,962 in the SEM Scanner arm, which includes the acquisition of the SEM Scanner (£44,735), training costs of £2,637 and scanning costs of £13,590. The submission reports amortising the costs of 23 devices assuming a lifetime of 3 years. However, the model applies the cost of (23/3 = 7.66) devices (at a quoted price of £5,835 per device).

- A per day cost for special mattress (£0.35), special chair (£ 0.89) and heel offloading (£0.22) is used in the model. The source cited is "Financial Forecast Model", which is not referenced. The EAC regards this to be of little impact, since only the cost of heel offloading is affected by the technology; the provision of appropriate mattress and chair is part of the care pathway for all at risk patients.

- Treatment costs for pressure ulcers for all the grades was estimated using the NHS Improvement pressure ulcer productivity calculator. The EAC think this is a valid tool to estimate the treatment costs, because it uses cost-results on the cost of pressure ulcers in UK taken from Bennett et al (2004) and inflated to 2016/17.

- The price of the SEM Scanner (£5,835) is the list price provided by the company.

Table 7 Cost parameters used in the company's model and changes made by the EAC

Parameter	Company value	EAC value	Source
Cost of purchasing SEM Scanner	£5,835	same	Company submission
Lifetime of scanner	3 years	same	Company submission
Number of scanners required	23	same	Company submission (assumes 1 per 9 beds)
Amortisation rate for scanner	0%	3.5%	NICE guidance
Total scanner cost	£44,735	£47,902	Impact of amortising at 3.5%
Band 5 nurse hourly cost	£18	£37	Unit Costs of Health & Social Care 2018
Training time per nurse	1 hour	same	The EAC accepts this figure but notes additional implementation costs for training described in the company's submission
Training cost	£2637	£5439	Revised band 5 costs
Time taken to reposition	10 minutes	same	NICE guidance CG179 appendix L
Staff required to reposition	1	2	NICE guidance CG179 appendix L
Cost of repositioning every 4 hours	£100.80	£414.40	Revised staff numbers and hourly cost
Cost of repositioning every 6 hours	£67.20	£276.26	Revised staff numbers and hourly staff cost
Heel offloading	£1.23	Not used	
Time for SEM Scanner assessment	5 minutes	same	EAC accepted the company's estimate but notes that time is required to prepare the machine and to clean it afterwards
SEM Scanner assessment	£1.50	£3.08	Revised staff cost

Proportion of stage II+ PU at stage II	0.67	same	NHS Safety Thermometer
Proportion of stage II+ PU at stage III	0.24	same	NHS Safety Thermometer
Proportion of stage II+ PU at stage IV	0.09	same	NHS Safety Thermometer
Cost of stage II PU	£6,770	same	The EAC accepts this figure derived from the NHS Improvement calculator but notes that inflation of the source data to 2017/18 prices generates lower estimates
Cost of stage III PU	£11,261	same	As above
Cost of stage IV PU	£16,250	same	As above
Cost of stage I assessment including nutrition after diagnosis	£0	£37	EAC estimate assumes 1 hour of nurse time
Cost of stage I treatment (excluding repositioning) (total)	£1.23	£28.36	EAC estimate assumes daily care taking 10 minutes of nurse time for duration of inpatient stay

Sensitivity analysis

The company reports undertaking univariate sensitivity analysis on a selection of cost, utility and probability variables in which each parameter was varied by 15%. Parameters were excluded if adjustment to the parameter by 1% had a marginal impact on the ICER for SEM Scanner. Probabilistic sensitivity analysis using Monte Carlo simulations was performed. The parameters included in the probabilistic analysis were:

- PU incidence rate (Beta distribution)
- Reduction in PU incidence following SEM Scanner introduction (Normal distribution – bounded at 0 and 100%)
- Total cost of prophylaxis and assessment under SOC (Normal distribution – bounded at £0)

- PU treatment costs by stage (Normal distribution – bounded at £0)
- SEM Scanner purchase price (Normal distribution – bounded at £4,000 and £12,000)
- Health state utility values according to PU grade (Normal distribution – bounded at 0)

Finally, a scenario analysis was performed in which a number of parameters were varied by 15%.

The EAC considers the sensitivity analysis to be rudimentary. The choice of 15% variation for all parameters in the one-way sensitivity analysis may not reflect the underlying uncertainty in each parameter. The probabilistic analysis is very basic. It is unclear why some parameters, such as the cost of prophylaxis and scanning in the SEM Scanner care pathway, are not included. Better distributions could have been selected for the included parameters that would have negated the need to bound distributions. The choice of standard deviations for parameters appears to lack justification. For instance, it is unclear why such a large variance in the purchase price for SEM Scanner is modelled. However, such variation might reflect differences in price *and* in the number of units acquired per ward.

9.3 *Results from the economic modelling*

Cost impact of SEM Scanner as an adjunct to VSA

Table 8 Summary of base case results

	Company's results			**EAC results**		
	Technology	**Comparator**	**Cost saving per patient**	**Technology**	**Comparator**	**Cost saving per patient**

Device and training	£47,372	£0	-£47,372	£53,341	£0	-£53,341
Additional scans	£13,590	£0	-£13,590	£64,037	£0	-£64,037
Prevention	£640,868	£550,215	-£90,653	£2,077,764	£1,794,281	-£283,483
Treatment	£197,129	£693,301	£496,172	£1,335,609	£1,509,837	£174,228
Total costs (Cohort)	£837,996	£1,243,516	£405,520	£3,530,751	£3,304,118	-£290,670
Cost per admitted patient	**£ 168**	**£249**	**£81**	**£707**	**£661**	**-£45**

The company's submission estimates a considerable cost saving per patient with the use of SEM Scanner. In contrast, the EAC model estimated an increase in costs. Both models estimated similar costs for the acquisition of the technology and training of staff. The EAC model estimated slightly higher costs for acquisition and training after amortising the acquisition price over three years at 3.5% and valuing nurse time for training at £37 compared with a value of £18 in the company's submission. The EAC estimated considerably higher costs for additional scanning time with SEM Scanner. There are two main reasons for this. Firstly, the EAC applied an hourly staff cost of £37 compared with £18 in the company's submission. Secondly, the company assumed that at risk patients would be scanned only once and that patients identified as high risk would incur further scans only at the heel or sacrum if this was the anatomical position identified as at risk. These scans were assumed to take 1 minute 15 seconds or two minutes 30 seconds, respectively. The EAC assumed that patients identified to have a stage I PU would be reassessed each day requiring an additional 5 minutes for patients assessed using SEM Scanner in addition to VSA.

The EAC estimated considerably higher prevention costs than those estimated by the company. The main constituent of these costs was repositioning. The EAC applied a higher unit cost for nurse time (£37 compared to £18 in the company's submission) and assumed that on average two nurses are required to reposition a patient. The company assumed that repositioning requires a single nurse. The EAC assumption on staff required for repositioning mirrors the assumption of two nurses for repositioning in the economic evaluation undertaken as part of NICE clinical guideline CG179 (appendix L).

The EAC estimated far higher treatment costs than those in the submission by the company. This was driven by an assumption of a higher prevalence of stage I PU in the EAC model. The EAC assumed that 8.05% of patients assessed as at risk will develop a stage I PU. The EAC assumed that in the absence of diagnosis, 50% of these would proceed to a stage II or greater PU, and that with diagnosis and treatment this would reduce to 36.5%. The company assumed that 1.64% of at risk patients would develop a stage II PU.

The company estimated a substantially larger saving in treatment costs than that estimated by the EAC. The company's submission assumes a reduction in the incidence of PU by 68.9% following the introduction of SEM Scanner. It also rounds down the numbers of patients at each PU stage calculated from data on the distribution of PU stage. The effect of rounding is a slight further increase in the assumed effectiveness of SEM Scanner (PUs in each of the categories 2 to 4 reduce by more than 70%). The EAC assumed a reduction of 27% in the risk of progression to stage II in patients diagnosed with a stage I PU following implementation of high risk management.

The overall impact of these changes is substantial. The company's submission estimates a cost saving of £81 per patient. The EAC estimates a cost increase of £45 following the introduction of SEM Scanner.

Sensitivity analysis results

The results of the company's univariate sensitivity analyses are not reported in detail; the company states that none generated a cost increase for SEM

Scanner. The results of the probabilistic sensitivity analysis are presented and indicate that 89% of model simulations generated a cost saving for SEM Scanner. The deterministic analyses are limited in their implementation by the arbitrary choice of 15% variation for each parameter. The probabilistic analysis is limited by the exclusion of a number of variables and limited justification of the variance modelled for the included parameters. However, the main limitation that is not addressed in sensitivity analysis is the structure of the model.

The EAC undertook extensive sensitivity analyses to explore the impact of uncertainty. Firstly, univariate sensitivity analysis was undertaken on all parameters considered subject to uncertainty. The results are tabulated below.

Table 9 Results of one-way sensitivity analysis for the EAC's model

Parameter	Base case	Variation in input	Variation in cost for SEM Scanner
Mean stage II+ PU treatment cost	£8,701	£5,000 to £15,000	£60 to £20
Cost to reposition	£12.33	£6 to £24	£26 to £82
Cost of stage I PU assessment	£37	£5 to £60	£36 to £52
Time taken for daily treatment of stage I PU	10 minutes	0 to 30 minutes	£37 to £61
Cost of nurse time per hour	£37	£28 to £45	£28 to £61
Training time for SEM Scanner	1h	0.5h to 2h	£45 to £46

Time to do SEM Scanner assessment	5 minutes	2 to 10 minutes	£38 to £58
Length of stay	5.6 days	3 to 25 days	£18 to £253
Stage I PU incidence	8.05%	4% to 20%	£62 to -£4
Proportion of stage I PU which heal without detection	0.5	0.25 to 0.75	£63 to £28
Relative risk of stage I PU healing with high risk management	0.73	0.25 to 0.95	-£17 to £74
Sensitivity of SEM Scanner and VSA combined	87.5%	75% to 95%	£55 to £40
Specificity of SEM Scanner and VSA combined	33%	25% to 55%	£61 to £1
Sensitivity of VSA	50.6%	35% to 65%	£33 to £57
Specificity of VSA	60.1%	45% to 75%	£17 to £73

Generous ranges were selected for parameters. In most cases SEM Scanner remained cost incurring but the impact on incremental costs was large. The one exception to this was training time for nurses – variation of this parameter had a negligible impact on incremental costs. In two sensitivity analyses SEM Scanner was cost saving at one extreme of the range: stage I PU incidence and the effectiveness of high risk management and treatment for stage I PU after diagnosis. For a further parameter, the specificity of SEM Scanner and VSA combined, the range was very close to indicating a cost saving at one extreme. SEM Scanner becomes cost neutral at an incidence of stage I PU of 19% (all other things, including length of stay, remaining the same). SEM Scanner is cost neutral if high risk management and treatment of stage I PU

following detection reduces the risk of progression by 62%. SEM Scanner becomes cost saving if specificity of the combined test increases to 56%.

The EAC undertook three further multiway sensitivity analyses. A two-way sensitivity analysis was undertaken in which the effectiveness of stage I PU treatment and the specificity of SEM Scanner were varied. The results are tabulated below. SEM Scanner became cost saving when specificity approached 50% and the relative risk of progression for a treated stage I PU approached 60%. A specificity of 35% was required when the relative risk of progression of stage 1 PU after diagnosis and high risk management was 0.4.

Table 10 Incremental cost of introducing SEM Scanner in two-way sensitivity analysis addressing specificity of SEM Scanner and effectiveness of treatment of stage I PU

		Specificity of SEM Scanner					
		25%	30%	35%	40%	45%	50%
Relative risk of progression of stage I PU with high risk management and treatment	0.85	£77	£67	£57	£47	£37	£27
	0.8	£70	£60	£50	£40	£30	£20
	0.75	£64	£54	£44	£34	£24	£14
	0.7	£58	£48	£37	£27	£17	£7
	0.65	£51	£41	£31	£21	£11	£1
	0.6	£45	£35	£25	£15	£35	-£5
	0.55	£38	£28	£18	£8	-£2	-£12
	0.5	£32	£22	£12	£2	-£8	-£18
	0.45	£25	£15	£5	-£5	-£15	-£25
	0.4	£19	£9	-£1	-£11	-£21	-£21

In a second sensitivity analysis, the above parameters were again varied over the same range of values. In this analysis, we considered a population likely to be at higher risk over a longer time period. Stage I PU incidence was set to 20% and length of stay to 15 days. The results are tabulated below. The results are very similar to the previous two-way sensitivity analysis – SEM Scanner becomes cost saving when specificity approaches 50% and the relative risk of progression for a treated stage I PU approached 60%. Again, a specificity above 30% is required when the relative risk of ulcer progression following diagnosis and high-risk management/treatment is 0.4. The impact of an increase in stage I PU incidence, which reduces the incremental cost of SEM Scanner, is offset by the increased length of stay, which has the opposite effect.

Table 11 Incremental cost of introducing SEM Scanner in two-way sensitivity analysis addressing specificity of SEM Scanner and effectiveness of treatment of stage I PU in scenario in which incidence of PU and length of stay is increased

		Specificity of SEM Scanner					
		25%	30%	35%	40%	45%	50%
Relative risk of progression of stage I PU with high risk management and treatment	0.85	£174	£153	£131	£110	£88	£67
	0.8	£158	£136	£115	£94	£72	£51
	0.75	£142	£120	£99	£78	£56	£35
	0.7	£126	£104	£83	£61	£40	£19
	0.65	£110	£88	£67	£45	£24	£2
	0.6	£94	£72	£51	£29	£8	-£14
	0.55	£78	£56	£35	£13	-£8	-£30
	0.5	£62	£40	£19	-£3	-£24	-£46

	0.45	£46	£24	£3	-£19	-£40	-£62
	0.4	£30	£8	-£13	-£35	-£56	-£78

In the third sensitivity analysis the EAC varied the incidence of stage I PU and LOS. The results are reported in Table 12. Over a very short length of stay of 3 days, SEM Scanner became cost saving when the incidence of stage I PU exceeded 12%. Over a length of stay of one week, SEM Scanner became cost saving when the incidence of stage I PU approached 24%. Pressure ulcer incidence increases as length of stay increases (Rondinelli 2018). Hence both incidence figures appear high over the length of stay specified. When length of stay was 2 weeks or more, SEM Scanner remained cost incurring when PU incidence reached 40%. The additional cost of turning every 4h instead of every 6h increases linearly with length of stay, and when length of stay is long this cost overwhelms costs averted through reduction in stage II+ PU incidence and treatment.

Table 12 Incremental cost of introducing SEM Scanner in two-way sensitivity analysis addressing incidence of PU and length of stay

		Length of stay					
		3d	7d	10d	14d	28d	56d
Incidence of stage I (%)	4	£35	£77	£108	£151	£299	£595
	6	£26	£69	£101	£143	£292	£590
	8	£18	£61	£93	£136	£286	£586
	10	£9	£52	£85	£128	£279	£581
	12	£1	£44	£77	£120	£272	£576
	16	-£16	£28	£61	£105	£259	£567

	20	-£33	£12	£45	£90	£246	£558
	24	-£50	-£4	£30	£75	£233	£549
	30	-£75	-£29	£6	£52	£213	£536
	40	-£117	-£69	-£34	£14	£180	£513

Cost impact of SEM Scanner in place of VSA

In the care pathway proposed by the company, SEM Scanner is used as an adjunct to VSA. The implied decision rule is that a positive result on either test signifies a stage 1 PU requiring treatment and high risk management. The consequence of this is that the specificity of the two tests cannot be higher than either test alone and is very likely to be lower. (Unless the results of one test influence the interpretation of the other test.) As a result of this the EAC did not consider specificity values above 0.6 for the combined test in sensitivity analysis.

The literature reviewed by the EAC indicated a much higher specificity for SEM Scanner when used alone. The EAC undertook analysis in which SEM Scanner is used *instead* of VSA and compared this to VSA alone. In this analysis, examination with SEM Scanner is assumed to take the same amount of time as examination with VSA. The sensitivity of SEM Scanner was taken as 86.51% and the specificity as 88.0%. These figures were calculated by the EAC using data from the study by Okonkwo et al (2018), in which the patients' PU-status was confirmed at baseline. VSA was not used in this study, so there is no equivalent sensitivity/specificity outcome for VSA (the figure of 60.1% is used from Pancorbo-Hildalgo et al, 2006). After keeping all other parameters the same, SEM Scanner is now associated with a per-patient saving of £70.

Table 13 Results of one-way sensitivity analysis for SEM Scanner in place of VSA

Parameter	Base case	Variation in input	Variation in cost for SEM Scanner
Mean stage II+ PU treatment cost	£8,701	£5,000 to £15,000	-£55 to -£94
Cost to reposition	£12.33	£6 to £24	-£53 to -£99
Cost of stage I PU assessment	£37	£5 to £60	-£62 to -£75
Time taken for daily treatment of stage I PU	10 minutes	0 to 30 minutes	-£63 to -£83
Cost of nurse time per hour	£37	£28 to £45	-£59 to -£79
Training time for SEM Scanner	1h	0.5h to 2h	-£70 to -£69
Length of stay	5.6 days	3 to 25 days	-£51 to -£206
Stage I PU incidence	8.05%	4% to 20%	-£58 to -£104
Proportion of stage I PU which heal without detection	0.5	0.25 to 0.75	-£53 to -£87
Relative risk of stage I PU healing with high risk management	0.73	0.25 to 0.95	-£130 to -£42

Sensitivity of SEM Scanner	86.5%	75% to 95%	-£61 to -£76
Specificity of SEM Scanner	88%	50% to 95%	£2 to -£83
Sensitivity of VSA	50.6%	35% to 65%	-£82 to -£58
Specificity of VSA	60.1%	45% to 75%	-£98 to -£42

The EAC undertook one-way sensitivity analysis to assess the sensitivity of results to parameter uncertainty in the scenario in which SEM Scanner replaces VSA. The results are tabulated above (Table 13). The inference that SEM Scanner is cost saving when used as a replacement for VSA was robust to uncertainty in each parameter apart from the specificity of SEM Scanner. When this parameter approached 50% SEM Scanner became cost incurring. The scanner remains cost saving even when the relative risk of ulcer progression following diagnosis and high risk management/treatment is increased to 1 (high risk management and treatment has no effect). The reason for this is the increased specificity of SEM Scanner alone, compared to VSA which reduces the considerable resource impact arising from increased repositioning of false positive patients. SEM Scanner alone remains cost saving until specificity falls to 51%.

SEM Scanner remains cost saving across the range of values considered for length of stay and incidence of stage I PUs. Savings increase as length of stay increases due to reductions in the cost of repositioning patients with SEM Scanner. Savings increase as incidence of stage I PUs increase due to reductions in the cost of treating stage II+ PUs. However, SEM Scanner remained cost saving even when the incidence of stage I PU was reduced to zero.

9.4 *The EAC's interpretation of the economic evidence*

The company concludes that SEM Scanner is highly likely to be cost saving on the basis of the cost estimates derived from the accompanying model. The company suggests that there are additional health benefits arising from a reduction in the incidence of PUs. These conclusions are consistent with the model results. However, the EAC has serious concerns regarding the validity of the model. The chief concern is the assumption that the introduction of SEM Scanner leads to a reduction in the incidence of PUs of 68%. This assumption is derived from a before-after comparison of the effectiveness of a pressure ulcer reduction programme (the PURP, Hancock & Lawrance 2019). There are a number of methodological limitations to this study, which are outlined in detail in sections 5 and 8. The contribution of SEM Scanner itself to the observed reduction is not estimable from the research design. However, the EAC considers it implausible that SEM Scanner would be entirely responsible for the observed reduction, and that it may have made a minor contribution alongside increased vigilance and attention to preventive measures such as repositioning.

The EAC notes the lack of evidence in the literature regarding the impact of treatment/preventive measures on the progression of PUs. There is evidence to indicate that SEM Scanner is able to diagnose a potential PU at an earlier stage than VSA. It is possible that earlier diagnosis improves the effectiveness of preventive measures. The EAC notes that SEM Scanner has been registered for use as a risk management tool. However, the mode of action appears to be through early detection of the formation of a PU. The EAC considered that for SEM Scanner to be effective it must be detecting PUs or nascent sites likely to form a PU more effectively than VSA. There is no clear clinical definition of what constitutes a nascent PU. One clinical expert suggested a new, pre-stage I category is required (see section 3). Therefore, the EAC considered the evidence on detection rates for stage I PU formation for which the literature provides some evidence and the likely effectiveness of interventions to halt or reverse the formation of PUs for which there is some limited evidence. This evidence was modelled to estimate the

potential impact on costs of improved detection of PUs by SEM Scanner, alone or in combination with VSA, compared to VSA. The model assumes increased effectiveness is achieved through improved detection of PUs prior to progression to stage II. It is possible that this approach fails to capture the increased likelihood of reversing the progression of a very early stage PU through earlier detection and implementation of treatment. The almost complete absence of evidence on the effectiveness of interventions to address stage I PU prevents assessment of the impact of earlier detection.

The EAC built its own decision model to estimate the impact of SEM Scanner on the costs of preventing and treating PUs. The model calculates the proportion of patients positively diagnosed with a stage I PU according to the prevalence of stage I PUs and the sensitivity of SEM Scanner in addition to VSA compared with VSA alone. The main impact of diagnosis in the care pathway submitted by the company is a change in the frequency of repositioning from every 6 to every 4 hours. Data on the impact of this is scant. However, a single trial reported a hazard ratio of 0.73 (95% CI: 0.53-1.02) (Defloor et al 2005). In the EAC's model, treatment costs are estimated on the assumption that the relative risk of stage I PU progression following treatment is 0.73. This parameter - along with a number of other parameters in the model - is subject to considerable uncertainty.

When SEM Scanner is used as an adjunct to VSA, the EAC estimates a cost increase of £45 per patient. Sensitivity analysis indicates a number of parameters in which uncertainty has a large impact on this estimate. The parameters with the largest impact are incidence of stage I PUs and length of stay. Higher incidence reduces the incremental cost of SEM Scanner, which becomes cost saving at an incidence of 19% (one-way sensitivity analysis, see Table 9). The incremental cost of SEM Scanner increases rapidly with increasing length of stay. It seems reasonable to assume that populations with a higher incidence are likely to have a longer stay in hospital. If this is the case, the finding that SEM Scanner is cost incurring when used as an adjunct to VSA is unlikely to change in higher risk populations.

The incremental impact of SEM Scanner on costs is highly sensitive to the specificity of the device. In the analysis of SEM Scanner as an adjunct to VSA, the EAC applied the same specificity as that assumed by the company and based on results by Okonkwo et al (2017). The EAC noted other studies where the specificity of SEM Scanner is estimated to be much higher than this (such as O'Brien et al 2018). The EAC assumed that when SEM Scanner is used as an adjunct to VSA a positive result on either test would be considered a positive diagnosis for a stage I PU. It follows from this assumption that the specificity of the combined test cannot be higher than the specificity of VSA and is highly likely to be lower. Uncertainty remains around the specificity of VSA. However, if the estimate of 60.1% for VSA is accurate it seems unlikely that the specificity of the combination of SEM Scanner and VSA could be much above 50%. In two-way sensitivity analysis SEM Scanner did not become cost saving until specificity approached 50% *and* the relative risk of stage I PU progression following treatment fell to 60%.

In the analysis of SEM Scanner as a replacement for VSA in which a specificity for the scanner of 88% was assumed, SEM Scanner became cost saving. SEM Scanner remained cost saving even when treatment and high risk management of stage I PU was assumed to have no effect on progression. The major cost driver is repositioning, and high specificity has a large impact on the cost burden of repositioning of patients falsely testing positive. The finding that SEM Scanner is cost saving when used as a replacement for VSA was robust to uncertainty in all parameters apart from specificity: SEM Scanner was cost saving until specificity fell to 51%. Notably, SEM Scanner remained cost saving at low incidence of stage I PUs and for short length of stay. The EAC thinks this result may indicate the most cost-effective implementation of the test (as a replacement rather than an adjunct to VSA).

Whilst the results of the scenario analysis were robust to parameter uncertainty in one-way sensitivity analysis, some caution in concluding that SEM Scanner is cost saving when used in this manner is warranted. The use of SEM Scanner as a replacement for VSA is not indicated by the IFU and is

not seen in any of the published evidence. The evidence on the use of SEM Scanner in this way extends only to the sensitivity and specificity of the test – data on the incidence of stage II+ PUs or the impact on costs of replacing VSA with SEM Scanner is absent.

Analysis of the impact of SEM Scanner as an adjunct or as a replacement for VSA is based on a simple decision tree. The very limited evidence on the progression of PUs and the impact of diagnosis and treatment limits the value of a more complex model. However, such a model does not explicitly capture the progression of PUs. There is evidence to indicate SEM Scanner diagnoses stage I PUs earlier than VSA. Whilst there is no evidence on the impact of this on progression, this would seem likely to improve the effectiveness of interventions to prevent progression.

In summary, the EAC estimates a cost increase of £45 per patient with the introduction of SEM Scanner into the care pathway for patients at risk of PU as an adjunct to VSA, and a saving of £70 per patient when SEM Scanner is used as a replacement for VSA. The EAC notes considerable uncertainty in parameters informing the analysis and the sensitivity of the results to these parameters. However, the EAC tested the sensitivity of results to variation of parameters over relatively wide ranges. The inference on costs when SEM Scanner is used as an adjunct to VSA was sensitive to only two parameters – the incidence of stage I PUs and the effectiveness of treatment/preventive measures in halting the progression of a stage I PU. The inference that SEM Scanner is cost saving when used in place of VSA was robust to all parameters tested except the specificity of SEM Scanner. Specificity is a key cost driver due to the high cost of increasing the frequency at which patients are turned. The results of the scenario analysis suggest that SEM Scanner might be best used as a replacement of VSA.

The evidence underpinning these findings is limited and further investigation of the effectiveness and cost-effectiveness of SEM Scanner as a replacement to VSA is warranted. In particular, it is possible that earlier detection of stage I PUs using SEM Scanner leads to fewer PUs progressing to stage II, regardless of whether these PUs would have been detected using VSA

(presumably at a slightly later point). Lack of evidence prevented the EAC from assessing this aspect of the performance of SEM Scanner.

10 Conclusions

10.1 *Conclusions from the clinical evidence*

The evidence base for SEM Scanner is entirely comprised of prospective observational studies (2 before-after comparative studies, 5 single-arm studies). The most clinically meaningful outcomes are reported in Raizman et al (2018) and Hancock & Lawrance (2019), both of which showed a reduction in PU incidence following the introduction of SEM Scanner. However, there are numerous methodological problems with these studies and the EAC has low confidence in these outcomes. The three studies reporting diagnostic outcomes were flawed in their use of VSA as the reference standard (see sections 5.2 and 8) and the EAC considers these outcomes should be viewed as a measure of agreement, rather than diagnostic accuracy. Three studies reported the 'time to test result' and showed SEM Scanner to be substantially quicker than VSA, although these studies did not go on to show the clinical significance of this apparent superiority.

- **Does the evidence present an unbiased estimate of the technology's treatment effect?**

The existing evidence base is very limited for SEM Scanner and there are several important limitations to consider in assessing the included studies. It is therefore difficult to estimate the effect of SEM Scanner in its primary goal (reducing PU incidence) with any confidence.

- **Was the treatment effect relevant to the population, intervention, comparators and outcomes in the decision problem?**

The EAC considered the populations of the studies to be highly relevant to the decision problem, with the care settings relevant to the NHS. There was some variation between the studies in how SEM Scanner was used (with regard to the cut-off used and the frequency of scans) and this may have increased the risk of performance bias in some studies. The comparator used in the two comparative studies was not well reported, although in Raizman et al (2018) the study was designed in such a way that there was some consistency of

care between the two groups; SEM Scanner was correctly used as an adjunct to the existing standard of care in the experimental arm. The evidence base is notably lacking in many of the outcomes listed in the scope, namely impact on clinical management decisions, rate of infection, quality of life, rate of complications, length of hospital stay, costs of treating PUs, patient compliance and ease of use.

- **Is there evidence on any important subgroups?**

The only sub-group analysis performed was on the variation shown between SEM Scanner readings of the heels and the sacrum. However, the studies that identified this variation did not go on to investigate how this phenomenon influenced other outcomes. None of the studies reported sub-group analyses for patients at high risk of developing PUs.

- **Are there any other important uncertainties in the clinical evidence?**

There are significant uncertainties over the outcomes of the two most clinically relevant studies. Raizman et al (2018) conducted the two phases of their study in different hospital settings and did not adequately report how the SEM Scanner results were used to influence care. Hancock & Lawrance (2019) did not report any demographic information for either phase, and no information about the standard of care in the control phase. This study also only included stage II-IV PUs in their analysis, which is a significant divergence from the other included studies.

10.2 *Conclusions from the economic evidence*

The economic evidence indicates that SEM Scanner is likely to be cost incurring when used as an adjunct of VSA and cost saving when used as a replacement of VSA, both for short stay and for long stay patients. The cost analysis utilises parameters for which there is considerable uncertainty. Most notably, it is not clear what impact the diagnosis and subsequent treatment of stage I PUs has on the likelihood of these ulcers progressing. The treatment of stage I PU would need to achieve a relative risk of progression of 0.38 for

SEM Scanner to become cost neutral when used as an adjunct of VSA, *ceteris paribus*. This is well below the lower confidence interval of 0.53 for the relative risk observed in the only trial comparing repositioning every 4 hours with every 6 hours (Defloor et al 2005). It is unclear what additional interventions might lower the risk of progression further. Therefore, the EAC concludes that the use of SEM Scanner as an adjunct to VSA is likely to increase the cost of prevention and treatment of PUs.

In contrast, SEM Scanner is cost saving when used as a replacement of VSA. This finding was robust to uncertainty in all parameters except specificity of SEM Scanner. It is conceivable that testing with SEM Scanner might require less training than VSA and is more easily documented, which could be an incentive to ensure regular implementation. The use of SEM Scanner as a replacement to VSA has the potential to reduce costs. It may also improve patient outcomes if its use translates into a reduction in the incidence of stage II+ PUs. However, as previously noted, the evidence on the use of SEM Scanner as a standalone technology is non-existent. Further investigation of the effectiveness and cost-effectiveness of SEM Scanner as a replacement to VSA is warranted.

11 Summary of the combined clinical and economic sections

There is a clear lack of high quality evidence for SEM Scanner, with only 2 low quality comparative studies and 5 single-arm studies included. The two comparative studies indicate there is potentially a significant benefit to adding SEM Scanner to SoC in the current pathway, although there are a number of important limitations to these studies, which makes it impossible to support the case for adoption. The before-after study from Canada by Raizman et al (2018) did not compare SEM Scanner in like-for-like care settings and the authors do not report how SEM Scanner readings were used to determine subsequent interventions. Hancock & Lawrance (2019) report the findings of a multi-centre before-after UK study, which is reported in two differing conference abstracts (supplemented by an unpublished report provided by the

company). There is very little information reported about the control phase of the study and it is impossible to determine the extent to which SEM Scanner influenced the reported reduction in PU incidence. The two studies are also heterogeneous in that Raizman et al included stage I PUs in their analysis, while Hancock & Lawrance do not. The outcomes reported in the non-comparative evidence – which is also methodologically flawed – do not add any certainty to the comparative studies.

The EAC revised the company's cost model and found that SEM Scanner is cost incurring when used as an adjunct to VSA and cost saving when used as a replacement to VSA. The EAC's analysis indicated an increased cost of £45 per patient when SEM Scanner is used as an adjunct to VSA. The company's cost model showed SEM Scanner to be cost saving when used as an adjunct to VSA, but this was based on optimistic assumptions of the impact of SEM Scanner on stage II+ PU incidence. The company's model did not utilise evidence of the diagnostic accuracy of SEM Scanner to estimate the impact on stage II+ PU treatment costs. The EAC built its own model to estimate the impact of diagnosis on maintenance/treatment costs and on the downstream costs of caring for PUs at stage II or higher. The model indicates that a much higher specificity of the combined test than that reported in the literature is required for SEM Scanner to be cost saving. The EAC notes the limitations in the evidence base that prevented consideration of any beneficial impact of earlier detection of PUs with SEM Scanner.

The EAC found SEM Scanner to be cost saving when use as a replacement to VSA. This finding was robust to parameter uncertainty. The key difference when SEM Scanner is used as a replacement rather than an adjunct to VSA is the potential for SEM Scanner to achieve higher specificity than VSA. This translates to a lower cost burden of increased turning for patients identified as high risk of PU. Use of SEM Scanner as a replacement of VSA may also translate into improved patient outcomes through reduced stage II+ PU incidence when compared to VSA alone. (However, sensitivity will be inevitably be maximised through use of SEM Scanner as an adjunct to VSA.)

Further investigation is warranted to assess the effectiveness and cost-effectiveness of SEM Scanner as a replacement to VSA.

12 Implications for research

The majority of the included studies do not report relevant outcomes on the clinical efficacy of SEM Scanner. In a systematic review, Pancorbo-Hidalgo et al (2006) reported the relative diagnostic performance of 4 methods of PU risk assessment (see Table) and found that clinical judgement (investigated in only 3 studies) performed worst for risk prediction. Future researchers should test the performance of SEM Scanner against the current standard of care (i.e. VSA), without basing interventions on the SEM reading. The methodology of Raizman et al (2018) implies that this was done, but the results are not reported. The studies that do report sensitivity and specificity of SEM Scanner have done so using VSA as the reference standard, which means it is impossible to test the relative diagnostic performance of SEM Scanner to VSA.

Table 14 Risk assessment scales performance (from Pancorbo-Hidalgo et al 2006)

Assessment tool	Sensitivity	Specificity	Odds ratio for risk prediction
Braden scale	57.1%	67.5%	4·08 (95% CI: 2·56–6·48)
Norton scale	46.8%	61.8%	2·16 (95% CI: 1·03–4·54)
Waterlow scale	82·4%	27·4%	2.05 (95% CI: 1·11–3·76)
Clinical judgement	50.6%	60.1%	1.69 (95% CI: 0·76–3·75)

The EAC highlights the fact that some of the key limitations to the Hancock & Lawrance study would be removed with better reporting. The study has been published in two separate conference abstracts and key information was taken from an unpublished report provided by the company. A well-reported full-text publication would be beneficial to providing clarity to this study.

The speed with which SEM Scanner identifies at-risk patients was shown, in three studies, to be substantially faster than VSA (an average of between 3 and 4.7 days faster). Future research should be designed to show differences in outcomes between patients who were identified earlier and how subsequent care differed for these patients.

The methodology used by Raizman et al (2018), although not without its flaws, suggests that it would be possible to carry out a randomised controlled trial for SEM Scanner. Consideration should be given to a trial comparing SEM Scanner alone with VSA. Such a trial should include the collection of cost data, which might then support a robust economic analysis of SEM Scanner. A primary outcome of PUs at stage II or greater would be sufficient to support an economic analysis without the need for complex modelling.

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14 Appendices

Appendix A – Search strategies

Appendix B – Included and excluded studies

Appendix C – Adverse events

Appendix D – Ongoing studies

Appendix A – Search strategies

Clinical evidence

Total records retrieved: 581

Total following de-duplication in EndNote X7.8: 382

- 7 records from MIB182

- 5 records from the company submission

- Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to October 04, 2019
- Search date: 7th October 2019

1	exp pressure ulcer/	11949
2	(pressure ulcer* or pressure sore* or pressure injur* or bed sore* or bedsore* or decubitus ulcer*).tw,kw,ot.	12862
3	1 or 2	16307
4	(detect* or assess* or risk* or diagnos* or eval* or determin* or measur* or judg* or objective*).tw,kw,ot.	12537346
5	3 and 4	8817
6	(biocapacitance or capacitance or impedance or dielectric or electrophysiolog* or surface electric*).tw,kw,ot.	186420
7	5 and 6	32
8	sem scanner*.af.	7
9	semscanner*.af.	0
10	semtm.af.	0
11	semr.af.	12
12	Bruin Biometrics.af.	6
13	BBI LLC.af.	2
14	(sub-epidermal moisture or subepidermal moisture).af.	19

15	or/8-14	33
16	7 or 15	60
17	(editorial or letter or case report or comment or news).pt.	1950874
18	16 not 17	60
19	animals/ not (animals/ and humans/)	4592008
20	18 not 19	53

- Embase 1974 to 2019 Week 40
- Search date: 7th October 2019

1	exp decubitus/	20022
2	(pressure ulcer* or pressure sore* or pressure injur* or bed sore* or bedsore* or decubitus ulcer*).tw,kw,ot.	15728
3	1 or 2	23653
4	(detect* or assess* or risk* or diagnos* or eval* or determin* or measur* or judg* or objective*).tw,kw,ot.	16309571
5	3 and 4	14123
6	(biocapacitance or capacitance or impedance or dielectric or electrophysiolog* or surface electric*).tw,kw,ot.	219065
7	5 and 6	68
8	sem scanner*.af.	8
9	semscanner*.af.	0
10	semtm.af.	1

11	semr.af.	57
12	Bruin Biometrics.af.	9
13	BBI LLC.af.	2
14	(sub-epidermal moisture or subepidermal moisture).af.	19
15	or/8-14	81
16	7 or 15	143
17	(editorial or letter or case report or comment or news).pt.	1723821
18	16 not 17	143
19	(animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not ((animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) and exp human/)	5874510
20	18 not 19	101

- Cochrane databases (CDSR and CENTRAL)
- Search date: 7th October 2019

ID	Search	Hits
#1	[mh "pressure ulcer"]	695
#2	(pressure ulcer* or pressure sore* or pressure injur* or bed sore* or bedsore* or decubitus ulcer*):ti,ab,kw	9740
#3	#1 or #2	9740
#4	(detect* or assess* or risk* or diagnos* or eval* or determin* or measur* or judg* or objective*):ti,ab,kw	1116694
#5	#3 and #4	8362
#6	(biocapacitance or capacitance or impedance or dielectric or electrophysiolog* or surface electric*):ti,ab,kw	8883
#7	#5 and #6	130
#8	sem scanner*	20

#9	semscanner*	0
#10	semtm	0
#11	semr	5
#12	Bruin Biometrics	0
#13	BBI LLC	2
#14	(sub-epidermal moisture or subepidermal moisture)	1
#15	{OR #8-#14}	28
#16	#7 or #15	158

- PubMed
- Search date: 7th October 2019

Search	Query	Items found
#17	Search (#7 or #15) Filters: Humans	41
#16	Search (#7 or #15)	63
#15	Search (#8 or #9 or #10 or #11 or #12 or #13 or #14)	37
#14	Search (sub-epidermal moisture[Title/Abstract] OR subepidermal moisture[Title/Abstract])	19
#13	Search BBI LLC	3
#12	Search Bruin Biometrics	10
#11	Search semr	12
#10	Search semtm	0
#9	Search semscanner*	0
#8	Search sem scanner*	7
#7	Search (#5 and #6)	31
#6	Search (biocapacitance[Title/Abstract] OR capacitance[Title/Abstract] OR impedance[Title/Abstract] OR dielectric[Title/Abstract] OR electrophysiolog*[Title/Abstract] OR surface electric*[Title/Abstract])	188759
#5	Search (#3 and #4)	8797
#4	Search (detect*[Title/Abstract] OR assess*[Title/Abstract] OR risk*[Title/Abstract] OR diagnos*[Title/Abstract] OR eval*[Title/Abstract]	12581777

	OR determin*[Title/Abstract] OR measur*[Title/Abstract] OR judg*[Title/Abstract] OR objective*[Title/Abstract])	
#3	Search (#1 or #2)	16276
#2	Search (pressure ulcer*[Title/Abstract] OR pressure sore*[Title/Abstract] OR pressure injur*[Title/Abstract] OR bed sore*[Title/Abstract] OR bedsore*[Title/Abstract] OR decubitus ulcer*[Title/Abstract])	12827
#1	Search pressure ulcer[MH]	11949

- Web of Science
- Search date: 7th October 2019

# 6	97	#4 OR #5 Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=1900-2019
# 5	64	TS=("sem scanner*" or semscanner* or semtm or semr or "Bruin Biometrics" or "BBI LLC" or "sub-epidermal moisture" or "subepidermal moisture") Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=1900-2019
# 4	38	#1 and #2 and #3 Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=1900-2019
# 3	753,444	TS=(biocapacitance or capacitance or impedance or dielectric or electrophysiolog* or "surface electric*") Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=1900-2019
# 2	20,753,413	TS=(detect* or assess* or risk* or diagnos* or eval* or determin* or measur* or judg* or objective*)

		Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=1900-2019
# 1	10,995	TS=("pressure ulcer*" or "pressure sore*" or "pressure injur*" or "bed sore*" or bedsore* or "decubitus ulcer*") Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=1900-2019

- CINAHL (Ebsco)
- Search date: 7th October 2019

Search Options	**Actions**		
S9	S7 OR S8	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	View Results (86) View Details Edit
S8	TX "sem scanner*" or semscanner* or semtm or semr or "Bruin Biometrics" or "BBI LLC" or "sub-epidermal moisture" or "subepidermal moisture"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	View Results (36) View Details Edit
S7	S5 AND S6	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	View Results (56) View Details Edit

S6	TX biocapacitance or capacitance or impedance or dielectric or electrophysiolog* or "surface electric*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	View Results (44,727) View Details Edit
S5	S3 AND S4	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	View Results (10,630) View Details Edit
S4	TX detect* or assess* or risk* or diagnos* or eval* or determin* or measur* or judg* or objective*	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	View Results (3,090,516) View Details Edit
S3	S1 OR S2	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	View Results (15,374) View Details Edit
S2	TX "pressure ulcer*" or "pressure sore*" or "pressure injur*" or "bed sore*" or bedsore* or "decubitus ulcer*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	View Results (15,301) View Details Edit
S1	(MH "Pressure Ulcer+")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	View Results (12,512) View Details Edit

- British Nursing Index (Proquest)
- Search date: 7th October 2019

Set	Search	Databases	Results
S6	4 OR 5	British Nursing Index	85
S5	"sem scanner*" or semscanner* or semtm or semr or "Bruin Biometrics" or "BBI LLC" or "sub-epidermal moisture" or "subepidermal moisture"	British Nursing Index	14
S4	1 AND 2 AND 3	British Nursing Index	71
S3	biocapacitance or capacitance or impedance or dielectric or electrophysiolog* or ("surface electrical")	British Nursing Index	3,623
S2	detect* or assess* or risk* or diagnos* or eval* or determin* or measur* or judg* or objective*	British Nursing Index	525,238
S1	"pressure ulcer*" or "pressure sore*" or "pressure injur*" or "bed sore*" or bedsore* or "decubitus ulcer*"	British Nursing Index	10,795

Grey literature:

Search date: 7th October 2019

- HMIC
- Global Health
- CAOD
- http://webarchive.nationalarchives.gov.uk/adv_search/
- http://www.opendoar.org/
- https://patents.google.com/

(search string "sem scanner") – **5 results**

Ongoing studies

Total records retrieved: 61

Total following de-duplication in EndNote X7.8: 59

- WHO ICTRP (default search)
- Search date: 7th October 2019

“sem scanner” – 2 results

- ClinicalTrials.gov (expert search)
- Search date: 7th October 2019

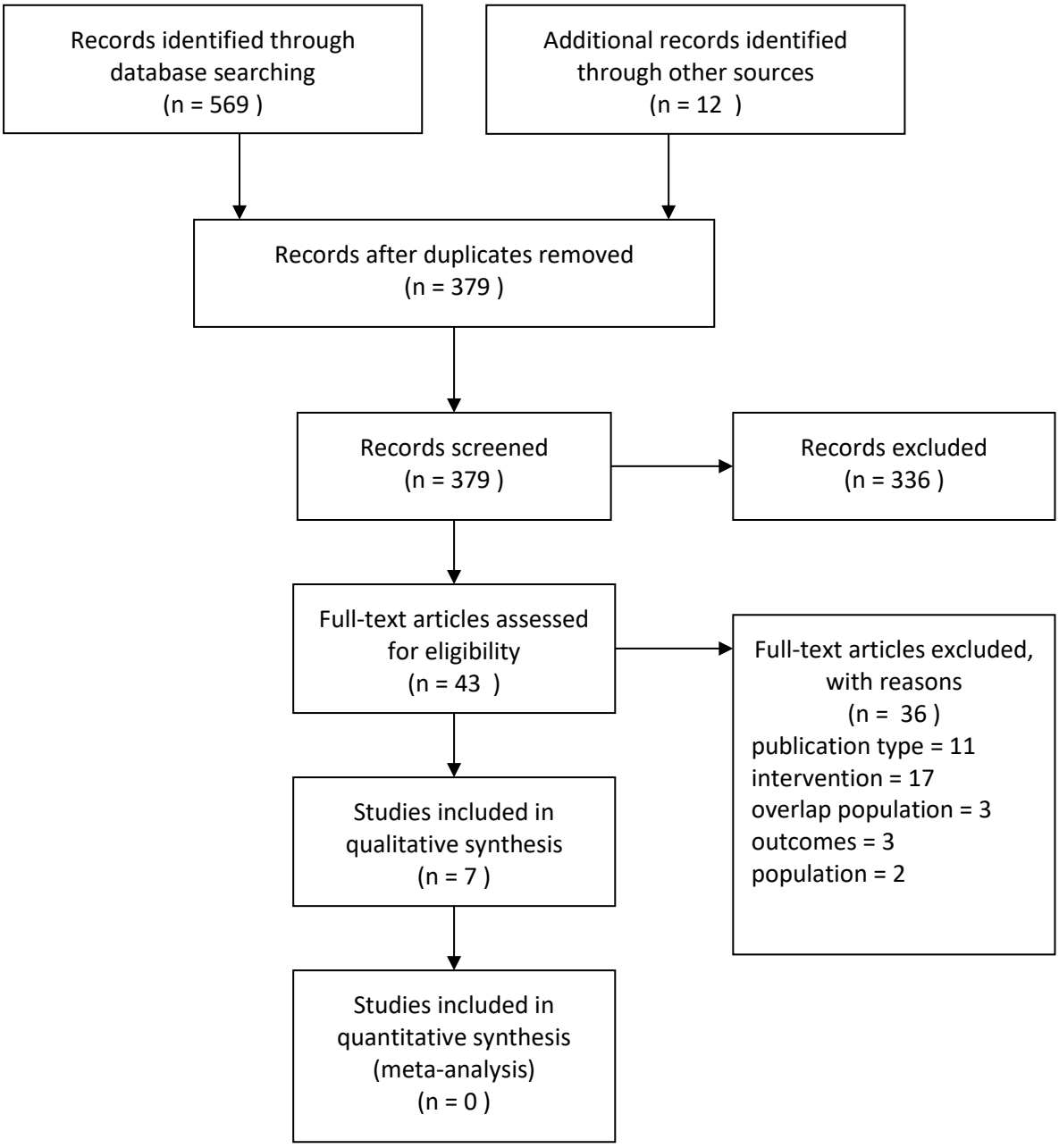
“sem scanner” – results

57 results from the CENTRAL search

Economics studies

The EAC did not run an additional search for economic evidence. The results of the clinical evidence searches (see Appendix A) were filtered in EndNote X7.8, using terms “econo*” and “cost*”. There were 44 results, which were sifted for relevance by two independent health economists.

PRISMA 2009 Flow Diagram



Appendix B – Included and excluded studies

Table 15 Included and excluded studies

Study and type	population	intervention	comparator	outcomes	Other (follow up, setting, versions of device etc.)	EAC comment
Raizman et al (2018) Canada	**Phase 1:** 89 participants (55% female, 60% incontinent) **Phase 2:** 195 participants (55% female, >90%	SEM Scanner	Standard Care	Number of patients that developed PUs	The two phases were in different hospital units and although the baseline demographics were similar between the groups, the authors state that phase 2 patients were overall at a higher risk for developing PUs.	Company included EAC included

	incontinent, Braden Mobility sub-score ≤3)					
Gefen et al (2018) USA	15 patients (66% female, mean age 74-years, 11 Caucasian, 4 black/African American)	SEM Scanner	VSA Ultrasound	Agreement between SEM Scanner and comparators Development of sDTIs		Company included EAC included
O'Brien et al (2018) Ireland	47 patients (61.5% female, mean age 74.7-years)	SEM Scanner	Standard Care	Sensitivity and Specificity		Company included EAC included

Okonkwo et al (2017) – **Study 008** USA and UK	182 in intention-to-treat (ITT) analysis; 170 per protocol 46.7% male, mean age 76-years, 66.5% Caucasian, 24.2% Asian, 4.4% Black/African American	SEM Scanner	Skin Assessment	Sensitivity and Specificity		Company EAC	included included
Okonkwo et al (2018) – **Study 003 (PUs) and**	175 patients in total	SEM Scanner	VSA and Braden Scale	SEM Scanner readings	The two different cohorts were recruited from different care settings (unaffected subjects from	Company EAC	included included

004 (unaffected) USA	125 patients with confirmed PUs (56% female, mean age 82.7-83.6-years) 50 Unaffected patients (50% female, mean age 66.8-years)		risk assessment	Sensitivity and Specificity	office setting, affected from care home).	
Hancock & Lawrance (2019) – **PURP**	1478 patients in PURP	SEM Scanner	Historical control	HAPU rate Percentage of changes in	15 acute care (AC) facilities, 1 hospice care (HC) facility.	Company included EAC included

UK	period vs. 12,128 patients in historical control Waterlow scale >10 or patients admitted to PURP ward (1 site used Braden scale).			clinical decision-making Number of additional interventions	The inclusion criteria are not uniform across the different sites.	
O'Keefe & McLuskey (2019) Ireland	32 patients	SEM Scanner	None	Number of patients with a positive SEM reading Number of patients developing PUs	Combined orthopaedic/plastic surgery ward	Company included EAC included

Smith (2019) UK	35 patients (9% aged 65–75-years, 74% were aged >75-years. 51% female)	SEM Scanner	Waterlow risk score	SEM delta readings Number of patients developing PUs	NHS Medical-surgical ward.	Company included EAC excluded The outcomes reported do not match the scope.
Moore et al (2018) UK	59 patients September-October 2017	SEM Scanner	None	Number of patients with deviated SEM reading Acceptability of device to clinical staff	Orthopaedic trauma ward Possible overlap with part of the population in Okonkwo et al (2017) (Study 008): the setting and the investigator mentioned (Northumbria NHS Trust, and Milne, J.) are the same.	Company included EAC excluded The outcomes reported do not match the scope.
Clendenin et al (2015)	31 healthy adults (≥18 years)	SEM Scanner	None	Inter-operator and inter-device agreement and reliability		Company included EAC excluded

USA						The study population does not match the scope (healthy volunteers).
Peko Cohen et al (2019) Israel	3D phantoms of human skull	SEM Scanner	None	SEM readings		Company included EAC excluded The study population does not match the scope (lab study)

Table 16 Methodological quality of observational studies

Study	Raizman (2018)	Gefen (2018)	O'Brien (2018)	Okonkwo (2017)	Okonkwo (2018)	Hancock & Lawrance (2019)	O'Keefe & McLuskey (2019)

Is the study based on a representative sample selected from a relevant population?	Yes	Yes	Yes	Yes	Yes	Unknown	Yes
Are criteria for inclusion explicit?	Yes	Yes	Yes	Yes	Yes	Unknown	No
Did all individuals enter the study at a similar point in their disease progression?	No	No	Yes	Yes	No	Unknown	Yes
Was follow up long enough for important events to occur?	Unknown	Yes	Yes	Unknown	Unknown	Unknown	Unknown
Were outcomes assessed using	Yes	Yes	Yes	Yes	Yes	Unknown	Unknown

objective criteria or was blinding used?							
If comparisons of sub-series are being made, was there sufficient description of the series and the distribution of prognostic factors?	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Include or attach any competed validated checklists in this section.

Appendix C – Adverse events

See also section 6. The MHRA Urgent Field Safety Notice is attached to this report.

MHRA - Urgent Field Safety Notice -

Appendix D – Ongoing studies

Table 17 Summary of all relevant ongoing or unpublished studies (from company submission)

Data source	Author, year (expected completion) and location	Study design	Patient population, setting, and withdrawals/lost to follow up	Intervention	Comparator(s)	Outcomes
Unpublished study manuscript Due to be submitted to *Wounds UK* by end September	**Effect of repositioning on subepidermal moisture measurement variation in healthy volunteers** Phil A Evans, BN (Hons) Queen Alexandra Hospital, Portsmouth, UK. Due to be submitted to *Wounds UK* by end September.	UK pilot study was to collect preliminary evidence about the effect of repositioning on the results of point-of-care devices that use subepidermal moisture (SEM) as a proxy indicator of PU risk.	22 healthy individuals.	SEM Scanner.	No comparators.	SEM delta did not differ significantly between time points. High variation was observed immediately after repositioning but did not show statistically significant variation with respect to time after repositioning.

Unpublished study manuscript Abstract submitted and presented at *Wounds UK* 2018. Due to be submitted to *Wounds UK* by end September.	**The impact of skin protectant cream on variation in sub-epidermal moisture readings** Phil A Evans, BN (Hons) Queen Alexandra Hospital, Portsmouth, UK. Due to be submitted to *Wounds UK* by end September.	The studies were exploratory, unblinded, controlled, prospective, cohort investigations of SEM Scanner 200. Participants acted as their own controls. This study investigated the effect of barrier cream application verses non-application on scanner delta values on directly	22 healthy volunteers aged 18–65 were recruited from the staff and student population of the University of Southampton and Portsmouth Hospitals NHS trust.	SEM Scanner.	No comparators.	Barrier cream applied evenly across the scan site, according to manufacturer instruction, does not appear to affect the SEM delta. Partial coverage may affect SEM delta though this risk appears to reduce with time and regular skin cleaning.

		comparable sites (heels) and the effect of full versus partial barrier cream application on delta values on the sacrum.				
Registry. BBI is the data controller of the Registry. Dendrite is the data processor.	The registry is a hypothesis generator based on structured datasets. It's a tool for further research on current methods of care for pressure ulcers. The registry is developed to provide data to answer the following research questions: • What is the predictive capacity of risk assessment methods? Do the specificity and sensitivity levels of current risk assessment tools make it mathematically	Text	Text	Text	Text	Text

	impossible to achieve full prevention? • What evidence supports the 5-step approach in treating and preventing pressure ulcers? • What can SEM Scanner readings teach us about the efficacy of the care pathway? Can the SEM Scanner, in conjunction with the current Standard of Care, help in reducing pressure ulcers? In addition, the following will be investigated using data generated from the pool of patients: • Are the current visual scales adequate or do the risk brackets require adjustment? • Which components/categories of risk assessment are the					

	more relevant in determining if a PU will develop? • How do we best assess sensitivity? • (Waterloo ≥10; Norton ≤18; Braden <15. What is sensitivity and specificity of these ratings?) • What are the components in risk assessment tools that are the most important to analyse? Data from the registry will also be used to assess the viability of risk assessed in 6 hours from admission; the components and efficacy of skin inspection. Was it done? How often? Types of abnormality detected. Type and efficacy of mechanical support will also be assessed.					

Merseycare Community District Nursing Service Pilot Implementation of SEM Scanner.	2019, Merseyside district community setting. Nicky Ore, Head of Clinical Operations. Abstract submitted and presented at EPUAP, Lyon, France, 2019. Award Winner for Quality Improvement Programme, EPUAP 2019	Two Health Care Assistants (HCAs) trained on use of SEM Scanner. Selection of patients on the caseload selected. Patients scanned four to five days per week over a three-month period. Algorithm used for decision making.	Mersey Care Pressure Ulcer Reduction Programme. The overall aim of the project is to demonstrate/evidence prevention and reduction of pressure ulcer development. Two district nurse bases identified for 12-week pilot: Sefton and South Liverpool. Focus on palliative care patients. Palliative care patients account for ~40–55% of caseload. Patients can remain on caseload for	SEM Scanner.	Waterlow visual assessment.	• 17 patients total during evaluation period • 697 readings taken and 2,788 data points captured for analysis • 26.9% reduction in PU in palliative care patients during the evaluation • 82% staff indicated the SEM Scanner

			varying periods of time: 50% may be on caseload for >4years; the other 50% on caseload for ~ 4 to 8 months.			impacted their clinical decision that day • 94% staff indicated additional interventions taken

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

Assessment report overview

SEM Scanner 200 for pressure ulcer prevention

This assessment report overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the External Assessment Centre (EAC) report. It includes **brief** descriptions of the key features of the evidence base and the cost analysis, any additional analysis carried out, and additional information, uncertainties and key issues the Committee may wish to discuss. It should be read along with the company submission of evidence and with the EAC assessment report. The overview forms part of the information received by the Medical Technologies Advisory Committee when it develops its recommendations on the technology.

Key issues for consideration by the Committee are described in section 6, following the brief summaries of the clinical and cost evidence.

This report contains information that has been supplied in confidence and will be redacted before publication. This information is highlighted in [redacted]. This overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Comments from professional bodies
- Appendix C: Comments from patient organisations
- [Appendix D: Additional analyses carried out by External Assessment Centre] [delete if no appendix D]

1 The technology

SEM Scanner 200 (BBI Europe Ltd) is a portable, hand-held, skin tissue assessment device that detects increased risk of pressure ulcer (PU) development by identifying early, pressure-induced tissue damage at the heel and sacrum. Pressure induced injuries can develop into pressure ulcers and deep tissue injuries. Published evidence suggests that damage to underlying soft tissues can happen 3-10 days before tissue damage shows at the epidermis (Moore et al. 2017). Tissue inflammation is the first response to damage and causes increased dilation and permeability of surrounding blood vessels. This leads to leakage of plasma and fluid, creating a layer of moisture under the skin called sub-epidermal moisture (SEM). As damage increases, so does the level of SEM. SEM Scanner measures changes in SEM values and reports it as a "delta" value, an SEM delta value of ≥0.6 intends to give an early sign of tissue damage and its severity.

The company are developing a new version of the device, the Provizio^{TM} SEM Scanner, which integrates readings into the electronic patient record and includes a barcode reader. The company assert that unpublished research comparing the new version with the current version has been performed in tissue phantoms. The EAC anticipate evidence will be generalizable due to the similar mechanism of action.

2 Proposed use of the technology

2.1 Disease or condition

PUs are injuries to the skin and underlying tissue, primarily caused by prolonged pressure on an area of the skin which can reduce the skin's blood supply. PUs are categorised by severity; stage I refers to intact skin with non-blanchable redness of a localised area, stage II refers to partial thickness loss of dermis presenting as a shallow open ulcer, stage III refers to full thickness tissue loss, and stage IV refers to full thickness tissue loss with exposed bone, tendon or muscle. PUs may also be classified as unstageable where the base of the ulcer is covered by slough or eschar in the wound bed. A purple area of

localised discoloured skin or blood-filled blister can indicate a suspected deep tissue injury.

2.2 Patient group

The SEM Scanner is intended for use in people at increased risk of developing PUs. The NICE guideline on pressure ulcers: prevention and management posits a simple 'at risk' and 'at high risk' categorisation, which combines "clinical judgement and/or a validated risk assessment tool". People with mobility issues and/or ageing skin are vulnerable to PUs, particularly people aged 70 years and over and those with disabilities affecting their physical, mental or cognitive capacities.

An NHS Safety Thermometer report states that from April 2014 to the end of March 2015, around 25,000 patients developed a new PU within the NHS in England. The NHS Safety Thermometer reported the national proportion of people with a category 2-4 PU in the UK to be 5.0%.

2.3 Current management

NICE's guideline on pressure ulcers: prevention and management recommends that a documented assessment for PU risk is carried in all those receiving care. Validated risk assessment tools are recommended to support clinical judgment in assessing a person's risk of PU development. Examples of risk assessment tools used with the NHS include the Braden scale, Waterlow score and Norton risk – assessment scale. The Braden-Q scale is recommended for use in children. NICE QS89 recommends that a risk assessment be carried out within 6 hours of admission in patients treated in hospital or care homes with nursing. Reassessment is recommended if there is a change in clinical status. Clinical experts confirmed that there is no existing consensus on the optimal risk assessment scale to be used for PUs.

The use of measures to prevent PUs is dependent on risk of PU risk of development. NICE recommends those deemed at risk should be repositioned at least once every 6 hours, this should be increased to once every 4 hours in those deemed at high risk.

The NPUAP/EPUAP/PPPIA Global Clinical Practice 2014 Guidelines state standard care for the detection of a PU is the visual skin assessment (VSA). A stage I PU is reported when nonblanchable reddening of the skin is detected visually.

2.4 Proposed management with new technology

SEM Scanner is intended to be used on of the heels and sacrum of people who are “at risk” or “at high risk” of developing a PU, as defined by NICE CG179 criteria. SEM Scanner is to be used on admission, during the patient stay and at discharge. The frequency of use is not defined and should be based on the care setting, such as daily in acute care settings compared with every 3 days in community care settings. An unpublished study (Burns et al. unpublished) shows a positive SEM Scanner result (i.e. delta ≥0.6) informs the clinical decision to action a “high risk” clinical care pathway. This leads to more frequent repositioning of the person, heel offloading (if the at-risk location is the heel) and increased use of SEM Scanner from weekly to daily in the at-risk location.

3 Company claimed benefits and the decision problem

These are described in the scope here (link to Appendix E). The company proposed two variation from the decision problem. The company propose the population described in the decision problem be clarified to only include people at risk of developing PU or with existing PUs where the skin remains intact and exclude people with existing PUs grade II or above. The company also propose to clarify the incorporation of diagnostic outcomes in the decision problem for the use of sensitivity and specificity data and state that the SEM Scanner is not to be considered a diagnostic tool. The EAC considered both variations to be valid. The below table presents the text used in the original decision problem, the company variation and the EAC’s view.

Decision problem	Variation proposed by company	EAC view of the variation
Population – People at risk of developing PUs or with existing PUs	The SEM Scanner can only be used on intact skin. This excludes existing PUs grade II or above.	The EAC accept this variation as valid.
Outcomes – Diagnostic outcomes	The SEM Scanner is not a diagnostic tool and the company wish the diagnostic outcomes to be used only for sensitivity and specificity data.	The EAC accept this variation as valid.

4 The evidence

4.1 Summary of evidence of clinical benefit

The evidence included in the company's submission consisted of 12 studies. The submission included 7 full text publications including, 1 prospective before and after comparator study (Raizman et al., 2018), 5 prospective observational studies (Gefan et al., 2018; O'Brian et al., 2018; Smith et al., 2019; Moore et al., 2018; Clendenin et al., 2015) and 1 in vitro study (Peko Cohen et al., 2019). The remaining 5 studies were abstracts including a prospective before and after study (Hancock and Lawrance, 2018) and 4 observational studies (Okonkwo et al., 2017; Okonkwo et al., 2018; O'Keefe et al., 2019; Gershon et al., 2014), 4 abstracts were submitted with additional unpublished information. The EAC completed a literature search and included 7 studies submitted by the company and excluded 5, no additional evidence was included. The rational for the selection of these studies is in section 4.2 of the assessment report. The below table presents the studies included and excluded in the assessment report.

Study	Type of publication	Type of study	Comment
Studies included by both EAC and company	7 studies were included by both: 3 full texts, 4 abstracts (2 unpublished manuscripts were supplied for 3 of the abstracts)	2 before and after studies, 5 prospective single-arm observational	*Raizman et al (2018)*, *Gefen et al (2018)* *O'Brien et al (2018)* *Okonkwo et al (2017)* *Okonkwo et al (2018*, *Hancock & Lawrance (2019)* *O'Keefe & McLuskey (2019)*
Studies in submission excluded by EAC	5 studies not included by EAC: 4 published full texts and 1 conference abstract with unpublished manuscripts	4 prospective single-arm observational and 1 in vitro	Smith (2019) - outcomes do not match the scope and overlapping data with Hancock and Lawrance (2019) Moore et al (2018) – outcomes do not match the scope. Gershon et al (2014) – earlier version of Okonkwo et al (2018) Clendenin et al (2015) – healthy population does not match scope. Peko Cohen et al (2019) – in vitro population and outcomes do not match scope

The EAC considered the evidence of 2 before and after studies (Raizman et al. 2018 and Hancock and Lawrence, 2019) and 5 observational studies (O'Brian et al., 2018; Okonkwo et al., 2017; Okonkwo et al., 2018; O'Keefe et al., 2019; Gershon et al., 2014). All studies included relatively homogenous populations relevant to the decision problem. There is heterogeneity in the interpretation of the SEM Scanner delta which increases the risk of performance bias.

The 2 before and after studies make up the strongest evidence for SEM Scanner. Both studies report the impact of introducing SEM Scanner into the clinical pathway on the incidence of PUs. The EAC calculated odds ratios for both studies and found them to be statistically significant (OR 0.06, p=0.0005, in Raizman et al 2018; OR 0.43, p=0.0023, in Hancock & Lawrance 2019). Although the Hancock and Lawrance study is a large multi-centre study including UK sites, the data are only available in abstracts and due to the lack of methodological detail reported in the abstracts the EAC consider the odds ratio to be unreliable. Similarly, both studies compare the impact of standard of care with and without the addition of the SEM Scanner. Standard of care is poorly defined in both studies, although the study design of Raizman et al (2018) address the consistency of care. Comparability between the studies is limited as there is heterogeneity in the reporting of PU incidence, Hancock and Lawrance (2019) did not report stage I PUs, whereas Raizman et al. (2018) did. O'Keefe and McLuskey (2019) also compared PU incidence following the use of SEM Scanner with a historical control cohort, due to lack of methodological detail in the abstract the EAC have categorised this study as a single-arm observational study.

The single arm observational studies reporting the sensitivity and specificity data use VSA as a reference standard. Due to the limited sensitivity and specificity of VSA, the EAC acknowledge that using VSA as a reference standard adversely affects the SEM Scanner specificity as all SEM Scanner positive results that are not visible stage I PUs will be considered false positives. The EAC did not identify any studies with a more appropriate reference standard, however, the EAC calculated a more accurate sensitivity and specificity using data from the Okonkwo et al (2018) study. O'Brien et al. also reported the correlation of results between VSA and SEM Scanner. The EAC consider the diagnostic and correlational outcomes irrelevant to the decision problem as the IFU states the device is to be used in adjunct with VSA and is not intended for the diagnosis of PUs.

Three studies reported that SEM Scanner can detect pressure induced damage earlier than VSA, however, the EAC note that the studies do not state

how faster identification impacts patient care or patient outcomes such as, length of stay or morbidity.

Summarise ONLY the pivotal studies in a table:

Study and design	Participants/ population	Intervention & comparator	Outcome measures and follow up	Results	Withdrawals	Funding	Comments
Raizman et al (2018) Prospective before and after comparison study	284 patients; Control arm (n=89) recruited from stroke/medical unit (55% female and >60% incontinent), interventional arm (n=195) recruited from hospital units following emergency room admission (n=166) or from alternative care unit (n=29) (55% women, >90% incontinent)	Risk assessment (Braden) plus SEM Scanner score 3 - 5 times per week (n=195) vs risk assessment score 5 times per week admitted (n=89)	Incidence of PUs for up to a month or until discharge	PU incidence was 13.5% for the standard care phase and 1% for the SEM Scanner arm.	N/A	Partly company funded	The cohorts used in this study, despite being matched closely for demographics, were recruited from different hospital units. The authors comment that those recruited into the interventional cohort were at a higher risk of developing a PU. SEM Scanner was used in both arms of the study, clinicians in the control arm were not blinded to the SEM Scanner score which could bias their scores; however, they had not been trained in use of the device or interpretation of the SEM Scanner score.

							The lack of randomisation increases the risk of selection bias. The standard care protocol is not adequately described, it is unclear whether the referenced daily nursing checks are specific to study protocol. The study was conducted outside of the UK so may not be generalisable to the NHS.
Gefen & Gershon (2018) Prospective single-arm observational study	15 patients (66% female, mean age 74 years, 11 Caucasian, 4 black/African American); group 1 patients were at risk of developing PU (n=7), group 2 patients had existing sacral stage I PU (n=6), group 3 had sDTIs (n=6),	Daily SEM Scanner assessment vs daily VSA and daily ultrasound imaging in a post-acute care setting	The taken for detection of increased risk of PU development and agreement between SEM Scanner readings, VSA and ultrasound. Follow up was 7±4 days.	There was consistent agreement between SEM Scanner but not VSA in group 3. In group 1, 1 patient developed sDTI. This patient's SEM reading was abnormal from day 1, while VSA indicated sDTI on day 3 and US on day 4.	N/A	Company funded	The small single-arm nature of this study limits its value in addressing the decision problem. The study was conducted in the USA and may not be generalisable to NHS care. The use of ultrasound to assess risk of PU development is outside of scope and is not considered standard care, however, VSA is within scope and used in NHS care settings.

	group 4 patients were not at risk of PU (n=2)						
O'Brien et al (2018) Prospective single arm observational study	47 patients (61.5% female) at risk of developing a PU (Norton scale)	Daily SEM Scanner measures diagnostic capability using daily VSA scores as reference	Device sensitivity and specificity. Correlation between VSA and SEM Scanner scores and time to detection of pressure injury using SEM Scanner compared with VSA.	Over a 4-week period, SEM Scanner achieved a sensitivity of 100% and specificity of 83.33%. Mean detection of pressure injury using VSA was 5.5 days and 2.1 days with SEM Scanner. Correlation between VSA and SEM Scanner was moderate (r=0.47, p=0.001). SEM Scanner: 2.1 days VSA: 5.5 days	n/a	Company funded	The single-arm nature of this study limits its value in addressing the decision problem. However, the correlation between VSA score and comparison of days to PU detection relevant. The criteria used to define an abnormal SEM Scanner, 3 consecutive says of >0.5 scores, is more stringent than described in the IFU. Nurses were blinded to the SEM Scanner score and scores were not used to inform clinical decisions about care. The study was conducted outside of the UK but the risk assessment measures described are equivalent to those used in the NHS.

				Sens 100% Spec 83.3% r =0.47, p=0.001			
Okonkwo 2017 Prospective single – arm observational study	182 patients at medium to high risk of developing a PU (46.7% make, mean age 76 years, 66% Caucasian, 24.2% Asian, 4.4% black/African American) from acute hospital and care home settings in the USA and UK	Daily SEM Scanner measures diagnostic capability using daily VSA scores as reference	Device sensitivity and specificity and time to detect PU using SEM Scanner and VSA. Follow up time was 20 days.	Sensitivity achieved by SEM Scanner was 87.2% and specificity was 32.55%. True positives were detected on average 4.7 days (± 2.4 days) earlier using SEM Scanner than VSA scores.	n/a	Company funded	The single-arm nature of this study limits its value in addressing the decision problem. The study includes UK data and reports relevant outcome measures. Validated scales of risk assessment were used to ascertain risk of PU development. The use of VSA as a reference standard means the diagnostic outcomes cannot be compared between the two measures. Non-visible PUs with SEM Scanner results of >0.5 were therefore reported as false positives. The cut off value of >0.5 for two consecutive days was in keeping with the IFU for the heels but diverged from IFU for the sacrum.
Okonkwo 2018	175 patients. Two cohorts,	SEM Scanner	Device was used once at	The device achieved a	3 patients excluded	Company funded	All patients recruited to the affected cohort had positive

Prospective single-arm observational study	people with existing PUs (n=125, stage I and II with intact skin, 56% female, mean age 82.7-83.6 years) recruited from a care home and people without PUs (n=50, 50% female, mean age 66.8years, 39 Caucasian and 9 black/African American) recruited from a physician's office.	measures diagnostic capability using daily VSA scores as reference	baseline and sensitivity and specificity were calculated by the EAC	sensitivity of 86.51% and specificity of 88%. Significant variability was calculated due to presence of callouses (p=0.0002) and race (p=0.003). In the cohort without PUs SEM "delta" scores ranged from 2.3 -2.5 in the sacrum and 1.7-2.0 in the heel. Variance was < 0.6			VSAs, this study reports the agreement between VSA and SEM Scanner scores and not the clinical effectiveness of SEM Scanner. The use of the SEM Scanner in the study protocol deviates from the IFU. The gluteal readings were not taken for the sacral PUs. The authors use a within-subject change in SEM Scanner of ±0.5 to identify tissue damage, this differs from the cut-off recommended in the IFU. The cohorts were recruited from different care settings.
Hancock and Lawrence (2019) Prospective before and after comparison study with	1478 patients in PU reduction programme compared to 12,128 patients in historical	SEM Scanner as part of a PU reduction programme (PURP) vs standard of care	Overall hospital acquired PU incidence impact on clinical decision making	Incidence of HAPUs dropped from 2.17% (263/12,128) in the standard of care arm to 0.95% (14/1478) in the	n/a	Company funded	This is a large real-world evidence prospective comparator study. The study includes UK NHS sites. The study has been reported in two conference abstracts and a supplementary

historical control	control across acute care facilities and one hospice facility			PURP arm and risk of developing a PU reduced by 23% (95% CI: 8.2-64.7%, p=0.01). 79% of centres reported 0 HAPUs during the PURP period. Clinical decision-making was impacted in 52% of cases.			unpublished report provided by the company. Information differs between the sources, such as, inclusion criteria, number of subjects and none describe the protocol for standard of care used. The cut off delta value is described >0.6 in the abstracts but corrected to ≥0.6 in the supplementary report. The study reports stage II-IV PUs, this differs from previous studies that have included stage I PUs and makes it difficult to compare the results of the studies.
O'Keefe & McLuskey (2019) Prospective single-arm observational study	32 patients from a combined orthopaedic and plastic surgery ward. Patient were at risk of PU development		SEM Scanner findings and VSA findings. Incidence of HAPU following	72% (n=23) had a positive SEM Scanner reading and 53% (n=17) had a positive VSA. All patients with a positive SEM Scanner reading received	n/a	Company funded	The single-arm nature of this study limits its value in addressing the decision problem. The study is only available as an abstract via the company's website, despite being accepted to the Tissue Viability Society, 2019.

				interventions, including those that did not have a positive VSA (n=5). No patients developed a PU during the study period. Historical rate is reported to be 12.2%.			The study reports using ≥0.6 as the delta cut off consistent with IFU. The abstract is limited in detail and does not report demographic data. Additional out of scope anatomical locations were assessed using SEM Scanner including hips and ischial tuberosities. No additional detail regarding the historical rate of PUs is reported.
Abbreviations used: DTI, deep tissue injury; HAPU, hospital-acquired pressure ulcer; IFU, information for use; sDTI, serious deep tissue injury; PU, pressure ulcer; VSA, visual skin assessment							

4.2 Summary of economic evidence

The company submission identified 10 economic studies as being relevant to the decision problem. The EAC reviewed the economic evidence submitted by the company and found 1 unpublished manuscript to be relevant to the economic assessment of SEM Scanner. The EAC conducted a literature search and found no additional economic evidence. The unpublished manuscript (Burns et al. unpublished) included as economic evidence used a decision analytic model and cost-utility methodology to assess the cost effectiveness of SEM Scanner as an adjunct to standard care and found the technology to be cost-saving.

De novo analysis

The company presented an economic model comparing the use of SEM Scanner for assessing a person's risk of PU development as an adjunct to standard NHS clinical practice compared with the cost of standard NHS clinical practice as described in the NICE PU clinical guideline (CG 174, 2014), in patients "at risk" of developing a PU. Initial patient risk assessment and daily clinical judgement in the standard care arm are combined with SEM Scanner assessment in the intervention arm. The company use a decision tree based on the NICE clinical guideline for pressure ulcers: prevention and management over a 1-year time horizon. Patient heels and sacrum are assessed for risk and categorised as "low risk, "at risk" or "at high risk". Patients allocated to "at risk" or "at high risk" receive repositioning every 6 or 4 hours, respectively. The decision tree assesses the impact of SEM Scanner on the cost of preventing PUs. The model structure is shown in figure 1. A full list of clinical and cost parameters is included in the final assessment report tables 6 and 7, respectively.

The EAC noted the company submission used uncertain parameters from an unpublished before and after study to estimate the impact of SEM Scanner on stage II PU incidence through the risk assessment of developing a PU leading to appropriate prevention measures. The EAC built a new model using the

SEM Scanner diagnostic accuracy data and VSA diagnostic accuracy data to model the impact of a combined SEM Scanner and VSA test on the incidence of PUs and the costs associated with maintenance and treatment of PUs. The EAC applied an “OR” decision rule where a positive score on either SEM Scanner or VSA would indicate the positive diagnosis of a stage I PU.

The SEM Scanner has been not been notified for the diagnosis of PU and is intended to be used as a risk assessment tool to detect pressure related injury at the heels and sacrum, the use of SEM Scanner to diagnose PUs does not reflect the intended use of SEM Scanner in the clinical care pathway.

Figure 1 Current standard of care and SEM Scanner "positive"

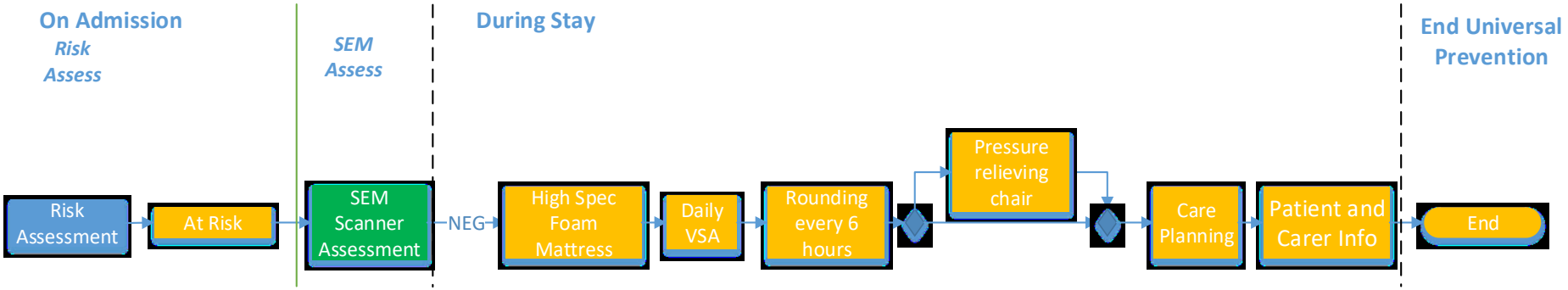


Figure 2 Current standard of care and SEM Scanner "negative"

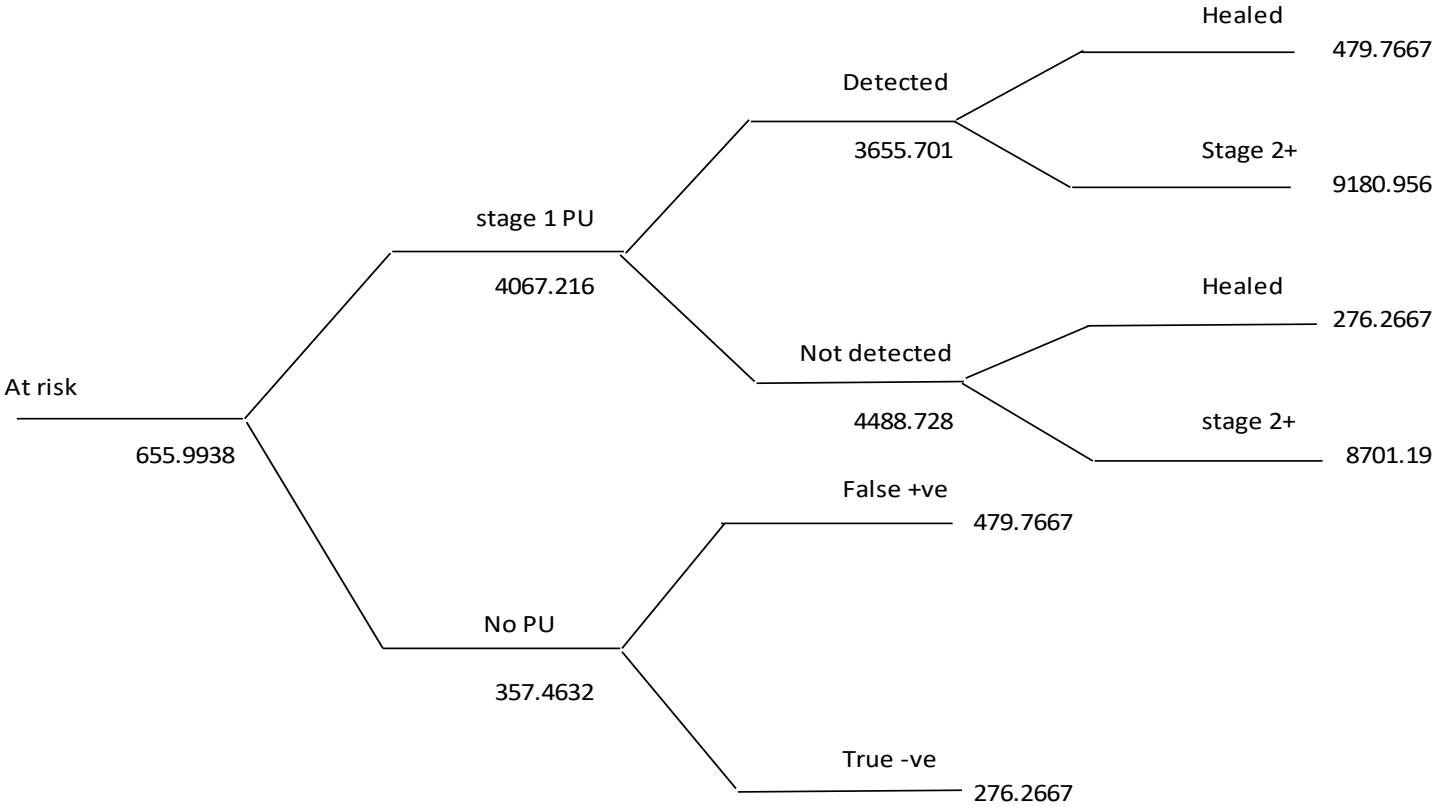


Figure 3 Decision tree built by the EAC with costs calculated for care including SEM Scanner

Model parameters

The main parameters included in the economic modelling were the incidence of pressure ulcers, the assumed impact of using SEM Scanner on PU incidence, the percentage of people classified as “at risk” and “at high risk”.

The company assume a PU incidence of 4.03% (Clark and Watts, 1994) at all stages and 4:09% in the “at risk” group based on the Hancock and Lawrance (2019) study. The EAC calculates an incidence of 8.05% in an at-risk population assuming a diagnostic odds ratio of 6.5 for initial assessment and incidence across all groups of 4.03%. The company assume a 68.9% reduction on the incidence of stage II+ PU in the SEM Scanner arm based on the unpublished Hancock and Lawrance 2019 before and after study. The EAC have considerable concern about the uncertainty of this assumption and built a new model using the combined diagnostic accuracy of SEM Scanner and VSA to estimate a reduction of 27% in the risk of progression to stage II PU following a stage I PU diagnosis. However, the SEM scanner is not intended to diagnose PUs.

Costs and resource use

The company submission states the cost of the SEM Scanner is £5,835 per device. The company estimates an additional cost of £60,962 in the SEM Scanner arm, this cost reflects the acquisition of 23 SEM devices (assuming 1 per 9 beds, based on 21 wards each with 10 beds) over a 3-year lifetime (£44,735 per annum), £2,637 for training costs and £13,590 for scanning costs. The EAC accept these costs but also apply a 3.5% amortisation rate resulting in an acquisition cost of £47,902.

The cost of nursing time were updated by the EAC. The company referenced the NICE costing statement for PUs published in 2014 and included a cost of £18 per hour for band 5 nurse time. The EAC believe this costing statement is outdated and recommend the recent estimate of £37 per hour which accounts for relevant overhead costs (Curtis & Burns 2018). This discrepancy has an impact on nursing time, training, SEM Scanner assessment and cost of repositioning. In addition to this, where the company have assumed 1 nurse

would be required for repositioning the EAC referenced the NICE clinical guideline for PU prevention and increased this figure to 2. The EAC also assumed an hour for the cost of a stage I assessment including nutrition after diagnosis and assumed an increase in the cost of treating a stage I PU based on 10 minutes of daily care by a band 5 nurse.

Treatment costs for PUs for all grades were estimated using the NHS improvement PU productivity calculator, the EAC confirms the validity of the tool. The company assumed 1.64% of at-risk patients would develop a stage II PU. However, the EAC estimated far higher treatment costs driven by an assumed prevalence of 8.05% of stage I PUs. The EAC assumed that 50% of wounds would progress into stage II or greater PUs without diagnosis and 36.5% with diagnosis and treatment. Table 7 in the assessment report presents a full list of cost parameters used in the company and EAC models.

Results

The company model concludes SEM Scanner is cost saving by £81 per patient. This cost saving is driven by an assumed reduction in PU incidence of 68%. The company model calculates the SEM scanner will result in an initial cost increase of £151,615 for the acquisition and use of the device plus increased preventative measures, these costs are offset by a saving of £496,172 in costs associated with PU treatment which results in a total cost saving of £405,502.

The EAC's model calculated the proportion of patients positively diagnosed with a stage I PU according to the prevalence of stage I PUs and the sensitivity of SEM Scanner in addition to VSA compared with VSA alone.The EAC's model found that SEM Scanner used in combination with VSA costs an additional £45 per patient compared with standard care alone. The EAC's model calculates the introduction of SEM Scanner to result in an additional cost of £283,483 associated with the prevention of PU in addition to £117,378 for cost of acquisition and associated utility costs. The EAC acknowledge that the revised model does not account for any potential clinical benefit in earlier identification and reversal of damage prior to stage I PU.

The company reported undertaking univariate sensitivity analyses of 15% on a selection of cost, utility and probability variables. Probabilistic sensitivity analyses using Monte Carlo simulations were performed. The EAC note the inclusion of some parameters into the probabilistic analysis and exclusion of others is unclear, better distributions could have been applied and the choice of standard deviation for parameters lacked justification. The results of the company's sensitivity analyses were not reported in detail; the company only stated that none had generated a cost increase for SEM Scanner. The probabilistic scenario analysis found that 89% of model simulations generated a cost saving of SEM Scanner.

The EAC undertook univariate and multivariate sensitivity analyses to explore the impact of uncertainty on the EAC's model. All parameters are assumed to be uncertain. A univariate analysis of all parameters in the model found SEM Scanner to be cost incurring in almost all cases. The model became cost-saving where PU incidence was >19% or where high-risk management and treatment of stage I PU following detection reduces risk of progression by 62%. SEM Scanner becomes cost-saving if specificity of the combined diagnostic test increases to 56%. Multivariate analyses identified that SEM Scanner was cost-saving when specificity of the combined test approached 50% and the relative risk of progression for a treated stage I PU approached 60%, the EAC tested this analysis with the inclusion of length of stay and found the cost-saving impact of an increased PU incidence was offset by an increased length of stay.

The use of SEM Scanner and VSA as a combined diagnostic test limits the specificity of the test. The EAC undertook a scenario analysis where the model uses the diagnostic accuracy of SEM Scanner alone to detect stage I PUs in place of VSA. This scenario suggests the SEM Scanner would be cost saving resulting in savings of £71 per patient. This scenario was robust to all parameters except for specificity; SEM Scanner became cost-incurring where specificity fell to 51%. The EAC acknowledge the IFU states the technology is not indicated for the diagnosis of stage I PUs and the clinical effectiveness of

using SEM Scanner as a replacement for VSA has not been explored in published literature.

5 Ongoing research

The company identified 2 unpublished manuscripts currently under development. Both manuscripts report single arm observational studies measuring the impact of preventative measures on changes in sub-epidermal moisture readings. No results have been published for the studies; the manuscripts are anticipated to be submitted for publication in September 2020. An NHS trust have presenting their results following the use of SEM Scanner in the Hancock and Lawrance (2019) PU reduction programme. The company also reference the use of a PU register to investigate the use of SEM Scanner in conjunction with the current standard of care, the usefulness of current risk assessment scales and the effectiveness of the current pathway.

6 Issues for consideration by the Committee

Clinical evidence

The evidence base is limited to before and after comparator studies and single arm observational studies. The strongest clinical evidence for SEM Scanner is from the before and after studies (Raizman et al, 2018; Hancock and Lawrance, 2019) that report the impact of SEM scanner on the incidence of PUs. There is limited detail where standard care has been described as a comparator and most studies do not adequately describe how the technology was incorporated into the care pathway or how the use of the device informed clinical decisions. There is uncertainty within the Hancock and Lawrance (2019) study about how much of the reduction in PU incidence is attributable to the use of SEM Scanner alone.

The single arm observational studies report the diagnostic accuracy of SEM scanner using VSA as a reference standard. The VSA is an assessment used for the diagnosis of PUs when damage becomes visible whereas the SEM

scanner is designed to detect increased risk of PU formation by measuring subepidermal moisture, the use of VSA as a reference standard means that all positive SEM scanner results where the skin is not visibly damaged would be classed as a false positive. Similarly, as the SEM Scanner has been designed to assess anatomies for risk of PU development the relevance of diagnostic outcome measures is questionable.

There are differences between the studies in the cut-off used to define a positive SEM Scanner result and the frequency of scanning, these variations increase risk of performance bias.

The impact of using validated scales to assess patient risk of PU followed by use of SEM scanner for anatomical risk of PU on the incidence of heel and sacrum PUs compared with using validated scales alone has not been assessed in a controlled trial. However, it would be considered unethical not to provide preventative measures for any patients at risk of PU.

Cost evidence

There is considerable disagreement between the parameters used, the model design and the findings of the company model and the EAC model. Both models are subject to considerable uncertainty and both model the use of SEM Scanner differently in the care pathway.

The company model shows SEM Scanner to result in a cost saving of £81 per patient, the model design and parameters used were based on data from Hancock and Lawrance (2019). The primary cost driver in the company model is the assumed 68% reduction in PUs following the introduction of SEM Scanner as a risk assessment tool that is intended to improve te prevention of PUs developing. This assumption is based on the unpublished Hancock and Lawrance (2019) study and is subject to considerable uncertainty, however, the real-world data are reflective of UK NHS practice.

The EAC built a model using the diagnostic accuracy data for SEM scanner and VSA, a combined sensitivity and specificity was used to estimate the number of stage I PUs detected, a positive result for either test was classed

as positive stage I PU diagnosis. The EAC model therefore presents SEM scanner as a diagnostic tool and the IFU clearly states the device should not be used to diagnose pressure ulcers limiting the relevance of this model to the clinical care pathway.

The EAC's model shows SEM Scanner to be cost incurring by £45 per patient. The primary cost driver in the EAC model is the specificity of SEM Scanner, a high number of false positives increases the cost of repositioning. The studies reporting sensitivity and specificity of the technology are acknowledged to be limited due to the use of VSA as a reference standard and the combined VSA and SEM Scanner diagnostic approach means the specificity can be no greater than either test alone.

7 Authors

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NICE Medical Technologies Evaluation Programme

February 2020

Appendix A: Sources of evidence considered in the preparation of the overview

A Details of assessment report:

- Erskine J, MacMillan T, et al. SEM Scanner 200 for pressure ulcer prevention, January 2020.

B Submissions from the following sponsors:

- Bruin Biometrics LLC

C Related NICE guidance

- Pressure Ulcers: prevention and management. NICE clinical guideline 174 (2014). Available from www.nice.org.uk/guidance/CG174

D References

Please see EAC assessment report for full list of references.

Appendix B: Comments from professional bodies

Expert advice was sought from experts who have been nominated or ratified by their Specialist Society, Royal College or Professional Body. The advice received is their individual opinion and does not represent the view of the society.

Mr Glenn Smith

Clinical Nurse Specialist for Nutrition and Tissue Viability, St Helen's Medical Centre

Ms. Trudie Young

Director of Education and Training, Welsh Wound Innovation Centre

Dr Yun Mei Lau

Education and Quality Improvement Fellow, Intensive Care Society

Prof. Michael Clark

Commercial Director, Welsh Wound Innovation Centre

Dr Fawad Hussain

Consultant Dermatologist and skin cancer lead, Barking, Havering and Redbridge University Hospital

Ms. Samantha Holloway

Reader/Programme Director, Cardiff University School of Medicine

Please see the clinical expert statements included in the pack for full details.

Appendix C: Comments from patient organisations

Advice and information was sought from patient and carer organisations.

The following patient organisations were contacted and no response was received.

- British Skin Foundation
- Leg Ulcer Charity
- Pressure Ulcers UK
- Leonard Cheshire Disability

Appendix D: Additional analyses carried out by the External Assessment Centre (delete section if none)

New economic evidence carried out after the External Assessment Report was initially submitted to NICE, considered relevant to fully address the issues in the scope.

Awaiting results – to be updated

Appendix E: decision problem from scope

Population	People at risk of developing pressure ulcers at the heel or sacrum, including people with existing pressure ulcers
Intervention	SEM Scanner 200 used as an adjunct to standard NHS clinical practice.
Comparator(s)	Standard NHS clinical practice for patients considered 'at risk' or 'at high risk' of pressure ulcers. This may involve a combination of: • Standard risk assessment using visual, tactile and biomarker tools. • Frequent repositioning (at least 6 hourly in people considered to be at risk and 4 hourly in people considered to be at high risk) • Pressure redistribution using devices such as high-specification foam mattress or pressure redistributing cushions.
Outcomes	The outcome measures to consider include: Intermediate/diagnostic outcomes • Diagnostic accuracy • Time to test result • Number of inconclusive results (including occasions where it is not possible to take 3 readings) • Impact on clinical management decisions Clinical effectiveness

	•Incidence of pressure ulcers at the heel and sacrum •Incidence of skin breakdown at the heel and sacrum •Stage of pressure ulcer developed (stage I – IV, unstageable) •Device related adverse events •Rate of infection •Quality of Life, and associated outcomes e.g. pain and discomfort; patient mobility; patient/carer satisfaction; patient depression and anxiety Systematic impact •Rate of complications avoided from pressure ulcer prevention e.g. Infection, abscess, septicaemia, bone infections, meningitis. •Length of hospital stay as a result of pressure ulcers, including ICU and conventional ward bed days. •Costs of treating pressure ulcers and their complications e.g. nursing, hospital, surgical and treatment costs Additional outcomes to those relevant to the benefits claimed by the company: •Patient compliance with and the use of pressure ulcer prevention strategies •Ease of use of product, including training requirements
Cost analysis	Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.
Subgroups to be considered	People at high risk of developing pressure ulcers such as those with mobility issues, those with comorbidities affecting cognition and communication, people with spinal injury, those in residential homes and those with darker skin.
Special considerations, including those related to equality	People with restricted mobility are at an increased risk of developing pressure ulcers and would likely benefit from this device. Category 1 pressure ulcers are identified by visual assessment of a non-blanching area of redness. In people with darker skin tones, it may not be possible to identify pressure ulcers by visual assessment. SEM Scanner assesses moisture levels and avoids subjective tests of skin colouration so may allow for earlier detection of tissue damage in people with dark skin tones.

Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic?	No
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No
	Is there anything specific that needs to be done now to ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance?	No
Any other special considerations	Not applicable	

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance scope

SEM Scanner 200 for pressure ulcer prevention

1 Technology

1.1 Description of the technology

SEM Scanner 200 (BBI Europe Ltd) is a portable, hand-held, skin tissue assessment device that detects increased risk of pressure ulcer development by identifying early, pressure-induced tissue damage at the heel and sacrum. This includes pressure ulcers and deep tissue injuries. Published evidence suggests that damage to underlying soft tissues can happen 3-10 days before tissue damage shows at the epidermis (Moore et al. 2017). Tissue inflammation is the first response to damage and causes increased dilation and permeability of surrounding blood vessels. This leads to leakage of plasma and fluid, creating a layer of moisture under the skin called sub-epidermal moisture (SEM). As damage increases, so does the level of SEM. SEM Scanner measures SEM and intends to give an early sign of tissue damage and its severity.

The technology consists of a single electrode sensor and an integrated pressure sensor. The SEM Scanner 200 assesses biocapacitance, a measure of the fluid content in the skin tissue using electrical capacitance, and displays a correlating SEM value between 0.3 and 3.9. To assess an area the SEM scanner 200 should be held against the tissue until an SEM value is reported, the pressure sensor guides the clinician to ensure the appropriate pressure is applied for an accurate reading. A minimum of 3 SEM measures are needed before the SEM scanner can report the SEM ‘delta’, the calculated difference between the minimum and maximum SEM values in the set of readings taken, of any given anatomical location. A delta value of greater than or equal to 0.6 suggest the anatomical site being assessed is at an increased risk of

developing a pressure ulcer. The results, as well as device status, are displayed on the device screen.

1.2 Relevant diseases and conditions

The SEM Scanner 200 is intended for use in the people at increased risk of developing pressure ulcers.

Pressure ulcers are injuries to the skin and underlying tissue, primarily caused by prolonged pressure on an area of the skin which is capable of impairing the skin's blood supply.

People with mobility issues and/or ageing skin are vulnerable to pressure ulcers, particularly people aged 70 years and over, those with disabilities affecting their physical, mental or cognitive capacities.

An NHS Safety Thermometer report states that from April 2014 to the end of March 2015, just under 25,000 patients developed a new pressure ulcer within the NHS in England. It is estimated that just under half a million people in the UK will develop at least one pressure ulcer in any given year. The NHS Stop the Pressure campaign (Midlands and East) launched in 2012 found measures to avoid the development of pressure ulcers resulted in a 50% reduction in pressure ulcer incidents in the first year. The national proportion of patients with a category 2-4 pressure ulcer in the UK in August 2012 was 6.0% and fell to 4.3% in August 2015. In July 2019 this proportion was reported to be 5.0%.

The NICE guideline on pressure ulcers: prevention and management notes that adults considered to be 'at high risk' of developing pressure ulcers will usually have multiple risk factors (such as significantly limited mobility, nutritional deficiency, inability to reposition themselves, and significant cognitive impairment) identified during risk assessment with or without a validated scale. Also considered to be at high risk are patients who have a history of pressure ulcers or those who already have a pressure ulcer.

1.3 Current management

NICE's guideline on pressure ulcers: prevention and management recommends that a documented assessment for pressure ulcer risk is carried out in adults, neonates, infants, children, and young people being admitted to secondary care, or care homes (adults), or tertiary care (neonates, infants, children, and young people), in which NHS care is provided; or receiving NHS care in other settings (such as primary and community care and emergency departments), if they have a risk factor. It recommends using a validated scale to support clinical judgement in those identified 'at risk' of developing pressure ulcers, and that risk is reassessed if the patient's clinical status changes. The guideline further defines a 'high risk' group for developing a pressure ulcer as those who usually have multiple risk factors such as significantly limited mobility and nutritional deficiency.

The guideline recommends strategies to prevent pressure ulcers, including regular patient repositioning, foam mattresses and pressure redistribution cushions. It also recommends the use of barrier creams to prevent damaged skin in people at high risk of developing moisture lesion or incontinence-associated dermatitis.

1.4 Regulatory status

The SEM Scanner 200 received a CE mark in November 2014 as a class IIb medical device for pressure ulcer prevention at the heel and sacrum only.

1.5 Claimed benefits

The following benefits to patients are claimed by the company as a result of a reduction in pressure ulcer incidence:

- Patient empowerment and engagement in care process
- Enabling rapid recovery and discharge
- Promoting functional recovery and mobility
- Increased ability to return to daily activities
- Maintenance of personal independence
- Reduced risk of social isolation

- Help to prevent patient distress
- Support prevention of patient pain
- Reduced risk of wound infection

The benefits to the healthcare system claimed by the company are:

- Consistent approach to risk assessment
- Objective and anatomically specific pressure ulcer data collection
- Reduced costs associated with medical and surgical interventions for treating pressure ulcers
- Reduced nursing and hospitalisation costs associated with the treatment of pressure ulcers

2 Decision problem

Population	People at risk of developing pressure ulcers at the heel or sacrum, including people with existing pressure ulcers
Intervention	SEM Scanner 200 used as an adjunct to standard NHS clinical practice.
Comparator(s)	Standard NHS clinical practice for patients considered 'at risk' or 'at high risk' of pressure ulcers. This may involve a combination of: • Standard risk assessment using visual, tactile and biomarker tools. • Frequent repositioning (at least 6 hourly in people considered to be at risk and 4 hourly in people considered to be at high risk) • Pressure redistribution using devices such as high-specification foam mattress or pressure redistributing cushions.
Outcomes	The outcome measures to consider include: Intermediate/diagnostic outcomes • Diagnostic accuracy • Time to test result • Number of inconclusive results (including occasions where it is not possible to take 3 readings) • Impact on clinical management decisions Clinical effectiveness

	•Incidence of pressure ulcers at the heel and sacrum •Incidence of skin breakdown at the heel and sacrum •Stage of pressure ulcer developed (stage I – IV, unstageable) •Device related adverse events •Rate of infection •Quality of Life, and associated outcomes e.g. pain and discomfort; patient mobility; patient/carer satisfaction; patient depression and anxiety Systematic impact •Rate of complications avoided from pressure ulcer prevention e.g. Infection, abscess, septicaemia, bone infections, meningitis. •Length of hospital stay as a result of pressure ulcers, including ICU and conventional ward bed days. •Costs of treating pressure ulcers and their complications e.g. nursing, hospital, surgical and treatment costs Additional outcomes to those relevant to the benefits claimed by the company: •Patient compliance with and the use of pressure ulcer prevention strategies •Ease of use of product, including training requirements
Cost analysis	Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.
Subgroups to be considered	People at high risk of developing pressure ulcers such as those with mobility issues, those with comorbidities affecting cognition and communication, people with spinal injury, those in residential homes and those with darker skin.
Special considerations, including those related to equality	People with restricted mobility are at an increased risk of developing pressure ulcers and would likely benefit from this device. Category 1 pressure ulcers are identified by visual assessment of a non-blanching area of redness. In people with darker skin tones, it may not be possible to identify pressure ulcers by visual assessment. SEM Scanner assesses moisture levels and avoids subjective tests of skin colouration so may allow for earlier detection of tissue damage in people with dark skin tones.

Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic?	No
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No
	Is there anything specific that needs to be done now to ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance?	No
Any other special considerations	Not applicable	

3 Related NICE guidance

Published

- The Debrisoft monofilament debridement pad for use in acute and chronic wounds. NICE medical technology guidance MTG17(2019). Available from www.nice.org.uk/guidance/MTG17
- Mepilex Border Heel and Sacrum dressings for preventing pressure ulcers. NICE medical technology guidance MTG40(2019). Available from www.nice.org.uk/guidance/MTG40
- Parafricta Bootees and Undergarments to reduce skin breakdown in people with or at risk of pressure ulcers. NICE medical technology guidance MTG20(2014). Available from www.nice.org.uk/guidance/MTG20
- Pressure Ulcers: prevention and management. NICE clinical guideline CG179(2014). Available from www.nice.org.uk/guidance/CG179.

In development

Not applicable

4 External organisations

4.1 Professional

The following organisations have been asked to comment on the draft scope:

- British Association of Dermatologists
- British Dermatological Nursing Group
- British Geriatric Society
- British Society for Dermatological Surgery
- Intensive Care Society
- Primary Care Dermatology Society (PCDS)
- Royal College of Nursing
- Royal College of Physicians
- Society of Chiropodists & Podiatrists (Feet for Life)
- Welsh Wound Network
- Wound Care Alliance UK

4.2 Patient

NICE's Public Involvement Programme contacted the following organisations for patient commentary and asked them to comment on the draft scope:

- British Skin Foundation (BSF)
- Leg Ulcer Charity
- Leonard Cheshire disability
- Pressure Ulcers UK

NICE National Institute for Health and Care Excellence

Adoption report: MTG533 SEM Scanner 200 for pressure ulcer prevention

Summary – for first meeting

Adoption levers

- Useful for people with darker skin tones.
- Patients' sleep less disturbed – it is reported to give night staff confidence that they don't need to reposition patients who are identified as not at risk.
- Gives an objective measure.

Adoption barriers

- Results need to be reconciled with electronic records which may take time and effort to set up. Necessary to revert to paper/end of bed recording in interim which is reported to be frustrating.
- Can take time to work out who to scan and how frequently.
- Variation in clinical acceptance
- Only evaluates two pressure ulcer risk areas.

1 Introduction

The adoption team has collated information from 4 tissue viability nurses (TVN) working within NHS organisations. Two of these work in acute settings (1 is a current user) and 2 work in the community (1 has experience of SEM scanner 200 and the other was aware of it).

This adoption report includes some of the adoption considerations for the routine NHS use of the technology.

2 Current practice in clinical area

All contributors use a risk assessment tool to evaluate patients and identify those at high risk of pressure ulcers. All reinforced the importance of

clinical judgement to supplement this and reported the purpose of identifying risk was to initiate preventative pressure ulcer care.

Contributors reported aiming to follow NICE guidance and doing risk assessment on every inpatient within 6 hours of admission and repeating weekly unless there is a change in condition. Those in an acute setting reported daily monitoring of skin.

Risk assessment tools in use were Braden (n=1), Waterlow (n=2) and Walsall (n=1).

District nursing teams carry out risk assessment and holistic assessment of skin on the first visit to all non-ambulatory patients in the community. They also apply clinical judgement (and in one case a nutrition screening tool) to identify patients at risk of pressure ulcers. The community user said the health care assistant (HCA) usually does the SEM scan and any high risk patients are reported on to community TVNs for further assessment.

3 Reported benefits

Contributors reported the following potential benefits of adopting SEM Scanner:

- Reduction in pressure ulcers (one site reported zero ulcers in 3 months vs. 1-2 per month prior to SEM Scanner, however one contributor reported no reduction in 4-5 months use)
- Earlier identification of skin breakdown (when compared with risk assessment and clinical judgement).
- Additional information to add to risk assessment and clinical judgement
- Useful for people with darker skin tones.
- Patients' sleep less disturbed – it gave night staff confidence that they didn't need to regularly reposition patients who were identified as not at risk.
- Gives an objective measure.

4 Insights from the NHS

Care pathway

SEM Scanner fits into the current care pathway for prevention of pressure ulcers in both acute and community setting as an additional task. It was reported that both nurses and HCAs carried out the scans.

The acute user recommended one scanner per ward (and spreading the task across am and pm shifts) but felt in larger wards with more than 30 beds that 2 scanners would be optimal.

Patient selection

One user in the acute setting said it can take time to work out who to scan and how frequently.

Clinician confidence/acceptance

There was variation in clinician confidence of SEM Scanner. While one user reported high levels of clinician confidence due to locally demonstrated benefits, another reported poor acceptance. It was reported that the TVN team should always be consulted in the purchasing decision for SEM Scanner as failure to do so can result in poor uptake of the technology. One contributor felt there was a lack of high-quality evidence and a lack of utility in that it can only be used to assess the heel and sacrum.

It was suggested that poor acceptance may occur where nurses believe preventative measures are already in place, however the objective measure of SEM before any signs of redness was thought to be a lever to adoption.

Three of the contributors (1 user and 2 non-users) felt there was a wider appetite for it and felt it had good potential.

Procurement and Commissioning

The cost of SEM Scanner may be a barrier to its adoption. Even if wider system savings are seen, local budget holders may be reluctant to invest.

One user had an initial business case refused. However, after securing charity funding to purchase and undertaking local pilot work demonstrating benefits, this site has gone on to successfully purchase more scanners and are about to bid for more to cover more clinical areas.

Training

Training is delivered free by a company nurse advisor using a “train the trainer approach”. The company report the implementation process takes approximately 4 weeks and includes a short meeting and clinical training with ward managers and key trainers (away from bedside) followed by bedside scanning led by company clinical specialists who are on site daily in the first week and then on request. Competency certificates are supplied.

Training was reported by users to be straight forward and the scanner was reported as easy to use.

Patient experience

One contributor reported that patients were engaged and interested in SEM scanner with some asking about their scan results.

Maintenance/quality control

SEM scanner is reportedly easy to clean and disinfection wipes were deemed compatible by infection prevention in 1 site. It was reported as needing minimal maintenance and the company provided good support. The current scanner is not serviceable. The company reports any faulty scanner failures will be replaced within 24 hours and that the next generation scanner is being developed that will be serviceable. After the 3-year warranty expires the company will replace the battery once free of charge. The cost of replacement batteries after this is not clear.

5 Comparators

No other comparators were reported by contributors that measure SEM.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technologies guidance

MT455 SEM Scanner

Company evidence submission

Part 1: Decision problem and clinical evidence

Company name	Bruin Biometrics (Europe) Ltd.
Submission date	02 October 2019
Regulatory documents attached	Please list regulatory documents submitted (CE certificate, Link provided to instructions for use.)
Contains confidential information	Yes

Contents

1 Decision problem

	Scope issued by NICE	Variation from scope (if applicable)	Rationale for variation
Population	People at risk of developing pressure ulcers or with existing pressure ulcers.	As discussed, the SEM Scanner can only be used on intact skin in adults.	As discussed this is the basis of our regulatory labelling and approved claims
Intervention	SEM Scanner used as an adjunct to standard NHS clinical practice.	Enter text.	Enter text.
Comparator(s)	Standard NHS clinical practice for patients considered 'at risk' or 'at high risk' of pressure ulcers. This may involve a combination of: • Standard risk assessment using visual, tactile and biomarker tools • Frequent repositioning (at least 6 times hourly in people considered to be at risk and 4 times hourly in people considered to be at high risk) • Pressure redistribution using devices such as high-specification foam mattress or pressure redistributing cushions	Enter text.	Enter text.
Outcomes	The outcome measures to consider include: Intermediate/diagnostic outcomes • **Diagnostic accuracy** • Time to test result • Number of inconclusive results (including occasions where it is not possible to take 3 readings) • Impact on clinical management decisions Clinical effectiveness • Incidence of pressure ulcers • Incidence of skin breakdown at the heel and sacrum • Stage of pressure ulcer developed (stage I – IV, unstageable)	As discussed this refers to sensitivity and specificity	Enter text.

	• Device related adverse events • Rate of infection • Quality of life, and associated outcomes e.g. pain and discomfort, patient mobility, patient/carer satisfaction, patient depression and anxiety Systematic impact • Rate of complications avoided from pressure ulcer prevention e.g. infection, abscess, septicaemia, bone infections, meningitis • Length of hospital stay as a result of pressure ulcers, including ICU and conventional ward bed days • Costs of treating pressure ulcers and their complications e.g. nursing, hospital, surgical and treatment costs Additional outcomes to those relevant to the benefits claimed by the company: • Patient compliance with and the use of pressure ulcer prevention strategies • Ease of use of product, including training requirements		
Cost analysis	Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be long enough to reflect differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and a combination of devices are needed.	Enter text.	Enter text.
Subgroups to be considered	People at high risk of developing pressure ulcers such as those with mobility issues, those with comorbidities affecting cognition and communication, people with spinal injury, those in residential homes and those with darker skin.	Enter text.	Enter text.
Special considerations, including issues related to equality	People with restricted mobility are at an increased risk of developing pressure ulcers and would likely benefit from this device. Category 1 pressure ulcers are identified by visual assessment of a non-blanching area of	Enter text.	Enter text.

	redness. In people with darker skin tones, it may not be possible to identify pressure ulcers by visual assessment. The SEM Scanner assesses moisture levels and avoids subjective tests of skin colouration so may allow for earlier detection of tissue damage in people with dark skin tones.		

2 The technology

Give the brand name, approved name and details of any different versions of the same device (including future versions in development and due to launch). Please also provide links to (or send copies of) the instructions for use for each version of the device.

Brand name	Bruin Biometrics (Europe) Ltd., abbreviated to "BBI"
Approved name	SEM Scanner
CE mark class and date of authorisation	Class IIa; medical device 11/Nov/2013

Version(s)	Launched	Features
200	2014	The SEM Scanner system includes the SEM Scanner 200 unit, the charging mat, and the charging mat AC power adapter. The SEM Scanner is a wireless, hand-held portable device measuring 2.8" (7.1 cm) wide and 6.4" (16.3 cm) in length, weighing 0.6 lbs. (0.3 kg), and contains an integrated circular coaxial sensor. The integrated software runs a user interface device screen that displays the device status, battery status, and readings. The device does not collect or display any identifiable or protected health information. A single (action) button is used to turn the device on, reset it, and turn the device off. The SEM Scanner assesses changes in tissue Biocapacitance and expresses the result in a unit-less SEM Value that ranges from 0.3 to 3.9. SEM Value is unitless (not an International System of Units measurement). The SEM Scanner is indicated to be used as an adjunct to the current standard of care (SOC), which includes Risk Assessment Tools (RATs) and visual skin assessment as detailed in NICE CG 179.

		The SEM Scanner is approved for use on the heels and the sacrum of adults, and is designed to be used on intact skin (accounting for >50% of all PUs). Instructions for use: https://sem-scanner.com/product/faqs/
[redacted]	[redacted]	[redacted]

		[redacted]

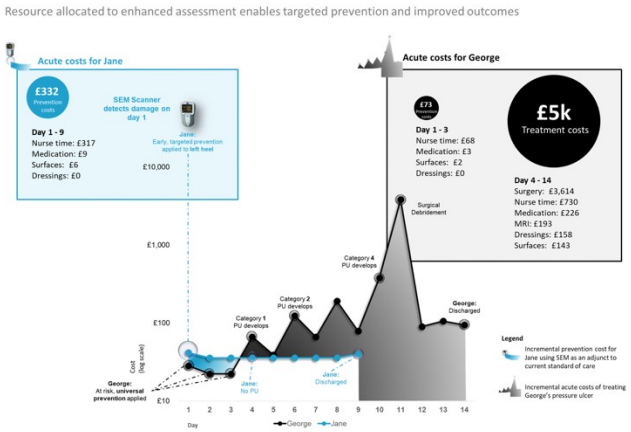
What are the claimed benefits of using the technology for patients and the NHS?

Claimed benefit	Supporting evidence	Rationale
Patient benefits		
Objectivity: The SEM Scanner can be used as an adjunctive device by providing objective data in the identification of increased risk of pressure ulcers. **Earlier anatomically specific data**: Current risk scales assess total body risk. Skin assessments suffer from not being able to confirm a PU diagnosis until the PU manifests. Both limitations of the current standard of care can be understood as a, "latency problem". Latency of detection and latency of knowing which antinomy. The SEM Scanner identifies increased risk of pressure ulcers days earlier than the current	Padula WV, Mishra MK, Makic MB et al. (2011) Improving the quality of pressure ulcer care with prevention: A cost-effectiveness analysis. Med Care 49(4):385–92 Raizman R, MacNeil M and Rappl L (2018) Utility of a sensor-based technology to assist in the prevention of pressure ulcers: A clinical comparison. Int Wound J 15(3):1033–44 O'Brien G, Moore Z, Patton D, et al. (2018) The relationship between nurse's assessment of early pressure ulcer damage and sub epidermal moisture measurement: A prospective explorative study. J Tissue Viability 27(4):232–7 Gefen A. (2018) The Sub-Epidermal Moisture Scanner: The principles of pressure injury prevention using novel early detection technology. Wounds International 9(3):30–5 Smith G (2019) Improved clinical outcomes in pressure ulcer prevention using the SEM scanner. J Wound Care 28(5):278–82 Okonkwo H, Milne J and Bryant R (2018) Evaluation of a novel device using capacitance of the detection of early pressure ulcers (PU), a multi-site longitudinal study [abstract]. In: Proceedings of the National Pressure Ulcer Advisory Panel (NPUAP) meeting, 2nd–3rd March 2018, Las Vegas, Nevada, USA (Manuscript in review process with Wound Repair and Regeneration. Manuscript ID WRR-18-06-0175.R1, entitled "A Blinded Clinical Study of SEM Scanner 200, a Capacitance Measurement Device, for Early Detection of Pressure Injury) Ross G and Gefen A (2019) Assessment of sub-epidermal moisture by direct measurement of tissue Biocapacitance. Medical Engineering and Physics: doi: 10.1016/j.medengphy.2019.07.011 Peko Cohen L and Gefen A (2019) Phantom testing of the sensitivity and precision of a sub-epidermal moisture scanner. Int Wound J 16(4):979–88 Oomens CWJ, Bader DL, Loerakker S et al. (2015) Pressure induced deep tissue injury explained. Annals of Biomedical Engineering 43(2):297–305	The key benefits to the patient are related to the prevention of pressure ulcers and thereby the avoidance of the challenges and complications caused by pressure ulceration. These include: • Reduction in incidence of hospital acquired pressure ulcers • Prevention means keeping the skin intact and therefore reducing recovery times and infection risks • Patient empowerment and engagement in care process • Enabling rapid recovery and discharge • Promoting functional recovery and mobility • Increased ability to return to daily activities • Maintenance of personal independence • Reduced risk of social isolation • Help to prevent patient distress

standard of care – in our most recent multi-centre clinical trial this was a median of 5 days earlier. **Earlier transition from universal to targeted interventions**: Using the SEM Scanner readings enables anatomically specific interventions as opposed to whole body interventions. **Better Outcomes**: When the SEM Scanner readings are acted upon the evidence from real-world usage show a substantial reduction of PU incidence especially stage III & IV pressure ulcers.		• Support prevention of patient pain • Reduced risk of wound infection
System benefits		
Released bed days	NICE. Costing statement: Pressure ulcers. Implementing the NICE guideline on pressure ulcers (CG179) [online; accessed 1 October 2019]	Prevention of pressure ulcers results in a reduction in excess bed day payments to hospitals where

	Burns M, King T, Tsang K et al. (2019) Modernising the pressure ulcer prevention care pathway: a cost-effectiveness analysis. Journal of Wound Care: in review (manuscript number jowc.2019.0193)	patients' length of stay exceeds the Healthcare Resource Group trim point. Patients with pressure ulcers stay in hospital an average of 5–8 days longer than other patients. Releasing bed days makes it possible to treat more patients within the same overall capacity, improving the efficiency of the organisation.
Reduced direct labour costs	NICE. Costing statement: Pressure ulcers. Implementing the NICE guideline on pressure ulcers (CG179) [online; accessed 1 October 2019] Burns M, King T, Tsang K et al. (2019) Modernising the pressure ulcer prevention care pathway: a cost-effectiveness analysis. Journal of Wound Care: in review (manuscript number jowc.2019.0193)	This device is a cost saving device. Current average costs of PU care by Grade in the NHS are: • £1,214 for PU Category I • £5,241 for Category II • £9,041 for Category III • £14,108 for Category IV (Bennett, et al., 2004; Dealey, et al., 2012; NICE costing statement, 2014). Costs of care increase significantly once the skin becomes broken. Nurse and healthcare assistant time accounts for 90% of the overall costs for treating pressure ulcers and 96% of the

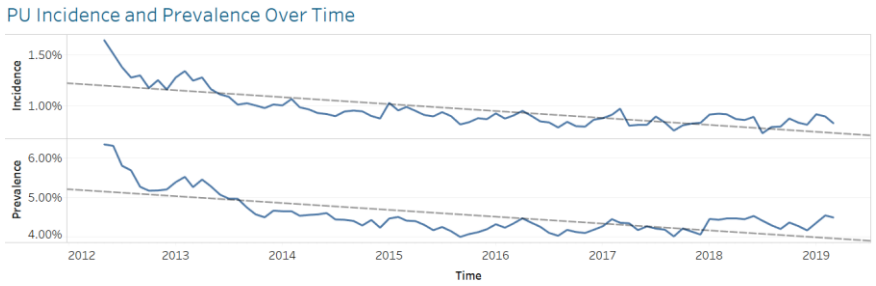
		cost in category I and II PUs. A proportion of this time is spent repositioning bed ridden patients or undertaking wound care treatments. Reducing the incidence of pressure ulcers in hospitals will release nursing time, enabling quality care time to be spent on other activities. The labour expense of treating Grade II-IV HAPUs is variable cost and can therefore be reduced in year.
Cost benefits		
Reduced material costs for the treatment of pressure ulcers	NICE. Costing statement: Pressure ulcers. Implementing the NICE guideline on pressure ulcers (CG179) [online; accessed 1 October 2019] Burns M, King T, Tsang K et al. (2019) Modernising the pressure ulcer prevention care pathway: a cost-effectiveness analysis. Journal of Wound Care: in review (manuscript number jowc.2019.0193)	By reducing the incidence of pressure ulcers, direct savings can be made from: • Reduction in the use of wound dressings; antibiotics; analgesic medication. These are largely variable costs • Reduced requirement for specialised assets for managing pressure ulcers such as foam mattresses

Reduced overall costs of care	NICE. Costing statement: Pressure ulcers. Implementing the NICE guideline on pressure ulcers (CG179) [online; accessed 1 October 2019] Burns M, King T, Tsang K et al. (2019) Modernising the pressure ulcer prevention care pathway: a cost-effectiveness analysis. Journal of Wound Care: in review (manuscript number jowc.2019.0193) Burns M (2019) Modelling Pressure Ulcer Prevention and Treatment Pathways: Costs and Savings [abstract]. In: Proceedings of the 21st Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, 18th–20th September 2019, Lyon, France Image Below Reflects A Visual Description of Analysis of 2 Alike Patients (Burns M. 2019) 	Implementing the SEM Scanner into the PU prevention care pathway using NICE CG 179 has been modelled via activity based and business impact modelling with and without the SEM Scanner. Analysis of 2 alike patients – whereby patient 1 develops Category 4 PU and patient 2 does not. Acute Care example. See Image to left. Patient 1 total cost £5k; Patient 2 total cost £332 • Cost of treatment far outweighs cost of prevention • Use of new technology as an adjunct to SOC is more effective and less costly than current SOC • Particular attention is drawn to variable costs in this analysis. These are clearly deliniated and are manageable in-year.
Sustainability benefits		

Reduced use of disposable materials for the management of pressure ulcers	NICE. Costing statement: Pressure ulcers. Implementing the NICE guideline on pressure ulcers (CG179) [online; accessed 1 October 2019] Burns M, King T, Tsang K et al. (2019) Modernising the pressure ulcer prevention care pathway: a cost-effectiveness analysis. Journal of Wound Care: in review (manuscript number jowc.2019.0193) Burns M (2019) Modelling Pressure Ulcer Prevention and Treatment Pathways: Costs and Savings [abstract]. In: Proceedings of the 21st Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, 18th–20th September 2019, Lyon, France	The early identification of increased risk of pressure ulcers enables healthcare professionals to effectively manage pressure ulcers early in the patient care pathway. This has the scope to mitigate the incidence of pressure ulcers that require treatment with single agent materials such as wound dressings and barrier creams. This approach has the scope to reduce the turnover of specialist items such as foam mattresses.

Briefly describe the technology (no more than 1,000 words). Include details on how the technology works, any innovative features, and if the technology must be used alongside another treatment or technology.

Pressure Ulcers (PU) have been defined by the National Pressure Ulcer Advisory Panel (NPUAP) in conjunction with the European Pressure Ulcer Advisory Panel (EPUAP) as localised injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure, or pressure in combination with shear (EPUAP, 2014). Resulting inflammation and localised oedema can occur from 3 to 10 days before damage and/or breakdown of skin is visible at the surface (Paek et al., 2002). As the level of skin damage increases, so does the inflammatory response. Subsequently, localised tissue oedema or water in the skin and tissue, termed sub-epidermal moisture (SEM), increases (Bates-Jensen et al., 2007; Moore et al., 2017; Schubert and Fagrell, 1989). NHS Improvement reported that 1,700 - 2,000 patients per month develop a PU whilst treating PUs costs the NHS more than £3.8m per day. Despite advances in education, awareness and knowledge the reduction in PU prevalence has stalled – see figure below which represents all Care Settings (NHS Safety Thermometer).



The SEM Scanner is a CE class IIa, portable, wireless, non-invasive, hand-held device for the detection of PUs. It has been designed to identify the SEM level of the extracellular space below the surface of the tissue. It compares multiple local measurements to determine the difference in SEM values between potentially damaged and nearby healthy tissue.

The device consists of a pair of concentric coplanar electrodes, an integrated pressure sensor, software that computes a delta value from a set of SEM measurements and a user interface screen that displays the most recent SEM reading, the calculated delta value and the device and battery status. (Bates-Jensen, et al., 2011; Bates-Jensen et al., 2007; Clendenin et al., 2015; Moore et al., 2017)

The SEM Scanner exploits differences between the dielectric constants of materials that constitute tissue. Dry tissue has a low dielectric constant, while tissue that has developed inflammation and localised oedema (also known as sub-epidermal moisture) is much higher. When the sensor is pressed against an area on the skin, the device measures the electrical capacitance of the sensor, which is affected by the moisture within the underlying skin tissue to a depth of approximately 3.8 mm, generating a delta value. (See images below)

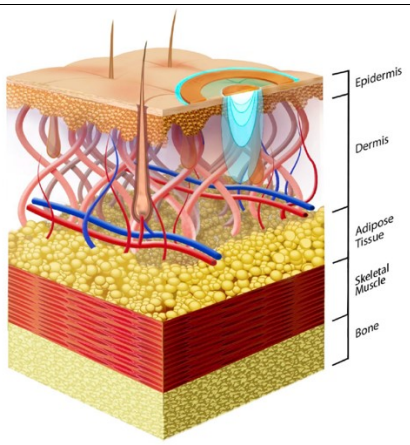
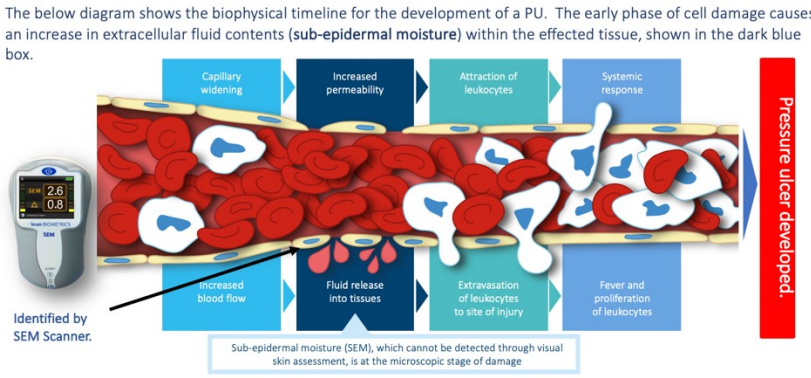


Illustration of the electric field used in the process of measurement of the local biocapacitance property of tissues, showing the shape and depth of penetration of the electric field of the SEM Scanner into the epidermis and dermal layers; BBI



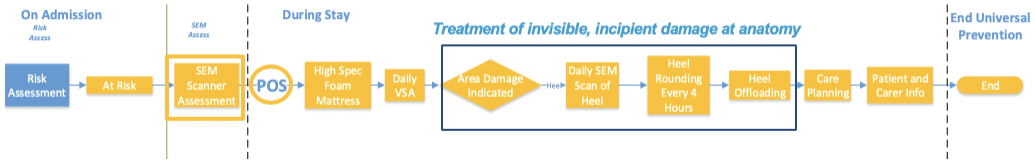
Repeated with kind permission of Prof A. Gefen

The delta value is a unitless measure of the difference in the SEM values between potentially damaged tissue and nearby healthy tissue. This computation eliminates common-mode effects in the local tissue, such as a change in the overall hydration level of a patient, as well as differences between patients and differences between body locations. The delta value is compared by the clinician to a threshold to identify tissue that is likely to develop into a pressure ulcer if an intervention is not implemented. Using delta values for PU evaluation eliminates sensitivity to variation between patients and PU localisation, as well as compensating for differences in user technique.

When patients have a delta value of ≥0.6 at an anatomical site, they may have tissue at increased risk for PU. This objective data facilitates earlier, and anatomically specific interventions designed to reverse the damaging effects of pressure ulceration. Delta values provide practitioners with days of advanced notice compared to visual skin assessment that a patient's skin and tissue is compromised over a given anatomy (Okonkwo et al., 2018). This is a clinically significant time advantage with considerable clinical utility for potential reversal of damage to skin and tissue prior to the breakage of the skin's surface. In comparison with visual skin assessment, the SEM Scanner supports clinicians to identify specific anatomical areas at increased risk of PU development 5 days (median) earlier (Okonkwo et al., 2018).

The SEM Scanner is designed to be used on intact skin on the heels and the sacrum. It is reported to have high inter-operator and inter-device agreement (Clendenin et al., 2015). Sensitivity and Specificity are reported as 87.5% and 32.9% (Okonkwo et al., 2018) as opposed to the reported challenges of existing methods such as Risk Assessment tools and Visual Skin Assessment (Fletcher et al., 2017; Moore et al., 2019).

The SEM Scanner is designed to be easily incorporated into existing care pathways (see figure below King T. et al 2018) and does not require additional procedures or technologies for the assessment of PUs and can readily be incorporated into standard of care procedures as an adjunct technology. Moreover, implementation of the SEM Scanner does not require additional staffing and does not require additional interventional equipment for the prevention of PUs.



The EPUAP/NPUAP/PPPIA PU Prevention Guidelines from which most national and local care pathways are derived are updated every 5 years. The latest update will be published in November 2019. The draft chapters have been released for Stakeholder review.

1. Aetiology Chapter – contains a full review of the Inflammatory Response to injury and the impact of localised oedema (sub-epidermal moisture). It describes this as “one of the earliest signs of cellular death in PUs” and states that it is “detectable via measurement of a biophysical marker called the Biocapacitance of tissues”
2. Skin and Tissue Assessment Chapter – contains 2 specific recommendations related to the assessment of sub-epidermal moisture. Recommendations 2.6 states “consider using a sub-epidermal moisture/oedema measurement device as an adjunct to routine clinical skin assessment”. Whilst recommendation 2.7 states “when assessing darkly pigmented skin, consider assessment of skin temperature and sub-epidermal moisture as important adjunct assessment strategies”

Strength of evidence for both recommendations is reported at B2 - which means that the “recommendation is supported by direct scientific evidence from properly designed and implemented clinical series on pressure ulcers in humans (or humans at risk for pressure ulcers) providing statistical results that consistently support the recommendation”.

These are in draft currently with the final version to be published November 15th 2019.

[redacted]

Briefly describe the environmental impact of the technology and any sustainability considerations (no more than 1,000 words).

Embedding the SEM Scanner into care pathways will require local PU Prevention protocols to be modestly updated to advise nurses to use their SEM Scanner informed clinical judgement to start anatomically specific interventions at a given anatomy. These protocol changes are very modest in their substance and their word count (see as an illustration the changes to the 2019 International Guidelines, presented above.). It is expected that local protocols will require updating after the publication of the revised EPUAP/NPUAP/PPPIA Guidelines in November 2019. Therefore, a combined updated process would be efficient.

The device itself has a warranted three-year lifespan and is returned to the manufacturer for disposal (where component parts are recycled as appropriate). The SEM Scanner is covered by a three-year warranty, which covers essentially all failure scenarios with the exceptions of theft and customer mishandling.

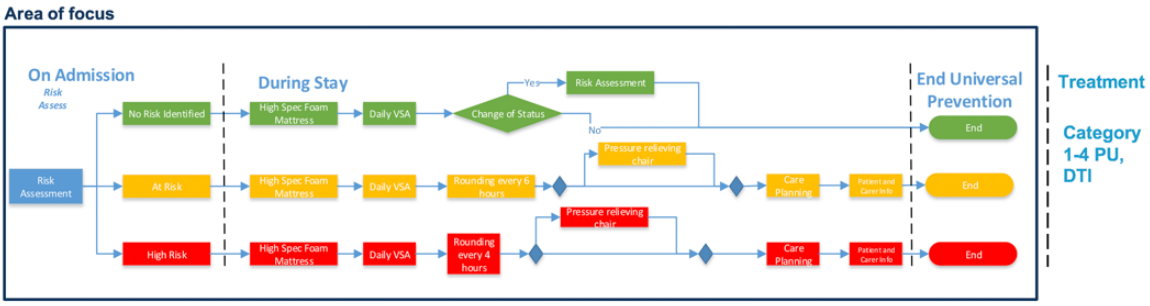
The SEM Scanner is fully complaint with Directive 2011/65/EU of the European Parliament and of the Council of 8 June 2011 on the restriction of the use of certain hazardous substances in electrical and electronic equipment (recast).

BBI has an environmentally friendly philosophy embedded into its management ethos. This philosophy that embraces a culture of not causing additional environmental impact runs through our R&D, Marketing and Clinical approaches. As one example we have recently embarked on a paper free approach to all scientific conferences/tradeshows. This was tested at EPUAP 2019 and gained tremendous support from the clinicians attending the event and will now be our “business as usual” approach.

Current standard of care for the treatment of PUs is associated with the considerable use and disposal of medical consumables including; wound dressings, alcohol wipes, barrier creams, and pharmaceuticals (antibiotics, analgesics). In addition, there is an increased use of resources associated with extended bedtime and hospital stay, including the frequent turnover of specialist foam mattresses. By utilising the SEM Scanner to alert healthcare practitioners to increased risk of PU, the use of these consumables falls considerably.

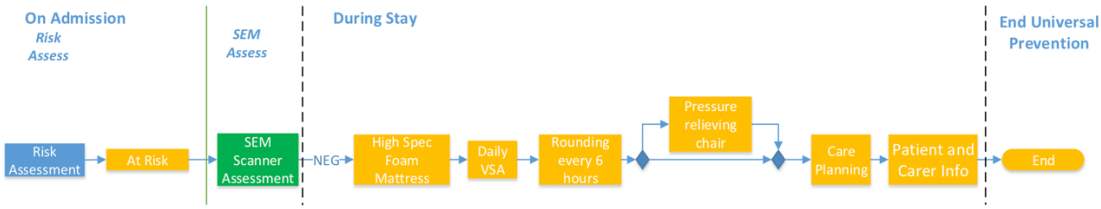
3 Clinical context

Describe the clinical care pathway(s) that includes the proposed use of the technology, ideally using a diagram or flowchart. Provide source(s) for any relevant pathways.*__Current Standard of Care; Universal Prevention Pathway (King T. et al 2018)__
(NHS Stop Pressure Ulcer Campaign, 2017; NICE Clinical Guidance, 2014)



- Based on NICE guidelines (CG179, 2014), local PU management and prevention protocols, and feedback from UK Tissue Viability Nurses

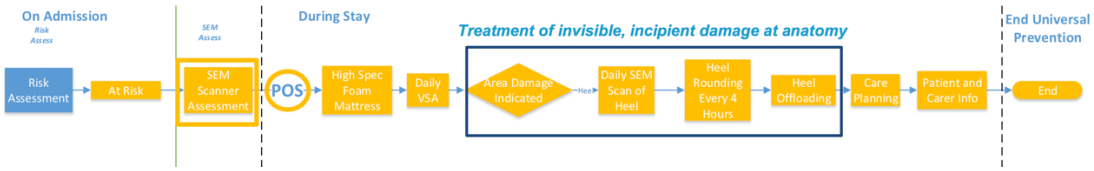
- The SEM Scanner is used in care settings where there is an incidence rate of pressure ulcers where the intention is to eliminate **ALL** avoidable cases and also where patients are identified as being at risk of developing a pressure ulcer
- In terms of the use within the current pathway, BBI recommends that the SEM Scanner should be used (in addition to standard of care):
  1) Upon admission – identifying increased risk or PU through raised deltas on admission
  2) During the patient's stay
  3) At discharge
- To assess risk, patients are scanned on admission and throughout their care as an adjunct to risk assessment protocols. The SEM Scanner is integrated as part of the patient risk assessment and is introduced into clinical workflow as represented by the image below **(**King T. et al 2018).



SEM Scanner as an adjunct to the Universal Prevention Pathway (see figure below **(**King T. et al 2018).

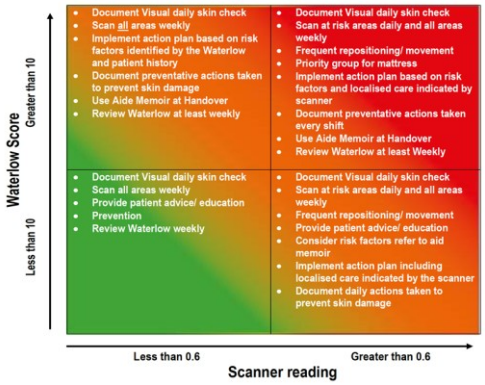
1. Risk assessment outcome=At Risk

2. If SEM assessment indicates risk of developing PU on left heel (example) (≥0.6 SEM Delta)
3. Use SEM Assessments to inform patient centred care:
    a. Implement anatomically targeted interventions as opposed to full body
    b. Perform daily SEM assessment of damaged area(s)



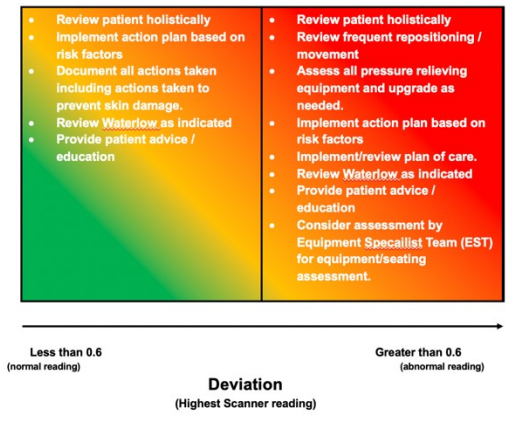
- The following graphics give an overview of how the SEM Scanner is being effectively used to enhance the holistic assessment of patients. Early identification of increased risk of PU and the relevant interventions aligned to the patient's care plan is resulting in the reduction of PU incidence.

Models for incorporating SEM Scanner readings into patient assessment protocols



(Littelfield S., Kellett N. Abstract submitted and presented at EWMA, Germany. 2016)

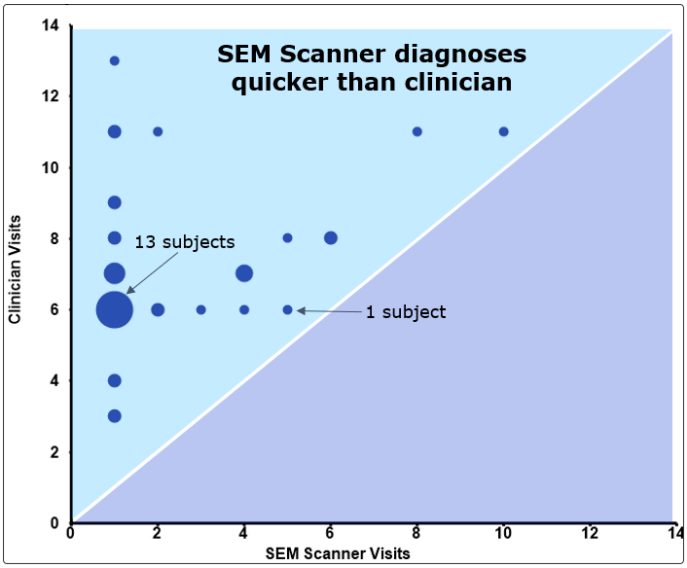
- In a Mersey Care Community District Nursing service evaluation of the SEM Scanner, patients in palliative care. 82% of staff indicated that SEM impacted clinical decisions.



Clinical judgement should always be utilised.
Review scanning frequency if clinical concerns / deterioration of condition.

(Ore N., Gallagher M. et al. QIP submitted and presented at EPUAP, Lyon, France. 2019)

- From clinical studies (SEM 200-003, 004 and 008), patients who were measured with an SEM delta of 0.6 and above, indicating elevated SEM levels, exhibited tissue that was either confirmed healthy (004), confirmed damaged (003) or inflamed (008)
- From clinical study SEM 200-008; (Okonkwo et al., 2018, submitted and in review process with Wound Repair and Regeneration) out of 42 identified pressure ulcers, for all of the pressure ulcers the SEM Scanner diagnosis was quicker than the clinician



Okonkwo H., et al. 2018

Describe any training (for healthcare professionals and patients) and system changes that would be needed if the NHS were to adopt the technology.

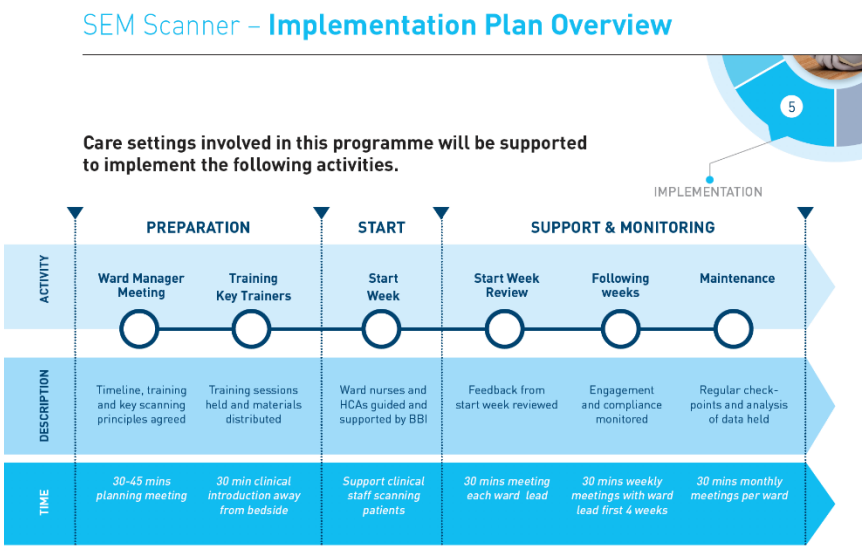
Using the technology enables earlier identification of increased risk of PU and anatomically targeted interventions intended to keep skin intact. Importantly the implementation of the SEM Scanner requires

- No new staff
- No additional equipment
- Interventional equipment remains the same (within the facility)

PU Prevention protocols would need to be updated to advise nurses to use their SEM Scanner informed clinical judgement to start anatomically specific interventions at a given anatomy. These protocol changes are very modest in their substance and their word count. They support the current standard of care.

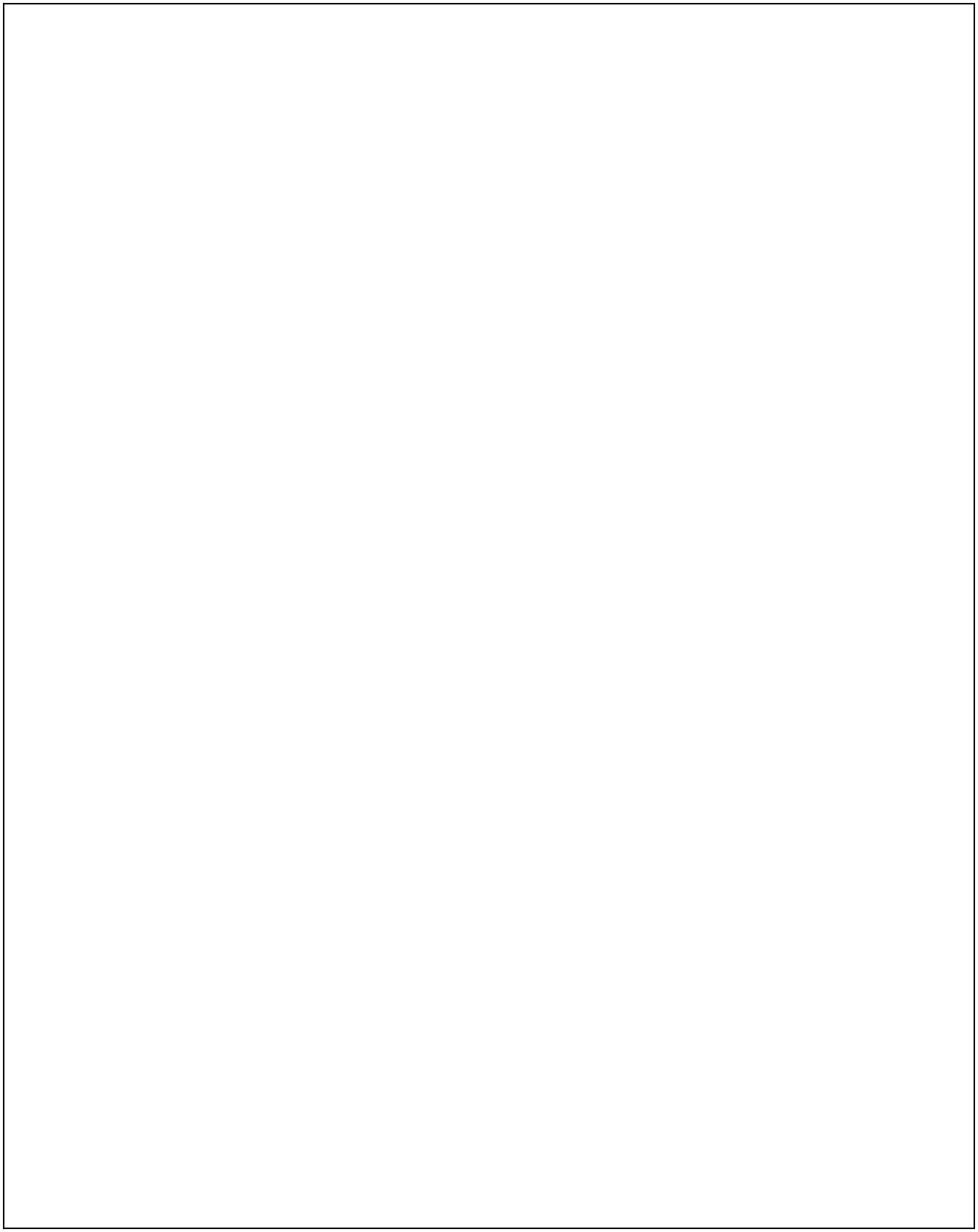
BBI's Health economic models highlight the time required to assess one patient with the SEM Scanner is approximately 5 minutes.

BBI work closely with the healthcare practitioners to ensure easy and efficient implementation of the technology. The images below detail an example of the support that is available.



Ward/Unit implementation plan

Activity	Content	Responsibility
Planning process	• Outline Implementation process • Identify key trainers • Set pre-implementation training dates and scanning start date • Confirm documentation to be used and PU pathway guidance	Project Lead Clinical Manager
Training	• Clinical Introduction – programme outline, ensure understanding of SEM • 'Hands on' practical session, how to scan correctly • SEM Implementation folder – outline content • Ensure understand PU pathway documentation	Clinical Manager Key Trainers
Week 1	• Work with Key Trainers only – observing, supporting good scanning technique • Complete Verification document and sign off • Observe key trainers teaching other staff, ensuring good practice upheld • Ensure compliance with pathway documentation and recording	Clinical Manager Key Trainers
Week 2	• Key Trainers – feedback, discuss experience, make any necessary updates • Clinical Manager – discuss the weeks findings, feedback from staff • Data Collection – reaffirm importance of good data, staff compliance	Clinical Manager Key Trainers
Week 3/4	• Assess adoption – plan time to overcome any training/compliance issues • Reduce support twice weekly dependent on confidence levels • Maintain weekly contact to review adoption progress	Clinical Manager Key Trainers
Maintenance	• Monthly meetings with Clinical Manager to review progress • Quarterly reviews with Project Lead, Clinical Manager, TVN – track progress on PU reduction	Project Lead Clinical Manager Matron/TVN



4 Published and unpublished clinical evidence

Identification and selection of studies

Complete the following information about the number of studies identified.

Please provide a detailed description of the search strategy used, and a detailed list of any excluded studies, in appendix A.

Number of studies identified in a systematic search.		805
Number of studies identified as being relevant to the decision problem.		35
Of the relevant studies identified:	Number of published studies (included in table 1).	6
	Number of abstracts (included in table 2).	6
	Number of ongoing studies (included in table 3).	6

List of relevant studies

In the following tables, give brief details of all studies identified as being relevant to the decision problem.

- Summarise details of published studies in table 1.
- Summarise details of abstracts in table 2.
- Summarise details of ongoing and unpublished studies in table 3.
- List the results of all studies (from tables 1, 2 and 3) in table 4.

For any unpublished studies, please provide a structured abstract in appendix A. If a structured abstract is not available, you must provide a statement from the authors to verify the data.

Any data that is submitted in confidence must be correctly highlighted. Please see section 1 of the user guide for how to highlight confidential information. Include any confidential information in appendix C.

Table 1 Summary of all relevant published studies

Data source	Author, year and location	Study design	Patient population, setting, and withdrawals/lost to follow up	Intervention	Comparator(s)	Main outcomes
Study SEM200–003	Gershon S, Okonkwo H, Rhodes S et al. (2014) SEM Scanner readings to assess pressure induced tissue damage [abstract]. In: Proceedings of the 17th Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, August 27th–29th 2014, Stockholm, Sweden (Manuscript submitted for publication to Advances in Skin and Wound Care, manuscript number D-19-00455) Okonkwo H (2018) Differentiating between healthy tissue and early	The SEM200–003 Protocol is a cross-sectional, data collection study of the SEM Scanner under clinical investigational as a non-significant risk device. The primary objective of this study was to compare SEM Scanner readings from the centres of confirmed stage I or II pressure ulcers or deep tissue injuries against SEM Scanner readings from the surrounding periwound areas. The secondary objectives were (1) to compare SEM Scanner readings from the centres of confirmed stage I or II pressure ulcers or deep tissue injuries in affected subjects against SEM Scanner readings from healthy subjects from a	A total of 125 participants were enrolled; 47% (n=59) had a heel pressure ulcer and 53% (n=66) had a sacral pressure ulcer. Three subjects were excluded from further analysis after determination that their PUs were clear fluid-filled blisters and did not meet the NPUAP definition for a stage 1 or DTI.	This was a non-blinded accuracy study. When combined with study SEM 200–004 looking at two cohorts of patients - those with and without PUs - validated by physical assessment of the skin and the ability of the SEM Scanner to accurately identify the presence or absence of tissue damage.	No comparator.	When combined with SEM200 study 004 the data collected suggest that spatial variability of SEM Scanner readings is effective for distinguishing wounded tissue from healthy tissue. Furthermore, the SEM Scanner readings are unlikely to be confounded by certain patient-specific factors and the SEM Scanner is safe and effective for use in diverse populations as an adjunct to the current standard of care for the detection of pressure-induced tissue damage. The difference in readings between the two cohorts was significant; p-value ≥0.064 for injured

	stage pressure injuries: A pilot study of effectiveness of the SEM scanner [abstract]. In: Proceedings of the 50th Annual Wound Ostomy and Continence Nurses (WOCN) society meeting, June 3rd–6th 2018, Philadelphia, USA (Manuscript Gershon S et al submitted to Journal of Wound Care)	previous study; (2) to assess the relationships, if any, between SEM Scanner readings and selected potential confounders; and (3) to assess the safety and patient tolerability of the SEM Scanner. There was no comparator for this study and there was no follow-up of study subjects. No blinding or masking was implemented. This study was designed to collect SEM Scanner readings at and around visually confirmed pressure ulcers or suspected deep tissue injury (collectively referred to as “wounds” in this report). Subjects were assessed with standard of care procedures for the identification of wounds (visual skin inspection, Braden scale, blanchability				tissue and as low as <0.001 for healthy uninjured regions (SEM Scanner delta values below 0.5 indicated normal tissue). Accuracy measures exceeded 80% for both the sacrum and heels.

		test, pain assessment) and with the SEM Scanner. SEM Scanner readings were collected at the centre of the wound, around the wound, and around the periwound region (“spatial” SEM Scanner readings).				

Study SEM200–004 Using sub-epidermal moisture (SEM) level as an indicator of early pressure damage to local skin and tissue.	Gershon S, Okonkwo H, Rhodes S et al. (2014) SEM Scanner readings to assess pressure induced tissue damage [abstract]. In: Proceedings of the 17th Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, August 27th–29th 2014, Stockholm, Sweden (Manuscript submitted for publication to Advances in Skin and Wound Care, manuscript number D-19-00455)	The study's primary objective was to collect SEM Scanner readings from unaffected tissue both at and contiguous to the bony prominences of the sacrum and heel to verify that a healthy population will have a generally constant level of SEM, indicating the absence of inflammation. This is an important comparator to patients who are at risk for pressure injury, or who have deep tissue injury, where SEM levels show elevated deltas. Non-interventional, cross-sectional data collection. Single time-point, no follow-ups.	25 females and 25 males from a private pain-management practice (no known observed pressure ulcers; "healthy tissue").	Non-interventional, cross-sectional data collection study.	No comparator.	Readings were collected at the centre and contiguous to the bony prominences of the heel and sacrum. When combined with the data from SEM 200 study 003 the data collected suggest that spatial variability of SEM Scanner readings is effective for distinguishing wounded tissue from healthy tissue. Furthermore, the SEM Scanner readings are unlikely to be confounded by certain patient-specific factors and the SEM Scanner is safe and effective for use in diverse populations as an adjunct to the current standard of care for the detection of pressure-induced tissue damage. The difference in readings between the two cohorts was significant; p-value ≥0.064 for injured tissue and as low as <0.001 for healthy

						uninjured regions (SEM Scanner delta values below 0.5 indicated normal tissue).
Study SEM200-008 Evaluation of a novel device using capacitance of the detection of early pressure ulcers (PU), a multi-site longitudinal study	Okonkwo H, Milne J and Bryant R (2018) Evaluation of a novel device using capacitance of the detection of early pressure ulcers (PU), a multi-site longitudinal study [abstract]. In: Proceedings of the National Pressure Ulcer Advisory Panel (NPUAP) meeting, 2nd–3rd March 2018, Las Vegas, Nevada, USA (Manuscript in review process with Wound Repair and Regeneration. Manuscript ID WRR-18-06-	• Multi-Site, longitudinal data collection study • Multi-site UK and US	Overall, 189 participants (46.7% males and 53.3% females) were enrolled, (22.2% UK 77.8% US, respectively). Seven participants' data were not analysable, resulting in an intent-to-treat population of 182.	The objective of the SEM200-008 study was to demonstrate that the SEM Scanner detects signs of pressure ulcers (SEM delta) earlier in patients than by clinical judgment using signs of pressure ulcer from visual skin assessments.	Standard of care based on scores from risk assessment scales (Braden scale, <15; Waterlow scale, ≥10; or Norton scale ≤18).	The study was successful in meeting the sensitivity endpoint with demonstration of earlier detection of damage before standard of care means. ITT study results demonstrated a sensitivity of 87.5% (95% CI: 74.8%–95.3%) for detecting pressure ulcers between the SEM Scanner and clinical judgment per visual skin assessment. This is in line with prior studies using the SEM Scanner 200 which showed sensitivity of 82% (003/004 study; 95% CI: 74%–88%) in subjects with pre-existing conditions (no

	0175.R1, entitled "A Blinded Clinical Study of SEM Scanner 200, a Capacitance Measurement Device, for Early Detection of Pressure Injury)					PU and intact-skin PU) for comparison. SEM scanner shown to detect PUs 5 days (mean) before nurse visual skin assessment.
Hancock K and Lawrance R (2019) In: Proceedings of the 21st Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, 18th–20th September 2019, Lyon, France	Hancock K and Lawrance R (2019) Reducing pressure ulcer (PU) incidence through introduction of new technology [abstract]. In: Proceedings of the 21st Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, 18th–20th September 2019, Lyon, France	The SEM scanner was introduced to healthcare facilities via pressure ulcer reduction programmes (PURP). A PU Reduction Program enables clinicians to evaluate the impact of including this innovative technology as an adjunct to SOC through a systematic process, without introducing additional staff or new prevention interventional equipment.	1160 patients included to date in 5 countries at 15 sites; 14 acute care, 1 hospice care. 46,000 data points. 1014 patients were in Acute Care facilities whilst 146 patients were in end of life care.	HAPU incidence for a define period was compared to hospital acquired pressure ulcers (HAPU) rates during the PURP.	Existing PU prevention protocols.	In the AC cohort >11,000 SEM assessments were taken, a 92% (weighted average) reduction in the incidence of HAPUs was achieved. • 79% of AC centres reported 0% HAPU during the PURP • Daily use of the device alerted to risk of PUs in 56% of assessments (Delta reading ≥0.6) • In 46% of assessments, patients were found to be at risk for PUs (Delta reading ≥0.6) but

						had no visual skin redness at that region • Clinical decision-making was impacted in 52% of cases • 63% of patients received additional interventions including increased mobilisation In HC, a 47% reduction in HAPUs was achieved. In one of largest PURPs to date 75% of healthcare practitioners described the new technology as easy to use 88% of healthcare practitioners reported that the new technology provided additional information to support clinical decision-making
J Tissue Viability 2018;27(4):232-237	O'Brien G, Moore Z, Patton D, et al. (2018)	To establish the relationship between visual skin	Patients (n=19) mean age 74.7 ± 14 years; mean Norton score,	Daily scans with SEM Scanner on the sacrum and	Preventative interventions were	• Medium correlation (r=0.47) between

	The relationship between nurse's assessment of early pressure ulcer damage and sub epidermal moisture measurement: A prospective explorative study. J Tissue Viability 27(4):232–7	assessment (VSA) and SEM measurements. To establish whether measurement of SEM was more accurate and timely in detecting skin changes when compared to visual skin assessment alone. **Methods**: • Setting: 2 wards in a 62-bed general hospital in Ireland • Participants: 47 consenting patients (18M, 29F) at high risk of PU (Norton score), without existing PU • Exclusions: Existing PU; non-consenting; not at risk (Norton score); active and mobile • Follow up: 4 weeks or until discharge or transfer • Assessment: Daily scans with SEM Scanner on	12; mean follow up 7.8 ± 4.2 days. • N=19 (40%) had abnormal skin by VSA • 21 Stage 1 PU developed on the sacrum (n=17; 91%) and heels (left, n=3; 14%. right, n=1; 5%); all had elevated SEM deltas before visual signs of damage (100% sensitivity) • Specificity was 83%; false positives had insufficient follow up time	both heels. A delta >0.5 indicated high risk of PU.	implemented according to local practice, but care plans were not altered based on the SEM scan results.	VSA and SEM outcomes for patients who developed a Stage 1 PU was recorded • VSA and SEM Scanner outcomes correlations: Strong for the sacrum (r=0.65); medium for the right heel (r=0.43); low for the left heel (r=0.23) • SEM Scanner detected damage on day 1.5 ± 1.4; VSA detected PU on day 5.5 ± 2.5, 4 days earlier than VSA

		the sacrum and both heels. A delta >0.5 indicated high risk of PU • Care plan and outcomes: Preventative interventions were implemented according to local practice, but care plans were not altered based on the SEM scan results. Nurses also conducted VSA. VSA and SEM measurements were correlated, and correlations categorised as low, medium or strong				
Smith G (2019) J Wound Care 28(5):278–82	Smith G (2019) Improved clinical outcomes in pressure ulcer prevention using the SEM scanner. J Wound Care 28(5):278–82	To test the reduction in the incidence of Grade 2+ Hospital Acquired Pressure Ulcers using the SEM Scanner in the hospital's PU Prevention and Management Protocol.	Patients: 35 consenting medical and non-elective surgical patients; 82% aged >65–75 and 74% >75 years. 51% M/49% F.	SEM Scanner: All patients were scanned by Healthcare Assistants on the sacrum and both heel once daily from admission. SEM delta ≥0.6 was taken to indicate early pressure damage. Registered nurses	Standard care: The existing PU prevention protocol required that all patients be risk assessed by the Waterlow scoring system. Those identified as very high-risk immobile patients with a PU are	All 35 patients scanned returned SEM deltas ≥0.6; none developed new PU during their in-patient stay – a 0% incidence. The use of the SEM Scanner became integrated as normal practice within ~2

				interpreted values reported by the SEM Scanner and adjusted care plans.	reassessed every 24 hours. Very high-risk immobile patients without a PU are reassessed every 7 days.	weeks of implementation. From authors: As a result of the evaluation and business case, the SEM scanners are being used on medical and surgical wards and with the tissue viability team, with a view to embed them as the objective measurement of risk, rather than risk stratification tools such as Braden or Waterlow. It is envisaged that over time a more objective approach to PU prevention can be taken with these devices. In addition, the tissue viability team intends to scan patients on admission to the hospital to determine how many patients are being admitted with developing damage

						that is not visually detectable.

Raizman R, MacNeil M and Rappl L (2018) Int Wound J 15(3):1033–44	Raizman R, MacNeil M and Rappl L (2018) Utility of a sensor-based technology to assist in the prevention of pressure ulcers: A clinical comparison. Int Wound J 15(3):1033–44	To evaluate the clinical utility of incorporating the SEM Scanner into clinical workflow and of associating interventions informed by the SEM Scanner with decreases in PU incidence.	Patients and setting, Phase 1: N=89; admitted to the medical/stroke unit. 55% F; 50% with 45–68 kg weight, 20–35% with 68–90 kg weight; majority >60, minority >80 years old. Outcome measure: The change in incidence of HAPU. Patients and setting, Phase 2: Patients with a score ≤3 in the Braden Mobility sub-score were enrolled from the alternative care unit (n=29) and from patients admitted to any unit in the hospital from the emergency room (n=166).	SEM Scanner.	Phase 1: Care plan: standard of care for risk assessment and interventions; SEM Scanner used but scores were not used to determine interventions, providing a baseline for PU incidence. Phase 2 care plan: As Phase 1 but the SEM scores were used in conjunction with risk assessment scores to guide appropriate interventions and care planning.	PU rates dropped significantly between Phase 1 and Phase 2 when the scanner was incorporated into initial and ongoing patient assessment. The 93% reduction in HAPU mirrors results reported by similar hospitals that used the SEM and achieved a reduction in HAPU of 100%. • Phase 1: 12/89 patients (13.5%) developed a PU indicating that the Hawthorne effect, whereby practice changes as a result of using the SEM Scanner, did not influence implementation of care • Phase 2: 2/195 patients (1%) developed a PU • Reduction in PU: 93% when SEM Scanner

						outcomes guided preventative interventions
Clendenin M, Jaradeh K, Shamirian A et al. (2015) J Tissue Viability 24(1):17–23	Clendenin M, Jaradeh K, Shamirian A et al. (2015) Inter-operator and inter-device agreement and reliability of the SEM Scanner. J Tissue Viability 24(1):17–23	To evaluate the repeatability of the SEM Scanner readings between operators and multiple devices. Comparison study evaluating the reliability of three different devices across three different operators in healthy volunteers. For each subject, each operator took three SEM Scanner readings at the following anatomical sites: Sacrum, sternum, left heel, and right heel. An average and maximum SEM Scanner value was recorded. An additional two replicate readings were also taken and recorded in the same manner, for a total of three readings per device, per operator and per anatomical site. Each operator then repeated this process for each of the three devices. An intraclass correlation (ICC) statistic was calculated to assess the inter-device and inter-operator reliability.	Healthy volunteers ≥18 years of age.	SEM scanner.		The results of this study demonstrate the high reliability and good agreement of the SEM Scanner across different operators and different devices. Given the limitations of current methods to prevent and detect pressure ulcers, the SEM Scanner shows promise as an objective, reliable tool for assessing the presence or absence of pressure-induced tissue damage such as pressure ulcers.

O'Keeffe S and McClusky P (2019) In: Proceedings of the Tissue Viability Society meeting, 1st–2nd May 2019, Southampton, UK	O'Keeffe S and McClusky P (2019) Evaluation Of Novel Sub-Epidermal Moisture (SEM) Technology In Early Pressure Ulcer Detection Versus Conventional Techniques [abstract]. In: Proceedings of the Tissue Viability Society meeting, 1st–2nd May 2019, Southampton, UK	To compare the clinical utility of using a SEM Scanning device versus subjective visual skin inspection. • 12-week period • 3 consecutive readings were taken over sacrum, heels and ischial tuberosities • SEM score ≥0.6 = increased risk of PU	Acute care patients in combined orthopaedic/plastic surgery ward. Waterlow score ≥10 (at risk to very high risk of PU.	SEM Scanner.	Visual Skin Assessment.	32 subjects enrolled – 72% (n=23) recorded positive SEM delta (≥0.6). 15 subjects with no visible signs of damage had a positive SEM Scan result – indictive of underlying PU Zero HAPU in study group. 12.2% HAPU rate pre evaluation 100% reduction in HAPU rate compared to historic rate.
Peko Cohen L and Gefen A (2019) Int Wound J 16(4):979–88	Peko Cohen L and Gefen A (2019) Phantom testing of the sensitivity and precision of a sub-epidermal moisture scanner. Int Wound J 16(4):979–88	Laboratory Study. To experimentally detect water content changes – to assess sensitivity and precision of the SEM Scanner in human phantoms of the heel and skull/face.	3 Dimensional (3D) printed phantoms of the skeleton of the heel/skull/face developed. To replicate the soft tissue – 0.7cm baby diapers were cut and attached to the phantoms - the thickness represents the thickness of the human heel or face.		Goal to determine if there was a statistically significant difference between SEM readings associated with water content at affected site vs another adjacent site.	For both phantoms the SEM Scanner was shown to be sensitive enough to detect the variation in water content" Increasing volume of water demonstrated a corresponding consistent trend of increasing deltas. The results were shown to be statistically significant.

						Locally increased water content at the body sites resulted in elevated SEM delta readings – confirms the SEM Scanner is able to detect fluid changes that are as small as 1ml.
Gefen A., Gershon S. OWM; 64 (9); 12-27	An Observational Prospective Cohort Pilot Study. To Compare the Use of Subepidermal Moisture Measurements versus Ultrasound and Visual Skin Assessment for Early Detection of Pressure Injury	An Observational Prospective Cohort Pilot Study	15 participants (10 women and 5 men). Post-Acute Setting. 4 Study groups recruited. Healthy Patients, DTI and Stage 3 monitored for 3 days. At risk patients monitored for 10 days. 3 anatomical locations (left heel, right heel and sacrum) by Ultrasound, SEM Scanner and VSA each day	SEM Scanner	Visual Skin Assessment (VSA). Ultrasound (US)	Among the 15 participants where lesions existed, SEM measurements always agreed with US and VSA findings. Authors found the US and SEM readings were similar but I the evolving SDTI case the SEM Scanner detected it earlier. SEM and US readings always agreed between themselves, they did not always agree with VSA which points to the limited capacity of VSA to assess the status of subepidermal (non visible) tissues

Table 2 Summary of all relevant abstracts

Data source	Author, year and location	Study design	Patient population, setting, and withdrawals/lost to follow up	Intervention	Comparator(s)	Main outcomes
The clinical impossibility of pressure ulcer prevention under the current standard of care.	Burns M, Tsang K and Grainger S (2020) The clinical impossibility of pressure ulcer prevention under the current standard of care [abstract]. In: Proceedings of the World Union of Wound Healing Societies (WUWHS) meeting, 8th–12th March 2020, Abu Dhabi, United Arab Emirates	The aim of this analysis was to assess the suitability of guidelines, if followed faithfully, to achieve complete PU prevention for in-patient acute-care populations. NHS England's Care Pathway for PU prevention and Management (CG179) was used for analysis. A clinical decision-tree analysis with transition probabilities was the resulting output.	All admitted patients to acute care setting based on the application of NICE CG 179.	SEM Scanner.	Standard of Care, NICE CG179 and published performance statistics	The results of this analysis highlight that Guidelines require universal, total body clinical interventions to be applied to patients deemed to be at PU risk. A positive confirmation of a PU by skin assessment brings anatomy-specific interventions designed to reverse damage at that anatomical site. Most pressure ulcers are considered preventable and reversible if identified in the early stage of ulceration. Anatomy-specific interventions applied only when a PU is visibly confirmed, as directed under the guidelines, may be too late for PU

						prevention to be achieved.
The mathematical impossibility of pressure ulcer prevention.	Burns M, Tsang K and Grainger S (2020) The mathematical impossibility of pressure ulcer prevention [abstract]. In: Proceedings of the World Union of Wound Healing Societies (WUWHS) meeting, 8th–12th March 2020, Abu Dhabi, United Arab Emirates	Most pressure ulcers (PUs) are considered preventable and reversible if identified in the early stage of ulceration. Early stage identification relies on patient screening, risk and skin assessments; the detection accuracy of which was analysed to determine if a full preventative state could be facilitated by such for an acute-care population.	All admitted patients to an in-patient episode of care. A static, probabilistic tree and 10,000 Monte Carlo distributions modelled practitioners' PU detection probabilities via patient screening, risk and skin assessment and resultant interventions using sensitivity and specificity values from published literature or clinical trial data.	SEM Scanner.	Standard of Care, NICE CG179 and published performance statistics	With 41.2% of the given population at risk for a PU, and known sensitivity (46.8%–82.4%) and specificity (27.4%–67.5%) rates of current detection standards, 25.98% of the population are falsely classified.
Pressure ulcer incidence in medium risk patients in acute care settings in the USA and UK.	Burns M (2020) Pressure ulcer incidence in medium risk patients in acute care settings in the USA and UK [abstract]. In: Proceedings of the World Union of Wound Healing Societies (WUWHS) meeting, 8th–12th March 2020, Abu	Report sub-set PU incidence data by risk-assessment category and associated interventions from an FDA trial across acute settings in the UK and USA.	A prospective, longitudinal multi-site study in twelve acute care settings was conducted in support of an FDA filing for a PU detection device. Data presented here are sub-sets of the study's overall data.	N/A	Standards of Care for PU Prevention and Management in the USA and UK	Most PUs formed on patients classed as "moderate-risk" followed by "high-risk" patients. Less than half (39%) of all patients received any type of anatomy-targeted interventions before their PU visibly manifested.

	Dhabi, United Arab Emirates					

Table 3 Summary of all relevant ongoing or unpublished studies

Data source	Author, year (expected completion) and location	Study design	Patient population, setting, and withdrawals/lost to follow up	Intervention	Comparator(s)	Outcomes
Unpublished study manuscript Due to be submitted to *Wounds UK* by end September	**Effect of repositioning on subepidermal moisture measurement variation in healthy volunteers** Phil A Evans, BN (Hons) Queen Alexandra Hospital, Portsmouth, UK. Due to be submitted to *Wounds UK* by end September.	UK pilot study was to collect preliminary evidence about the effect of repositioning on the results of point-of-care devices that use subepidermal moisture (SEM) as a proxy indicator of PU risk.	22 healthy individuals.	SEM scanner.	No comparators.	SEM delta did not differ significantly between time points. High variation was observed immediately after repositioning but did not show statistically significant variation with respect to time after repositioning.
Unpublished study manuscript Abstract submitted and presented at *Wounds UK* 2018. Due to be submitted to *Wounds UK* by end September.	**The impact of skin protectant cream on variation in sub-epidermal moisture readings** Phil A Evans, BN (Hons) Queen Alexandra Hospital, Portsmouth, UK. Due to be submitted to *Wounds UK* by end September.	The studies were exploratory, unblinded, controlled, prospective, cohort investigations of SEM Scanner 200. Participants acted as their own controls. This study	22 healthy volunteers aged 18–65 were recruited from the staff and student population of the University of Southampton and Portsmouth Hospitals NHS trust.	SEM scanner.	No comparators.	Barrier cream applied evenly across the scan site, according to manufacturer instruction, does not appear to affect the SEM delta. Partial coverage may affect SEM delta though this risk appears to reduce with time and regular skin cleaning.

		investigated the effect of barrier cream application verses non-application on scanner delta values on directly comparable sites (heels) and the effect of full versus partial barrier cream application on delta values on the sacrum.				
Registry. BBI is the data controller of the Registry. Dendrite is the data processor.	The registry is a hypothesis generator based on structured datasets. It's a tool for further research on current methods of care for pressure ulcers. The registry is developed to provide data to answer the following research questions: • What is the predictive capacity of risk assessment methods? Do the specificity and sensitivity levels of current risk assessment tools make it mathematically impossible to achieve full prevention?	Text	Text	Text	Text	Text

	• What evidence supports the 5-step approach in treating and preventing pressure ulcers? • What can SEM scanner readings teach us about the efficacy of the care pathway? Can the SEM scanner, in conjunction with the current Standard of Care, help in reducing pressure ulcers? In addition, the following will be investigated using data generated from the pool of patients: • Are the current visual scales adequate or do the risk brackets require adjustment? • Which components/categories of risk assessment are the more relevant in determining if a PU will develop? • How do we best assess sensitivity? • (Waterloo ≥10; Norton ≤18; Braden <15. What is sensitivity and specificity of these ratings?) • What are the components in risk assessment tools that are the most important to analyse? Data from the registry will also be used to assess the viability of risk assessed in 6 hours from admission; the components and efficacy of skin inspection. Was it					

	done? How often? Types of abnormality detected. Type and efficacy of mechanical support will also be assessed.					
Merseycare Community District Nursing Service Pilot Implementation of SEM Scanner.	2019, Merseyside district community setting. Nicky Ore, Head of Clinical Operations. Abstract submitted and presented at EPUAP, Lyon, France, 2019. Award Winner for Quality Improvement Programme, EPUAP 2019	Two Health Care Assistants (HCAs) trained on use of SEM Scanner. Selection of patients on the caseload selected. Patients scanned four to five days per week over a three-month period. Algorithm used for decision making.	Mersey Care Pressure Ulcer Reduction Programme. The overall aim of the project is to demonstrate/evidence prevention and reduction of pressure ulcer development. Two district nurse bases identified for 12-week pilot: Sefton and South Liverpool. Focus on palliative care patients. Palliative care patients account for ~40–55% of caseload. Patients can remain on caseload for varying periods of time: 50% may be on caseload for >4years; the other 50% on caseload for ~ 4 to 8 months.	SEM Scanner.	Waterlow visual assessment.	• 17 patients total during evaluation period • 697 readings taken and 2,788 data points captured for analysis • 26.9% reduction in PU in palliative care patients during the evaluation • 82% staff indicated the SEM scanner impacted their clinical decision that day • 94% staff indicated additional

						interventions taken

Table 4 Results of all relevant studies (from tables 1, 2 and 3)

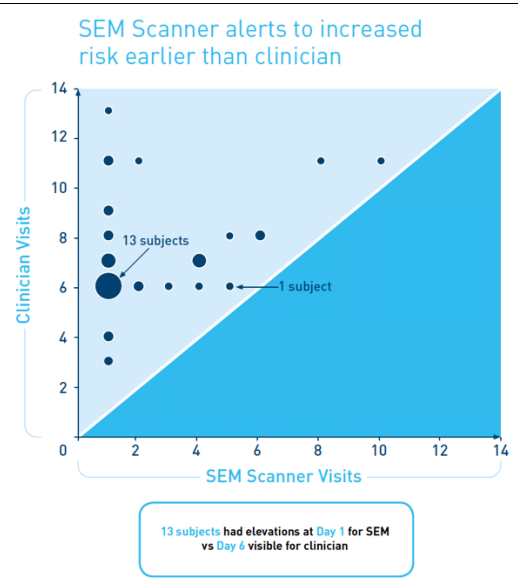
Study	Results	Company comments

SEM200–003:SEM 200–004
 	
Gershon S, Okonkwo H, Rhodes S et al. (2014) SEM Scanner readings to assess pressure induced tissue damage [abstract]. In: Proceedings of the 17th Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, August 27th–29th 2014, Stockholm, Sweden (Manuscript submitted for publication to Advances in Skin and Wound Care, manuscript number D-19-00455)
 	
Okonkwo H (2018) Differentiating between healthy tissue and early stage pressure injuries: A pilot study of effectiveness of the SEM scanner [abstract]. In: Proceedings of the 50th Annual Wound Ostomy and Continence Nurses (WOCN) society meeting, June 3rd–6th
	• Cohort 1:
	  ○ 47% had a heel PU and 53% a sacral PU
	  ○ 3 patients (did not meet inclusion criteria); evaluable subjects N=122
	  ○ 32% of patients with heel PU and 21% with a sacral PU had diabetes
	  ○ Evaluable patients with PU, 4 had PU on both heels. Total PU assessed N=126
	  ○ Heel ulcers: Stage 1 (20.6%); DTPI (79.4%)
	  ○ Sacral PU: Stage 1 (66.7%); DTPI (28.5%)
	  ○ Because of asymmetry in sacral PU the rings of assessment were unequal on left and right. There was less variability for heel PU
	  ○ SEM readings were higher for sacral PU than for heel PU. Average readings increased with increasing distance from the ulcer. In the centre of the PU readings were significantly lower than average peripheral readings
	
	• Cohort 2:
	  ○ There were significant issues in obtaining measurements at the sternum, patella and C7 spinous process (modesty concerns and difficulties in placement of the scanner probe in good contact with the skin)
	  ○ Readings differed between gender only for sternal readings
	
	• Graphically the readings from sacral PU form a “V” shaped spatial distribution where an ulcer was assessed but readings from normal skin gave a relatively level spatial pattern
	• In heel PU all readings were elevated compared with normal heel skin
	• Interim results from subjects with PUs suggested that fewer than 16 readings could be informative and would be less burdensome
	• SEM Scanner accuracy: When a delta >0.5 SEM units was used, the SEM Scanner demonstrated 90.5% accuracy in detecting PU and 86% accuracy for detecting the presence or absence of a PU at the sacrum. In heels the corresponding outcomes were 82.5% accuracy for damage and 90% accuracy for healthy tissue
		Accuracy exceeded 80% for both sacrum and heels when a within-subject change in SEM Scanner readings of >0.5 is utilised.
		
		SEM Scanner readings are unlikely to be adversely affected by patient-specific factors, such as comorbidities or skin-tone.
		
		The use of within-subject change as the distinguishing factor minimises the potential for influence by other patient-specific characteristics.
		
		The SEM Scanner was shown to be a very effective device. It brings objective information that would be helpful as an adjunct to clinical judgement and the current standard of care.
		
		Early identification of increased risk of PU is key to prevention of injury progression and in the development of effective prevention and treatment plans. Because the SEM Scanner provides measurable quantitative data prior to the visual identification of the presence or non-presence of tissue injury, the implication is that the paradigm for framing the approach to PU prevention is disrupted and must be reconsidered.

2018, Philadelphia, USA Gershon S. Using sub-epidermal moisture (SEM) level as an indicator of early pressure damage to local skin and tissue. Submitted and in review process with Advances in Skin and Wound Care: Manuscript number D-19-00455		

SEM200–004
 	
Gershon S, Okonkwo H, Rhodes S et al. (2014) SEM Scanner readings to assess pressure induced tissue damage [abstract]. In: Proceedings of the 17th Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, August 27th–29th 2014, Stockholm, Sweden (Manuscript submitted for publication to Advances in Skin and Wound Care, manuscript number D-19-00455)
	• Sacral readings: Did not differ significantly; the differences between median values were well below 0.6 SEM units
	• Heel readings: Generally lower than sacrum readings
	  ○ Sites around the heel locations had more variability among readings; variance between the median values was well below 0.6 SEM units
	  ○ Medial side of the heel: Lower than readings on the lateral side; the difference was not statistically significant
	• Measurements from all anatomical locations were similar by gender except for the centre of the bony prominence of the heel where the reading taken above the bony prominence of the heel was lower in males than in females
	• No associations between readings at the heel and gender were observed
	• There were no statistically significant variations based on gender, age, race, ethnicity, BMI, smoking status, diuretics, surgery, or osteoarthritis between the subjects' measurements at the sacrum; among those factors, only race indicated a variation between groups for heel measurements
	• Callouses on the heel and race may be two potential confounders for heel readings
	• Callouses on the heel decrease the readings at the centre, laterally and medially of the bony prominence, but not on the plantar surface
		The relatively flat spatial pattern of SEM values around the bony prominence in both heels and the sacrum in healthy subjects supports the hypothesis that in healthy tissue there is no inflammation. There was greater variability in average SEM readings at the heels compared with the sacrum, possibly because of recognised differences in vasculature at this anatomic location.
		
		This study supports the notion that single absolute SEM Scanner readings are insufficient to assess tissue viability. The status of tissue (e.g., tissue damage) is more appropriately represented by the spatial SEM Scanner readings. Care should be exercised where callouses, which confound SEM readings, are present. African Americans returned generally lower SEM readings than non-African Americans, but the reduction was equivalent at all sites. The delta value used to indicate risk of PU is therefore valid.

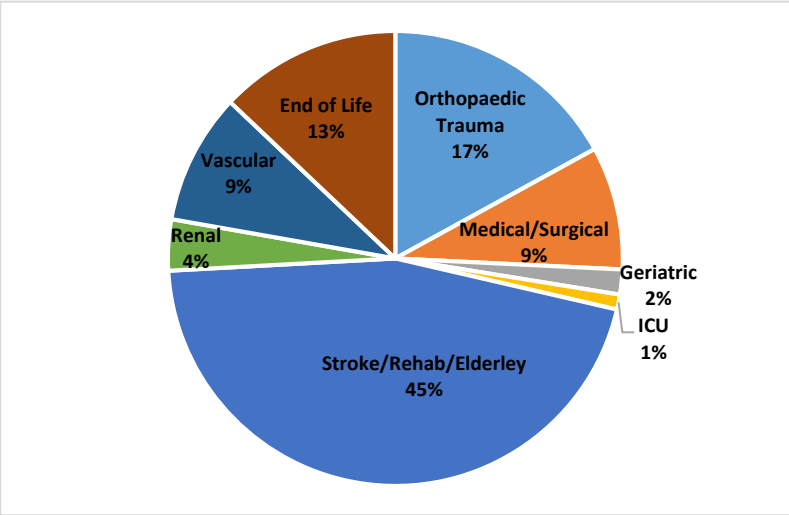
Study SEM200–008 Okonkwo H, Bryant R and Milne J (2018) Evaluation of a novel device using capabilities of the detection of early pressure ulcers (PU), a multi-site longitudinal study [abstract]. In: Proceedings of the 50th Annual Wound Ostomy and Continence Nurses (WOCN) society meeting, June 3rd–6th 2018, Philadelphia, USA (Manuscript in review at Wound Repair and Regeneration, manuscript number WRR-18-06-0175.R1)	The primary endpoint of sensitivity was achieved by comparing the SEM deltas to visual inspection for PU diagnosis. The secondary endpoint supports that the SEM scanner is helpful in detecting pressure damage earlier than when the standard of care identifies the damage visually. Results from the 008 clinical study from each assessed anatomy were classed as: ○ True positives - a visible pressure ulcer and a localised SEM delta of 0.6 or above ("abnormal levels of SEM") ○ True negatives - no visible pressure ulcer and a localised SEM delta below 0.6 ("flat values") ○ False negatives - a visible pressure ulcer and a localised SEM delta below 0.6 ("flat values") ○ False positives - no visible pressure ulcer and a localised SEM delta of 0.6 or above ("abnormal levels of SEM") • 82.4% of patients were moderate- to high-risk of PU by standard risk assessment methods; 22.2% had pre-existing PU • Compared with standard skin assessment, the SEM Scanner had >80% sensitivity and between 30% and 40% specificity • The SEM Scanner detected damage to the sacrum, left heel and right heel 4.7 ± 2.6, 5.1 ± 2.3, and 4.3 ± 2.4 days, respectively, sooner than skin assessment did (Figure)	Prevention of PU remains a major challenge in all health care settings. Prophylactic measures currently rely on Risk Assessment Tools and clinical assessments of skin temperature, rigidity, and visible characteristics, which are plagued by poor inter-rater reliability. Additionally, the Risk Assessment Tools assess the whole body rather than a specific anatomy. By objectively identifying subdermal changes that precede palpable or visible indicators of PU, Biocapacitance measurement may prove useful in PU prevention initiatives as a method for early identification of increased risk of PU. The data provided by the SEM Scanner is objective and anatomically specific.



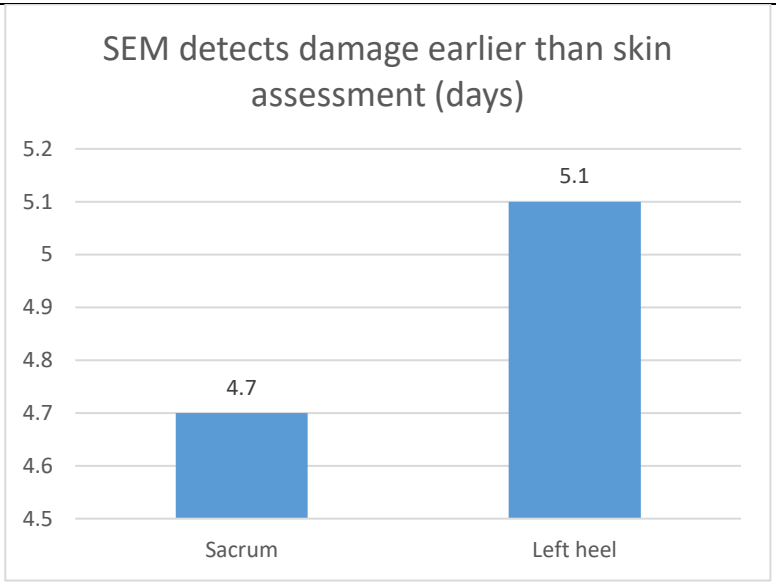
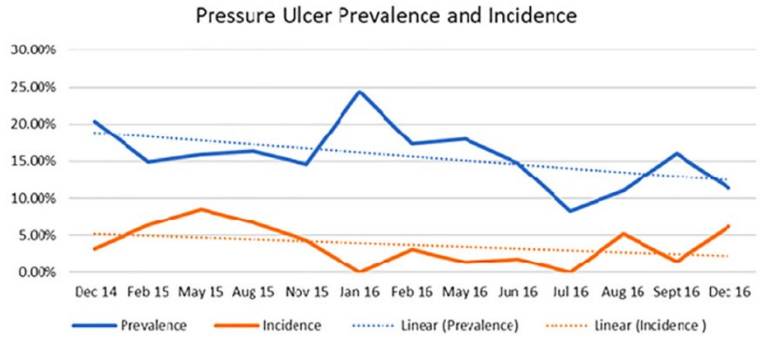
SEM Scanner detected PUs 5 days, on average, before nurse Skin Assessment.

Table Sourced from Okonkwo H. et al. 2018

Days Between VSA+ and SEM Detection				
	All	Sacrum	Left Heel	Right Heel
N	42	13	17	12
Mean (SD)	4.74 (2.39)	4.69 (2.59)	5.06 (2.33)	4.33 (2.39)
Median	5.00	5.00	5.00	4.50
Min, Max	1.00, 12.00	2.00, 12.00	1.00, 10.00	1.00, 9.00

Hancock K and Lawrance R (2019) Reducing pressure ulcer (PU) incidence through introduction of new technology [abstract]. In: Proceedings of the 21st Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, 18th–20th September 2019, Lyon, France	Pressure Ulcer Reduction Programme (PURP) Database • 1160 patients: 5 countries • 15 sites; 14 acute care; 1 hospice care • 11 different clinical care settings • HAPU data collected for defined pre-PURP period - compared to PURP period • Acute Care subset; 14 sites; 1014 patients • 46,000 data points • Patients scanned daily- heels and sacrum • Prevention interventions in at risk patients implemented according to local policy • No additional staffing or resources required Results: • 92% weighted reduction in HAPU • 79% sites reported zero HAPU during PURP • 63% patients received additional preventative interventions Figure Below represents the clinical care settings 	From a real-world perspective, the SEM Scanner used in this multicentre evaluation increases reliability and objectivity in an otherwise complex but essential skin and risk assessment platform. It is a tool that can be deployed at the point of admission, during patient stay, on discharge and in the community for an accurate determination of the risk of HAPU; essential for root cause analysis and for tracking the value of quality initiatives. Most importantly, the SEM Scanner can be integrated into existing care pathways and utilised by bedside caregivers to provide real-time information about tissue integrity. Informed clinical decision-making is vital when striving to reduce the number and severity of PU, irrespective of where they originate.

		
O'Brien G, Moore Z, Patton D, et al. (2018) The relationship between nurse's assessment of early pressure ulcer damage and sub epidermal moisture measurement: A prospective explorative study. J Tissue Viability 27(4):232–7	• Patients and follow up: Mean age 74.7 ± 14 years; mean Norton score, 12; mean follow up 7.8 ± 4.2 days • n=19 (40%) had abnormal skin by VSA • 21 Stage 1 PU developed on the sacrum (n=17; 91%) and heels (left, n=3, 14%; right, n=1, 5%); all had elevated SEM deltas before visual signs of damage (100% sensitivity) • Specificity was 83%; false positives had insufficient follow up time • Medium correlation (r=0.47) between VSA and SEM outcomes for patients who developed a Stage 1 PU was recorded • VSA and SEM Scanner outcome correlations: Strong for the sacrum (r=0.65); medium for the right heel (r=0.43); low for the left heel (r=0.23) • SEM Scanner detected damage on day 1.5 ± 1.4; VSA detected PU on day 5.5 ± 2.5, 4 days earlier than VSA (Figure)	This study confirms the feasibility of SEM measurement adjunctive to current methods of assessing for early stage PUs, enabling improved methods of risk assessment to quantify patient risk for PUs. SEM measurement detected damage, on average, 4 days sooner than Stage 1 PUs were visually detected. The SEM Scanner had high sensitivity and specificity scores for Stage 1 PUs.

		
Raizman R, MacNeil M and Rappl L (2018) Utility of a sensor-based technology to assist in the prevention of pressure ulcers: A clinical comparison. Int Wound J 15(3):1033–44	• Phase 1: 12/89 patients (13.5%) developed a PU indicating that the Hawthorne effect, whereby practice changes as a result of using the SEM Scanner, did not influence implementation of care • Phase 2: 2/195 patients (1%) developed a PU • Reduction in PU: 93% when SEM Scanner outcomes guided preventative interventions  **FIGURE 2** Monthly prevalence and incidence rates for SHN Dec 2014 to Dec 2016. Abbreviations: SHN, Scarborough Health Network [Colour figure can be viewed at wileyonlinelibrary.com]	PU rates dropped significantly between Phase 1 and Phase 2 when the scanner was incorporated into initial and ongoing patient assessment. The 93% reduction in HAPU mirrors results reported by similar hospitals that used the SEM and achieved a reduction in HAPU of 100%. Working towards a goal of zero was not only ethical but also seemed reachable. In Phase I nurses did not change their practice in

		prevention strategies and nosocomial rates did not decrease. The addition of scanning did not significantly impact assessment time, and interventions followed standard protocols from risk assessment and visual inspection. The 93% decrease in PU incidence was attributed to the use of the SEM Scanner to guide interventions.

5 Details of relevant studies

Please give details of all relevant studies (all studies in table 4). Copy and paste a new table into the document for each study. Please use 1 table per study.

Study SEM200–003	
How are the findings relevant to the decision problem?	Most pressure ulcers are considered preventable and reversible if identified in the early stage of ulceration. The generally accepted methods for detecting or diagnosing pressure ulcers include a Risk Assessment Tool and a comprehensive skin and tissue assessment, commonly known as a "visual skin assessment" (VSA). These are regarded as a non-quantitative and unreliable assessment. This study showed that the SEM Scanner was shown to be a very effective device in the quantitative detection of pressure ulcers. Accuracy exceeded 80% for both sacrum and heels when a within-subject change in SEM Scanner reading of >0.5 is utilised. SEM Scanner readings are unlikely to be adversely affected by patient-specific factors, such as comorbidities or skin-tone. The use of within-subject change as the distinguishing factor minimises the potential for influence by other patient-specific characteristics.
Does this evidence support any of the claimed benefits for the technology? If so, which?	The SEM200–003 protocol is a cross-sectional, data collection study of the SEM Scanner under clinical investigational use as a non-significant risk device. It brings objective information that would be helpful as an adjunct to clinical judgement and the current standard of care. Early identification of increased risk of PUs is key to prevention of injury progression and in the development of effective prevention and treatment plans. Because the SEM Scanner provides measurable quantitative data prior to the visual identification of the presence or non-presence of tissue injury, the implication is that the paradigm for framing the approach to PU prevention is disrupted and must be reconsidered.
Will any information from this study be used in the economic model?	Yes
What are the limitations of this evidence?	No limitations
How was the study funded?	The study was funded by BBI LLC

SEM200–004	
How are the findings relevant to the decision problem?	Improvement in the absolute (quantitative early detection of pressure ulcers over current visual-based standard of care. When combined with the SEM study 003 the results identify the variation in the healthy tissue being represented as flat whilst unhealthy tissue is inflamed.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Accurate and quantitative early detection of pressure ulcers.
Will any information from this study be used in the economic model?	Yes
What are the limitations of this evidence?	No limitations
How was the study funded?	This study was funded by BBI LLC

SEM200–800	
How are the findings relevant to the decision problem?	Improvement in the absolute (quantitative) early detection of pressure ulcers over current visual-based standard of care.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Demonstrates the sensitivity and specificity of the SEM Scanner for detection of early pressure ulcers in patients before pressure ulcers are diagnosed through clinical judgment, giving a window of 5 days earlier awareness of increased risk. Enables anatomically specific interventions.
Will any information from this study be used in the economic model?	Yes
What are the limitations of this evidence?	No limitations
How was the study funded?	This study was funded by BBI LLC

Pressure Ulcer Reduction Programme	
How are the findings relevant to the decision problem?	Current visual assessment to detect pressure ulcers is inadequate. The subsequent burden of treatment is time and labour intensive with significant cost-utility implications to the NHS.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Yes, in terms of overall reduction in PU incidence: 92% weighted reduction in HAPU was identified. In addition, the healthcare practitioners reported that 63% patients received additional preventative interventions. 79% sites reported zero HAPU during the PURP.
Will any information from this study be used in the economic model?	Yes
What are the limitations of this evidence?	No limitations
How was the study funded?	The PURPs were supported by loan of the SEM Scanners in most circumstances. BBI personnel supported through training and education.

6 Adverse events

Describe any adverse events and outcomes associated with the technology in national regulatory databases such as those maintained by the MHRA and FDA (Maude). Please provide links and references.

On December 20th, 2018, the FDA classified and authorised the SEM Scanner (Model 200) under Section 513(f)(2) (*de novo*) with a classification product code "QEF" (Pressure Ulcer Management Tool) (https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN170021.pdf).

The FDA database was searched for the product code "QEF" returning only the SEM Scanner (Model 200) in the results.

Search of the FDA recall database with the term "capacitance" returned one result. For recall event ID 69369 and recall number Z-0149-2015, a class 2 device named Freedom Evo 2 was recalled in 2014.The Freedom EVO is an open automation platform product for general laboratory use. It is intended for routine laboratory tasks, such as general-purpose pipetting and general-purpose liquid handling and robotic processes. As such, this device does not bear any resemblance either in principle or practice to the SEM 200 series. Also, the Freedom Evo 2 and the SEM Scanner do not fall under the same product classification category.

Based on this search, the market data shows that capacitance-based devices are safe, as there have been no injuries reported since 1976.

A search of the FDA adverse databases (MAUDE, MDR and MedSun) with search dates from 1976 to April 30th, 2019 using the product code "" QEF" and, or "Capacitance" did not return any adverse events. Therefore, we can conclude that the device is safe when used as intended.

Critical Evaluation of The Safety Data from Literature Search

Several different devices were used in the reviewed articles, none being exactly the same as the SEM Scanner and no safety-related issues were identified in those reviewed articles. However, in functional principles and electrical properties, the SEM Scanner is equivalent to the devices used as research tools in these articles. Biocapacitance monitoring using small amplitude signals from a battery-operated device, such as the SEM Scanner, pose little safety risk for clinicians or patients**.**

Safety Data from Use of Sem Scanner

Since product launch of the SEM Scanner in commercial distribution in the European Union, no incidents have been reported with the SEM Scanner. Furthermore, no adverse events have been observed from use of the device during the clinical studies (over 270 subjects) conducted thus far. The SEM Scanner continues to demonstrate its safety from use on patients as well as users.

Describe any adverse events and outcomes associated with the technology in the clinical evidence.

The clinical studies listed in section 4 (Tables 1 and 4) and reviewed in the qualitative data synthesis (in section 7) demonstrates that devices comparable to the SEM Scanner are generally safe. To further ensure safety, patient-contacting material components of the SEM Scanner were tested for biocompatibility and the results show that the materials are biocompatible. In addition, no adverse events to patients or users have been reported from SEM Scanner use during clinical studies or post-commercial use in the clinic. Patient acceptance of skin scanning is similar to visual inspection and using colour scales.

The Risk Management process indicates that no significant risks have gone unmitigated. The main benefit of the SEM Scanner is that, if it is used as directed and intended, its introduction to the market should modernise the care pathway in order to support a decrease in the total prevalence of tissue damage and pressure ulcers. BBI asserts that the benefits of the SEM Scanner outweigh the minimal risks.

SEM Scanner continues to demonstrate its safety both from commercial use in the clinic and observed under investigations described above. And thus, risks are clinically and significantly negligible and have remained unchanged from the original Risk Management analyses conducted for this device.

7 Evidence synthesis and meta-analysis

Although evidence synthesis and meta-analyses are not necessary for a submission, they are encouraged if data are available to support such an approach.

If an evidence synthesis is not considered appropriate, please instead complete the section on qualitative review.

If a quantitative evidence synthesis is appropriate, describe the methods used. Include a rationale for the studies selected.

Please see qualitative review in section, Qualitative review”

Report all relevant results, including diagrams if appropriate.

Please see qualitative review in section, Qualitative review”

Explain the main findings and conclusions drawn from the evidence synthesis.

Please see qualitative review in section, Qualitative review”

Qualitative review

Please only complete this section if a quantitative evidence synthesis is not appropriate. Explain why a quantitative review is not appropriate and instead provide a qualitative review. This review should summarise the overall results of the individual studies with reference to their critical appraisal.

Presented here is a full qualitative review of the results that includes a limited quantitative review synthesis. This was deemed the most appropriate way to present the overall objectives of the clinical programme, based on previous evidence, and the evidence itself, derived from the key clinical studies.

This section provides the product's safety and effectiveness for its intended use based on device performance under clinical investigational use labelling and commercial use. Clinical data validating the product's effectiveness is referenced in **Table 1** below. The following sub-sections present a detailed discussion of the respective studies and demonstration of clinical utility for reducing PUs that have been observed to date upon implementation of the SEM Scanner into the clinical setting.

Table 1: Clinical Testing

Sub-sections	Subsection Name	Number of Subjects/Patients	Product Performance - Evidence
7.3.1	SEM200–003 & SEM200–004	125 (SEM200–003) 50 (SEM200–004)	Development of cut-off algorithm (SEM Delta)
7.3.2	SEM200–008	182 (Intent-to-Treat, ITT)	Primary support of indications for use and labelling claims
7.3.3	Clinical Impact of Real-World Use	1160 patients	Clinical impact from introduction of SEM Scanner into the care facility worldwide

BBI developed the SEM Scanner to provide objective, quantitative information about the physiological condition of tissue most susceptible to pressure induced injury, and to do so significantly earlier than is possible via current clinical judgement alone. By alerting practitioners to increased risk of PU earlier in development, the SEM Scanner can inform the clinical judgement of preventive care timing, anatomical site, and intensity of intervention measures needed.

No single solution addresses the lack of objective evidence to confirm early tissue damage; therefore, we proceeded with a sequence of evaluations to converge on demonstrating product performance in the clinical setting. The first was to demonstrate the ability of the SEM Scanner to determine differences in pressure-damaged tissue (study SEM200–003) and no pressure-damaged tissue (study SEM200–004). And lastly, demonstrate that there was "agreement" between SEM Scanner and VSA to identify pressure ulcers and to confirm number of days of early detection (study SEM200–008). The study, SEM200–008, was constructed as a prospective, longitudinal

comparison to VSA.

The determination of sensitivity, and not specificity, in the SEM200–008 study was the focus due to the device's ability to measure against an objective evidence of a true positive, but the absence of sufficient evidence to invalidate a false positive. To clarify, visible pressure damage compared with the SEM Scanner is a comparison between two definitive outcomes and thus serves to confirm prior study results (the SEM200–003 and SEM200–004 studies). However, due to the inability of the current standard of care to detect early reversible damage, the studies on no-wound status between VSA and the SEM Scanner are highly subjective at best, which can give the false impression of low specificity. Therefore, the evaluations as discussed above form the evidence needed to demonstrate performance of the SEM Scanner for a product of this kind that is used as an adjunct to clinical judgment.

The SEM Scanner has been evaluated in three key clinical studies (discussed below), totaling 357 subjects. These studies have demonstrated that the SEM Scanner has considerable clinical benefit for use as an adjunct to the standard of care for early identification of increased risk of pressure ulcers.

SEM200–003 & SEM200–004

Two preliminary clinical studies were conducted in human subjects to demonstrate device feasibility for safety and performance of its intended use in measuring differences between tissues noted with pre-existing pressure ulcers, adjacent tissue, and tissue without pressure ulcers. Based on Investigators' feedback, the heel and sacrum were primarily chosen for SEM Scanner measurements in these studies as these locations are most frequently impacted by pressure-induced tissue damage.

The first study (SEM003 Final Study Report, **Appendix**) was conducted in 125 residents of nursing homes or similar care facilities with confirmed stage I or II pressure ulcers or suspected deep tissue injuries. The primary objective of the study was to compare SEM Scanner readings from the centres of confirmed stage I or II pressure ulcers or deep tissue injuries (hereon collectively referred to as "wounds") against SEM Scanner readings from the area surrounding the wound ("spatial readings"). The secondary objective was to assess the safety and patient tolerability of the SEM Scanner. Based on the interim data, an additional objective was included to compare spatial readings in subjects affected and unaffected by wounds. To accomplish this additional objective, 50 subjects unaffected by wounds were recruited under a separate protocol (SEM200–004). A copy of SEM004 Final Study Report is enclosed in **Appendix**.

Subjects enrolled in SEM200–003 were on average 82 years old and 58% female. The subjects were predominantly white (67%) followed by Asian (18%) and Hispanic (7%). Subjects were either residents at long-term nursing facilities (96%) or residents at assisted living facilities (4%); 65% of the subjects were fully dependent upon a caregiver for daily activities and 94% were at risk for pressure ulcers based on the Braden scale (total score ≤18).

All enrolled subjects were evaluated at a single anatomical (wound) location except for four subjects who presented with wounds on both heels and were assessed at both heels. Therefore, the study enrolled 125 subjects and assessed 129 wounds. Just over 10% of both heel and sacral wounds were considered recurring. Distribution of the classified wounds is summarised in **Table 2** below.

Table 2: Distribution of Classified Wounds

SEM200–003 Enrolled Subjects, 129 wounds		
"Wound" Classification	Heels	Sacrum
Stage I	21%	64%
Stage II (with intact blisters)	0%	4.5%
Suspected Deep Tissue Injury (sDTI)	79%	32%

SEM Scanner readings were collected at the centre of the wound and at up to 16 points around the wound. The wound was defined as the discoloured tissue at and around a bony prominence (usually heel or sacrum). The discoloured tissue of the wound is noted by reddened tissue known as erythema (early stage pressure ulcer) or purple/maroon tissue (sDTI). The region outside the wounded area was defined as the non-discoloured tissue surrounding the discoloured tissue. In this study, the "edge of erythema" refers to the demarcation between the discoloured and the non-discoloured tissue, regardless of whether the wound is a pressure ulcer or sDTI. In this study, SEM Scanner readings collected outside of the edge of erythema were hypothesised to represent readings from tissue unaffected by the wound.

For a given wound, SEM Scanner readings were collected at the centre of the wound and at up to 8 points within the wound as shown in the figure below (Rings 1 and 2, boxes 1–8) and 8 points outside of the edge of erythema (Rings 3 and 4, boxes 9–16) in each of the Northern, Southern, Western and Eastern directions (**Figure 1**).

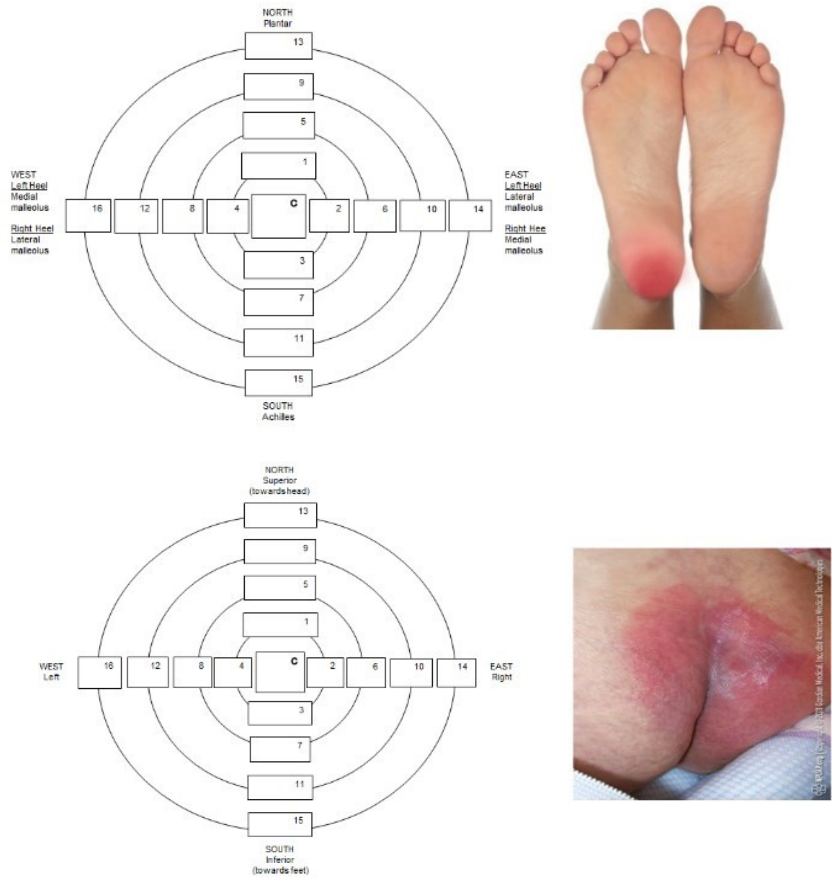


Figure 1: Spatial Guide to SEM Scanner Readings on the Heel and Sacrum

In addition to the collection of SEM Scanner readings, clinicians determined the stage and severity of the wound using VSA, the current standard method for diagnosing pressure damage. Pressure ulcer risk assessment tools — the Braden Scale and the skin type question of the Waterlow Scale — were also completed to categorise risk of the enrolled subjects.

To demonstrate the study's primary objective, SEM Scanner readings were collected at the centers of wounds for comparison to readings taken at designated points within the wound (inside the edge of erythema) and outside the wounded area (outside the edge of erythema). The mean SEM Scanner reading at the center of the heel wounds was 1.87 (standard deviation, SD=0.84). The mean SEM Scanner reading from wound center was lower and increased with each subsequent Ring distance away as it moved towards outside the edge of erythema, indicating that the SEM Scanner was detecting changes in moisture levels from the center of the wound to the periphery. SEM Scanner readings at the center of heel wound were statistically significantly lower than the average of the SEM Scanner readings collected at Rings 2, 3, and 4 (all p-values <0.01). The results observed in heel wounds are summarised in **Table 3** below (as an example). Similar results were observed for wounds on the sacrum.

Table 3: Summary of Results by Ring for Wounds on Heels

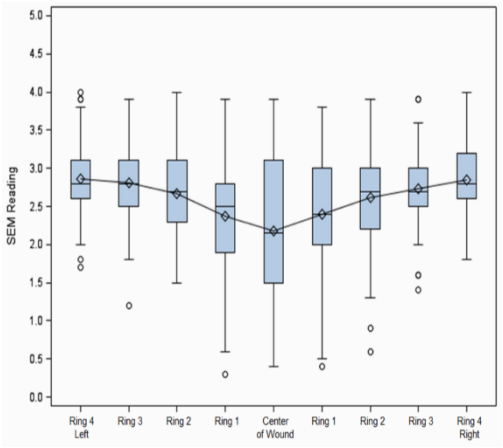
	SEM Scanner Placement				
	Centre	**Ring 1**	**Ring 2**	**Ring 3**	**Ring 4**
Estimates					
Mean (SE)	1.87 (0.09)	1.97 (0.08)	2.07 (0.08)	2.13 (0.08)	2.19 (0.08)
95% CI	(1.70, 2.05)	(1.82, 2.12)	(1.92, 2.22)	(1.98, 2.28)	(2.05, 2.34)
Comparisons to Centre					
Difference (SE)		0.10 (0.07)	0.19 (0.07)	0.25 (0.07)	0.32 (0.07)
95% CI		(-0.03, 0.23)	(0.06, 0.32)	(0.13, 0.38)	(0.19, 0.45)
2-sided p-value		0.139	0.004	< 0.001	< 0.001

Abbreviations: CI=confidence Interval; SE=standard error

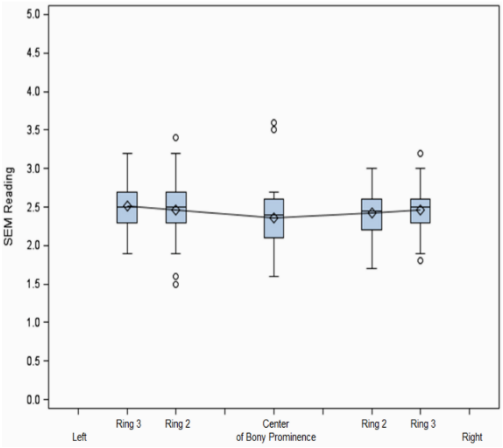
An exploratory analysis was completed to evaluate the spatial three-dimensional nature of wounds and how it relates to SEM Scanner readings by comparing each assessment point to the centre of the wound. Therefore, evaluation of each assessment point was performed by comparing the SEM Scanner readings in the left to right plane to readings in the superior to inferior plane. In sacral wounds, all of the assessment points outside of the edge of erythema (Rings 3 and 4) were statistically significantly different from the centre (all p values <0.05). When summarised graphically, a V-shaped pattern from the data points was observed (left figure below) with lower SEM Scanner readings at the centres of wounds and higher readings at the periphery. This V-shaped pattern reflects the nature of pressure damage whereby the SEM Scanner readings were lower at and around the centre of the wound (lower moisture, cell death) as compared to those in the periphery of the wound. A similar pattern was observed for wounds on heels.

For comparison to subjects with wounds discussed above, a companion study was conducted on subjects without wounds (SEM200–004). The hypothesis was that a different pattern would be observed in subjects without wounds. Under the companion SEM200–004, clinicians used the centre of the bony prominence (just above the gluteal cleft) to approximate the "centre" of a wound for subjects unaffected by wounds. Spatial SEM Scanner readings were collected to include the

centre and adjacent points from the centre to assess whether the same V-shaped pattern is observed in subjects without wounds (**Figure 2**). Similar spatial pattern analysis (described above) was performed for SEM200–004, whereby a different pattern emerged – generally level (or flat) pattern – for subjects unaffected by wounds (right figure below). This generally level (or flat) spatial pattern indicates that the moisture levels in subjects without wounds did not vary greatly from the centre of the bony prominence to the periphery, which is as expected in tissue unaffected by tissue damage ("healthy").



SEM Scanner Readings from Wounded Tissue at the Sacrum
Source: SEM200–003 Final Study Report, Fig 14



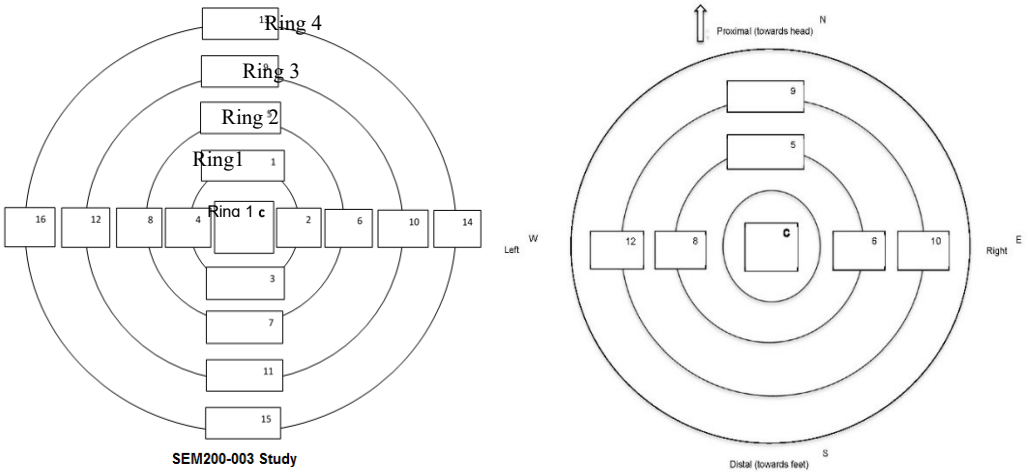
SEM Scanner Readings from Healthy Tissue at the Sacrum
Source: SEM200–004 Final Study Report, Fig 4

Figure 2: Box Plot of SEM Scanner Readings for Sacrum With and Without Wounds

The different spatial patterns in subjects with and without wounds demonstrate that the SEM Scanner 200 does accurately detect differences in moisture (also known as sub-epidermal moisture or localised oedema) levels under the skin, an early indicator of pressure damage.

The comparison of spatial SEM Scanner readings between subjects affected with wounds (SEM200–003) and subjects unaffected (SEM200–004) led to the consideration of within-subject variation as an identifying feature of pressure ulcers. A range of algorithms was constructed and assessed to best determine how to classify subjects as having "wounded" tissue or "healthy" tissue based on within-subject variation in SEM Scanner readings.

The size of the wound was calculated from SEM200–003 to proxy reading locations that would most likely capture the within-subject SEM values for centre of the wound and the tissue around it (damaged or healthy) to detect a large enough difference in tissue health surrounding the bony prominence. To develop the appropriate algorithm, locations for SEM Scanner readings were selected from affected wounds data and unaffected wounds data for inclusion in the algorithm analysis. Based on this analysis and practicality of use in the care facility (since measuring 16 points is impractical), 6 points was selected at the sacrum and 4 points at the heel to serve as the measurement locations for detecting SEM changes in tissue with signs of early damage. For pressure ulcers, it was assumed that readings within the edge of erythema (centre, Ring 1, and Ring 2) would constitute "wounded" tissue and that readings outside the edge of erythema (Ring 3 and Ring 4) would constitute "unwounded" tissue. These locations are identified in the table (**Table 4**) and figure (**Figure 3**) below.



SEM200–004 Study
Figure 3: Spatial Locations for SEM Scanner Readings

Table 4. Locations for SEM Scanner Readings

	Centre	**Ring 2**				**Ring 3**			
	C	5	6	7	8	9	10	11	12
Sacrum	√	√	√		√		√		√
Heel	√					√	√		√

Further, a variety of cut-off thresholds was reviewed for desirable performance on sensitivity and specificity (**Table 5**):

Table 5: SEM200–003/–004 Cut-off Thresholds

SEM Delta Cut-off (Positive*)	**SEM200–003/–004 Sensitivity and Specificity - Combined Sacrum and Heels**			
	Sensitivity	95% CI	Specificity	95% CI
$\Delta \geq 0.6$	82%	74%, 88%	51%	41%, 61%
$\Delta \geq 0.7$	80%	72%, 86%	56%	46%, 66%
$\Delta \geq 0.8$	74%	65%, 81%	70%	60%, 78%

* Positive here refers to indication of presence of damage

The SEM Scanner algorithm demonstrated sensitivity as high as 91% and specificity as high as 70%. To validate the algorithm in future studies and compare against existing tools, a single cut-off value of $\Delta \geq 0.6$ with sensitivity of 82% and specificity of 51% was selected. The $\Delta \geq 0.6$ cut-off was intended to be conservative, with the understanding of a trade-off between sensitivity versus specificity. Given the low-risk nature of potential interventions in the event of a false positive (e.g., more frequent turning), the cut-off of $\Delta \geq 0.6$ ensures as many patients as possible are detected, since the risks of a false negative are greater than those of a false positive.

SEM200–008

Prior to designing SEM200–008 protocol (Rev 1), new learnings from Gillian O'Brien's independent investigator study pointed towards viability of clinical interpretation using the $\Delta \geq 0.6$ cut-off. Gillian O'Brien first presented her results at the 2015 Annual Meeting of the European Pressure Ulcer Advisory Panel (EPUAP). Ms. O'Brien's study demonstrated that the SEM Scanner detects skin changes earlier when compared to nurses' visual skin assessment alone. Of the 47 patients enrolled into Ms. O'Brien's study, 19 of her study patients who were noted with consecutive days indicating elevated SEM levels (SEM delta of $\Delta \geq 0.6$ and above) went on to develop visual signs of pressure ulceration. And, more importantly, the SEM Scanner identified early damage on average 3.9 days earlier than the nurses' visual skin assessments. Therefore, the SEM200–008 (Rev 1) study was designed to demonstrate the safety and sensitivity and specificity (effectiveness) of the SEM Scanner.

A copy of the SEM200–008 clinical study report is provided in the **Appendix**.

Study Objectives

The objective of the SEM200–008 study was to demonstrate that the SEM Scanner detects signs of pressure ulcers (SEM delta) earlier in patients than by clinical judgment using signs of pressure ulcer from visual skin assessments (standard of care). This study was conducted under Institutional Review Board (IRB) approved SEM200–008 protocol. The study's primary and secondary objectives are presented below.

- **Primary:** Demonstrate the sensitivity and specificity of the SEM Scanner for detection of early pressure ulcers in patients before pressure ulcers are diagnosed through clinical judgment ("diagnose PU before clinical judgment")

- **Secondary:** Determine the average number of days between detection of early pressure ulcers using the SEM Scanner and diagnosis of pressure ulcers through clinical judgment ("time to detection")

Study Execution

A total of 12 study sites, 3 UK and 9 US centres, participated in this multi-site, longitudinal study. In total, 22.2% were from UK centres and 77.8% of the enrolled subjects were from US centres. This study enrolled a total of 189 subjects, who had provided their written informed consent or by verbal/written consent of the subjects' legally authorised representative, from April through November 2016.

The study was carried out by a clinical study team at each participating site comprised of a Principal Investigator, Study Coordinator, and individuals acting in study roles of "Generalists" and "Specialists." Daily assessments were limited to up to two assessors within each assessment team. Comprising one team, the role of the "Specialist" was assigned to nursing staff who were the facility's experts on wound care to continue "standard of care" evaluations. Comprising a second team, the role of the "Generalist" included individuals who did not provide pressure ulcer care to the enrolled subjects and consisted of a wider range of healthcare providers; wound experts, ward nurses, nursing assistants, or medical assistants. The intent of elevating the role of the Specialist for comparison to the SEM Scanner was to demonstrate the diverse usability of the device for detecting early pressure ulcer in comparison to the "gold standard." The "gold standard" in this case is the clinical judgment of the wound/tissue viability experts.

To evaluate the study's objectives, blinding between assessment teams – the Specialists and Generalists – following standard of care and teams collecting SEM Scanner data was required to ensure that no bias is introduced to clinical judgment by the SEM Scanner results. The Study Coordinator acted as the "gate-keeper" to help maintain blinding. Blinding was successfully upheld between the assessors as it was a straightforward and simple process to follow. In addition to blinding between Specialists and Generalists, the study was also blinded to staff at BBI during enrolments by an independent consultant to BBI (PhD Epidemiologist) managing the Medrio database, an electronic data capture system.

The study allowed for an interim analysis review of sensitivity and specificity after 40 pressure ulcers were identified by the Specialists via visual skin assessments. Enrolments continued while interim analysis was being performed and BBI staff continued to remain blinded until there was a decision to cease enrolments. BBI staff was only alerted of results when the interim analysis was completed. The results are discussed below.

Results – Primary and Secondary Endpoint ITT

Of the 189 subjects, a total of 182 subjects contributed to the intent-to-treat (ITT) data analysis performed per this study's Statistical Analysis Plan (SAP) (SEM200–008 study report in **Appendix**). **Table 6** reflects the distribution of pressure ulcers identified by VSA per Specialists' judgment that went into the ITT analysis.

Table 6: Pressure Ulcer (PU) Classification Included in ITT Analysis

	ITT (N = 182*)					
	All		Sacrum		Heels	
PU Classification, n = 48**	n	%	n	%	n	%
Stage I	32	66.7%	12	25%	20	41.7%
Stage II	3	6.3%	3	6.3%	0	0.0%
Stage III - IV	0	0.0%	0	0.0%	0	0.0%
Unstageable	2	4.2%	0	0.0%	2	4.2%
sDTI	11	22.9%	1	2.1%	10	20.8%

Table Source: Table 8b in SEM200–008 Final Study Report
*Excludes 8606 and 8707 pressure ulcers because of non-analysable data; not part of ITT
**Excludes Sacrum PUs w/insufficient SEM valid series for comparison: 81418, 81609, 81610, 8607, 8608

- The study was successful in meeting the sensitivity endpoint with demonstration of earlier detection of damage before standard of care. The SEM Scanner detected PUs 5 days (median) before nurse Visual Skin Assessment

- ITT study results demonstrated a sensitivity of 87.5% (95% CI: 74.8%–95.3%) for detecting pressure ulcers between the SEM Scanner and clinical judgment per visual skin assessment. This is in line with prior studies using the SEM Scanner that showed a sensitivity of 82% (003/004 study; 95% CI: 74%–88%) in subjects with pre-existing conditions (no PU and intact-skin PU) for comparison

- **Table 7** presents the primary endpoint analysis based on two out of three observation days ("2 out of 3 days") with SEM delta values of greater than $\Delta \geq 0.6$ (e.g., $\Delta \geq 0.7$, etc.)

Table 7: ITT Population - Primary Endpoint Sensitivity and Specificity (SEM delta >0.5); 2 out of 3 days

Number of Days Positive - 2 out of 3; ITT (N = 182)		
	All Locations	
Parameter	SPC+	SPC-
SEM+	42	257
SEM-	6	124
Sensitivity	87.5%	
(95% CI)	(74.8% - 95.3%)	
Specificity	32.6%	
(95% CI)	(27.9%–37.5%)	

Table Source: Table 8c in SEM200–008 Final Study Report (showing all locations per SAP)

Key:
SPC+ = Specialist visual skin assessment identification of a pressure ulcer
SPC- = Specialist visual skin assessment with no identification of a pressure ulcer
SEM+ = SEM Scanner with SEM delta $\Delta \geq 0.6$
SEM- = SEM Scanner with SEM delta $\Delta < 0.6$

Secondary endpoint is only analysed for subjects identified with positive detection (pressure ulcer by Specialist and SEM Scanner with delta $\Delta \geq 0.6$). The number of days is the difference between pressure ulcer diagnosis by clinical judgment of the Specialist and the first day of SEM delta $\Delta \geq 0.6$ ("time to detection") with the first valid series per SAP analysis rule. **Table 8** presents the mean, standard deviation, median, and range of days analysed for the secondary endpoint from this study. The data showed that of the 42 pressure ulcers identified as "true positive" in the ITT population, the SEM Scanner detected the first signs of pressure damage under the skin by a median of 5 days earlier (mean 4.74, SD 2.39) than visual evidence by skin assessments. In some cases, the first indication of damage by SEM Scanner was up to 12 days earlier than by visual skin assessment of the Specialists. With an advantage of 5 median days earlier than visually identifiable signs suggests that the SEM Scanner would provide a tremendous benefit to clinicians to instigate anatomically specific interventions earlier than standard of care today.

Table 8: Secondary Endpoint Results (n = 42 pressure ulcers; ITT)

Days Between First SEM Scanner Delta $\Delta \geq 0.6$ to Specialist Confirming a Pressure Ulcer	**All (combined heels & sacrum)**
N	42
Mean (SD)	4.74 (2.39)
Median	5.00
Min, Max	1.00, 12.00

Table Source: Table 9 from SEM200–008 Final Study Report (showing all only per SAP)

The ITT study results showed a specificity of 32.6% (95% CI: 27.9%–37.5%) in this study. This is lower than results from prior studies (SEM200–003/–004) involving subjects that were enrolled with pre-determined pressure ulcers ("positives") and no pressure ulcers ("negatives"), whereby results

showed a specificity of 51% (95% CI: 41%–61%). Interestingly, the specificity noted in this study was likely impacted by several contributing factors that are further discussed below.

Consistent with all prior studies, no device related adverse events were reported in this study from use of the SEM Scanner.

Discussion

The primary endpoint of sensitivity was achieved by comparing the SEM deltas to visual inspection for PU diagnosis. Achieving the secondary endpoint reinforces that the scanner is helpful in detecting pressure damage earlier than the current standard of care.

These data promoted the question, “Why did sensitivity show broad agreement, but specificity showed lower agreement of 33%?” The following factors were considered to have contributed to the observed specificity in this study.

(1) Damage threshold: A positive SEM delta and negative VSA for the same suspected PU may both be true; changes in tissue consistency may be present even if not detected by VSA

Research on the damage threshold demonstrates that tissue damage occurs before it is visible. Refer to **Figure 4** below. For that reason, the 2014 international NPUAP/EPUAP/PPPIA guideline recommends consideration of other signs in addition to inspecting skin for erythema (e.g., oedema, skin temperature change, change in tissue consistency), especially in darker skin toned individuals whereby signs of blanchable erythema is difficult to perform.

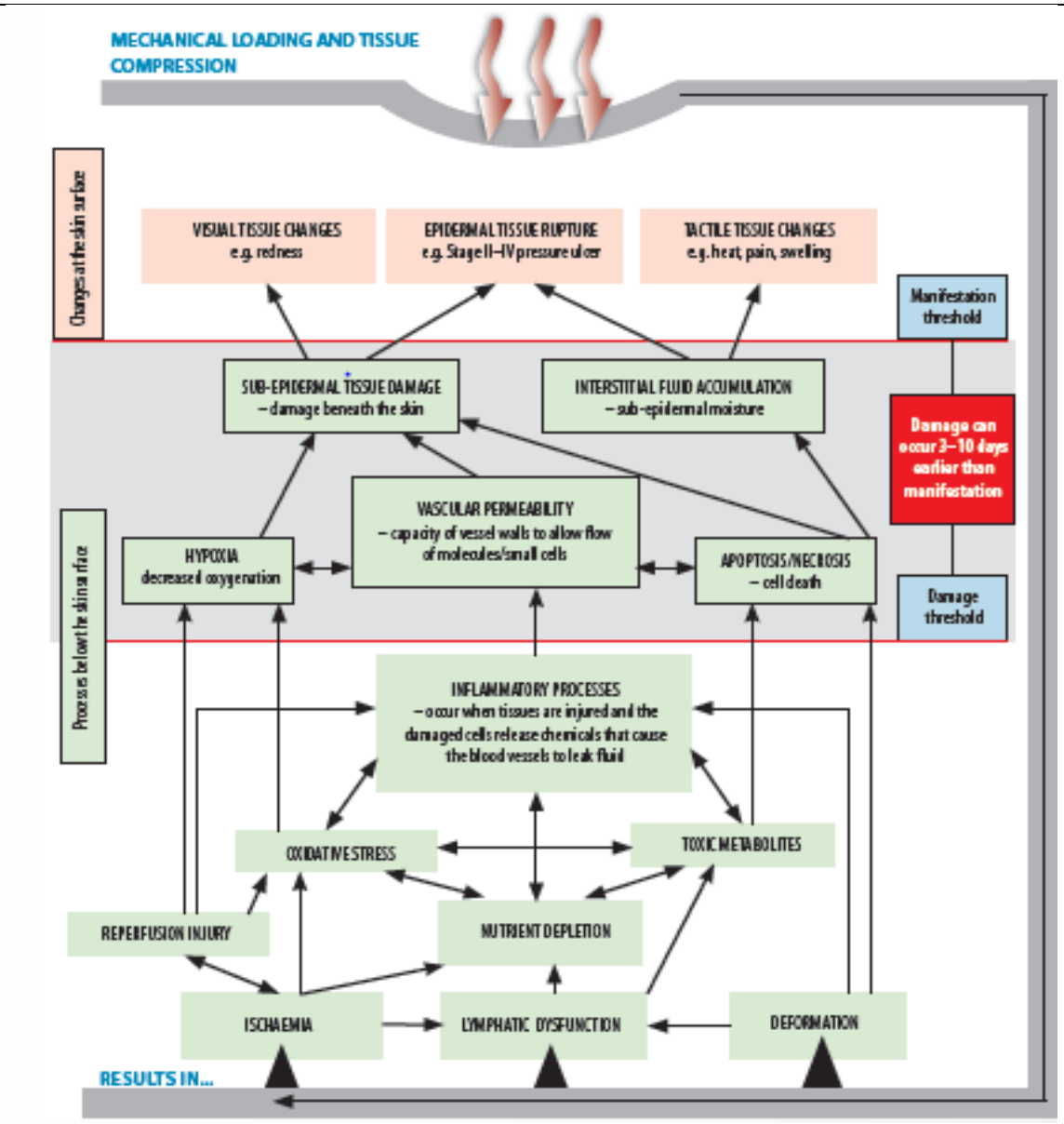


Figure 4: Conceptual Illustration of Biological Processes that Lead to Tissue Damage (Adapted from Moore et al., 2017)

(2) Reversibility and self-resolution: Independent researchers demonstrated the inherent reversible nature of early pressure damage

As illustrated in the conceptual figure above, and as stated by Oomens et al., 2015, "…tissue damage is initiated at the cellular level" and "unloading the tissue will restore the supply of oxygen and nutrients to the tissue" to return tissue to homeostasis. For example, Halfens et al., 2001, showed epidemiologically that of all grade 1 pressure ulcers in his study (n=68, acute-care), a portion, upon later re-examination, resolved (22.1%); a portion deteriorated (22.1%); a portion stayed the same (35.3%); and a portion (20.6%) disappeared (thought to be an initial misdiagnosis or resolution). Although it is not possible to distinguish between damage that will and will not reverse, application of the right interventions (e.g., unloading) provided before the damage threshold is reached results in tissue "resetting" to "normal homeostasis," via the restoration of oxygen supply and nutrients to the tissue and removal of waste products. In addition, Swisher et al., 2015, published a rat study demonstrating that impedance technology could measure non-visible tissue damage also showed that pressure damage to tissue can, and will, reverse when the tissue is unloaded. In Swisher's study, they induced pressure ulcers in rats and observed evidence of

reversibility in their 1-hr ischaemia cycle compared to those with irreversible damage in their 3-hr ischaemia cycle group.

Whether a wound will result depends on the balance between damage and the repair capacity and this can be different for each individual patient. Factors including individual metabolism, tissue properties, medical conditions, and the degree of ischaemia are known to affect the recovery period in which tissue can be restored to its unloaded state and functional integrity.

In this study, it is highly likely (see next point) that early detection of damage was reversed by interventions. The advantage of the SEM Scanner as an adjunct to the clinician's judgment is informative up to five days earlier of damage before VSA; therefore, providing an earlier trigger for decision-making on prevention measures to implement, with high certainty, at the specific anatomical site.

(3) Interventions: In this study, it would have been unethical to withhold prevention measures

The data show that intensive forms of prevention measures (repositioning every 1 or 2 hours, heel boots and elevations, and active and low air mattress support systems) were provided to 89.6% of the enrolled subjects (**Table 9**) while 10.4% received less intense forms of preventive care (e.g., static bed mattress, topical agents, lower turning frequency). Studies have shown that high levels of intervention and preventive care can significantly reduce the incidence of pressure ulcers.

The high level of interventions in SEM200–008 likely led to reversals of tissue damage, as noted above, and therefore, even if the SEM Scanner was able to detect changes in tissue damage, VSA alone was not.

Table 9: Preventive Measures (ITT, N = 182)

	Preventive Measures, ITT (N = 182)		
Patients receiving high level of prevention	**n**	**%**	**Weighted Average of total stay***
	163	89.6%	70.0%
Repositioning			
Turn every 1 hour	5	2.7%	38.4%
Turn every 2 hours	154	84.6%	93.0%
Support System			
Active Air Mattress	32	17.6%	81.3%
Low Air Loss Mattress	119	65.4%	86.5%
Heel Off-Loading			
Heel Boot	34	18.7%	55.9%
Heel Elevation	121	66.5%	65.3%

*Weighted average is calculated from each individual patient's interventions recorded each day

Table Source: Table 10 in SEM200–008 Final Study Report

A review of the level of preventive measures provided to the subjects relative to risk assessment suggests that an overwhelming number of interventions were provided despite their risk scores (as shown in **Table 10**; number of 2 or more preventive measures).

Table 10: High Tier Preventive Measures vs. Day 0 Risk Assessment (Total Score)

	ITT (N = 182)									
Number of High Tier Level of Preventive Measures Provided	Braden ≤18 (n=155)		Braden >18 (n=2)		Waterlow ≥10 (n=13)		Waterlow <10 (n=3)		No D0 - Risk Assessment (n=9)	
	n	%	n	%	n	%	n	%	n	%
0	6	3%	0	0%	11	6%	2	1%	0	0%
1	4	2%	0	0%	2	1%	0	0%	0	0%
2	32	39%	1	1%	0	0%	1	1%	6	3%
3	87	48%	0	0%	0	0%	0	0%	3	2%
4	26	14%	0	0%	0	0%	0	0%	0	0%
5	0	0%	1	1%	0	0%	0	0%	0	0%

Table Source: Table 11 in SEM200–008 Final Study Report

Given that early pressure damage can be reversed, it is likely that interventions in this study were a contributing factor in pressure damage not manifesting into visible damage.

(4) Variable nature of clinical judgement: PU prevention includes risk assessment scales such as Waterlow, Braden, and Norton; visual skin assessment; and clinical judgment, all of which are subjective, dependent on training and experience

This study utilised clinicians with a high level of experience in VSA, and still in 4% (7/182) of the ITT population, there were negative diagnoses from VSA that under the international guidelines would have classified as a pressure ulcer. This represents an additional 7 instances of a positive instance of a pressure ulcer to the 48 PUs classified by VSA.

A review of other signs of skin changes, particularly red and blanchable, skin temperature and firmness, were noted that did not get classified as a pressure ulcer is presented in **Table 11**. These other signs may indicate early pressure damage, and as such would represent an almost threefold increase in the potential for diagnosis of pressure ulcer damage. The data showed that 94% of subjects who were identified with these other skin changes by VSA also had SEM delta values indicating presence of damage (positive). Similarly, in 74% of cases identified with no other signs of skin changes by VSA, SEM deltas also indicated absence of damage (negative). However, currently there is no standard of care method for Specialists to classify pressure ulcer with non-visible damage.

Table 11: Other Signs of Skin Changes vs. Diagnosed Pressure Ulcer of Red and Non-Blanchable

	ITT (N = 182)		
	All	**Sacrum**	**Heels**
Current NPUAP/EPUAP/PPIA (2014)	n	n	n
Diagnosed PU's	48	16	32
Red and Non-Blanchable (No PrU)	7	1	6
Total	55	17	38
Other signs of skin changes (No PrU)			
Red and Blanchable	67	21	46
Changes in skin temperature (either cool/warm)	57	13	44
Changes in skin firmness	15	4	11
Total	139	38	101

Table Source: Table 12 in SEM200–008 Final Study Report

(5) Device performance: We additionally considered the possibility that the device failed to perform for specificity as targeted for analysis at a single cut-off

In determining the broadest cut-off to use for clinical interpretation of the SEM delta, a range of cut-offs had been explored and considered. The SEM delta of >0.5 cut-off was decided upon as it provided the most conservative value, since the goal was to detect as early and as many for prevention. A review of the range of SEM delta cut-offs in this study is summarised in **Table 12** Inclusion of a range of cut-off provides a scale for clinical decision making depending upon clinical care risk profiles of the patient.

Table 12: SEM200-008 Range of SEM Δ

SEM Positive 2 of 3 days	**ITT (N = 182)**					
	Sensitivity			**Specificity**		
SEM Δ	n	%	95% CI	n	%	95% CI
Δ ≥0.6	42	87.5%	74.8%, 95.3%	124	32.6%	27.9%, 37.5%
Δ ≥0.7	39	81.3%	67.4%, 91.1%	170	44.6%	39.6%, 49.8%
Δ ≥0.8	32	66.7%	51.6%, 79.6%	227	59.6%	54.5%, 65.6%

Conclusion

The primary objective of this study was to demonstrate the sensitivity and specificity of the SEM Scanner compared to standard of care via visual skin assessments. A total of 189 subjects were enrolled in the SEM200–008 study under Rev 1 protocol. Enrolments were completed between April to November 2016 from 12 clinical facilities with three in the UK and nine in the US.

Data collected from 182 of those subjects were included into the ITT population endpoint analysis. In the ITT population, 48 subjects were identified by visual skin assessments performed by the study's Specialists. The study met its primary sensitivity endpoint with positive detection success yielding a sensitivity of 87.5% (CI: 74.8% - 95.3%) and its secondary endpoint of demonstrating that the SEM Scanner can detect signs of pressure ulcers on an average of 4.74 days (SD 2.39; range: 1.00–12.00) earlier than visual skin assessments by the Specialists.

This study did not meet the targeted endpoint for specificity of at least 55%. Given the comparison of non-visual to visual skin damage it is not surprising that a lower specificity is observed in this study. Particularly, when one reviews the contributing factors:

1. Pressure ulcer is classified based on visual signs of damage
2. Device is designed to measure tissue changes under the skin relative to damage that is not yet visible
3. Study design was structured to observe how early the SEM Scanner can detect signs under the skin before visual damage as determined by standard of care means
4. Pressure ulcer is reversible when prevention measures are implemented early – published in multiple literature sources
5. High level of prevention measures (repositioning every 1 or 2 hours, heel boots and elevations, and active and low air mattress support systems) were provided to 89.6% of the enrolled subjects

In addition, data from the 003/004 studies clearly show that the SEM Scanner does have discriminating powers. In these studies, the device was used to scan 50 healthy subjects (004) and 125 PUs (003). The studies showed strong agreement between the SEM Scanner and clinical truth (damaged or healthy tissue), with 87% agreement for the positives/damaged (sensitivity) and 88% agreement for the negatives/healthy (specificity).

The results in this study continue to demonstrate the product's performance to correctly identify pressure ulcers with high agreement ("sensitivity") to standard of care using visual signs, and the device is capable of early detection of pressure ulcers. Despite the lower than expected specificity observed in this study, coupled with little to no risk from use of the device, one can appreciate the potential benefit of its intended use as an adjunct to clinical decision-making for early detection of pressure ulcers.

Clinical Impact of Real World Use

When the SEM Scanner was launched in the European Union (EU) in 2014, BBI introduced the Pressure Ulcer Reduction Programme (PURP) as part of the clinical evaluation process of the impact in a variety of care settings.

Programme Objective

The objective of the SEM Scanner PURP is to provide healthcare practitioners with the option to evaluate the clinical impact of implementation of the SEM Scanner when incorporated into the clinical workflow of care facilities for pressure ulcer prevention and management care procedures over a 1 to 6-month period. This clinical evaluation programme allows clinicians a systematic approach to assess several factors prior to purchasing the SEM Scanner, including:

1. Clinical Impact – as measured by hospital-acquired pressure ulcers (HAPU) change (e.g., reduction from historical)

2. Financial Impact – as measured by cost-savings and productivity

3. Nurse Experience (e.g., ease of use, safety) – as provided in post-evaluation surveys and verbally from the users of the SEM Scanner after PURP completion, and by PIs as presented in scientific posters and presentations

PURPs have now been conducted at care facilities in the UK, Ireland, Spain, Belgium and Canada.

Programme Structure

PURP is structured for evaluation of the SEM Scanner when used as an adjunct to clinical assessment with a target to reduce avoidable hospital-acquired pressure ulcers (HAPUs). The programme was structured to include the following elements in Parts 1 and 2.

Part 1 – Preparation:

PURP Evaluators	Individuals (“participants”) who were selected by the hospital and consisted of wound care specialists, nurses and clinicians as they represent the intended user profiles.
Lead Clinician	The main contact liaison between the hospital and BBI.
Training	Participants completed a series of training activities including device training. Representatives from BBI’s Clinical Specialist Team provided support throughout the evaluation period. Training activities included elements involving:

	a. Clinical orientation – a didactic review and education on the role of sub-epidermal moisture in pressure-induced tissue damage b. Product demonstration – detailed didactics and hands-on demonstration with "tips" on proper positioning of device on skin (e.g., what is good vs better placement position). Included in demonstration is a review on device operations, cleaning, placement locations, and clinical interpretation of SEM delta (0.6 and above may indicate damage). Participants were asked to demonstrate comprehension on use of the device by completing a reverse hands-on exercise by demonstrating on the participants and/or each other
Pressure Ulcer Mapping Exercise	Participants completed a device placement exercise by using it on patients with an existing Stage I pressure ulcer. This exercise was recommended to assist clinicians with understanding the relationship of spatial readings using the SEM Scanner in areas with visible damage versus adjacent tissue.
Collate pre-PURP HAPU data	Data is collated for a defined period to act as a comparison for the PURP period.

Part 2 – Evaluation:

a. Take daily SEM Scanner readings on patients identified at risk for developing HAPU on the wards of PURP evaluators. Scan sacrum and both heels (when applicable)

b. Record daily SEM delta values on sacrum and both heels (when applicable), Visual Skin Observations of tissue health (e.g., redness), identification of HAPU (if observed), and indicate if prevention/intervention measures had been provided for that day

c. Along with clinical assessments, PURP evaluators were to provide preventive measures when SEM delta scores of 0.6 or above were noted. Patients were intervened upon using hospital's pressure ulcer prevention and management protocol

d. Evaluate performance by assessing the "pre"/"post" HAPU rates. The "pre" rate for each PURP centre was based on the historical monthly HAPU rates (all grades) for up to 1-year prior of the ward in the program

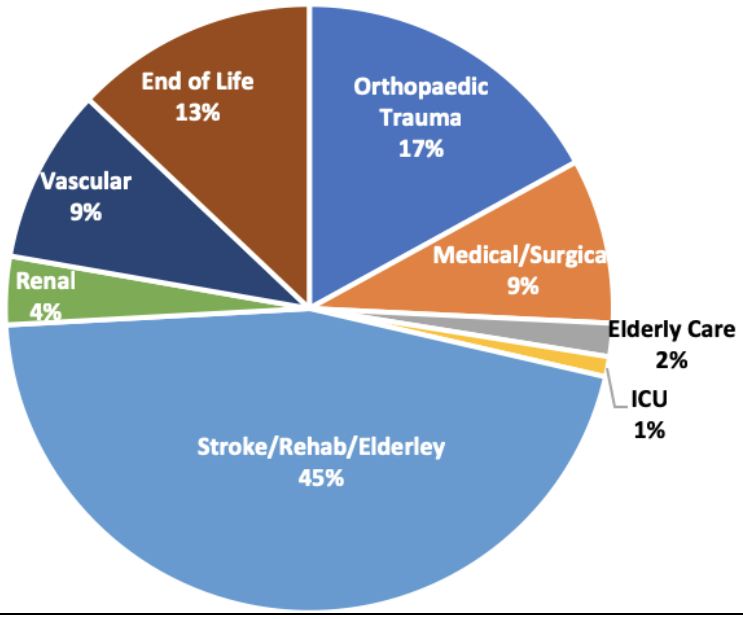
PURP Data Collection

PURP data collection included daily data review and completion of participant questionnaire after the completion of the individual's evaluation. PURP participants collected daily review of sacrum and heel(s) as well as their skin assessments, interventions provided, and diagnosis of skin status (no pressure ulcer or pressure ulcer by classification). PURP participants recorded the information on data record sheets they utilised for their respective PURP evaluations. BBI asked PURP participants to complete a questionnaire post-evaluation regarding their experience with use of the SEM Scanner and its clinical utility.

Results

The summary of aggregated data collected from 15 care facilities involved in PURP from 2014 to 2019 included a variety of departments which represent the patient population in the NHS (Figure 5). In total, 1160 patients are included in this aggregate data.

Figure 5: Percentage of Patients Per Care Setting: PURP To Date



PURP results show:

- 79% of the participating hospitals observed zero HAPUs during the evaluation period
- Weighted reduction in HAPU of 92% was reported from 14 acute care sites
- 1 end of life care site achieved a 47% reduction in HAPU
- 63% patients received additional preventative interventions
- 52% healthcare practitioners reported that the data impacted on their clinical decision making

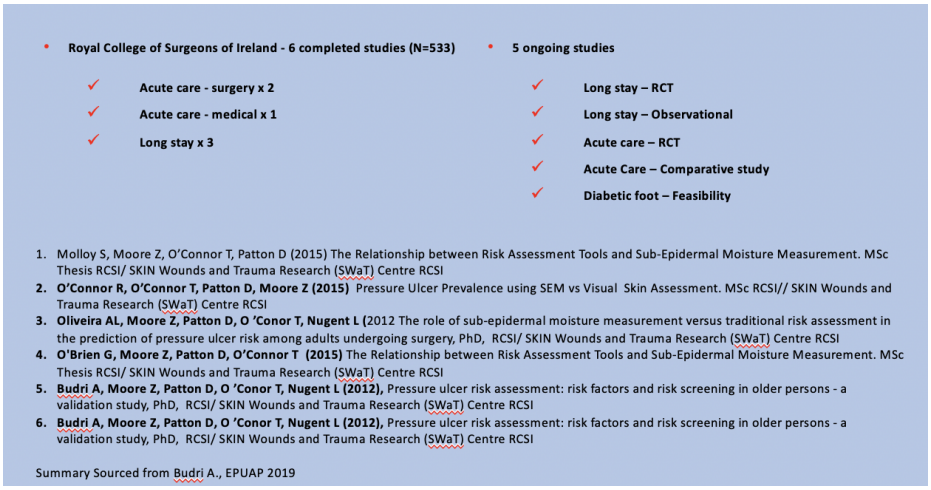
Discussion

The objective of the PURP programme is to provide real-world evidence of use of SEM Scanner as an adjunct in a prevention focused protocol to:

- From visually manifested to earlier: Identify increased risk of PU earlier than visual skin assessment
- From subjective to objective: Act on objective, anatomically specific data
- From total body, to anatomy specific: Allows shift from whole body preventions to anatomically specific interventions
- No increase in staff numbers. No new staff needed
- No additional interventional equipment required
- Limitations – varying length of PURP programmes, small number for short time period – analysis shows impact remains

PURP users have shown the benefits observed from use of the SEM Scanner. From real-world perspective, the data suggest that the SEM Scanner aids in clinical assessment and decision making for prevention of pressure ulcer by providing quantitative, real-time information about patient's tissue health to facilitate earlier and targeted intervention. This is reflective of the intended use of the SEM Scanner as an adjunct to clinical judgment for early identification of increased risk of pressure ulcers.

The Royal College of Surgeons of Ireland have also conducted a series of studies including the SEM Scanner – the data below is a summary of the current and ongoing activities.



8 Summary and interpretation of clinical evidence

Summarise the main clinical evidence, highlighting the clinical benefit and any risks relating to adverse events from the technology.

Summary of evidence from clinical studies

The SEM Scanner has been evaluated in three key clinical studies in the United Kingdom and United States, totalling 357 subjects. For early stage pressure ulcer risk identification, it was necessary to perform a series of evaluations that in total would provide the necessary evidence. First was to *characterise* differences in confirmed pressure-damaged tissue (study SEM200–003) and no pressure-damaged tissue (study SEM200–004) with the SEM Scanner. Then, demonstrate *agreement* between SEM Scanner and VSA and early identification of pressure ulcer risk (study SEM200–008) in a prospective, longitudinal multi-site study within the clinical setting. The determination of sensitivity, and not specificity, in this last study was the focus due to our ability to have objective evidence of a true positive but the absence of sufficient evidence to invalidate false positive. Therefore, the evaluations as discussed above, when combined, form the evidence needed to demonstrate performance of the SEM Scanner for a product of this kind that is used as an adjunct to clinical judgment for early identification of increased risk of pressure ulcers.

In two initial clinical studies conducted by the company, the SEM Scanner was used to assess sacral and heel regions in persons affected and unaffected by pressure ulcers. These studies enrolled 125 subjects with pressure ulcers, involving 129 wounds (e.g., Stage I/II and deep tissue injury), as well as 50 unaffected study subjects. An algorithm was developed with a range of cut-off thresholds from the results

indicating a sensitivity of 82% and a specificity of 51% at the conservative cut-off of SEM delta of >0.5. These results indicate that SEM Scanner readings have considerable clinical utility by providing an objective means of aiding a clinician in the early identification of increased risk of PU.

BBI conducted a multi-site clinical study designed to demonstrate that the SEM Scanner could detect pressure ulcers in patients before pressure ulcers are diagnosed through clinical judgment alone ("diagnose PU before clinical judgment") and the average number of days of early detection ("time to detection"). Study assessments included (i) daily Risk Assessment and (ii) daily Skin Assessment performed by the Specialist blinded to the SEM readings; and (iii) daily SEM Scanner readings collected by the Generalist blinded to the Risk and Skin assessments. The presence or absence of a pressure ulcer was ultimately diagnosed by the Specialist based upon clinical judgment via skin assessment.

This study showed a sensitivity of 88% (95% CI: 75–95%) and a specificity of 33% (95% CI: 28–38%) for early detection of pressure ulcers observed in the intent-to-treat population. The range was also calculated for a $\Delta \geq 0.7$ cut-off showing a sensitivity of 81.3% and specificity of 44.6%; and for a $\Delta \geq 0.8$ cut-off showing a sensitivity of 66.7% and a specificity of 59.6%. The data also demonstrated that the SEM Scanner identified signs of potential pressure damage on average as early as 4.74 days (SD 2.39; range: 1.00, 12.00) before visual skin assessment alone.

Summary of real-world evidence

When the SEM Scanner was launched in the European Union and Canada, BBI introduced the Pressure Ulcer Reduction Programme (PURP) to provide an opportunity for potential customers to conduct evaluations of the product. PURP was conducted at multiple hospitals in the United Kingdom, Ireland, Belgium, Spain, and Canada. The programme was structured to evaluate the impact on the rate of hospital-acquired pressure ulcers (HAPU) and the ability to incorporate use of the SEM Scanner into the existing care pathways over a period of one to six months.

In total, aggregated data was shared with BBI from 15 participating PURP hospitals, which included 1160 patients who were scanned (heel, sacrum) using the SEM Scanner. The 15 PURP hospitals comprised of a diverse range of acute facilities units from emergency, elderly care, orthopaedic trauma, and intensive care unit (ICU) departments and, additionally, one end of life facility. In 79% of PURP participating hospitals the nurses observed zero HAPUs during the evaluation period whilst a 92% weighted HAPU reduction rate was achieved in the Acute Care Facilities.

In summary, BBI has presented robust data to demonstrate that the SEM Scanner is safe and effective for its proposed indication for use. These data demonstrate that the benefits of the device outweigh the risks. These data provide a strong basis for NICE to publish a MedTech Guidance supporting the use in clinical practice, which will allow clinicians and patients to benefit from this greatly needed tool to aid in reducing the incidence of PUs in the NHS. Each time a PU is prevented it preserves a patient's quality of life and averts the possibility of a life- threatening injury occurring.

Briefly discuss the relevance of the evidence base to the scope. This should focus on the claimed benefits described in the scope and the quality and quantity of the included studies.

The SEM Scanner is used as an adjunct to standard NHS clinical practice. It is recognised by the NHS that collecting and understating data on the causes of harm is a key tenet of quality improvement approaches in healthcare. Accurate measurement must accompany a quality improvement method to make changes and improve outcomes for service users and patients (NHS Pressure Ulcers: Revised definition and measurement, 2018).

The decision problem therefore centres on the limitations of current strategies to predict the development of pressure ulcers based on visual skin assessment techniques and Risk Assessment Tools. The use of the SEM Scanner in clinical studies 003, 004, 008 and the real-world data generated for the PURP (see section 4) directly addresses the benefit of using the SEM Scanner according to the following criteria laid out in the decision problem:

- Complications avoided by pressure ulcer prevention
- Additional length of hospital stay due to development of pressure ulcers (including ICU and conventional ward days)
- Patient compliance and the use of pressure ulcer prevention strategies
- Ease of use

Healthcare providers currently have no objective, accurate and anatomically specific options to i**dentify increased risk of PU**. Current options primarily include visual and tactile assessments that, as previously noted, have varying outcomes based on the skill and training of the individual performing the assessment.

Early identification of increased risk can benefit patients by leading to the potential reversal of tissue damage, and by allowing healthcare practitioners to manage the tissue damage while the skin is still intact. If the damage is not detected early, it can result in broken skin, which often requires medical or surgical interventions to heal, at greater risk to the patient and greater costs to the healthcare system. The clinical studies reviewed in section 4 have shown that the SEM Scanner can accurately distinguish between damaged and undamaged skin, and, when used as an adjunct to clinical judgment, it can do so approximately 5 days prior to detection by v**isual skin assessment** alone, and, in some instances, up to 12 days earlier.

Identify any factors which might be different between the patients in the submitted studies and patients having routine care in the UK NHS.

NHS Improvement (2019) highlights that pressure ulcers can affect anyone from newborns to those at the end of life. Pressure ulcers can cause significant pain and distress for patients and can contribute to longer stays in hospital, increasing the risk of complications, including infection. The NHS recognise that pressure ulcers may occur in a variety of care settings including acute care settings, hospices, ICUs and care homes. It is recognised by the NHS that collecting and understanding data on the causes of harm is a key tenet of quality improvement approaches in healthcare. Accurate measurement must accompany a quality improvement method to make changes and improve outcomes for service users and patients (NHS Pressure Ulcers: Revised definition and measurement, 2018).

Describe any criteria that would be used in clinical practice to select patients for whom the technology would be most appropriate.

In the current SOC patients are identified at risk of pressure ulcers through the use of Risk Assessment Tools (Waterlow, Braden, Purpose T and Norton being the most common.) and Visual Skin Assessment. The SEM Scanner should be used as an adjunct to these tools. The technology can be used on admission to help identify those at risk and then daily thereafter.

Briefly summarise the strengths and limitations of the clinical evidence for the technology.

For patients with tissue damage, early **identification of risk** is critical to prevent manifestation **of the pressure ulcer at the skin surface.**

Healthcare providers currently have limited options to detect pressure damage. These options primarily include visual and tactile assessments that, as previously noted, have varying outcomes based on the skill and training of the individual performing the assessment. The SEM Scanner…..

1. From subjective to objective
2. From acting on visually manifest PUs to acting on the biomarker (earlier)
3. From whole body to anatomy specific
4. From treating broken skin ulcers to keeping skin intact

Early identification of risk can benefit patients by leading to the potential reversal of tissue damage, and by allowing HCPs to manage the tissue damage while the skin is still intact. If the damage is not detected early, it can result in broken skin, which often requires medical or surgical interventions to heal, at greater risk to the patient and greater costs to the healthcare system.

The clinical studies reviewed in section 4 have shown that the SEM Scanner can accurately distinguish between damaged and undamaged skin, and, when used as an adjunct to clinical judgment, it can do so approximately 5 days prior to detection by VSA alone, and, in some instances, up to 12 days earlier.

At the proposed cut-off of ≥0.6 the sensitivity of the device ranges from 88% to 67%. These sensitivity levels all demonstrate a high likelihood of a patient experiencing one or more benefits from use of the SEM Scanner; in all cases, the likelihood of a patient experiencing one or more benefits from use of the SEM scanner is higher than the likelihood of a patient experiencing a benefit from the current standard of care; clinical judgment alone.

The benefits to the patient can be realised without any corresponding device-related serious or non-serious adverse events. To date, there have been no device-related serious or non-serious adverse events associated with use of the SEM Scanner. The probability of a harmful effect from use of the device is extraordinarily low, given that the device is used on intact skin and is not intended to be relied upon for diagnosis or treatment. The only potential for a harmful effect may stem from cross-contamination of the device, in the event the clinician does not properly sterilise the device between uses. Because the device is intended for use only in healthcare settings, should cross-contamination occur, the patient would receive immediate care to prevent development of an infection, e.g., antibiotics. To date, there have been no reported incidents of cross contamination from use the SEM Scanner.

Risks

The SEM Scanner is intended to be used by an HCP as an adjunct to clinical judgment and is not meant to be used as a stand-alone diagnostic. To date, there have been no device-related serious adverse events associated with use of the SEM Scanner. No device related events have been reported during clinical investigational use in studies, nor commercially reported. All potential device-related risks associated with use of the SEM Scanner have been mitigated to the lowest extent possible.

If the SEM deltas indicate increased risk of tissue damage (e.g., SEM delta of 0.6 and above), the values must be viewed with consideration of the clinician's expertise and judgment based on other clinical signs of patient's overall health and tissue state. And thus, a couple of likely outcomes from clinician's decision would ensue:

1) If the clinician determines that no tissue damage is present, the prevailing standard of care procedures are followed per the healthcare facility's pressure ulcer prevention and management programme. The patient would continue to receive the standard care plan
2) If the clinician chooses to provide intervention measures to the patient and the intervention is not necessary, there exists no additive risk to the patient. Instead, the patient could receive a higher level of intervention measures such as more frequent turning of the patient or use of a heel boot
3) Potentially, there is more risk associated with a false negative result, but this risk is mitigated by the intended adjunctive use of the device. As noted, the clinician will be responsible for determining whether to intervene based not only on the SEM delta, but also on his or her own judgment. Therefore, if the SEM delta indicates the absence of tissue damage, but the clinician assesses the patient and determines the presence of tissue damage, the clinician may properly intervene. If both the SEM Scanner and the clinician determine the absence of pressure damage, when such damage does exist, the patient is no worse off than if the clinician defers to their judgment

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Please include all references below using NICE's standard referencing style.

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Moore Z, Patton D, Rhodes SL et al. (2017) Subepidermal moisture (SEM) and bioimpedance: A literature review of a novel method for early detection of pressure-induced tissue damage (pressure ulcers). Int Wound J 14(2):331–7

Moore Z and Patton D (2019) Risk assessment tools for the prevention of pressure ulcers. Cochrane Database Systematic Review: doi: 10.1002/14651858.CD006471.pub4

NICE. Clinical guideline CG179 [online; accessed 1 October 2019]

NICE. Costing statement: Pressure ulcers. Implementing the NICE guideline on pressure ulcers (CG179) [online; accessed 1 October 2019]

NHS Improvement. Stop the pressure. Helping to fight pressure ulcers [online; accessed 1 October 2019]

NHS: Pressure ulcers: Revised definition and measurement summary and recommendations June 2018 [online; accessed 1 October 2019]
NHS Safety Thermometer Analysis – Deloitte Health Analytics on behalf of BBI LLC

NHS. Stop Pressure Ulcer Campaign [online; accessed 1 October 2019]

O'Brien G, Moore Z, Patton D, et al. (2018) The relationship between nurse's assessment of early pressure ulcer damage and sub epidermal moisture measurement: A prospective explorative study. J Tissue Viability 27(4):232–7

O'Keeffe S and McClusky P (2019) Evaluation Of Novel Sub-Epidermal Moisture (SEM) Technology In Early Pressure Ulcer Detection Versus Conventional Techniques [abstract]. In: Proceedings of the Tissue Viability Society meeting, 1st–2nd May 2019, Southampton, UK

Okonkwo H, Bryant R and Milne J (2018) Evaluation of a novel device using capabilities of the detection of early pressure ulcers (PU), a multi-site longitudinal study [abstract]. In: Proceedings of the 50th Annual Wound Ostomy and Continence Nurses (WOCN) society meeting, June 3rd–6th 2018, Philadelphia, USA (Manuscript in review at Wound Repair and Regeneration, manuscript number WRR-18-06-0175.R1)

Okonkwo H (2018) Differentiating between healthy tissue and early stage pressure injuries: A pilot study of effectiveness of the SEM scanner [abstract]. In: Proceedings of the 50th Annual Wound Ostomy and Continence Nurses (WOCN) society meeting, June 3rd–6th 2018, Philadelphia, USA (Manuscript Gershon S et al submitted to Journal of Wound Care)

Okonkwo H, Milne J and Bryant R (2018) Evaluation of a novel device using capacitance of the detection of early pressure ulcers (PU), a multi-site longitudinal study [abstract]. In: Proceedings of the National Pressure Ulcer Advisory Panel (NPUAP) meeting, 2nd–3rd March 2018, Las Vegas, Nevada, USA (Manuscript in review process with Wound Repair and Regeneration. Manuscript ID WRR-18-06-0175.R1, entitled "A Blinded Clinical Study of SEM Scanner 200, a Capacitance Measurement Device, for Early Detection of Pressure Injury)

Ore N, Gallagher M and Fox-Smith C (2019) Striving for Perfect Care – Preventing skin breakdown in the community setting in the UK [abstract]. In: Proceedings of the 21st Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, 18th–20th September 2019, Lyon, France

Oomens CWJ, Bader DL, Loerakker S et al. (2015) Pressure induced deep tissue injury explained. Annals of Biomedical Engineering 43(2):297–305

Padula WV, Mishra MK, Makic MB et al. (2011) Improving the quality of pressure ulcer care with prevention: A cost-effectiveness analysis. Med Care 49(4):385–92

Paek R, Chang DS, Brevetti LS et al. (2002) Correlation of a simple direct measurement of muscle pO(2) to a clinical ischemia index and histology in a rat model of chronic severe hindlimb ischemia. Journal of Vascular Surgery 36(1):172–9

Peko Cohen L and Gefen A (2019) Phantom testing of the sensitivity and precision of a sub-epidermal moisture scanner. Int Wound J 16(4):979–88

Raizman R, MacNeil M and Rappl L (2018) Utility of a sensor-based technology to assist in the prevention of pressure ulcers: A clinical comparison. Int Wound J 15(3):1033–44

Ross G and Gefen A (2019) Assessment of sub-epidermal moisture by direct measurement of tissue Biocapacitance. Medical Engineering and Physics: doi: 10.1016/j.medengphy.2019.07.011

Schubert V and Fagrell B (1989) Local skin pressure and its effect on skin microcirculation as evaluated by laser–Doppler fluxmetry. Clinical Physiology and Functional Imaging 9(6):535–45

Smith G (2019) Improved clinical outcomes in pressure ulcer prevention using the SEM scanner. J Wound Care 28(5):278–82

Swisher SL, Lin MC, Liao A et al. (2015) Impedance sensing device enables early detection of pressure ulcers in vivo. Nature communications 17(6):6575

10 Appendices

Appendix A: Search strategy for clinical evidence

Describe the process and methods used to identify and select the studies relevant to the technology. Include searches for published studies, abstracts and ongoing studies in separate tables as appropriate. See section 2 of the user guide for full details of how to complete this section.

Date search conducted:	September 2019
Date span of search:	1980-Present

List the complete search strategies used, including all the search terms: text words (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean). List the databases that were searched.

Data Search Strategy
PubMed
Queries performed using PubMed automatically assume use of a AND operator between separate terms unless quotation marks are used to group terms. Hence, the term pressure ulcer will be interpreted as a search for both terms pressure AND ulcer appearing anywhere within an article, whereas the term “pressure ulcer” will produce a search where the words pressure ulcer appear together. In addition, most articles in the PubMed database have medical subject headings (MeSH) assigned to them. Relevant search words or strings were selected from the PubMed MeSH listing, and when used in this search strategy such terms are indicated by an accompanying [MeSH].
The search terms chosen were selected based upon knowledge of general terms used in clinical description of localized tissue edema and pressure ulcer detection methodologies. Additionally, terms related to scientific methods related to bioelectrical capacitance measurement principles were selected.
The following queries will be used in the literature search:

1. “Pressure Ulcer” AND detection AND erythema
2. “Pressure Ulcer” AND detection AND edema
3. Skin AND impedance AND edema
4. Skin AND impedance AND “pressure ulcer”
5. Skin AND impedance AND erythema
6. Skin AND capacitance AND edema
7. Skin AND capacitance AND “pressure ulcer”
8. Skin AND capacitance AND erythema
9. Skin AND dielectric AND edema
10. Skin AND dielectric AND erythema
11. Skin AND dielectric AND “pressure ulcer”
12. "Pressure Ulcer/prevention and control"[Mesh] AND detection
13. "Erythema/diagnosis"[Mesh] AND skin
14. "Erythema/diagnosis"[Mesh] AND” pressure ulcer”
15. "Erythema/diagnosis"[Mesh] AND impedance

16. "Electrophysiology"[Mesh] AND skin
17. "Electrophysiology"[Mesh] AND edema
18. "Electrophysiology"[Mesh] AND “pressure ulcer”
19. "Dielectric Spectroscopy"[Mesh] AND skin
20. "Dielectric Spectroscopy"[Mesh] AND edema
21. "Dielectric Spectroscopy"[Mesh] AND “pressure ulcer”
22. "Pressure Ulcer"[Mesh] AND ("Electric Impedance"[Mesh] OR "Electric Capacitance"[Mesh])
23. “Pressure Ulcer” AND moisture AND damage
24. Epidermal AND moisture AND damage
25. Erythema AND skin AND moisture
26. “Pressure induced” AND damage AND tissue
27. “Pressure induced” AND damage AND skin
28. “Pressure Ulcer” AND damage AND tissue
29. “Pressure Ulcer” AND “Pressure induced”
30. “Surface electrical capacitance” AND “Damage” AND “tissue”
31. “Surface electrical capacitance” AND “Damage” AND “skin”

Brief details of any additional searches, such as searches of company or professional organisation databases (include a description of each database):

Not applicable

Inclusion and exclusion criteria:

For the PubMed literature search, all articles recovered using these search terms will be inspected and only articles meeting all of the following acceptance criteria will be included for analysis in the clinical evaluation report.

- Uses electrical capacitance techniques on the skin of human subjects.
- Full articles (not simply abstracts) with a comprehensible methods section.
- The capacitance measurements had to be made on a local region of human skin, as opposed to “whole body” capacitance techniques that are commonly used to estimate edema of a limb or for body fat analysis.
- Articles are written in English
- At least 20 patients are present within each subgroup examined in the publication. For the FDA database searches, all reports will be included in the analysis.

Data abstraction strategy:

PubMed Search
The PubMed literature search will be executed by methodically querying the PubMed database with each of the queries identified in the protocol.
An excel table will be maintained to capture the search results and selection decisions. For each PubMed query,

- The full listing of results will be captured (bibliographic reference only) and placed into a table (see Template, Clinical Literature Search Reporting Worksheet) that has the Query number and date searched identified
- If the title shows any potential relevance to our selection criteria, the abstract will be reviewed. If the abstract indicates that the article may meet the article selection criteria, the article shall be retrieved
- Upon review of the article there may be discovered additional queries that might be useful in identifying articles. Additionally, specific articles may be listed in the bibliographies of the retrieved articles that did not come up in the database search. These articles may be considered and will be identified in the "Ad-hoc" table

FDA Database Search
For the FDA database queries, an excel export of the results are maintained. The excel reports will be integrated with the PubMed search Excel table. If the search returns no results it will be so noted.

Data Selection Process
A table of all query hits will be generated. The title and abstract will be reviewed and assessed to see if it meets the acceptance criteria. If it doesn't meet the acceptance criteria the reason for exclusion will be provided in the table. If the article merely duplicates clinical data from another article, the reviewer shall make a determination as to which article provides the most relevant detailed data and exclude the other articles that have duplicate data. This reason shall be provided in the table. If the abstract does not provide enough information to determine if the acceptance criteria are met, the full article will be retrieved for further review to see if the acceptance criteria are met.

For articles that meet acceptance criteria the article will be assessed for suitability. Article suitability will be appraised based on the following factors:

- Appropriate Device – were the data generated from the device in question?
- Appropriate Patient Group – were the data generated from a patient group that is representative of the intended treatment population (e.g. age, sex, etc.) and
- Data Source Type – Was the design of the study appropriate?
- Statistical Rigor – Has a statistical analysis of the data been provided and is it appropriate?

For each individual factor a ranking between 1 and 4 is given based upon the table below and the sum of the scores is calculated. A low overall score (under 6 total) means the article is most suitable, whereas a higher score indicates less suitability. The suitability score will be considered during analysis of the articles for the clinical evaluation. Articles with suitability scores greater than 9 will not be included in the final list of clinical literature that is used for assessing performance and safety data.

Ranking	Appropriate device or technique	Appropriate Patient Group	Study Design	Statistical Rigor
1.	Same device as SEM Scanner	Patients are at risk of pressure ulcers	Randomized clinical trials	Clearly defined, statistically significant results
2.	Similar capacitance technique applied to skin	Patients may have localized tissue edema.	Case Control Study	Lack of statistical detail, potentially significant results
3.	Related capacitance technique	Patient's skin is treated to induce tissue irritation/edema.	Case Series	Unclear statistical details
4.	Unclear capacitance technique, but results may support general safety	Patients have unrelated conditions or are normal population.	Individual reports	No statistical detail or not presented

Excluded studies

List any excluded studies below. These are studies that were initially considered for inclusion at the level of full text review, but were later excluded for specific reasons.

Excluded study	Design and intervention(s)	Rationale for exclusion	Company comments
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text

Report the numbers of published studies included and excluded at each stage in an appropriate format (e.g. PRISMA flow diagram).

Enter text.

Structured abstracts for unpublished studies

Study title and authors

Introduction

Objectives

Methods

Results

Conclusion

Article status and expected publication: Provide details of journal and anticipated publication date

Sent as full manuscripts in the data pack

Appendix B: Search strategy for adverse events

Date search conducted:	September 2019
Date span of search:	1980-present

List the complete search strategies used, including all the search terms: text words (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean). List the databases that were searched.

FDA databases
The following criteria will be used in the FDA database searches:

- Product codes = QEF
- The product code classifies Pressure Ulcer Management Tools and is the most relevant type of device to obtain FDA safety data.
- For the MedSun database, they do not accept product codes and thus the term capacitance was searched.

PubMed
Queries performed using PubMed automatically assume use of a AND operator between separate terms unless quotation marks are used to group terms. Hence, the term pressure ulcer will be interpreted as a search for both terms pressure AND ulcer appearing anywhere within an article, whereas the term “pressure ulcer” will produce a search where the words pressure ulcer appear together. In addition, most articles in the PubMed database have medical subject headings (MeSH) assigned to them. Relevant search words or strings were selected from the PubMed MeSH listing, and when used in this search strategy such terms are indicated by an accompanying [MeSH].
The search terms chosen were selected based upon knowledge of general terms used in clinical description of localized tissue edema and pressure ulcer detection methodologies. Additionally, terms related to scientific methods related to bioelectrical capacitance measurement principles were selected.

1. "Pressure Ulcer/prevention and control"[Mesh] AND detection
2. "Erythema/diagnosis"[Mesh] AND skin
3 "Erythema/diagnosis"[Mesh] AND” pressure ulcer”
4. "Erythema/diagnosis"[Mesh] AND impedance
5. "Electrophysiology"[Mesh] AND skin
6. "Electrophysiology"[Mesh] AND edema
7. "Electrophysiology"[Mesh] AND “pressure ulcer”
8. "Dielectric Spectroscopy"[Mesh] AND skin
9. "Dielectric Spectroscopy"[Mesh] AND edema
10. "Dielectric Spectroscopy"[Mesh] AND “pressure ulcer”
11. "Pressure Ulcer"[Mesh] AND ("Electric Impedance"[Mesh] OR "Electric Capacitance"[Mesh])
12. “Pressure Ulcer” AND moisture AND damage
13. Epidermal AND moisture AND damage

14. Erythema AND skin AND moisture
15. “Pressure induced” AND damage AND tissue
16. “Pressure induced” AND damage AND skin
17. “Pressure Ulcer” AND damage AND tissue
18. “Pressure Ulcer” AND “Pressure induced”
19 “Surface electrical capacitance” AND “Damage” AND “tissue”
20. “Surface electrical capacitance” AND “Damage” AND “skin”

Brief details of any additional searches, such as searches of company or professional organisation databases (include a description of each database):

Not applicable

Inclusion and exclusion criteria:

For the PubMed literature search, all articles recovered using these search terms will be inspected and only articles meeting all of the following acceptance criteria will be included for analysis in the clinical evaluation report.

- Uses electrical capacitance techniques on the skin of human subjects
- Full articles (not simply abstracts) with a comprehensible methods section
- The capacitance measurements had to be made on a local region of human skin, as opposed to “whole body” capacitance techniques that are commonly used to estimate edema of a limb or for body fat analysis
- Articles are written in English
- At least 20 patients are present within each subgroup examined in the publication. For the FDA database searches, all reports will be included in the analysis

Data abstraction strategy:

PubMed Search
The PubMed literature search will be executed by methodically querying the PubMed database with each of the queries identified in the protocol.
An excel table will be maintained to capture the search results and selection decisions. For each PubMed query,

- The full listing of results will be captured (bibliographic reference only) and placed into a table (see Template, Clinical Literature Search Reporting Worksheet) that has the Query number and date searched identified
- If the title shows any potential relevance to our selection criteria, the abstract will be reviewed. If the abstract indicates that the article may meet the article selection criteria, the article shall be retrieved
- Upon review of the article there may be discovered additional queries that might be useful in identifying articles. Additionally, specific articles may be listed in the bibliographies of the

retrieved articles that did not come up in the database search. These articles may be considered and will be identified in the “Ad-hoc” table

FDA Database Search
For the FDA database queries, an excel export of the results are maintained. The excel reports will be integrated with the PubMed search Excel table. If the search returns no results it will be so noted.

Data Selection Process
A table of all query hits will be generated. The title and abstract will be reviewed and assessed to see if it meets the acceptance criteria. If it doesn’t meet the acceptance criteria the reason for exclusion will be provided in the table. If the article merely duplicates clinical data from another article, the reviewer shall make a determination as to which article provides the most relevant detailed data and exclude the other articles that have duplicate data. This reason shall be provided in the table. If the abstract does not provide enough information to determine if the acceptance criteria are met, the full article will be retrieved for further review to see if the acceptance criteria are met.

For articles that meet acceptance criteria the article will be assessed for suitability. Article suitability will be appraised based on the following factors:

- Appropriate Device – were the data generated from the device in question?
- Appropriate Patient Group – were the data generated from a patient group that is representative of the intended treatment population (e.g. age, sex, etc.) and
- Data Source Type – Was the design of the study appropriate?
- Statistical Rigor – Has a statistical analysis of the data been provided and is it appropriate?

For each individual factor a ranking between 1 and 4 is given based upon the table below and the sum of the scores is calculated. A low overall score (under 6 total) means the article is most suitable, whereas a higher score indicates less suitability. The suitability score will be considered during analysis of the articles for the clinical evaluation. Articles with suitability scores greater than 9 will not be included in the final list of clinical literature that is used for assessing performance and safety data.

Ranking	Appropriate device or technique	Appropriate Patient Group	Study Design	Statistical Rigor
1.	Same device as SEM Scanner	Patients are at risk of pressure ulcers	Randomized clinical trials	Clearly defined, statistically significant results
2.	Similar capacitance technique applied to skin	Patients may have localized tissue edema.	Case Control Study	Lack of statistical detail, potentially significant results
3.	Related capacitance technique	Patient’s skin is treated to induce tissue irritation/edema.	Case Series	Unclear statistical details
4.	Unclear capacitance technique, but results may support general safety	Patients have unrelated conditions or are normal population.	Individual reports	No statistical detail or not presented

Enter text.

Adverse events evidence

List any relevant studies below. If appropriate, further details on relevant evidence can be added to the adverse events section.

Study	Design and intervention(s)	Details of adverse events	Company comments
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text
Text	Text	Text	Text

Report the numbers of published studies included and excluded at each stage in an appropriate format (e.g. PRISMA flow diagram).

Enter text.

Appendix C: Checklist of confidential information

Please see section 1 of the user guide for instructions on how to complete this section.

Does your submission of evidence contain any confidential information? (please check appropriate box):

No	☐	If no, please proceed to declaration (below)
Yes	☒	If yes, please complete the table below (insert or delete rows as necessary). Ensure that all relevant sections of your submission of evidence are clearly highlighted and underlined in your submission document, and match the information in the table. Please add the referenced confidential content (text, graphs, figures, illustrations, etc.) to which this applies.

Page	Nature of confidential information	Rationale for confidential status	Timeframe of confidentiality restriction
6-7	☒ Commercial in confidence ☐ Academic in confidence Details Enter text.	Page 6-7 referring to Provizio™ SEM Scanner	Commercial Launch during 2020
16	☒ Commercial in confidence ☐ Academic in confidence Details Enter text.	Page 16 referring to BBI Patents Pending	Ongoing

Confidential information declaration

I confirm that:

- all relevant data pertinent to the development of medical technology guidance (MTG) has been disclosed to NICE
- all confidential sections in the submission have been marked correctly
- if I have attached any publication or other information in support of this notification, I have obtained the appropriate permission or paid the appropriate copyright fee to enable my organisation to share this publication or information with NICE.

Please note that NICE does not accept any responsibility for the disclosure of confidential information through publication of documentation on our website that has not been correctly marked. If a completed checklist is not included then NICE will consider all information contained in your submission of evidence as not confidential.

Signed*: ** Must be Medical Director or equivalent*		**Date:**	October 2nd 2019
Print:	Kate Hancock	**Role / organisation:**	Vice President, Marketing and Clinical Communications
Contact email:	K Hancock@bruinbiometrics.com		

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technologies guidance

MT455 SEM Scanner

Company evidence submission

Part 2: Economic evidence

Company name	BBI Europe Ltd
Submission date	30 October 2019
Contains confidential information	Yes / No

Contents

1 Published and unpublished economic evidence

Identification and selection of studies

Complete the following information about the number of studies identified.

Please provide a detailed description of the search strategy used, and a detailed list of any excluded studies, in appendix A.

Number of studies identified in a systematic search.		34 in Total 28 (from Pubmed) 6 in publication process (from BBI)
Number of studies identified as being relevant to the decision problem.		7
Of the relevant studies identified:	Number of published studies.	4 published 4 submitted (by BBI)
	Number of abstracts.	-
	Number of ongoing studies.	2 (PURP and community)

List of relevant studies

In table 1, provide brief details of any published or unpublished economic studies or abstracts identified as being relevant to the decision problem.

For any unpublished studies, please provide a structured abstract in appendix A. If a structured abstract is not available, you must provide a statement from the authors to verify the data provided.

Any data that is submitted in confidence must be correctly highlighted. Please see section 1 of the user guide for how to highlight confidential information. Include any confidential information in appendix C.

Table 1 Summary of all relevant studies (published and unpublished)

Data source	Author, year and location	Patient population and setting	Intervention and comparator	Unit costs	Outcomes and results	Sensitivity analysis and conclusion
SEM200-003/004 004 Manuscript D-19-00455 has been accepted for publication in Advances in Skin and Wound Care. 003/004 Manuscript is in the review process with Journal of Wound Care	Gershon S, Okonkwo H, Rhodes S et al. (2014) SEM Scanner readings to assess pressure induced tissue damage [abstract]. In: Proceedings of the 17th Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, August 27th–29th 2014, Stockholm, Sweden	A total of 125 participants with known pressure ulcers were enrolled into the 003 study; 47% (n=59) had a heel pressure ulcer and 53% (n=66) had a sacral pressure ulcer. Whilst a total of 50 patients without pressure ulcers were enrolled in the 004 study.	SEM Scanner	Capital purchase price is set at £5835 per unit ex VAT	Combining the SEM200 studies 003 and 004 (see clinical data application) the data collected suggests that spatial variability of SEM Scanner readings is effective for distinguishing wounded tissue from healthy tissue. Furthermore, the SEM Scanner readings are unlikely to be confounded by certain patient-specific factors and the SEM Scanner is safe and effective for use in diverse populations as an adjunct to the current standard of care for the detection of pressure-induced tissue damage.	The SEM Scanner has been shown to be an effective device, bringing objective data as an adjunct to the existing care pathway. Early identification of increased risk of pressure ulcers is key to prevention of injury progression and in the development of effective prevention care pathways. As the SEM Scanner provides measurable, quantitative data prior to visual identification of the presence or non-presence of PU, the implication of this finding is that the paradigm for re-framing the approach to pressure ulcer prevention should be reconsidered.

Study SEM200-008 Evaluation of a novel device using capacitance for the detection of early pressure ulcers (PU), a multi-site longitudinal study	Okonkwo H, et al (2018) Evaluation of a novel device using capacitance for the detection of early pressure ulcers (PU), a multi-site longitudinal study [abstract]. In: Proceedings of the National Pressure Ulcer Advisory Panel (NPUAP) meeting, 2nd–3rd March 2018, Las Vegas, Nevada, USA (Manuscript in review process with Wound Repair and Regeneration. Manuscript ID WRR-18-06-0175.R1, entitled "A Blinded Clinical Study of SEM Scanner 200, a Capacitance Measurement Device, for Early Detection of Pressure Injury)	Overall, 189 participants (46.7% males and 53.3% females) were enrolled, (22.2% UK 77.8% US, respectively). Seven participants' data were not analysable, resulting in an intent-to-treat population of 182.	Intervention SEM Scanner. Standard of care based on scores from risk assessment scales (Braden scale, <15; Waterlow scale, ≥10; or Norton scale ≤18).	Capital purchase price is set at £5835 per unit ex VAT	Measurements of the sub-epidermal moisture biomarker using the SEM Scanner demonstrated sensitivity of 87.5% in identifying PIs, relative to the reference standard of skin assessment by wound care specialists. Additionally, SEM scanning produced a positive finding 4.74 days ± 2.39 days earlier than the diagnosis of a PU by skin assessment. This data agrees with the temporal delay of 3-10 days between SEM changes and the appearance of visible or palpable skin changes demonstrated in other studies.	Sensitivity of the SEM Scanner exceeds that of skin assessments alone in its ability to detect the antecedents of a developing PU at particular anatomies. The corroborative finding in this study of an elevation in SEM deltas suggests SEM as a reliable, sub-clinical biomarker of later manifestation of a PU. False negative rates were low (n=6; 3.3%). Sensitivity and specificity of the SEM test in the aggregate as measured by the 67.13% area under the curve exceed that of clinical judgement alone. The SEM test provides 4.74 days of lead time to enable clinicians to take additional preventative initiatives on an anatomically specific location.

Pressure Ulcer Reduction Programme	Hancock K and Lawrence R (2019) Reducing pressure ulcer (PU) incidence through introduction of new technology [abstract]. In: Proceedings of the 21st Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, 18th–20th September 2019, Lyon, France	1160 patients included to date in 5 countries at 15 sites; 11 different care settings. 14 acute care, 1 hospice care. 46,000 data points. 1014 patients were in Acute Care facilities whilst 146 patients were in end of life care.	The SEM Scanner was introduced to healthcare facilities via pressure ulcer reduction programmes (PURP). A PURP enables clinicians to evaluate the impact of including this innovative technology as an adjunct to SoC through a systematic process, without introducing additional staff or new prevention interventional equipment.	Capital purchase price is set at £5835 per unit ex VAT	In the Acute Care cohort the weighted reduction in HAPU was 92%. 79% of sites experienced zero HAPU during the PURP whilst 63% of patients received additional interventions. In the Hospice Care cohort a reduction in HAPU of 47% was achieved.	The results demonstrate that introducing the SEM Scanner as an adjunct in a prevention focused protocol can: • Identify increased risk of PU earlier than visual skin assessment • Enable clinicians to act on objective, anatomically specific data • Allows shift from whole body preventions to anatomically specific interventions • Achieve the results with no increase in staff numbers or additional interventional equipment • 2 sites have tested for the Hawthorne effect and found no Hawthorne effect in place

The cost of pressure ulcers in the United Kingdom Published	Dealey C, Posnett J, Walker A. The cost of pressure ulcers in the United Kingdom. J Wound Care 2012;21(6):261–66.	Resource use was derived from a bottom-up methodology, based on the daily resources required to deliver protocols of care reflecting good clinical practice, with prices reflecting costs to the health and social care system in the UK. This approach was used to estimate treatment costs per episode of care and per patient for ulcers of different severity and level of complications.	Data from this paper would be used to establish the cost of treating pressure ulcers in the UK as a baseline for incorporation to the cost utilisation model.	NA	The cost of treating a pressure ulcer varies from £1214 (category 1) to £14 108 (category IV). Costs increase with ulcer severity because the time to heal is longer and the incidence of complications is higher in more severe cases. "Episode costs increase substantially in the presence of complications, partly because of the higher daily costs of treatment and partly because of the longer episode length."	"Treating PUs represents a significant resource cost to the health and social care system in the UK
The Cost of Pressure Ulcers in the UK. Published.	Age and Ageing Vol. 33. No 3. 2004. Bennett G. Dealey C. Posnett. J	Health and Social. Care System in the UK	Bottom-up methodology, based on daily resources required to deliver protocols of care reflecting good clinical practice in the UK	NA	Total cost is estimated at £1.4 to £2.1bn, 4% of NHS expenditure. Cost per category varies from £1064 for a category 1 to £10551 for a category IV	Pressure Ulcers result in significant costs to the NHS, and are likely to increase as the population ages. A high proportion of the cost is nurse time.

Cohort study evaluating pressure ulcer management in clinical practice in the UK following initial presentation in the community: costs and outcomes. Published	BMJ Open. 2018:8. Guest. J. Fuller G. Vowden P. Vowden K.R	209 community patients who developed a PU identified via The Health Improvement Network (THIN) Database	Retrospective cohort analysis of patient records	NA	Healing time varied according to category of PU from 1 month for category 1 to 10 months for an Unstageable PU. Mean NHS cost of wound care over 12 months was £1400 Category 1 to >£8500 for other Categories. Costs of managing unhealed wounds was 2.4 times that of healed wounds	This analysis identifies the challenges, time and costs of healing pressure ulcers in a cohort of patients.
Health economic burden that wounds impose on the National Health Service in the UK Published	Guest JF, Ayoub N, McIlwraith T, et al. Health economic burden that wounds impose on the National Health Service in the UK. BMJ Open 2015;5:	This was a retrospective cohort analysis of the records of patients in The Health Improvement Network (THIN) Database. Records of 1000 adult patients who had a wound in 2012/2013 were randomly selected and matched with 1000 patients with no history of a wound (controls).	Data from this paper was used to establish the prevalence of pressure ulcers within the NHS for input into the cost utilisation model.	N/A	Estimate: NHS managing 153 000 pressure ulcers per annum. With a national annual prevalence of 0.0031 within UK adult population.	The study identified the prevalence of PU and the incidence of new wounds. The study also reports the resource use particularly that of nurse time. An extrapolation of the data identified a potential volume of 2.2m patients with wounds at an adjusted cost of £5.1bn

Healthy Life-Years Lost and Excess Bed-Days Due to 6 Patient Safety Incidents Empirical Evidence From English Hospitals Published	Hauck KD, Wang S, Vincent C, Smith PC. Med Care. 2017 Feb;55(2):125-130	A cross-sectional analysis of medical records of all inpatients treated in 273 English hospitals in period 2005/6 to 2009/10. Patients with 6 types of preventable incidents were identified: Death in low mortality HRGs; pressure ulcers: central line infections; DVT/PE: post-operative sepsis: post-operative hip fracture	Statistical analysis of Hospital Episode Data	NA	Authors calculated attributable deaths; estimated healthy life years (HLYs) lost and excess bed days. The most relevant outcome to the model is the excess bed days identified in the Pressure Ulcer data which showed the greatest loss in both healthy life years lost and excess bed days at 26 HLYs and 555 days per 100,000 population on average	The authors conclude that to address financial burden concerns then a focus on PU prevention and treatment should be a high priority.
The Determinants of Costs and Length of Stay for Hip Fracture Patients	Castelli A. Daidone S. Jacobs R. Kasteridis P. Street A.D PLoS One. 2015 Jul 23;10(7)	60,000 hip fracture patients in 152 hospitals in England 2009/10	Retrospective analysis of Hospital Episode Data	NA	Authors constructed a care pathway for the cohort and mapped the costs using healthcare resource group data. The costs were allocated per patient. Pressure ulcers were identified to increase length of stay by 8.42 days	Pressure ulcers are reported consistently in the literature to increase patient length of stay – this paper adds to this consensus in a specific cohort of hip fracture patients. This cohort are at particular risk of pressure ulcers and therefore this analysis is of particular relevance to the model

Modernising the pressure ulcer prevention care pathway: a cost-effectiveness analysis	Burns M. King T. Tsang K. Grainger S. Tang S. Submitted to Journal of Wound Care. In review process – manuscript number jowc.2019.0193	Model of 1 year 210 bed acute care hospital	SEM Scanner as an adjunct to standard of care (SoC) compared with standard of care alone	Capital purchase price is set at £5835 per unit ex VAT	Over a 1-year time horizon, the SoC plus SEM Scanner was a dominant option compared with SoC alone. The incidence of HAPUs was lower by 67.4% and costs were lower by £93 per patient at risk. The probability that the SEM Scanner was dominant or cost-effective at a willingness-to-pay threshold of £20,000/QALY was 90%.	The SEM Scanner as an adjunct to standard of care provides important clinical benefits and is a more effective and less costly treatment strategy versus SoC alone in the UK acute care setting.

2 Details of relevant studies

Please give details of all relevant studies (all studies in table 1). Copy and paste a new table into the document for each study. Please use 1 table per study.

SEM200-003/004	
What are main differences in resource use and clinical outcomes between the technologies?	When combined with SEM200 study 004 (see clinical data application) the data collected suggest that spatial variability of SEM Scanner readings is effective for distinguishing wounded tissue from healthy tissue. Furthermore, the SEM Scanner readings are unlikely to be confounded by certain patient-specific factors and the SEM Scanner is safe and effective for use in diverse populations as an adjunct to the current standard of care for the detection of pressure-induced tissue damage. The difference in readings between the two cohorts was significant; p-value ≥0.064 for injured tissue and as low as <0.001 for healthy uninjured regions (SEM Scanner delta values below 0.5 indicated normal tissue). Accuracy measures exceeded 80% for both the sacrum and heels.
How are the findings relevant to the decision problem?	Most pressure ulcers are considered preventable and reversible if identified in the early stage of ulceration. The generally accepted methods for detecting or diagnosing pressure ulcers include a Risk Assessment Tool and a comprehensive skin and tissue assessment, commonly known as a “visual skin assessment” (VSA). These are regarded as a non-quantitative and unreliable assessments. This study demonstrated that the SEM Scanner was an effective device in the quantitative detection of pressure ulcers. Accuracy exceeded 80% for both sacrum and heels when a within-subject change in SEM Scanner reading of >0.5 is utilised. SEM Scanner readings are unlikely to be adversely affected by patient-specific factors, such as comorbidities or skin-tone. The use of within-subject change as the distinguishing factor minimises the potential for influence by other patient-specific characteristics.
Does this evidence support any of the claimed benefits for the technology? If so, which?	The SEM200–003 protocol is a cross-sectional, data collection study of the SEM Scanner under clinical investigational use as a non-significant risk device. It brings objective information that would be helpful as an adjunct to clinical judgement and the current standard of care. Early identification of increased risk of PUs is key to prevention of injury progression and in the development of effective prevention and treatment plans. Because the SEM Scanner provides measurable quantitative data prior to the visual identification of the presence or non-presence of tissue injury, the implication is that the paradigm for framing the approach to PU prevention is disrupted and must be reconsidered.

SEM200-003/004	
Will any information from this study be used in the economic model?	Yes
What cost analysis was done in the study? Please explain the results.	No cost analysis – results used in clinical outcome parameters in model
What are the limitations of this evidence?	No limitations in context of study
How was the study funded?	This study was funded by Bruin Biometrics LLC

SEM200-800	
What are main differences in resource use and clinical outcomes between the technologies?	The study was successful in meeting the sensitivity endpoint with demonstration of earlier detection of damage over current visual-based standard of care. ITT study results demonstrated a sensitivity of 87.5% (95% CI: 74.8%–95.3%) for detecting pressure ulcers between the SEM Scanner and clinical judgment per visual skin assessment. This is in line with prior studies using the SEM Scanner 200 that showed sensitivity of 82% (003/004 study; 95% CI: 74%–88%) in subjects with pre-existing conditions (no PU and intact-skin PU) for comparison. SEM Scanner shown to detect PUs 5 days (median) before nurse visual skin assessment.
How are the findings relevant to the decision problem?	Improvement in the absolute (quantitative) early detection of pressure ulcers over current visual-based standard of care.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Demonstrates the sensitivity and specificity of the SEM Scanner for identification of increased risk of pressure ulcers 5 days earlier than visual skin assessment. It also enables anatomically specific interventions.
Will any information from this study be used in the economic model?	Yes
What cost analysis was done in the study? Please explain the results.	No cost analysis – results used in clinical outcome parameters in model

SEM200-800	
What are the limitations of this evidence?	Future studies should consider additional body locations.
How was the study funded?	This study was funded by Bruin Biometrics LLC.

Pressure Ulcer Reduction Programme (PURP)	
What are main differences in resource use and clinical outcomes between the technologies?	In the AC cohort >11,000 SEM assessments were taken, a 92% (weighted average) reduction in the incidence of HAPUs was achieved. • 79% of AC centres reported 0% HAPU during the PURP • Daily use of the device alerted to risk of PUs in 56% of assessments (Delta reading ≥0.6) • In 46% of assessments, patients were found to be at risk for PUs (Delta reading ≥0.6) but had no visual skin redness at that region • Clinical decision-making was impacted in 52% of cases • 63% of patients received additional interventions including increased mobilisation In HC, a 47% reduction in HAPUs was achieved. In one of largest PURPs to date 75% of healthcare practitioners described the new technology as easy to use. 88% of healthcare practitioners reported that the new technology provided additional information to support clinical decision-making.
How are the findings relevant to the decision problem?	Current visual assessment to detect pressure ulcers is inadequate. The subsequent burden of treatment is time and labour intensive with significant cost-utility implications to the NHS.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Yes, in terms of overall reduction in PU incidence: 92% weighted reduction in HAPU was identified. In addition, the healthcare practitioners reported that 63% of patients received additional preventative interventions. 79% sites reported zero HAPU during the PURP.
Will any information from this study be used in the economic model?	Yes

Pressure Ulcer Reduction Programme (PURP)	
What cost analysis was done in the study? Please explain the results.	No cost analysis – results used in clinical outcome parameters in model
What are the limitations of this evidence?	Limitations – the PURPs have been conducted for a varying length of time generally between 1 to 6 months.. A small number of PURPs were for a short time period – an analysis shows impact remains consistent even when the shorter time period PURP data is removed.
How was the study funded?	This study was funded by Bruin Biometrics LLC.

The cost of pressure ulcers in the UK. Age and Ageing Vol. 33. No 3. 2004. Bennett G. Dealey C. Posnett. J	
What are main differences in resource use and clinical outcomes between the technologies?	This was a bottom up methodology rather than a comparative approach. The goal was to identify the costs per episode of care and per patient of different severities of pressure ulcers
How are the findings relevant to the decision problem?	The findings are fundamental to the understanding of the costs of pressure ulcers within the UK Health and Social Care System. The cost of the NHS is identified. This data may be regarded as the seminal data in pressure ulcer understanding in the UK in terms of cost impact.
Does this evidence support any of the claimed benefits for the technology? If so, which?	NA
Will any information from this study be used in the economic model?	Text
What cost analysis was done in the study? Please explain the results.	This was a bottom up methodology rather than a comparative approach. Costing assumes patients are within an institutional care setting. The following resources were costed: Nurse Time; Dressings; Antibiotics: Diagnostic Tests: Support Surfaces and Inpatient Days
What are the limitations of this evidence?	There are a number of limitations identified: 1. Only includes patients in institutional care – patients in the community are not included and therefore incidence rates may well be higher 2. No surgical costs are included 3. Potential over estimation on resource use
How was the study funded?	Published manuscript – unable to ascertain funding. Please note Bruin Biometrics did not fund any part of this study.

Dealey C, Posnett J, Walker A. The cost of pressure ulcers in the United Kingdom. J Wound Care 2012;21(6):261–66	
What are main differences in resource use and clinical outcomes between the technologies?	This was a bottom up methodology rather than a comparative approach. The goal was to update earlier estimates to reflect the costs of treating PUs of different severity at prices current in mid-2011.
How are the findings relevant to the decision problem?	The findings are fundamental to the understanding of the costs of pressure ulcers within the UK Health and Social Care System. It is clear that costs increase with increasing PU severity and with additional complications. This data may be regarded as the seminal data in pressure ulcer understanding in the UK in terms of cost impact.
Does this evidence support any of the claimed benefits for the technology? If so, which?	NA
Will any information from this study be used in the economic model?	Yes
What cost analysis was done in the study? Please explain the results.	Bottom up methodology using protocols of care that reflected good clinical practice. Costs using UK NHS Unit. Prices were allocated to specific resources.
What are the limitations of this evidence?	Update to 2004 analysis – specific limitations on patient management such as surgery to close and ulcer. In addition care protocols were not updated for the addition of new technologies. Despite the 2012 timeline this is regarded as the most relevant data in terms of PU cost in the UK.
How was the study funded?	Published paper states the following “Heron Evidence Development Ltd. was funded for this work by Mölnlycke Health Care (UK). The authors have no other conflicts of interest to declare”. Please note Bruin Biometrics did not fund any part of this study.

Healthy Life-Years Lost and Excess Bed-Days Due to 6 Patient Safety Incidents Empirical Evidence From English Hospitals. Hauck KD, Wang S, Vincent C, Smith PC. Med Care. 2017 Feb;55(2):125-130	
What are main differences in resource use and clinical outcomes between the technologies?	This analysis of hospital episode data from the period 2005/6 to 2009/10 from 273 English hospitals. The most relevant analysis to this model is the excess bed days from pressure ulcers at 555 per 100,000 population which importantly was the highest of 6 different patient safety events analysed
How are the findings relevant to the decision problem?	The results of the analysis identify the financial impact that pressure ulcers have on hospital lengths of stay (“excess bed days”) in England and identifies that prevention of Pus should be a priority to focus upon. Pus account for an additional 15.5 days extended LoS (Table 1: 2005/06-2009/10)

Healthy Life-Years Lost and Excess Bed-Days Due to 6 Patient Safety Incidents Empirical Evidence From English Hospitals. Hauck KD, Wang S, Vincent C, Smith PC. Med Care. 2017 Feb;55(2):125-130	
Does this evidence support any of the claimed benefits for the technology? If so, which?	Yes. The extended length of stays
Will any information from this study be used in the economic model?	No. We chose to adhere to the more conservative extended length of stay values of 5-7 days from Dealey. Adding longer LoS values only adds to the overall estimate of costs for the existing PU burden and adds more economic support for the use of the SEM Scanner in a PU prevention focussed pathway.
What cost analysis was done in the study? Please explain the results.	NA
What are the limitations of this evidence?	Firstly it is recognised that the Hospital Episode Data has inherent weakness's that will be reflect within any data analysis. Secondly the report does not include the impact on long term health.
How was the study funded?	The study Supported by The Health Foundation, the Centre for Patient Safety and Service Quality (National Institute for Health Research), and the National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Modelling Methodology at Imperial College London in partnership with Public Health England (PHE). Please note Bruin Biometrics did not fund any part of this study.

The Determinants of Costs and Length of Stay for Hip Fracture Patients. Castelli A. Daidone S. Jacobs R. Kasteridis P. Street A.D. PLoS One. 2015 Jul 23;10(7)	
What are main differences in resource use and clinical outcomes between the technologies?	In this analysis of 60,000 hip fracture patients the authors constructed a care pathway for the cohort and mapped the costs using healthcare resource group data. The costs were allocated per patient. Of particular interest to the model was the impact of pressure ulcers in terms of increased length of stay which was reported to be by 8.42 days
How are the findings relevant to the decision problem?	Hip Fracture patients are a high risk group for pressure ulceration. The increase in length of stay in this cohort is reflected in higher costs of care and therefore aligns itself to the urgent requirement to focus on PU prevention.
Does this evidence support any of the claimed benefits for the technology? If so, which?	No
Will any information from this study be used in the economic model?	Yes

The Determinants of Costs and Length of Stay for Hip Fracture Patients. Castelli A. Daidone S. Jacobs R. Kasteridis P. Street A.D. PLoS One. 2015 Jul 23;10(7)	
What cost analysis was done in the study? Please explain the results.	The costs were mapped using healthcare resource group data. Patients with pressure ulcers had higher costs of care (£1943. – see table 3).
What are the limitations of this evidence?	3 key limitations identified: firstly the care pathway is incomplete – particularly subsequent to discharge. Secondly the authors were unable to include social care costs, finally by using Reference cost data does not accurately capture the costs of care.
How was the study funded?	Commissioned and funded by the Policy Research Programme in the English Department of Health from the Economics of Social and Health Care Research Unit (ESHCRU) (Ref 103/0001). Please note Bruin Biometrics did not fund any part of this study.

Modernising the Pressure Ulcer Prevention Care Pathway: A Cost Effectiveness Analysis Burns M. King T. Tsang K. Grainger S. Tang S. Submitted to Journal of Wound Care. In review process – manuscript number jowc.2019.0193	
What are main differences in resource use and clinical outcomes between the technologies?	Over a 1-year time horizon, the SoC plus SEM Scanner was a dominant option compared with SoC alone. The incidence of HAPUs was lower by 67.4% and costs were lower by £93 per patient at risk. The probability that the SEM Scanner was dominant or cost-effective at a willingness-to-pay threshold of £20,000/QALY was 90%.
How are the findings relevant to the decision problem?	The model reflects a 210 bed acute facility. Based on 12182 admissions, average length of stay of 5.6 days and 89% occupancy. This reflects well an NHS facility and identifies the potential clinical and financial outcome improvements that can be gained by the integration of the SEM Scanner into the existing care pathway.
Does this evidence support any of the claimed benefits for the technology? If so, which?	Yes Reduction of HAPUs Improved QALY Cost saving solution
Will any information from this study be used in the economic model?	Yes
What cost analysis was done in the study? Please explain the results.	Firstly treatment costs for all HAPU categories were taken from the 2016/17 PU productivity calculator provided by NHS Improvement. Prevention costs were estimated by costing all labour and material costs across each element of the prevention pathway. Costs of staff training, and amortised asset cost were included. QALYs, derived from Padula et al (2011) and based on EQ-5D index scores, were used to reflect the utility of patients. The primary output of the model was the incremental cost

Modernising the Pressure Ulcer Prevention Care Pathway: A Cost Effectiveness Analysis Burns M. King T. Tsang K. Grainger S. Tang S. Submitted to Journal of Wound Care. In review process – manuscript number jowc.2019.0193	
	per QALY gained with SoC plus SEM Scanner compared with SoC alone, expressed as the incremental cost-effectiveness ratio.
What are the limitations of this evidence?	Estimates of sensitivity and specificity are taken from a controlled clinical study which may well therefore be different in real world use. Costs of PU are assumed on a single episode of PU – it does not allow for progression to a more severe state. Costs of PU care may differ between care centres.
How was the study funded?	The study was funded by Bruin Biometrics LLC.

Guest JF, Ayoub N, McIlwraith T, et al. Health economic burden that wounds impose on the National Health Service in the UK. BMJ Open 2015;5: e009283. doi:10.1136/ bmjopen-2015-009283	
What are main differences in resource use and clinical outcomes between the technologies?	This was a retrospective cohort analysis of patient records from the THIN database. 1000 patients without a wound were matched with 1000 patients with a wound. Outcomes / resource use and NHS costs were estimated at 2013/2014 levels.
How are the findings relevant to the decision problem?	The study identified the prevalence of PU and the incidence of new wounds. The study also reports the resource use particularly that of nurse time.
Does this evidence support any of the claimed benefits for the technology? If so, which?	NA
Will any information from this study be used in the economic model?	Yes – to provide an overall perspective and cross check of data points
What cost analysis was done in the study? Please explain the results.	A computer based model was created depicting the care pathways. A 12 month period was mapped, and unit costs applied. 2 forms of sensitivity analysis was conducted. 76% patients presented with new wounds – extrapolate to UK adult population = 2.2million patients (4.5% adult population). Cost extrapolation = £6bn compared with £0.7bn for the matched cohort – hence the authors state “Hence, the total annual NHS cost of managing 2.2 million wounds and associated comorbidities was estimated to be £5.3 billion”. After sensitivity analysis it is adjusted to £4.5 to £5.1bn
What are the limitations of this evidence?	The data reflects a wide range of wound rather than a specific analysis of pressure ulcer data. The analysis is based upon clinician entries into patient records – these have been reported to be lacking in detail and not precise. Secondly the THIN database is restricted to GP records – patients in Institutional care are not included.

Guest JF, Ayoub N, McIlwraith T, et al. Health economic burden that wounds impose on the National Health Service in the UK. BMJ Open 2015;5: e009283. doi:10.1136/ bmjopen-2015-009283	
	Finally the analysis reflects a limited time period (12months) a portion of wounds did not heal within the time period.
How was the study funded?	The published paper states the study was funded by multiple sources – please note Bruin Biometrics did not fund any part of this study.

Cohort study evaluating pressure ulcer management in clinical practice in the UK following initial presentation in the community: costs and outcomes. BMJ Open. 2018:8. Guest. J. Fuller G. Vowden P. Vowden K.R	
What are main differences in resource use and clinical outcomes between the technologies?	Retrospective cohort analysis designed to evaluate the patient pathways and associated resource use, health outcomes and corresponding costs attributable to managing PUs over 12 months . Note the cohort is a sample of patients from the THIN database. 50% of patients healed within the 12 month period with healing times varying from 1 month for a category 1 to 10 months for an unstageable pressure ulcer. Mean NHS costs over the 12 month period ranged from £1400 for a category 1 to over £8500 for the other categories of pressure ulcers.
How are the findings relevant to the decision problem?	This analysis identifies the challenges, time and costs of healing pressure ulcers
Does this evidence support any of the claimed benefits for the technology? If so, which?	
Will any information from this study be used in the economic model?	Yes – to provide an overall perspective and cross check of data points in the community
What cost analysis was done in the study? Please explain the results.	NHS costs of care were calculated using 2015/16. For the 209 patients the mean costs of resources were then combined in order to estimate the mean NHS cost of managing a PU over 12 months from initial presentation in the community. Additionally the cost of wound care was also estimated by segmenting patients according to category of PU.
What are the limitations of this evidence?	Firstly the cohort is identified via the THIN database – this is limited to GP records and the inherent limitations. Secondly the analysis is limited to a 12 month period.
How was the study funded?	The published paper states the study was funded by multiple sources – please note Bruin Biometrics did not fund any part of this study.

3 Economic model

This section refers to the de novo economic model that you have submitted.

Description

Patients

Describe which patient groups are included in the model.

NICE CG179[1] recognizes that all patients are potentially at risk of developing a pressure ulcer.

Patients in active care are included in the models submitted here. These comprise patients in 1.) acute care in-patient facilities, 2.) long-term step-up or step-down community hospitals and skilled-nursing facilities, 3.) community-based patients cared for by district nurses, and 4.) End of Life Palliative Care patients.

Rather than leave the models at the "all population" level, we have taken the step to narrow the focus in **Model A** to patients deemed to be "at-risk" (as assessed via a validated risk-assessment tool, such as Waterlow) of developing a reportable PU. In settings 1 and 2, above, this means an at-risk population of 41% (Vanderwee, 2007[2]). For the model only, PU incidence is deemed to occur exclusively in this, "at-risk" population set. SEM Scanner readings are taken from this at-risk population set.

Given the disparate patient sites of service and cohorts, no one model can satisfactorily represent all patient in a single modelled structure; the complexity being high for even one site of service. Note that additional models have been completed for activity-based-costing estimates (a bottom-up costing) of PU costs, savings and consequences for settings 1, 2 and 3.

Technology and comparator(s)

State the technology and comparators used in the model. Provide a justification if the comparator used in the model is different to that in the scope.

The SEM Scanner (BBI LLC) is a handheld medical device that measures Biocapacitance to assess changes in sub-epidermal moisture (SEM). The SEM Scanner offers an objective and reliable method for the assessment of local SEM using Biocapacitance. Changes in SEM are associated with early pressure-induced tissue damage before the damage becomes visible to the unaided eye (Moore *et al* 2017[3]).

The SEM Scanner is approved for use as an adjunct to the current standard of care for assessing risk of a specific anatomy developing a PU.

The direct comparator of the SEM Scanner, and the current standard of care, is the ability of nurses, post risk-assessing a patient, to identify pressure ulcer (PU) damage via skin assessment, per Guidelines (NICE CG179, 2014[1] and NPUAP/EPUAP/PPPIA Clinical Practice Guidance 2014[4]). Skin assessments are visual and palpation tests.

The aims of the modelling analyses are to assess the cost effectiveness of the SEM Scanner when used as an adjunct to clinical guidelines (standard of care [SoC] plus SEM Scanner) compared with the current SoC alone (adapted from NICE CG179, 2014[1] for the prevention and management of HAPUs from the perspective of UK care settings).

Model structure

Provide a diagram of the model structure you have chosen in Appendix B.

Justify the chosen structure of the model by referring to the clinical care pathway outlined in part 1, section 3 (Clinical context) of your submission.

NICE CG179 Pressure Ulcers: Prevention and Management (NICE GC179 2014[1]) is the care pathway relevant to this subm CG179 details the individual steps required to screen and prevent pressure ulcers in patients admitted to the pathway. It th steps required to manage patients with incidents of PUs, with varying degrees of skin and tissue deterioration, from intact s PUs to full-thickness Grade 4 ulcers and unstageable ulcers.

The focus of the SEM Scanner is to aid in nurses' decision-making to prevent PUs, particularly of reportable grades 2-4 an unstageable PUs. Keeping the skin intact is the prevention aim of the SEM Scanner. Complexity of care and recovery incre considerably after skin breakage.

The economic model was therefore developed to evaluate the cost-effectiveness of using the SEM Scanner as an adjunct t standard of care (SoC) to detect and, when the data is acted on, to prevent HAPUs from the perspective of the CG179. The horizon of the analysis is 1 year.

Prevention Costs – Current Standard of Care
Currently, patients are initially screened on admission into two PU groups: 1.) patients admitted with an existing PU or, 2.) without a PU at admission. A patient presenting with a PU formed prior to admission will undergo a variety of treatments, ea dependent on the condition of the patient's skin and tissue, the clinical goals being, healing, pain management and, avoida chronic wound cascade, and infection.

Those without an existing PU are further assessed, typically using validated risk-assessment tools (e.g., Purpose-T, Braden (Figure 1). Depending on assessed risk, patients will receive a bundle of "universal preventions" designed to reduce PU ris whole patient. Universal prevention activities are those clinical interventions intended to assess overall risk (e.g., Braden sc condition of the patients in conjunction with whole-body offloading and care planning. They are applied when patients are d at risk of a PU, but where no PU is diagnosed at any particular anatomy. The intensity of universal prevention, prior to a PU changes in CG179 according to the assessed risk.

Risk assessments are supplemented by a skin assessment—visible and palpation tests—intended to diagnose a develope skin assessment diagnoses a PU, then anatomy-specific interventions (e.g., at the left heel) are initiated.

A subtle insight of consequence is that the diagnostic standard currently in use (Figure 1) suffers from "latency":

1. Diagnostic latency: This is the gap between the time when the damage actually begins and the time, under the curr of care, at which it is detected and confirmed. Risk assessment tools tell nurses that a patient is at risk; the questio that patient is at risk goes unanswered.
2. Anatomical latency: Prevention (keeping the patient's skin intact, rescuing and reversing the damage) requires kno on the body to intervene, when and how intensively, not only that the patient is at risk. Skin assessments achieve t diagnostic threshold required to trigger anatomy-specific interventions once the wound has developed and can be skin assessment.

To our knowledge, no publications exist which cost preventative activities. The company worked with Deloitte LLP, Risk Ad to model the initial screening, risk assessment, skin assessment and "universal prevention" activities in a clinical decision-t (Figure 1).

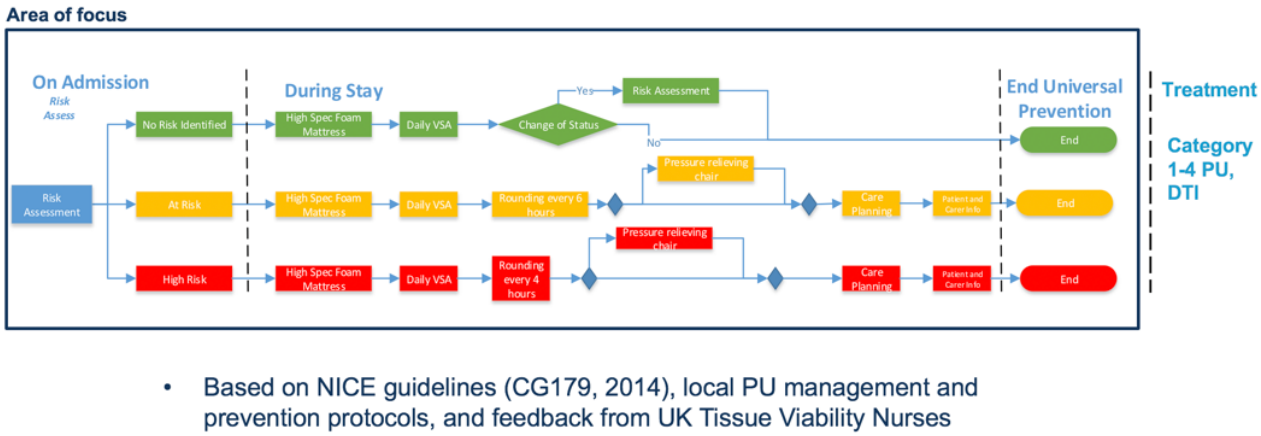


Figure 1: Current Standard of Care Universal Prevention Pathway (NICE, 2014), presented at WCICT June 18, 2018 and s submitted for publication[5].

Costs for each activity in Figure 1 came from Tissue Viability nurses at NHS sites, or NHS sources where the SEM Scanne implemented and are fully cited in the model. These costs are shown in the model (Model A) in the tab, 'Universal preventio

Prevention Costs – Current Standard of Care and SEM Scanner
Introduction of the SEM Scanner into the clinical care pathway is detailed extensively in the clinical submission. Readers of economic submission will benefit from a short clinical, care pathway, and economic cost narrative: that follows.

The device is used at admission, during the episode of care and at discharge. The "on admission" use case is shown in Fig 3. SEM Scanner values are recorded as an integral component of the patients' record and are passed with the patient betw settings between discharge and admission.

The SEM Scanner has been designed to integrate – be adjunctive – to the current standard of care such that, if a patient is being at risk then SEM Scanner readings are obtained from heels and sacral areas (accounting for 86.5% of all PUs, Vand 2011[6]). One of two binary outcomes then result:

1. SEM Scanner negative (a localized SEM delta Δ<0.6). In this case, the anatomy in question is at lower risk for a PU preventions under the current standard of care continue (Figure 2). These standard of care costs are shown in, "Sc 'Universal prevention activities' of Model A.

Figure 2: Current Standard of Care and SEM Scanner negative ("neg"), presented at WCICT June 18, 2018 and subsequer submitted for publication[5].

2. SEM Scanner positive (a localised SEM delta $\Delta \geq 0.6$). In this case, the anatomy in question is at increased risk for no visible or palpable signs of a PU are evident to the assessing nurse. Universal preventions continue and anatom interventions are started for that anatomy (Figure 3). These anatomy specific costs are shown in, "Scenario B" in 'U prevention activities' of Model A.

Figure 3: Current Standard of Care and SEM Scanner positive ("POS"), presented at WCICT June 18, 2018 and subseque
submitted for publication[5].

Impact of SEM Scanner implementation
The clinical submission extensively details the impact of SEM Scanner implementation. The Company gathers and reports
reduction data on a quarterly basis. The preponderance of sites using the Scanner report a 100% reduction in reportable P
the implementation period (see Pressure Ulcer Reduction Program "PURP", report attached to the clinical submission). The
reports both weighted average and straight-average incidence reductions compared to a control period for the same site of

Following review by J Posnett, Model A used an observed PU incidence computed reduction of 68.9%. The calculation of t
is shown in Model A, 'PU Costs, Incidence and Dist", cells E31-H38.

George & Jane
A patient-level, bottom-up analysis of the difference in the prevention phase of the care pathway is provided as a presentat
micro-site under the title of George and Jane. This analysis shows the current standard of care for an admitted fractured ne
patient, George. This is compared against Jane's case, also admitted for a fractured neck of femur, but into a care pathway
with the SEM Scanner.

Implementation clinical requirements and SEM Scanner costs
Scanning and interventions are undertaken in NHS Trusts (from real world implementation experience) is done by Health C
Assistants or qualified nursing staff. No new staff are required. Existing preventive and treatment equipment are used.

SEM Scanner unit purchase, staff training, and usage costs are shown in Model A, 'RESULTS - SoC vs SEM Adjunct' (cell

Treatment Costs
Costs for treatment of grades 1-4 and unstageable ulcers are well accepted from publications written by Dealey C., Posnett
Walker A. (2012)[7]. These cost figures are published on the National Health Service's website for their NHS Improvement (N
Improvement 2019)[8] division. Figures shown there are indexed up from the 2012 values to 2016/17 values.

Measures of Interest
Modelled outcomes of interest are listed below.

1. Changes in the incidence from the pre-deployment period and the deployment period.
2. The Cost impact of the change in incidence:
    a. The overall change in costs
    b. The change attributable to materials cost savings which tend towards variable expense
    c. The change attributable to freed up resources (nursing time). These are not calculated as cost savings, rat
       identified as productivity and freed-up time to care.
    d. The change in bed utilization from shorter lengths-of-stay
3. Cost metrics of deployment:
    a. Total per annum deployment costs
    b. Costs per admitted patient (not-at-risk and at-risk)
    c. Costs per at-risk patient
    d. Cost per scan
4. The Return on Investment from deployment of the Scanner in Year 1 and out years.
5. The Incremental Cost Effectiveness Ratio (ICER) expressed as an ICER per Quality Adjusted Life Year (QALY).

Results are shown in Model A, ' RESULTS - SoC vs SEM Adjunct'.

A Final Note on Prudence Prudence is built into the model from choosing conservative model inputs. Exclusion of litigation costs and shorter extended stay than the 15.5 extended bed occupancy days arising from patients with PUs as reported by Hauck (2017)[9] are two exam modelling choices made which were detrimental to the Scanner's economic case. Extensive sensitivity analyses and Monte Carlo simulations.

Table 2 Assumptions in the model

In this table, list the main assumptions in the model and justify why each has been used.

<table>
<tr><th>Assumption</th><th>Justification</th><th>Source</th></tr>
<tr><td colspan="3">As a general note to readers, all assumptions in the model are shown in the “inputs” tabs, of which there are three: 1. ‘ Base Scen. - Model Inputs’, 2. ‘ Universal Prevent Activities’, and 3.) ‘ Inputs - Monte Carlo’</td></tr>
<tr><td>Population clinical characteristics in acute and palliative care</td><td>A total of 1129 acute and 146 palliative care patients were recruited into an evaluation designed to assess whether the introduction of the SEM Scanner into routine clinical practice would be associated with a reduction in the incidence of HAPUs. Over a 4-year period, 14 sites in the UK (11), Canada (1), Belgium (1) and Spain (1) implemented a PU reduction programme using the SEM Scanner as part of their SoC. Data were collected prospectively from 13 acute sites and one hospice, and the incidence of HAPUs at category 2 or above was compared with historic controls in the same facilities.
In the Acute Care facilities, 79% achieved zero HAPUs during the PU reduction programme with an overall weighted HAPU reduction of 92% (0.5% incidence), resulting in only 5/983 patients developing a HAPU. The observed incidence reduction (the rate used in the model) was 68.9%.
In the hospice care setting, a HAPU reduction of 47% was achieved in a care for end of life patients. Setting.</td><td>Hancock K, Lawrence R. Integrating early detection of pressure ulcers (PU) into
universal prevention pathways. Abstract 25 presented at NPUAP, St Louis, USA, March 1–2,2019. https://sem-scanner.com/wp-content/uploads/2019/03/NPUAP-Poster-2019-RWE-VFpresented. pdf. Accessed September 3, 2019.[10]</td></tr>
<tr><td>Incidence rate of category ≥2 ulcers</td><td>Use
PU Observed Incidence Calculation (data from pre-PURP facilities Hancock K, et al (2019)[10])<table><tr><td>Pre-PURP count of reportable PUs</td><td></td><td>171</td></tr><tr><td>Pre-PURP count of admitted patients to same facilities</td><td></td><td>10447</td></tr><tr><td>Observed Incidence Pre-PURP</td><td></td><td>1.637%</td></tr><tr><td>PURP count of reportable PUs</td><td></td><td>5</td></tr><tr><td>PURP count of admitted patients to same facilities</td><td></td><td>983</td></tr><tr><td>Observed Incidence PURP</td><td></td><td>0.509%</td></tr><tr><td>Observed Incidence reduction % Pre-PURP to PURP</td><td></td><td>68.925%</td></tr></table>Hancock K, et al. Integrating early detection of pressure ulcers (PU) into universal prevention pathways.
Abstract submitted and presented at NPUAP, St Louis, USA, 1–2 March 2019.[10]</td><td>Hancock K, Lawrence R. Integrating early detection of pressure ulcers (PU) into
universal prevention pathways. Abstract 25 presented at NPUAP, St Louis, USA, March 1–2,2019. https://sem-scanner.com/wp-content/uploads/2019/03/NPUAP-Poster-2019-RWE-VFpresented. pdf. Accessed September 3, 2019. [10]</td></tr>
<tr><td>Number of “predicted”</td><td>The number of PUs modelled in the analysis is 0.509% with the scanner compared with 1.8% with SoC. In the costing analysis, ulcers are distributed across four possible health states: healthy (no ulcer), category 2 (partial thickness skin loss), category 3</td><td>“Predicted” incidence is taken from the real-world experience of use of the Scanner in clinical practice (PURP).</td></tr>
</table>

PUs	(full thickness skin loss), and category 4 (full thickness tissue loss). The distribution of ulcers is 67% category 2, 24% category 3, and 9% category 4. When the SEM Scanner is used to detect an early sign of tissue damage beneath the skin, the current SoC (prevention and management) is not otherwise changed, but the SEM Scanner directs nurses/clinicians towards earlier and anatomically more precise intervention where pressure damage has been detected.	Hancock K, Lawrence R. Integrating early detection of pressure ulcers (PU) into universal prevention pathways. Abstract 25 presented at NPUAP, St Louis, USA, March 1–2,2019. https://sem-scanner.com/wp-content/uploads/2019/03/NPUAP-Poster-2019-RWE-VFpresented.pdf. Accessed September 3, 2019. [10]
Setting	The analysis is based on an acute care setting with 10 inpatient wards, each with 21 beds (210 beds total). Assuming an average length of stay of 5.6 days and that hospital beds are occupied 89% of the time, there will be 12,182 admissions for the year. Of these admissions, 41% of patients are deemed to be at risk of developing a PU on the basis of a PU risk score (Waterlow, Braden, or Norton). The analysis assumes 147 nurses requiring training on use of the SEM Scanner. This was calculated by assuming a bed to nurse ratio of five: one and nurses operating over three shifts per day, with a 14% headroom in staffing levels. Each nurse required 1 hour of training to use the SEM Scanner. Using prior UK implementations of the SEM Scanner, where each nurse station covered nine beds and had one SEM Scanner, implied a total of 23 SEM Scanners would be required.	NHS England. Bed availability and occupancy data. November 2018. https://www.england.nhs.uk/statistics/statistical-work-areas/bed-availability-and-occupancy/beddata-overnight/. Accessed 4 September 2019[11] NICE. Costing statement: pressure ulcers: implementing the NICE guideline on pressure ulcers (CG179). 2014. https://www.nice.org.uk/guidance/cg179/resources/costing-statement-pdf-248688109. Accessed September 2, 2019.[12]
Costs	Costs were calculated for the 4995 patients deemed to be at risk of developing a PU in the base case scenario. Treatment costs for all HAPU categories were taken from the 2016/17 PU productivity calculator provided by NHS Improvement.20 Prevention costs were estimated by costing all labour and material costs across each element of the prevention pathway outlined in **Figures 1, 2 and 3** In addition to ulcer treatment and prevention costs, the cost of training staff to use the SEM Scanner and amortised asset costs for the SEM Scanner were included. The first year of the SEM Scanner implementation was chosen to provide a prudent evaluation as training costs associated with the SEM Scanner are expected to be greatest during this period. The unit price of one SEM Scanner was £5835 and the device cost was amortised over 3 years.	NHS Improvement. Pressure ulcer productivity calculator. 2019. https://improvement.nhs.uk/documents/2483/Pressure_ulcer_productivity_calculator.xlsx. Accessed April 9, 2019.[8]
Utilities	QALYs, derived from Padula et al and based on EQ-5D index scores, were used to reflect the utility of patients. It was assumed that an average inpatient with no skin complications (i.e. no PU) had two chronic conditions and a median health utility value of 0.827 per year (Table “QALY Source” in **Model A**).	Padula WV, Mishra MK, Makic MB, et al. Improving the quality of pressure ulcer care with prevention: a cost-effectiveness analysis. Med Care. 2011;49:385–392.[13]

	Patients with a category 1 or 2 and 3 or 4 HAPU had lower utility scores: 0.778 and 0.597 per year, respectively.	

Table 3 Clinical parameters, patient and carer outcomes and system outcomes used in the model

In this table, describe the clinical parameters, patient and carer outcomes and system outcomes used in the model.

Parameter/outcomes	Source	Relevant results	Range or distribution	How are these values used in the model?
Interventions	NICE CG179.	Current SoC:Regular risk assessment and visual skin inspection, with appropriate prevention protocols; SEM Scanner + SoC Same as current SoC, plus SEM Scanner measurements at the sacrum and heels, with appropriate prevention protocols	N/A	Base case clinical input parameter
Baseline incidence 1.6%	As Table 2, above	From PURP implementations	No range	Pressure ulcer incidence input used in scenario setting
Underlying incidence of hospital acquired category ≥2 pressure ulcers	The cost of pressure ulcers in the UK (Bennett G, Age and Ageing 2004; 33: 230–235)[14]	Underlying incidence 4.0%	No range	Base case clinical input parameter

Sensitivity of anatomy specific skin assessment and of SEM Scanner	Garcia-Fernandez FP, Pancorbo-Hidalgo PL, Agreda JJ. Predictive capacity of risk assessment scales and clinical judgment for pressure ulcers: a meta-analysis. Journal of wound, ostomy, and continence nursing : official publication of The Wound, Ostomy and Continence Nurses Society. 2014 Jan-Feb;41(1):24-34.[15] Sub-Epidermal Moisture Detection as an Adjunct to a Clinical Pathway for Prevention and Management of Hospital-Acquired Pressure Ulcers in the UK: A Cost- Effectiveness Analysis, Value in Health 2019.[5]	50.6% current SoC; 87.5% SEM Scanner	N/A	Base case clinical input parameter
Specificity of risk assessment	Garcia-Fernandez FP, Pancorbo-Hidalgo PL, Agreda JJ. Predictive capacity of risk assessment scales and clinical judgment for pressure ulcers: a meta-analysis. Journal of wound, ostomy, and continence nursing : official publication of The Wound, Ostomy and Continence Nurses Society. 2014 Jan-Feb;41(1):24-34.[15] Burns M. King T. Tsang K. Grainger S. Tang S. Modernising the pressure ulcer prevention care pathway: a cost-effectiveness analysis. Submitted to Journal of Wound Care. In review process – manuscript number jowc.2019.0193[5]	60.1% current SoC 33% SEM Scanner	N/A	Base case clinical input parameter

If any outcomes listed in table 4 are extrapolated beyond the study follow-up periods, explain the assumptions that underpin this extrapolation.

Not applicable

Table 4 Other parameters in the model

Describe any other parameters in the model. Examples are provided in the table. You can adapt the parameters as needed.

Parameter	Description	Justification	Source
Time horizon	1 year	Costs of the implementation are most acute in the first year. Costs of implementation diminish after year one, so the first-year test is the most stringent for the SEM Scanner. If it passes the first-year deployment test, then the subsequent years are only more beneficial for the SEM Scanner case	N/A
Discount rate	N/A	1 year model obviates need to compute the time value of money	N/A
Perspective (NHS/PSS)	Yes, but partly	PUs occur in the community and at people's homes. However, the SEM Scanner is only for use by health-care practitioners. It is not for use by patients on themselves.	SEM Scanner Instructions for Use
Cycle length	N/A	PUs are not experienced on a cycle, rather are discrete, cycle-independent, safety events	N/A
Transition probabilities	N/A	It is true that approximately 22% (Halfens, 2001[16]) Grades 1-2 PUs deteriorate to Grades 3-4 PUs. These deterioration states have been excluded from the model since they have a singular economic effect of making the "current standard of care costs" (i.e., before the SEM Scanner) more costly. The SEM Scanner case only gets stronger.	Halfens RJ, Bours GJ, Van Ast W. Relevance of the diagnosis 'stage 1 pressure ulcer': an empirical study of the clinical course of stage 1 ulcers in acute care and long-term care hospital populations. Journal of clinical nursing. 2001 Nov;10(6):748-57[16]
Health states	The preponderance of PU cases are Complexities and Comorbidities, rather than primary causes for admissions. Health states are therefore limited to:	The preponderance of PU cases are Complexities and Comorbidities, rather than primary causes for admissions. A patient is either admitted to a care setting with a PU or not. If not they are then risk assessed; clinical-interventions will follow post risk and	CG179

	1. PU on admission 2. No PU and no PU risk 3. No PU and at risk for a PU These states have been modelled.	skin assessments	
Sources of unit costs	Peer reviewed publications, NHS listings or directly from NHS care settings for all non-SEM Scanner costs SEM Scanner costs from Bruin Biometrics LLC	These costings are the most reliable sources (direct evidence) of unit costs	Please see the references in the model input tabs for line item references.

Explain the transition matrix used in the model and the transformation of clinical outcomes, health states or other details.

This text is replicated from an earlier section, "Model Structure". Please also see Appendix B to this document.

Currently, patients are initially screened on admission into two PU groups: 1.) patients admitted with an existing PU or, 2.) patie without a PU at admission. A patient presenting with a PU formed prior to admission will undergo a variety of treatments, each dependent on the condition of the patient's skin and tissue, the clinical goals being, healing, pain management and, avoidance chronic wound cascade, and infection.

Those without an existing PU are further assessed, typically using validated risk-assessment tools (e.g., Purpose-T, Braden, W **(Figure 1).** Depending on assessed risk, patients will receive a bundle of "universal preventions" designed to reduce PI risk for whole patient. Universal prevention activities are those clinical interventions intended to assess overall risk (e.g., Braden scale) condition of the patients in conjunction with whole-body offloading and care planning. They are applied when patients are deem at risk of a PU, but where no PU is diagnosed at any particular anatomy. The intensity of universal prevention, prior to a PU dia changes in CG179 according to the assessed risk.

Risk assessments are supplemented by a skin assessment—visible and palpation tests—intended to diagnose a developed PU skin assessment diagnoses a PU, then anatomy-specific interventions (e.g., at the left heel) are initiated.

A subtle insight of consequence is that the diagnostic standard currently in use (**Figure 1**) suffers from "latency":

3. *Diagnostic latency:* This is the gap between the time when the damage actually begins and the time, under the current of care, at which it is detected and confirmed. Risk assessment tools tell nurses that a patient is at risk; the question of that patient is at risk goes unanswered.
4. *Anatomical latency:* Prevention (keeping the patient's skin intact, rescuing and reversing the damage) requires knowing on the body to intervene, when and how intensively, not only that the patient is at risk. Skin assessments achieve that diagnostic threshold required to trigger anatomy-specific interventions once the wound has developed and can be diag skin assessment.

To our knowledge, no publications exist which cost preventative activities. The company worked with Deloitte LLP, Risk Adviso to model the initial screening, risk assessment, skin assessment and "universal prevention" activities in a clinical decision-tree a **(Figure 1).**

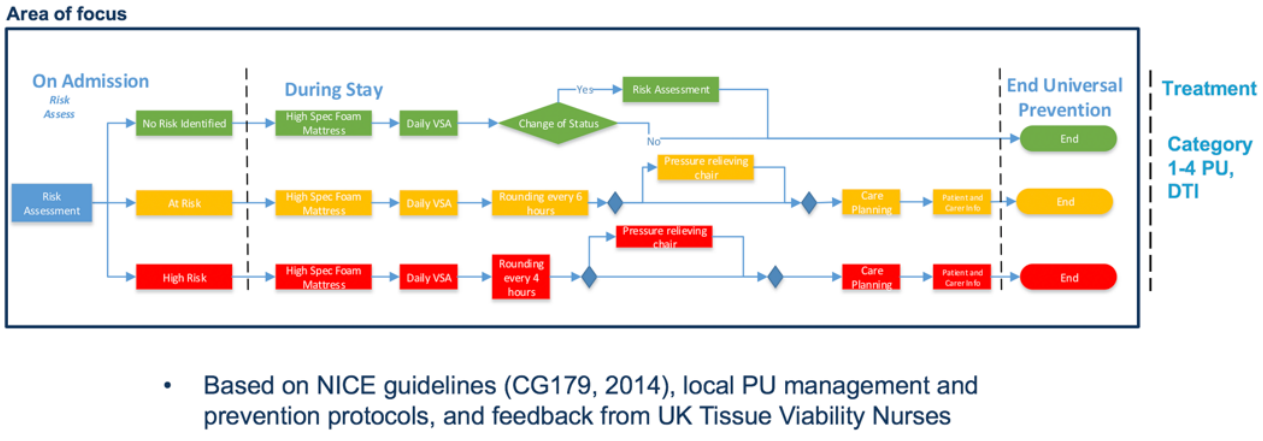


Figure 1: Current Standard of Care Universal Prevention Pathway (NICE, 2014), presented at WCICT June 18, 2018 and subs submitted for publication[5].

Costs for each activity in Figure 1 came from Tissue Viability nurses at NHS sites, or NHS sources where the SEM Scanner ha implemented and are fully cited in the model. These costs are shown in the model **(Model A)** in the tab, '*Universal prevention a*

Prevention Costs – Current Standard of Care and SEM Scanner
Introduction of the SEM Scanner into the clinical care pathway is detailed extensively in the clinical submission. Readers of this economic submission will benefit from a short clinical, care pathway, and economic cost narrative: that follows.

The device is used at admission, during the episode of care and at discharge. The "on admission" use case is shown in Figures 3. SEM Scanner values are recorded as an integral component of the patients' record and are passed with the patient between settings between discharge and admission.

The SEM Scanner has been designed to integrate – be adjunctive – to the current standard of care such that, if a patient is ass being at risk then SEM Scanner readings are obtained from heels and sacral areas (accounting for 86.5% of all PUs, Vanderwe 2011[6]). One of two binary outcomes then result:

1. SEM Scanner negative (a localized SEM delta Δ<0.6). In this case, the anatomy in question is at lower risk for a PU. U preventions under the current standard of care continue (**Figure 2).** These standard of care costs are shown in, "*S A*" in '*Universal prevention activities'* of **Model A**.

Figure 2: Current Standard of Care and SEM Scanner negative ("neg"), presented at WCICT June 18, 2018 and subsequently submitted for publication[5].

2. SEM Scanner positive (a localised SEM delta $\Delta \geq$0.6). In this case, the anatomy in question is at increased risk for a PU no visible or palpable signs of a PU are evident to the assessing nurse. Universal preventions continue and anatomy sp interventions are started for that anatomy (**Figure 3**). These anatomy specific costs are shown in, "*Scenario B*" in '*Univ prevention activities'* of **Model A**.

Figure 3: Current Standard of Care and SEM Scanner positive ("POS"), presented at WCICT June 18, 2018 and subsequently submitte publication[5].

Resource identification, measurement and valuation

Technology costs

Provide the list price for the technology (excluding VAT).

List price for a capital purchase of one SEM Scanner is £5835 ex VAT. The device is warranted for 3 years by the Company.

If the list price is not used in the model, provide the price used and a justification for the difference.

List price as stated above is used in the model.

NHS and unit costs

Describe how the clinical management of the condition is currently costed in the NHS in terms of reference costs, the national tariff and unit costs (from PSSRU and HSCIC). Please provide relevant codes and values (e.g. OPCS codes and ICD codes) for the operations, procedures and interventions included in the model.

- HRG codes for skin disorders JD07 A-K (http://www.bad.org.uk/healthcare-professionals/clinical-services/nhs-tariffs-2017 Accessed October 29, 2019)

Admitted patient care and outpatient procedure prices 2019/20 Return to contents

							Prices to be used for blended payment for emergency care					
HRG code	HRG name	Outpatient procedure (£)	Combined day case / ordinary elective spell (£)	Day case spell (£)	Ordinary elective spell (£)	Ordinary elective long stay trim point (days)	Non-elective spell (£)	Non-elective long stay trim point (days)	Per day long stay payment (for days exceeding trim point) (£)	Reduced short stay emergency tariff applicable?	% applied in calculation of reduced short stay emergency tariff	Reduced short stay emergency tariff (£)
JD07A	Skin Disorders with Interventions, with CC Score 12+	-	9,119	-	-	81	9,764	80	248	YES	25%	2,441
JD07B	Skin Disorders with Interventions, with CC Score 8-11	-	6,202	-	-	35	5,698	39	248	YES	25%	1,425
JD07C	Skin Disorders with Interventions, with CC Score 4-7	-	3,408	-	-	16	3,903	23	248	YES	25%	976
JD07D	Skin Disorders with Interventions, with CC Score 0-3	-	2,093	-	-	6	2,441	10	248	YES	45%	1,098
JD07E	Skin Disorders without Interventions, with CC Score 19+	-	6,873	-	-	121	7,359	75	248	YES	25%	1,840
JD07F	Skin Disorders without Interventions, with CC Score 14-18	-	4,951	-	-	48	5,301	46	248	YES	25%	1,325
JD07G	Skin Disorders without Interventions, with CC Score 10-13	-	1,308	-	-	10	3,745	31	248	YES	25%	936
JD07H	Skin Disorders without Interventions, with CC Score 6-9	-	656	-	-	5	2,789	21	248	YES	25%	697
JD07J	Skin Disorders without Interventions, with CC Score 2-5	-	384	-	-	5	1,655	10	248	YES	45%	745
JD07K	Skin Disorders without Interventions, with CC Score 0-1	-	319	-	-	5	601	5	248	NO	.	.

- ICD-10 for pressure ulcers include L89.0, L89.1, L89.2, L89.3, L89.9 for stage I–IV pressure ulcers, respectively.

Resource use

Describe any relevant resource data for the NHS in England reported in published and unpublished studies. Provide sources and rationale if relevant. If a literature search was done to identify evidence for resource use then please provide details in appendix A.

All resource use data are provided in Appendix A, and in the Model's input tabs.

In general, all resource data are from NHS sources or from peer reviewed publications.

Describe the resources needed to implement the technology in the NHS. Please provide sources and rationale.

Health Care Assistants or qualified nursing staff perform the scanning concurrent to scheduled skin assessments. SEM Scanner readings are taken at the same time as the skin assessments are performed. Scanning time has been factored into the model. No new nurse resource is needed.

Existing clinical interventions are used once an SEM Scanner positive result is obtained. No new clinical interventions are required to be obtained.

Tissue Viability nurses will update local protocols for PU prevention and management. This has not been costed in the Model, since updates are a normal course of business expense for local NHS providers. The next major update will be in response to the 2019 NPAUP/EPUAP Guidance document release on November 16th, 2019.

Describe the resources needed to manage the change in patient outcomes after implementing the technology. Please provide sources and rationale.

Tissue Viability nurses will update local protocols for PU prevention and management. This has not been costed in the Model, since updates are a normal course of business expense for local NHS providers. The next major update will be in response to the 2019 NPAUP/EPUAP Guidance document release on November 16th, 2019.

The most successful PURP implementations have been sponsored by the Deputy Chief or Chief nurses. This level of management sponsorship increases the compliance to cutting over from the old standard of care to the new standard of care.

Limited IT involvement is required SEM deltas are recorded in patients' notes by nurses. The next generation SEM Scanner will link to Electronic Health Records. IT involvement for the next generation device is also expected to be limited to supervising initial installation support provided by the Company. No release date is scheduled for the next generation device, hence no costs are included in Model A.

EBME involvement is limited to the initial intake and support of any product recalls.

Describe the resources needed to manage the change in system outcomes after implementing the technology. Please provide sources and rationale.

Tissue Viability nurses will update local protocols for PU prevention and management. This has not been costed in the Model, since updates are a normal course of business expense for local NHS providers. The next major update will be in response to the 2019 NPAUP/EPUAP Guidance document release on November 16th, 2019.

TVNs at the local level have oversight over PU prevention and management policy and system outcomes.

We have not contemplated NHS England costs of national deployment since such a costing is presumed to be beyond the scope of this submission.

Table 5 Resource use costs

In this table, summarise how the model calculates the results of these changes in resource use. Please adapt the table as necessary.

	Technology costs	Comparator 1 costs	Comparator 2 costs (N/A)	Difference in resource use costs (technology vs comparator 1)	Difference in resource use costs (technology vs comparator 2)
Note: All values are for the 210-bed case in Model A for one year. Per admitted at-risk values are provided in the final row of this table.					
	SEM Scanner	**Nurse skin assessment**	**N/A**	**-**	**N/A**
Cost of resource use to implement technology	£60,962	£0 (marginal cost)	N/A	£60,962	N/A
Cost of resource use associated with patient outcomes	Prevention: £144,614 + £431,292= £579,906 Treatment: £197,129 Total= £777,035	Prevention: £230,175 + £320,040 = £550,215 Treatment: £693,301= £640,868 Total= £1,243,516	N/A	(£466,481)	N/A
Cost of resource use associated with system outcomes	Included immediately above	Included immediately above	N/A	Included immediately above	N/A
Total costs	**£837,996** **£168/**admitted at-risk patient	**£1,243,516** **£249/** admitted at-risk patient	N/A	**£405,520** **(£81) per admitted patient**	N/A

Adverse event costs

If costs of adverse events were included in the analysis, explain how and why the risk of each adverse event was calculated.

Since the deployment of the device in 2014, no adverse events, or serious adverse events have been reported. No costing for adverse events has therefore been included in Model A.

Table 6 Adverse events and costs in the model

In this table, summarise the costs associated with each adverse event included in the model. Include all adverse events and complication costs, both during and after long-term use of the technology. Please explain whether costs are provided per patient or per event.

Adverse event	Items	Cost	Source
NOTE: This section is not applicable to the SEM Scanner based on all implementations to date.			
Adverse event 1	Technology	Text	Text
	Staff	Text	Text
	Hospital costs	Text	Text
	[Other items]	Text	Text
	Total	Text	Text
Adverse event 2	Technology	Text	Text
	Staff	Text	Text
	Hospital costs	Text	Text
	[Other items]	Text	Text
	Total	Text	Text
			[Add more rows as needed]

Miscellaneous costs

Describe any additional costs or resource considerations that have not been included elsewhere (for example, PSS costs, and patient and carer costs). If none, please state.

None

Are there any other opportunities for resource savings or redirection of resources that have not been possible to quantify?

Yes.

1. The Model presumes that all PUs occur exclusively in the at-risk population. PUs also occur, however, in patients deemed to not be at risk (e.g., maternity patients). These costs have not been modelled or included. An opportunity for the use of the SEM Scanner is to use all of the data being imputed to the Company's PU Registry to better risk-stratify patients to decrease the number of patients' anatomies missed by the current standard of care.
2. The beneficial patient-effect of patients' own involvement in their care plans. Anecdotally, patients respond to numbers and the technology and are more actively curious about their own care and "what the numbers mean". See the patient's response in this BBC video as an example, https://www.bbc.com/news/av/uk-england-hampshire-41065539/the-bedsore-scanner-which-could-save-thousands-of-lives
3. The societal benefit of the increase in QALYs from prevention of PUs.
4. The cost optimisation arising from having objective evidence of the efficacy of clinical interventions for a given patient cohort, e.g., one heel boot having higher prevention efficacy as measured by SEM values versus the efficacy of another heel boot.

Total costs

In the following tables, summarise the total costs:

- Summarise total costs for the technology in table 7.
- Summarise total costs for the comparator in table 8. This can only be completed if the comparator is another technology.

Table 7 Total costs for the technology in the model

Description	Cost	Source
Cost per treatment/patient over lifetime of device "scanning episode" = "treatment/patient"	3year warranted life of device. 23 devices/4995 at risk patients/year = 217 patients per year per device 217*3= 651 scanning episodes (3 anatomies,14 scans per scanning episode)/device **£5,835/651 =£8.96/scanning episode**	Model A

Consumables per year (if applicable) and over lifetime of device	NA	N/A
Maintenance cost per year and over lifetime of device	£0	NA
Training cost over lifetime of device	Costed at £18 for 1-hour training per band 5 on implementation £18 *3=£54 1 device per every 6.4 nurses Total nurse training per device £54 *6.4= £**345.60/651 scanning episodes/device = £0.53/scan/device**	Model A
Other costs per year and over lifetime of device	£1.50/scanning episode scanning time 651 scanning episodes * **£1.50** = **£976.50/year**	Model A
Total cost per treatment/patient over lifetime of device	**£8.96 + £0.53 + £1.50 = £10.99/treatment/patient/device**	Model A

Table 8 Total costs for the comparator in the model

Please note that the values shown below are for daily skin assessment by a nurse. This is the closest comparator but as represented appears to be more expensive than the SEM Scanner £16.80 versus £10.99 for the Scanner. Readers are reminded that MODEL A adds all scanning time to the daily skin inspection (as an adjunct). While this is not truly reflective of the reality – scanning is done in approximately 5 minutes as part of the skin assessment – the Company wanted to be very conservative in its costing, so added the two values. Therefore, a better comparison is skin assessment alone £16.80/treatment/patient vs skin assessment and SEM as adjunct £16.80+£10.99 = £27.79/treatment/patient. Recall that only at risk-patients are scanned in the model. This is a considerable overstatement of the costs of SEM as an adjunct to the current standard of care. It is true that adding the SEM Scanner adds cost to the prevention stage of the care pathway and that it saves costs in the overall pathway because of incidence reduction.

Description	Cost	Source
Cost per treatment/patient over lifetime of device – note costed per high risk patient – comparator is standard of care	Daily skin assessment of £16.80	QALY Model using NICE/NHS standard costs
Consumables per year (if applicable) and over lifetime of device	N/A	N/A
Maintenance cost per year and over lifetime of device	N/A	N/A
Training cost over lifetime of device	No specific device – Nurse training includes PU prevention	N/A
Other costs per year and over lifetime of device	NA	N/A
Total cost per treatment/patient over lifetime of device	£16.80	QALY Model using NICE/NHS standard costs

Results

Table 9 Base-case results

In this table, report the results of the base-case analysis. Specify whether costs are provided per treatment or per year. Adapt the table as necessary to suit the cost model. If appropriate, describe costs by health state.

Costs per treatment ("scan")

	Mean discounted cost per patient using the technology (£)	Mean discounted cost per patient using the comparator (£)	Mean discounted cost per patient using the comparator (£)	Difference in mean discounted cost per patient (£): technology vs comparator 1*	Difference in mean discounted cost per patient (£): technology vs comparator 2*
Device cost	£8.96	£0	N/A	(£8.96)	N/A
Training cost	£0.53	included as standard training £0	N/A	(£0.53)	N/A
Administration cost	£1.50	Text	N/A	(£1.50)	N/A
Monitoring costs	N/A	Text	N/A	Text	N/A
Consumables	N/A	Text	N/A	Text	N/A
Adverse events	N/A	Text	N/A	Text	N/A
Total	£10.99	Text	N/A	£10.99	N/A
* Negative values indicate a cost saving. Adapt this table as necessary.					

Scenario analysis

If relevant, explain how scenario analyses were identified and done. Cross-reference your response to the decision problem in part 1, section 1 of the submission.

A range of scenario analyses were performed. PU incidence reduction rates – observed incidence reduction rates, a 10% reduction rate, and a 100% reduction rate – we modelled. Most other variables were fixed. This therefore was the main driver in measuring the effectiveness of the SEM Scanner in the prevention focused pathway.

The Incidence reduction rate has to be fixed at 11% to obtain the same cost outcomes as the current standard of care.

Describe the differences between the base case and each scenario analysis.

The base case remained the same in each analysis. Please see the tab, 'Results – SoC vs SEM Adjunct'

Describe how the scenario analyses were included in the cost analysis.

They established, particularly on the lower boundary, the threshold beyond which the current standard of care is as effective as the SEM adjunct standard of care. In reality none of the PURP implementation have had incidence reductions of reported ulcers below the threshold value, so the value of the scenario analyses have been limited to establishing threshold values.

Describe the evidence that justifies including any scenario analyses.

The real-world usage of the device (PURP report provided in the clinical submission) is highly informative.

Table 10 Scenario analyses results

In this table, describe the results of any scenario analyse that were done. Adapt the table as necessary.

	Mean discounted cost per patient using the	Mean discounted cost per patient using the	Difference in cost per patient (£)*

	technology (£)	comparator (£)	
Scenario 1 (total costs)	Text	Text	Text
Scenario 2 (total costs)	Text	Text	Text
* Negative values indicate a cost saving. Adapt this table as necessary.			

Sensitivity analysis

Describe what kinds of sensitivity analyses were done. If no sensitivity analyses have been done, please explain why.

We performed sensitivity and threshold analysis on the base scenario to identify the impact that variation in assumptions would have on the base case outcome. It should be noted that the base case represents a conservative savings case.

Sensitivity analysis (+/- 15%)
Univariate analysis for each cost, probability, and utility variable was performed. The +/- 15% variation of each variable did not change the outcome of the result: a SEM Scanner implementation continued to dominate the current standard of care.
A further sensitivity scenario was performed where all variables listed below were adjusted by 15% to reduce the effectiveness of SEM Scanner implementation.

- Number of hours of training required per nurse increased by 15% to 1.15 hours;
- Number of band 5 nurses treating the 12,181 patients across three shifts increased by 15% to 168 nurses;
- Price of the SEM Scanner increased by 15% to £6,710.25;
- Nurse band 5 wage increased by 15% to £20.70;
- Time taken to scan the patient increased by 15% to 5.75 minutes;
- Pressure ulcer reduction from implementing the SEM Scanner reduced by 15% to 68%;
- Specificity rate when using the SEM Scanner reduced by 15% to 51%;
- Decreased the number of days it takes for a PU to heal (Dealey, Posnett, and Walker, 2012) by 15%;
- Increased the PU cost per episode by 15% for each PU grade (Dealey, Posnett, and Walker, 2012);
- Increased the number of intentional rounding's per day and the time it takes a nurse per rounding by 15%; and
- Decreased difference in total QALY between healthy and non-healthy patients by 15%.

Summarise the variables used in the sensitivity analyses and provide a justification for them. This may be easier to present in a table (adapt as necessary).

The top-10 most sensitive variable are shown in the table below.

If any parameters or variables listed in table 3 were omitted from the sensitivity analysis, please explain why.

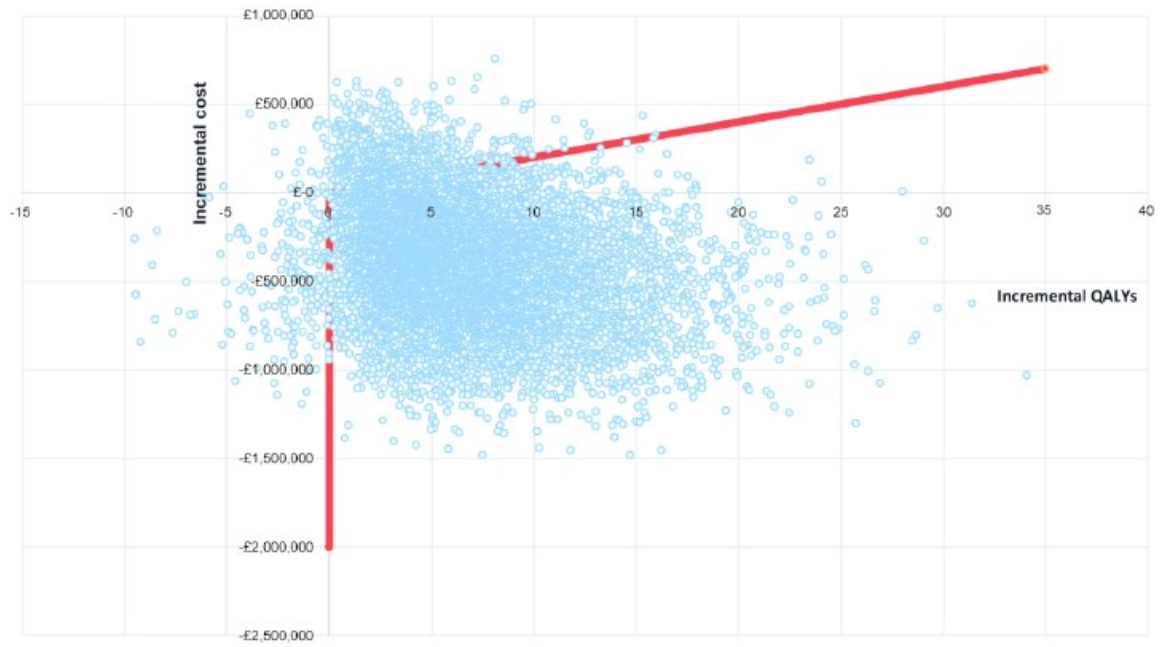
The variables below were not included in the above threshold analysis:

- Training per Nurse (hours) because a 1% change in this variable did not affect the ICER value.
- Number of Nurses because a 1% change in this variable did not affect the ICER value.
- Average Length of Stay because this only affects the number of admissions, which is a measure of scale rather than impact.
- Time per SEM Scan (mins) because the SEM Scanner was still cost saving when the Time per SEM Scan was over an hour.
- Specificity rate because the +/- 15% sensitivity testing is more applicable for this variable.

Sensitivity analyses results

Present the results of any sensitivity analyses using tornado plots when appropriate.

Sensitivity Analysis
The cost plane chart below shows the results of the probabilistic sensitivity analysis (10,000 iterations). In 89% of iterations, the SEM Scanner was dominant, and in a further 1% (90%) the SEM Scanner was cost effective at a willingness-to-pay threshold of £20,000 per QALY gained.



What were the main findings of each of the sensitivity analyses?

The cost plane chart below shows the results of the probabilistic sensitivity analysis (10,000 iterations). In 89% of iterations, the SEM Scanner was dominant, and in a further 1% (90%) the SEM Scanner was cost effective at a willingness-to-pay threshold of £20,000 per QALY gained.

What are the main sources of uncertainty about the model's conclusions?

The main source of uncertainty is the starting observed incidence rate. A 1.6% rate as used is a good indicative value. Cleary some sites of service have lower values, while others higher. Sites of service with very low starting observed incidence (0.23) increase the uncertainty of the cost savings or cost-effective nature of the SEM Scanner as an adjunct case.

Miscellaneous results

Include any other relevant results here.

Enter text.

Validation

Describe the methods used to validate, cross-validate (for example with external evidence sources) and quality assure the model. Provide sources and cross-reference to evidence when appropriate.

Validation scope and process are discussed below.

Model design and health economic validation
The underlying philosophy was to build the model using only peer reviewed publications and standard NHS publicly available costings to ensure accuracy and validity. Secondly the model utilises NICE CG 179 as the standard of care for Pressure Ulcer Prevention and Treatment to ensure that the standard of care comparator was the most valid and relevant possible. In addition the model has undergone a variety of detailed sensitivity analysis in order to represent faithfully the variances that will most likely impact cost efficiencies.

The model has been further validated via the following methodologies:

- 1:1 review with individual clinical experts in pressure ulcer management
- Public presentation at International Scientific Conference (WCICT 2018)
- 1:1 review with two globally recognised health economic experts. Prof J Posnett who acted as advisor on the development of the manuscript submitted to Journal of Wound Care and Prof W Padula who has subsequently supported the development of a “like” model based on the US health system – a manuscript is in preparation and will be submitted for publication shortly.
- Reviewed by Health Innovation Manchester (HinM)– reviewed as part of a submission to the Manchester Innovation & Prioritization Monitoring Committee under the auspices of Ben Bridgewater, and Bradley Quinn, Insight and Intelligence Lead, Health Innovation Manchester
- PURP sites – customised site and care setting specific site reports at end of PURP include ROI elements and have been reviewed at each PURP site by nurse leaders for real world application.

Clinical validation

Give details of any clinical experts who were involved in validating the model, including names and contact details. Highlight any personal information as confidential.

The following clinical experts have been involved in validation of various elements of the model: please note we have not included in this document contact details due to GDPR.

- Isle of Wight Hospital, Isle of Wight. Glenn Smith – Formerly Lead Tissue Viability & Patient Safety St Marys' NHS Trust, Isle of Wight
- Marie Curie. Gillian Raine – Lead Nurse, Marie Curie Hospice, Marie Curie Drive, Newcastle upon Tyne NE4 6SS
- Virgin Care (7 Community Hospitals in Kent, Bath and Surrey). Matt Hodson, Chief Nurse Virgin Care Ltd, London
- Northumbria Healthcare NHS Foundation Trust (Northumberland Specialist Emergency Care Hospital, North Tyneside Hospital, Wansbeck Hospital). Jeanette Milne – formerly Lead Tissue Viability Nurse Northumbria Healthcare NHS Foundation Trust
- Lancashire Teaching Hospitals NHS Foundation Trust (Royal Preston Hospital). Elaine Entwistle – Lead Tissue Viability Nurse

Model functionality validation
Both the company and Deloitte LLP, Risk Advisory have put the model through our respective quality assurance processes.

4 Summary and interpretation of economic evidence

Describe the main findings from the economic evidence and cost model. Explain any potential cost savings and the reasons for them.

Results are shown in the table below. For an at-risk population of 4995, introduction of the SEM Scanner is expected to save £405,520 in the first year, or £81 per at risk admitted.

The incremental cost of the scanner itself is £60,962 and this includes the capital cost of the SEM Scanner amortised over 3 years, the costs of training in year 1 and the cost of the additional time required for the scan. The incremental costs of the prevention phase of the PU prevention and management pathway are estimated at £90,653 or £18.15 per at-risk patient.

The number of ulcers is expected to be lower with the SEM Scanner by 57 (80-23) (68.9% observed reduction) and the savings in treatment costs is estimated at £496,172. The reduction in PU incidence is associated with an improvement in quality of life. The QALY gain is estimated at 0.046 per 100 patients at risk.

Cost Savings
Cost savings were divided into materials costs savings and labour/overhead. The latter are classed in the model as freed-up time to care, not a cost-reduction. Materials costs, by contrast, are classed as variable in the near term. While this is not always true (e.g., mattresses can be on a fixed-term rental contract and therefore behave as fixed costs), it is true that other materials e.g., dressings and supplies vary in their use according to incidence. A table of cost savings is shown below:

	Current standard of care material costs	SEM Scanner adjunct to CSoC material costs	Estimated savings in year of deployment from material costs (dressings, supplies being variable costs. Surfaces are variable costs over the medium term)
Grade 1	£0.00	£0.00	£0.00
Grade 2	£98,078.10	£29,060.18	£69,017.92
Grade 3	£98,681.99	£25,968.95	£72,713.05
Grade 4	£100,604.64	£28,744.18	£71,860.46
Total	**£297,364.73**	**£83,773.31**	**£213,591.43**

Results of the base case analysis suggest that use of the SEM Scanner alongside current SoC is a dominant, cost-saving option. The main driver of these results are:

1.) the greater sensitivity of the SEM Scanner in detecting tissue damage earlier than is possible with visual inspection alone. In the base case, the reduction in the incidence of HAPUs is 68.9%. The SEM Scanner option remains dominant at a reduction of anything above 11%.
2.) The catastrophic patient, treatment and cost consequences of treating PUs with broken skin. Once a PU exceeds Grade 2, the complexities and therefore costs of treatment rise nonlinearly.

The economic incentive is therefore to prevent rather than treat. At the modelled values, the SEM Scanner is the dominant quality intervention that subordinates all others.

Briefly discuss the relevance of the evidence base to the scope.

The scope as related to the cost-analysis were considered from an NHS service and personal social services perspective. The time horizon for the cost-analysis was long enough to reflect differences in costs and consequences of the technologies being compared.

This analysis is deliberately conservative. We have assumed an incidence rate of 1.6% for hospital acquired ulcers following a widely accepted clinical pathway for HAPU prevention and management [3,7,9,12, 14,17-24]. Other sources suggest the annual incidence rate in the UK may be as high as 4.0–5.7%[17]. In addition, category 1 ulcers are excluded from the analysis. Management and treatment of category 1 ulcers come at a cost and reduction of these ulcers would result in additional cost savings and improvements in health-related quality of life. The estimated reduction in the incidence of hospital acquired ulcers (68.9%) was derived from the sensitivity and specificity results of the SEM200-008 study[12]. UK hospitals using the SEM Scanner have shown a reduction of more than 95% in community hospitals over a 6-month period[23] and seven out of ten acute care hospitals observed a 100% reduction HAPUs in a SEM Scanner programme in the UK, Spain and Canada, with an average reduction of 86.2%[24].

Therefore, in a UK acute care setting with costs analysed over 1 year, the SEM Scanner used as an adjunct to a commonly accepted prevention pathway is a dominant intervention for preventing HAPUs compared with SoC alone. The SEM Scanner as a part of a standardised and evidence-based PU prevention and management programme has the potential to produce cost savings by preventing avoidable PUs and by halting the possible progression of early stage ulcers by detecting them earlier than the current standard method of visual assessment.

Briefly discuss if the results are consistent with the published literature. If they are not, explain why and justify why the results in the submission be favoured over those in the published literature.

Inconsistencies
The main inconsistency is the imputed incidence reduction rate of 68.9% (and higher). These types of incidence reduction results are reported in short deployments of other quality interventions, but are (to our knowledge), not common. The reported PURP results are therefore of particular value and are recognized as unusual.

Consistencies
Demarre. L et al (2017[25]) showed that prevention is better than treatment. These modelled results also demonstrate
those results.

Describe if the cost analysis is relevant to all patient groups and NHS settings in England that could potentially use the technology as identified in the scope.

CG179 states that all patients are potentially at risk of developing a PU.

This analysis is relevant to all patient groups, although caution is provide here that the device is not yet approved for use on pediatric patients.

Briefly summarise the strengths and limitations of the cost analysis, and how these might affect the results.

The analysis has a number of limitations. Estimates of the sensitivity and specificity of the SEM Scanner are taken from a well-designed clinical study in which participants were trained and practice followed a defined protocol. In normal clinical practice results may be different.

The costs of treating an incident ulcer assume a single episode which does not allow for the possibility that an incident ulcer may progress over time into a more severe state leading to additional costs. The costs of a standard prevention protocol will also vary between centres. More significantly, the full benefits of the SEM Scanner can only be realised if prevention practice is adapted to the new information provided by the SEM scanner.

Detail any further analyses that could be done to improve the reliability of the results.

Extend the analysis to the community (district nursing) setting.

5 References

Please include all references below using NICE's standard referencing style.

Bruin Biometrics LLC Health Economic Submission MT 455 SEM Scanner Reference List

Note: reference list does not include excluded studies listed in Appendix A

1. NICE. Pressure ulcers: implementing the NICE guideline on pressure ulcers (CG179). (2014) Available at https://www.nice.org.uk/guidance/cg179/resources/pressure-ulcers-prevention-and-management-pdf-35109760631749. Accessed October 2019
2. Vanderwee, K., Clark, M., Dealey, C. et al. (2007). Pressure ulcer prevalence in Europe: a pilot study. J Evaluation in Clinical Practice 13; 227-235
3. Moore Z, Patton D, Rhodes SL, et al. (2017). Subepidermal moisture (SEM) and bioimpedance: a literature review of a novel method for early detection of pressure-induced tissue damage (pressure ulcers). Int Wound J. 14:331–337
4. National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance. Prevention and Treatment of Pressure Ulcers: Clinical Practice Guideline. Emily Haesler (Ed.). Cambridge Media: Osborne Park, Western Australia: 2014
5. Burns M. King T. Tsang K. Grainger S. Tang S. Modernising the pressure ulcer prevention care pathway: a cost-effectiveness analysis. Submitted to Journal of Wound Care. In review process – manuscript number jowc.2019.0193
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7. Dealey C, Posnett J, Walker A. (2012). The cost of pressure ulcers in the United Kingdom. J Wound Care. 21:261–266
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11. NHS England. Bed availability and occupancy data. November 2018. https://www.england.nhs.uk/statistics/statistical-work-areas/bed-availability-and-occupancy/beddata-overnight/. Accessed October 2019
12. NICE. Costing statement: pressure ulcers: implementing the NICE guideline on pressure ulcers (CG179). 2014. https://www.nice.org.uk/guidance/cg179/resources/costing-statement-pdf-248688109. Accessed October, 2019
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14. Bennett G, Dealey C, Posnett J. (2004). The cost of pressure ulcers in the UK. Age Ageing. 33:230–235
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17. Gorecki C, Brown JM, Nelson EA, et al. (2009). Impact of pressure ulcers on quality of life in older patients: a systematic review. J Am Geriatr Soc. 57:1175–1183
18. Padula WV, Gibbons RD, Valuck RJ, et al. (2016). Are evidence-based practices associated with effective prevention of hospital-acquired pressure ulcers in US academic medical centers? Med

Care. 54:512–518
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20. Posnett J, Gottrup F, Lundgren H, et al. (2009). The resource impact of wounds on health-care providers in Europe. J Wound Care. 18:154–161
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23. Littlefield S, Kellett N. Chasing zero: results from a new pressure ulcer prevention bundle. (2016). Poster presented at EMWA Conference, Bremen, Germany, May 11–13.. ://bruinbiometrics.com/images/Littlefield_VC-Results-from-New-PU-Prevention-Bundle.pdf. Accessed April 9, 2019
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25. Demarre L. Van Lancker A. Van hecke A. Verhaeghe S. Grypdonck M. Lemey J. Annemans L. Beeckman D. (2015). The cost of prevention and treatment of pressure ulcers: A systematic review. Int J Nurs Stud. Nov;52(11):1754-74

6 Appendices

Appendix A: Search strategy for economic evidence

Describe the process and methods used to identify and select the studies relevant to the technology being evaluated. See section 2 of the user guide for full details of how to complete this section.

Date search conducted:	Friday, October 26, 2019. Note, we conduct searches frequently (approximately every 6 months) to make sure we are current on all publications. This most recent search was to confirm we have not missed a recent, relevant publication.
Date span of search:	January 2012-Present Day The cut-off of January 2012 was chosen because the seminal Dealey (2012) paper established nationally recognized health economic statistics in 2012. Costs per PU stage before that paper are outdated.
List the complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean). List the databases that were searched.	
PUBMED (NCBI) Pressure Ulcers AND Costs AND economics AND United Kingdom NOT incontinence-associated dermatitis NOT diabetic foot ulcer NOT venous leg ulcer (((((("pressure ulcer"[MeSH Terms] OR ("pressure"[All Fields] AND "ulcer"[All Fields]) OR "pressure ulcer"[All Fields] OR ("pressure"[All Fields] AND "ulcers"[All Fields]) OR "pressure ulcers"[All Fields]) AND ("economics"[Subheading] OR "economics"[All Fields] OR "cost"[All Fields] OR "costs and cost analysis"[MeSH Terms] OR ("costs"[All Fields] AND "cost"[All Fields] AND "analysis"[All Fields]) OR "costs and cost analysis"[All Fields])) AND ("united kingdom"[MeSH Terms] OR ("united"[All Fields] AND "kingdom"[All Fields]) OR "united kingdom"[All Fields]) AND ("economics"[Subheading] OR "economics"[All Fields] OR "economics"[MeSH Terms]) NOT (incontinence-associated[All Fields] AND ("dermatitis"[MeSH Terms] OR "dermatitis"[All Fields]))) AND ("01/2012"[CRDAT] : "3000"[CRDAT])) NOT ("diabetic foot"[MeSH Terms] OR ("diabetic"[All Fields] AND "foot"[All Fields]) OR "diabetic foot"[All Fields] OR ("diabetic"[All Fields] AND "foot"[All Fields] AND "ulcer"[All Fields]) OR "diabetic foot ulcer"[All Fields])) NOT ("varicose ulcer"[MeSH Terms] OR ("varicose"[All Fields] AND "ulcer"[All Fields]) OR "varicose ulcer"[All Fields] OR ("venous"[All Fields] AND "leg"[All Fields] AND "ulcer"[All Fields]) OR "venous leg ulcer"[All Fields]	

Brief details of any additional searches, such as searches of company or professional organisation databases (include a description of each database):
Bruin Biometrics analysis of the NHS's Safety Thermometer database (NHS Digital) for the periods 2012-2018). The NHS Safety Thermometer database is a measurement tool for the improvement in healthcare with a focus on the most common patient harms. Bruin Biometrics sponsored analysis of Hospital Episode Statistics. Source NHS Digital 2016/17. Hospital Episode Statistics is a database containing details of all admissions, A and E attendances and outpatient appointments at NHS hospitals in England.
Inclusion and exclusion criteria:
NHS Safety Thermometer- Classic version Inclusion: Pressure Ulcer statistics 2012 to 2018 Exclusion: Non-PU related statistics – the NHS Safety Thermometer Classic version also collates data on patient falls, UTI, VTE Hospital Episode Statistics. Source NHS Digital 2016/17 Inclusion: ICD-10: L890, L891, L892, L893, L899 Exclusion: all other codes not related to PU
Data abstraction strategy:
NHS Safety Thermometer The focus was to investigate the trends of pressure ulcer incidence and prevalence via detailed analysis of the data from 2012 to 2018. The analysis was designed to demonstrate national and regional geographic data along with care setting analysis. Hospital Episode Statistics. Source NHS Digital 2016/17 Abstraction strategy was focused upon the following data • PU's incurred during stay in hospital • Top 10 primary reasons for admission to an NHS Hospital Leading to a PU • Total PU by type (ICD-10) activity over the last 12 months in NHS England • By CCG Nationally, and by hospital provider • Average length of stay • Average patient wait time for treatment/referral • Average age of patient • Age bands • Bed days • Type of admission – i.e. emergency or elective

Excluded studies

List any excluded studies below. These are studies that were initially considered for inclusion at the level of full text review, but were later excluded for specific reasons.

Excluded study	Design and intervention(s)	Rationale for exclusion	Company comments
NHSLA litigation in hip fractures: Lessons learnt from NHSLA data. Ring J, Talbot C, Cross C, Hinduja K. Injury. 2017 Aug;48(8):1853-1857	Purpose of the study was to assess the reasons for litigation surrounding hip fractures, A request was made to the NHSLA for data from the financial years 1995–2012 relating to all orthopaedic claims, using the Freedom of Information Act (2000).	Focus of publication is on litigation costs of orthopaedic trauma	Not included due to litigation focus rather than cost of care
Pressure ulcer prevention is everyone's business: the PUPS project. Blenman J, Marks-Maran. Br J Nurs. 2017 Mar 23;26(6):S16-S26	Descriptive narrative of pressure ulcer prevention project	Based upon previously published costs that are already included in the analysis in this submission	The model and submission has already included the data from the original publication referenced
Pressure Relieving Support Surfaces: a Randomised Evaluation 2 (PRESSURE 2): study protocol for a randomised controlled trial. Brown S. et al. Trials. 2016 Dec 20;17(1):604.	Study protocol description	This publication did not include costing of PU and therefore was not deemed relevant.	Not relevant to the model development

Quality improvement in health care: how to do it. Walsh K, Helm R, Aboshady OA. Br J Hosp Med (Lond). 2016 Sep 2;77(9):536-8	Descriptive narrative of the PDSA Quality Cycle – example of a PDSA in PU prevention included	Based upon previously published costs that are already included in the analysis in this submission	The model and submission has already included the data from the original publication referenced
Profile and costs of secondary conditions resulting in emergency department presentations and readmission to hospital following traumatic spinal cord injury. Gabbe BJ, Nunn A. Injury. 2016 Aug;47(8):1847-55	Retrospective cohort study utilising population level data.	Focus upon secondary conditions requiring readmission in spinal cord injury patients. The costs included in this publication are based in Australia and therefore not relevant	Not relevant to the model development
Parafricta Bootees and Undergarments to Reduce Skin Breakdown in People with or at Risk of Pressure Ulcers: A NICE Medical Technologies Guidance. Meads C, Glover M, Dimmock P, Pokhrel S. Appl Health Econ Health Policy. 2016 Dec;14(6):635-646. Review.	NICE Guidance Review MTG20	NICE Guidance document – no individual cost data available	Model has used relevant published data

A cost-effectiveness analysis of two different repositioning strategies for the prevention of pressure ulcers. Marsden G. et al. J Adv Nurs. 2015 Dec;71(12):2879-85	Cost utility model using data derived from a systematic review of the literature to analyse two different repositioning techniques	Based upon previously published costs that are already included in the analysis in this submission	The model and submission has already included the data from the original publication referenced
The psychometric performance of generic preference-based measures for patients with pressure ulcers. Palfreyman S, Mulhern B. Health Qual Life Outcomes. 2015 Aug 1;13:117.	Patient survey investigating quality of life impact of pressure ulcers	This publication focuses upon quality of life impact via a patient survey in both acute and community settings. It. Is not relevant to the model development	Not relevant to the model development
A quality improvement programme to reduce pressure ulcers. Heywood N. et al. Nurs Stand. 2015 Jul 15;29(46):62-70	Descriptive narrative of a pressure ulcer prevention project using the Rapid Spread Methodology which is used to help the NHS introduce evidence-based care at scale and pace across a whole organisation.	This is a descriptive narrative however it also comment upon previously published costs that are included in the analysis included in this submission.	The model and submission has already included the data from the original publication referenced
Recording pressure ulcer risk assessment and incidence. Plaskitt A, Heywood N, Arrowsmith M. Nurs Stand. 2015 Jul 15;29(46):54-61.	Descriptive narrative of the introduction of electronic record system – publication describes impact on pressure ulcer incidence	Based upon previously published costs that are already included in the analysis in this submission	The model and submission has already included the data from the original publication referenced

Pressure ulcers. Nurs Stand. 2015 Jul 1;29(44):17	Clinical supplement – general description of the extent of the issue of pressure ulcers	Based upon previously published costs that are already included in the analysis in this submission. Note this publication does estimate number of PU per annum in England at 700,000	The model and submission has already included the data from the original publication referenced
Introducing A Care bundle To prevent pressure injury (INTACT) in at-risk patients: A protocol for a cluster randomised trial. Chaboyer W. et al. Int J Nurs Stud. 2015 Nov;52(11):1659-68	Descriptive narrative of a pending RCT	Description of a pending RCT – no cost data included	Model has used relevant published data
Reconciling increasing wound care demands with available resources. Dowsett C, Bielby A, Searle R. J Wound Care. 2014 Nov;23(11):552, 554, 556-8	This publication reports an analysis using a variety of published data sources to estimate future demand – note this is a wider wound care focus rather than specifically pressure ulcers	Based upon previously published costs that are already included in the analysis in this submission.	The model and submission has already included the data from the original publication referenced
Point prevalence of complex wounds in a defined United Kingdom population. Hall J. et al. Wound Repair Regen. 2014 Nov-Dec;22(6):694-700	Report of a prevalence survey of complex wounds in one UK City. note this is a wider wound care focus rather than specifically pressure ulcers	The publication does not identify new costings of PU	The model and submission has already included data based on seminal publications

A systematic review of economic evaluations assessing interventions aimed at preventing or treating pressure ulcers. Palfreyman SJ, Stone P. W. Int J Nurs Stud. 2015 Mar;52(3):769-88		Based upon previously published costs that are already included in the analysis in this submission	The model and submission has already included the data from the original publication referenced
The return on investment of implementing a continuous monitoring system in general medical-surgical units. Slight S. P. et al. Crit Care Med. 2014 Aug;42(8):1862-8.	ROI model analysis. Two models developed - base case model which estimated total cost savings of intervention effects, model (B) a conservative model which only included the direct variable cost component for the final day of length of stay and treatment of pressure ulcers	This publication is USA based and therefore not relevant	The model uses UK based published data
“Spin" in wound care research: the reporting and interpretation of randomized controlled trials with statistically non-significant primary outcome results or unspecified primary outcomes. Lockyer S. Trials. 2013 Nov 6;14:371	Report of analysis into the reporting of RCT results – not relevant to the development of the model	This publication does not include relevant data	The model and submission has already included UK published data
Introduction to economic assessment. McMahon A, Sin CH. Nurs Manag. 2013 Nov;20(7):32-8	Descriptive narrative	This is a methodological analysis – there is no relevant PU costing data	The model and submission has already included UK published data

Pressure ulcer prevention in the community setting. Jones. D. Nurs Stand. 2013 Sep 18-24;28(3):47-55	Descriptive narrative of pressure ulcer prevention methods	Based upon previously published costs that are included in the analysis included in this submission.	The model and submission has already included the data from the original publication
Pressure redistribution devices: what works, at what cost and what's next? Clancy M. J Tissue Viability. 2013 Aug;22(3):57-62	Report that reviews the development of and impact of preventative solutions. Expenditure was modelled on a £500 bed UK hospital using previously published data	Based upon previously published costs that are already included in the analysis in this submission	The model and submission has already included the data from the original publication referenced
Working towards clinical excellence. Pressure ulcer prevention and management in primary and secondary care. Benbow M. J Wound Care. 2012 Sep;21(9 Arjohuntleigh Suppl):S26-39.	Descriptive narrative of a pressure ulcer prevention project in one UK hospital	This publication does not include relevant data.	This is a commercially sponsored supplement
Methods to assess cost-effectiveness and value of further research when data are sparse: negative-pressure wound therapy for severe pressure ulcers. Soares M. O. et al. Med Decis Making. 2013 Apr;33(3):415-36.	Decision analytic modelling. Data identified from a literature search, expert opinion and data from a pilot trial	Focus of this publication is on the evidence supporting the use of NPWT rather than explicitly the challenge of pressure ulcer prevention.	The model and submission has already included the data from the original publication referenced.

Pressure ulcer risk assessment. Guy H. Nurs Times. 2012 Jan 24-30;108(4):16, 18-20.	Descriptive Narrative	This publication does not include data (especially costs data)	The model and submission has already included UK published data
Cost-effective non-surgical treatment of chronic pressure ulcers in the community. Dale M. et al. Br J Community Nurs. 2014 Mar;Suppl:S6, S8-12.	Comparative cost. Model comparing 2 potential models of care one of which includes the provision of an outreach service designed to reduce recurrence of pressure ulcers.	Based upon previously published costs that are already included in the analysis in this submission	The model and submission has already included the data from the original publications referenced

Report the numbers of published studies included and excluded at each stage in an appropriate format (e.g. PRISMA flow diagram).

An economic data review as per the above exclusion and inclusion criteria was conducted as a keyword search in Pubmed and for appropriate NHS and NICE publications, not a systematic review. The objective was to locate data pertinent and specific to the construction of the economic cost model in terms of patient selection, clinical scenarios, and data related to UK PU prevalence and NHS material and utilisation cost of current treatments. The studies are presented in Table 1 and in the references in sections 2 to 4.

Structured abstracts for unpublished studies

Study title and authors
Introduction
Objectives
Methods
Results
Conclusion
Article status and expected publication: Provide details of journal and anticipated publication date

Appendix B: Model structure

Please provide a diagram of the structure of your economic model.

Appendix C: Checklist of confidential information

Please see section 1 of the user guide for instructions on how to complete this section.

Does your submission of evidence contain any confidential information? (please check appropriate box):

No X If no, please proceed to declaration (below)

Yes ☐ If yes, please complete the table below (insert or delete rows as necessary). Ensure that all relevant sections of your submission of evidence are clearly highlighted and underlined in your submission document, and match the information provided in the table. Please add the referenced confidential content (text, graphs, figures, illustrations, etc.) to which this applies.

Page	Nature of confidential information	Rationale for confidential status	Timeframe of confidentiality restriction
#	☐ Commercial in confidence ☐ Academic in confidence	Enter text.	Enter text.
Details	Enter text.		
#	☐ Commercial in confidence ☐ Academic in confidence	Enter text.	Enter text.
Details	Enter text.		

Confidential information declaration

I confirm that:

- all relevant data pertinent to the development of medical technology guidance (MTG) has been disclosed to NICE
- all confidential sections in the submission have been marked correctly
- if I have attached any publication or other information in support of this notification, I have obtained the appropriate permission or paid the appropriate copyright fee to enable my organisation to share this publication or information with NICE.

Please note that NICE does not accept any responsibility for the disclosure of confidential information through publication of documentation on our website that has not been correctly marked. If a completed checklist is not included then NICE will consider all information contained in your submission of evidence as not confidential.

Signed*: ** Must be Medical Director or equivalent*		**Date:**	October 30th 2019
Print:	Kate Hancock	**Role / organisation:**	VP Marketing and Clinical Communications
Contact email:	khancock@bruinbiometrics.com		

NICE National Institute for Health and Care Excellence

Medical technologies guidance

Collated expert questionnaires

Technology name & indication: **SEM Scanner 200 for pressure ulcer prevention**

Experts & declarations of interest (DOI)

<table>
<tr><td rowspan="2">Expert #1</td><td>Dr Fawad Hussain, Consultant Dermatologist and Skin cancer lead, Barking, Havering and Redbridge University Hospitals NHS Trust, , British Association of Dermatologists</td></tr>
<tr><td>DOI: None</td></tr>
<tr><td rowspan="2">Expert #2</td><td>Professor Michael Clark, Commercial Director, Welsh Innovation Centre, European Pressure Ulcer Advisory Panel; European Wound Management Association</td></tr>
<tr><td>DOI: Yes
<table>
<tr><th rowspan="2">Type of interest *</th><th rowspan="2">Description of interest</th><th colspan="2">Relevant dates</th></tr>
<tr><th>Interest arose</th><th></th></tr>
<tr><td>Direct - financial</td><td>Potential for future departmental involvement with the company around clinical education</td><td>Potential only</td><td></td></tr>
</table></td></tr>
<tr><td rowspan="2">Expert #3</td><td>Mrs Samantha Holloway, Reader/ Programme Director, Cardiff University School of Medicine, Tissue Viability Society</td></tr>
<tr><td>DOI: None</td></tr>
<tr><td>Expert #4</td><td>Glenn Smith, Advanced Nurse Practitioner, St Helen’s Medical Centre ,</td></tr>
</table>

	DOI: None
Expert #5	Dr Yun Mei Lau, Education and Quality Improvement Fellow, Intensive care Society,
	DOI: None
Expert# 6	Ms Trudie Young, Director of Education and Training, Welsh Wound Innovation Centre
	DOI: Yes

Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Choose an item.	I have a potential role in providing education on the technology for the company	16th April 2019	

How NICE uses this information: the advice and views given in these questionnaires are used by the NICE medical technologies advisory committee (MTAC) to assist them in making their draft guidance recommendations on a technology. It may be passed to third parties associated with NICE work in accordance with the Data Protection Act 2018 and data sharing guidance issued by the Information Commissioner's Office. Expert advice and views represent an individual's opinion and not that of their employer, professional society or a consensus view (unless indicated). Consent has been sought from each expert to publish their views on the NICE website.

For more information about how NICE processes data please see our privacy notice.

1. **Please describe your level of experience with the technology, for example: Are you familiar with the technology? Have you used it? Are you currently using it? Have you been involved in any research or development on this technology? Do you know how widely used this technology is in the NHS?**

Expert #1	I have read about it as part of this consultation, I have not seen it being used before.
Expert #2	I am familiar with the technology and the supporting scientific and clinical publications. As a non- clinician I have not used the technology. No involvement with prior research or development on the technology. My understanding is that the technology is currently limited in use in the NHS with growing interest in its potential.
Expert #3	I am familiar with the research supporting the technology but have not used it personally, neither have I been directly involved with any research or development. The technology is not currently widely used in the NHS in Wales.
Expert #4	In my previous role as TVN in an integrated Trust we did a two month trial on a medical surgical ward which showed positive results. We purchased four scanners. We have also developed separate unpublished data sets related to pt risk on admission. I have written or co authored several papers on the subject of the scanner. I have a proposed cost base analysis document in publication. I was highly commended on March 2017 in the Pressure Area Care Award and won the Best Product or innovation for patient Safety award with Bruin for work on the scanner and accompanying health economic models. I am aware of several trusts across the UK using the scanners and I am in contact with a number of TVNs.
Expert #5	No prior experience with SEM Scanner. No prior involvement in research or development of this said technology. Not aware of its usage in the NHS.
Expert#6	I have seen and had the technology and had its functionality described and discussed with me by the company. I have not used it in clinical practice. I have not been involved in the research or development of the technology. There is growing interest within the NHS, although currently used is isolated sites.

2. Has the technology been superseded or replaced?

Expert #1	No
Expert #2	No
Expert #3	Not that I am aware of
Expert #4	No
Expert #5	N/A
Expert#6	Not that I am aware of

Current management

3. How innovative is this technology, compared to the current standard of care? Is it a minor variation or a novel concept/design?

Expert #1	It is an innovative intervention, and I believe if it is shown to be effective by research, it will help with prevention of deeper pressure sore and allow for earlier treatment mostly in community
Expert #2	This is a novel concept which potentially could help target pressure ulcer preventive care
Expert #3	The SEM scanner represents a novel concept.
Expert #4	There is currently nothing else on the market like the scanner. Superficially there are similarities to the Delfin MMC device however the Delfin device does not provide the appropriate data set to inform front line clinicians. The scanner is novel and I am not aware of a comparable alternative.
Expert #5	Current practice involves a indicating on a body map on admission. This remains subjective and reliant on continuous checks by nursing staff. This technology would be an innovative.

Expert #6	It has potential however there needs to be further research that proves the technology prevents pressure ulceration.

4. Are you aware of any other competing or alternative technologies available to the NHS which have a similar function/mode of action to the notified technology? If so, how do these products differ from the technology described in the briefing?

Expert #1	None
Expert #2	No similar technology, closest alternative may be high frequency ultrasound which may also identify early stages of soft tissue changes
Expert #3	No
Expert #4	See above
Expert #5	No
Expert #6	Potentially high frequency ultrasound They are not comparable

Potential patient benefits

5. What do you consider to be the potential benefits to patients from using this technology?

Expert #1	Early detection of pressure sore and timely treatment.
Expert #2	Potentially earlier use of pressure ulcer preventive care
Expert #3	Early detection of impending tissue damage which may be missed by visual assessment alone.
Expert #4	Reduction in pressure ulcers

	Recognition of patient risk of skin breakdown.
Expert #5	Objective measure and allows for future planning.
Expert#6	Detection of early onset pressure damage

6. Are there any groups of people who would particularly benefit from this technology?

Expert #1	Patients who are bed ridden and have restricted mobility or are living in nursing homes.
Expert #2	All patients at risk of developing pressure ulcers
Expert #3	Any group of patients currently deemed to be at risk of developing a pressure ulcer
Expert #4	Patients potentially at risk of developing pressure ulcers.
Expert #5	Frail, malnourished patients. Long-term ventilated patients.
Expert#6	Individuals ‘at risk’ of developing pressure ulceration

7. Does this technology have the potential to change the current pathway or clinical outcomes? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?

Expert #1	Yes, I believe it has the potential to prevent pressure sores related complications hence reducing morbidity and mortality associated with these.
Expert #2	Potentially reduced pressure ulcer incidence and severity
Expert #3	There is a range of well-established evidence to support the detrimental effects of pressure damage to the patient i.e. pain, odour, leakage and extended hospital stay. Early detection of impending tissue damage could facilitate more timely pressure ulcer prevention interventions to maintain skin integrity thereby reducing the need for invasive treatment.

Expert #4	Yes. The data suggests avoidance of pressure ulcers, reduction in hospital and community costs and improvement of pt's quality of life.
Expert #5	Yes, it could potentially lead to fewer pressure sores/earlier identification and subsequent presentation of pressure sores which would contribute to length of stay.
Expert#6	It could reduce the need for community care if the technology is proven to prevent pressure ulcers

Potential system impact

8. What do you consider to be the potential benefits to the health or care system from using this technology?

Expert #1	Reduced need for referral to secondary care by allowing earlier intervention where there is evidence of sub-epidermal moisture in patients with risk of pressure sores, which can reduce duration of stay in hospital by preventing higher grade pressure sores and allow for associated cost savings and improved patient outcomes. Will also have limited role in secondary care in units such as rehab.
Expert #2	Potentially reduced avoidable harm (pressure ulcers) and improved quality of care
Expert #3	If an individual develops a pressure ulcer this presents a significant financial cost to the healthcare service in terms of increased length of stay, need for surgery intervention, potential requirement for antibiotics to treat infection. Early detection of impending tissue damage could facilitate more timely pressure ulcer prevention interventions to maintain skin integrity.
Expert #4	Reduction in length of stay. Productivity release. Cash release from non use of treatment products. Reduction in wound infection. Reduction in community visits.

	I have data to support these claims.
Expert #5	Improved patient outcomes
Expert#6	Potential to improve pressure ulcer prevention

9. Considering the care pathway as a whole, including initial capital and possible future costs avoided, is the technology likely to cost more or less than current standard care, or about the same?

Expert #1	I believe it would cost less.
Expert #2	Potentially increase in cost of care through use of the technology.
Expert #3	I would envisage that the costs would decrease over time as the incidence of pressure ulcers should also decrease if the technology is adopted as part of the pathway for patient assessment.
Expert #4	Less in the long run provided you are using the appropriate health economic analysis model and the current ones are not fit for purpose, e.g. Posnett et all, and the NHS calculator.
Expert #5	Over a long-term period, I believe it would be cost-efficient when balancing out length of stay and involvement of experts ie. Tissue viability team, plastic surgeons.
Expert#6	Difficult to answer until the benefits are realised, at this moment in time an additional cost.

10. What do you consider to be the resource impact from adopting this technology? Could it, for example, change the number or type of staff needed, the need for other equipment, or effect a shift in the care setting such as from inpatient to outpatient, or secondary to primary care?

Expert #1	I believe it will have a favourable impact, I believe the amount of specialist input from dermatology, tissue viability, district nurses and plastics would be reduced if the device helps diagnose pressure ulcers earlier and allow for earlier interventions in the community.
Expert #2	Potentially limited resource impact

Expert #3	I would see the main resource being training of staff to use the technology, but I would also expect there to be support from the company to support training. It would seem that the preferred approach is that the technology is used by specialists but I do wonder if there is scope to train other levels of staff to undertake the assessment and report back. I wonder if in time it's also feasible to train patients and carers to use the technology as there are similarities between this intervention and that of asking patients with diabetic foot disease to check their foot temperature in order to detect an impending ulcer.
Expert #4	Reduction in real costs of dressings and antibiotics Reduction in length of stay in hospital settings. Reduction in use of pressure relieving resources and appropriate utilisation Reduction in face to face contacts by community nurses. Productivity release.
Expert #5	As above
Expert#6	None of those listed, improvement in pressure ulcer prevention

11. Are any changes to facilities or infrastructure, or any specific training needed in order to use the technology?

Expert #1	The staff in the clinical settings where the device will be used will require training, it will also require charging points and safe storage of equipment
Expert #2	Training in use of the technology required
Expert #3	Specific training would be required but I would expect this to be provided by the company with ongoing arrangements for technical support much like is in place for pressure re-distributing equipment and prior to that training / support for use of Negative Pressure Wound Therapy.
Expert #4	Replace pressure ulcer risk assessment tools such as Waterlow or Braden with the Scanner.
Expert #5	Yes, specific and continuous training to extract maximum buy in to the technology.

Expert#6	Training by the company on the use and interpretation of result

12. Are you aware of any safety concerns or regulatory issues surrounding this technology?

Expert #1	None
Expert #2	None known
Expert #3	The device is not indicated for the paediatric population.
Expert #4	No
Expert #5	No. but keen to know
Expert#6	No

General advice

13. Please add any further comments on your particular experiences or knowledge of the technology, or experiences within your organisation.

Expert #1	I believe this device is going to be useful in early detection of pressure ulcers and has a potential to improve care of patients at risk of developing pressure ulcers.
Expert #2	No further comment
Expert #3	Blank
Expert #4	Happy to talk further in more detail. Too much to put into paper of this sort.
Expert #5	Blank

Expert#6	Blank

Other considerations

14. Approximately how many people each year would be eligible for intervention with this technology, either as an estimated number, or a proportion of the target population?

Expert #1	Not sure
Expert #2	Around 30% of in-patients would be at risk of pressure ulcer development.
Expert #3	Based on local data (over a 4 day period), the prevalence of hospital acquired pressure ulcers (HAPU) is 5.3% in a population of approximately 1570 patients. The data also suggests that approximately one-third of patients are deemed to be at low risk (based on the use of a risk assessment scale) of developing a pressure ulcer, one-third are medium risk and the remaining patients are high – severe risk. Therefore a large percentage of these would be eligible for the intervention would this technology. Of the 5.3% HAPU 28% were category 1 and 39% category 2. Use of the technology has the potential to detect any impending damage early to decrease the prevalence.
Expert #4	100% should be screened and those indicating risk to be followed up.
Expert #5	Almost all in ICU and majority of patients reduced mobility and with hospital stays >5 days.
Expert#6	It is difficult to quantify this at this moment in time.

15. Would this technology replace or be an addition to the current standard of care?

Expert #1	In addition to current standards
Expert #2	Addition to current standard of care
Expert #3	I would see this is addition to the current standard of care.

Expert #4	Replace current risk stratification tools for identifying patients at risk
Expert #5	To replace
Expert#6	addition

16. Are there any issues with the usability or practical aspects of the technology?

Expert #1	Staff will need to be trained; it will require charging points and safe storage.
Expert #2	Potentially the increased cost of making the technology widely available within care facilities
Expert #3	Training is required but I would see the technology as any more complicated than other automated devices use routinely in clinical practice. Users need to be aware of the requirement for skin to be clean and dry.
Expert #4	Integration into ward or clinical routine takes time as people understand and trust the evidence that the technology gives ward staff.
Expert #5	Concerns would be surrounding the longevity of the device.
Expert#6	Having to share the technology between patients

17. Are you aware of any issues which would prevent (or have prevented) this technology being adopted in your organisation or across the wider NHS?

Expert #1	None
Expert #2	Cost and uncertainty over the value of the information provided by the technology
Expert #3	No
Expert #4	The main issue is understanding that it needs to replace standard assessment tools such as Waterlow.

	The second element is that healthcare organisations so poorly understand their health economic outcomes and outcome/process/balance/structural measures that they cannot see that adopting the technology will significantly change patient safety.
Expert #5	No
Expert#6	no

18. Are you aware of any further evidence for the technology that is not included in this briefing?

Expert #1	None
Expert #2	Unpublished MSc and Phd theses described during presentations at the 2019 EPUAP conference (September 2019)
Expert #3	No
Expert #4	We have unpublished data at the moment which is awaiting publication regarding use on admission to hospital settings.
Expert #5	No
Expert#6	No

19. Are you aware of any further ongoing research or locally collected data (e.g. audit) on this technology? Please indicate if you would be able/willing to share this data with NICE. Any information you provide will be considered in confidence within the NICE process and will not be shared or published.

Expert #1	None
Expert #2	No awareness of local data collection
Expert #3	No
Expert #4	RCSI are using the scanner to look at diabetic foot ulcers.

	I presented anecdotal evidence that the scanner can pick up oedema and cellulitis. I am happy to share all of my information with NICE for their review.
Expert #5	No
Expert#6	no

20. Is there any research that you feel would be needed to address uncertainties in the evidence base?

Expert #1	Yes, I believe more research is needed to show efficacy of this device in detection of pressure sores and factors that will affect the sub-epidermal moisture readings, which might lead to false positive or false negative readings
Expert #2	The technology reports changes in water content within soft tissue; there is a gap between this information and being clear when tissue damage has occurred
Expert #3	Requirement for the technology to be used by specialists. Clinimetric assessment with other levels of healthcare professionals and also patients / carers would be useful to determine reliability.
Expert #4	Health economic analyses are urgently needed. There is a dearth of properly structured clinical papers that explore health economics of pressure ulcers in detail.
Expert #5	Will need to review current evidence
Expert#6	There still needs to be evidence that the technology prevents pressure ulcer formation.

National Institute for Health and Care Excellence

External Assessment Centre correspondence

[SEM Scanner]

The purpose of this table is to show where the External Assessment Centre relied in their assessment of the topic on information or evidence not included in the sponsors' original submission. This is normally where the External Assessment Centre:

a) become aware of additional relevant evidence not submitted by the sponsor
b) need to check "real world" assumptions with NICE's expert advisers, or
c) need to ask the sponsor for additional information or data not included in the original submission, or
d) need to correspond with an organisation or individual outside of NICE

These events are recorded in the table to ensure that all information relevant to the assessment of the topic is made available to MTAC. The table is presented to MTAC in the Assessment Report Overview, and is made available at public consultation.

Submission Document Section/Sub-section number	Question / Request *Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.*	Response *Attach additional documents provided in response as Appendices and reference in relevant cells below.*	Action / Impact / Other comments
Sections 2, 3, 4.2, 8.1	**Initial questions to company – 10.10.19** **Device** 1. In the rationale column on page 8, a "Reduction in incidence of hospital acquired pressure ulcers" is given as a patient benefit. Some of the evidence on SEM scanner was collected in social and tertiary care settings. Could you confirm that the SEM scanner is intended for use both in hospitals and in other care settings? 2. On page 15 of the report it states the "device consists of a pair of concentric coplanar electrodes", while in the Instructions for Use it states the device "consists of a single electrode sensor" – could you explain the discrepancy? Which is correct? 3. Based on the Instructions for Use, the device only gives a delta reading to 1-decimal place. Is this the case or can the device deliver readings to greater	**Response from company – 18.10.19** Device Questions – BBI Answers In the rationale column on page 8, a "Reduction in incidence of hospital acquired pressure ulcers" is given as a patient benefit. Some of the evidence on SEM scanner was collected in social and tertiary care settings. Could you confirm that the SEM scanner is intended for use both in hospitals and in other care settings? The SEM Scanner can be used in all care settings for adults. It IS in use in all care settings today (including acute, skilled nursing, community, end-of-life). Both CE and FDA authorisations provide for on-label use in all settings. Please note the product is labelled for adults not children. On page 15 of the report it states the "device consists of a pair of concentric coplanar electrodes", while in the Instructions for Use it states the device "consists of a single electrode sensor" – could you explain the discrepancy? Which is correct? We understand that this can be confusing – in fact both statements are correct. The SEM Scanner contains 2 single electrodes that are coplanar that form one electrode sensor. The two "electrodes," each of which is a single conductive area, that together form a "sensor." One electrode is the round	

Submission Document Section/Sub-section number	Question / Request *Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.*	Response *Attach additional documents provided in response as Appendices and reference in relevant cells below.*	Action / Impact / Other comments
	accuracy? For example, could the device give a reading of 0.59 or 0.61? 4. Is the SEM Scanner used on both heels and the sacrum in every patient (if a PU hasn't already broken the skin there)? 5. On page 89, it states that the results indicated "a sensitivity of 82% and a specificity of 51% at the conservative cut-off of SEM delta of >0.5". How was the cut-off point optimised? Was this calculated using a ROC curve or by another method? 6. On page 91, it refers to acting on "the biomarker" – does this refer to the bio-capacitance measurements? **Pathway** 1. In section 3 (Clinical Context), the implication from the diagrams is that SEM Scanner would be employed in patients who are "at risk", but not in "high risk" or "no risk identified" patients. Could you clarify (a) that this is the correct assumption and (b) how the three risk categories are	centre "dot" while the second electrode is the "doughnut" that is concentric around the dot. The two electrodes are on a common surface of the printed circuit board (PCB), i.e. coplanar. Based on the Instructions for Use, the device only gives a delta reading to 1-decimal place. Is this the case or can the device deliver readings to greater accuracy? For example, could the device give a reading of 0.59 or 0.61? In development cycle we started with 2 decimal places however BBI removed that feature in 2013 as we found that 1.) more than one decimal point had negligible limited clinical utility, 2.) was distracting users from looking at the delta value even more than if we just had one decimal point. Is the SEM Scanner used on both heels and the sacrum in every patient (if a PU hasn't already broken the skin there)? As a rule, yes to both sacrum and both heels – typically patients are scanned on admission to identify any increased risk of PU at the specific anatomies on admission. Dependant on the patient status and local policy the patient is then scanned on both heels and sacrum going periodically: daily in acute settings or at	

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	determined? Does it correspond to the risk assessment recommendations in NICE CG179? 2. It is mentioned that the SEM scanner is recommended to be used upon admission, during the patient's stay and at discharge (also section 3, pg20). How frequently during the patient's stay should the scanner be used? Is this at the nurse's discretion or related to the risk level? 3. On page 71, it states that readings are taken from centre of and around the wound, which is "defined as the discoloured tissue at and around a bony prominence (usually heel or sacrum)". Does this suggest that the SEM scanner is being used on areas where a developing PU is already apparent? Is the scanner used on non-discoloured skin as well? 4. On page 90, the submission asks the company to "Identify any factors which might be different between the patients in the submitted studies and	change of condition; once every 3 days in community/step-down facilities or at change of condition (per Virgin Care). This is very important as it is anatomically specific, with risk assessment tools they only identify risk for the whole body whereas the SEM Scanner works on an anatomically specific perspective. So for example the left heel could be identified as being at increased risk and interventions can therefore be focussed. Intact skin can be scanned; Scanning over broken skin is contraindicated. So, a category one where the skin is reddened can still be scanned but once the skin is broken scanning over the broken skin should not occur. On page 89, it states that the results indicated "a sensitivity of 82% and a specificity of 51% at the conservative cut-off of SEM delta of >0.5". How was the cut-off point optimised? Was this calculated using a ROC curve or by another method? To start we should explain that the development process identified that what we are trying to identify is an invisible process i.e. the sub-epidermal moisture and currently there is no gold standard test we can compare too. Here is the path we followed: 1. Tested the device in a laboratory setting to make sure of reliable, repeatable measures on known controlled,	

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	patients having routine care in the UK NHS." As most of the submitted studies were carried out in the US, we require some more detail about how care might differ between the study populations and the UK. Would you be able to provide some more information on how risk assessment and prevention for PUs may differ between the UK and the US? **Evidence** 1. The submission refers to a publication in review (*Burns M, King T, Tsang K et al. (2019) Modernising the pressure ulcer prevention care pathway: a cost-effectiveness analysis. Journal of Wound Care: in review (manuscript number jowc.2019.0193)*) – is it possible to send KiTEC a copy of this? It would be treated as academic in confidence and marked as such in the report. 2. Is the image on page 12 of the submission from the above publication? It is not included in the	exact substances – please refer to the publication by Ross and Gefen, Medical Engineering & Physics, July 2019. 2. Then progressed to human subject studies and tested the reliability using a method whereby there was 3 devices and 3 users who were blinded to the same patient with the same anatomy – which gave 3. an inter rater reliability score – this is documented in our 002 and is approximately 83% (Clendenin, 2015) 4. Patients with known healthy tissue were compared to patients with category 1 PU or DTI (intact skin)– this is documented in our 003 (healthy tissue) and 004 studies (damaged tissue). This is where the delta is derived from; a series of readings were taken, and we compare the highest and lowest. The spatial variation of SEM over the anatomy in question was identified and this allowed us to identify the delta cut–off point. 003/004 derived deltas for a range of values 82% sensitivity 51% specificity	

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	abstract (*Burns M (2019) Modelling Pressure Ulcer Prevention and Treatment Pathways: Costs and Savings [abstract]. In: Proceedings of the 21st Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, 18th–20th September 2019, Lyon, France*). 3. On page 17 there is a reference to *King T. et al 2018*, but the full citation is not given in the reference list. Could you provide the full citation and/or the full-text article? 4. Could you clarify the references to the studies labelled 'SEM200-003', 'SEM200-004' and 'SEM200-008'? Should SEM200-008 be treated as academic in confidence? 5. 'SEM200-003', 'SEM200-004' are referred to together and separately at different points in the submission – do these refer to the two cohorts in the 2018 WOCN abstract: "W03 Differentiating between Healthy Tissue and Early Stage Pressure	**Table 21 (from FDA submission). SEM200-003/-004 Cutoff Thresholds** **SEM200-003/-004 Sensitivity and Specifi Sacrum and Heels** SEM Delta **Cutoff (Positive*)** / Sensitivity / 95% CI / Specifici Δ ≥0.6 / 82% / 74%, 88% / 51% Δ ≥0.7 / 80% / 72%, 86% / 56% Δ ≥0.8 / 74% / 65%, 81% / 70% * Positive here refers to indication of presence of damage 5. Why is greater than Δ ≥0.6 the cut-off point: this is chosen to the highest sensitivity (interventions being very low risk, cost effective and minimally disruptive to patients while the complications of a full-thickness ulcer being potentially catastrophic) to capture subjects with abnormal SEM balanced with specificity. We chose the cut-off point (Δ ≥0.6) and prospectively tested it in study 008 in an at-risk cohort of patients (risk levels were recorded and reported). The choice of cut-off value was also informed results from by O'Brien G. et al. Journal of Tissue Viability, 2018 6. We tested delta value in 12 centres, including 3 in the UK, each its own PI and study personnel. A generalist	

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	Injuries: A Pilot Study of Effectiveness of the SEM Scanner"? 6. Is there any crossover in the patient populations of the 2018 WOCN abstract by Okonkno & Lester: "W03 Differentiating between Healthy Tissue and Early Stage Pressure Injuries: A Pilot Study of Effectiveness of the SEM Scanner" and the 2014 EPUAP abstract by Gershon et al: "P22 SEM Scanner Readings to Assess Pressure Induced Tissue Damage"? 7. In section 4 (Identification and selection of studies) it states that 805 studies were identified by systematic search – does this refer to the PubMed search? Is this the result of combining the lines in the search with the OR command? What was the total before/after de-duplication? 8. Was there a separate search carried out specifically for abstracts (for example in EMBASE or Web of Science, or by searching individual conference proceedings websites)?	and a specialist at each centre were blinded to each other whereby the generalist assessed the patient with the SEM Scanner whilst the specialist used the existing method (visual skin assessment). From there we produced sensitivity and specificity calculations and ROC curves. 008 87.5% sensitivity 32.5% specificity at the Δ ≥0.6 delta cutoff Table 7. – from submitted publication (Okonkwo, Bryant *et al*, 2019) SEM200-008 Range of SEM Δs ITT (N = 182) Sensitivity / Spe SEM Δ | n | % | 95% CI | n | % Δ ≥0.6 | 42 | 87.5% | 74.8%, 95.3% | 124 | 32.6% Δ ≥0.7 | 39 | 81.3% | 67.4%, 91.1% | 170 | 44.6% Δ ≥0.8 | 32 | 66.7% | 51.6%, 79.6% | 227 | 59.6% Source: Table 13 from SEM200-008 Final Study Report	

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	9. On page 26 it states there are 6 abstracts included in table 2, but there are only 3 in the table itself – could you clarify? 10. Table 4 does not include the results of all the studies included in table 1. Could you explain why only some studies were selected? 11. In relation to question 8, on page 27 it states there were 125 patients, but in the abstract, it states 175 patients. Does this refer to the specific cohort? Is SEM200-003 the cohort of patients with PUs and the SEM200-004 the cohort of healthy volunteers? 12. In Table 2 (starting on page 44) there are three abstracts (all with Burns M. as the lead author) listed with the publication date 2020 – is it possible to share this with KiTEC? They will be treated as academic in confidence and marked as such in the report. 13. In section 5 (Details of relevant studies), only some studies are	Is there an official cut off ? Yes it is greater than 0.5 **expressed as Δ>0.6**. The latter is our standard representation and is stated in the instructions for use – see below. ***3.6.1. Interpretation of the Δ Symbol*** ➢ A Δ < 0.6 at an anatomical site may suggest the tissue is at lower risk for pressu ➢ A $\Delta \geq 0.6$ at an anatomical site may suggest increased risk for pressure ulcers On page 91, it refers to acting on "the biomarker" – does this refer to the bio-capacitance measurements? The biomarker is the actual sub-epidermal moisture (localised oedema) change itself whilst the Biocapacitance measurement is how we produce objective data on the change in the biomarker. We are exploiting the electrical properties underneath the skin to represent the change in sub-epidermal moisture. Please refer to the publications by Prof A Gefen: i. Ross G. and Gefen A., Medical Engineering & Physics, July 2019 ii. Gefen A. EWMA Journal, 2018 iii. Gefen A. Wounds International, 2018 Pathway Questions – BBI Answers In section 3 (Clinical Context), the implication from the diagrams is that SEM Scanner would be employed in patients who are "at risk", but not in "high	

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	selected i.e. not all those included in Table 4. Could you explain why? 14. Can you confirm that the study described as "Pressure Ulcer Reduction Programme" refers to the 2019 NPUAP abstract by Hancock & Lawrance: "Integrating Early Detection of Pressure Ulcers (PU) into Universal Prevention Pathways"?	risk" or "no risk identified" patients. Could you clarify (a) that this is the correct assumption and (b) how the three risk categories are determined? Does it correspond to the risk assessment recommendations in NICE CG179? Diagrams were produced by developing a deep understanding of NICE CG 179 breaking down each step which we then mapped, costed and are 100% aligned to CG 179. We then undertook a series of validation steps with clinical partners to ensure it was aligned and accurate. In terms of risk categories – risk assessment tools (RATS) firstly screen patients in a binary method to identify if a patient is at risk – it then categorises at risk populations in a series of risk categories such as low risk, medium risk, high risk etc. BBI has approached this from the perspective that you are either at risk or not and do not further discriminate further because RATs are reported to be unreliable with low sensitivity and specificity, secondly there is a data that shows there is a little correlation between patients who developed a PU and their Risk Assessment score. We actually found in our 008 data that the medium risk category of patients actually had the highest incidence of pressure ulcers. Knowing the limitations of RATs and the whole body approach rather than anatomically specific approach what we do in	

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		clinical practice therefore is ensure that any patient that is at risk is scanned. The direct comparison for the SEM Scanner is not therefore the RATs, rather clinical judgement informed by skin assessments (see the submitted 008 paper). It is mentioned that the SEM scanner is recommended to be used upon admission, during the patient's stay and at discharge (also section 3, pg20). How frequently during the patient's stay should the scanner be used? Is this at the nurse's discretion or related to the risk level? On admission to care and discharge from care, yes in all cases regardless of sites of service. For in-patient stays, frequency of scanning is based on patient status and type of facility. Site of service is hugely important in defining frequency. In acute care scanning is coincident with the existing frequency of skin assessments (usually daily) so fits with existing clinical steps, albeit adding the scanning procedure to the existing protocol. Community and step-down facilities have reported scanning less frequently – for example at Virgin Care it is every 3 days, at Mersey Care they started scanning every 5 days but have	

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		shortened that time-frame to every 3 days. Both groups review scanning frequency if there is a change in patient condition. On page 71, it states that readings are taken from centre of and around the wound, which is "defined as the discoloured tissue at and around a bony prominence (usually heel or sacrum)". Does this suggest that the SEM scanner is being used on areas where a developing PU is already apparent? Is the scanner used on non-discoloured skin as well? Refer back to the notes on 003/4/8 studies earlier to give background to answer this question. The primary clinical benefit of the SEM Scanner is to give nurses objective information associated with damage occurring underneath the skin, at scanned anatomies, which cannot be seen by skin assessments alone such as visual or palpation. This information is a.) more accurate and, b.) earlier than skin assessments alone provide (sensitivity and specificity of skin assessments for correct diagnosis of a manifested PU with intact skin is 50.6% and 60.1%, respectively. Please see the 008 manuscript). This then allows the nurse to use this objective information to give anatomically specific interventions to prevent the skin from breaking. There is a specific method of scanning that we teach to all of our customers and is detailed in the instructions for use – see page 22 and 24.	

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		On page 90, the submission asks the company to "Identify any factors which might be different between the patients in the submitted studies and patients having routine care in the UK NHS." As most of the submitted studies were carried out in the US, we require some more detail about how care might differ between the study populations and the UK. Would you be able to provide some more information on how risk assessment and prevention for PUs may differ between the UK and the US? In the 008 study, 3 sites were within the UK (see 008 study manuscript). Included in our submission pack we have also included a number of other publications based in the UK such as Smith G. Journal of Wound Care, 2019: Ore N. EPUAP 2018 and Evans P. Additionally in our real world evidence file, the vast majority of sites who have entered a pressure ulcer reduction programme have been UK based – in our latest analysis this equates to: 1. 15 sites 2. 1180 patients 3. 11 different care settings 4. 75% sites achieved zero HAPU during the programme 5. Overall weighted HAPU reduction of 93% BBI will be adding to the Cloud site further documents including scientific conference presentations and a more detailed	

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		explanation of the PURP process and results for the UK sites for your review. In this care environment i.e. PU prevention the care is harmonised under International Clinical Guidelines published by EPUAP; NPUAP and PPPIA in a combined effort are generally used to then determine national and local policies (to our knowledge, CG179 is also informed by such Guidelines). International Clinical Guidelines are updated every 5 years and are due to be published in November 2019. Please refer to page 16 of the BBI Clinical Submission for key elements of the draft chapters of the updated Guidelines relevant to the SEM Scanner. Due to this harmonised approach we do not see material differences in the following: iv. Standard of care in terms of risk assessments tools are standardised – using one of the most common versions such as Braden or Waterlow for example v. Skin assessment is the same method globally as in the UK, which necessitates visual and palpation tests vi. Nurse staff are the same in terms of their focus and skills sets WOCN in the USA, TVN in UK vii. Interventions are also harmonised for example the use of specialised support systems from companies	

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		such as Arjo or Hill-Rom, barrier creams and preventative dressings from companies such as Molnlycke or Smith and Nephew Evidence Questions 1. The submission refers to a publication in review (*Burns M, King T, Tsang K et al. (2019) Modernising the pressure ulcer prevention care pathway: a cost-effectiveness analysis. Journal of Wound Care: in review (manuscript number jowc.2019.0193)*) – is it possible to send KiTEC a copy of this? It would be treated as academic in confidence and marked as such in the report. We have included this paper to the data pack found on the link above. 2. Is the image on page 12 of the submission from the above publication? It is not included in the abstract (*Burns M (2019) Modelling Pressure Ulcer Prevention and Treatment Pathways: Costs and Savings [abstract]. In: Proceedings of the 21st Annual European Pressure Ulcer Advisory Panel (EPUAP) meeting, 18th–20th September 2019, Lyon, France*). This data is the output of the abstract referenced above – the abstract was accepted as an oral presentation at EPUAP, France,	

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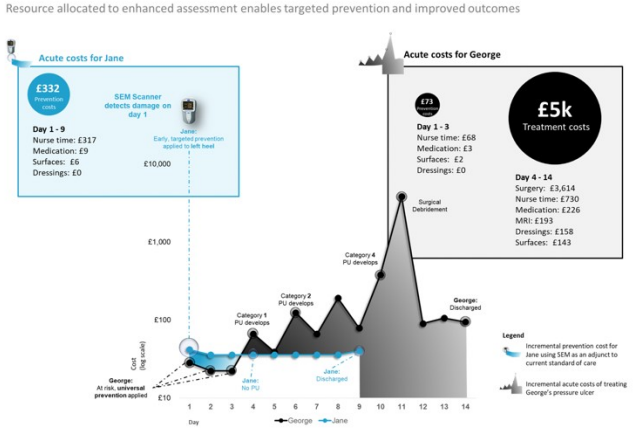
		September 2019. We have added to the link above a copy of the full presentation.  3. On page 17 there is a reference to *King T. et al 2018*, but the full citation is not given in the reference list. Could you provide the full citation and/or the full-text article? The full reference is King T. et al. (2018). An Initial Overview of a QALY: Reporting the Impact of the SEM Scanner in PU Prevention. Presented at WCICT, Manchester, UK. Please note the manuscript referred to in question 1 relates to this analysis. We have added to the link above a copy of the full presentation.	

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		4. Could you clarify the references to the studies labelled 'SEM200-003', 'SEM200-004' and 'SEM200-008'? Should SEM200-008 be treated as academic in confidence? 003, 004 studies have been cited first as the original conference poster abstract then as full publication, which are in review in the relevant journal. SEM -800 should not be treated as academic in confidence. The study has been presented either as an oral or as a poster at a number of academic conferences such as: Okonkwo H, Milne J and Bryant R (2018) Evaluation of a novel device using capacitance of the detection of early pressure ulcers (PU), a multi-site longitudinal study [abstract]. In: Proceedings of the National Pressure Ulcer Advisory Panel (NPUAP) meeting, 2nd–3rd March 2018, Las Vegas, Nevada, USA. The full paper is in review: Wound Repair and Regeneration. Manuscript ID WRR-18-06-0175.R1, entitled "A Blinded Clinical	

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		Study of SEM Scanner 200, a Capacitance Measurement Device, for Early Detection of Pressure Injury). We have added to the link above a copy of the manuscript. 5. 'SEM200-003', 'SEM200-004' are referred to together and separately at different points in the submission – do these refer to the two cohorts in the 2018 WOCN abstract: "W03 Differentiating between Healthy Tissue and Early Stage Pressure Injuries: A Pilot Study of Effectiveness of the SEM Scanner"? SEM200-003 and SEM200-004 are two separate studies however the data is often reported jointly as the data supported the analysis that derived the Delta cut-off point – please refer back to question 5 in the Device question and answer sheet. SEM200-003 included 125 patients with healthy skin whilst SEM200-004 included 50 patients with wounds. 6. Is there any crossover in the patient populations of the 2018 WOCN abstract by Okonkwo & Lester: "W03 Differentiating between Healthy Tissue and Early Stage Pressure Injuries: A Pilot Study of Effectiveness of the SEM Scanner" and the 2014 EPUAP abstract by Gershon et al: "P22 SEM Scanner Readings to Assess Pressure Induced Tissue Damage"?	

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		These are two different studies with no crossover. 7. In section 4 (Identification and selection of studies) it states that 805 studies were identified by systematic search – does this refer to the PubMed search? Is this the result of combining the lines in the search with the OR command? What was the total before/after de-duplication? The 805 number refers to results from all search parameters and the result of combining the lines in the search with the OR command after de-duplication. 8. Was there a separate search carried out specifically for abstracts (for example in EMBASE or Web of Science, or by searching individual conference proceedings websites)? No- a separate search was not conducted 9. On page 26 it states there are 6 abstracts included in table 2, but there are only 3 in the table itself – could you clarify? The number on page 26 should be 3 (as the number in the table)	

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		10. Table 4 does not include the results of all the studies included in table 1. Could you explain why only some studies were selected? In table 4 we included the main pivotal trial data and real-world evidence used to define clinical outcomes using the SEM Scanner in key and NHS-relative populations. 11. In relation to question 8, on page 27 it states there were 125 patients, but in the abstract, it states 175 patients. Does this refer to the specific cohort? Is SEM200-003 the cohort of patients with PUs and the SEM200-004 the cohort of healthy volunteers? We can confirm this is a combination of the two patient populations. As stated earlier at times these studies are reported jointly when it is relevant. 12. In Table 2 (starting on page 44) there are three abstracts (all with Burns M. as the lead author) listed with the publication date 2020 – is it possible to share this with KiTEC? They will be treated as academic in confidence and marked as such in the report. We have included these abstracts to the data pack found on the link above.	

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		13. In section 5 (Details of relevant studies), only some studies are selected i.e. not all those included in Table 4. Could you explain why? Similarly, as in table 4, we included the main pivotal trial data and real-world evidence used to define clinical outcomes using the SEM Scanner in key and NHS-relative populations. 14. Can you confirm that the study described as "Pressure Ulcer Reduction Programme" refers to the 2019 NPUAP abstract by Hancock & Lawrance: "Integrating Early Detection of Pressure Ulcers (PU) into Universal Prevention Pathways"? We can confirm this.	

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Sections 2, 3	**Questions to expert advisers – 17.10.19** ***Standard Care*** 1) How do you identify pressure ulcers in your clinical practice? 2) How often do you assess patients for potential pressure ulcers? Does this depend on their risk category? 3) Do you use the risk assessment categories outlined in NICE's guidance CG179 (https://www.nice.org.uk/guidance/cg179/chapter/1-Recommendations) – "no risk", "at risk" and "high risk"? 4) In what ways does care differ for patients in different risk categories?	**Response from Professor Michael Clark – 21.10.19** 1) How do you identify pressure ulcers in your clinical practice? I'm not in clinical practice. 2) How often do you assess patients for potential pressure ulcers? Does this depend on their risk category? Not in clinical practice 3) Do you use the risk assessment categories outlined in NICE's guidance CG179 (https://www.nice.org.uk/guidance/cg179/chapter/1-Recommendations) – "no risk", "at risk" and "high risk"? Not in clinical practice 4) In what ways does care differ for patients in different risk categories? Use recommendations in International Pressure Ulcer Guidelines 2014 (NPUAP, EPUAP, PPPIA) when teaching on this point 5) Does care differ for patients with different categories of pressure ulcer? Use recommendations in International Pressure Ulcer	

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	5) Does care differ for patients with different categories of pressure ulcer? 6) What other guidelines (if any) do you adhere to in your practice regarding pressure ulcers? For example, NPUAP/EPUAP/PPPIA. 7) Are there any differences in risk assessment of pressure ulcer between lighter and darker skin tones? 8) Do you believe that pressure ulcer risk assessment, prevention and treatment are consistent internationally? What potential differences are there between the US and the UK? ***SEM Scanner*** 9) The SEM scanner is designed to be used in social and tertiary care settings, as well as in hospitals. Do hospital acquired pressure ulcers differ from those developed in other care settings, in terms of severity or probability of development?	Guidelines 2014 (NPUAP, EPUAP, PPPIA) when teaching on this point 6) What other guidelines (if any) do you adhere to in your practice regarding pressure ulcers? For example, NPUAP/EPUAP/PPPIA. Not in clinical practice 7) Are there any differences in risk assessment of pressure ulcer between lighter and darker skin tones? More use of thermal cues in darker skin 8) Do you believe that pressure ulcer risk assessment, prevention and treatment are consistent internationally? What potential differences are there between the US and the UK? Generally consistent at guideline level, US tended to use more reactive support surfaces than Europe for patients at high risk. ***SEM Scanner*** 9) The SEM scanner is designed to be used in social and tertiary care settings, as well as in hospitals. Do hospital acquired pressure ulcers differ from those developed in other care settings, in terms of severity or probability of development? No 10) The SEM scanner is only for use on the heel or sacrum – can PUs develop in other areas of the body? Are there benefits of "anatomically specific interventions as opposed to whole body interventions", as claimed by the manufacturer? Main development	

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	10) The SEM scanner is only for use on the heel or sacrum – can PUs develop in other areas of the body? Are there benefits of "anatomically specific interventions as opposed to whole body interventions", as claimed by the manufacturer? 11) If a patient is deemed to be 'at risk' (i.e. by NICE CG179 criteria), what steps are taken to address this in your practice? How could care differ when a patient is deemed to be at risk by SEM Scanner? 12) Do you know of any other similar technologies to SEM Scanner i.e. devices which objectively assess a patient's risk of developing pressure ulcers?	is on sacrum and heels, of other anatomical locations where the SEM Scanner could be useful would be the ischial tuberosities 11) If a patient is deemed to be 'at risk' (i.e. by NICE CG179 criteria), what steps are taken to address this in your practice? How could care differ when a patient is deemed to be at risk by SEM Scanner? Not in clinical practice but can't envisage any changes to preventive care with or without data from SEM Scanner 12) Do you know of any other similar technologies to SEM Scanner i.e. devices which objectively assess a patient's risk of developing pressure ulcers? No but I'm not convinced the SEM Scanner objectively assesses risk of pressure ulcer development. It denotes local fluid concentration in tissue and the link between this and PU development requires exploration. **Response from Mrs Samantha Holloway – 22.10.19** ***Standard Care*** 1) How do you identify pressure ulcers in your clinical practice? All patients have a risk assessment undertaken within the first six hours following the patient's admission to the acute care sector. Risk assessment is ongoing and frequency of re-assessment is dependent on any change in the patient's condition. In the Primary Care setting all patients have a risk assessment undertaken on the first assessment visit.	

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		Skin inspection is based on a visual assessment of the most vulnerable areas of risk for each patient, typically, heels, sacrum, ischial tuberosities, femoral trochanters and occiput, early signs of pressure damage are documented on a body map. Use of the SKIN bundle as a documentation tool 2) How often do you assess patients for potential pressure ulcers? Does this depend on their risk category? Inspection of the skin (by a registered nurse) is conducted at least every 8 hours (or at every District nurse visit in the primary care setting) for patients who are at risk of developing pressure ulcers. In the acute care setting inspection of the skin for those at higher risk is undertaken more often. 3) Do you use the risk assessment categories outlined in NICE's guidance CG179 (https://www.nice.org.uk/guidance/cg179/chapter/1-Recommendations) – "no risk", "at risk" and "high risk"? Risk assessment categories are based on the Waterlow Pressure Ulcer Scale (2005) 4) In what ways does care differ for patients in different risk categories? Type of pressure re-distributing device(s) provided. Frequency of repositioning Frequency of skin inspection Use of transfer aids to reduce friction and shear	

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		Use of 30 degree side tilted position when repositioning and avoiding 90 degree semi recumbent lying Avoiding pressure on the heels Patients who are at elevated risk of pressure ulcers will restrict sitting time to less than 2 hours in a chair even with appropriate pressure relief. 5) Does care differ for patients with different categories of pressure ulcer? Yes, whilst principles of skin care and management of incontinence may be the same across all categories there are differences. Refer to responses for previous question. 6) What other guidelines (if any) do you adhere to in your practice regarding pressure ulcers? For example, NPUAP/EPUAP/PPPIA. The NPUAP/EPUAP/PPPIA (2014) guidelines 7) Are there any differences in risk assessment of pressure ulcer between lighter and darker skin tones? There is no difference in terms of the process / procedure. Patients with darkly pigmented skin pressure damage may present as: purplish / bluish localised areas on skin localised heat, localised oedema and localised induration	

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		8) Do you believe that pressure ulcer risk assessment, prevention and treatment are consistent internationally? What potential differences are there between the US and the UK? The NPUAP/EPUAP/PPPIA have gone some way in improving consistency for some aspects of risk assessment, prevention and treatment. However there are subtle differences in terminology i.e. Pressure Ulcers versus Pressure Injuries. There's also no consensus about risk assessment in relation to a gold standard, however this may be justified as risk is related to the specific population. In my opinion prevention is probably the one area where there is more agreement on the principles i.e. skin inspection, skin care, repositioning. The range of treatments available does vary considerably depending on reimbursement and procurement arrangements as well as availability of dressings and devices on the local formulary. ***SEM Scanner*** 9) The SEM scanner is designed to be used in social and tertiary care settings, as well as in hospitals. Do hospital acquired pressure ulcers differ from those developed in other care settings, in terms of severity or probability of development?	

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		In my opinion no, irrespective of the setting there will be individuals who acquire a pressure ulcer in their own home, or a social / nursing care setting. 10) The SEM scanner is only for use on the heel or sacrum – can PUs develop in other areas of the body? Are there benefits of "anatomically specific interventions as opposed to whole body interventions", as claimed by the manufacturer? Common locations of Pus include the ischial tuberosities, femoral trochanters and occiput. I'm not entirely sure what the manufacturers mean by that statement but in terms of prevention / treatment interventions there are principles which would apply to any part of the body that is at risk. See responses to question 4. 11) If a patient is deemed to be 'at risk' (i.e. by NICE CG179 criteria), what steps are taken to address this in your practice? How could care differ when a patient is deemed to be at risk by SEM Scanner? See response to question 4. I would not see care differing otherwise. 12) Do you know of any other similar technologies to SEM Scanner i.e. devices which objectively assess a patient's risk of developing pressure ulcers? No. **Response from Dr Fawad Hussain – 06.11.19**	

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		Standard Care 1) How do you identify pressure ulcers in your clinical practice? A Registered Nurse/Midwife assesses all patients using the Braden Pressure Ulcer Risk Assessment Tool and completes a skin assessment within two hours of arrival in the Trust (in the Emergency Departments this is done at secondary assessment). This is than documented within the nursing documentation used in each relevant area. A body map is also completed, following a skin assessment, for all in-patients to show their skin status on admission to the hospital. Pressure ulcers on admission are identified during this first assessment; following this assessment, any pressure ulcers identified will be termed hospital acquired, unless there is clear evidence to suggest the pressure ulcer was already known to exist. A new body map will be completed if new damage or changes in skin integrity is identified and /or weekly. Existing body maps are not added to as this causes confusion. 2) How often do you assess patients for potential pressure ulcers? Does this depend on their risk category? Braden Pressure Ulcer Risk Assessment Tool and complete a skin assessment within two hours of arrival in the Trust. A Braden Risk Assessment is than undertaken and recorded in the 7 day patient assessment, planning and evaluation booklet when the patient is moving to/from another area e.g. prior to or following transfer to theatre, another ward/discharge lounge, nursing/residential home.	

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		All patients have their Braden score re-assessed daily and this is documented in the 7 day patient assessment, planning and evaluation booklet. If the patient's condition changes then re-assessment must occur. Repeat skin assessments will be conducted more frequently in patients deemed at risk. Re-assessment of skin condition will be undertaken at each change of position for patients who have prevention and/or treatment strategy in place (deemed at risk of pressure damage). Patients with Unstageable Pressure Ulcers and/or Suspected Deep Tissue Injuries (SDTI's) are reviewed weekly, by a clinician with the appropriate skills, to help identify a definitive pressure ulcer category. Where a patient declines to have a skin assessment undertaken, it is clearly documented in the nursing records. Where possible patients are given relevant information to help them make an informed decision and this is clearly documented. For those patients who lack capacity to understand the risk of declining care, a Mental Capacity Assessment is undertaken to evidence that the intervention is being undertaken in the person's best interest. 3) Do you use the risk assessment categories outlined in NICE's guidance CG179 (https://www.nice.org.uk/guidance/cg179/chapter/1-Recommendations) – "no risk", "at risk" and "high risk"? Yes, Braden Risk Assessment tool is used to categorise the risk. 4) In what ways does care differ for patients in different risk categories?	

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		Risk assessment tools are only used as an aide memoire and do not replace clinical judgement. All patients at risk of pressure ulcers have preventative strategies put in place. These will include regular skin inspection, ensuring the patient is nursed on a suitable surface, repositioning, moisture/incontinence is managed and nutrition is monitored. Interventions for prevention of pressure ulcers are clearly documented on the Comfort Round/ Skin care monitoring tool found in 'Essential Patient Assessment, Care Plans and Evaluation' 7 or 4 day nursing booklet, and in neonatal and paediatric nursing documentation. Nursing staff inform patients, carers and relatives of the need for pressure area care and give them the patient information leaflet 'Skin Matters', which is available on the Trust intranet. Where it is not appropriate to give this written information, then this will be documented on the nursing documentation e.g. patients with reduced consciousness, intubated patients, or where there are no relatives/carers visiting. Where possible patients are given verbal information to make an informed decision regarding pressure ulcer prevention and treatment and a record of this conversation is recorded in the nursing notes. Where patients are unable or unwilling to concord with the preventative strategies this is clearly documented by clinical staff and escalated to a senior professional e.g. senior sister/charge nurse/Midwife in charge/matron within 24 hours. The Malnutrition Universal Screening Tool (MUST) is used within the Trust for nutritional screening. AtmosAir 'hybrid' mattresses are used to nurse patients with a Braden score of 10 and above. Heels are floated for patients who are bedbound, nursed predominantly in bed, and/or are at high risk of pressure ulcers or have existing heel wounds.	

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		Heels can be elevated using either heel protectors or free-floated using pillows to facilitate this. Patients with pressure damage to the seating area (sacrum, buttocks and ischial tuberosity's) will have a pressure reducing/relieving cushions. Patients are assessed individually for this equipment. Patient's with skin damage to the seating area have a reduced sitting time of a maximum of 2 hour periods. Pressure relieving devices are changed in response to altered level of risk, clinical condition or needs. 5) Does care differ for patients with different categories of pressure ulcer? The first action for pressure ulcers is to identify, and where possible, remove the cause. Preventative strategies are followed. Wound charts are completed by the assessing nurse showing the demographics of the wound, plan for treatment and evaluation of the treatment. Treatment plans are based on individual assessment. AtmosAir mattresses are used for patients with pressure damage up to and including a healing category 3 pressure ulcer. Patients, who have category 3 or 4 pressure damage have a dynamic mattress and this is in place within 4 hours of a request via the identified ordering route. The Tissue Viability team receives all Tissue Viability incident reports, which includes both hospital and inherited pressure ulcer incidents, and this team decides if any further assessment is required, based on the information given. The Tissue Viability team may reclassify a pressure ulcer on their first assessment if, in their opinion, this had been incorrectly staged originally and following review of all previous documentation relating to the pressure damage. The Tissue Viability Team maintains a database of referred	

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		patients which shows whether the patient has been assessed by the team, if verbal advice has been given or if the patient was not assessed. Patients are referred for a Surgical opinion on the basis of: • Failure of previous conservative management interventions • Level of risk (anaesthetic and surgical intervention, recurrence) • Patient preference (lifestyle, abilities and comfort) • Ulcer assessment • General skin assessment • General health status • Competing care needs • Assessment of psychosocial factors regarding the risk of recurrence • Practitioner's experience • Previous positive effect of surgical techniques 6) What other guidelines (if any) do you adhere to in your practice regarding pressure ulcers? For example, NPUAP/EPUAP/PPPIA. NICE (2014) and NPUAP/EPUAP/PPPIA (2014) European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel. Prevention of pressure ulcers: quick reference guide Washington DC: National Pressure Ulcer Advisory Panel (2009) 7) Are there any differences in risk assessment of pressure ulcer between lighter and darker skin tones? No 8) Do you believe that pressure ulcer risk assessment, prevention and treatment are consistent internationally? What potential differences are there between the US and the UK? In our trust we use the Braden Scale which was developed in US, I am however am not able to comment on the differences in prevention and	

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		treatment between US and UK, which I believe would vary with in organisations. ***SEM Scanner*** 9) The SEM scanner is designed to be used in social and tertiary care settings, as well as in hospitals. Do hospital acquired pressure ulcers differ from those developed in other care settings, in terms of severity or probability of development? Potentially any patient who is unable to effectively reposition or is exposed to prolonged moisture at the skin-surface interface is at risk of pressure ulcers. In particular, Hospital acquired pressure ulcers can lead to decreased quality of life, pain, suffering and increased morbidity, and in some cases mortality. In addition, these can increase patient length of stay and health care costs and may expose the hospital to litigation. Patients being admitted to hospital are generally becoming older and have more comorbid conditions and consequently require more complex care and hence have a higher risk of developing in hospital pressure ulcers. Seriously ill patients present to the hospitals with illness and/or injury and trauma that is potentially life threatening, such conditions also result in a higher risk of developing Pressure ulcers. In addition to this, the use of medical devices such as cervical collars and backboards in cases where there is suspected spinal injury is also a significant risk for the development of pressure ulcers because of their hard and unyielding surfaces. Also, relatively innocuous devices such as oxygen tubing, CPAP masks, nasogastric tubes, and urinary catheters can also pose risk to patients if not safely positioned and managed.	

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		10) The SEM scanner is only for use on the heel or sacrum – can PUs develop in other areas of the body? Are there benefits of "anatomically specific interventions as opposed to whole body interventions", as claimed by the manufacturer? Other sites that can be affected by pressure ulcers are back of head, shoulder blades elbows, heels, ears, hips, lower back. 11) If a patient is deemed to be 'at risk' (i.e. by NICE CG179 criteria), what steps are taken to address this in your practice? How could care differ when a patient is deemed to be at risk by SEM Scanner? Steps taken to address patients at risk of developing pressure ulcers have already been stated above. If the SEM scanner can reliably detect very early tissue damage (not clinically visible to the eye) than these interventions can implemented earlier to avoid further tissue damage. In cases where no tissue damage has been detected, cost and staff time can be saved by avoiding putting in place such detailed interventions 12) Do you know of any other similar technologies to SEM Scanner i.e. devices which objectively assess a patient's risk of developing pressure ulcers? I am not aware of any other similar technologies.	

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Sections 4.2	**Further questions to company – 23.10.19** 1. Am I correct in thinking the 50 healthy subjects referred to in each of these three documents is the same cohort (the baseline characteristics are the same in all three)? 2. Does this group of 50 subjects constitute study 003? 3. Does study 003 correspond to this CT.gov record: https://clinicaltrials.gov/ct2/show/NCT01965444? 4. Are any of the "affected subjects" (n=46) mentioned in the *gershon – EPUAP-2014-abstracts_pg56.pdf* file the same patients as the sacral (n=66) and heel (n=59) subjects with PUs mentioned in the *Gershon_Differentiating between.doc* file?	**Response from company – 28.10.19** 004 cohort was 50 patients with healthy skin whilst 003 was 125 patients with pressure ulcers https://clinicaltrials.gov/ct2/show/NCT01965444 - refers to the 004 the manuscript of which has just been accepted for publication in Advances in Skin and Wound Care. We do not yet have a publication date but I will confirm as soon as I hear. **Further response from company – 01.11.19** The variance in the number of patients is due to the fact that this was interim data set hence only being 46 patients.	

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	5. Does the group of 125 patients (66+59, sacral and heel) with PUs constitute study 004?		
Section 9	**Further questions to company – 04.11.19** 1. Could you send over Figure 2 and 3 please as these are missing from the submission. 2. What were the inclusion and exclusion criteria used for the economic evidence?	**Response from company – 07.11.19** 1.See appendix 1 for figures 2 and 3. ***2. Inclusion and Exclusion Criteria*** *41% of patients are shown as at risk. Those at-risk patients are included. All else are excluded.* *The inputs are on "Base Scen. - Model inputs", cell F16. The formula puts all at risk (28%) and all at high risk (13%) into the at-risk admissions (28%+13% = 41%). Those are then eligible for screening by the standard of care (skin assessment) and by the SEM Scanner.* *The source for the 41% is Vanderwee, 2007 (Vanderwee K, Clark M, Dealey C, Gunningberg L, Defloor T. 2007. Pressure ulcer prevalence in Europe: a pilot study. Journal of Evaluation in Clinical Practice, 13, 227-235.). This is cited on page 21 of the written document. Worsely and Smith (2016) quote a lower number of at risk patients (~14%) for Isle of Wight. But remember that is for a general hospital, not an acute hospital. As they say, "patients who require complex surgical medical or orthopaedic support are*	

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		transferred to nearby specialist centres on the UK mainland.". The break-down of 14% at-risk and 13% high-risk came from Virgin and from Glenn Smith at Isle of Wight, but neither number is used in isolation in our model for NICE. Please note therefore that the straight number of 41% of admissions is used. *Consequence: The lower the at-risk population, the worse the current standard of care is costed at, because all of the fixed costs have fewer patients to spread the costs over. It also hurts the SEM Scanner case, but nowhere near as much, when a lower "at-risk" population is shown. Why? Because the fixed costs of the SEM Scanner (purchase price and training) are spread across the number of at-risk patients (bad for SEM Scanner case if few at-risk patients), but the costs of scanning are variable and decrease linearly with the decrease in the number of at-risk patients.*	
Section 9	**Further questions to expert advisers – 04.11.19** 1. Would SEM be part of the initial assessment at admission or would assessment be undertaken with an existing tool and SEM only used to categorise patients at moderate or high risk?	**Response from Professor Michael Clark – 05.11.19** 1. Would SEM be part of the initial assessment at admission or would assessment be undertaken with an existing tool and SEM only used to categorise patients at moderate or high risk? I would anticipate that, at present the SEM Scanner would be used in conjunction with a pressure ulcer risk assessment tool (for example Waterlow scale). If the SEM Scanner was found to be predictive of future PU	

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	2. Is there clinical value in a positive SEM diagnosis in addition to identifying a high risk patient? 3. Would the patient get additional care specific to the location of that positive reading, in addition to the routine 'roundings'? 4. Is there any difference in care for patients identified as high risk compared with those identified as moderate risk, apart from increased frequency of rounding? 5. How effective is rounding every 4 hours at preventing ulcers compared to rounding every 6 hours?	development, then it is possible in future for the Scanner to replace typical risk assessment scoring. 2. Is there clinical value in a positive SEM diagnosis in addition to identifying a high risk patient? Yes, not all PU develop in patients at high risk. Caution should be considered here though, it may be that the Scanner could indicate that patients are likely to develop PU but for this to be a false positive result. 3. Would the patient get additional care specific to the location of that positive reading, in addition to the routine 'roundings'? I would anticipate greater attention would be paid to anatomical areas that show a positive SEM result. 4. Is there any difference in care for patients identified as high risk compared with those identified as moderate risk, apart from increased frequency of rounding? The International PU guidelines recommends changes in the care allocated to patients at high risk of PU development compared to those people at lower risk. For example, "Use an active support surface (overlay or mattress) for individuals at higher risk of pressure ulcer development when frequent manual repositioning is not possible. (Strength of Evidence = B; Strength of Recommendation =C) "	

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		5. How effective is rounding every 4 hours at preventing ulcers compared to rounding every 6 hours? Limited evidence to help answer this question. A Cochrane review found no difference between 4 and 6 hour repositioning but the evidence was considered to be of very low quality (Gillespie et al 2014) **Response from Dr Fawad Hussain – 06.11.19** 1. Would SEM be part of the initial assessment at admission or would assessment be undertaken with an existing tool and SEM only used to categorise patients at moderate or high risk? I believe it should part of initial assessment for all patients deemed to be at risk of developing sacral and heel ulcers and then should be part of regular re-assessments based on scoring tools such as Braden Risk Assessment. 2. Is there clinical value in a positive SEM diagnosis in addition to identifying a high risk patient? It would be helpful in diagnosing sub-clinical tissue damage allowing for earlier interventions. 3. Would the patient get additional care specific to the location of that positive reading, in addition to the routine 'roundings'?	

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		Use of appropriate mattresses, heel float or pressure relieving devices, enhanced nutrition, extra nursing care, enhanced skin care and earlier input from tissue viability 4. Is there any difference in care for patients identified as high risk compared with those identified as moderate risk, apart from increased frequency of rounding? Depending on local guidelines there might be extra interventions in place such as type of mattresses used and when such patients are referred to tissue viability teams. 5. How effective is rounding every 4 hours at preventing ulcers compared to rounding every 6 hours? I am not able to comment on this. **Response from Mrs Samantha Holloway – 06.11.19** 1. Would SEM be part of the initial assessment at admission or would assessment be undertaken with an existing tool and SEM only used to categorise patients at moderate or high risk? I would see SEM being used as part of the initial assessment using the existing tool including visual assessment for all patients	

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		2. Is there clinical value in a positive SEM diagnosis in addition to identifying a high risk patient? Yes in my opinion as the SEM can provide objective evidence which must be acted upon 3. Would the patient get additional care specific to the location of that positive reading, in addition to the routine 'roundings'? I'm not sure there would be anything in addition provided but I would expect specific documentation related to the anatomical location and the condition of the skin 4. Is there any difference in care for patients identified as high risk compared with those identified as moderate risk, apart from increased frequency of rounding? Repositioning schedules and choice of re-distributing equipment may differ potentially depending on the local policies / protocols 5. How effective is rounding every 4 hours at preventing ulcers compared to rounding every 6 hours? There is a lack of evidence to provide a judgement on the frequency of rounding, however there is some evidence on repositioning in terms of this being every 3 hours using the 30 degree tilt: Reference: A randomised controlled clinical trial of repositioning, using the 30° tilt, for the prevention of pressure ulcers. Zena Moore Seamus Cowman Ronán M Conroy, 27 June 2011 https://doi.org/10.1111/j.1365-2702.2011.03736.x	

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		Call with Dr. Fawad Hussain 20/11/2019 ***Attendees; TM: Tom Macmillan, JE: Jamie Erskine, AC: Anastasia Chalkidou, FH: Fawad Hussain*** TM – Thank you Fawad for responding to the written questions and for taking the time for this call. This is an opportunity for us to get some more detail from you about your opinion of the SEM Scanner and where it may be used in practice. Can you give us a quick summary of your thoughts? FH – I've never used the device; my background is as a dermatologist and also as a medical director, so my work includes the tracking of hospital acquired PUs. Hospital acquired PUs are still more common than they should be and are when these develop during Hospital stay and are reported as serious incidents. Sacral ulcers and ulcers of the Heels are most common. The main problem is that visual inspection is always prone to human error. I'm generally positive about the SEM Scanner as an objective measurement means that readings can be documented and checked over time. However, I've not seen research based evidence that shows the scanner is superior to standard visual checks and current care yet. Although there is risk of such devices giving false positive or false negative readings because of conditions such as oedema of the sites could affect readings. But I'm generally positive that digitising things would be a good thing.	

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		TM – I agree that evidence is limited, we are hoping that we can start to fill in the gaps by asking you a few questions. Firstly, when SEM identifies someone as being at risk: there are currently 2 pathways in NICE guidance, 1 is for people at risk and 1 is for people at high-risk, what's the difference in intervention? FH – I don't think that quantifying risk of pressure ulcers would be covered by these guidelines it is the function of the device.. My understanding is that SEM scanner is used to identify when tissue damage has already happened but is not visible to eyes in people already at risk (grade 1 ulcers). So, you can then treat early, prior to the sores becoming grade 2, 3 or 4 sores. TM – Some studies use the device differently, i.e. to look for patients at risk. FH – from what I have read, SEM is not relevant as a risk assessment tool, it should be used to diagnose sub-clinical grade 1 non-visible ulcers (or perhaps an earlier than stage 1 ulcer i.e. stage 1a maybe). The manufacturer needs to make clear if SEM is a diagnostic tool or a risk assessment tool. They should also show the scanner's superiority to other scanners like US (although this may not be available in nursing homes for example). Current risk assessment tools (such as Braden scale) are much cheaper so I wouldn't recommend that SEM scanner be used as a risk assessment tool, unless research shows superiority to current methods.	

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		TM – You've mentioned that you use the Braden scale – how do different risk assessment scales compare? FH – I have looked online previously as I am only aware of Braden: all scales appeared to take consideration of similar metrics and had similar outcomes. TM – We couldn't find any consensus on what the best scale may be. FH – Nor could I. PUs are still one of the biggest group of incidents in hospitals however, so we need to do better. PUs can have a very negative effect on QoL. Early interventions could be huge help. Risk assessments are based on various metrics but not on current damage. TM – Once PU is stage 2 or higher, is there a significantly different cost? FH – Absolutely, at stage 3 we need surgery (flap or graft). Could find mortality data but in past I've read that rates go up significantly in higher stages as well as degradation in QoL. A grade 3 on heel may take years to heal. AC – How long does it take to develop from grade 1 to 2 to 3 to 4? Do the patients 'comorbidities affect this? FH – Yes, would depend in comorbidities most likely (may be research on this). There might also be variation in how easy it is to detect early damage (depending on seniority and experience of nurses etc doing the assessment). SEM could reduce this variation but there needs to be more research in this area. We need to assess the clinical data – how will	

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		management change if early tissue damage from pressure is detected before it is visible to the eye? TM – The majority of PUs, as you mentioned, are on the heels and Sacrum – could PUs develop in other areas? SEM is only instructed to be used on those 2 areas, could ulcers in other areas be missed? FH – If SEM is only licenced in those areas then it will have to be used there. I can't see it being used on occipital scalp because of hair, but really PUs can develop anywhere on the body where prolonged pressure is placed. I.e. where a hard collar after neck injury has been placed or babies in incubation and so on. TM – Are there any likely safety concerns? FH – Are the pads adhesive and if so what kind of adhesive is used, this can result in contact allergic dermatitis or contact irritant dermatitis? Can False negatives or positives be caused by skin colour tones or can local oedemas and in general oedema affect readings? Dermatitis could also affect readings? JE – What would be the best way to assess the diagnostic accuracy of the SEM Scanner? As you've mentioned it should be used in conjunction with Visual Assessment so Visual Assessment alone shouldn't be used as a reference standard.	

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		FH – The gold standard would probably be animal models, inducing pressure ulcers and taking biopsies. There are obviously ethical concerns here and this wouldn't be possible in human trials.	

[Insert additional rows if required]

Appendix 1

Minutes from company teleconference on 14 October 2019

MT445_SEM
Scanner company TC

Document received from company by e-mail on 21 October 2019:

Supplementary Data - PURP Backgrc

Documents received from company by e-mail on 23 October 2019:

Fig 1. Modelled clinical pathways for prevention and management of hospital-acquired pressure ulcers in the UK
NEG, negative; POS; positive; SEM, sub-epidermal moisture; VSA, visual skin assessment

Fig 2. Cost-effectiveness plane with a willingness-to-pay threshold of £20,000 per quality adjusted life year (QALY) gained

BBI12276 FIGURE 01.tif

BBI12276 FIGURE 02.tif

Documents received from company by e-mail on 7 November 2019:

Figure 1 and 2 Nov 6th 2019.pptx

NICE National Institute for Health and Care Excellence

National Institute for Health and Care Excellence
Centre for Health Technology Evaluation

Pro-forma Response

External Assessment Centre Report factual check

SEM Scanner 200 for pressure ulcer prevention

Please find enclosed the assessment report prepared for this assessment by the External Assessment Centre (EAC).

You are asked to check the assessment report from [insert EAC] to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by 12pm, **28th January 2020** using the below proforma comments table. All your comments on factual inaccuracies will receive a response from the EAC and when appropriate, will be amended in the EAC report. This table, including EAC responses will be presented to the Medical Technologies Advisory Committee and will subsequently be published on the NICE website with the Assessment report.

20th January 2020

NICE National Institute for Health and Care Excellence

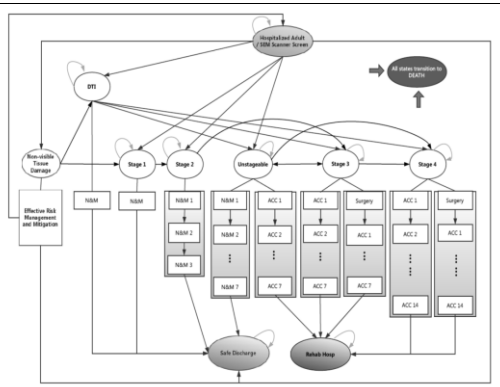
Issue 1

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 8. The EAC notes that the IFU states the device is not to be used for diagnosing or detecting PUs	A clearer statement about the Intended use should be included as per Justification	We also note the comments about the SEM Scanner being a risk assessment device, rather than a diagnostic device. Notwithstanding the high (>80%) sensitivity and specificity of the device to discriminate healthy from PU damaged tissue reported in initial studies, the company deliberately chose a very conservative clinical claim and Intended Use Label for three reasons. 1. A PU is an accumulation of dead and dying cells over an anatomy exposed to deformation, ischemia and shear forces described in detail in the 2019 International Clinical Practice Guidelines. A physical biopsy and histological assessment would be required for a differential diagnosis of the early stages of such. The SEM Scanner by contrast measures the inflammatory response associated with early damage.	This section has been reworded for clarity.

		There are many analogues in use in other medical fields today (e.g., assessing a patient's risk of a heart attack by reference to blood pressure, or the Xpert1MTB/ RIF Ultra assay (Ultra) for tuberculosis (TB) diagnosis. 2. The positive predictive value of the SEM test as reported in Okonkwo H., et al. 2020 was confounded by necessary trial design (comparison of an objective test of SEM against a subjective diagnostic standard, where the latter is the index value) and continuation of regular, ethically required preventative measures. Researchers of the epistemological conundrum of establishing a new diagnostic test in the absence of an objective gold standard, and where interventions necessarily continue uninterrupted suggest the 'clinical test validity'[i], meaning looking at the results of the test – the SEM Scanner – in clinical practice and observe	

		agreement that way. Validation via this method involves the scientific and clinical community defining a point in the validation process, whereby the information gathered is considered sufficient to allow clinical use of the test as a replacement to the current standard of diagnosis with confidence. Published research of the SEM Scanner in clinical use, the PURP data, and independent research using the SEM Scanner are doing exactly this. 3. To date, no pre-category 1 PU classification exists in the classification taxonomy (2019 International Clinical Practice Guidelines; ICD-10 or HRG Codes for Skin Disorders JD07 A-K). The clinical advantage offered by the SEM Scanner is early indication of incipient damage for which no neatly defined classification exists. Please note however, that Padula's submitted manuscript (2019, Journal of	

		Patient Safety) expressly mentions and models a pre-stage 1 phase. Specifically, Figure 1 therein shows a Markov model of hospital-acquired pressure ulcer outcomes in hospital care with and without the use of a sub-epidermal moisture scanner to detect early tissue deformation. Stages correspond to the standardized scale of pressure ulcer severity. Patients who undergo care for pressure ulcers either receive nursing and monitoring (N&M) or acute and chronic care (ACC) in addition to surgery; numbering after N&M and ACC corresponds to the consecutive day(s) or additional care in a specific state prior to transition to other possible health states. All health states have Death as a potential outcome. The Markov model extends to 365 days in total. Padula et al (submitted 2019, Journal of Patient Safety) refers to pre-stage 1 as, "Pre-stage 1 refers to non-visible tissue deformation either on the surface or in soft tissue underneath the skin, by which moisture levels can still increase."	

Issue 2

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 8 Unpublished study authored by the CEO of the company	Please add that the manuscript was also authored by a team from Deloitte	Misleading statement that suggests the paper was only authored by a BBI team member. The co-authors from Deloitte are highly qualified and are bound by ethics of independence. Separately, please also see the attached submitted manuscript by Padula et al (submitted 2019, Journal of Patient Safety), which uses a Markov modelling approach for the costs and benefits of PU prevention,	This has been clarified.

		specifically for the SEM Scanner. Padula's model uses a 365-day duration. Padula's prior papers (2011 and 2018, attached) established a robust method of evaluating the costs-benefits of PU prevention. The UK's National Institute for Health Research's, Centre of Reviews and Dissemination issued a CRD Commentary (PubMedID 21368685), on the method and analysis utilized in the 2011 Padula paper, finding them to be, "The methods were adequate, and the results were well reported. The authors could have given more details of how the effectiveness estimates were identified but given the scope of the study the authors' conclusions appear to be valid."	

Issue 3

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 8 However, the evidence shows that SEM Scanner does not reduce PU incidence to the	Notwithstanding the company's strong disagreement with the EAC's assertion, we believe the more accurate phrasing of the point EAC is	Could you reconsider the phrasing of this sentence? From reading other sections of this report, we believe you mean to write that "the evidence does	This has been amended to read: "However, the evidence does not support the reduction in PU

extent claimed by the company.	making is, "the evidence does not support the company's claim that the SEM Scanner reduces PU incidence to the extent claimed."	not support the company's claim that the SEM Scanner reduces PU incidence to the extent claimed". Separately, we question such a conclusion and restate the validity of the real-world evidence as presented and the Raizman paper, which does support the company's claim of PU incidence reduction.	incidence that the company claim is due to SEM Scanner."

Issue 4

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 14. The EAC notes that the standalone use of the device is not supported by the IFU and is not seen in any of the published evidence.	Please amend to reflect the Intended Use Labelling	See our comments in Issue 1, above. The device is adjunctive. Clinical judgement retains primacy over diagnosis. Many analogues exist in medicine for adjunctive devices (blood pressure for heart attack risk, for example, or the Xpert1MTB/ RIF Ultra assay (Ultra) for tuberculosis (TB) diagnosis.	The EAC accepts this description of the device but no change is required in the context.

Issue 5

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 8. The instructions for use (IFU) highlight the fact that the standard of care, visual skin assessment (VSA), only detects the presence of PUs once they are visible at the skin level.	Please reword to reflect that this is well recognised and understood in the published literature, not only in the IFU.	This has been well represented in published literature for decades, not only in the IFU	This has been clarified.

Issue 6

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 8 SEM Scanner is designed to be used as an adjunct to the standard of care for assessing patients' anatomies for PU risk	"SEM Scanner is designed to be used as an adjunct to the standard of care for assessing patients' anatomies for PU risk prior to visible or palpable signs of damage manifesting at the skin's surface"	This is a vital point. The SEM Scanner does not assess patients for risk - Braden, Waterlow, Purpose-T and other risk assessment tools do that – rather patients' anatomies. Rather, the SEM Scanner test provides anatomy specific and does so earlier than skin and tissue assessment.	This has been clarified.

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Issue 7

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
P.15 One clinical expert suggested that there might be scope for an additional PU category that describes pre-stage I damage that is not visibly apparent, but which will progress to higher stages if no intervention occurs. However, there is no existing evidence that describes this.	Please revise final sentence to show the depth of research regarding the lack of pre stage 1 undertaken	Please refer to the etiological chapter of the most recent 2019 guidelines NPIAP/EPUAP/ PPPIA Prevention and Treatment of Pressure Ulcers/Injuries: A Clinical Practice Guideline. National Pressure Injury Advisory Panel. 2019. Available at: https://guidelinesales.com/. Access date: November 23, 2019 No mention of the phrase pre-stage 1 is made. The reasons for directing the EAC to this reference is the substantially expanded aetiology chapter therein. Also please see the lab work performed by Gray, Robert & Voegeli, David & Bader, Daniel. (2015). Features of Lymphatic Dysfunction in Compressed Skin	This has been clarified.

		Tissues – Implications in Pressure Ulcer Aetiology. Journal of Tissue Viability. 25. 10.1016/j.jtv.2015.12.005 Theirs and other lab work suggest an equivalent pressure threshold of 60mmHg (8kPa) above which direct deformation damage is induced. Offloading and reperfusion returned the subjects assaulted areas to normal. Please also see the systematic review of inflammation and oedema following the onset of sustained mechanical loading by Van Damme et al (2019) Physiological processes of inflammation and edema initiated by sustained mechanical loading in subcutaneous tissues: A scoping review. Wound Repair and Regeneration Finally, we again point you to the work of Padula (submitted in 2019) and his clinical colleagues	

		who do describe and model the pre-stage 1 phase.	

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Issue 8

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response

p. 16 and 19, Table 1: International NPUAP/EPUAP Pressure Ulcer Classification System Specifically, we reference the descriptions of Category 1 and Deep Tissue Injuries	We agree with the reported descriptions of PU classifications, so are not asking for a change to any wording. Rather, we point out the significance of updates to PU aetiology in recent years. The current classification scheme fails to reflect the current understanding of PU categories. The understanding of PUs is that there are physiological processes invisibly occurring under the skin's surface hours to days before damage manifests visually or palpably. Deep tissue injuries are undermined ulcers which initially present with intact skin as purple/maroon bruise. Clinical judgement informed by Skin and Tissue Assessment "STA" fail to capture information about those sub-clinical processes in the pre-stage 1 phase. In the category 1 phase of a PU, clinical judgement has a sensitivity and specificity of 50.6% and 60.1%, respectively. For dark skin tone patients, the odds are worse. We conclude that diagnostic standards for these early categories of PU development approach randomness.	The 2019 NPIAP/EPUAP Clinical Guidelines state, "skin and soft tissue assessment is the basis of pressure injury prevention and treatment" (p.74) Note here the dependence on visual and tactile skin inspection ("Skin and Tissue Assessment", "STA") to confirm the presence of developed damage as indicated by the non-blanchability of the erythema at the site. Current diagnostic standards - clinical judgement informed by STA – wait for STA to observe damage. STA assumed the patients' anatomy is normal until it is visibility and tactilely confirmed not to be, in spite of sub-epidermal and sub-clinical processes of damage being present. Prevention – which we define as keeping the skin intact and avoiding the progression to a later stage PU with broken skin	The EAC asserts the current classification scheme is the best reference point because all literature referred to subsequently in the report used the 2014 guidelines to describe/categorise PUs.

		– is hindered by this late, post-damage diagnostic standard. The 2019 Clinical Guidelines aetiology chapter describes the antecedent processes extensively	

Issue 9

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 20. The company describes the introduction of the SEM Scanner in patients who are 'at risk' or 'at high risk' (there is no difference between the two in the company's assertion) of developing PUs (according to the NICE CG179 criteria).	Please reword in line with our justification	It is unclear where this statement derives. The Company, to our knowledge, has never conflated or disregarded the two risk categories. Rather, we reference a minimum threshold - at risk – at or above which patients satisfying this threshold would benefit from being scanned by the SEM Scanner. The workflow diagrams presented in the submission clearly show a difference	The EAC's assertion derives from Figure 2 (taken from the company's submission). This has been clarified.

		between at-risk and at high-skin patient states (Figure 7, SEM positive with resultant increase in the turning regime from 6 to 4 hours; and, figure 8, at-risk but SEM negative).	

Issue 10

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 20. The frequency with which patients are scanned during the patient's stay is not defined.	Please reword to reflect the justification	This appears inconsistent with subsequent sentences in the EAC's report. Practically, the frequency is set by the clinical site leaders and is generally coincident with the frequency of STAs for that site of service.	This has been clarified.

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Issue 11

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 21. Clinical experts highlighted the ischial tuberosities, femoral trochanters and occiput as other anatomical locations that are important to check for signs of PUs. However, the IFU does not contain any instructions for taking SEM readings from locations other than the heel and sacrum.	Please add a statement to reflect the fact that Sacrum/Heel PUs represent the majority of PUs (~87%) and that the company have a clinical plan to expand labelling	We agree and have a clinical plan to expand the label to these sites and to medical device related pressure ulcers. Please note that heel and sacral ulcers account for >80% of all PUs. Vanderwee et al (2011) cite 87% in their study Vanderwee K, Defloor T, Beeckman D, Demarre L, Verhaeghe S, Van Durme T, Gobert M. Assessing the adequacy of pressure ulcer prevention in hospitals: a nationwide prevalence survey. BMJ Qual Saf. 2011;20(3):260-7	This has been clarified.

Issue 12

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 21. For suspected heel PUs, heeling offloading is also added to the pathway following a positive result. It is notable that in some of the published studies (Okonkwo et al 2018) the device is used on the heels and sacrum of patients who already have visible reddening of the skin and would therefore, already have been identified as being at risk of developing a PU by the standard of care alone.	Please re word according to the justification	We are concerned that centrally important misunderstandings of the utility of the device exist. For clarity: 1. the primary clinical utility of the SEM Scanner is to provide anatomy specific, sub-clinical data prior to category 1 manifestation to clinicians. They can then act on those data at the anatomy in question; 2. a second clinical utility is in aiding clinical-practitioners overcome the near randomness of clinical judgement for correctly classifying category 1 PUs (Pancorbo-Hildalgo et al (2006)) if unaided by the SEM Scanner. This is particularly necessary for dark skin-tone patients	The EAC accepts this description of the device but no change is required in this context.

		3. the purpose of the Okonkwo 2018 study was to establish sensitivity and specificity for known clinical states (PU damaged vs not PU damaged as confirmed by an expert). Meeting the study's end-points necessitated taking readings over intact, pressure-damaged skin. Design was informed by the epistemological conundrum of developing a diagnostic device in the absence of a gold standard which necessitated a method of 1) taking SEM readings from confirmed pressure damaged anatomies (heels and sacrum). Confirmation was performed by an expert, 2.) taking SEM readings from confirmed healthy anatomies (heels and sacrum). Confirmation	

		was performed by an expert, 3.) comparing the two. This is where the delta calculation was developed, then 4.) performing a prospective, blinded, longitudinal study showing sensitivity and specificity of the delta (Okonkwo 2020, published in Wound Repair and Regeneration). The accuracy of ward-level practitioners is very low 50.6% and 60.1% sensitivity and specificity, respectively (Pancorbo-Hidalgo) Pancorbo-Hidalgo PL, Garcia-Fernandez FP, Lopez-Medina IM, Alvarez-Nieto C. Risk assessment scales for pressure ulcer prevention: A systematic review. J Adv Nurs. 2006;54(1):94-110	

Issue 13

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 21. However, it should be noted that there are no substantial differences to the pathway when SEM Scanner is added, compared to the pathway following the existing standard of care	Wording should be amended to describe the change in care pathway as per justification. Suggested wording could be, "However, it should be noted that when the SEM Scanner is added to the assessment and prevention phases of the care pathway, the change compared to the pathway following the existing standard of care is limited."	We do not understand this comment. The care pathway change when the SEM Scanner is added is focused the assessment and prevention end of the care pathway, per Figure 2 in this document. The change is focused, limited and only marginally disruptive, which is how we have interpreted this comment. The impact of the SEM Scanner on clinical decision making and its effect on prevention, however, is not. The 2019 NPIAP/EPUAP Clinical Guidelines state, "skin and soft tissue assessment is the basis of pressure injury prevention and treatment" (p.74).	This has been clarified.

		The device provides objective data, before the wound manifests on the skin's surface and it does so for specific anatomies. The three advantages to healthcare practitioners are: 1. Objective data; 2. Earlier; and, 3. anatomy specific. All advantages are necessary for successful PU prevention.	

Issue 14

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 22. However, with the exception of the Delfin Moisture Meter (Bates-Jensen et al 2007; Guihan et al 2012), SEM Scanner is the only CE-marked device of its kind available in the UK.	Please add clarification that Delfin Moisture Meter is not authorised for sale for PU assessment in patients.	All other devices are experimental, lab-based devices. The Delfin device is not authorised for sale for PU assessment per publicly available documentation.	The EAC accepts this description of the Delfin device but no change is required in this context.

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Issue 15

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 27. Raizman Study The two phases were in different hospital units and although the baseline demographics were similar between the groups, the authors state that phase 2 patients were overall at a higher risk for developing PUs. The standard care protocol is not adequately reported. There are references to daily nursing checks, but it is not clear if this is usual practice or specific to this study.	We should be grateful if you would reconsider your conclusion that this paper be entirely dismissed. Systematic reviews and Cochrane reviews frequently include contacting the author for clarifications where the paper is insufficiently detailed. Did the EAC take this step?	Please revisit this publication and contact the authors for clarification. We are concerned this publication and the structure of the study were too readily, entirely dismissed. Please look particularly at: 1. In response to concerns raised about the 2 phases of the study, even with the watchfulness of the SOS team and collection of SEM Scanner data in both phases, the only change to practice between the two phases was the use of the scanner readings in phase 2 to intervene on subjects' anatomies with an SEM delta of 0.6 or above ($\Delta \geq 0.6$). The incidence effect was a	The EAC maintains its assertion that the study is not adequately reported on the matter of the standard of care protocol.

		92.6% reduction (13.5%-1%), in a higher-risk cohort in phase 2 compared to the first phase. 2. In response to the concern if the inadequacy of reporting of the standard of care protocol, please review Table 4 (page 6), and the pre-penultimate paragraph in section 5 (p. 10), "Interventions [in Phase 1] continued to be implemented based on standard protocols based mainly on Total Braden Score, Mobility Subscale, and clinical judgement." Regardless of the abbreviated description of the protocol, the authors indicate protocol consistency in each of the phases, with the exception of addition of Scanner triggered interventions. 3. In response to the expressed concern (p27, EAC), "There are references to daily nursing checks, but it is not clear if this is usual	

		practice or specific to this study, please view the sentence, "This product evaluation compared outcomes from using a standard prevention and intervention hospital protocol with interventions supplemented by information from the scanner." Raizman 2018 Section 2, page 4.	

Issue 16

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg. 92. Raizman et al (2018) conducted the two phases of their study in different hospital settings and <u>did not report how the SEM Scanner results were used to influence care</u> [underline added by Company for emphasis]	We should be grateful if you would reconsider your conclusion that this paper be entirely dismissed.	Please review the sentence, "In Phase 2, of the study, examiner used SEM delta values of 0.6 or greater as indicators of high-risk or tissue damage, even if the Braden score and subscales indicated low risk. These SEM values triggered increased interventions such as more advanced support surfaces, increased turning and repositioning schedules, more frequent full-body assessment	This has been clarified.

		by the SOS team member, heel boots or positioning devices, and a special sacral dressing. The subscales of the Braden and the SEM value at the individual body site directed targeted interventions." Please view Table 4, in particular, which has columns for various risk scales according to the Braden mobility subscale from low-risk to high-risk.	

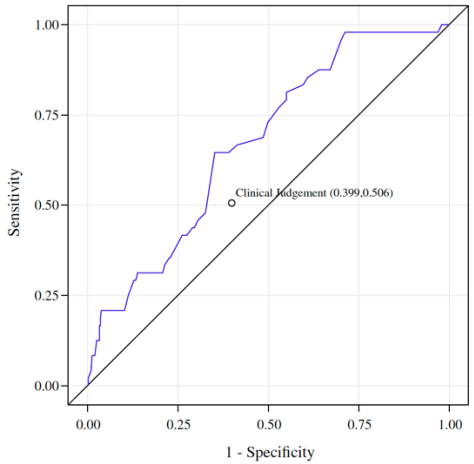
Issue 17

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 30. O'Brien Study Norton scale and VSA used as standard practice. SEM Scanner used separately with a cut off >0.5 for 3 or more days (a more stringent cut off than the IFU describes).	Please rephrase – the cut off is mathematically equivalent	Please expand. Although using different descriptions of the delta calculation, the definitions of the SEM delta as >0.5 or $\Delta \geq 0.6$ are mathematically equivalent.	This has been clarified.

Issue 18

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 32. Okonkwo 2017 The reference standard is VSA, which means this study does not measure the diagnostic performance of SEM Scanner versus VSA.	BBI requests clarification	Does EAC mean, "measures", rather than "does not measure"? If, "does not measure…", please understand that visual skin and palpation tests informing clinical judgement is the current diagnostic standard. Please further understand the epistemological conundrum of the absence of an objective gold standard test against which to compare SEM Scanner readings (VSA – better named as skin and tissue assessment (STA) is it). This problem is discussed in Okonkwo et al 2020, the published version of this study specifically in the section, "Limitations of the Evaluative Rubric of Sensitivity and Specificity". The classic approach (46, 47) to evaluating the accuracy of a diagnostic accuracy is to compare the results of the test under evaluation (index test) with the results of a reference standard; the best available	This has been clarified.

		method to determine the presence or absence of the condition or disease of interest. This reference standard is ideally, a 'gold standard', viz one that is without error. The performance of a new thermometer, for example, can be tested against an existing, objective measurement of temperature. A pure test for a new diagnostic device benefits from assessing a disease state that is not susceptible to being confounded by reversal or healing and can be objectively diagnosed, without error. The rubrics of "sensitivity" and "specificity" do not neatly apply to the epistemological objectives central to this study, but nonetheless remain the paradigm statistical measures for a new diagnostic. The use of specificity as an end point was recognised, before study inception, as a worst-case assessment for the SEM test because it classes all results in which a pressure ulcer did not visibly manifest (skin and tissue assessment negative) but where changes in subepidermal moisture were observed (SEM positive) as false positive results. No presently available alternative to the design was possible."	

		The endpoints of the Okonkwo 2020 study were 1.) sensitivity and specificity, and 2.) time to detect. Endpoint 1 resulted in the ROC curve, below (Okonkwo 2020, p9). SEM Scanner tests of PU risk result in more accurate PU diagnosis and the difference is significant.  **AUC** **CI** **p-value** 0.6713 (0.5969, 0.7457) <.0001 **FIGURE 1** Receiver operating characteristic curve for performance of the study device relative to the gold standard of skin and tissue assessment. Receiver operating characteristic curve illustrating diagnostic sensitivity and specificity of the investigational device in detecting pressure injury. AUC, area under the curve. CI, confidence	

		Citations 46 and 47 in the Okonkwo paper are: FDA. Guidance for Industry and Food and Drug Administration Staff; Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests. Food & Drug Administration. 2007.	

Issue 19

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 34 Okonkwo 2018 The addition of a ±0.5 bound is highly questionable and seriously impairs the reliability of this evidence. The cut-off used is unclear – the authors describe adding a ±0.5 bound to the averaged readings, which is contrary to the IFU.	Please add clarification regarding the role of study according to the justification as the statement is misleading	This was an exploratory study from which the Delta calculation was derived. A submitted publication in the Journal of Wound Care in the peer review comments process currently. The ±0.5 bound was exploratory and ultimately not used in later studies or clinical practice, hence the difference between it and the IFU. For context, this study ("003/04") was designed to address the first three steps (1-3) of resolving the	This has been clarified.

		epistimological conundruum described above and again here: Design was informed by the epistemological conundrum of developing a diagnostic device in the absence of a gold standard which necessitated a method of 1) taking SEM readings from confirmed pressure damaged anatomies (heels and sacrum). Confirmation was performed by an expert, 2.) taking SEM readings from confirmed healthy anatomies (heels and sacrum). Confirmation was performed by an expert, 3.) comparing the two. This is where the delta calculation was developed, then 4.) performing a prospective, blinded, longitudinal study showing sensitivity and specificity of the delta (Okonkwo 2020 Wound Repair and Regeneration).	

Issue 20

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 41. Smith 2019 Waterlow scores that indicated all patients were at risk.	No wording changes proposed	Waterlow is a whole-body risk assessment which does not seek to address the question of "where is the patient at risk for a PU?". Rather, the score simply seeks to answer the question of "is the patient at risk for a PU, yes or no?" The SEM Scanner by contrast is an anatomy-specific test. The two tests (whole patient risk assessment vs anatomy-specific SEM) are not directly comparable. A proper comparison is between Skin and Tissue Assessment (sometimes rereferred to as Visual Skin Assessment. This naming convention does not adequately cover the palpation tests associated with the skin	This has been clarified to reflect the differences between Waterlow and SEM Scanner.

		assessment. We prefer to use the terms STA and SEM)	

Issue 21

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
5.1 The overall evidence base is very weak	BBI request a re-review of the evidence and a review of this conclusion, particularly in light of our efforts to lay out the necessary sequence of studies.	A response universally applicable to the EAC's report is that the initial studies were designed to establish device performance and sensitivity and specificity. These were necessary, non-optional steps in the development of the device. Raizman; Smith; and the PURP data – real world evidence – is designed to address the issues of effectiveness and efficacy. We do not agree with the EAC's position to exclude all of these data from consideration.	This has been amended to read: "The overall evidence base is weak."

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Issue 22

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Section 5.1 Hancock & Lawrance (2019) also carried out a before-after study design but the methodology and other information are poorly reported, and this study is not considered reliable.	BBI request that this statement reflects the additional data sent as it is misleading to suggest the work is not reliable	NICE, the NHS and the USA's FDA are increasingly relying on Real-World Evidence in decision making. Please see the links for NICE and FDA guiding the use of Real-World Evidence. http://nicedsu.org.uk/methods-development/real-world-data/ Food & Drug Administration (FDA) Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices August 31, 2017 https://www.fda.gov/media/99447/download Where possible, the PURP process followed these best practices. Specifically: 1. A historical controls reference period was used in the PURPs for the same sites of evaluation (pre, during and post PURP) 2. Selection bias was addressed in many of the PURPs by including all admitted patients to the wards the PURP 3. PURP methods followed those described in the PURP pack, with some site variability in the	The EAC accepts this description of real-world evidence but no change is required in this context. The published and unpublished studies relating to the PURP are poorly reported, which affects any assessment of the reliability of the study. This is also addressed in section 12.

provision of evaluation project managers (e.g., at Chelsea & Westminster)

4. Individual patient data SEM values, interventions, VSA and risk scores were gathered on the data capture sheets (see PURP pack provided to NICE) and aggreged by site to per-site report.
5. Homogeneity was controlled for within each PURP to assure comparison of the sample to the pre and during PURP period
6. Data handling methods, data lock procedures and audit mechanisms were performed by an external statistician
7. Given the relatively rare incidence of PUs, our own power analyses showed exceptionally large sample sizes for an 80% power at p=<0.05. Specifically, we present a range of scenarios relating to a range of true PU rates and indicate how many patients would be required in the pre-PURP and the PURP periods in order to show that a 40% reduction (say) in the PU rate was statistically significant at p<0. We have provided illustrations below for sample sizes to have 80% power to show a significant effect, and have done this assuming that we would have 2- or 3-times as many patients in the pre-PURP period when compared with the PURP period.

True Prior	True PU		Size of prior PU	Sample size to show

PU rate	rate with SEM scanner	True PU reduction	relative to PURP	p<0.05 with 80% power	
				Prior PU	PURP
2%	1.2%	40% reduction	2-fold larger	6,000	3,000
			3-fold larger	7,900	2,700
2%	1%	50% reduction	3-fold larger	5,100	1,700
2%	0.5%	75% reduction	3-fold larger	1,950	650
2%	0.2%	90% reduction	3-fold larger	1,140	380

The number of patients needed is incredibly large unless a.) the incidence rate is high, and/or b) the PU reduction >90%.

Additionally, we performed analyses using the method of Miettinen and Nurminen (1985); a method of analysis

		which is generally good at handling small sample sizes or low number of events, and have presented the treatment effects as a risk difference (prior PU rate – PURP PU rate) as this is a way of presenting the information when there are zero PUs in the PURP period. We did this for three of the largest UK based PURPs 1. Acute Care at Chelsea & Westminster (n=697), 2. Community Hospitals at Virgin Care (n=234), and 3.) palliative end-of-life care at Marie Curie (n=146). Reported results for p value, and Risk Difference at 95% CI are presented. See attached spreadsheet, "PURP results for NICE 26Jan2020"; PURP Summary and the presentation by the team at Marie Curie. PURP sites have or are in the process of publishing or have presented their individual site data: *1.* Chelsea and Westminster (publication in draft) *2.* Marie Curie (publication in draft) *3.* Marie Curie Marie Curie – Oral presentation of clinical work with SEM Scanner: Raine, G. Prevention; Prevention; Prevention. Tackling The Number One Patient Safety Issue Presented at Patient Safety Congress, Manchester, UK, July 10, 2018 (PPT previously provided) *4.* Virgin Care, United Kingdom – The site has released public discussions with their payor (the	

		Commissioning Group[1]) regarding their PURP data. Peer-reviewed publications are in the draft stage. The Virgin Care report, titled "Virgin Care First Signs Project Launch Presentation," was previously provided to NICE. *5.* NSECH - Two oral presentations of clinical work with SEM Scanner: "Pressure Ulcers: An Outcome Based View On Risk Assessment Tools, Timely Detection and Prevention", Wounds UK, November 2017 "Getting Ready for A New World of PI Prevention Using Early Detection Technology: Translating Risk Assessment of Early Detection Technology to Clinical Practice", National Pressure Ulcer Advisory Panel (NPUAP), March 2018 *6.* The aggregate data were also presented at the 2017 EPUAP Awards Session at the EPUAP Conference Belfast presentation by BURNS. The conference book is not available on the EPUAP website. https://www.epuap.org/19th-epuap-annual-meeting-2017-belfast-northern-ireland/. http://epuap2017.org/fileadmin/user_upload/EPUAP/Katalog_EPUAP_2017_FINAL.pdf. The company can provide the presentation as needed.	

[1] http://www.kssahsn.net/what-we-do/better-quality-and-safer-care/pressure-damage/Pressure%20Damage%20%2026%20May%202016/Embracing%20new%20technology%20to%20enhance%20quality%20-%20Simon%20Littlefield.pdf

		7. The latest aggregate data were also presented most recently at the 2019 EPUAP Conference. The company can provide the presentation as needed	

Issue 23

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 52 Using VSA as the reference standard means that SEM Scanner can be shown, at best, to match the sensitivity/specificity of VSA and in most of the reported studies	Please review based on our comments in the justification section.	Please reconsider the logic of this statement. For the purposes of the company's studies, the principal investigators spent considerable time undertaking detailed skin and tissue assessments (with detailed written Case Report Forms for each assessment, subsequently audited by site monitors) to confirm the presence or absence of PUs. The time spent on the assessments in the studies and the extensive, relevant expertise of the Principal Investigators is far exceeded the constraints imposed by regular clinical practice by routine ward-level practitioners. Comparing a	The EAC maintains this assertion.

		generalist's time-constrained assessment without the detailed case report forms used in the company's studies are not equivalent the patient assessments used in the company's studies. Reported sensitivity and specificity of VSA in Pancorbo-Hidalgo is for ward-level clinical practitioners, not experts who were able to take their time to a detailed assessment. Sensitivity and Specificity of clinical judgement as reported in this paper (50.6% and 60.1%) are for healthcare practitioners who in routine practice have a limited time to assess their patients and have limited PU expertise, rather than for wound care experts. Garcia-Fernandez FP, Pancorbo-Hidalgo PL, Agreda JJ. Predictive capacity of risk assessment scales and clinical judgment for pressure ulcers: A meta-analysis.	

		J Wound Ostomy Continence Nurs. 2014;41(1):24-34.	

Issue 24

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 52 The low specificity (32.55%) reported by Okonkwo et al (2017) suggests that SEM Scanner may not be a reliable tool for ruling out PUs.	Please amend statement to reflect the justification	The specificity calculation in that paper was the proportion of measured anatomies from at-risk patients exhibiting SEM deltas of 0.6 or above, substantially all of whom were receiving intensive preventative interventions who but did not develop a PU during the study period. Interventions were ethically necessary. Recall the SEM Scanner measures the biomarker of incipient damage, rather than directly measure the accumulation of dead and dying cells of a PU. Not every patient already receiving interventions who exhibit deltas above 0.6 will	The EAC maintains this assertion. This matter is explored in more detail, also on page 52.

		go on to develop a full-thickness PU. 1. It is for this reason the Company prefers to claim the device as an adjunctive risk assessment tool. Costs for such were modelled in the model provided to NICE for this MTG. The Company is following best practice for such diagnostic situations, namely 'clinical test validity' meaning looking at the results of the test – the SEM test via the SEM Scanner – in clinical practice and observe agreement that way. Validation via this method involves the scientific and clinical community defining a point in the validation process, whereby the information gathered is considered sufficient to allow clinical use of the test with confidence. Published research of the SEM Scanner in clinical use, the PURP data, and independent research	

		using the SEM Scanner do exactly this.	

Issue 25

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 53 However, none of these studies investigated the subsequent use of further interventions, so it is impossible to verify the company's claim with the existing evidence.	Please re write to reflect the evidence that is available as per the justification	None of the studies referenced in that section of the EACR had an efficacy endpoint. The claim from these studies is the "window of 5 days earlier". The existing evidence as presented in the evidence tables, above, demonstrate this "window of opportunity" claim (i.e. earlier). Those initial studies were not designed to test the effect of the interventions taken in that window, rather just to determine the existence (or not) of early indications of incipient pressure damage. The effectiveness and efficacy of the SEM Scanner in clinical practice as provided in the Raizman/Smith/ PURP evidence	This has been amended to read: "However, none of these studies investigated the subsequent use of further interventions, so the clinical utility of the device cannot be ascertained from these studies."

		was intended to show the effect of intervening at specific anatomies within the "window of opportunity". Please consider rewording this sentence.	

Issue 26

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 53 One clinical expert highlighted the potential for contact allergic dermatitis or contact irritant dermatitis.	This statement should be removed as it is not accurate	The device has been tested to and complies with ISO 10993-1:2003 Biological Evaluation Of Medical Devices - Part 1: Evaluation And Testing https://www.iso.org/standard/44908.html All materials used on the device are non-cytotoxic. This was a necessity for CE marking. No Adverse events or Serious Adverse Events have been reported in any country in over four years of clinical use.	This has been clarified.

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Issue 27

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 53 Due to the lack of high quality studies, no meta-analysis has been carried out.		Please see earlier comments about the sequence of studies. First was diagnostic accuracy followed by effectiveness and efficacy. Diagnostic studies call for sensitivity and specificity studies. RCTs in diagnostic studies are rare and, in our case, ill suited (lack of objective gold standard, randomness of skin and tissue assessments, dark skin-tone limitations). See, specifically "Randomised Controlled Trials are regarded as the gold standard of study methodology in pharmaceutical or interventional studies but are rare in the evaluation of diagnostic tests." Misra, S et al Validation and regulation of point of care devices for medical applications, in Medical	The EAC maintains this assertion.

		Biosensors for Point of Care (POC) Applications, 2017 For our diagnostic accuracy studies, we broadly followed the process described in Misra (2017). The caveat is that diagnostic accuracy studies typically rely on cross-sectional data. We utilised those data sets in the early work described in this report. From these studies the delta was derived and then tested longitudinally as reported in Okonkwo 2020.	

Issue 28

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 56 Firstly, SEM Scanner is intended to be used as an adjunct to VSA, so using VSA as the reference standard does not deliver a clinically useful outcome measure	Please revisit this language to accurately reflect the claim in the IFU. Note in particular the SEM as adjunct to the standard of care, rather than VSA alone. Additionally, please reflect the facts that: 1. the SEM test is objective over the subjective VSA; 2. is more accurate than skin and tissue assessments, which approach	Please revisit this language. Section 2.2 of the IFU "Indications for Use" states: "The SEM Scanner 200 is intended to be used	This has been amended to read: "Firstly, SEM Scanner is intended to be used as an adjunct to standard practice. Using this as the reference standard does not deliver a clinically useful measure of diagnostic accuracy."

	randomness; 3. applies to all skin tones, when VSA is severely challenged for dark skin-toned patients, and 4. is earlier than VSA. Please reference the ROC curve provided earlier in this document. We are uncertain why these utilities are not seen as vitally clinically relevant relative to the current standard of care.	by healthcare professionals as an adjunct to the standard of care when assessing the heels and sacrum of patients who are at increased risk for pressure ulcers." Additionally we presume this comment relates to the effectiveness and efficacy part of the EAC's assessment? We maintain that an outcome measure of "earlier" than skin assessment is highly clinically relevant. If the statement relates to the earlier diagnostic tests, please recall the epistemological limitations that skin and tissue assessment is the gold standard index test for the diagnosis of a PU or the absence of such.	

		No other diagnostic index test exists.	

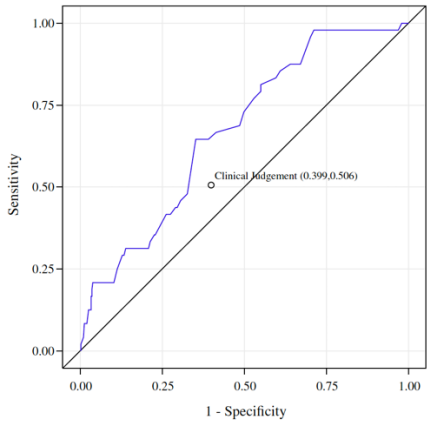
Issue 29

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 56 However, this result is unreliable due to the fact patients were selected specifically due to their PU status (and therefore not representative of usual clinical environment) and it is not clear how the cut-off delta was used in this study.		This was a necessary step to establish diagnostic accuracy in these studies. There is no other epistemological method available in the early stage of establishing a diagnostic test. Use of randomization in establishing diagnostic accuracy is rare and, in our case, ill suited (lack of objective gold standard, randomness of skin and tissue assessments, dark skin-tone limitations). See, specifically "Randomised Controlled Trials are regarded as the gold standard of study methodology in pharmaceutical or interventional studies but are rare in the evaluation of diagnostic tests." Misra, S et al Validation and regulation of	The EAC maintains its assertion.

		point of care devices for medical applications, in Medical Biosensors for Point of Care (POC) Applications, 2017	

Issue 30

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 56 The EAC notes that the IFU for the device states: "WARNING: This device is not intended to be used for detecting or diagnosis of pressure ulcers." The EAC considers the evidence on diagnostic outcomes reported by Okonkwo et al and O'Brien et al should be treated as measures of agreement between SEM Scanner and VSA		See our response letter dated January 28th, 2020. For our diagnostic accuracy studies, we broadly followed the process neatly described in Misra (2017). Diagnostic accuracy studies typically rely on cross-sectional data. We utilised those data sets in the early work described in this report. From these studies the delta was derived and then tested as reported in Okonkwo 2020. Diagnostic sensitivity and specificity measures resulted and a ROC curve produced, provided again, below.	The EAC maintains its assertion.

		 **AUC** **CI** **p-value** 0.6713 (0.5969, 0.7457) <.0001 **FIGURE 1** Receiver operating characteristic curve for performance of the study device relative to the gold standard of skin and tissue assessment. Receiver operating characteristic curve illustrating diagnostic sensitivity and specificity of the investigational device in detecting pressure injury. AUC, area under the curve. CI, confidence Misra reference: Misra, S et al Validation and regulation of point of care devices for medical applications, in Medical Biosensors for Point of Care (POC) Applications, 2017	

Issue 31

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 57 One clinical expert highlighted the possibility that the presence of oedema could impair the accuracy of SEM Scanner, meaning the device should be contraindicated in these patients.	Please reword as this is a misleading statement. Further, the independent clause does not logically nor necessarily lead to the subsequent conclusion in the dependent clause of the sentence.	If the reviewer is referring to systemic oedema, then please understand that the delta calculation at the specific anatomy accounts for the spatial variation of oedema when the tissue is deformed through pressure. The pattern is dead and dying tissue over or contiguous to the bony prominent area surrounded by an inflammatory area. The result is a delta at or exceeding 0.6 in in pressure damaged tissue, and a delta of less 0.6 in tissue without damage. Please see the accepted manuscript Gershon 2020, attached (manuscript accepted in Advances in Skin and Wound Care awaiting publication date). If the reviewer is referring to localised oedema as a confounding factor, please re-	This has been clarified.

		review the basis of the device. The device is designed to measure localised oedema/SEM (see aetiology chapter of the 2019 Clinical Practice Guidelines). In a parallel example, a thermometer is designed to measure surface skin or core temperature and so wold not be contraindicated for febrile patients, rather would be used on those patients.	

Issue 32

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Pg 28. Raizman Study – a trainer was present throughout the study to assist clinicians in the use and interpretation of SEM Scanner.	The wording needs reworking to reflect more accurately the role of the trainer as per justification "A trainer was present throughout the study however the role was limited to the skill of the use of the SEM Scanner"	This sentence implies the trainer helped clinicians use the device in routine patient assessment. In rereading the paper, the role of the trainer was limited to skills checks (point 3, page 8).	This has been clarified.

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Centre for Health Technology Evaluation

Pro-forma Response

External Assessment Centre Report factual check

SEM Scanner 200 for pressure ulcer prevention

Please find enclosed the assessment report prepared for this assessment by the External Assessment Centre (EAC).

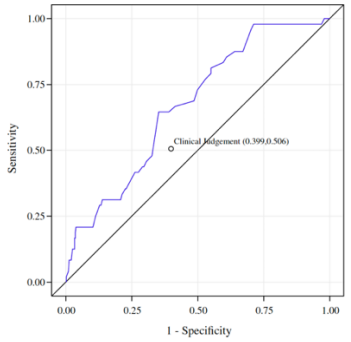
You are asked to check the assessment report from [insert EAC] to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by 12pm, **28th January 2020** using the below proforma comments table. All your comments on factual inaccuracies will receive a response from the EAC and when appropriate, will be amended in the EAC report. This table, including EAC responses will be presented to the Medical Technologies Advisory Committee and will subsequently be published on the NICE website with the Assessment report.

20th January 2020

NICE National Institute for Health and Care Excellence

Issue 1

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
PU incidence reduction changed from 68.9% reduction overall to reduction of 27% in the risk of progression to stage II in patients diagnosed with a stage I PU following implementation of high risk management. 'The company concludes that SEM Scanner is highly likely to be cost saving on the basis of the cost estimates derived from the accompanying model. The company suggests that there are additional health benefits arising from a reduction in the incidence of PUs. These conclusions are consistent with the model results. However, the EAC has serious concerns regarding the validity of the model. The chief concern is the assumption that the introduction of SEM	75% from the better sensitivity and specificity provided by the SEM Scanner. Or Results from either Raizman or PURP (after the EAC is provided with the explanations and clarifications requested)	The EAC's change is a significant change in our assumptions and is likely to be the key driver that is changing the results. The 68.9% is from Hancock K, et al. Integrating early detection of pressure ulcers into universal prevention pathways - Abstract submitted and presented at NPUAP, St Louis, USA, 1–2 March 2019.10. Which shows the reduction in incidence of reportable PUs from PURPs carried out at the time of publication. We are unclear how the EAC has derived the 27% PU reduction rate used in the EAC model, but we have identified two variables in the EAC model that significantly lower PU reduction %. These variables are: (1) proportion of undetected stage 1 PU healing = 50% and (2) Relative risk of PU healing after detection and high-risk management/treatment = 73%. Applying the 73% PU prevention (variable 2) to the SOC+SEM pathway is disputable since the SEM Scanner provides earlier, anatomically specific risk assessments that drive targeted prevention activities. These targeted prevention activities result in a PU prevention % that is greater than the 73% achieved by universal,	Regarding the estimation of PU incidence: The calculation indicates the number of patients who will proceed to a PU and would be identified by SEM scanner. The EAC does not dispute this calculation. However, identification of patients at risk of PU formation is not the same as prevention of PU progression to stage II or beyond. The EAC does not accept that identification of patients who have progressed to early formation of a PU is sufficient to prevent further progression. Further treatment must be implemented for prevention of progression of the PU. The EAC could find only limited evidence on such treatments and utilized this evidence to assess the impact of interventions on the likelihood that patients will progress to a PU at stage II or greater. Regarding the two studies (Mallah et al 2015; Crawford et al 2014): The EAC accepts that these interventions were resource intensive. Nevertheless, the EAC

Scanner leads to a reduction in the incidence of PUs of 68%.' 'The EAC takes the view that a significant proportion of the reduction of 68% in the incidence of PUs in the study cited by the company is attributable to improved attention to general care and preventive measures. Hence an assumption of a 68.9% reduction in the incidence and hence the costs of treating PUs following the introduction of SEM Scanner is an overestimate. The magnitude of this overestimation is difficult to specify but the existing literature would indicate it may be large.' 'The EAC notes that reductions of similar magnitudes to the study cited by the company have been observed in other reports on the impact of PU reduction programmes that did not include SEM Scanner (Mallah et al 2015; Crawford et al 2014).'		whole body prevention. BBI's real-world PURP evidence supports this. Incidence reduction can be computed in two different manners, 1) directly from the real-world evidence. This is detailed in the clinical fact-check section, or 2.) computing an incidence reduction as derived from the increase in sensitivity and specificity achieved by the SEM Scanner compared to the current standard of care. The ROC curve in Okonkwo 2020 shows improved performance over the current standard of care, resulting in more damaged patients properly receiving interventions.  AUC 0.6713 CI (0.5969, 0.7457) p-value <.0001 **FIGURE 1** Receiver operating characteristic curve for performance of the study device relative to the gold standard of skin and tissue assessment. Receiver operating characteristic curve illustrating diagnostic sensitivity and specificity of the investigational device in detecting pressure injury. AUC, area under the curve. CI, confidence	remains of the view that a before and after study of PURP which included the use of SEM scanner will conflate the effectiveness of SEM scanner with the effectiveness of other aspects of the PURP. The resulting estimate of effectiveness is highly likely to overestimate the contribution of SEM scanner in isolation. The EAC notes that increased detection of early formation of PUs is not in itself a preventive measure. Prevention is reliant on appropriate intervention to halt progression of the PU. The EAC modelled the impact of increased rounding frequency on the progression of PUs after detection. The EAC could not find evidence on any additional intervention to halt the progression of PUs. The EAC believes that a trial in which both treatment and control hospitals introduced PURPs and the treating hospitals utilized SEM scanner would be necessary to quantify the additional impact of SEM scanner on PU reduction in addition to other aspects of the PURP. The EAC cited studies of

'The EAC built its own decision model to estimate the impact of SEM Scanner on the costs of preventing and treating PUs. The model calculates the proportion of patients positively diagnosed with a stage I PU according to the prevalence of stage I PUs and the sensitivity of SEM Scanner in addition to VSA compared with VSA alone. The main impact of diagnosis in the care pathway submitted by the company is a change in the frequency of repositioning from every 6 to every 4 hours. Data on the impact of this is scant. However, a single trial reported a hazard ratio of 0.73 (95% CI: 0.53-1.02) (Defloor et al 2005). In the EAC's model, treatment costs are estimated on the assumption that the relative risk of stage I PU progression following treatment is 0.73. This parameter - along with a number of other parameters		The PU reduction can be calculated based on the sensitivity of SEM vs VSA resulting in a 75% PU reduction. This is based on the method agreed with John Posnett for the QALY publication (Burns et al 2019, submitted. Modernising the pressure ulcer prevention care pathway: a cost-effectiveness analysis Burns M. King T. Tsang K. Grainger S. Tang S. Submitted to Journal of Wound Care. In review process – manuscript number jowc.2019.0193) and the assumption that 100% (instead of 73%) of PUs detected by the SEM Scanner are prevented. Computing PU incidence reduction rates based on the observed incidence rate; the sensitivity of the risk assessment; and the specificity of the risk assessment, for both the current standard of care and the current standard of care with the SEM Scanner as an adjunct results in an estimated PU incidence reduction of **75%** when compared to the current standard of care. The calculation is as follows: the underlying incidence rate of the current standard of care is estimated by taking the observed incidence rate 1.64% (PURP) divided by the sensitivity of the risk assessment 50.6% (Pancorbo-Hildalgo 2006), which is 3.3%. To calculate the incidence rate under the current standard of care with the SEM Scanner as an adjunct, the underlying incidence	other PURPs to evidence the potential of such programmes to yield substantial reductions in PU incidence without improved detection technology. The EAC believes such studies evidence the real risk of confounding of estimates of the effectiveness of SEM scanner with the effectiveness of other aspects of the PURP when interpreting the data provided by the company on the effectiveness of SEM scanner. Regarding SEM Scanner being able to detect pressure damage before it is visible: The EAC accepts this mechanism of intervention. However, the EAC was only able to identify evidence of effectiveness in preventing the progression of PUs for one intervention – turning frequency – and the available evidence suggests a modest reduction in the likelihood of progression of a PU after a change from rounding every 6h to every 4h. The EAC considered the possibility of undertaking a more complex model of PU progression to determine the impact of SEM scanner. The EAC was aware of

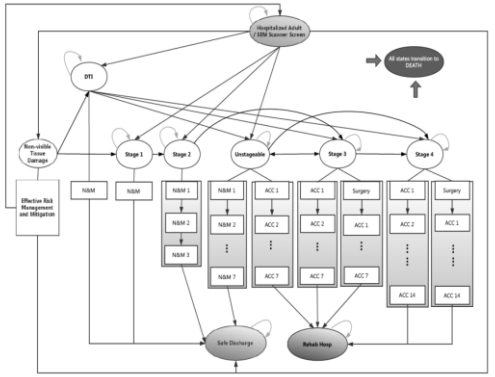
in the model - is subject to considerable uncertainty.'		rate (3.3%) is multiplied by one minus the sensitivity of the SEM Scanner 12.5% (Okonkwo et al 2020) i.e. those PUs that are missed, which is 0.4%. This is a reduction of 75% when compared to the current standard of care. **PURP and Incidence Reduction** As suggested by the EAC, manuscripts for publication of these SEM Scanner aided results are well advanced. We believe that the issues raised of homogeneity and bias are already controlled for in the PURP process documents and study methodologies. Detailed explanations of such will help overcome objections. **EAC Cited Studies and Their Limitations** We recognise the impact in both studies (Mallah et al 2015; Crawford et al 2014) of having a dedicated team of practitioners taking preventative measures well beyond those guided in CG179. In Mallah, a wholly dedicated team of practitioners ("twenty nurse champions" for 486 inpatients) were required to take intensive interventions (e.g., 2 hour turning, skin assessment repeated at every shift per Table 1). We consider these to be relatively unlimited resources and application of high-intensity interventions, notwithstanding the point they	previous publications which utilized such a model. The EAC considered the evidence on the impact of the timing of detection on the risk of progression of PUs to be insufficient to justify such an approach. Specifically, the EAC acknowledges in their report the possibility that earlier detection improves the likelihood of preventive interventions to halt the progression of PU. However, the EAC could find no evidence to support this assumption. In the absence of evidence, the EAC considered interventions implemented 'pre stage 1' and at stage 1 to be equally effective in halting the progression of PUs to stage 2 or above. Given this assumption a model distinguishing the two states would not change the estimation of the impact of detection (at stage 1 or 'pre stage 1') on the cost of treating PUs that progress to stage 2 or further. In the light of this the EAC considered the additional complexity of a Markov model to be insufficiently justified.

		made in the publication about compliance. Given these facts and the patient cohort presumably consistent with a tertiary care centre they reported an ending 5.5% (p110) incidence rate (2.96% prevalence) and a prevalence reduction of 55% from the start point to the end. We note that even in spite of utilising a large dedicated team, intensive observation, and intensive interventions (e.g., 76% being turned every 2 hours) the study group still ended up their study period with a high ending incidence. We do not agree with this study as being an equal comparator to the PURP results; the interventions far exceed NICE CG179 and the resultant incidence was materially higher than those of PURPs, or Raizman 2018. Interesting, Mallah's results mirror the incidence results in Okonkwo 2020, where 26% of the study population developed a PU during the study period in spite of 89.6% of enrolled subjects receiving intensive forms of intervention, far beyond those in CG179. Crawford also utilised a 2-hour turning regime and a multidisciplinary team. Again, these measures far exceed the standards stipulated in CG179. Crawford reports an incidence reduction of 67% (all PU categories).	

		Why in all of these separate studies, where patients received intensive forms of interventions under vigilant observation were high PUs incidences (in Mallah 2015 and Okonkwo 2020) observed? The evidence of PURPS and Raizman in combination with the Company's diagnostic studies inform our assessment that even a legion of the very best nurses unaided by early, anatomy specific evidence of insipient damage cannot achieve a full preventative state. By contrast SEM PURPs conducted with NHS customers utilised the prevailing standards of care at their NHS facilities (minimally stipulated in CG179). No new staff were added (Chelsea & Westminster dedicated a Health Care Assistant for Project Management). The standard interventions were used. The only change was SEM Scanner informed interventions. Marie Curie - palliative, end of life, oncology cohort – reported a >40% reduction in their first year of use and are reporting a 69% reduction in their second year of use.	

		NHS Chelsea & Westminster (acute) reported a 100% reduction over 6-months at their Chelsea site and a 62% reduction at their Middlesex site. Analysis of NHS Safety Thermometer data shows that the incidence of pressure ulcers has remained static since 2014 across England, although campaigns such as Stop the Pressure have been promoting the preventative methods for PU. This is an indication that under current prevention protocols and resources there is little scope for further reduction of PUs without a change to the current protocols. Through interviews with current users of the SEM Scanner who have seen large reductions in their incidence rates, the preventative methods that have been used for each risk cohort of patients has not changed, it is the early detection from the SEM Scanner that has allowed the preventative methods to be implemented earlier than before. It would be possible to escalate all patients to the highest risk rating to reduce the current PU incidence rate, however, this is limited by resources available and as we observe in Mallah (2015), Crawford (2014) and Okonkwo (2020), even in spite of the most intensive interventions (at large cost) being applied to the right anatomy early enough, PUs still result.	

		WORK FLOW There may be a misunderstanding of how the SEM Scanner is implemented. The SEM Scanner is not intended to change the medical interventions that are used for each patient cohort based on their PU risk rating, its purpose is to better allocate patients to each risk cohort and to do this sooner than is the case under the current standard of care. By the SEM Scanner being able to detect pressure damage, before it is visible, preventative measures can be introduced earlier, therefore stopping the progression of the pressure damage into an identifiable PU. A more suitable model than that presented in the EACR, and potentially by the Company – one reflective of the SEM Informed workflow – is presented by Padula et al (manuscript submitted November 2019). The UK's NIHR has commented favourably on previous versions of Padula's model, "Value of hospital resources for effective pressure injury prevention: a cost-effectiveness analysis" BMJ 2018. Padula's 2018 paper, published in the British Medical Journal was awarded the best paper Annual International Society of Pharmacoeconomics and Outcomes Research	

		(ISPOR) Awards Program 2019 Award for Excellence in Application of Health Economics and Outcomes Research. https://qualitysafety.bmj.com/content/28/2/132 Padula et al (submitted 2019, Journal of Patient Safety) includes all categories (including pre-stage 1) for the SEM Scanner pathway under a Markov model.  We respectfully suggest EAC consider Padula's modelling of the clinical state of "pre-stage 1", category 1 and higher (particularly later stages) and the associated interventions in their modelling.	

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Issue 2

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
A band 5 nurse is costed at £18 per hour, sourced from the NICE costing statement for pressure ulcers published in 2014. This is based on mid-point Agenda for Change pay scales 2013–14. The EAC believe that this estimate is outdated and recommend the recent estimate of £37/hour for band 5 nurse (Curtis & Burns 2018	**£21.18.** We respectfully request that NICE provide guidance to the EAC and BBI about the source and appropriate per hour/nursing time metric.	We accept that a 2019/20 rate is needed for our model. We respectfully request that NICE provide guidance to the EAC and BBI about the source and chosen metric of the per hour/nursing time. We agree with the integrity of the source EACR used. Rather we point out the inconsistencies in which source and chosen metric of the per hour cost for nursing time are used; an inconsistency which pre-dates the EACR. The inconsistency results in an accounting error of comparing PU prevention costs against treatment costs where nursing time is central and significant (90%) but using two different hourly wage metrics for time spent on prevention versus time spend on treatment for the same nurse resource. **Detail** We re-read the following papers: Bennett et al (2004), Dealey et al (2012), and the NICE PU Costing statement, none of which explicitly state what hourly nursing cost is used in the total costs associated with treating each PU category. Bennett et al (2004) and Dealey et al (2012) are silent on which hourly rate is used in their calculations of costs and that nurse time accounts for approximately 90% of treatment interventions for Categories I and II PUs. Recall the calculations in these papers underpin all NICE PU costing estimates. Dealey's (2012) paper references PSSRU 2011 prices in Table 1 for "Nurse and Healthcare Assistant time for risk-assessment, monitoring and repositioning".	The EAC considered the data from Dealey (2012) to provide the best estimate of the costs of treating PUs at stages II to IV. The EAC accepts that it is unclear what hourly cost for nurse time was applied in Dealey 2012. The EAC undertook sensitivity analysis which examined variation in the cost of treating PUs over a wide range. The results of the EAC models were robust to this variation. The EAC maintains a view that the cost of a band V nurse should reflect the full overhead costs rather than only including salary and oncosts, and that these costs are most accurately reported in the Unit Costs of Health and Social Care.

		Reverse engineering Bennett et al (2004), Dealey et al (2012) suggests they used base wages/salary plus the salary on costs metric divided by 1,573 working hours per year, (per the NICE CG179 2014, Costing statement). The logic supporting this statement is that the costs of repositioning alone from Table 4 (CG 179, Appendix L) multiplied by the recommended frequency of 4 times per day (every 6 hours) exceed the entire quoted cost in Dealey et al (2012) of the daily cost to treat a Grade 1 PU: £11.67 x 4 = £46.68/day, which the same source considers a reasonable approximation of the costs of prevention. Risk-assessments, monitoring, and all other non-labour preventative interventions (e.g., heel boots) are incremental. Further, NICE CG179 2014, Costing statement: Pressure ulcers (April 2014, Section 3.4 "Costs of Repositioning" expands on both the number of nurses required (0-4) for repositioning and their 2013/14 pay grades (Bands 5-7, at £18-26/hour, including on-costs) (their source: "mid-point Agenda for Change pay scales 2013–14" https://www.nhsemployers.org/pay-pensions-and-reward/agenda-for-change/pay-scales/hourly. **A Possible Explanation** Between the time of BBI's 2019 submission and the EACR 2020 report and the Bennett et al (2004) and Dealey et al (2012) papers, *"…NHS England and NHS Improvement has advocated mandating patient-level costs (known as PLICS) rather than reference costs as PLICS offers a much richer source of cost data, linkable at patient level, to improve value in the NHS*". Curtis, Lesley A. and Burns, Amanda (2019) Unit Costs of Health and Social Care 2019. Unit Costs of Health and Social Care. PSSRU, Kent, UK, 176 pp. ISBN 978-1-911353-10-2. (p.8)	

Appendix L, NICE CG179 2014 has seemingly utilised PLCIS, hence the hourly salary figure of £35/hour used to calculate the costs of repositioning in Table 4.

All other PU treatment values used by NICE predated this recommended change to PLCIS. NICE CG179 2014, Costing statement: Pressure ulcers (April 2014) exclusively utilises Bennett et al (2004); and, Dealey et al (2012), to establish the costs of treatment for each category of PU used by NICE (see Table 5 excerpt immediately below). This timing difference may explain the comment in Appendix L, NICE CG179 2014, "*The GDG were concerned that the costs for category 3 and 4 ulcers may be too low – but the group agreed these costs should be used as a starting point*".

Table 5: Cost of pressure ulcers

Category of pressure ulcer	Proportion of pressure ulcers in each category[a]	Expected time to healing[a]	Expected cost[c]
Category 1	37.20%	28 days	£1,214
Category 2	29.10%	94 days	£5,241
Category 3	20.90%	127 days	£9,041
Category 4	12.80%	155 days	£14,108
Weighted average		**84 days**	**£5,672**

(a) Derived from a review of clinical literature[3]
(b) Based on nurse time (dressing changes, repositioning, and assessment), dressings, antibiotics, diagnostic tests, surfaces, debridement, and inpatient days (where appropriate – only for patients who develop complications).

We accept that a 2019/20 rate is needed for our model. The current (2019-2020) salary range for is £24,214-£30,112. On-costs are not listed in the source used by NICE. https://www.nhsemployers.org/pay-pensions-and-reward/agenda-for-change/pay-scales/annual. The Kent Academy Repository (PSSRU source https://kar.kent.ac.uk/79286/1/KAR%20version%20with%20front%20cov

		er2019%20%281%29.pdf) shows (presumably, mid-point) Band 5 base salary reported £26,894. This is consistently within the range reported via NHS Employers, above. Including Salary On costs in the amount of £6,416 provides a total salary plus on costs in the amount of £33,310. This equates to a 2019/20 Band 5 hourly rate of £33,310/1,573 = **£21.18.**	

Issue 3

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
The company's probabilistic/sensitivity analysis substantially discounted	To be determined based on the response to issues 1 and 2.	The savings produced by the Company's model were significant, therefore, the sensitivity analysis that was conducted aimed to a.) "break the model", b.) determine the magnitude of parameter changes required to reverse the result to cost increasing, rather than saving, and, c.) identify the key drivers of changes to the model's outcomes. The level of uncertainty in the Company's model was low, hence our choice of sensitivity analysis. This was the reasoning behind the simultaneous change in all	The EAC notes that this method of determining uncertainty in each parameter is ad hoc rather than evidence based. The EAC accepts that evidence may be lacking to estimate uncertainty in many of the model parameters. The EAC notes that an assumption of 20% variation around the mean value is commonplace when implementing one-way sensitivity analysis. The EAC remains of the view that a range of plus or minus 15% may have been insufficient to capture the full extent of uncertainty in some variables.

		variables by 15%; the change was in the direction that would disfavour the SEM Scanner against the current standard of care. This simultaneous change in variables was to determine if the outcome (the SEM Scanner generating cost savings) would change if all of the variables were negatively adjusted. Due to a lack of literature on variability of many of the detailed parameters used in the analysis, high-level parameters covering the core components of the analysis were chosen for the probabilistic sensitivity analysis. The parameters cover total prevention cost and treatment costs, which include the cost of prophylaxis and scanning in the SEM Scanner care pathway. The reasoning for the distributions of the probabilistic parameters in the individual parameter sensitivity testing used in the Monte Carlo analysis was as follows: • PU reduction rate - Standard deviation was determined on the basis	

		that in the unlikely event, three parts of standard deviation away from the mean would result in a near 0 reduction rate. • Total prevention cost - Standard deviation was determined on the basis that in the unlikely event, three parts of standard deviation away from the mean would result in a maximum prevention cost of £1,585,395. This was generated by having 100% of the patient population to be at high risk, which means all prevention activities are performed on the entire population. • Total treatment cost by PU grade - Standard deviation was determined on the basis that in the unlikely event, three parts of standard deviations away from the mean would result in a near £0 treatment cost.	

		• Utility scores - Standard deviation was determined on the basis that in the unlikely event, three parts of standard deviation away from the mean would result in a near 0 utility score. All utility scores restricted to be at least greater than 0. Healthy utility score is always higher than grade 1-4 utility scores.	

Issue 4

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
The model estimates that 50.45% of the at-risk cohort are diagnosed to be at high risk (and hence repositioned every four hours) under SoC The EAC is unable to determine how the parameter of 50.45% for SoC was estimated.	Please see the method in the adjacent column	The 50.45% of patients being high risk is calculated by the following method: 1. We observe an incidence rate of 1.6% in the data. 2. The sensitivity of the current standard of care is 60%. 3. The underlying incidence rate (if no preventative measures were used) is	Regarding point 3: The EAC notes that this step of the calculation is incorrect. If the sensitivity of the test is 60%, the true prevalence is observed rate/sensitivity NOT observed rate /(1-sensitivity). The above calculation assumes that incidence is based on the test results rather than longer term observation of the patient AND that the specificity of the test is 100%.

		estimated to be 4.1% (1.6%/(1-60%)). 4. It is crudely assumed for this purpose only that all patients deemed to be high-risk do not develop a PU due to the heightened preventative measures used. Therefore, the underlying incidence in the high-risk population is 2.5% (4.1% - 1.6%). 5. The matrix must total 100%, therefore, the population that will not develop a PU will account for 96% (100% - 4.1%). 6. To split the 96% between at-risk and high-risk the specificity of the current standard of care must be used, which is 50%. 7. Therefore, the 96% of the population that will not get a PU, is halved across the two risk categories. The total population estimated to be at risk is, therefore, 50.45%.	Regarding point 4: The EAC notes that an assumption that all identified PUs are prevented is a very strong assumption Regarding point 8: The EAC understand that this figure comprises half of the 95.9% of patients who will not go on to develop a PU to which 2.5% has been added. The EAC notes that a sensitivity of 60% and a true incidence rate of 4.1% would generate a true positive proportion of 2.46% of the cohort. The EAC accepts the method of calculation but notes the error in step 3 – the underlying incidence rate should be 2.67%. This would generate a high risk result for 50.27% of the cohort assuming a sensitivity of 60% and a specificity of 50%. The EAC notes that this is little different to the company's estimate.

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Issue 5

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
The model structure is not used to estimate the impact of SEM Scanner on the cost of treating patients with PUs. Instead, an assumption is made that the introduction of SEM Scanner results in a reduction in the incidence of PUs of 68%. The EAC considers the model structure to be adequate to estimate the additional costs of preventive care arising from the deployment of SEM Scanner….The EAC considers the model to be inadequate to estimate the impact of SEM Scanner on the costs of treating PUs.	Please revise the wording to remove the suggestion that the SEM Scanner is used in treatment.	The SEM Scanner is not intended to be used in the treatment of PU. Through interviews with current users of the SEM Scanner who have seen large reductions in their incidence rates, the treatment of the individual stages of PU have not changed when using the SEM Scanner. The incidence reduction has been attributable to the early detection of pressure damage from the SEM Scanner that has allowed the preventative methods to be implemented earlier than before. It would be possible to escalate all patients to the highest risk rating and preventative measures to reduce the current PU incidence rate; however, this is limited by resources available in the NHS.	The EAC accepts there is a potential for interventions to be more effective when delivered earlier in the development of the PU. However, the EAC was unable to support this potential mechanism with any direct clinical evidence.

Issue 6

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
The EAC estimated considerably higher costs for additional scanning time with SEM Scanner. There are two main reasons for this.	Amend total costs of scanning depending on the response to Issue 2	The company assumed that at risk patients would be scanned only once and that patients identified as high risk would incur further scans only at the heel or sacrum if this was the anatomical position identified as at risk. These scans were modelled to take 1 minute 15 seconds or two minutes 30 seconds, respectively. The EAC assumed that patients identified to have a category I PU would be reassessed each day requiring an additional 5 minutes for patients assessed using SEM Scanner in addition to VSA. Further, EAC used a different wage/hour cost for Band 5 nurses (see Issue 2). The model did not include stage I PUs in the analysis as these are not recorded in the NHS Safety Thermometer. Padula's model includes category 1 PUs. The company advocates for including category 1 PUs in modelling.	See responses to issues 1 and 2.

		The inclusion of category I PUs in the analysis would be beneficial for the case of the SEM Scanner, as their inclusion will increase the overall incidence rate of PU. Through early identification of pressure damage the SEM Scanner would reduce the incidence of category I PU. Once a category I PU is identified it would be treated, this treatment will not change if the SEM Scanner was used.	