National Institute for Health and Care Excellence

Medical technologies evaluation programme

MT445 SEM Scanner 200 for pressure ulcer

Consultation comments table

Final guidance MTAC date: 24th July 2020

There were 102 consultation comments from 6 consultees:

- 1 company representative
- 1 consultant for the company
- 3 healthcare professionals
- 1 professional organisation

The comments are reproduced in full, arranged in the following groups –

- Recommendations – General (comments 1 to 5, n=5)
- Recommendations – New evidence to address research recommendations (comments 6 to 12, n=7)
- Recommendations – research design (comments 13 and 14, n=2)
- Wording (comments 15 and 16, n=2)
- Mechanism of action and pressure ulcer (PU) aetiology (comments 17 to 35, n=19)
- Standard care (comments 36 and 37, n=2)
- Risk assessment (comments 38 to 46, n=9)
- Clinical unmet need (comments 47 to 51, n=5)
- Equality (comments 52 to 54, n=3)
- Strength of clinical evidence (comments 55 to 66, n=12)
- Diagnostic outcomes (comments 67 to 70, n=4)
- New clinical evidence (comments 71 to 78, n=8)
- Existing economic evidence (comments 79 to 87, n=9)

- New economic evidence (comments 88 and 89, n=2)
- Updated version of scanner Provizio (comments 90 and 91, n=2)
- COVID-19 (comments 92 to 94, n=3)
- Device usage (comments 95 to 102, n=8)

#	Consultee ID	Role	Section	Comments	NICE response DRAFT/FINAL
Recommendations – General					
1.	2	Professional organisation	1	*Recommendations* We agree that there is insufficient evidence to support widespread implementation of this device.	Thank you for your comment.
2.	2	Professional organisation	4.14	*Further research is needed to address the uncertainty about the efficacy of SEM Scanner 200 in reducing pressure ulcer incidence* Agree with all these points, particularly in respect of effectiveness in community settings and in relation to non-white skin. We suggest that there also needs to be more mixed methods research to understand the 'active ingredients' of this device and the mechanisms of effect, to understand how, in what contexts and for whom, the SEM impacts case management and care outcomes. For example, is it the engagement of qualified staff in skin assessment and using the scanner, rather than the use of the SEM scanner per se that impacts care processes and outcomes? This work could be undertaken before, or in parallel with a much needed RCT by a research team skilled in this field.	Thank you for your comment. A research recommendation identifies further evidence which could support a recommendation for wider adoption. The committee considers the most important evidence gaps and the value of the information, current ongoing research, ethical and practical aspects and the likely costs and benefits, when making research recommendations. The design protocol is created by the MTEP research commissioning team following publication of the medical technologies guidance
3.	3	Company	n/a Thank you for your comment.	Thank you to the Chair, Committee, NICE programme team, EAC, and experts for the time, analysis, and considerable thought committed to our application, MT455.	Thank you for your comment.

				We take NICE's comments in the draft consultation document very seriously and have reexamined each element of our supporting clinical and economic data. Our application is, on the one hand, narrowly focused on NICE's evaluation of the role, efficacy and health economy of the SEM Scanner in aiding pressure ulcer prevention in the hands of NHS healthcare practitioners. We have learned from and accepted some of the draft comments in their entirety. A detailed response to the economic conclusions presented in the draft consultation document is provided separately. On the other hand, NICE's consideration of our application is occurring at a time when the fundamental concepts of pressure ulceration (PUs) and their prevention have shifted and continue to do so with increasing pace and materiality. Our application is necessarily best understood in the context of these shifts rather than separate from them. The EAC's clinical scope of literature review was too narrow to include relevant and vital evidence, about PU aetiology and the role of SEM test (as distinct from the SEM Scanner) in particular. A broader search would have potentially answered a number of NICE's research questions and the Committee's questions. The majority of this letter is limited to using materials already submitted to characterize those shifts. This document comments a. on the draft consultation document's interpretation of clinical materials already submitted, and then b. engages with NICE's research recommendations as drafted. Details supporting these comments are provided in the Consultation Document and Addendum Pack. A. Interpretation of clinical materials previously submitted This is a shift catalysed by significant advances in the science of PU aetiology and pathophysiology, and an acknowledgement of the inside-out mechanisms of PU development. On the back of these shifts, the 2014 and 2019 International Clinical Guidelines describe a damage threshold beyond which pressure damage manifests; before which skin and tissue may return to homeostasis if timely, anatomy specific interventions are applied. NICE's clinical guidelines, CG 179, are yet to be updated with these advances. Readers of the remaining commentary will benefit from referencing Figure 1 from Padula et al (2020) which has been excerpted, modestly adapted	

				and presented by permission- this figure is shared in the file submitted separately to NICE. Figure 1: A visual portrayal of pressure ulcer states. The red line depicts the dividing line between intact skin and blistered or broken skin states of pressure ulceration. (Excerpted, Adapted from Padula, W., et al. The cost-effectiveness of sub-epidermal moisture scanning to assess pressure injury risk in U.S. health systems. Journal of Patient Safety and Risk Management. OnlineFirst, pp. 1-9. Copyright © 2020 by the Authors. Reprinted by permission of SAGE Publications, Ltd.)	
4.	3	Company	1	*NICE ask for comment on the following point - Are the recommendations sound and a suitable basis for guidance?* We have a number of concerns about the EAC interpretation of the evidence which underpins the recommendations of the committee, and in particular about their evaluation of the economic evidence. BBIs comments are noted against the specific point in the Consultation Document with summary files shared with NICE separately"	Thank you for your comment. Please see the individual comment for NICE's response.
5.	3	Company		We believe that many of NICE's research recommendations have been addressed in publications issued since the EAC's report and the draft consultation document were issued. We fully accept that more research is needed. Indeed, the research journey may never stop. Our ambition extends far beyond repeating studies to validate the SEM device to collaborating with health systems to achieve and maintain PU prevention, at scale, while reducing costs to payors. In the NHS that means collaborating with providers of care in primary, secondary and tertiary sectors strategically (i.e., by making choices about where and how to target prevention efforts). We are already doing this in the UK and are expanding our collaborations. The traditional model of RCT, cohort, site of service analysis is one method of achieving scientific assurance of validity. In a separate	Thank you for your comment. For NICE's response to comment regarding research design please see response to comment 2. Section 8.2 of the Medical Technologies Evaluation Programme methods guide describes the types of recommendations the committee can make.

				document we describe the cost (at least £7.7 million) and time (6.5 years) of our interpretation of the research NICE has proposed (n=1,712). The value of the additional clinical data is low. The return on investment is substantially negative. These time and cost estimates assume a post-pandemic world. A formal, pragmatic path forward We believe that the scientific rationale for measuring sub-epidermal moisture as an indicator of pressure damage and as part of a programme to reduce harm to patients is sound, but we recognise that the clinical evidence base is still developing. We believe that a conditional recommendation with review after two-three years (pandemic dependent) would facilitate new studies in the NHS specifically designed to more formally evaluate the magnitude of the benefits which can be achieved. Section 2.2.3 in NICE's Decision Support Unit Report dated 12th December 2016,"The Use Of Real World Data For The Estimation Of Treatment Effects In Nice Decision Making " (12th December 2016), offers a helpful, pragmatic path forward. Five criteria were defined to validate or refute the role of Real World Evidence: a. "An adverse outcome is likely if the person is not treated (evidence from, for example, studies of the natural history of a condition)" –Ignoring the microscopic non-visible SEM changes early, even before visual discoloration on the skin surface may result in delayed SoC interventions that increase the risk of a subject developing PUs. Conversely, STAs are key in visual confirmation of a developing PU. They are an integral part of the SoC care bundle which also includes other risk assessment tools, anatomic interventions (Blackburn et al., 2020, Coleman et al., 2013, Lyder CH, 2008, Bale et al., 2007). Randomising subjects into separate arms where STAs may not be provided may result in adverse outcomes. b. "The treatment gives a dramatic benefit that is large enough to be unlikely to be a result of bias (evidence from, for example, historically controlled studies)"- Foundational clinical studies of the SEM summarised in various sections of this report and in data submitted previously to NICE provide evidence of the increased clinical utility in using the SEM scanner in routine clinical practice. In a blinded clinical study aggregate sensitivity and specificity of the SEM Scanner exceeded clinical judgment alone with observed SEM changes 4.7 (± 2.4 days) earlier than diagnosis of a PU via STA alone (Okonkwo et al., 2020). SEM was associated with concurrent	

				and future (1 week later) skin damage and was significantly higher ($p<0.05$) in stage I PUs compared to no injury and blanching erythema (Kim et al., 2018). c. "The side effects of the treatment are acceptable (evidence from, for example, case series)" – The SEM Scanner is a non-invasive, non-significant risk Class IIa (CE marked) device. There are no side effects in using the SEM Scanner. Patient risk is low. False positives result in offloading a patient's anatomy. False negatives mean the patient is no worse off since STA diagnose the patient. No adverse events were reported in any study using the SEM Scanner till date. d. "There is no alternative treatment"- There are no direct competitors to our dielectric constant biocapacitance measurement technology with the intended use of detecting early stage pressure ulcers (viz, pre-category 1, Category 1, DTI). No other device has the legal claim required by the Medical Device Regulations to legally market their devices as a competitor to BBI's SEM Scanner without making "off-label" claims. We are aware of other impedance devices (e.g., Delfin) but to our knowledge, none have regulatory authority to market their devices for PU detection and are unaware of validation studies of any such devices. e. "There is a convincing pathophysiological basis for treatment"- The delta value is a 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 healthcare practitioner 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, this indicates 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 healthcare practitioners with days of advanced notice compared to visual skin assessment that a patient's skin and tissue is compromised over a given anatomy. 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., 2020). Concluding comments: A formalisation and extension of our existing PURP programs (real-world evidence of prevention) and an extension of the existing PU Prevention Registry (overview of which is submitted separately) would achieve these data aims at scale well beyond the projected sample size of 1,712.	
6.	3	Company	1.1	*However, there is not enough good-quality evidence to support the case for routine adoption in the NHS.* In a Statement of Intent issued in 2019 (Widening the evidence base: use of broader data and applied analytics in NICE's work) the use of broader sources of data and analytic methods was confirmed, separately in January 2020 NICE stated "We recognise the value of traditional 'hierarchies of evidence' but take a comprehensive approach to assessing the best evidence that is available to answer the questions we face" (Our Principles NICE). Evidence in the form of Observational; Experimental; Qualitative and Real World are all identified as being acceptable. It is BBIs assertion that the EAC reports and the Consultation Document subsequently issued do not appear to be living up to these principles and therefore the inclusion of BBIs wider evidence base should be reconsidered. Since the original BBI submissions to NICE a further 18 peer review publications that are relevant to the Consultation have been published: • 5 relate to the aetiology of pressure ulceration relevant to the SEM Scanner mode of operation and therefore highly relevant to the scope • 10 focus on the concept of sub-epidermal moisture or the SEM Scanner technology and therefore highly relevant to the scope- these include an independent Systematic review • 2 present the health economics of the SEM Scanner technology applied in prevention care pathways • 1 publication describes the challenges of the standard of care Additionally a further 6 manuscripts are submitted (or in process of) - the majority of these manuscripts detail the pragmatic real world studies conducted at multiple sites. The combination of these publications bring new data that must be analysed as part of a review of the original	Thank you for your comment. The aetiological studies, proof of concept studies and studies describing the challenges of standard care are outside the scope of the assessment. The independent systematic review (Scafide, 2015) did not include any studies that used SEM Scanner 200 to measure sub epidermal moisture and NICE medical technologies guidance evaluates a single medical technology. It is not a multiple technology assessment and does not compare evidence for all similar technologies in a broader class. The External Assessment Centre reviewed the unpublished data and reported that their conclusion regarding the clinical evidence remained unchanged. The committee considered the additional evidence and concluded it does not answer the

				Guidance decision making process. A re-review of the total evidence is required to ensure that the principles stated by NICE are reflected in this Consultation – there are now: o Minimum of 36 peer review publications on the concept of sub-epidermal moisture or the SEM Technology o Minimum of 34 Scientific abstracts accepted on the concept of sub-epidermal moisture or the SEM Technology o 7 healthcare practitioners have reported on the implementation of the SEM Scanner in pragmatic real world studies at Scientific Conferences o 3 Health Economic peer review publications which utilised both Markov and Probabilistic Modelling Therefore BBI challenge whether all the "relevant evidence has been considered" nor that the summaries are "reasonable interpretations of the evidence" (page 1 Consultation Document. BBI share the most recent publications listed in order of those we believe most acutely address NICE and EAC comments in the table submitted separately to NICE - note some of this content is submitted academic in confidence.	uncertainties which led to their recommendation for further research.
7.	3	Company	1.1	*the risk of pressure ulcer formation using SEM scanner without visual skin assessment compared with visual skin assessment alone* Bearing the comments in mind made by BBI at point 4.14 but with the intention of answering this research question BBI share 3 sets of data: 2 as academic in confidence. o SUBMIT AS ACADEMIC IN CONFIDENCE Calvo Aguirre J. J. In review at the Journal of Long Term Care including new data since submission and should be considered within a review of the Guidance. Prospective, comparison study undertaken at a Long Term Care Facility in Spain. BBI recognise this is not undertaken within the NHS however it is an important contribution to the evidence base: o Prospective comparison design o Standard of care (SoC) described similar to the SoC within NICE CG179 o Results are presented in the file submitted separately to NICE o Budri A., et al May 2020 Journal of Clinical Nursing. Observational, prospective, nonexperimental study. This is new data since submission and should be considered as part of a review of the Guidance.	Thank you for your comment. The External Assessment Centre was asked to comment on the additional references supplied by the consultee: Aguirre, unpublished, Budri (2020) and Bennet et al, (unpublished). The committee considered the additional evidence and concluded it does not answer the uncertainties which led to their recommendation for further research.

				o 150 subjects enrolled - Long term care setting o Followed up for 20 days or until visual skin assessment (VSA) PU develops o SoC remained as planned by the nursing care team o 3 days of elevated SEM delta considered a PU event o PU incidence reported by VSA 12.7% n=19; SEM assessment reported incidence 78.7% n=118 o Odds of detection of PU was 25 times greater with SEM than VSA o Statistically significant reduction of 6.2 days in the time that SEM took to detect a PU [95%CI: -10.5days to -2.35days, p=.002] o SUBMIT AS ACADEMIC IN CONFIDENCE Bennett S., et al. Open label, prospective, randomised design study. This represents significant new data since submission and should be considered as part of a review of the Guidance. o The results are presented in the file submitted to NICE separately - BBI also refer NICE to the file submitted presenting a summary of the studies led by RCSI- this study is presented in more detail in that file. Given the data above it is BBIs belief that research question should now be removed."	
8.	3	Company	1.1	*how changes in clinical decision making from using SEM scanner lead to reduction in the incidence of pressure ulcers* "BBI share with the NICE Committee and EAC new data published or developed since submission that will answer this research question. BBI have demonstrated consistent and repeatable results from a variety of care settings including Acute; Community and Palliative care. o In these pragmatic real world studies standard of care was unchanged apart from the inclusion of the SEM Scanner into the care pathway. Graph 1 included in the file sent to NICE separately demonstrates the repeatability of the reduction of incidence of pressure ulcers across a high number of sites with varying clinical challenges. The healthcare practitioners involved will articulate their experiences in having already integrated additional preventive interventions, education programmes and awareness campaigns. However on addition of the SEM Scanner into their care pathways consistent and repeatable incidence rate reductions are demonstrated. Note Graph 1 only refers to specific UK sites where permission to share the data has been given – further data is available from sites in USA; Canada: Belgium; Spain and Ireland.	The External Assessment Centre was asked to comment on the additional references and concluded the additional unpublished data did not change their conclusions about the clinical evidence. The committee considered the additional evidence and concluded it does not answer the uncertainties which led to their recommendation for further research.

				In total to December 2019 2,115 subjects; 28 sites enrolled. Overall Implementing the SEM Scanner into routine clinical practice has resulted in a weighted average 90.5% PU Incidence reduction. 1x Palliative Care site 47% HAPU reduction; 1x Community Care site 26.7% CAPU reduction o In the Acute Care cohort (n=26), 1952 subjects scanned, <35,000 SEM assessments □ SEM delta ≥ 0.6 noted in 58% of these SEM: 21% of these assessments noted visual discoloration □ 73% (19/26) hospitals had ZERO HAPUs during the study period - 100% reduction rate □ 88% (23/26) had a reduction in HAPUs of >80% □ 92% (24/26) hospitals had a HAPU incidence rate of 3% or less □ 77% (n=1503) SEM Scanner readings influenced nurse's decision in increasing SoC interventions It should be noted that the data collection has evolved over time – earlier PURPs did not collect decision making data therefore this response includes a sub section of data Acute Care Summary: clinical decision data was recorded for 1252 patients across 17 sites and Intervention data for 1491 subjects across 22 sites o 77% (n=923 subjects) SEM Scanner readings influenced the nurse's decision in increasing SoC interventions o Mobilisation or turning was increased in 80% subjects (n=738) o Specialist surface or mattress was introduced in 51% subjects (n = 471). o Heel support or elevation of heels was introduced in 73% subjects (n=674) o Prophylactic dressing or barrier cream was introduced in 70% subjects (n= 646) Community Care Summary: 1 site, 17 subjects o Clinical judgement informed by skin and tissue assessments (STAs) and SEM deltas - 94% (n=16) subjects, receiving interventions based on the trust decision algorithm o 71% Mobilisation or turning was increased (n=10) o 71% Specialist surface or mattress (n=10) o 86% Heel support or elevation (n=12) o 60% Prophylactic dressing or barrier cream (n=9)	

				o Clinical judgement informed by SEM deltas alone, where STAs did not show visible discoloration, resulted in changed clinical decision making in 82% subjects (n=14/17) o Verbal feedback from two UK sites share the day to the day impact- this feedback from clinicians using the SEM Scanner on a daily basis is critically important for NICE and the EAC to understand the impact in the real world setting. Contact details will be shared with NICE directly to maintain confidentiality. o "Proactive way of managing PI/PUs" o "SEM measurement gives clinicians the initiative to react earlier than before" o "Influences the decision-making process and gives clearer guidance of what steps staff need to take next" o "SEM gives a level of information that was previously unknown" o "SEM allows for individualised care rather than blanket care planning from RAT" o "SEM make people more likely to conduct a VSA as they don't assume there is/isn't damage Latest data on year 3 of usage from Marie Curie who implemented the SEM Scanner into their care pathway has resulted in a continued reduction in the incidence of PU. In the last 6 months the team have reported a 3 month period with a 100% reduction in PU incidence – they are now finalising the data for the whole 6 month period - this is highly relevant given the high risk status of this patient cohort. o SUBMIT AS ACADEMIC IN CONFIDENCE Bennett S., et al open label, prospective, randomised design study. Significant new data since submission and should be considered as part of a review of the Guidance. Results are in the file submitted to NICE separately - BBI also refer NICE to the file submitted presenting a summary of the studies conducted by RCSI where this study is shared in more detail. o SUBMIT AS ACADEMIC IN CONFIDENCE Calvo Aguirre J. J. In review at the Journal of Long Term Care including new data since submission and should be considered within a review of the Guidance. Prospective, comparison study undertaken at a Long Term Care Facility in Spain. BBI recognise this is not undertaken within the NHS however it is an important contribution to the evidence base: o Prospective comparison design	

				o Standard of care (SoC) described similar to the SoC within NICE CG179 Results are in the file submitted to NICE separately. o Lancashire Teaching Hospitals NHS Foundation Trust, Royal Preston Hospital: recently initiated a new Change Bundle for PU prevention. Under the Always Safety First initiative the team are targeting a 50% reduction in PU incidence across the collaborative wards. An integral component of the Change Bundle is to assess the skin using the SEM Scanner every 24 hours (Figure 1 which is included in the file sent separately to NICE). Given the new data above BBI pose the question – what more is needed to answer this research question? What advantage would be gained by not recommending the SEM Scanner at this time? BBI propose that a conditional approval with review after two years would facilitate new studies in the NHS specifically designed to evaluate the magnitude of the benefits which can be achieved. BBI Propose that the PU Registry documented in a separate comment could act as a data repository."	
9.	3	Company	1.1	*the clinical benefits and resource impact of using the scanner in different care settings* "BBI share with NICE Committee and EAC new data published or developed since submission that will answer this research question Clinical benefits: The most important benefit is the reduction in pressure ulceration- the subsequent consequences of such injuries to health systems, patients and their families are widely reported in the published literature. BBI have demonstrated consistent and repeatable results from a variety of care settings including Acute; Community and Palliative care. o In these pragmatic real world studies standard of care was unchanged apart from the inclusion of the SEM Scanner into the care pathway. Graph 1 included in the file submitted to NICE separately demonstrates the repeatability of the reduction of incidence of pressure ulcers across a high number of sites with varying clinical challenges. The healthcare practitioners involved will articulate their experiences in having already integrated additional preventive interventions, education programmes and awareness campaigns. However on addition of the SEM	Thank you for your comment. Please see NICE's response to comment 6, 7 and 8. The External Assessment Centre reviewed the additional economic evidence. The committee decided not to change the guidance in response to this comment

				Scanner into their care pathways consistent and repeatable incidence rate reductions are demonstrated. Note Graph 1 only refers to UK sites where permission to share their data was granted – further data is available from sites in USA; Canada: Belgium; Spain and Ireland. 2,115 subjects; 28 sites up to December 2019. Overall Implementing the SEM Scanner into routine clinical practice has resulted in an weighted average 90.5% PU Incidence reduction. 1x Palliative Care site 47% HAPU reduction; 1x Community Care site 26.7% CAPU reduction o In the Acute Care cohort (n=26), 1952 subjects scanned, <35,000 SEM assessments □ SEM delta ≥ 0.6 noted in 58% of these SEM: 21% of these assessments noted visual discoloration □ 73% (19/26) hospitals had ZERO HAPUs during the study period - 100% reduction rate □ 88% (23/26) had a reduction in HAPUs of >80% □ 92% (24/26) hospitals had a HAPU incidence rate of 3% or less □ 77% (n=1503) SEM Scanner readings influenced nurse's decision in increasing SoC interventions o Latest data on year 3 of usage from Marie Curie who implemented the SEM Scanner into their care pathway has resulted in a continued reduction in the incidence of PU. In the last 6 months the team have reported a 3 month period with a 100% reduction in PU incidence – they are now finalising the data for the whole 6 month period - this is highly relevant given the high risk status of this patient cohort. • SUBMIT AS ACADEMIC IN CONFIDENCE ""Clinical Impact of SEM Scanner Real-World Use in the United Kingdom"". Musa L. et al in review at Journal of Wound Care. Authors summarise the method and outcomes of the pragmatic real world approach in which the SEM Scanner was implemented into a variety of care settings. Further detail is presented in the file submitted separately to NICE. • Individual manuscripts based on these real world experiences with the SEM Scanner and the impact of PU Incidence, clinical benefit and resource impact have been developed by the lead co-ordinator at each site. These manuscripts represent a mix of care settings and represent new data since submission and help to serve to answer the research question raised. A table summarising the manuscripts is submitted to NICE separately -SUBMITTED AS ACADEMIC IN CONFIDENCE	

				• A Budri et al "Identification of increased risk of pressure damage with the SEM Scanner: definition and evidence of clinical outcomes and cost-effectiveness" accepted for publication by the British Journal of HealthCare Management. Author reviews the quantitative biophysical criteria and operation methodologies that define risk-assessment protocols of the SEM Scanner when used in the identification of increased risk of PI/PU. Clinical case studies, and cost evaluation summary are presented. SUBMITTED AS ACADEMIC IN CONFIDENCE - further detail is in the file submitted to NICE separately • BBI refer NICE and the EAC refer to a report submitted by the Royal College of Surgeons of Ireland -the team have conducted a series of controlled studies with the SEM Scanner and have detailed the outcomes in a variety of care settings • https://www.nice.org.uk/about/who-we-are/our-principles, Principle 6, point 20 "recognise the value of traditional hierarchies of evidence": systematic review is typically positioned at the top of the pyramid. Since submission, an independent systematic review has been published (Scafide K et al. JWOCN 2020;00(0):1-9). Authors reviewed the published data on a number of bedside technologies in early detection of pressure injuries. Of the SEM Studies included it reported that the reliability of instruments application and associated measurements were formally evaluated in all SEM Studies. The authors state that " the evidence from our review supports the use of SEM measurements as a potential tool for the early identification of PI" – they also concluded that "a body of research regarding SEM measures which includes multiple high quality studies increases the reliability of the findings identified in our review". This is a significant development due to the methodology, independent nature and is new data since submission. Resource Impact o Since submission and the subsequent EAC report the following was published in Wounds International (Gefen A. et al WI Vol 11 Issue 1 2020) Modelling the Cost-Benefits Arising from Technology-Aided Early-Detection of Pressure Ulcers. Lead author Prof A Gefen details the cost benefits of implementing the SEM Scanner as an adjunct to standard of care. The authors used a Probabilistic Model and Decision Trees with subsequent Monte Carlo Simulations. Conclusion includes: "Implementation of SEM Scanner technology as an adjunct to the current care practice of VSAs is highly likely to lead to significant financial benefits	

				and cost savings". This newly published analysis specifically answers the resource impact portion of the research question. o Since submission and the subsequent EAC report the following was published in the Journal of Patient Safety and Risk Management (JPSRM 0(0) 1-9). Lead author Prof W Padula modelled the implementation of the SEM Scanner technology in 3 different care settings. Using a Markov model on a simulated patient cohort the authors concluded that "SEM Scanners are a cost effective means of documenting pressure injury risk" and this "technology circumvents the high cost of most pressure injuries in facilities and may achieve ROI in less than 1 year". BBI recognise that this publication is based on US Health Care System however the standard of care for PU prevention is consistent to the International Clinical Practice Guidelines and therefore there is value in including this publication for the review by the EAC and NICE. This newly published analysis specifically answers the resource impact portion of the research question. o New analysis developed specifically to ensure the relevant data was available to answer the above research question. This data (titled Georges Story) is to BBIs understanding the first time a patients journey has been mapped from Acute through to Community care and then on to End of Life care – including both Acute and Social care costs. Relevant documents are submitted to NICE separately. This modelling compares two care pathways – current standard of care (SoC) and SoC with the SEM Scanner as an adjunct. The modelling identifies resource use in terms of bed days, materials costs and healthcare practitioner time. Demonstrating reductions possible when SEM scanning technology is built into the care pathway o Reduced material costs such as dressings o Reduced equipment costs such as specialised support surfaces o Freed up healthcare practitioner time o Reduced acute length of stay This is a significant new element of analysis and therefore must be included in a review by NICE and the EAC and answers the evidence gap suggested in the Consultation document. o Lothian Health Board conducted a Pressure Ulcer Reduction Program (PURP) in 2 clinical settings at the Western General Hospital (WGH), Edinburgh and Edinburgh Royal Infirmary (RIE).	

				o The PURP at RIE was in a ward which had been involved in a large number of quality improvement programmes and changes had been made, however they were still the highest reporters of HAPU in the Health Board. The aim was to determine if the use of the SEM Scanner could reduce the incidence of hospital acquired pressure injuries/ulcers (HAPU) where other interventions had been less effective. o The PURP at WGH was in a ward which had achieved zero HAPU in the previous year but were the highest users of therapy mattresses in the organisation. The aim was to determine if their decision making and results were linked to high use of equipment or if decision making could be improved and also impact potentially inappropriate and excessive use of high cost intervention products, specifically dynamic mattress surfaces. o At the same time a separate intervention using a decision pathway for equipment was tested in similar wards in the organisation, with either high reporting of HAPU or high use of equipment. Using only an assessment and equipment decision pathway, without the SEM scanner intervention, there was an increase in the use of dynamic mattress surfaces and other interventions and results were deemed to be inconsistent with intervention costs rising. o Pre PURP information for the prior year 2018-2019 recorded an HAPU incidence rate in the SEM testing wards of 0% at the WGH and HAPI/U incidence rate of 2.4% at RIE. o Excellent results were achieved at RIE where a 100% HAPU reduction was reported. Significantly an 11% reduction in the usage of dynamic mattresses was noted. In the Western General Hospital, 0% percent HAPU was maintained and a 33% reduction in the use of dynamic system usage was noted. o Combined results for both sites showed a 0% HAPU rate with a 15% reduction in equipment usage compared to the pathway wards which showed an 86% relative reduction in HAPU with a 16% increase in equipment usage which continued. o Given the outcomes achieved when using the SEM Scanner, the economic value has been fully reviewed compared to the reported cost of treatment of HAPU within the Health Board. A positive return on	

				investment is achievable as well as reduced length of stay and avoidance of potential litigation costs. o The introduction of SEM Scanner technology is to be recommended to the Executive Board for implementation to relevant wards within acute hospitals initially with a view to widening the remit to include patients in the post-acute setting. This is new data since submission and therefore should be included in a review by NICE and the EAC and answers the evidence gap suggested in the Consultation document. Given the data above BBI pose the question – what more is needed to answer this research question? What advantage would be gained by not recommending the SEM Scanner at this time? BBI believe that a conditional approval with review after two years would facilitate new studies in the NHS specifically designed to evaluate the magnitude of the benefits which can be achieved."	
10.	3	Company	1.1	*the clinical benefits for different skin tones* "BBI share with NICE Committee and EAC new data published or developed since submission that will fully answer this research question o Visual skin assessment is frequently reported in published literature to be challenging in dark skin tone patients as identification of skin redness (typical visual diagnosis of category 1 PU) is difficult. This is of higher interest currently due to COVID 19 to the extent that we understand that the current Stop The Pressure campaign of React to Red is under review. Repeated calls have been made in published literature for an objective method of assessing dark skin tone patients due to the high impact in the group of patients. o BBI draw NICE Committee and the EAC to the Prevention and Treatment of Pressure Ulcers/Injuries Clinical Practice Guideline (CPG) (EPUAP/NPIAP/PPPIA 2019). Section 5 Skin and Tissue Assessment, Page 79 recommendation 2.7 “When assessing darkly pigmented skin, consider assessment of skin temperature and sub-epidermal moisture as important adjunct assessment strategies”. BBI recognise that NICE referred to this in point 4.7 of the Consultation document – however BBI believe that whilst NICE were correct to point out a weak positive recommendation it should be clarified that this is further described by the CPG as “Probably do it” and is only second in strength of recommendation	Thank you for your comment. Please see response to comment 7 and 8. The External Assessment Centre was asked to comment on the additional references supplied by the consultee and reported that the Bates-Jenson et al. studies use alternative technologies to measure subepidermal moisture. NICE medical technologies guidance evaluates a single medical technology based on the claimed advantages of introducing the specific technology compared with current management of the condition. It is not a multiple technology assessment and does not compare evidence for all

				to Strong positive recommendation: “Definitely do it” and is supported by a B2 Strength of Evidence level. BBI assert that the strength of the recommendation has been misunderstood and therefore a review with feedback from a wider range of clinical experts to fully understand the importance of this piece of evidence is required. o CPG reference B Bates Jenson WOCN 2009; 36(3);277-284 in their strength of evidence. Descriptive cohort study including pooled data from 2 pervious Nursing Home studies, n=66. Goal to compare SEM values in persons with dark skin tone versus lighter skin tone. Author concluded: o Higher SEM Values was associated with both concurrent and incident (1 week later) skin damage in persons with dark skin tones o When more skin damage was observed, SEM values were higher at all anatomic locations. o BBI share additional evidence that supports the low probability of SEM assessments being confounded by skin pigmentation/tones or ethnicity. 417 subjects enrolled/19 facilities: (29% African American, 12% Asian American, 21% Hispanic). This indicates that SEM is consistent and similar in varied skin tones as opposed to current SoC STAs where it is more challenging to detect skin discoloration in individuals with dark skin tones as a measure of tissue injury. (Bates-Jensen B. et al Int Wound J, 15, 297-309 and Bates-Jensen B. et al Wound Repair Regen, 25, 502-511). o Prof Bates Jensen is available to speak to the NICE /EAC team to share her experiences and discuss the findings of her research in more detail, BBI refer NICE and the EAC to the video by Prof B Bates-Jensen for a summary. https://vimeo.com/436348696 o BBI also refer NICE and the EAC to a recent educational Webinar held by NPIAP featuring Dr J Black focussed on assessing dark skin tone patients. Dr Black highlighted the challenges – “The ICG says if you have darkly pigmented skin that maybe you need to use adjunctive measures to help figure out what’s going on, one of these measures is SEM” referring to the importance of technology to assist in assessment. Referring to the SEM Scanner Dr Black stated, “Trans epidermal water loss is greater in dark skin than white skin”….”the guideline does suggest you consider measuring SEM as earlier work by BBJ 2009 matches pretty well the work from 2020”.	similar technologies in a broader class.

				https://www.youtube.com/watch?v=kzEcOhnL6Ak&feature=youtu.be o BBI point out that the SEM Scanner's unique mode of operation in that enables detection of SEM changes in underlying tissue via Biocapacitance of the tissue is not influenced by epidermal skin pigmentation. o Since submission, an independent systematic review has been published in the Journal of Wound Ostomy and Continence Nursing (Scafide K et al. JWOCN 2020;00(0):1-9). The authors reviewed the published data on a number of bedside technologies in early detection of pressure injuries. With reference to this specific research question the authors commented upon the challenges of visual skin assessment in dark skin toned patients and reviewed the work by B Bates Jensen stating that the science suggested "darker skin tone favouring a greater likelihood of detection". Given the data above BBI pose the question – does not the data above answer the research question? The challenges for assessment of dark skin tone are well documented as are the impacts of pressure ulceration in this group of patients. What is being gained by continuing to request further research in dark skin tone patients rather NICE could ask what would be gained by implementing this technology in this specific group of patients?"	
11.	3	Company	1.1	*how well the scanner works across populations with a range of comorbidities* "BBI share with NICE Committee and EAC new data published or developed since submission that will fully answer this research question. BBI draw attention to multiple published reports of the impact of the SEM Scanner across a variety of populations and care settings which present with a wide range of comorbidities. BBI have demonstrated consistent and repeatable results from a variety of care settings including Acute; Community and Palliative care. o In these pragmatic real world studies standard of care was unchanged apart from the inclusion of the SEM Scanner into the care pathway. Graphs 1 and 2 included in the file sent separately to NICE demonstrate the repeatability of the reduction of incidence of PU across a high number of sites with varying clinical challenges. The healthcare practitioners involved will articulate their experiences in having already integrated additional preventive interventions, education programmes and	Thank you for your comment. The External Assessment Centre was asked to comment on the additional references supplied by the consultee They reviewed new data from Musa (unpublished), Guy (unpublished) and Budri (2018) – The External Assessment Centre reported that this study has been published under another title (Budri, 2020) and concluded that their conclusions regarding the clinical evidence is unchanged. Please see response to comment 7. .

				awareness campaigns. However on addition of the SEM Scanner into their care pathways consistent and repeatable incidence rate reductions are demonstrated. Note Graph 1 submitted in a separate file to NICE only refers to UK sites where permission has been received to share data– further data is available from sites in USA; Canada: Belgium; Spain and Ireland. Graph 2 submitted in a separate file to NICE identifies the variety of care settings included to date – this represents patients with a wide range of co-morbidities in order to answer the research question. Up to December 2019 2,115 subjects; 28 sites. In the Acute Care cohort (n=26), 1952 subjects scanned, <35,000 SEM assessments Overall Implementing the SEM Scanner into routine clinical practice has resulted in an weighted average 90.5% PU Incidence reduction. 1x Palliative Care site 47% HAPU reduction; 1x Community Care site 26.7% CAPU reduction o In the Acute Care cohort (n=26), 1952 subjects scanned, <35,000 SEM assessments ▯ SEM delta ≥ 0.6 noted in 58% of these SEM: 21% of these assessments noted visual discoloration ▯ 73% (19/26) hospitals had ZERO HAPUs during the study period - 100% reduction rate ▯ 88% (23/26) had a reduction in HAPUs of >80% ▯ 92% (24/26) hospitals had a HAPU incidence rate of 3% or less ▯ 77% (n=1503) SEM Scanner readings influenced nurse's decision in increasing SoC interventions o Latest data on year 3 of usage from Marie Curie who implemented the SEM Scanner into their care pathway has resulted in a continued reduction in the incidence of PU. In the last 6 months the team have reported a 3 month period with a 100% reduction in PU incidence – they are now finalising the data for the whole 6 month period - this is highly relevant given the high risk status of this patient cohort. o SUBMIT AS ACADEMIC IN CONFDENCE ""Clinical Impact of SEM Scanner Real-World Use in the United Kingdom"" Musa L. et al in review at Journal of Wound Care. Authors summarise the method and outcomes of the pragmatic real world approach in which the SEM Scanner was implemented into a variety of care settings. Further detail is in the file submitted separately to NICE. o 5 Individual manuscripts based on these real world experiences with the SEM Scanner and the impact of PU Incidence, clinical benefit and	

				resource impact (full details are in the table submitted separately to NICE) have been developed by the lead co-ordinator at each site. These manuscripts represent a mix of care settings and represent new data since submission and help to serve to answer the research question raised SUBMITTED AS ACADEMIC IN CONFIDENCE o SUBMIT AS ACADEMIC IN CONFIDENCE Data from a pilot in a Mental Health Care setting (abstract submitted and accepted by 2020 EPUAP Conference, Guy R. et al. Hertfordshire Mental Health NHS Trust) o 20.5% PU incidence prior to piloting the SEM Scanner o Zero pressure ulcers occurred during the pilot (95%CI, 0%, 18%) o Nursing staff involved reported the impact on clinical decision making with additional interventions utilised such as increased patient repositioning or the use of heel boots o This is new data since submission and provides detail of the impact of the SEM Scanner in a population not usually considered in PU prevention projects. o BBI has undertaken further sub cohort analysis of the data from within the Foundational Studies (SEM 200-003 and SEM 200-004) based on the queries raised in the Consultation document. Submitted as a scientific abstract to the 2020 EPUAP Conference. This is new data since submission. There was no significant association of SEM readings at the centre of PUs by PU age (Heel PUs (t=-1.605, p =0.122); Sacral PUs (t=-0.257, p =0.798)). No significant association was seen with SEM readings by stage 1 PU vs. deep tissue injury (Heel PUs (t = 1.71, p= 0.093); Sacral PUs (t = -1.93, p = 0.059), PU category (all p > 0.10), PU severity (all p > 0.40), pain levels (all p > 0.45), Braden total score (p = 0.149) and Waterlow skin type (p = 0.912). In healthy subjects, repeated measures analysis of variance showed no association between subject characteristics and spatial SEM readings (all p > 0.12). Heel callouses were a potential confounder for SEM readings (p = 0.0002) as was race (p = 0.003). Lower SEM readings at the calcaneus of males (p = 0.0468) and in the heel for African Americans (p = 0.0122) were attributed to chance alone (Type 1 error) (Geffen & Gershon, 2018). o SUBMIT AS ACADEMIC IN CONFIDENCE A Budri et al "Identification of increased risk of pressure damage with the SEM Scanner: definition and evidence of clinical outcomes and cost-effectiveness" accepted for publication by the British Journal of HealthCare Management. Further detail is submitted to NICE in a separate file.	

				o BBI refer NICE and the EAC refer to a report submitted by the Royal College of Surgeons of Ireland -the team have conducted a series of controlled studies with the SEM Scanner and have detailed the outcomes in a variety of care settings; populations and subsequently comorbidities o Budri A., et al May 2020 Journal of Clinical Nursing. Observational, prospective, nonexperimental study. This is new data since submission and should be considered as part of a review of the Guidance. o 150 subjects enrolled - Long term care setting o Followed up for 20 days or until visual skin assessment (VSA) PU develops o SoC remained as planned by the nursing care team o 3 days of elevated SEM delta considered a PU event o PU incidence reported by VSA 12.7% n=19; SEM assessment reported incidence 78.7% n=118 o Odds of detection of PU was 25 times greater with SEM than VSA o Statistically significant reduction of 6.2 days in the time that SEM took to detect a PU [95%CI: -10.5days to -2.35days, p=.002] o https://www.nice.org.uk/about/who-we-are/our-principles, Principle 6, point 20 “recognise the value of traditional hierarchies of evidence”: systematic review is typically positioned at the top of the pyramid. Since submission, an independent systematic review has been published (Scafide K et al. JWOCN 2020;00(0):1-9). Authors reviewed the published data on a number of bedside technologies in early detection of pressure injuries. Of the SEM Studies included it reported that the reliability of instruments application and associated measurements were formally evaluated in all SEM Studies. The authors state that “ the evidence from our review supports the use of SEM measurements as a potential tool for the early identification of PI” – they also concluded that “a body of research regarding SEM measures which includes multiple high quality studies increases the reliability of the findings identified in our review”. This is a significant development due to the methodology, independent nature and is new data since submission. Given the data above BBI pose the question – what more is needed to answer this research question? What advantage would be gained by not recommending the SEM Scanner at this time? BBI believe that a conditional approval with review after two years would facilitate new studies in the NHS specifically designed to evaluate the magnitude of the benefits which can be achieved."	

12.	3	Company	1.1	*patient-related outcome measures.* "BBI request clarification on the detail of this research question. The current wording is very broad and BBI need more detail to be able to fully comment however the below data serves to answer the research question as we understand it. o BBI has undertaken QALY analysis within decision tree modelling based on NHS simulations of a 21 bedded facility. However as it was stated in the NICE Guidance documentation not to submit QALY data BBI did not submit this data; BBI will share the modelling with NICE o 210 beds o 12,181 admissions o 1.6% incidence rate o 80% reduction of incidence of Category 2-4 pressure ulcers o Increase of 4.3 QALYs o Per NICE evaluation scales, an ICER result as calculated for use of the SEM Scanner as adjunct indicates a dominant QI, as it is 'more effective and less costly than the current standard of care' o Also since submission and the subsequent EAC report the following was published in the Journal of Patient Safety and Risk Management (JPSRM 0(0) 1-9). Authored by Prof W Padula this publication modelled the implementation of the SEM Scanner technology in 3 different care settings. Using a Markov model on a simulated patient cohort the authors concluded that "integration of the SEM Scanners yielded cost savings of $4054 and 0.35 quality-adjusted life years gained per acute. Admission – suggested the sub-epidermal moisture scanners are a dominant strategy compared to standard of care". BBI recognise that this publication is based on US Health Care System however the standard of care for pressure ulcer prevention is consistent to the International Clinical Practice Guidelines and therefore there is value in including this publication for the review by the EAC and NICE. o New analysis developed specifically to ensure the relevant data was available to answer the above research question. This is a significant new element of analysis and therefore must be included in a review by NICE and the EAC and answers the research questions above. This data (titled Georges Story) is to BBIs understanding the first time a patients journey has been mapped from Acute through to Community care and then on to End of Life care – including both Acute and Social care costs. Relevant documents are submitted in separately to NICE. This modelling	Thank you for your comment. The rational and context for cost-consequence analysis is described in section 7.3.1 of the Medical Technology Evaluation methods guide. The External Assessment Centre was asked to comment on the additional references supplied by the consultee. Please see response to comment 6.

				compares two care pathways – current standard of care (SoC) and SoC with the SEM Scanner as an adjunct. The modelling identifies resource use in terms of bed days, materials costs and healthcare practitioner time. Demonstrating reductions possible when SEM scanning technology is built into the care pathway o Reduced material costs such as dressings o Reduced equipment costs such as specialised support surfaces o Freed up healthcare practitioner time o Reduced acute length of stay o Lothian Health Board conducted a Pressure Ulcer Reduction Program (PURP) in 2 clinical settings at the Western General Hospital (WGH), Edinburgh and Edinburgh Royal Infirmary (RIE). o The PURP at RIE was in a ward which had been involved in a large number of quality improvement programmes and changes had been made, however they were still the highest reporters of HAPU in the Health Board. The aim was to determine if the use of the SEM Scanner could reduce the incidence of hospital acquired pressure injuries/ulcers (HAPU) where other interventions had been less effective. o The PURP at WGH was in a ward which had achieved zero HAPU in the previous year but were the highest users of therapy mattresses in the organisation. The aim was to determine if their decision making and results were linked to high use of equipment or if decision making could be improved and also impact potentially inappropriate and excessive use of high cost intervention products, specifically dynamic mattress surfaces. o At the same time a separate intervention using a decision pathway for equipment was tested in similar wards in the organisation, with either high reporting of HAPU or high use of equipment. Using only an assessment and equipment decision pathway, without the SEM scanner intervention, there was an increase in the use of dynamic mattress surfaces and other interventions and results were deemed to be inconsistent with intervention costs rising. o Pre PURP information for the prior year 2018-2019 recorded an HAPU incidence rate in the SEM testing wards of 0% at the WGH and HAPI/U incidence rate of 2.4% at RIE.	

				o Excellent results were achieved at RIE where a 100% HAPU reduction was reported. Significantly an 11% reduction in the usage of dynamic mattresses was noted. In the Western General Hospital, 0% percent HAPU was maintained and a 33% reduction in the use of dynamic system usage was noted. o Combined results for both sites showed a 0% HAPU rate with a 15% reduction in equipment usage compared to the pathway wards which showed an 86% relative reduction in HAPU with a 16% increase in equipment usage which continued. o Given the outcomes achieved when using the SEM Scanner, the economic value has been fully reviewed compared to the reported cost of treatment of HAPU within the Health Board. A positive return on investment is achievable as well as reduced length of stay and avoidance of potential litigation costs. o The introduction of SEM Scanner technology is to be recommended to the Executive Board for implementation to relevant wards within acute hospitals initially with a view to widening the remit to include patients in the post-acute setting. This is new data since submission and therefore should be included in a review by NICE and the EAC and answers the evidence gap suggested in the Consultation document. o Two expert clinicians (Smith G and Raine G) have also provided BBI with details on the impact on patient empowerment – anecdotal and based on their experiences Implementing the SEM Scanner into clinical practice. G Raine: “The Marie Curie team saw the potential of the SEM scanner, took the initiative and used new technology to transform how we care for patients at risk of pressure damage. The SEM Scanner takes people of the subjective boxes that the Braden and Waterlow places them in and allows staff to plan care based on the individuals response to pressure. This has resulted in a reduction of pressure incidents in one of the highest risk patients groups there is”. The “ scanner enables “new level to practice” and “allows individualise care rather than blanket care planning from risk assessment tools”	

				G Smith: “Summarising how the SEM Scanner impacts clinical practice from my experience. I liken it to a blood pressure monitor. You cannot look at a patient and simply know that their blood pressure is up or down – there are external signs such as redfaced or fainting, but you cannot objectively know that a patient’s blood pressure is to blame for those symptoms unless you actually take their blood pressure. For that you need an instrument to do that – a sphygmomanometer manual automatic or otherwise. There is no other way of collecting that objective data. I would suggest the SEM Scanner is of the same utility. You wouldn’t imagine just giving someone a blood pressure tablet and never measuring objectively that the tablet is having a positive impact. You would check the patient’s blood pressure over time to measure objectively that the tablet (and the resource you are putting into it) are having a positive impact. Otherwise it is a costly resource used without any evidence that it is making a difference. Why then do we do the same with pressure relieving mattresses, repositioning regimes, electric profiling beds, low friction garments, limb elevation devices etc.?? It seems ridiculous to me that we can now objectively measure with a device that the interventions are having a positive impact within 24 hours of implementation and yet we stick with traditional models of care which disregard this ability to target interventions and know conclusively that the return on investment is reduction on pressure ulcer risk. My recommendation is to revisit the Guidance to an approval status for this device.” o The recently published CCG12: Assessment and Documentation of Pressure Ulcer Risk for Community Hospital inpatients and NHS funded residents in Care Homes sets out clear practice for assessing pressure ulcer risk and acting upon any risks identified. Based upon existing Risk Assessment Tools whose challenges of specificity and sensitivity are now well documented – BBI would propose that inclusion of the SEM Scanner in CCG12 would further improve patient related outcomes and would welcome the opportunity to pilot the impact in identified sites o NICE CG179 states the requirement to assess risk of pressure ulceration within 6 hours of admission to hospital or at the first face to face assessment in the community. BBI would propose that inclusion of the SEM Scanner in a review of NICE CG179 (which has not been updated	

				since 2014) would further improve patient related outcomes especially the ability to identify present on admission ulceration which under the current standard of care would not be possible to identify and would allow earlier and anatomically specific interventions. BBI believe that a conditional approval with review after two years would facilitate new studies in the NHS specifically designed to evaluate the magnitude of the benefits which can be achieved."	
13.	3	Company	1	*NICE ask for comment on the following point - Are the recommendations sound and a suitable basis for guidance?* *The committee is recommending research to address uncertainties about the clinical benefits of using SEM Scanner 200 compared with standard risk assessment. This should assess:* • *the risk of pressure ulcer formation using SEM scanner without visual skin assessment compared with visual skin assessment alone* The scope of the appraisal specified use of the scanner as an adjunct to skin and tissue assessment, a combination of tactile and visual assessment (for simplicity herein abbreviated to "VA") rather than as a substitute for it, so this recommendation addresses a different decision problem. Nonetheless, if visual assessment means that the clinician observes the skin for signs of possible pressure damage, we don't believe it is possible to separate visual assessment from use of the scanner. It would not be feasible for a clinician to take a reading with the scanner without at the same time observing the skin, and it would be unethical simply to ignore signs of skin damage observed in this way. We have taken note of the arguments of the EAC that viewing the scanner as a substitute for visual assessment increases the specificity of the SEM reading and improves its cost-effectiveness. We cannot see how this can be the case. • *how changes in clinical decision making from using SEM scanner lead to reduction in the incidence of pressure ulcers* • *the clinical benefits and resource impact of using the scanner in different care settings* • *the clinical benefits for different skin tones* • *how well the scanner works across populations with a range of comorbidities* • *patient-related outcome measures* We agree that all these issues are important, but to design a study (or series of studies) to address all these uncertainties would demand very	Thank you for your comment. With regards to the scope of the assessment please see NICE's response to comment 6. With regards to comment regarding research design please see NICE's response to comment 2. With regards to comment about the type of recommendation please see NICE's response to comment 5.

				large sample sizes and would be prohibitively expensive. Results could not realistically be expected in less than two years. We discuss separately the interpretation of the current evidence, but we believe that given the current evidence base the time and expense required to address all these issues would be disproportionate. The cost of the proposed research would likely significantly outweigh the value of the additional information. We suggest that a more focussed approach to future research could aim to address the key question of whether introduction of the SEM Scanner into NHS clinical practice reduces the incidence of pressure ulcers. A conditional approval of the case for SEM with a review after 2 years would facilitate new studies in the NHS to assess the magnitude of the benefits achieved."	
14.	3	Company	4.14	*Further research is needed to address the uncertainty about the efficacy of SEM Scanner 200 in reducing pressure ulcer incidence* "We believe the scientific rationale for measuring sub-epidermal moisture as an indicator of pressure damage and as a part of a programme to reduce harm to patients is sound, but we recognise that the clinical evidence base is still developing. We believe that a conditional approval with review after two years would facilitate new studies in the NHS specifically designed to evaluate the magnitude of the benefits which can be achieved. BBI propose that as an option in capturing such relevant data the following should be considered. BBI are sponsors of the world's first Global Pressure Ulcer Registry which is currently resident on UK IT servers. Developed by Dendrite Clinical Systems – this group are responsible for 179 National or International databases including a high number of UK base registries. The Registry is a hypothesis generator based on structured datasets. It is a tool for further research on current methods of prevention, management and care for pressure ulcers and for better stratification of patients across primary, secondary and tertiary care. The Registry links select patient pressure ulcer (PU) risk data with biometric readings of skin and tissue condition from the SEM Scanner. The Registry is developed to provide data to initially answer the following research questions:	Thank you for your comment. Please see NICE's response to comment 2.

				• What is the predictive capacity of existing risk assessment methods? • Do the specificity and sensitivity levels of current risk assessment tools make it mathematically impossible to achieve full prevention? • What evidence supports the SSKIN in treating and preventing PUs? • What can SEM Scanner readings teach us about the efficacy of the care pathway for particular patient cohorts and clinical sites of service • What are the rolling percentage reductions in the incidence of Grades 2-4 PUs where the SEM Scanner have been deployed in conjunction with the current Standard of Care for PU diagnosis, prevention and management 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? The existing Real World Evidence data currently managed by an independent Biostatistical Company is uploaded to the Registry, typically once per calendar quarter. The Registry then forms the ongoing database for the real-world data with Dendrite acting as a Data Processor. To review the Pressure Ulcer Prevention Registry please click on the link below: https://rs2.e-dendrite.com/csp/purp/frontpages/index.html"	

15.	1	Healthcare professional	4.1	*SEM Scanner 200 can reduce pressure ulcer incidence but there are considerable uncertainties* "The sentence "whether a reduction in pressure ulcer incidence was due to the scanner results guiding care management decisions or the increased nursing care associated with using the scanner" does not make sense to me, because regardless of whether it is "due to the scanner results guiding care management decisions" or "the increased nursing care associated with using the scanner" these are two sides of the one coin, the SEM scanner guiding care, or nurses pay more attention to pressure ulcer prevention because they see that there is an abnormal SEM. I think the key thing here is whether any different interventions were added or whether the current interventions were increased. One way or the other the use of the SEM scanner is affecting change, which is resulting in a reduction in PU development. Our experience in our RCT shows that use of the SEM scanner to detect early PU development enables a targeted intervention based on the result of the assessment, such as off loading of the heels, and increased repositioning. In the control group, although part of the clinical trial, nursing care did not change, suggesting, that over time, nurses become less aware of the presence of the researcher and continue with the provision of usual care."	Thank you for your comment. The committee decided to change the wording of section 4.1 in response to this comment.
16.	3	Company	1.1	*measures differences in moisture deep under the skin of the heels and the area around the base of the spine (sacrum)* "BBI Comment - this is a misunderstanding – the SEM Scanner actually only measures to a depth of approximately 4mm. Therefore this statement should be corrected to ensure Committee Members are aware of the correct mode of operation and allay any concerns that the depth of measurement may make."	Thank you for your comment. The committee changed the wording in section 1 in response to this comment.
17.	1	Healthcare professional	4.9	*The rationale for using SEM Scanner 200 needs further clinical testing* "The question of oedema comes up all the time, but given the principles of SEM measurement, it should make no difference in the SEM deltas, just the SEM readings will be higher but the deltas will not be abnormal unless there is an anatomical area exposed to sustained unrelieved pressure/shear.	Thank you for your comment. With regards to the inclusion of aetiological studies and proof of concept studies please see comment 6.

				Disruption of cell homeostasis can cause cell death, triggering the inflammatory process (Bates-Jensen, McCreath, & Patlan, 2017). Local inflammation is a normal response to any cell injury and is essential for tissue repair at a microscopic level (Gefen, 2018b). Each single damage pathway, or combination of damage pathways, can set off the inflammation process (Gefen, 2018b). During this process, plasma leaks as a response to the increased blood vessel permeability, which increases the water content around the affected area. This local oedema, SEM, and the local increase of moisture changes the electrical capacitance of the tissues which can be measured using an electrical bio impedance device (Bates-Jensen, McCreath, Kono, Apeles, & Alessi, 2007; Gefen, 2018b; Goretsky, Supp, Greenhalgh, Warden, & Boyce, 1995; Moore et al., 2017). The key thing to understand, is that the SEM scanner measures responses to localised pressure and shear forces, thus, even if an individual has a generalised oedema, it will still be possible to determine SEM changes over a localised boney prominence."	The committee decided not to change the guidance in response to this comment.
18.	3	Company	1.1	*Increased moisture under the skin is thought to reflect inflammation and may indicate an increased risk of pressure ulcer formation*. "BBI Comment – as this underpins the mode of operation it is important to clarify this point. The role of the inflammatory response and the damage spiral are now well reported in the literature – the most relevant and recent summary can be found in the 2019 International Clinical Practice Guidelines – this statement suggests that the scientific foundation of SEM and the ability of the SEM Scanner to identify via Biocapacitance biomarker methodology is undermined. A restatement is required."	Thank you for your comment. Please see NICE's response to comment 178.
19.	3	Company	4.5	*The committee also considered that the presence of comorbidities and conditions associated with skin damage or swelling may influence subepidermal moisture levels and affect the clinical accuracy of the SEM Scanner 200 to identify pressure ulcer risk.* "It is critical to clarify that the principles of operation of the SEM Scanner specifically identify the localised SUB-EPIDERMAL MOISTURE not the SYSTEMIC OEDEMA. While systemic oedema may develop due to a variety of causes , localised oedema in a person who is at-risk for PUs will very likely indicate a forming PU. The SEM Scanner is specifically detecting a localised oedema (as opposed to a systemic oedema) (see figure below in file submitted to NICE) by comparing the Biocapacitance marker which correlates with the interstitial fluid content across different	Thank you for your comment. Please see NICE's response to comment 178.

				tissue locations, e.g. in multiple tissue sites around the sacrum. The difference between the Biocapacitance readings acquired at multiple different tissue locations, which is quantified by the SEM-delta measure, represents the inhomogeneity in interstitial fluid distribution which only increases if one specific site – a PU formation site – starts accumulating plasma due to a locally inflamed, leaky vasculature. In view of the above clarification this point should be restated as it will undermine the views of Committee members regarding the efficacy of the SEM Scanner. It should also retract the request for research on this point due to the above clarification. For further detail please refer to the Letter from Prof A Gefen. Gefen & Soppi 2020 suggest that ....this content is submitted as Academic In Confidence - it is in the file submitted to NICE. Given the healthcare practitioner workload, the redeployment of staff and the engagement of staff to unfamiliar care pathways. the need for a simple to use, objective tool to identify increased risk of PU could not be more important."	
20.	3	Company	4.9	*Although the committee accepted the rationale for this hypothesis, it considered that patients may have oedema from other causes and the principles need to be further tested in well-constructed clinical studies* "As with point 4.5 this statement reflects a significant misunderstanding on the aetiology of PU and the science behind the mode of operation of the SEM Scanner. It is critical therefore to clarify that the principles of operation of the SEM Scanner specifically identify the localised SUB-EPIDERMAL MOISTURE not the SYSTEMIC OEDEMA. While systemic oedema may develop due to a variety of causes , localised oedema in a person who is at-risk for PUs will very likely indicate a forming PU. The SEM Scanner is specifically detecting a localised oedema (as opposed to a systemic oedema) by comparing the Biocapacitance marker which correlates with the interstitial fluid content across different tissue locations, e.g. in multiple tissue sites around the sacrum. The difference between the Biocapacitance readings acquired at multiple different tissue locations, which is quantified by the SEM-delta measure, represents the inhomogeneity in interstitial fluid distribution which only increases if one specific site – a PU formation site – starts accumulating plasma due to a locally inflamed, leaky vasculature. In view of the above clarification this point should be restated as it will undermine the views of Committee members regarding the efficacy of the SEM Scanner. Secondly the call for research on this point should be rescinded.	Thank you for your comment. Please see NICE's response to comment 178.

				Figure included in the document submitted to NICE is reproduced with Permission from Prof A Gefen"	
21.	3	Company		1) Healthy tissue is not inflamed. This is well established. It is also pivotal. 2) PUs are localised damage to skin and tissue caused by deformation and ischemia in combination with shear. The first stage of a developing PU is a localised inflammatory response. 3) The first categories of PUs include Category 1 and suspected Deep Tissue Injuries (DTIs). Both have intact skin. Figure 1 also shows a transition stage of "non-visible tissue damage" which ties to the current aetiological discussion. This is not (currently) a recognised category of ulcer. 4) Category 1 and suspected Deep Tissue Injuries have varying accumulations of dead and dying cells. DTIs are potentially catastrophic since they are undermined ulcers which can rapidly deteriorate to full thickness ulcers. Note, this topic was discussed extensively at the last Committee meeting at which I caused confusion by stating and then withdrawing my description of intact skin PUs (Category 1 and DTIs) as those including dead cells. Dead cells are indeed present in DTIs in particular. Aetiological experts have confirmed this.	Thank you for your comment. Please see NICE's response to comment 178.
22.	3	Company		12) In response to skin and tissue damage, the body's inflammatory response is to vasodilate and increase vascular permeability, thereby causing plasma (comprised of approximately 90% water) to leak through the vessels into the surrounding tissue. Now known as the Damage Spiral (Figure 2 presented in the file submitted separately to NICE)- some local interstitial fluid comes from cell rupture: it is microscopic in proportion. i. Oomens et al (2015) note that during prolonged deformation, arteries and capillaries, the main pathway for inflammatory fluids, and lymph vessels are blocked resulting in localised death of skin and tissue, and the inability of this tissue to inflame. ii. Factors such as duration of pressure, patient physiology, and prevention/intervention measures applied to patient care, contribute to how skin and tissue respond. iii. Alleviation of deformation and ischemia in sufficient time prior to tissue death ("the damage threshold") can return the damaged area to its homeostasis state ("reversibility"). Figure 2: The Damage Spiral (Figure Reproduced with Permission from Prof A Gefen)	Thank you for your comment. Please see NICE's response to comment 178. The External Assessment Centre was asked to comment on the additional references. Okonkwo (2020) – The External Assessment Centre reported that the AUC values are new but the paper appears to add little to the already reported results included in the assessment. The committee considered the additional evidence and concluded it does not answer the uncertainties which led to their

				13) Etiological studies show that early pressure damage does not always manifest into a visible PU (19, 31-33). Researchers of early-stage PUs and PU biomechanics demonstrated the inherent reversible nature of early pressure damage (19, 31-33). Reversibility and self-resolution are known phenomena PU (19, 31-33). Some early damage will progress to a PU and some will reverse back to a healthy state, depending on a variety of factors including a patient's overall health and whether an intervention is taken to alleviate pressure and or shear. Moreover, some pressure damage can be; a) stable, b) not progressing or c) reversing (31). Ultimately this means that increases in SEM delta values will not always lead to a PU, but a PU will be preceded by a change in SEM. Complications to end-point analysis from these etiological realities were considered during trial design and in interpretation of the data. 14) Early stage pressure related damage can be reversed when detected and intervened upon early enough. The International Clinical Practice Guidelines refer to this as the damage threshold. Given the known aetiology of PU development (detailed separately in this Consultation feedback) even the best nursing skills and diligence relating to skin care would be ineffective in achieving timely detection of sub-epidermal injuries. In other words, without insight into deep tissue viability, there is no feasible way for a healthcare practitioner relying on current risk assessment scales and STAs to detect the developing injury in a timely way (Gefen A. 2018) nor take the appropriate, anatomy-specific interventions necessary. The resulting insight therefore is that PU prevention – more simply termed keeping the skin intact – is improbable under the current standard of care (Gefen A. et al 2020). 15) Time matters where deformation is involved. No affirmative data are available, which show that waiting to intervene at an anatomy exhibiting signs of early-stage damage is a successful clinical strategy. Waiting to intervene risks prolonging the ischemic and deformatory processes responsible for ulceration 16) The clinical challenge has been to know whether, where and when to intervene when the signs of early-stage pressure damage are sub-clinical. 17) Bench testing of the SEM Scanner showed that its measurement field is responsive to materials introduced to the field of the SEM Scanner to a depth of ~6mm from the sensor. And, SEM readings increased linearly with the presence of moisture and decreased linearly with the absence of moisture. 18) SEM Scanner clinical studies, SEM200-003 and -004, demonstrated	recommendation for further research. .

				that confirmed damaged tissue in Category 1 and DTI PUs(-003) and confirmed healthy tissue (-004) show different spatial measurement patterns using the SEM Scanner 200 device. SEM Scanner clinical study SEM200-004 demonstrated that confirmed healthy tissue at bony prominences showed spatially consistent absolute SEM values (a SEM "flat" pattern). In other words, healthy skin and tissue over bony prominences have an even distribution of moisture. Healthy tissue showed locally consistent values ("flat") while damaged tissue showed spatially deviated SEM values. From these observations, the SEM delta cutoff was derived. Results of SEM 004 are now published in Advances in Skin and Wound Care March 2020, were submitted to NICE, were used to gain FDA authorization between 2017-2018. A combined manuscript of SEM 003 and 004 is in final review with Journal of Wound Care. 19) SEM200-008 study (Okonkwo 2020 and FDA DEN170021) demonstrated the longitudinal performance of SEM delta cutoff in at-risk patients in providing an early indication of damage compared to visual skin assessment. And, assuming the cutoff is used as an adjunct, how much earlier the SEM delta identifies pressure damage before visual skin assessment. Results of SEM 008 are published in Wound Repair and Regeneration Jan 2020 (Okonkwo 2020). 20) Receiver Operating Characteristic Curves for SEM200-003/04 and 008 show: i) Statistically significantly superior area under the curve statistics than clinical judgement alone for Category 1, DTI PUs and for non-visible tissue damage. ii) AUC for Category 1, DTI PUs (003/004) is 0.7809 (95% CI 0.7221, 0.8397, p<0.0001) iii) AUC for longitudinal deterioration through non-visible tissue damage to a confirmed Category 1, DTI PUs is 0.6713 (95% CI 0.5969-0.7457, P < 0.0001) iv) The higher AUC for 003/004 resulted from diagnosis of PU state by expert opinion (the gold standard). v) The lower AUC for 008 may have resulted from the confounding effect of interventions in the study populations (Okonkwo, 2020). 21) Inflammation - "moisture" (simply stated as water) - is not yet suited for use as a differential diagnosis of the early stages of PUs. • Other diagnostic tests, such as chemical, physical or histological biopsies, may be better suited to testing inflammatory mediators, cellular interactions, localized hypoxia, or apoptosis. Such testing is not the SEM	

				Scanner's intended use. • The SEM Scanner measures changes in levels of moisture (deviating from the flat pattern of healthy tissue) at local tissue over and surrounding the bony prominences susceptible to PUs to give an early indication of tissue damage. This provides the clinician with important targeted information to act upon.	
23.	4	Healthcare professional	2	"Variation between readings reflects sub epidermal tissue inflammation and potential tissue damage"	Thank you for your comment.
24.	4	Healthcare professional	2	"These are the two locations on the body that have the highest incidence of PU developing. This is a worldwide findings in all studies"	Thank you for your comment.
25.	4	Healthcare professional	4	"Agree it is important to rule out other cause of oedema, however this device is identifying a microscopic level of oedema rather than the gross oedema that is often associated with heart conditions, lymphoedema etc. As it is a ratio rather than a direct number it is comparing the patients own readings over an area of tissue and calculating the delta. It would therefore be comparing areas with oedema due to an underlying cause but there could still be differences due to the inflammatory process of the cells in that area which are unlinked to the general oedema but linked to pressure on the area causing the damage."	Thank you for your comment. Please see NICE's response to comment 178.

26.	6	Company consultant	n/a	During 2018-2019 [redacted] the Aetiology Working Group responsible for writing the Aetiology Chapter of the 2019 International Guideline for Pressure Ulcer/Injury Prevention and Treatment and have led this panel of experts to publication of the most comprehensive, rigorous and up-to-date work thus far on the aetiology of pressure ulcers (analyzing over than a 100 recent research papers in the field). For information of the committee, to enable a more informed discussion, I summarized below the contemporary, mainstream published knowledge on pressure ulcer aetiology which is detailed in the above International Guideline. Pressure ulcers (PUs) are injuries which may develop over a timescale of minutes to hours under sustained tissue deformations. Tissue damage in PUs does not appear instantaneously, but rather, develops from the cell scale to the mesoscale and grows to the tissue level and finally, presents itself on the skin surface and often causes skin and underlying tissue breakdown. This implies that in PUs, the damage spiral onsets and progresses from the micro to the macro. Our current fundamental understanding described in the above 2019 Guideline is that this damage spiral ultimately leading to PUs is triggered and then driven by cell and tissue exposure to sustained mechanical deformations, or, in bioengineering terms, to mechanical stress concentrations in soft tissues.	Thank you for your comment. Please see NICE's response to comment 178.
27.	6	Company consultant	4.9	Any bodyweight or device-related forces which cause sustained soft tissue distortions generate large deformations of the cells contained within the affected tissues, with the greatest tissue and cell deformations occurring where these forces are concentrated. With respect to sustained bodyweight forces, the most influenced soft tissue sites are typically found in deep tissue layers under bony prominences, where the highly curved and 'sharp' bone surfaces come into contact with easily deformable soft tissues. The bodyweight forces which are transferred through the sharp and rigid bony elements cause large distortions in the soft tissue structures that they encounter, such as under the sacral or calcaneal (heel) bones, with the highest distortions occurring near the sharpest bony surfaces. This is the reason for the tissue damage to typically occur first in the deeper tissues and only then progress towards more superficial layers, until eventually presenting itself on the skin. At the cell scale, the continuous exposure to such mechanical forces that deform soft tissues would gradually damage the integrity of the cytoskeleton - the complex protein scaffold which makes the structural framework of cells. The	Thank you for your comment. Please see NICE's response to comment 178.

				exterior walls of the cell, called the plasma membrane, are structurally supported by the cytoskeleton. When the cytoskeleton becomes unable to continue providing the sufficient mechanical support to the plasma membrane, pores will form on the membrane. Poration of the plasma membrane will rapidly lead to abnormal transport of ions and molecules from within cell bodies extracellularly, and from the extracellular space inwards into the cell bodies. The inability of multiple cells to control - 3 - their mass transport yields loss of homeostasis which results in *en masse* apoptosis within a timeframe of just minutes. When these multiple cells have been damaged or have died as a direct result of the sustained tissue deformations as described above, the damaged cells and nearby immune cells release pro-inflammatory cytokines, which are signaling proteins that function to attract additional immune cells. This signaling is a programmed normal response which is essential for healing. Recruitment of a large number of immune cells is primarily aimed at counteracting pathogens, clearing dead cell debris and preparing the ground for tissue regeneration. However, in the specific context of PU aetiology, the inflammatory singling itself is a potential contributor to the injury spiral, considering the effects of the pro-inflammatory cytokines on the endothelium in the vasculature adjacent to the initial damage site. Specifically, the secreted pro-inflammatory cytokines act to dilate capillaries and increase the permeability of capillary walls near the initial damage site, by relaxing endothelial cell tight-junctions. This endothelium relaxation facilitates leukocyte extravasation - the migration of immune cells from the blood circulation to the initial damage site. However, the endothelium relaxation also results in leakiness of the vasculature near the damage site and so, plasma fluids build-up in the interstitial tissue spaces, which forms localised oedema. Of note is that this localised oedema which results from the mechanical insult is fundamentally different from a systemic oedema. Systemic oedematous conditions are typically caused by sodium retention in tissues which is associated with heart, liver or kidney dysfunction, or due to a lymphatic disease resulting in lymphoedema, whereas a localised oedema is a characteristic result of a normal immune response trigged by localised tissue damage to allow leukocyte extravasation, as explained above (in response to point 4.9 in the Consultation Document).	

28.	6	Company consultant		Often in a developing PU, soft tissue expansion due to a forming localised oedema is mechanically limited, for example because the soft tissues are constrained between a bony element and a support surface (e.g. between the sacrum and a mattress). If the affected soft tissues cannot sufficiently expand in volume, the interstitial pressures would increase sharply, causing further cell deformation and thereby, additional deformation-induced cell death. Under such conditions, the inflammatory process would then cause release of reactive oxygen and nitrogen species to degrade the extracellular matrix in an effort to relieve the rising interstitial pressures, which will cause further tissue damage, now to the extracellular structures. At a certain stage, the growing interstitial pressures may reach a level that would cause obstruction of the vasculature itself, which will impair blood perfusion into the affected tissue site and thereby, trigger ischaemic damage. These synergistic interactions between sustained cell and tissue deformations, inflammation and ischaemia form the vicious cycle of the development and progression of PUs as we currently understand it. The description of the aforementioned vicious cycle, depicted in the Figure here, is the core of the Aetiology Chapter of the 2019 Guideline. The contents of the 2019 Aetiology Chapter visualized in the Figure represent the contemporary understanding from the past decade – a vast change and progress with respect to earlier knowledge.	Thank you for your comment. Please see NICE's response to comment 178.
29.	6	Company consultant		Of note, inflammation is a critical juncture where the post-injury cascade of events is determined, i.e., whether an early-stage, developing PU will heal normally (without leaving clinically significant tissue damage) or otherwise, would shift to a chronicity state (Cutting & Gefen, 2019). Specifically, the nature of the inflammatory signaling and the associated localised oedema (Figure) are central factors in any healing process and will ultimately determine the 'fate' of the wound, that is, a good healing and closure outcome, or alternatively, chronicity (Cutting & Gefen, 2019). Conditions of uncontrolled inflammation such as those reported in COVID-19 augment the tissue swelling or the increase in interstitial pressure levels, which then causes a wider spread of the secondary cell death and tissue damage, due to the resulting high cell distortions (Figure). Inflammatory signaling further impacts the lymphatic system and as commonly known, typically causes swelling of lymphatic nodes, which adds to the mechanical loading on adjacent cells and therefore, to the potential for cell damage. The SEM Scanner is designed to function based upon this contemporary aetiological understanding of PUs and targets the inflammatory phase in the formation of PUs which is characterised by localised accumulation of	Thank you for your comment. Please see NICE's response to comment 187.

				plasma in the interstitial compartments. Noteworthy is that the localised nature of plasma fluid accumulation in soft tissues due to a forming PU is inherently different from a systemic oedema mechanism, in both the pathophysiology and clinical outcomes, as described earlier. As mentioned in multiple places in the 2019 Guideline, there are a number of physical and chemical biomarkers that characterize the inflammatory phase in PU formation and among these biomarkers, biocapacitance is a very robust biophysical measure of the localization and extent of the tissue damage.	
30.	6	Company consultant		- 4 - While systemic oedema may develop due to a variety of causes e.g. heart failure, low protein levels, liver or kidney diseases, a localised oedema in a person who is at-risk for PUs will very likely indicate a forming PU. The SEM Scanner is specifically detecting a localised oedema (as opposed to a systemic oedema) by comparing the biocapacitance marker which correlates with the interstitial fluid content across different tissue locations, e.g. in multiple tissue sites around the sacrum. The difference between the biocapacitance readings acquired at multiple different tissue locations, which is quantified by the SEM-delta measure, represents the inhomogeneity in interstitial fluid distribution which only increases if one specific site – a PU formation site – starts accumulating plasma due to a locally inflamed, leaky vasculature (Figure). Currently, there is no other feasible technological alternative to use of biocapacitance as the biophysical measure of the build-up of this local inflammatory cell and tissue damage which points to an early-stage, but still likely reversible damage.	Thank you for your comment. Please see NICE's response to comment 1~~8~~7.
31.	6	Company consultant		The process by which serious, hospital-acquired deep PUs form under intact skin, spread in deep tissues and eventually present themselves as full-thickness wounds has been rigorously described in the medical literature in the last decade, from a basic science and aetiological perspectives. A compilation of this contemporary knowledge is provided in the most recent (2019) version of the Etiology Chapter in the International Clinical Guideline for Pressure Ulcer/Injury Prevention/Treatment which [redacted] has authored as Chair of the Aetiology Working Group. The mechanobiology of such PUs is that soft tissue damage initiates near bony prominences – typically the sacrum and heels. The force of concentrated bodyweight under these bony prominences causes intensified and sustained cell and tissue deformations which compromise cell integrity,	Thank you for your comment. Please see NICE's response to comment 1~~7~~8.

				transport function, leading to cell death and eventually, to massive tissue death (Figure).	
32.	6	Company consultant		The SEM Scanner (Figure) measures the biocapacitance of the local skin and subdermal tissues under its sensor. As mentioned above, the biocapacitance is a temporal and spatial physical property of the tested tissue region, and more specifically, a bioelectrical property that is the ratio of the change in an electric charge in the scanned tissue region to the corresponding change in its electric potential (Gefen, 2018; Peko Cohen & Gefen, 2019; Ross & Gefen, 2019; Gefen & Ross, 2020). A large self-biocapacitance of a tissue region indicates that this tissue region is able to hold more electric charge at a given voltage than a different region with a low self biocapacitance. The biocapacitance is a function of the geometry and architecture, which in the context of a SEM Scanner measurement is the area of the sensor of the device and the composition of the examined soft tissues in the immediate vicinity of the sensor, especially the dielectric properties of these tissues. For tissues, as with many dielectric materials, the biocapacitance is independent of the electrical potential applied by the SEM sensor. The biocapacitance of tissues is, however, variable and highly sensitive to the interstitial water content of the tissue (Gefen, 2018; Peko Cohen & Gefen, 2019; Ross & Gefen, 2019; Gefen & Ross, 2020). The dielectric constant of water (which is approximately 80) is 10 to 20-times greater than that of all solid tissue components, e.g. collagen and elastin. In a certain anatomical region, with a given anatomical configuration, the SEM Scanner reading of biocapacitance will be predominantly affected by the dielectric tissue properties, which are, in turn, highly sensitive to the amount of water in the examined tissues. Accordingly, any inflammation-related increase in the permeability of the vascular and/or lymphatic walls will almost immediately be measureable due to its impact on the effective dielectric property of the affected tissues. Hence, the tissue biocapacitance will increase rapidly and dramatically even if the inflammatory response has just been initiated and despite visible (clinical) signs of it have not developed yet (Gefen, 2018; Peko Cohen & Gefen, 2019; Ross & Gefen, 2019; Gefen & Ross, 2020). The SEM Scanner reports the level of biocapacitance of a tissue site as a non-dimensional 'SEM value.' A comparison of the SEM values at the inflamed tissue site with those from adjacent, healthy tissue sites will identify the maximum difference between the SEM values, which is called the 'SEM-delta.' The greater the SEM-delta, the greater the extent of the	Thank you for your comment. Please see NICE's response to comment 178.

				developing inflammatory oedema and therefore, the potential tissue damage to be expected at the scanned site	
33.	6	Company consultant		The SEM-delta is an objective, quantitative and standardized reading of the tissue health conditions, wherein a low SEM-delta indicates healthy tissue and a high SEM delta points to a local inflammation as a result of localized cell and tissue death. In particular, a trend of increase in SEM-delta values acquired at a common body site over time (i.e. from one day to another) may indicate an increasing, spreading inflammation that is the response to an ongoing tissue degradation process. Noteworthy is that if there is a condition of systemic oedema e.g. lymphoedema or heart or kidney dysfunction, the SEM values acquired at adjacent points will be similar and hence, the SEM-delta would be low. Accordingly, selection of the SEM-delta measure (rather than the individual SEM values) allows to distinguish a localized inflammatory process which most likely indicates a forming PU from any systemic increase in interstitial fluid contents, either normal or abnormal (Ross & Gefen, 2019; Gefen & Ross, 2020). Using laboratory bioengineering phantoms of soft tissues in organs (the head and heels), we have demonstrated in our published work (Peko & Gefen, 2019; 2020) that indeed, the SEM Scanner is able to detect intra-tissue fluid content changes that are as small as 1 milliliter and that the SEM-delta reading is sensitive to these changes. The latter findings were shown to be robust and reproducible for both the SEM-200 (1st-generation) model and the new SEM-250 (2nd-generation) Scanner model (Peko & Gefen, 2019; 2020).	Thank you for your comment. Please see NICE's response to comment 178.
34.	6	Company consultant		• The SEM Scanner is built upon well-established physiological and biophysical principles which were explained here. The SEM Scanner is targeting a specific stage in the PU injury cascade in which there is a window of opportunity for detection of a localized change in the biocapacitance property of a tissue region at risk. Such change in the local tissue biocapacitance would indicate inflammatory - 10 - micro-damage that may still be reversible (Figure). This is in stark contrast with the conventional clinical thinking of documenting an existing macroscopic, structural tissue damage which occurs much later in the injury spiral (typically days after the onset of the micro-damage) and only then, that structural damage can be spotted by VSAs or ultrasound examinations.	Thank you for your comment. Please see NICE's response to comment 178.
35.	6	Company consultant		There is no current feasible technological alternative to use of biocapacitance, the biophysical measure used by the SEM Scanner	Thank you for your comment

				technology, for detecting the inflammatory stage of cell and tissue damage in PUs.	
36.	3	Company	4.8	*nvolves the combined use of validated scales and clinical judgement* "This is commonly reported as the standard of care (SoC) in PU prevention however it is important for the Committee Members to be aware of the widely reported challenges of the SoC (Moore Z. et al 2019) so they are equipped to make an informed decision regarding the clinical applicability of the SEM Scanner. SoC utilises risk assessments supplemented by a skin and tissue assessment—visible and palpation tests— (STA) intended to diagnose a developed PU. STAs appraise skin colour, blanchability, temperature, hardness, and other visible or palpable indicators of injury (particularly challenging in dark skin tone patients)– which form the basis of clinical judgement. Clinical judgment of healthcare practitioners related to PU prevention was analysed in a systematic review in 2006 which identified "high inter-examiner variability" (Pancorbo -Hidalgo P.L. et al). Whilst a later meta-analysis (Garcia-Fernandez F.P. et al. 2014) reported that clinical judgement of nurses informed by risk tools and skin and tissue assessment "achieved inadequate capacity to assess PU risk". Furthermore Pancorbo -Hidalgo identified that clinical judgement has a sensitivity of 50.6% and specificity of 60.1% because of the skill dependency of skin and tissue assessment. Finally correct identification of a Stage I pressure ulcer has been observed as low as 60% in a diverse group of 1,452 nurses (Beeckman D. et al. 2007). Given the known aetiology of PU development (detailed separately in this Consultation feedback) even the best nursing skills and diligence relating to skin care would be ineffective in achieving timely detection of sub-epidermal injuries. In other words, without an insight into deep tissue viability, there is no feasible way for a healthcare practitioner relying on current risk assessment scales and STAs to detect the developing injury in a timely way (Gefen A. 2018) nor take the appropriate, anatomy-specific interventions necessary. The resulting insight therefore is that PU prevention – more simply termed keeping the skin intact – is improbable under the current standard of care (Gefen A. et al 2020). The SEM Scanner significantly reduces the variation in the process of PU risk	Thank you for your comment. For comment regarding pressure ulcer aetiology please see NICE's response to comment 17.~~8~~

				assessment and provides objective documentation supporting care planning. Okonkwo H. et al (2020) reported the SEM Scanner as follows: Sensitivity was 87.5% (95% CI: 74.8%-95.3%) Specificity 32.9% (95% CI: 28.3%-37.8%) Area Under the Receiver Operating Characteristic Curve (AUC) 0.6713 (95% CI 0.5969-0.7457, p <0.001) Receiver Operating Characteristic Curve for SEM 008 (Okonkwo et al 2020) graph is within the document submitted to NICE. A figure within the document submitted to NICE presents a visual portrayal to demonstrate the “Non-visible Tissue Damage” referred to above. Due to the subjective, latent nature of STAs and subsequent anatomy-specific interventions, the need for the SEM Scanner providing objective, point-of-care data on at-risk patients before the invisible, sub-clinical, damage manifests at the skin’s surface as visible damage is clear. Figure reference - Padula, W., et al. The cost-effectiveness of sub-epidermal moisture scanning to assess pressure injury risk in U.S. health systems. Journal of Patient Safety and Risk Management, OnlineFirst, pp. 1-9. Copyright © 2020 by the Authors. Reprinted by permission of SAGE Publications, Ltd."	
37.	4	Healthcare professional	2	"Standard care across the UK is through use of a recognised risk assessment tool and the SSKIN bundle. This includes: S = Skin assessment S= Surface in contact with skin - e.g. mattress, cushion etc. all clinical areas would have high specification foam as baseline standard if they are NHS facilities. K = Keep moving - mobilisation or repositioning I = Incontinence or Increased moisture (from sweat or other body fluids) N = Nutrition and fluids. All staff would use these as standard care."	Thank you for your comment.
38.	3	Company		5) Risk assessments are the whipping boy of PU prevention and management. A great deal has been written about the validity of risk assessment tools, their sensitivity, specificity and other performance characteristics. A whole Cottage industry of upholding, criticising, validating, re-validating risk assessment tools has evolved to the point	Thank you for your comment.

				where there are now more than 97 risk assessment tools available to practitioners. Publications extend to the many hundreds. The debate quickly becomes personal among advocates of risk assessment tools versus those who want rid of them. Those debates are irrelevant here. 6) Risk assessment tools play their role in stratifying patients into varying degrees of risk from no risk to very high risk. Generalised “universal preventions” result where a patient is deemed to be at risk. 7) Risk assessment tools ask the wrong question to be completely useful in directing care for PU prevention. They do not ask, nor are able to answer the question of “where?” a patient is at risk of developing a PU. “Is my patient’s left heel going to develop a PU?” Risk assessments do not seek to, nor can they answer that question	
39.	3	Company		9) Risk assessments are supplemented by a skin and tissue assessment—visible and palpation tests— (STA) intended to diagnose a developed PU. If the STA diagnoses a PU, then anatomy-specific interventions (e.g., a heel boot at a patient’s left heel together with a bundle of other interventions) are initiated . STAs appraise skin color, blanchability, temperature, hardness, and other visible or palpable indicators of injury. Clinical judgment of nurses, informed by risk tools and skin and tissue assessment, however, “achieved inadequate capacity to assess PU risk ” and suffered from “high inter-examiner variability . Clinical Judgement has a sensitivity of 50.6% and specificity of 60.1%, as noted by the EAC: a standard approaching randomness for diagnosis of Category 1 and suspected Deep Tissue Injuries . 10) Consider the guidance to nurses for their diagnoses: i) A Category 1 PU is “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.” (EPUAP classification system. Emphasis and underlines added by BBI) ii) How could a nurse reliably diagnose a condition with inherent contradictory characteristics in its definition: (a) redness, but not if dark skin toned, (b) firm or soft, and (c) warmer or cooler? 11) Differential diagnosis of the early stages of damage and intact PUs cannot occur using any method until these definitional characteristics are sufficiently refined to achieve a mutually exclusive, but collectively	Thank you for your comment.

				exhaustive differential rubric within PU states or between PUs and other potential wounds. More refined definitional characteristics cannot be identified, tested, and refined without objective data of skin and tissue state, such as those from objective devices like the SEM Scanner. For the first time using the SEM, an objective metric of health or damage is available.	
40.	6	Company consultant	n/a	Since these PUs may not form initially on skin, even the best nursing skills and diligence relating to tissue care will be ineffective in achieving timely detection of sub-epidermal injuries. In other words, without an insight into deep tissue health status and viability, there is no feasible way for a nurse relying on current risk assessment scales and visual skin assessments (VSAs) to detect the developing injury in a timely way (Gefen, 2018; Gefen & Ross, 2020; Gefen et al., 2020). It is not surprising therefore that these deep PUs, which emerge at the skin surface only after considerable deeper tissue damage has already been caused, are the ones associated with the majority of the global expenditure on treating PUs (Gefen et al., 2020).	Thank you for your comment.
41.	6	Company consultant	n/a	Importantly, even for patients correctly identified to be at-risk by risk assessments, who receive a high-specification support surface as well as other best-practice prophylactic interventions and repositioning, nursing staff will never be able to detect a deep tissue injury (DTI) evolving under intact skin by means of the VSAs. The VSAs currently used in practice are only able to detect the DTI once the damage has reached the skin, which is clearly too late. This simple logical flaw in classic PUP strategies points to the true barrier to effective PUP and to the associated cost reductions: the lack of a reliable technology, based on solid physical and physiological foundations, to evaluate the tissue health of patients under an apparently normal skin at specific anatomies	Thank you for your comment.
42.	6	Company consultant		Importantly, as per the medical claims made by the manufacturer, the SEM Scanner is currently being suggested as an adjunct to VSAs, not as a replacement of these conservative manual examinations. Practically, with reference to the comment made in the NICE EAC Consultation Document (Section no. 1.1; first bullet point), there is no point in validating the SEM Scanner measurements against VSAs since VSAs document existing macroscopic structural tissue damage, whereas the SEM Scanner detects early, microscopic-scale damage. The latter event occurs at an earlier time point on the timeline of the PU damage cascade (Figure) and so, the technology-aided SEM-delta readings will always be abnormally elevated prior to a positive (and subjective) VSA diagnosis, as in the	Thank you for your comment. The committee heard from expert advisers that it would not be realistic to use SEM scanner without also assessing the skin. The committee have amended their recommendation to reflect this. Changes were made to the wording in sections 1.1, 4.4 and 4.14 in response to this comment.

				above example study. Indeed, a large volume of other, independent clinical studies have been reported in the literature and are reviewed in the published work of [redacted] all consistently demonstrated the early-detection feature of the SEM Scanner, which is not surprising based on the known PU aetiology (Figure).	
43.	1	Healthcare professional	4.3	*There is uncertainty about the diagnostic accuracy of SEM Scanner 200* This is confusing, if using skin assessment would confound results, then why recommend it in future research? Pragmatically, how can I scan the heels and sacrum without actually looking at the skin, because I would need to look to ensure that I am placing the device in the right place! Earlier research has examined the reliability of pressure ulcer grading using different grading systems among a wide variety of individuals (n=2,480) (nursing students, clinical, education and research staff) (Nixon et al., 2005b, Defloor et al., 2006, Russell Localio et al., 2006, Stausberg et al., 2007, Beeckman et al., 2007, Beeckman et al., 2008). Overall, the reliability of pressure ulcer grading varies enormously k =1.0 (Nixon et al., 2005b), k = .52 (Defloor et al., 2006), r =.69 (Russell Localio et al., 2006), k =.50 (Stausberg et al., 2007), k=.33 (Beeckman et al., 2007) and k =.56 (Beeckman et al., 2008). Thus, in the main, there is only moderate agreement among this large number of diverse research participants. Thus, the suggestion that VSA is the gold standard really needs to be challenged. In the practice of assessing an individual with the SEM scanner one cannot avoid looking at the skin, thus it will not be possible to separate skin assessment from that of the SEM scanner, unless the SEM readings can be transmitted safely and securely to an independent outcome assessor, who is unaware of the condition of the skin.	Thank you for your comment. Please see NICE's response to comment 42
44.	3	Company		Claim language We need to make you aware of a change to the Claim Language for the SEM Scanner. This change was registered some months ago. The revised language reads: "The SEM Scanner 200 is intended as an adjunct to current standard of care for the detection of deep and early-stage pressure-induced	Thank you for your comment. Please see NICE's response to comment 42

				injuries/ulcers by health care professionals” The language retained a fundamental principle of the SEM Scanner being an adjunct to the current standard of care. Why? i) Definitional challenges of what Category 1, DTI and early-stage damage comprise sufficient to unambiguously diagnose the presence or absence of ulceration mean that subjective characteristics of each PU category need to be augmented with objective characteristics of skin and tissue status (e.g., SEM). The current definitions include contradictory characteristics (firm/soft, warm/cold, red/not red if dark skin toned) of skin and tissue status. These contradictions make a clear diagnosis, not least a differential diagnosis, highly challenging. We fully anticipate objective measures of skin and tissue status will provide clear definitional differences between states (e.g., SEM flat values showing healthy tissue, SEM deltas showing damaged tissue etc.) We recognise such change is a gradual process involving the scientific and clinical research communities. ii) The absence of an objective gold standard and the challenge that poses for the clinical diagnostic accuracy paradigm is described in other parts of the submission. Proving a diagnostic in the absence of a gold standard test presents an epistemological and regulatory challenge: one that recognises the clinical need for the SEM Scanner, while at the same time having responsibility to uphold established scientific norms and assure patient safety. Researchers of this epistemological suggest the ‘clinical test validity,’9 meaning looking at the results of the test – SEM from the SEM Scanner – in clinical practice and observe the results 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. iii) Safety System and Professionalism principles suggest value in the primacy of clinical judgement over diagnosis when both conditions described immediately above exist. Warnings about use of SEM Scanner data for PU diagnoses were removed. In agreement with our Notified Body this language frees up healthcare practitioners to exercise qualified greater clinical judgement about the role of the SEM Scanner data in their care pathway in the context of a bolus of publications.	

				Why change now? A bolus of publications about SEM, the SEM Scanner (sponsored and independent) demonstrating scientific principles of observability and repeatability have been published in late 2019 and early 2020. The gradual process of validation has moved along quite considerably which the claim language reflects.	
45.	4	Healthcare professional	1.1	"This would be a very difficult process to assess. To use the SEM scanner you have to be looking at the patient's skin to ensure the scanner is in contact with the skin and in the correct location. As a nurse you would be viewing the skin during the process and basing you judgement on this combined information of sight and SEM score."	Thank you for your comment. Please see NICE's response to comment 42.
46.	4	Healthcare professional	4	"I think that this would be very difficult to do (as mentioned in first section) as the individual undertaking the scan has to see the skin to use the scanner. To do this sort of study would involve bringing in non-clinicians to take readings or have the readings sent off site to a non-clinician who was not visualising the skin. Bringing in someone non-clinical would change the dynamics of care unless the scanning was undertaken at the usual time with a clinician. However the non-clinician would still see the skin even if they were not reporting on it. It may be possible but a complex piece of work. The work we completed recently noted the number of visual skin changes when undertaking the scan compared to SEM scanner reading results. We had a total of 126 patients over 2 wards and a total of 3211 scans took place during the 6 week period across the wards. In one ward only 14% of patients would have been picked up with visual inspection alone compared to 67% with SEM scanner reading. In the second ward 45% with visual assessment alone vs. 71% with SEM scanner reading."	Thank you for your comment. Please see NICE's response to comment 42.
47.	4	Healthcare professional	4	*There is NHS interest in the SEM Scanner 200 because community and hospital-acquired pressure ulcers remain a significant problem* "Agree, after more than 5 years of focused PU prevention improvement work , there continue to be areas who have not seen the improvement expected. This may be due to population, increasing frailty and immobility. This device would improve outcomes for patients in this group who are highly vulnerable to tissue damage due to their underlying comorbidities."	Thank you for your comment.
48.	4	Healthcare professional	4	*SEM Scanner 200 provides an objective measure of pressure ulcer risk*	Thank you for your comment.

				"This would be an excellent tool to improve measurement of risk compared to the poor inter-rater reliability for staff at present assessing patients using recognised PU risk assessment tools such as Waterlow, Braden etc. Also clinical judgement is subjective and depends on a range of issues such as past experience, knowledge, competence etc."	
49.	6	Company consultant	n/a	The benefits of a quantitative, standardized and objective risk assessment and early detection of PUs using a technological tool - the SEM Scanner – to aid and support the currently subjective process of PU identification are significant, and the risks in using the device, if any, are negligible.	Thank you for your comment.
50.	6	Company consultant		The BBI LLC (Bruin Biometrics) SEM Scanner technology addresses a major and unmet medical need in prevention of PUs and supports healthcare professionals who are currently not supported by any other technology to aid in their clinical decision-making with regards to the PU risk at specific anatomical sites of individuals.	Thank you for your comment.
51.	6	Company consultant	n/a	□ Risk assessment and early-detection are the two essential foundations for effective PUP, which can finally be based on modern and relevant medical technology - the SEM Scanner - rather than just the art and subjective clinical skills.	Thank you for your comment.
52.	4	Healthcare professional	4	The evidence does not address how SEM scanner 200 performs across different populations “Definitely agree, dark skin is difficult to assess for early signs of skin changes such as redness as this does not show on the darker pigmented skins. In this population group it would be an invaluable tool to assess and provide clear guidance to staff on which patients required interventions reviewed.”	Thank you for your comment.
53.	3	Company		Page 1 of the Consultation Documents also asks, “Are there equality issues that need special consideration and are not covered in the medical technology consultation document?”. BBIs response is that the Consultation document has not considered all the evidence especially for dark skin toned patients whose health disparities are more pronounced in PU prevention and especially impacted due to COVID 19. Please see the individual comments in the Consultation Document and the Addendum pack for detailed responses.	Thank you for your comment. The committee considered the possible equality issues related to recommending research is done to assess the clinical efficacy of SEM Scanner. The committee decided that the guidance addresses all equality issues and decided not to amend the guidance.
54.	6	Company consultant	n/a	Another common misconception hindering the timely clinical diagnosis of PUs is that patients who develop PUs will complain about discomfort or pain. Pain is not a good predictor of PUs, particularly where there is an	Thank you for your comment.

				impaired sensation due to central or peripheral neural damage caused by injury or disease or anaesthetics, sedation or any medications which affect sensation. Pain only becomes relevant where a person is able to sense (but not necessarily move), which is not the case for the majority of the at-risk patients. For example, one (relatively rare) condition where discomfort or pain may predict a later onset of a PU would be a locked-in syndrome (pseudocoma) where a person loses their ability to move, but can still sense discomfort (Gefen & Soppi, 2020).	Please see NICE's response to comment 53
55.	2	Professional organisation	4.1	*SEM Scanner 200 can reduce pressure ulcer incidence but there are considerable uncertainties* We agree that it is not clear whether use of this device actually results in a reduction in pressure damage. Or if there is a reduction in pressure damage incidence, whether this is due to the device or some other intervention such as more focused visual monitoring etc.	Thank you for your comment.
56.	2	Professional organisation	4.5	*The evidence does not address how SEM Scanner 200 performs across different populations* We agree there is a need for more testing in non-white skin.	Thank you for your comment.
57.	5	Healthcare professional	3.2	*Raizman et al, 2018* The published report was a quality improvement initiative thus I did not have support as usual research studies had, so I used my experience to determine sample size.	Thank you for your comment.
58.	5	Healthcare professional	3.2	*Raizman et al., 2018* As a result of the evaluation we purchased SEM scanners and use them to decrease incidence of Ulcers: units that do not practice SEM scanning have higher incidence so I am advocating to get more devices.	Thank you for your comment.
59.	4	Healthcare professional	2	*represent clinically significant levels of sub epidermal tissue inflammation and potential tissue damage.*	Thank you for your comment.
60.	1	Healthcare professional	4.1	*The 2 before and after studies are relevant to the decision problem and report pressure ulcer incidence* However, I'm not sure what difference it really makes if one reports stage 1 and the other doesn't?	Thank you for your comment. The committee reviewed the guidance and concluded that the assessment of the evidence was fair. The committee did not change

				The issue of whether one study author reports stage one and above, and another study author reports stage two and above only influences the numbers of pressure ulcers included in the data reported, rather than influencing how well the SEM Scanner 200 works. Indeeed, the impact of this relates to the comparison of gross figures between studies, however, so long as the study authors report the number of PUs per grade, then comparisons can be made between studies related to stage 2 and above. Given that, in many clinical settings, it is mandatory to report stage 2 and above PUs, then it likely that many research studies will follow this pattern. Further, this reflects what clinicians will be looking for in the data, so that they may compare results with their own data derived from their mandatory PU reporting results.	the guidance in response to this comment.
61.	3	Company		8) The result is generalised, whole body interventions, sporadically applied. Okonkwo 2020 showed that of the Intent To Treat population, 26.4% developed a PU during the study; 66.7% classified as Stage 1 injuries, 23% deep tissue injuries, the remaining being Stage 2 or Unstageable. All (100%) of subjects received some form of preventative interventions. The high level of offloading measures noted in the study potentially led to reversals of tissue damage . Intensive forms of offloading measures (repositioning every 1 or 2 hours, heel boots & elevations and active and low air mattress support systems) were provided to 89.6% of the enrolled subjects while 10.4% received less intense forms of preventive care (e.g., static bed mattress, topical agents, less turning frequency). i) Of the 48 PUs that developed, 22 (46%) developed in patients deemed to be “moderate risk”, followed by 18 (38%) in the “high-risk” category, then 6 (13%) in the “very high risk” category. The balance occurred in the “mild risk” category.	Thank you for your comment. Please see NICE’s response to comment 60.
62.	3	Company	4.7	*The committee also noted that, based on evidence, the guideline only proposed a weak positive recommendation for these devices when assessing risk in people with dark skin.* BBI point out that this is further described by the CPG as “Probably do it” and is only second in strength of recommendation to Strong positive recommendation: “Definitely do it” and is supported by a B2 Strength of Evidence level. BBI assert that the strength of the recommendation has been misunderstood and therefore a review with feedback from a wider range of clinical experts to fully understand the importance of this piece of evidence is required to ensure a deeper understanding of the significance.	Thank you for your comment. The committee heard from expert advisers that the clinical practice guidelines recommendations are not solely reflective of the evidence. The committee decided not to change the guidance in response to this comment.

				Secondly the Consultation Document do not mention that this is one of two recommendations within the CPG (page 78; Recommendation 2.6. Strength of Evidence B2; No specific recommendation). Given the strength of evidence behind both statements BBI believe the current wording undermines the importance of the statements and a clarification is required to ensure Committee members views are not uninformed.	
63.	3			22) As shown from real-world data from the clinical setting, PURP investigators demonstrated the clinical impact of using the SEM Scanner as an adjunct to standard of care. When nurses act on the SEM Scanner's quantitative information: 1. The SEM Scanner provides days of early detection of localised inflammation at anatomical locations that are susceptible to PU development (heel and sacrum). This is an advancement in PU clinical practice. 2. Nursing teams can achieve zero or near zero incidences of reportable PU. 3. Manuscripts detailing results of the PURP Pragmatic approach to date are in final review with Journal of Wound Care whilst individual site outcome manuscripts have been submitted (or in the process of submission) to a number of UK based nursing journals - BBI refer NICE to the summary file submitted separately. Increasing number of NHS facilities are now adopting this technology under formal PURP processes (i.e., real-world evidence gathering and reporting methods). 4. BBI's real-world evidence are more robust than EAC's clinical review asserted. 23) The link between SEM test results to specific clinical actions and clinical results have been established. See the protocols from NHS users about their use of the device's results. Broadly, when SEM delta positive, treat as you would category 1 PU. Patient already deemed to be at risk.	Thank you for your comment. Please see NICE's response to comment 60.
64.	6	Company consultant	n/a	Indeed, in our published - 7 - work, we could identify the formation of a heel PU in a patient under their intact skin (i.e. a heel DTI) through a consistent rise in the SEM-delta readings at the examined heel, 2 days before VSA indicated tissue damage and importantly, 3 days before the appearance of a hypoechoic lesion demonstrating the fully-developed macroscopic oedema in an ultrasound examination of that same heel (Gefen & Gershon, 2018). This is strong evidence of the detective power of the SEM Scanner in identifying the forming oedema under a spotless	Thank you for your comment. Please see NICE's response to comment 60.

				skin, already at the initial, microscopic phase of the oedematous development.	
65.	6	Company consultant	n/a	It is a striking fact that the SEM Scanner technology has been tested in clinical trials more than any other emerging preventative technology in the PU arena which is known to [redacted]. The NICE EAC report evaluating the SEM Scanner should be adjusted to accurately reflect the state of the science and the rigorous testing that this particular technology underwent in both the basic science and medical-clinical aspects. Specifically, there are multiple large-scale clinical trials published in the peer-reviewed medical (wound care) literature which reported a significant diagnostic value of the SEM Scanner, leading to improved health care and reduction in treatment costs post implementation of the device. The published literature is reviewed in the work of [redacted] cited below. One of these clinical studies, [redacted] (Gefen & Gershon, 2018), is summarized below to provide an example for the clinical importance, applicability and usefulness of the SEM Scanner in different clinical settings. A clinical study was conducted to evaluate consistency between the SEM Scanner and ultrasound examinations of suspected deep PUs under intact skin, known as deep tissue injuries (DTIs). Specifically, using an observational, prospective cohort study design, patients >55 years of age were recruited. In addition to SEM Scanner measurements, we also performed conventional VSAs as well as ultrasound assessments. These examinations were performed daily for a minimum of 3 and maximum of 10 consecutive days following patient enrollments. The ultrasound results were considered indicative of a DTI if hypoechoic lesions were present in the acquired images. The SEM Scanner readings were considered abnormal when the SEM-delta at a specific body region (sacrum or each of the heels) was equal or greater than 0.6 for at least 2 consecutive days. Boolean analysis was utilized to systematically determine the consistency between the ultrasound and SEM Scanner readings where DTI was the clinical judgment. Among the 15 participants (10 of whom were women, mean age 74 ± 10.9 years), which were, in general, a nursing home population at a high risk for PUs, there was consistent agreement between the SEM Scanner readings and ultrasound when DTIs existed. Noteworthy is a case of a patient which has been reported in our article (Gefen & Gershon, 2018), where the patient developed a heel DTI during the study. Their SEM Scanner readings in that case were abnormal 2 days before	Thank you for your comment. Please see NICE's response to comment 60.

				VSA indicated tissue damage and 3 days before the appearance of a hypoechoic lesion in the ultrasound. - 8 - Given our current aetiological knowledge, the ability of the SEM Scanner to detect the injury at such an early stage, prior to it being visible on the skin or even detectable under the skin by means of ultrasound, is due to the fact that the SEM Scanner targets early, microscopic damage associated with inflammation, whereas both ultrasound and VSAs document existing, macroscopic structural damage to tissues (Figure). It is not surprising therefore that with respect to subdermal tissue damage or DTIs, ultrasound and SEM Scanner results in Gefen & Gershon (2018) were similar, and in an evolving DTI case monitored during our aforementioned study, the SEM Scanner detected a lesion earlier than the ultrasound. This published study was included within the EAC review but the results appear to be disregarded by the NICE EAC for some reason, but should be considered along with the entire contemporary body of literature reviewed here	
66.	6	Company consultant	n/a	Published literature by [redacted] and by others clearly shows that the above theoretical basis is well supported by clinical data, including laboratory bioengineering work as well as large clinical trials.	Thank you for your comment.
67.	1	Healthcare professional	3.3	*In 3 of the observational studies SEM Scanner 200 detects subepidermal moisture changes earlier than visual skin assessment* I think that this is a misinterpretation of the intention of these studies. The aim was not to determine what difference this makes to clinical practice in these studies, rather it was to see what the SEM scanner actually does in the clinical setting, in terms of if there is a sustained abnormal delta, then what happens to the patient in terms of pressure ulcer development, ie. Do they go on to develop a visual pressure ulcer? As with the earlier studies of Norton, in validating risk assessment, the design of the studies were focused on what information the risk assessment would identify, but was not focused on the impact of risk assessment, given that risk assessment was not routinely used in practice. It was only after clarifying the information that was relevant to practice that risk assessment was then formally adopted and the expectation arose that once risk assessed, the patient should receive appropriate intervention strategies. So, too, in the early studies on SEM, the intention was to understand what information could be gained from the use of the SEM	Thank you for your comment. The External Assessment Centre agree that the diagnostic studies were to improve understanding at an earlier stage in the evidence generation than RCTs and do not assess the effect on clinical practice. The External Assessment Centre noted that this does not impact the conclusions drawn in their assessment. The committee decided not to change the guidance in response to this comment.

				scanner, given that this was not known from a clinical perspective. Once this had been established, then studies have moved forward in terms of RCTs to determine what difference the SEM scanner makes when compared with use of VSA alone. This type of work mimics the work on risk assessment, whereupon no changes to patient care is made based on the scores from the risk assessment, rather the patient is assessed to see if they did develop a pressure ulcer or not. Given that these SEM studies are among the first studies of SEM, it is reasonable that in these first studies, an exploration of what SEM is picking up is essential to understand, before one would actually adopt the device into practice and make changes to clinical care based on the SEM scores.	
68.	1	Healthcare professional	3.3	*Diagnostic accuracy is reported in 3 of the observational studies but they use an inappropriate reference standard* I would agree and this is challenge that we have faced throughout all the work on SEM, because it is assumed if the patient did not go on to develop a visual PU that a positive SEM was then a false positive. However, this does not allow for the impact of prevention strategies, and this is the exact same problem faced during the validation of risk assessment tools When validating risk assessment tools, a major issue arises which impacts negatively on the ability to validate the assessment tool. In contemporary practice, clinical care changes (or should change) as a result of the risk score achieved following the assessment of the individual. It is unethical to deny an individual care, for example, just to determine if when the individual is deemed to be at risk, do they actually develop a PU. Given these challenges, and as recommended by Defloor (2004), preventative strategies employed need to be included as a core element of the instrument validation. Thus, it is argued that the true "test" of the instrument should not be that the individual developed a PU, rather it is that the individual did not develop a PU, because the preventative interventions, driven by the risk assessment, were appropriate and thus the individual was protected from harm. (Ref: Defloor T, Grypdonck MF. Validation of pressure ulcer risk assessment scales: a critique. J Adv Nurs. 2004;48(6):613-621. doi:10.1111/j.1365-2648.2004.03250.x)	Thank you for your comment. Please see NICE's response to comment 67.

				However, given that the SEM scanner is picking up early signs of pressure ulcer development, then it is reasonable that it be compared to the gold standard – visual assessment, where using visual assessment stage 1 is theoretically meant to be evidence of early pressure ulcer development.	
69.	3	Company	3.4	*The studies provided no additional information about the effect of these findings on clinical management or on the clinical benefits of earlier detection*. BBI find it hard to understand the inclusion of this statement – it has been clarified in the Fact Check submissions that the intention of these studies was specifically to support the mode/principles of operation of the device during the development phase NOT to determine the ongoing impact. This data is provided separately. BBI believe this is an inaccurate statement and requires restating especially in light of the new additional data submitted during the Consultation process.	Thank you for your comment. Please see NICE's response to comment 67.
70.	3	Company	4.1	*There is uncertainty about the diagnostic accuracy of SEM Scanner 200* "Predictive accuracy of the SEM Scanner An assessment of the cost-effectiveness of the scanner starts with a comparison of the predictive accuracy of the SEM reading plus visual assessment (SEM+VA) compared with visual assessment (VA) alone. Four studies included as part of the manufacturer's submission address the timeliness and the sensitivity and specificity of the SEM reading compared with VA alone. The EAC considers this evidence to be irrelevant to the decision problem (EAC report 5.3, page 51). We disagree. Sensitivity reflects the proportion of at-risk patients who are correctly identified. The greater the sensitivity the more patients may be prevented from developing a stage II+ ulcer. Similarly, if a test incorrectly identifies patients as being at high risk, this is likely to result in unnecessary costs associated with enhanced prevention protocols. An analysis of the cost-effectiveness of the scanner compared with visual assessment depends critically on having information about the predictive characteristics of both. In the studies which report the sensitivity and specificity of the SEM Scanner the gold standard is visual assessment. The EAC considers this to be an inappropriate standard because at best the SEM Scanner can only give results which are as good as VA. They cannot be better. We agree that VA is not an ideal standard but bearing in mind the nature of the problem it is difficult to see what an alternative could be. Identification of a	Thank you for your comment. Please see NICE's response to comment 67.

				stage I ulcer is based on visual and tactile signs ("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." EPUAP classification system). There are no other means currently available in routine NHS practice (or anywhere else in the world for that matter) to make the assessment except visual and tactile assessment. Even if we accept the premise that the sensitivity and specificity of SEM+VA can only be as good as VA alone, the evidence in the literature consistently confirms that the scanner is able to identify tissue damage 3-5 days before any damage is visible. Clinicians consulted by NICE point to the fact that earlier detection offers an opportunity for earlier intervention and, assuming early intervention is preferred to later intervention, there are important benefits to patients. However, we do not agree that estimates of the characteristics of the SEM readings are based on an inappropriate gold standard. In their base case economic analysis EAC cite the sensitivity and specificity of the scanner as 87.5% and 33% respectively, taken from an unpublished paper (Okonkwo, 2017). Full details of the study on which these parameters are based is available in a recent publication which was not available at the time of the EAC assessment (Okonkwo 2020). In this study a SEM delta ≥0.6 is taken as an indication of underlying pressure damage and this is compared with visual observation of the skin by a specialist tissue viability nurse. There is evidence (e.g. Beekman 2007; Defloor 2006; Defloor 2004) that assessment by a specialist nurse is more accurate than assessment by a generalist without any special training in wound care, and for this reason we believe that VA by a specialist nurse is an appropriate gold standard. In this case the predictive accuracy of the SEM reading can exceed routine VA and the SEM Scanner offers the possibility that in routine practice it can detect more presumptive stage I ulcers than VA alone and can detect them earlier. The SEM Scanner Receiver Operating Characteristic Area Under The Curve statistic of 0.6713 (95% CI 0.5969, 0.7457); p<0.0001 shows a combined sensitivity and specificity of SEM as one demonstrating clinical utility exceeding that of VA alone (Okonkwo 2020)."	
71.	1	Healthcare professional	4.1	*SEM Scanner 200 can reduce pressure ulcer incidence but there are considerable uncertainties*	Thank you for your comment.

				Our experience is that it may not reduce pressure ulcer incidence rather you will see a difference in the mean SEM deltas from start to completion of the trial, in favour of the SEM group. If we believe that SEM is doing what it says on the tin, which we do, then a reduction in mean SEM deltas is fundamental. In other words, when you detect an abnormal delta, and act on it, what happens? Evidence from our clinical study (yet to be published) showed the following: data was undertaken to explore the relative risk (RR) of SEM PU between the study groups. The RR of SEM PU is [redacted] indicating a [redacted]% reduction in the risk of SEM PU in the experimental group, with the true population parameter lying from [redacted]% to [redacted]%. This finding is statistically significant [redacted]Analysis of the data was undertaken to determine the mean difference in SEM scores from baseline to end of study. [redacted]Further analysis was undertaken to determine the difference in mean SEM scores at study completion between the control and experimental group. [redacted] *The evidence does not address how SEM Scanner 200 performs across different populations* In our research we are looking at ICU patients which would address the co-morbidity question.	For comment regarding new unpublished data please see NICE's response to comment 6.
72.	3	Company	4.1	*SEM Scanner 200 can reduce pressure ulcer incidence but there are considerable uncertainties*	Thank you for your comment.

				BBI refer to the report sent separately to NICE reviewing a series of clinical research projects undertaken by the team at RCSI School of Nursing and Midwifery/Skin Wounds and Trauma (SWaT) Research centre. Since 2015 RCSI have led on 10 research projects- the report focuses on 8 studies (as 2 are in infancy). These projects refer to the following care settings: 4 Acute Care Studies 1 Community Care Study 2 Residential Care Studies This report contains new data for NICE and the EAC to consider as part of a review of the Guidance as the data helps to answer the uncertainties and is submitted as Academic In Confidence.	Please see NICE's response to comment 6.
73.	3	Company	4.1	SEM Scanner 200 can reduce pressure ulcer incidence but there are considerable uncertainties "In a Statement of Intent issued in 2019 (Widening the evidence base: use of broader data and applied analytics in NICE's work) the use of broader sources of data and analytic methods was confirmed, separately in January 2020 NICE stated ""We recognise the value of traditional 'hierarchies of evidence' but take a comprehensive approach to assessing the best evidence that is available to answer the questions we face"" (Our Principles NICE). Evidence in the form of Observational; Experimental; Qualitative and Real World are all identified as being acceptable. It is BBIs assertion that the EAC reports and the Consultation Document subsequently issued do not appear to be living up to these principles and therefore the inclusion of BBIs wider evidence base should be reconsidered. Since the original BBI submissions to NICE a further 18 peer review publications that are relevant to the Consultation have been published: • 5 relate to the aetiology of pressure ulceration relevant to the SEM Scanner mode of operation and therefore highly relevant to the scope • 10 focus on the concept of sub-epidermal moisture or the SEM Scanner technology and therefore highly relevant to the scope- these include an independent Systematic review • 2 present the health economics of the SEM Scanner technology applied in prevention care pathways • 1 publication describes the challenges of the standard of care	Thank you for your comment. Please see NICE's response to comment 6.

				Additionally a further 6 manuscripts are submitted - the majority of these manuscripts detail the pragmatic real world studies conducted at multiple sites. The combination of these publications bring new data that must be analysed as part of a review of the original Guidance decision making process. A re-review of the total evidence is required to ensure that the principles stated by NICE are reflected in this Consultation – there are now: o Minimum of 36 peer review publications on the concept of sub-epidermal moisture or the SEM Technology o Minimum of 34 Scientific abstracts accepted on the concept of sub-epidermal moisture or the SEM Technology o 7 healthcare practitioners have reported on the implementation of the SEM Scanner in pragmatic real world studies at Scientific Conferences o 3 Health Economic peer review publications which utilised both Markov and Probabilistic Modelling Therefore BBI challenge whether all the "relevant evidence has been considered" nor that the summaries are "reasonable interpretations of the evidence" (page 1 Consultation Document.) BBI share the most recent publications listed in order of those we believe most acutely address NICE and EAC comments in the table submitted separately"	
74.	4	Healthcare professional	1.1	We have just completed a piece of work, that has not yet been written up due to current COVID-19 situation. In this the staff used SEM scanner readings to guide decision making and we then recorded if they changed decisions based on score and what that decision was. e.g. repositioning/moving more often, changing surface, introducing a heel off loading device or barrier product to protect skin. We saw a 100% decrease in PU incidence during the 6 week trial period in a ward that had had multiple previous interventions to reduce PU previously with little success. We also saw a decrease in therapy surface use which we had not expected and an increase in repositioning or heel off loading devices because they could target their interventions to specific part of the body; compared to a risk assessment tool which give a general risk for the whole patient.	Thank you for your comment.
75.	4	Healthcare professional	1.1	We recorded clinical decisions and our outcomes of 0 (Zero) HAPU during 6 week evaluation which is 100% relative reduction in HAPU during the trial period indicate improved patient outcomes.	Thank you for your comment.

76.	4	Healthcare professional	3.4	*In 3 of the observational studies SEM Scanner 200 detects subepidermal moisture changes earlier than visual skin assessment* The work we did showed that in two wards, one showed 75% of the time and the other 79% of the time, that the increased delta reading led to a change in clinical decision making and care for the patient.	Thank you for your comment.
77.	4	Healthcare professional	4	I believe there are a number of pieces of unpublished work which could add to the review. It depends what is meant by 'research' whether this is on a large scale or small local studies where results could be combined as real world data.	Thank you for your comment.
78.	4	Healthcare professional	4	"I think that the challenge is not about the efficacy of this scanner in reducing PU incidence but about whether this is actually something that can be measured in practice. Ignoring the scanner for a moment, if I use clinical judgment or a risk assessment tool and I add interventions into a care plan and a patient does not develop a PU how can you prove that my intervention affected the outcome for that individual? Conversely if I don't intervene and there is no change in outcome for the patient how do we know whether the action or inaction had any effect on the outcome? Can we ever prove that in this area of healthcare?"	Thank you for your comment.
79.	2	Professional organisation	4.13	*Uncertainties about the clinical benefit of SEM Scanner 200 results in uncertain cost-effectiveness* Agree - more work is needed	Thank you for your comment.
80.	3	Company	3.5	*Incidence rate of 1.637%* Re 1.637% incidence rate. BBI have undertaken a literature search to validate the Acute Care 1.637% average incidence rate used in the BBI HE submission. o PubMed, Google and BBI's databases were searched for literature on the incidence and prevalence of PUs = 20 results. Search criteria = pressure ulcers, prevalence and incidence; conducted March 10 2020 There are varied methodologies utilised in the published literature, there is also mixed PU Category reporting – some reports focus solely on Category 2-4 whilst others include Category 1. Finally rates vary considerably between care settings – the combination of these factors makes it challenging to draw clear conclusions.	Thank you for your comment. In response to this comment, the External Assessment Centre commented that the incidence used in their approach to modelling the cost of SEM scanner was higher than the incidence reported by the company to reflect the inclusion of early stage PUs. The committee decided not to change the guidance in response to this comment.

				Incidence • Range 0.9% (Fletcher J. 2018) drawn from NHS Safety Thermometer (all care settings) to 11.3% (Ferris A. et al. 2019), systematic review (palliative care patients) • NHS Safety Thermometer data (accessed July 8, 2020) New Pressure Ulcer data point range 0.8% March 2019 to 1.1% March 2020- these reported data are recognised as having many challenges in terms of accuracy o Important to note – Incidence reduction has plateaued over time- with higher cost PU Category 3-4 PU constant over time o Due to the sample collection method of the NHS Safety Thermometer, it is expected that the actual total number of PUs will be higher than that data shown above, particularly due to the COVID pandemic. o Note BBI has already conducted a detailed analysis of Safety Thermometer data 2018-2019 – BBI will be pleased to share the data with NICE – e.g. demonstrating incidence and absolute count by care setting; geographical heat maps Prevalence o Range 4.5% (Fletcher J. et. Al 2018) to 32.1% (NHS CG 179 2014) o NHS Safety Thermometer data (accessed July 8 2020) All Pressure Ulcer data point at 4.6% March 2019 to 4.9% March 2020- as above due to the sample collection method of the NHS Safety Thermometer, it is expected that the actual total number of PUs will be higher than that data shown above o Note BBI is working with one large UK urban conurbation (population 4 million, of which ~900,000 discharges) – a analysis of their data via NHS Safety Thermometer shows an absolute count of 5233 (Category 2-4 PU March 2018-March 2019) for acute care only. o Academic In confidence BBI understand that from the recent NHS Audit .....this statement is within the file submitted to NICE o Conclusion: the average rate used by BBI is reflective of the incidence rate in the mix of care settings the analysis was reporting on – BBI propose a review of the EAC analysis of this element is required	
81.	3	Company	3.5	*A 68% reduction* The table included in the files submitted separately to NICE clearly demonstrates the repeatability of the reduction of incidence of pressure ulcers across a high number of sites with varying clinical challenges. The	Thank you for your comment. In response to this comment, the External Assessment Centre commented that it was their

				EAC report commented that the 68.9% rate reduction used in the BBI HE model was an over estimation (Page 65) - additionally at the Committee Meeting it was commented that rate reductions of this magnitude were rarely seen. The purpose of this table is to demonstrate that the implementation of the SEM Scanner into an otherwise unchanged care pathway consistently achieves rate reductions over and above the 68.9% figure used. Of the 18 sites only 3 sites were substantially below the 68.9% data point and all bar 1 site are above the 27% rate reduction identified by the EAC report. The healthcare practitioners involved in the pragmatic real world evidence projects in the table will articulate their experiences in having already integrated additional preventive interventions, education programmes and awareness campaigns. However on addition of the SEM Scanner into their care pathways consistent and repeatable incidence rate reductions are demonstrated.	assessment that the pressure ulcer reduction programme data used in the model inflated the effect of SEM Scanner with the impact of increased attention to pressure ulcers. The committee decided not to change the guidance in response to this comment.
82.	3	Company	3.5	*A 68% reduction* BBI have also undertaken a review of a mix of peer review publications based on a number PU prevention interventions included in the International Clinical Practice Guidelines 2019. These studies feature new technologies or approaches, including cohorts from a mix of care settings with sample sizes ranging from 165 - 1312. The reduction rates range from ~45% to 100%. The objective is to emphasise that a comment made during the February Committee meeting that a 5% reduction rate is the rate of reduction most seen in PU prevention efforts is 1.) not reflective of these data, and 2.) is an overly conservative estimate. BBI poses the question as to whether there are differences between calculation methodologies? BBI proposes that the challenges are to a.) be familiar with PU prevention data as published, and b.) change the mindset and view the reduction rates in terms of a paradigm shift where new technologies are embraced in comparison to existing potentially outdated care pathways. Additionally BBI share this data to confirm that the 68.9% rate used by BBI in the economic modelling is indeed a reasonable and valid rate to use for the economic modelling. (Note the list of publications reviewed in this analysis can be supplied).	Thank you for your comment. Please see NICE's response to comment 81
83.	3	Company	3.6	*The EAC also added a 3.5% depreciation rate for the device that had not been included in the company submission.*	Thank you for your comment.

				The EAC suggested a number of changes to the assumptions employed in the manufacturer's submission. For example, the hourly cost of a Band 5 nurse is increased from £18 to £37 and the EAC rejects the evidence that the scanner could lead to a 68.9% reduction in stage II ulcer. The discussion document also notes that the EAC added a 3.5% depreciation rate which had been omitted. We are confused about this point because by writing-off the full capital value of the device over three years the manufacturer's model already assumed depreciation at 33% per year. However, this is a minor point.	In response to this comment, the External Assessment Centre explained that they amortised the cost of SEM scanner across 3 years at a rate of 3.5%. The committee decided not to change the guidance in response to this comment.
84.	3	Company	3.8	*The EAC modelled the cost of SEM Scanner 200 using preferred assumptions, the technology was cost incurring by £45 per person* "• We have not been able to reproduce the results of the economic model reported by the EAC. Adopting the same assumptions and the same parameter values we find the model predicts a net cost of the SEM Scanner of +£14 per patient at risk, rather than +£45. • In normal clinical practice we believe introduction of the SEM Scanner is most likely to be broadly cost neutral. The economic model assumes patient repositioning requires two Band 5 nurses four or six times daily. In most situations our implementation experience has borne out that at least one nurse would be replaced by a clinical assistant, and even a small reduction in the cost of repositioning results in cost neutrality. • The EAC does not present an assessment of the cost-effectiveness of the SEM Scanner. The EAC report presents only a cost analysis, although the benefits are implicit in their model. The EAC model predicts an additional 148 patients (72%) will be classified as high risk using the scanner and a total of 20 stage II+ ulcers are prevented (11.5%). The costs of ulcer treatment are reduced, and the overall incremental cost per ulcer prevented is £3,437. Where cost neutrality is a reasonable expectation the SEM Scanner would be a dominant option. • Reducing the incidence of iatrogenic tissue damage is a priority for the NHS and system benefits include avoiding litigation, reducing excess length of stay and avoiding the need for some surgical procedures. Benefits to patients include alleviation of pain and discomfort and a reduction in the risk of infection or other serious complications. • The NICE scope specifies a comparison of the SEM Scanner as an adjunct to visual assessment. The consultation document recommends that research should compare the risk of pressure ulcer formation using	Thank you for your comment. In response to this comment, the External Assessment Centre completed additional sensitivity analyses and reported that reducing the cost of repositioning has a considerable impact on the cost of SEM Scanner and usual care. The committee changed section 3.9 of the guidance in response to this comment.

				the SEM Scanner without visual assessment compared to visual assessment, and the EAC show a case in which this comparison would lead to significant cost savings. Unfortunately, we do not believe this option is feasible. Taking a SEM Scanner reading necessarily involves the nurse observing the skin on the heels and sacrum and it would not be possible to separate the act of scanning from a visual assessment of the skin. • The consultation document also recommends research to encompass the effect of the SEM Scanner on incidence of pressure ulcers in different care settings, in patients with different skin tones, and in patients with a range of comorbidities. We believe that to design a study (or studies) to address all these topics as well as collecting patient-related outcome measures would be prohibitively expensive and disproportionate. The costs of the research would most likely outweigh the value of any additional information which could be generated. We believe the scientific rationale for measuring sub-epidermal moisture as an indicator of pressure damage and as a part of a programme to reduce harm to patients is sound, but we recognise that the clinical evidence base is still developing. We believe that a conditional approval with review after two years would facilitate new studies in the NHS specifically designed to evaluate the magnitude of the benefits which can be achieved."	
85.	4	Healthcare professional	2	The scanner can now be leased or rented as well as purchased	Thank you for your comment.
86.	5	Healthcare professional		*Raizman et al, 2018* I want to let you know that the company only provided a free scanner and little to know frontline education during the evaluation period.	Thank you for your comment.
87.	6	Company consultant	n/a	The SEM Scanner technology has a proven cost-effectiveness, demonstrated in comprehensive published work which has been summarized above.	Thank you for your comment.
88.	6	Company consultant	n/a	In terms of nursing time, VSAs cost approximately £6 per patient, per skin check session (Gefen et al., 2020). Accordingly, conducting routine VSAs for each and every hospitalized patient is financially implausible, and hence, regular VSAs are only conducted for patients who are determined to be at-risk - 6 - for PUs based on the outcome of a risk assessment tool upon admission. If VSAs would have been hypothetically implemented for all patients	Thank you for your comment. Please see NICE's response to comment 9.

				routinely during their hospitalization period, the result will be spending of many billions of pounds sterling on patients who will never be at a meaningful risk, as only a small fraction are at a true risk for PUs. Indeed, current risk assessments typically classify up to 2 of 5 of all hospitalized patients as being at a high risk for developing PUs, but the sensitivity and specificity of risk assessments is often criticized, given the unacceptable extent and rate of deaths from PUs and the total expenditure on PUs (Oliveira et al., 2017; Gefen et al., 2020).	
89.	6	Company consultant	n/a	In collaboration with the manufacturer and a panel of external expert health economists, [redacted] has published a comprehensive cost-benefit analysis focusing on the financial savings associated with implementation of the SEM Scanner technology in hospital settings (Gefen et al., 2020). The latter paper is, in fact, the first ever to report the predicted savings that a diagnostic PUP technology may achieve. Specifically, in the above study, implementation of the SEM Scanner technology as an adjunct to the current VSA standard of care practice has been tested using probabilistic cost-benefit modelling. We developed a decision-tree model type and Monte Carlo simulations representing the various pathways of care that 10,000 patients, admitted to National Health Services (NHS) hospitals in the United Kingdom, may experience. We tested two alternate acute hospital scenarios, of lower (1.6%, Categories 1-4) and higher (6.3%, Categories 1-4) PU incidence rates. Under a conservative range of assumptions and input parameters, we found that implementation of the SEM Scanner technology as an adjunct to the current standard of care is highly likely to lead to significant financial benefits and cost savings. For example, our modelling demonstrated that the expected saving per patient, by routine implementation of the SEM Scanner in care facilities with the above low and high incidence rates, is £15.23 and £80.68 per admission, respectively. For an average UK Trust with 40,802 admissions (excluding day cases) per annum, the estimated total financial savings from implementing the SEM Scanner, using the assumptions and inputs set out here, would range between £0.6-million to £3.3-million per annum. These cost reductions, even under our conservative modelling assumptions, reflect the above explained (i) detection and treatment of anatomy-specific, non-visible tissue damage which is not possible without the SEM Scanner, (ii) higher rates of detection of category-1 PUs than possible without the technological aid of the SEM Scanner, and (iii) avoidance of some unnecessary treatments of	Thank you for your comment. Please see NICE's response to comment 9.

				patients without PUs, due to higher confidence by clinicians to rule out PUs with the SEM Scanner readings than without. The fundamental basis of the above cost-benefit analyses is that patients are in a given PU-state (no damage, sub-clinical damage, Stage 1 or later damage) and accordingly we modelled changes in the probability of correct detection of that state with and without the SEM Scanner. Savings from the aforementioned factors (i) and (ii) arise from earlier and more sensitive diagnostic accuracy of skin and tissue deterioration in the earliest phases of damage, as indicated by the SEM Scanner as an adjunct to VSA, however, we assumed that the efficacy of treatments remains the same as without the SEM Scanner in place. In other words, these considerable savings are from properly including patients with - 9 - developing but invisible PUs into the care pathway and properly excluding patients without developing PUs from the care pathway who would otherwise have been deemed at risk (which is saving point no. iii above). Accordingly, the work described in Gefen et al. (2020) clearly demonstrates that wide implementation of the SEM Scanner technology in the UK, as well as in other countries, is well justified from a financial perspective and will lead to cost savings. While more research is in need to further establish the cost-benefits of the SEM Scanner, in particular in specific clinical settings e.g. geriatric or rehabilitation centers, no other diagnostic PUP technology has ever been investigated so rigorously as the SEM Scanner was (Gefen et al., 2020) for its financial justification. It is therefore unreasonable to ask at this stage for "*more research … to establish the clinical and cost benefits of the SEM Scanner*" as stated in the NICE EAC Consultation Document (p. 12, point 4.13) given that there is no other PUP diagnostic technology with cost-benefit evidence which is even near to that of the SEM Scanner, in both breadth and depth.	
90.	3	Company	2.4	*The cost of purchasing the SEM Scanner 200 is £5,835 per device.* Please note since original submission BBI have now launched the next generation of the device - Called Provizio SEM Scanner - please see the detail previously submitted as Company in Confidence	Thank you for your comment. The committee heard that the Provizio is available to NHS. The committee decided not to include Provizio SEM scanner in the guidance.
91.	6	Company consultant	n/a	In the second-half of 2019, Bruin Biometrics LLC introduced a 2nd-generation SEM Scanner model called Provizio™ SEM Scanner. This new	Thank you for your comment.

				version of the SEM Scanner is elegantly designed to include an improved user interface and better wireless connectivity. We have conducted a bioengineering study to evaluate the sensitivity of Provizio™ SEM Scanner in identifying fluid content changes in laboratory phantoms of a human heel and skull/face, relatively to their 1st-generation SEM measurement device (also known as the SEM 200 model). We performed SEM measurements on the aforementioned physical phantoms described in our published work (Peko & Gefen, *International Wound Journal* 2019). Following the experimental protocol detailed in the latter publication, we injected 1ml ('reference'), 2, 3 and 4ml of water to the 'soft tissue' substitutes in each phantom and location. Next, we calculated the corresponding SEM-delta, which quantifies the dimensionless difference in these experiments between the biocapacitance properties of the 'soft tissues' at the reference (1ml) site versus each of the 2, 3 and 4ml sites simulating inflammatory oedema. Finally, we conducted Bland-Altman (B&A) statistical analyses to determine the levels of statistical agreement between the Provizio™ SEM Scanner and previous (200 model SEM Scanner) device readings, for each phantom type and location. Consistent with our published work concerning the 200 model of the SEM Scanner, the Provizio™ SEM Scanner device was shown to be sensitive enough to detect water content variations that were as small as 1ml. Furthermore, the above B&A analyses established that any differences in readings between the Provizio™ and 200 model of the SEM Scanner were clinically negligible. In addition, these differences did not tend to become larger as the mean of the two device readings increased, which indicates stability and precision of both devices. Hence, the Provizio™ SEM Scanner was shown to perform identically to the 200 model SEM Scanner in laboratory experiments evaluating its sensitivity to small water content variations within physical phantoms of human body tissues. Furthermore, the Provizio™ SEM Scanner is also substantially more compact and user-friendly, has a smaller sensor which facilitates easier access to small and/or curved body sites, and it features improved connectivity with other medical data systems in hospital settings. We recently published our findings described above with regards to the performances of the Provizio™ model, in a follow-up publications in the *International Wound Journal* (Peko & Gefen, 2020).	Please see NICE's response to comment 90.
92.	2	Professional organisation	4.10	*SEM Scanner 200 needs cleaning between patients*	Thank you for your comment.

				Cleaning may be even more problematic in a post-COVID age. We note that the scanner has a 'medium risk of cross-contamination'. Given that those most at risk of pressure damage are likely to be at high risk of COVID, this is likely to be an issue.	The committee were informed by the company that the Provizio has a disposable cap that reduces bioburden levels and has a less time-consuming cleaning regime. The committee decided not to change the guidance in response to this comment.
93.	6	Company consultant		Based on recent Italian data reported in the literature, a rate of 12% of all positive coronavirus disease 2019 (COVID-19) cases required admission in an intensive care unit (ICU) and the ICU length of stay with this diagnosis is relatively long. At the time of writing this LoS, there are already nearly 10-million positive COVID-19 cases (www.worldometers.info accessed on June 25th, 2020) which is indicative of approximately 1.2-million ICU patients who have been added or will be added to healthcare systems worldwide since the outbreak of the pandemic in the western hemisphere, in February 2020. In the context of this current widespread of the first wave of COVID-19, where many of the newly admitted ICU patients are anesthetized for mechanical ventilation and are therefore, by definition, at-risk for PUs, it is important and relevant to discuss how COVID-19 interacts with the known aetiological factors described above. First, COVID-19 activates the immune system promptly and sharply, which positions COVID-19 patients with a cytokine release syndrome (also known as 'cytokine storm') at a high risk for developing PU-related inflammatory tissue damage. This is because their inflammatory response is unleashed and their cytokine sensitivity thresholds are therefore disrupted. In addition, COVID-19 patients are also at a high risk for PU-related ischaemic tissue damage as their oxygen saturation levels are typically low and their cardiac output may be abnormal, e.g. due to myocarditis, acute myocardial infarction or heart failure, all of which are reported cardiovascular complications of COVID-19. Another potential contributor to tissue ischaemia in COVID-19 is the hypercoagulability leading to a tendency for thrombosis in these patients. These timely examples illustrate how COVID-19 interacts directly with two of the three primary etiological factors in the vicious cycle of PUs, inflammation and ischaemia and further suggest that COVID-19 may be a confounder of PUs. Indeed, anecdotal clinical data collected with clinical collaborators of ********** over the last three months suggest that the	Thank you for your comment. The committee heard from expert advisers that additional devices, like SEM Scanner are unlikely to be used on wards with patients that are COVID-19 positive to reduce the risk of transmission. The committee decided not to change the guidance in response to this comment.

				prevalence rate of PUs in ICUs among COVID-19 patients could be 10-times or more the respective PU rates at the same ICUs prior to the COVID-19 outbreak. Considering that already before the COVID-19 outbreak, PUs were a well-recognized independent prognosticator of death among ICU patients, the interaction of the cytokine storm in COVID-19 with the inflammatory damage factor in the PU spiral underpins the importance of PUP for this particular patient population. Based on its underlying physical and physiological principles described above, the SEM Scanner as an adjunct to clinical judgment can be a very effective tool for this task	
94.	3	Company		Page 1 of the Consultation Documents also asks, “Are the recommendations sound and a suitable basis for guidance to the NHS?” BBI response is No; a review is required of the draft recommendations which, in BBIs assessment, do not take into account the full evidence base especially as this has expanded during the past few months. It must be noted that the need for enhanced PU prevention is greater now more than ever due to COVID 19 – existing prevention pathways are challenged based on subjective and outdated tools - please see the individual comments in the Consultation Document and the Addendum pack for detailed responses.	Thank you for your comment. Please see NICE’s response to comment 93.
95.	2	Professional organisation	4.11	*SEM Scanner 200 has a battery life of 3 hours and a lifespan of over 3 years* A 3 hour battery life seems short. While the product ought to be stored on its charger, in busy clinical practice this may not happen. In community practice, this is highly unlikely as clinicians are likely to be travelling for more than 3 hours.	Thank you for your comment. The committee heard from expert advisers that the battery life has not been an issue when used in a hospice setting but this may differ in the community, The committee decided not to make any changes to the guidance in response to this comment.
96.	2	Professional organisation	4.12	*The company provides free training* While the training may be provided free, has time for clinicians to receive training been costed into the economic modelling?	Thank you for your comment. In response to this comment, the External Assessment Centre advised the committee that training costs were included in the economic model.

					The committee made no changes to the guidance in response to this comment.
97.	3	Company	2.3	*admission, during the patient's stay and on discharge* Note when in the Community the device may be used on a ongoing basis	Thank you for your comment.
98.	3	Company	4.6	At the February Committee Meeting a number of statements were made that need to be clarified. Statement 1 Expert Advisor Stated that as the new CPG included recommendations on the use of prophylactic dressings there is a risk that to undertake the scanning by the SEM Scanner the dressing will need to be removed – this may cause damage to vulnerable skin and therefore is an added risk. BBI has spoken to a number of other experts in this area including SEM Scanner users– their guidance is as follows: 1. Scanning would be undertaken with other care procedures such as structured hygiene 2. During which time the skin under the dressing would be assessed as per care Guidelines 3. Therefore there is no additional dressing removal required to facilitate scanning 4. Advanced dressings have specialised adhesives which ensure the vulnerable skin is not damaged on removal 5. As the scanning is undertaken at the same time there is a very limited impact on nurse time and patient disturbance Additionally 2 experts commented on the time to scan – both stated that the scanning was conducted as part of personal care so it is not seen as time consuming. Given the above feedback BBI believe that this misleading statement should revisited to ensure that Committee members are aware of the reality in clinical practice to ensure that this misunderstanding does not undermine the views regarding the SEM Scanner. Statement 2 Expert Advisor At the Committee Meeting one Expert Advisor was asked to comment on the fact that the SEM Scanner is only approved for Sacrum and Heel. Is this a limitation? The Expert Advisor commented that 25% PU are on the heel and 25% are on the Sacrum and therefore other body locations are not included – its limited as it cannot be used on other areas. BBI share	Thank you for your comment.

				additional data on this important point – literature search: o Medline, Google and BBI's databases were searched for literature on the distribution of PUs across the heel and sacrum = 8 results. Search criteria = Pressure Ulcers, Prevalence, Incidence, Heels Sacrum; conducted March 11 2020. There are varied methodologies utilised in the published literature, there is also mixed PU Category reporting – some reports focus solely on Category 2-4 whilst others include Category 1. Finally rates vary considerably between care settings – the combination of these factors makes it challenging to draw clear conclusions. • Heel range 12% to 61% (of all reported PUs)- average 34.6% • Sacrum range 17% to 57.9% (of all reported PUs)- average 35% • Rates ~40% on removal of the two dated sources (Vangilder 2009 & Vanderwee 2007) Conclusion: Heel and sacral PUs are the majority of reported PUs. Rates quoted in the February Committee Meeting reflected 2007/2009 data of around 25% per anatomical location. Removing the two oldest sources then the rates are closer to 40% per anatomical location. It is BBIs assertion that this higher rate is now reflective of the real challenges in PU prevention and therefore the SEM Scanner current Indications for Use will have meaningful impact on PU prevention by targeting the two sites which represent the highest percentages of PU occurrence. Note BBI also have a Post Market Study Plan (Figure included in document submitted to NICE). Expansion to additional body locations is one element of that plan once company bandwidth and funding allows. Note this plan includes a number of ongoing independent studies – these are the ones BBI are aware off and may not be a comprehensive list. Statement 3 It was also questioned that could other conditions such as Venous Stasis affect Biocapacitance? BBI refer the team to the CPG 2019 Etiology chapter pages 16-27 for an understanding of the aetiology of PU and the role of Biocapacitance – once this understanding is clear the Committee will understand that diseases processes such as Venous Stasis do not affect Delta readings. As with other comments BBI believe there is a need for a better understanding of the Aetiology and mode of operation of the SEM Scanner to enable an informed decision to be made on the potential impact the SEM Scanner can have on PU prevention. BBI have discussed	

				the questions raised with other experts in the field – the feedback is that there is a lack of understanding that could prejudice the opportunity for the SEM Scanner in this process.	
99.	3	Company	4.14	*This research should assess using the SEM Scanner 200 (without visual assessment) for assessing the risk of pressure ulcers compared with standard risk assessment using validated scales and skin assessment. Pressure ulcers occur in acute and community care so research should address the effect of adopting SEM Scanner 200 in each of these settings independently. Research should be sufficiently powered to include subgroups of people with dark skin and those with a range of comorbidities known to influence fluid levels in the subepidermis and underlying tissues.* "BBI acknowledges the Committee's draft research recommendations. In considering these recommendations BBI asked ourselves and our academic expert advisors a logical sequence of questions. We have replicated these questions below together with a summary of our analyses. Our analyses have tried to faithfully reflect the intent of NICE's draft recommendations. 1. Does the draft report reflect the current science of risk assessments, skin and tissue assessments and the SEM test such that the research questions are by informed by current science and conceptual clarity? 2. Has each research question already been answered elsewhere? 3. What is the relative clinical utility to PU prevention science of addressing each research recommendation? 4. What is the relative benefit/cost/risk beyond clinical utility to PU prevention science of addressing each research recommendation? 5. What accepted and recommended alternative scientific methods are available to answer the research questions in the near-term and at reasonable cost to the BBI? The first conclusion of these analyses is that uncertainties about the overall clinical benefits of using the SEM Scanner compared to standard risk assessment have generally already been addressed and widely published. Specifically, we know: 1. Risk assessment tools seek to assess the overall risk of the patient of developing a PU. Risk assessment tools are known to be inadequate and unreliable tools for PU prognosis and assessment. Their limitations are very clearly established in the literature.	Thank you for your comment. Please see NICE's response to comment 2.

				2. Risk assessment tools are general, not anatomy specific in nature, so do not seek to answer the question of "where is my patient at risk of developing a PU"? PUs by contrast are anatomy specific. A patient may therefore be risk assessed to be at risk of developing a PU, but the location of such is illusive to the healthcare practitioner. Generalised risk assessments result in generalised interventions until a PU is positively diagnosed by skin and tissue assessments at which time anatomy specific interventions are applied. 3. Specific recommendations about SEM versus risk assessment tools and skin and tissue assessments for dark skin tones patients and community/post-acute settings have also been broadly, but admittedly not fully, addressed in published articles. Dark skin toned patients, for example, have a four times higher mortality rate from pressure ulcers than light skin toned patients. The second conclusion is that the cost/benefit calculation falls definitively in the cost category with interesting but limited clinical benefits. The SEM Scanner provides earlier, anatomy specific assessments of damage before the skin is visibly or tactically assessable as damaged: this is already established. The cost/risk/benefit of earlier and anatomy specific interventions clearly fall into the benefit category. The third conclusion is that NICE's recommendations about the clinical veracity and utility of real-world evidence apply to these research needs. Real World Evidence using formal controls over sources of bias are suited for purpose, per existing guidance: in other words, an extension of what BBI is already doing via its PURPs. An RCT is, unquestionably the paradigm research method, but in this case is neither necessary, nor recommended in NICE's other guidance documents. It is also infeasible for the company to take on. At £4,500 per enrolled patient, the per patient cost of BBI's last clinical study, the minimum cost of a multi-arm study is £7.7 mm; cost prohibitive to conduct. With a 12-month period to first patient enrolled (after trial design, site selection and enrolment, IRB approvals, PI selection, training, site initiation visits etc.) and then 30 patients/month enrolment rate, the study period would extend to almost 60 months. Presuming a further 6 months of data analysis, statistical analysis and report writing in combination tallies 78 months (6.5 years). These data are based on rates and costs of our last clinical study in the UK and are reflective of incidence rates, enrolment rates (especially in community settings and of dark-skin toned patients), and effect sizes.	

				Such a trial would of course only possible after COVID-19 has passed or been significantly mitigated to the point where patient enrolment could start further adding to the already lengthy timeline. NHS patients meanwhile continue to suffer from preventable PUs as a direct consequence of a chronically deficient diagnostic standard reliant on subjective tests of subcutaneous damage. BBI have investigating with the support of a number of external experts how to develop a study of this nature and share the following comments/challenges: o NICE Statement of Intent: 2019 “Widening the evidence base: use of broader data and applied analytics in NICE’s work”. use of broader sources of data and analytic methods was confirmed. January 2020 Our Principles. ""We recognise the value of traditional ‘hierarchies of evidence’ but take a comprehensive approach to assessing the best evidence that is available to answer the questions we face"". Evidence in the form of Observational; Experimental; Qualitative and Real World are all identified as being acceptable – it is BBIs assertion that the EAC reports and the Consultation Document subsequently issued do not live up to these principles by requesting this large multi arm study with sufficient power to capture dark skin tone and multiple co-morbidity impacts. o RCT design: as pointed out during the February Committee Meeting by one of the expert advisors it is extremely challenging to accomplish in wound care studies and specifically in PU Prevention. This is also confirmed by a newly published Cochrane Review. (Walker R. et al. Cochrane Reviews, Journal Tissue Viability https://doi.org/10.1016/j.jtv.2020.05.004). BBI have researched the options (further detail is in Addendum Pack): i. Challenge to Define Study Groups: given the current prevention care pathway ii. Randomisation, Control groups and Ethical Concerns iii. Blinding - given the nature of the SEM Scanner – the mode of operation and the need to assess the skin during operation leads to the conclusion that the potential to limit bias is almost impossible iv. Sample Size and Sample Population: our research suggest minimum of 1712 subjects – given the nature of the potential subjects enrolling to this level will be highly challenging and lead to a length study period with the added challenge of informed consent- expectation of high screening to enrolment ratios	

				v. Time, Cost and Scope: At £4,500 per enrolled patient, the per patient cost of BBI's last clinical study, the minimum cost of a multi-arm study is £7.7 mm; a cost prohibitive to conduct. With a 12-month period to get to the first patient enrolled and then 30 patients/month enrolment rate, the study period would extend to almost 60 months. A further 6 months of data analysis, statistical analysis and report writing in combination tallies 78 months (6.5 years). These data are based on rates and costs of our last clinical study in the UK and are reflective of incidence rates, enrolment rates (especially in community settings and of dark-skin toned patients), and effect sizes."	
100.	4	Healthcare professional	4	"Agree, it is a diagnostic tool that gives a numerical value to indicate where there is deviation from normal level of sub epidermal moisture which is linked to the tissue inflammatory process. This enables clinicians to review and change care interventions as required. Similar to a BP monitoring identifying a rise in BP which triggers the clinician to confirm the readings on a regular basis and change care and interventions as required."	Thank you for your comment.
101.	4	Healthcare professional	4	*SEM Scanner 200 needs cleaning between patients* All multi-use medical devices require cleaning between patients, this is standard practice	Thank you for your comment.
102.	4	Healthcare professional	4	We did not encounter any issues with battery life during out 6 week evaluation period.	Thank you for your comment. Please see NICE's response to comment 95

"Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees."