External Assessment Centre report

Title: Parafricta Bootees and Undergarments to reduce skin breakdown in people with frail skin or at risk of pressure ulcers

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

Contents

1. Summary 4
1.3 Summary critique of clinical evidence submitted by the sponsor 6
1.4 Summary of economic evidence submitted by the sponsor 6
1.5 Summary critique of economic evidence submitted by the sponsor 7
1.6 External Assessment Centre commentary on the robustness of evidence submitted by the sponsor 8
1.7 Summary of any additional work carried out by the External Assessment Centre 8
2. Background 9
2.1 Overview and critique of sponsor's description of clinical context 9
2.2 Overview of sponsor's description of ongoing studies 11
2.3 Critique of sponsor's definition of the decision problem 11
3. Clinical evidence 14
3.1 Critique of the sponsor's search strategy 14
3.2 Critique of the sponsor's study selection 14
3.3 Included and excluded studies 14
3.4 Overview of methodologies of all included studies 16
3.5 Overview and critique of the sponsor's critical appraisal for each study 17
3.6 Results 22
3.7 Does each relevant study include the patient population(s), intervention(s), comparator(s) and outcomes as defined in the final scope? 27
3.8 Description of the adverse events reported by the sponsor 27
3.9 Description and critique of evidence synthesis and meta-analysis carried out by the sponsor 28
3.10 Additional work carried out by the External Assessment Centre in relation to clinical evidence 28
3.11 Conclusions on the clinical evidence 30
4. Economic evidence 30
4.1 Critique of the sponsor's search strategy 30
4.2 Critique of the sponsors study selection 31
4.3 Included and excluded studies 31
4.4 Overview of methodologies of all included economic studies 34
4.5 Overview and critique of the sponsor's critical appraisal for each study 34
4.6 Does the sponsor's review of economic evidence draw conclusions from the data available? 35
4.7 De novo cost analysis 35
4.8 Results of de novo cost analysis 50
4.9 Subgroup analysis 54
4.10 Model validation 54
4.11 Interpretation of economic evidence 55
4.12 Additional work undertaken by the External Assessment Centre in relation to economic evidence 55
4.13 Conclusions on the economic evidence 61

5. Impact on the cost difference between the technology and comparator of additional clinical and economic analyses undertaken by the External Assessment Centre....62
6. Conclusions....63
7. Implications for research....63
8. References....65
9. Appendices....67

1. Summary

1.1 Scope of the sponsor's submission

The sponsor's submission conforms to the scope for the assessment report as published by NICE, except that the patient population in the NICE final scope is any adults and children. The sponsor has excluded very young children because Parafricta Bootees and Undergarments do not fit them. The sponsor also manufactures bedsheets and baby nests but these are not part of this evaluation. The intervention is Parafricta Bootees and Undergarments used with pressure reducing devices as in standard NHS clinical practice and the three comparators were pressure reducing devices used in standard NHS clinical practice alone or with sheepskin or with pressure-relieving bootees. The sponsor's submission only evaluated the first comparator and not sheepskin or pressure relieving bootees. The sponsor's report did not modify the outcome measures but some of the outcomes listed in the NICE final scope have clinical evidence and some do not (for comparator 1 only). There was information on incidence of developing pressure ulcers, incidence of grade 1 or 2 pressure ulcers progressing to grade 3 or 4 pressure ulcers, incidence of skin breakdown, severity of pressure ulcers, length of hospital stay and patient comfort. There was no useful information on time to healing, patient compliance, quality of life, morbidity and device-related adverse events.

1.2 Summary of clinical evidence submitted by the sponsor

There were seven studies submitted by the sponsor and three of these were included in the quantitative analysis. There was also an unpublished clinical audit found. Of the seven submitted studies, three were single case studies, two were small uncontrolled case series, one was a small partially controlled case series and one (Smith 2010) was a larger case series with documented historical controls. The three single case studies and the small uncontrolled case series with very little information are not discussed further here.

Hampton (2009) was a case series of 25 nursing home residents. A single Parafricta Bootee was used on the right heel in 10 patients, with the left heel used as comparator. Eighteen patients had Parafricta Undergarments and there was no comparison group. The duration of follow up was four weeks. The outcomes were measured in three ways 1. Bogginess and redness of skin as assessed by tissue viability nurse 2. Colour photographs and 3. High frequency ultrasound. The reason for three different ways for measuring outcomes was because of the difficulty of assessing skin oedema. Bogginess and redness was judged to be very subjectively assessed. Colour photographs did not reproduce the nature of the skin damage well as the colour reproduction depended on ambient light levels. The ultrasound graphs

were an attempt to measure thickening of the skin from oedema and were felt to be the most reliable outcome measure.

Smith 2010 recruited 165 patients in three months, compared with 204 historical controls recruited in the previous three months, having similar conditions and in the same hospital wards (two medical and one orthopaedic wards). All patients were at high risk of pressure ulcers (Waterlow score of ≥15), some had pressure ulcers on admission and some did not. All were unable to reposition independently. The intervention was the addition of Parafricta Bootee or/and Undergarment to standard pressure ulcer preventative measures. Outcomes were the incidence improvement and deterioration of pressure ulcers, length of stay (and cost savings). It presented results as pressure ulcer incidence, improvement and deterioration The results suggest that the Parafricta cohort had fewer patients who developed pressure ulcers in patients without pressure ulcers on admission, but no difference in the development of additional pressure ulcers in patients who already had a pressure ulcer. Also the results suggest that fewer pressure ulcers deteriorated in the Parafricta cohort. There were no statistically significant differences in length of stay between cohorts 1 and 2 but the lengths of stay were not given in the published Smith (2010) paper.

Stephen-Haynes (2011) was a case series of 25 nursing home residents evaluating Parafricta Bootees or/and Undergarment added to standard approach as outlined by NICE guidance 2005. There was no comparator. Outcomes were skin improvement, ease of use, garment retention and patient comfort. The results suggested that there was some skin improvement, the garments were on average easy to use, to keep on and reasonably comfortable.

For the clinical audit:

[redacted]

1.3 Summary critique of clinical evidence submitted by the sponsor

For Hampton (2009) the colour graphs and their captions are difficult to interpret. The axes report pixel number by intensity and do not appear to report skin thickness. It is unclear whether the graphs are depicting skin oedema and its resolution or not. Differences could be oedema, skin thickness or pixel number.

For Smith (2010) there were no numbers of deaths or demographic characteristics in either cohort, and no numerical results of length of stay by cohort were given. So it is impossible to tell how similar the cohorts were as there is no information on confounding factors. The only information we do have is the Waterlow score from the Sponsor's economic submission which suggests that the cohort not given Parafricta may have been more at risk of pressure ulcers than those given Parafricta. The difference in pressure ulcers could also be because the Parafricta cohort patients were less ill than those in the historical comparison cohort. Therefore, it cannot be inferred that any change in pressure ulcer incidence, improvement or deterioration was due to the use of Parafricta Bootees and/or Undergarments. Also, if patients couldn't reposition (an inclusion criterion for the study) then movement would be limited so it would be likely that any pressure ulcers occurring would have been caused by pressure rather than friction.

As Stephen-Haynes (2011) was an uncontrolled study it is impossible to tell whether any improvement in pressure ulceration or skin improvement was temporary or permanent or whether it was due to the Parafricta Undergarment or would have happened anyway.

Gleeson (2014) evaluating the use of Parafricta Bootees in an unknown number of patients on [redacted], but how it was conducted was unclear as there are no details in the manuscript.

1.4 Summary of economic evidence submitted by the sponsor

A literature search was carried out by the sponsor to identify published health economic studies related to the use of Parafricta Undergarments and/or Bootees in the management of pressure ulcers. The sponsor applied their inclusion and exclusion criteria and identified only one relevant study (Smith 2010) which is used to support their submission. This study compared the costs of 165 patients who used Parafricta Undergarment or Bootee in addition to standard pressure ulcer preventative measures with the costs of 204 historical controls who did not use Parafricta Undergarment and/or Bootee but received the same standard care. The use of Parafricta was found to save £630 per 'at risk patient'.

The sponsor's *de novo* cost model drew heavily on the data provided by Smith (2010). This simple cost model, submitted as an Excel spreadsheet, estimated expected costs of managing patients at risk of developing pressure ulcers in hospital and community settings, with and without the use of Parafricta in addition to current practice (use of pressure reducing devices). The differences in these expected costs were the benefit (cost-savings) to the NHS of using Parafricta garments. The hospital model showed that the costs without Parafricta were £5,306.76 per at risk patient and with Parafricta £4,549.65 per at risk patient, yielding a net saving of £757.11 per at risk patient. The respective figures in the community models were without Parafricta = £5,899.92 per prevalent case; with Parafricta = £2,444.93 per prevalent case; net cost saving of £3,454.99 per prevalent case.

The sponsor's cost model assumed that the use of Parafricta would: (a) reduce the incidence and prevalence of pressure ulceration; (b) shorten patients' length of stay (due to the further assumption that if a patient develops a pressure ulcer, they would require an extended hospital stay); (c) delay time to develop a new ulceration; and (d) stop deterioration of existing ulceration.

1.5 Summary critique of economic evidence submitted by the sponsor

Strengths of the economic evidence:

The chosen model structure reflects the Smith (2010) data, which was the only source available at present (confirmed by the EAC). It charted the incidence of pressure ulcers, whether existing on admission or developed during the hospital stay. Expected differences in length of stay for a patient using Parafricta versus not using Parafricta, in addition to standard clinical practice (pressure relieving mattresses plus usual nurse care and assessment), reflected the potential cost savings. The model inherently assumed that if a patient develops a pressure ulcer, they will require an extended hospital stay. The Smith (2010) data as well as the inputs received from one of the EAC clinical experts supports this assumption, to a degree. Dealey (2012) also concludes that delayed discharge is a contributor to additional costs.

The EAC judged the *de novo* cost model relevant to the decision problem as outlined in the NICE Final Scope. The sponsor was able to acquire and supply raw data from Smith (2010) which, when the EAC reanalysed it, showed a small, important but not statistically significant difference in length of stay between the group using Parafricta in addition and the group only receiving standard care.

Weaknesses of the economic evidence:

The economic modelling conducted by the sponsor and built on the Smith (2010) data, suffers from the deficiencies in the study design used to collect this data. The EAC discusses this in more detail in Appendix 3 and tried to adjust for known patient characteristics. The reanalysis was still not fully able to account for potential biases resulting from unequal study groups.

The submission stated that the time horizon was one year in both hospital and community settings. However because of the use of the Smith (2010) data, the hospital model time horizon is limited to the inpatient stay of an 'at risk patient'. This was clarified by the sponsor. Costs were estimated on a per patient basis. This is not explicitly represented as potential cost savings over a longer fixed period of time.

The EAC challenge the validity of using median length of stay in a modelling exercise of this kind, even if length of stay data may be skewed. In some instances, the number of patients in each pathway is very low. The resulting length of stay is likely to be highly uncertain. Subsequently, the uncertainty in the length of stay data has not been fully accounted for as only via arbitrarily (and not very wide) confidence intervals have been placed around the weighted length of stay. Each component is highly uncertain. The EAC ran extra analyses attempting to adjust the length of stay data for patient characteristics and accounting better for uncertainties.

1.6 External Assessment Centre commentary on the robustness of evidence submitted by the sponsor

The evidence is not robust, given the problems identified with relying on Smith (2010) data. The effect size appears to be smaller than the sponsors' use of data suggests. The EAC has revised the model to allow for more robust input parameters/methods using the same dataset and structure of the model. This revised analysis confirms that the use of Parafricta Bootees and Undergarments is cost-saving; however the scale of savings is smaller than those estimated in the sponsor's submission.

1.7 Summary of any additional work carried out by the External Assessment Centre

For clinical effectiveness – additional work involved rerunning searches and sifting for additional relevant studies, re-analysing the Smith (2010) incidence results as relative risks, and analysis of Waterlow scores from Smith (2010) based on the spreadsheet in the economic submission.

With regard to the economic submission, the EAC verified the sponsor's search strategy, reconstructed their decision tree for clarity, verified their

economic model, reanalysed Smith (2010) data to estimate overall effect size and additional summary statistics, and finally produced a refined version of the model, accounting for uncertainties in length of stay more fully.

The revised cost-saving figures are £595 per 'at risk' patient in the hospital setting, compared to the sponsor's figure of £757. The corresponding figures in the community models were: £2,510and £3,455 respectively per prevalent case (per year).

2. Background

2.1 Overview and critique of sponsor's description of clinical context

The clinical context is the development of pressure ulcers through skin breakdown, these are also known as bedsores or pressure sores. Although anyone can develop a pressure ulcer, patients are at increased risk if they have significantly limited mobility (for example, people with a spinal cord injury), a previous pressure ulcer, are at risk of nutritional deficiency, are unable to reposition themselves or have a neurological condition or significant cognitive impairment. Pressure ulcers usually develop in people who have underlying health conditions or who have frail skin for whatever reason. Pressure ulcers tend to affect people with health conditions that make it difficult to move, especially those confined to lying in a bed or sitting for prolonged periods of time. They tend to occur more often in the elderly but can occur at any age. Conditions that affect the flow of blood through the body, such as type 2 diabetes, can also make a person more vulnerable to pressure ulcers. It is estimated that 412,000 people will develop a new pressure ulcer annually in the NHS (Bennett 2004).

Pressure ulcers can develop when a large amount of pressure is applied to an area of skin over a short period of time or when less pressure is applied over a longer period of time and tend to develop over bony prominences, particularly heels and the sacrum. The extra pressure disrupts the flow of blood through the skin. Without a blood supply, the affected skin becomes starved of oxygen and nutrients and begins to break down, leading to an ulcer forming. Skin damage is also believed to be caused by friction, shear and moisture (NICE 2005), but the extent of the contribution of these is low – 7.5% in a sample of 28,299 hospital patients (Lahmann 2011a) and 13.9% in a sample of 17,966 long term care residents (Lahmann 2011b).

Grading of pressure ulcers is by four grades (Anon 2014):

- Grade 1 – The affected area of skin appears discoloured and is red in white people, and purple or blue in people with darker coloured skin.

They do not turn white when pressure is placed on them and skin remains intact but may hurt or itch. It may also feel either warm and spongy, or hard.

- Grade 2 – Some of the epidermis or the dermis is damaged, leading to skin loss. The ulcer looks like an open wound or a blister.
- Grade 3 – Skin loss occurs throughout the entire thickness of the skin and the underlying tissue is also damaged but muscle and bone are not damaged. The ulcer appears as a deep, cavity-like wound.
- Grade 4 - The skin is severely damaged and the surrounding tissue becomes necrotic. The underlying muscles or bone may also be damaged. People with grade 4 pressure ulcers have a high risk of developing a life-threatening infection.

For some people, pressure ulcers are an inconvenience that requires minor nursing care. For others, they can be serious and lead to life-threatening complications, such as blood poisoning or gangrene. In people with diabetes mellitus it is a cause of foot amputations. Pressure ulcers can lead to delayed hospital discharge but it is currently unclear as to how much of this is happening in the NHS. It is estimated that the cost per patient to heal an ulcer varies from £1,214 for Grade 1, £5,241 for Grade 2, £9041 for Grade 3 to £14108 for Grade 4 (Dealey 2012).

Treatment for pressure ulcers includes regularly changing a person's position, the use of dressings, creams and gels designed to speed up the healing process and relieve pressure, and using equipment to protect vulnerable parts of the body, such as specially designed mattresses and cushions. Regarding the latter, draft NICE guidance states "Pressure redistributing devices are widely accepted methods of trying to prevent the development of pressure areas for people assessed as being at risk. These devices include different types of mattresses, overlays, cushions and seating. They work by reducing pressure, friction or shearing forces. There is limited evidence on the effectiveness of these devices" (NICE 2013). For the most serious cases, surgery is sometimes recommended. One issue with all pressure relief equipment is the impact it has on the patient's ability to self-reposition and move around the bed. Much of the equipment currently in use in the NHS addresses the offloading issues in pressure ulcer prevention but does not address repositioning.

The sponsor's description of the clinical context is appropriate and relevant to the decision problem.

2.2 Overview of sponsor's description of ongoing studies

There is an ongoing audit at St Helen's & Knowsley NHS Trust of the use of Parafricta Bootees for patients considered at risk of a heel pressure ulcer, compared to current practice of using a protective hydrogel dressing, which has not yet been published (Gleeson 2014). This audit was started in 2013 and is planned to go on for two years, but the first year's results are available. This was sent to us as an unpublished manuscript. No other relevant ongoing trials were found.

2.3 Critique of sponsor's definition of the decision problem

2.3.1 Population

The patient population in the NICE final scope is any adults and children. The sponsor has excluded very young children because the Bootees and Undergarments do not fit them. The sponsor also manufactures bedsheets and baby nests but these are not part of this evaluation.

The patient population in the submitted studies is in line with the NICE final scope. However, the only comparative study with a described comparison group considers one subgroup specified in the scope only - patients who were unable to reposition independently. None of the included studies describe the population characteristics sufficiently adequately to ensure generalizability with the patient population in England. Where there are historical controls, it is unclear how similar these are to the patients using Parafricta.

2.3.2 Intervention

The intervention is Parafricta which can be one or two Bootees and/or Undergarment. The NICE final scope does not specify whether this refers to a single garment only, or the use of two or three garments together. Parafricta is used an adjunct additional to pressure reducing devices used in standard NHS clinical practice as described in the scope.

The intervention described in the submission is Parafricta Bootees and Undergarments. The submitted studies evaluate one Parafricta Bootee, one or two Bootees, or Undergarments, or a combination of Bootees and Undergarments.

2.3.3 Comparator(s)

The comparators in the NICE final scope are pressure reducing devices used in standard NHS clinical practice, and also one of the following three options:

1. No Parafricta (ie pressure reducing devices alone)

2. Sheepskin

3. Pressure-relieving bootees

Evidence has been submitted in the case of comparator 1 but not comparators 2 or 3.

2.3.4 Outcomes

The sponsor's report has not modified the outcome measures in NICE's final scope. However, it should be noted that some of the outcomes listed in the NICE final scope have clinical evidence and some do not (for comparator 1 only). There is information on incidence of developing pressure ulcers, incidence of grade 1 or 2 pressure ulcers progressing to grade 3 or 4 pressure ulcers, incidence of skin breakdown, severity of pressure ulcers, length of hospital stay and patient comfort. There is no useful information on time to healing, patient compliance, quality of life, morbidity and device-related adverse events. (Please note that lack of reports of adverse events does not imply no events have occurred unless there is positive confirmation in study reports).

2.3.5 Cost analysis

The sponsor submission includes two models, one reflecting a hospital setting and one reflecting a community setting.

The sponsor's statement on the cost analysis (p.12 of the submission) largely reflects the scope. The comparator and perspectives are included within *de novo* model appropriately. In the hospital model the costs are estimated on a per patient basis, but are not explicitly represented as potential cost savings over a longer period of time. The model time horizon is thus limited to the inpatient stay of an at risk patient.

The submission states that Parafricta products are re-usable and therefore costs of care and laundry of the products are considered. In the hospital model, it is assumed that at any time a patient will have access to six different Parafricta garments in rotation. In the base case it was assumed the six garments can be washed and used by a total of three different successive patients. This may be a conservative estimate, based on experience of users.. This means that over the product lifetime garments are washed twice for re-use. Laundry costs are not included in the community model.

The submission states that sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed. This should include consideration of confidence intervals around length of stay (the main

driver of costs in the model) as well as explicitly justified variation in the numbers and combinations of devices. The sensitivity analysis carried out by the sponsor is around some arbitrary (and not very wide) confidence intervals defined for weighted length of stay and although the cost of garments is subject to sensitivity analysis, this is not explicitly explored as a number of garments needed by each patient.

2.3.6 Subgroups

The subgroups in the NICE final scope are:

- people with restricted mobility who may be bedbound
- people who may have skin damage due to musculoskeletal or neurological conditions where repetitive motion is present.

There is no variation from the NICE Final Scope described in the sponsor's statement of the decision problem.

The main clinical evidence (Smith 2010) evaluated patients who were unable to reposition independently so addresses the first subgroup, but this is not described in the Sponsor's statement of the decision problem. The second subgroup is not mentioned.

2.3.7 Special considerations, including issues related to equality

The special considerations on equality in the NICE final scope are as follows:

"It should be noted that people with chronic wounds, including pressure ulcers, may be protected under the Equality Act 2010. The device may have particular advantages for people who have chronic wounds and may be classed as having a disability under the 2010 Equality Act. Other groups covered by the Equality Act are people with diabetes who may have foot ulcers as a result and people who have spinal injuries and may have pressure ulcers. This device would not restrict the access for treatment for these groups of people."

There is no additional discussion of this in the submission. The equality issues are already addressed within the evaluation and there are no further equality issues relevant.

2.4 Description of the technology

Parafricta is a patented smooth woven material which is claimed to reduce skin friction and shear in skin. The proprietary Parafricta fabric has a friction coefficient of 0.2 (the friction coefficient of polycotton is 3 to 5 times greater). The sponsor's rationale for the Parafricta technology is that friction and sheer as well as pressure are factors in pressure ulcer development (Lahmann 2011a and Lahmann 2011b). Hence Parafricta garments are intended to

reduce friction and sheer on the assumption that this will reduce the development and progression of pressure ulcers.

This material is made into underpants for the sacral area and bootees for the foot. The Underpants have no hem over the sacrum but the Bootees have a hem over each side of the heel. Both Undergarments and Bootees have CE marks. All relevant documents have been submitted.

Parafricta garments (Bootees and Undergarment) are used as an adjunct to pressure reducing devices used in standard NHS clinical practice

3. Clinical evidence

3.1 Critique of the sponsor's search strategy

3.1.1 Description of the Sponsors search strategy

The search strategy is described in 10.1 Appendix 1 and 10.2 Appendix 2 of the report and covers more than 6 pages and is unnecessarily long. The most effective way to find evidence on Parafricta is to use this term as a key word in database searches then review reference lists of the most recent studies found.

A long list of databases and sources of unpublished material is presented (see sponsor's submission p98 and p101) and these may have been searched from 2004 to 2014. It is possible that wider date ranges were searched then results limited to the specific dates of 2004-14. Only English language references were used. The manufacturer is British so foreign language publications this early in the product's development are unlikely.

3.2 Critique of the sponsor's study selection

The inclusion criteria are copied from the NICE scope (population, intervention, outcomes, study design) but do not include the comparators.

The sponsor has included all relevant studies found on Parafricta Bootees and Undergarments. The lack of comparator in the inclusion criteria suggests that the sponsor was looking for any evidence in the intervention irrespective of whether there was a comparator.

3.3 Included and excluded studies

3.3.1- Studies included in the sponsor's submission

There were seven included studies found from the searches and three of these were included in the quantitative analysis. Included studies are shown in Table 1 and Table 2. The evidence is generalizable to the UK setting.

Bree-Aslan 2008 is a case study of one nursing home resident aged 85 from the UK.

Hampton 2007 is a case study of one nursing home resident aged 82 from the UK.

Hampton 2009 is a case series of 25 nursing residents (ages not given) from the UK.

Kerr 2008 is a case study of one nursing home resident aged 70 from the UK.

Loehne (2013) is a case series of an unknown number of nursing home residents from USA.

Smith 2010 is a case series of 165 patients from UK hospital wards (ages not given) compared to 204 historical controls from the same wards.

Stephen-Haynes (2011) is a case series of 25 nursing home residents (age not given) from the UK.

3.3.2 – Studies excluded from the sponsor's submission

No relevant studies were excluded by the sponsor. Excluded were:

- Reviews and methods (31 studies
- Friction and sheer v pressure debate (17 studies)
- 'off piste' (92 studies)
- Heel & sacral pads and dressings (17 studies)
- Sheets and pillowcases on non-Parafricta material (7 studies)
- Stockings (1 study)
- Parafricta sheets and pillowcases (2 studies)

Details of these studies were not given, quite correctly, as they are irrelevant to the evaluation of Parafricta Bootees and Undergarments.

3.3.3. - Additional relevant studies identified by the EAC

Independent searches by the EAC found no additional relevant studies (see additional work undertaken by the EAC section below).

There was one additional study found via the Sponsor - an ongoing audit at St Helen's & Knowsley NHS Trust of the use of Parafricta Bootees for patients considered at risk of a heel pressure ulcer, compared to current practice of using a protective hydrogel dressing, which has not yet been published (Gleeson 2014). This audit was started in 2013 and is planned to go on for two years, but the first year's results are available. Gleeson D (2014) is a

clinical audit of the use of Parafricta Bootees at St Helens and Knowsley NHS trust between January and December 2012.

3.4 Overview of methodologies of all included studies

There were seven included studies in the submission of which three were single case studies, two were small uncontrolled case series, one was a small partially controlled case series and one (Smith 2010) was a larger case series with documented historical controls. There was also the unpublished audit by Gleeson (2014). See Table 1 and Table 2 for an overview of these studies.

The three single case studies (Bree-Aslan 2008, Kerr 2008, Hampton 2007) need no further description. The case series by Loehne (2013) gives no information on the study design other than that it is a case series of the use of Parafricta Bootees in nursing home patients.

Hampton (2009) was a case series of 25 nursing home residents. A single Parafricta Bootee was used on the right heel in 10 patients, with the left heel used as comparator. Eighteen patients had Parafricta Undergarments and there was no comparison group. The duration of follow up was four weeks. The outcomes were measured in three ways 1. Bogginess and redness of skin as assessed by tissue viability nurse 2. Colour photographs and 3. High frequency ultrasound graphs. The reason for three different ways for measuring outcomes was because of the difficulty of assessing skin oedema. Bogginess and redness was judged to be very subjectively assessed. Colour photographs did not reproduce the nature of the skin damage well as the colour reproduction depended on ambient light levels. The ultrasound graphs were an attempt to measure thickening of the skin from oedema and were felt to be the most reliable outcome measure.

Smith 2010 recruited 165 patients in three months, compared with 204 historical controls recruited in the previous three months of similar conditions in same hospital wards (two medical and one orthopaedic wards). All patients were at high risk of pressure ulcers (Waterlow score of ≥15), some had pressure ulcers on admission and some did not. All were unable to reposition independently. The intervention was the addition of Parafricta Bootee or/and Undergarment to standard pressure ulcer preventative measures. Outcomes were the incidence improvement and deterioration of pressure ulcers (and cost effectiveness – see later sections of this report).

Stephen-Haynes (2011) was a case series of 25 nursing home residents evaluating Parafricta Bootees or/and Undergarment added to standard approach as outlined by NICE guidance 2005. There was no comparator. Outcomes were skin improvement, ease of use, garment retention and patient comfort.

Gleeson (2014) was a clinical audit evaluating the use of Parafricta Bootees in an unknown number of patients on [redacted], but how it was conducted was unclear as there are no details in the manuscript.

3.5 Overview and critique of the sponsor's critical appraisal for each study

Critical appraisal was presented for three of the studies – Hampton 2009, Smith 2010 and Stephen-Haynes 2011 using the suggested table for observational studies in the NICE template. The critical appraisal for these three studies is not very accurate, for example in response to the question 'was the outcome accurately measured to minimise bias', none of the three critical appraisals mention that there was no report of blinding of outcome measurement in the studies. Also, for the question 'has the authors identified all important confounding factors' there is no mention that none of the studies adequately describe the background characteristics of the patients, for example their ages, genders and other participant characteristics. There was no mention of the strengths and weaknesses of the different study designs (see Appendix 1).

The largest comparative study (Smith 2010) was a case series with historical controls, ie a single centre controlled before after study, and forms the basis of the economic model (see later in this report) so is discussed further here. The critical appraisal missed the following important details. The Cochrane Collaboration says of study designs as used in Smith (2010) "In studies with only one intervention or control site the intervention (or comparison) is completely confounded by study site making it difficult to attribute any observed differences to the intervention rather than to other site-specific variables" (EPOC 2014), so this study design provides relatively weak comparative evidence as results may arise from confounding. Important confounding factors in this instance may have arisen from a variety of unknown issues that result from not having an adequate control group. Additionally, as the patients in the study could not reposition themselves, they represent only a subset of the population who might potentially benefit from Parafricta. Also that no numerical results of length of stay by cohort, no numbers of deaths in either cohort and no demographic characteristics in either cohort or combined were given. This is important to determine whether the two cohorts were sufficiently similar to determine whether any change in pressure ulcers were due to Parafricta use or confounding factors.

Table 1. Comparative studies

Primary study (acronym)	Population	Intervention	Comparator	Outcomes measured and their results	Comment
Hampton S (2009)- (JCN2009)	Case series of 25 nursing home residents with grade 2-3 pressure ulcers on one or more heels (10 patients) or the sacral area (18 patients). All patients had appropriate pressure ulcer equipment for at least 2 weeks prior to the study start. No information on ages, medical conditions or durations of pressure ulcers.	Single Parafricta Bootee on right heel, or undergarment according to damage location Duration 4 weeks but unclear whether this was for all patients.	For heel: comparator was patient's untreated left heel. For sacral ulcers – historical comparison only	Skin oedema and damage as assessed by: 1. Bogginess and redness of skin as assessed by tissue viability nurse 'in 100% of the heel cases the 'bogginess' of the skin was reduced' 2. Colour photographs 3. High frequency ultrasound graphs These show an apparent improvement in the Parafricta Bootee'd heels compared to a control heel	Bogginess – subjective outcome. Colour photograph results not presented as they were not always representative of nurse assessment of the skin. Ultrasound – no independent validation presented, would need to link improvement curve shown in graphs presented to clinical improvement in the patient. Therefore graphs difficult to interpret clinically.
Smith (2010) - (JWC2010)	Case series of 165 patients recruited in 3 months, compared with 204 historical controls (previous 3 months) of similar condition in same hospital wards (2 medical and 1 orthopaedic wards, UK hospital). All patients were at high risk of pressure ulcers (Waterlow score of ≥15), some had pressure ulcers on admission and some did not. All were unable to reposition independently.	Cohort 2. Addition of Parafricta Bootee or/and Undergarment to standard pressure ulcer preventative measures.	Historical comparison Cohort 1: standard pressure ulcer preventative measures (without the addition of Parafricta Bootees and Undergarments)	For incidence of pressure ulcers and deterioration see separate table. No statistically significant differences in length of stay between cohorts 1 and 2	If patients couldn't reposition then movement would be limited so likely that pressure ulcers caused by pressure rather than friction. No numerical results of length of stay by cohort. No numbers of deaths in either cohort. No demographic characteristics in either cohort or combined. Cannot tell how similar the cohorts were.

Table 2. Case studies or series with no comparative groups described

Primary study (acronym)	Population	Intervention	Comparator	Outcomes measured and their results	Comment
Bree-Aslan (2008). (NRC3)	Case study of one nursing home diabetic patient aged 85 with arterial and venous insufficiency and a Grade 4 heel pressure ulcer measuring 3.5x3.3cm, being nursed on a dynamic air mattress and using a soft fibre bootee.	Cavilon spray, Hydrogel dressing then Versiver dressing on top. Plus Parafricta Bootee over it for one week.	Historical comparison from the same person only	'marked improvement in the wound bed and no further damage to the surrounding tissues'.	Impossible to determine whether the improvement was temporary or permanent or was due to the hydrogel dressing, the Parafricta Bootee or unrelated to either and would have happened anyway.
Gleeson (2014) (unpublished manuscript)	Clinical audit of [redacted] of pressure ulcers.	[redacted] on pressure ulcers	[redacted] not described	[redacted]	The decrease in pressure ulcers was probably not due to a decrease in hospital activity but may be related to education and training initiatives and investment in a range of pressure reducing products. It is unclear how much of [redacted] was due to Parafricta Bootees and how much was due to the other initiatives taking place at the Trust.

Primary study (acronym)	Population	Intervention	Comparator	Outcomes measured and their results	Comment
Hampton S (2007) (NRC1)	Case study of one nursing home patient aged 82 with multiple sclerosis and with sore and broken skin over the buttocks for several months, being nursed on an air mattress.	Parafricta Undergarment for one week	Historical comparison from the same person only	'in less than one week the soreness had disappeared and the skin was clear'	Impossible to tell whether the improvement was temporary or permanent or whether it was due to the Parafricta Undergarment or would have happened anyway.
Kerr A (2008). (NRC2)	Case study of one nursing home patient aged 70 years with poor mobility and with at least 3 month's history of macerated and excoriated buttocks with deep split wounds and inflammation. Sudocreme had been applied.	Parafricta Undergarment	Historical comparison with Sudocreme on the same person only	'reduced inflammation with the open areas showing signs of closure'	Impossible to tell whether the improvement was temporary or permanent or whether it was due to the Parafricta Undergarment or previous allergy to Sudocreme or would have happened anyway.
Loehne, H.B. (2013). (SAWC1)	Case series of an unknown number of US nursing home patients. No information on sex, age, current condition, duration, grade or site of pressure ulcers. Excluded were patients with, or at risk of, pressure ulcers on the heel or foot due to pressure only.	Parafricta Bootee. Unclear if both feet or only one. Dressings (not specified) in some patients. Follow up at 30 days.	Unclear.	None of the unknown number of patients had developed pressure ulcers or had re-opening of closed wounds.	This does not present any evidence of effectiveness as there is minimal information on patients.

Primary study (acronym)	Population	Intervention	Comparator	Outcomes measured and their results	Comment
Stephen-Haynes (2011) (WUK2011)	Case series of 25 nursing home patients at-risk of pressure ulcers (n=5) or with a pressure ulcer (n=20, 10 with category 1 ulcer, 10 with category 2 ulcer). Characteristics included steroid use (n=1), CVA (n=6), dementia (n=3), multiple sclerosis (n=3).	Parafricta Bootee or/and Undergarment added to standard approach.	None	Skin improvement: 76% improvement, 24% same. Ease of use: very easy in 64% patients, easy in 16%, fairly easy in 16% and difficult in 4%). Garment retention: 48% clinicians found it very easy to keep garments in place, 16% easy, 20% fairly easy, 16% not easy. Patient comfort: 76% very comfortable, 24% comfortable.	Impossible to tell whether any improvement in pressure ulceration was temporary or permanent or whether it was due to the Parafricta Undergarment or would have happened anyway.

3.6 Results

The numbers of patients in each study, outcomes and results are shown in Table 1 and Table 2.

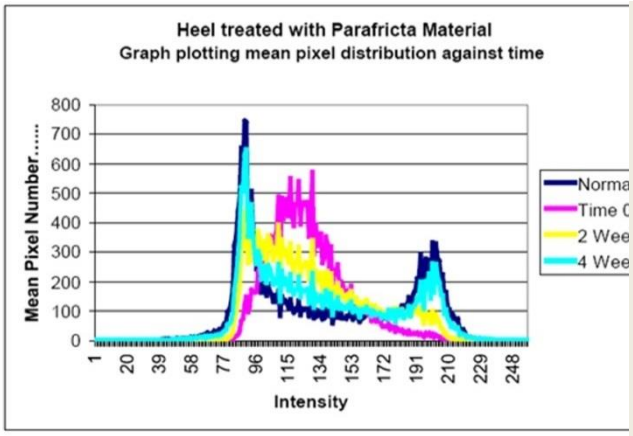
Results for the three single case studies (Bree-Aslan 2008, Kerr 2008, Hampton 2007) are in Table 2. It is impossible to determine whether the improvements claimed were temporary or permanent or was due to the hydrogel dressing, the Parafricta Bootee or unrelated to either and would have happened anyway. These case studies therefore do not make a useful contribution to the evidence on effectiveness and need no further description. The case series by Loehne (2013) gives no useable results as we do not know the number of patients to which they are referring. Contact with the author yielded no further information. The Sponsor's submission states that there were six patients in the case series but it is unclear where this number came from.

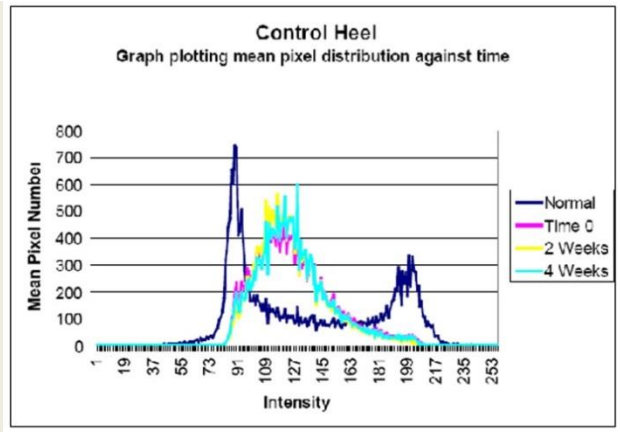
Hampton 2009 reported three types of outcomes, as described above.

- 'bogginess' of skin. For heels in the 10 patients wearing Parafricta Bootees on the right heel – 100% of the patients had bogginess reduced on the right heel. No information about the left heel was reported. No information about the 18 patients with sacral redness for this outcome measurement was reported.

- Colour photographs – results not given

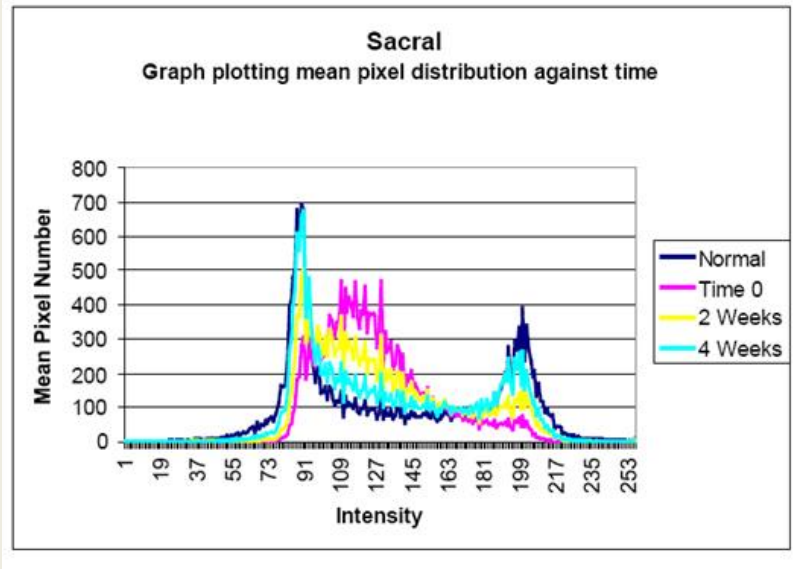
- High frequency ultrasound. Three graphs were provided that are reproduced below in Figure 1, along with their captions.





The right 'study' heel. Normal is shown as the dark blue line and it can easily be seen how each week the tissues grow toward the normal line and by week 4 the turquoise line matches the dark blue line. This demonstrates how the right heels all gradually improved weekly.

The left 'control' heel does not progress from inflammation to 'normal' as seen in the right foot. In fact, it remains very static and where it was oedematous on day 1 it remained oedematous at week 4.



The graph clearly shows that the tissues regain 'normal' status by week 4 when the turquoise line achieves the same pathway as the dark blue or normal tissue line.

Figure 1. Hampton (2009 high intensity ultrasound results

The statistical analyses of these results are shown below (see Table 3).

Table 3. Statistical analysis of Hampton 2009 high frequency ultrasound results

	Statistic	Normal Heel	Control 0	Control 4 weeks	Treated 0	Treated 4 weeks
Normal Heel	Diff		30.4	30.9	29.7	9.4
	p value		0	0	0	0.2
Control 0	Diff	30.4		3.91	9.8	36.72
	p value	0		0.98	0.16	0
Control 4 weeks	diff	30.9	3.91		9	34.38
	p value	0	0.98		0.24	0
Treated 0	Diff	29.7	9.8	9		31.2
	p value	0	0.16	0.24		0
Treated 4 weeks	Diff	9.4	36.72	34.38	31.2	
	p value	0.2	0	0	0	

Critique: These colour graphs and their captions are difficult to interpret if the reproduction is in monochrome. The axes report pixel number by intensity and do not appear to report skin thickness. There are four curves – one a 'normal' heal or sacrum and three from the study reporting the affected tissues at time 0, 2 and 4 weeks. It is unclear whether the graphs are depicting skin oedema and its resolution or not. The results in Table 3 are difficult to interpret as it is unclear what 'Diff' refers to (oedema, skin thickness or pixel number).

Smith (2010) analysed results in pressure ulcer incidence, improvement and deterioration using differences in incidence. These are reproduced in Table 4. As incidence differences are difficult to interpret these were recalculated using relative risks (in Revman 5.2) and the results shown in

Table 5. The results from the study, whichever way it is analysed suggest that the Parafricta cohort had fewer patients who developed pressure ulcers in patients without pressure ulcers on admission but no difference in the development of additional pressure ulcers in patients who already had a pressure ulcer. Also the results suggest that fewer pressure ulcers deteriorated in the Parafricta cohort. There were no statistically significant differences in length of stay between cohorts 1 and 2 but the lengths of stay were not given.

Critique: There were no numbers of deaths or demographic characteristics in either cohort, and no numerical results of length of stay by cohort were given. So it is impossible to tell how similar the cohorts were as there is no information on confounding factors. The only information we do have is the Waterlow score from the Economic submission (see additional work carried out by the EAC below) which suggests that the cohort not given Parafricta may have beenmore at risk of pressure ulcers than those given Parafricta. The difference in pressure ulcers could also be because the Parafricta cohort patients were less ill than those in the historical comparison cohort. Therefore, it cannot be inferred that any change in pressure ulcer incidence, improvement or deterioration was due to the use of Parafricta Bootees and/or Undergarments. Also, if patients couldn't reposition (an inclusion criterion for the study) then movement would be limited so it would be likely that any pressure ulcers occurring would have been caused by pressure rather than friction.

For Stephen-Haynes (2011) the results were as follows:

- Skin improvement: 76% improvement, 24% same.
- Ease of use: very easy in 64% patients, easy in 16%, fairly easy in 16% and difficult in 4%.
- Garment retention: 48% clinicians found it very easy to keep garments in place, 16% easy, 20% fairly easy, 16% not easy.
- Patient comfort: 76% very comfortable, 24% comfortable.

Critique: As this was an uncontrolled study it is impossible to tell whether any improvement in pressure ulceration or skin improvement was temporary or permanent or whether it was due to the Parafricta Undergarment or would have happened anyway.

Table 4. Reported results from Smith (2010)

	Subgroups	Historical controls incidence (%)	Parafricta cohort incidence (%)	% difference (Parafricta – control)	P value
No pressure ulcer on admission	A, Did not develop a pressure ulcer	67 (59)	58 (75)	16	0.03
	B. Developed a pressure ulcer	46 (41)	19 (25)		
Pressure ulcer on admission	C. Did not develop an additional pressure ulcer	67 (74)	73 (83)	9	0.18
	D. Developed an additional pressure ulcer	24 (26)	15 (17)		
Subgroup B.	The pressure ulcer improved	16 (33)	14 (74)	41	0.01
	The pressure ulcer stayed the same or deteriorated	32 (67)	5 (26)		
Subgroup D.	The pressure ulcer deteriorated	18 (27)	4 (6)	-21	0.001
	The pressure ulcer stayed the same or improved	49 (73)	69 (94)		

The results for the Gleeson (2014) unpublished clinical audit are as follows:

There were 232 Bootees purchased during the year and used in six wards with patients at high risk of pressure ulcers. There were 600 allocations made to patients during the year on these wards. At the Trust there was also a general investment in pressure reducing/relieving products including 4-sectional electric profiling beds, pressure-reducing foam, alternating air mattresses, heel troughs and cushions. There was also an initiative on policy guideline development driven through education and training, and also key performance indicators. It is stated in the article that there was a 32% reduction in reportable hospital-acquired grade 2 pressure ulcers compared to the previous year, presumably on these wards. Overall there was a Trust-wide drop in pressure ulcers of 76%. There was a 9% increase in Trust-wide activity in 2012, presumably compared to 2011.

Critique: This is an unpublished manuscript of an interim report and some details are missing, for example there is no information on the number of patients who were allocated Parafricta Bootees. The decrease in pressure ulcers was probably not due to a decrease in hospital activity but may have been related to education and training initiatives and investment in a range of pressure reducing products. It is unclear how much of this [redacted] in pressure ulcers in the Trust overall was due to Parafricta Bootees, if at all, and how much was due to the other initiatives taking place at the Trust.

3.7 Does each relevant study include the patient population(s), intervention(s), comparator(s) and outcomes as defined in the final scope?

All of the studies included the correct patient populations and the correct intervention of Parafricta Bootees and/or Undergarments. In all the included studies evidence is provided for only one of the three comparators - Parafricta versus no Parafricta in a background of pressure reducing devices used in standard NHS clinical practice and there is no evidence with comparators of sheepskin or pressure-relieving bootees. Some relevant outcomes have been reported but not all those listed in the NICE final scope. The main problem with the evidence available is difficulty with confounding factors. We do not know whether change in pressure ulcer incidence, improvement, deterioration or healing is due to differences in populations, or due to the use of Parafricta, from any of the included studies.

3.8 Description of the adverse events reported by the sponsor

The sponsor considers that adverse events are unlikely. No adverse events were recorded in the presented studies. The EAC searched the FDA Maude database for the brand name “Parafricta” on 3.4.2014. No reports of adverse

events were found. If Parafricta Bootees and Undergarments are used on more than one person, there is a risk of cross-infection if the garments are not adequately washed.

Expert Advisers were asked about adverse events. D Gleeson confirmed that she thought there were no side effects and all patient groups could use Parafricta Bootees and Undergarments.

3.9 Description and critique of evidence synthesis and meta-analysis carried out by the sponsor

The evidence synthesis was narrative. Meta-analysis was not conducted and not possible or appropriate as only one comparative study was available making it impossible to calculate weighted estimate of effect from more than one study.

3.10 Additional work carried out by the External Assessment Centre in relation to clinical evidence

1. Literature Searches

Additional searches were conducted for already published clinical evidence on 19th February 2014 using the key term 'parafricta'. The results were Medline – 1 reference, Web of Science – 1 reference, Embase 4 references, The Cochrane Library (all databases) 0 references. In all, 4 references and 2 duplicates were found. Of these two were already in the submission, one was a conference abstract for a study already in the submission and the fourth was a case series evaluation by Barrett et al (2012) on Durafiber (Smith and Nephew) – a type of wound dressing. The searches did not add any useful information to that already in the submission. Additional searches for ongoing trials were conducted in the meta-register of Current Controlled Trials (all five databases) using the search term Parafricta. No ongoing studies were found.

2. Recalculation of results for Smith 2010

Recalculation of results with relative risks and 95% confidence intervals was necessary in Smith 2010 because the publication used unusual results calculations using percentage differences in incidence which were difficult to interpret. Incidence differences vary depending on the underlying event rate such that a difference of 2% maybe clinically meaningful if the underlying rate is 2% but not if it is 80%. Relative risks were calculated instead which are much more easily interpreted and not subject to this difficulty.

Table 5. Calculated relative risks for Smith 2010

		Cohort 1 (no Parafricta)	Cohort 2 (Parafricta)	Relative risk (95%CI)*
Pressure ulcer on admission	That pressure ulcer deteriorated	18/67	4/73	4.90 (1.75-13.75)
Pressure ulcer on admission	Developed an additional pressure ulcer	24/91	15/88	1.55 (0.87-2.75)
No pressure ulcer on admission	Developed pressure ulcer	46/113	19/77	1.65 (1.05-2.59)
No pressure ulcer on admission but one developed during hospital stay	Pressure ulcer same or deteriorated	32/48	5/19	2.53 (1.16-5.52)
Calculated in Revman 5.2				

3. Analysis of Waterlow scores from Smith (2010) based on the spreadsheet in the economic submission.

This information appears in the clinical evidence section as it is the only indication of the different clinical characteristics of the two cohorts in Smith (2010). A higher Waterlow score indicates more risk from pressure ulceration (see Appendix 2). The Waterlow scores are reported in categorical form and the results are as follows (see Table 6):

Table 6. Waterlow scores from Smith (2010)

All incidences			
	Waterlow score	Number	Percentage
Cohort 1 Pre Parafricta products	15-19 20-24 25+	103 82 21	50.00% 39.81% 10.19%
Total		206	
Cohort 2 Post Parafricta products	15-19 20-24 25+	94 52 19	56.97% 31.52% 11.52%
Total		165	
Chi Square Test result P value	0.2553898 p-value from Chi-square test (implies non-difference if > 0.05)		

These results indicate that the cohort without Parafricta may have been more at risk of pressure ulceration than the cohort given Parafricta garments.

3.11 Conclusions on the clinical evidence

Seven studies were submitted by the sponsor and one clinical audit was also assessed in this report. None of the studies were of high quality – the best evidence being a relatively large case series with historical controls. Parafricta Bootees and Undergarments were compared to UK clinical practice without Parafricta Bootees and Undergarments. There was no evidence submitted where the comparator was sheepskin or other pressure relieving bootees.

There is insufficient evidence to demonstrate that Parafricta Bootees and Undergarments are associated with a decreased incidence, improvement, deterioration or better healing of pressure ulcers compared to no Parafricta, and no information on Parafricta compared to sheepskin or pressure-relieving bootees.

The main development of Parafricta is the material having less friction and shear than standard materials such as bed linen and cotton. However, the evidence suggests that only a small proportion of pressure ulcers are due to this (7.5% to 13.9%) so it in small case series, any differential effects are unlikely to be demonstrated. The largest case series evaluated patients who were unable to reposition so again was unlikely to show any difference. We do not know whether confounding factors rather than clinical effectiveness of Parafricta Bootees and Undergarments are responsible for any differences observed.

4. Economic evidence

4.1 Critique of the sponsor's search strategy

The search strategy to identify relevant economic studies is described in 10.1 Appendix 3 in the sponsor's submission. The searches were conducted on 10th March 2014. The key words used includes a strategy that combines 'condition' (ulcer OR sore) with (friction OR shear) and (cost OR economic OR benefit). However, the texts on p. 126 of sponsor's submission mentions 'budget' instead of 'benefit'. A follow-up strategy replacing (friction or shear) with 'pressure' was used and the sponsors conclude that this strategy resulted in hits that were too general indicating the use of pressure reducing devices and none were related to use of Parafricta. The databases used were Medline, Embase, MEDLINE (R) In-Process, EconLit and NHS EED. In Pubmed, the search was restricted to only 'reviews'. Appendix 10.3 indicates that they also included a Cochrane Library search restricting to only

‘economic evaluations’ but it is not explicit in the list of databases they mention on p.125. The date span of the search was not limited. No unpublished literature was sought. Although not specifically mentioned, the searches were restricted to English language only.

The EAC considered whether a more comprehensive search would have been achieved by including additional databases such as CRD (which includes HTA, DARE and NHS EED) or HEED and changing key words, for example, from “cost” to “cost*”. The EAC tested this on CRD and HEED and could not identify any relevant study over and above those that the sponsors identified.

The sponsors did not do any formal searches to identify resource measurement and valuation.

4.2 Critique of the sponsors study selection

The inclusion criteria are consistent with the scope. The exclusion criteria for evaluating economic studies were the same as those used to evaluate clinical studies. Of the three aspects that were excluded are language (non-English), time span (before 2005), and specific intervention that may have confounded Parafricta’s effects by ‘materially changing the type or quality of nursing and /or wound care provided’. No additional information was provided as to the nature of those interventions. The EAC considers the Sponsor’s selection of relevant economic studies adequate.

4.3 Included and excluded studies

4.3.1 Studies included in the sponsor submission

The sponsor included only one study- Smith 2010 - after applying the selection criteria. This study is described in Table 7 and met the study selection criteria for health economic studies. Smith (2010) was a case series of 165 patients recruited in three months, compared to 204 historical controls (recruited in the previous three months) of similar condition in same hospital wards (two medical and one orthopaedic wards, UK hospital). All patients were at high risk of pressure ulcers (Waterlow score of ≥15), some had pressure ulcers on admission and some did not. All were unable to reposition independently. Both received the same standard care (pressure reducing devices) but Parafricta was used in group 2. The health economic outcome was the difference in expected costs in each group comprising of the following resource use: bed day costs, dressing costs, cost of garment and cost of mattress. These expected costs were derived from median lengths of stay over the treatment pathway, weighted by the corresponding incidence, and valued using unit costs of the above resource use. A positive difference in

expected costs between group 1 and group 2 was considered to be cost-saving. In this study, this was £630 per ‘at risk patient’.

4.3.2 Studies excluded from the sponsor submission

The excluded paper in the sponsor’s submission is a CRD critique of the included study and thus is not relevant.

4.3.3 Additional relevant studies identified by the EAC

No other relevant studies were identified by the EAC.

4.3.4 Studies excluded by the EAC

No studies that were identified by the sponsor were excluded by the EAC

Table 7. Comparative studies included in economic appraisal

Primary study (acronym)	Population	Intervention	Comparator	Costs and resource use	Comment
Smith (2010) - (JWC2010)	Case series of 165 patients recruited in 3 months, compared to with 204 historical controls (previous 3 months) of similar condition in same hospital wards (2 medical and 1 orthopaedic wards, UK hospital). All patients were at high risk of pressure ulcers (Waterlow score of ≥15), some had pressure ulcers on admission and some did not. All were unable to reposition independently.	Cohort 2. Addition of Parafricta Bootee or/and Undergarment to standard pressure ulcer preventative measures.	Historical comparison Cohort 1: standard pressure ulcer preventative measures (without the addition of Parafricta bootees and undergarments)	For economic analysis, the outcomes were expected costs in each cohorts comprising of the following resource use: • Bed day costs • Dressing costs • Cost of garment • Cost of mattress These expected costs were derived from median lengths of stay over the treatment pathway, weighted by the corresponding incidence, and valued using unit costs of the above resource use.	The economic model used in the paper to show net cost-savings attributable to Parafricta use relied heavily on the two cohorts being different from each other in terms of "median" length of stay. Therefore, the authors' description in the journal article that "there were no statistically significant differences between the lengths of stay in the corresponding pathways between cohorts 1 and 2" does not make sense.

4.4 Overview of methodologies of all included economic studies

There was one included study (Smith 2010) which was a case series with historical controls. In the first half of the 6-month study period, subjects (those at very high risk of developing pressure ulcers on hospitalisation) were followed up for new incidence or additional incidence of pressure ulcer, lengths of stay, changes in pressure ulcer grading, time to develop an ulcer, and dressing needs. These patients (n=206) were managed with current practice (pressure reducing devices) and served as controls (group 1). In the beginning of the 4th month, Parafricta garments were introduced on top of the current practice and the same data were collected for the new patients who arrived in the hospital between 4th and 6th months of the study period. This group of patients served as intervention group (n=165).

A simple decision tree was constructed to model the actual treatment pathways. Starting from the likelihood of whether pressure ulcer was developed after hospitalisation, the pathway went to include development of additional pressure ulcer and whether the existing pressure ulcer stayed the same, or improved or deteriorated. Median lengths of stay were recorded for each terminal point (the final outcome in the pathway) and rolled back to estimate the 'expected costs of treatment' in both arms. These costs were compared to indicate net cost-savings attributable to Parafricta use. Best and worst case scenario analysis was carried out to indicate uncertainty around the cost-savings estimate. No adjustments to median lengths of stay were made, ignoring the fact that lengths of stay could have been confounded by patients' background characteristics, such as the Waterlow score. The Smith (2010) paper contains little information on their background characteristics.

4.5 Overview and critique of the sponsor's critical appraisal for each study

The sponsors present their critical appraisal on the Smith (2010) using standard criteria (Drummond and Jefferson 1996). Their critical appraisal failed to identify a number of important aspects of the study. For example, no comments were made about the effect size, both in terms of how it was generated (e.g. non-randomisation as a design issue) and whether the effect size was net of confounders (statistical adjustment). No appraisal was presented for use of weighted median, instead of mean in the effect size estimate in the model. Also, no critical appraisal was presented about identification of all relevant resource use and how each resource use was valued. The EAC's critical appraisal of this study is in Appendix 3.

4.6 Does the sponsor's review of economic evidence draw conclusions from the data available?

The results presented in Smith (2010) paper suggested that there is a potential for Parafricta garments to reduce the costs of pressure ulcer management in the hospital settings. They estimated that Parafricta garment use may help the NHS to save £637 per at risk patient (net of the cost of the garments), as the use of garments led to a reduction in pressure ulcers and/or reduction in hospital length of stay. Although other costs are included in the model, these savings are largely driven by reduction in lengths of stay. The sponsors used the data as well as conclusions drawn in this paper to produce their economic analysis in the current submission. The main reason for this is that despite their weaknesses, Smith (2010) is the only large study providing comparative data to enable researchers to model the cost-consequence of Parafricta garments. It is therefore important to note that any conclusions based on the available economic evidence may still be subject to significant uncertainty.

4.7 De novo cost analysis

The sponsor conducted a cost analysis based on data from Smith (2010) to assess potential cost saving associated with use of Parafricta Undergarments and Bootees. Separate analyses were conducted to reflect their use in both a hospital setting and a community setting.

In the hospital setting, expected differences in length of stay for a patient using Parafricta Bootees and Undergarments, reflected the potential cost savings. In the community setting, a reduced prevalence rate amongst those using Parafricta, and the effect on nurse/ carer interventions reflected the potential cost savings.

The sponsor produced a quantitative *de novo* model for both these settings operationalised in MS Excel. It allowed cost savings to be estimated and sensitivity analysis around parameters inputs to be conducted to assess uncertainty.

4.7.1 Patients

In the cost analysis, the sponsor defined the patient group as per the scope:

People (adults or children of any age) in a community or hospital setting who:

a. Have a grade 1 or 2 pressure ulcer and are at risk of progressing to grade 3 or 4 pressure ulcer

b. do not have a pressure ulcer but are at risk of developing pressure ulcers caused by friction and shear forces, including but not limited to patients who:

- have frail skin and are at risk of skin breakdown or damage
- have impaired sensation and are at risk of skin breakdown or damage
- have peripheral arterial disease, who have very high risk of developing ulcers
- have medical condition where skin frailty is a primary factor and where friction and shear could cause skin damage

All of the data regarding incidence and length of stay which populated the hospital model and informed the community model came from Smith (2010). It is therefore relevant to assess how well the population in this study fits that defined in the scope.

The patient population included in Smith (2010) study were those with a Waterlow score ≥ 15 (at high or very high risk of pressure ulceration) (see Appendix 2). The Waterlow score is an additive scoring system, which factors risk due to BMI (obese or underweight), skin type (ranging from healthy to broken), sex (female at higher risk), age (highest risk 81+), malnutrition, continence and mobility. “Special risks” are considered to be: tissue malnutrition (terminal cachexia, organ failure, and peripheral vascular disease), neurological deficit (diabetes, motor/sensory and paraplegia) and major surgery or traumas, which add significantly to the score.

In the two groups included in Smith (2010) (one without Parafricta [group 1] and one with the addition of Parafricta [group 2]) the majority of ulcers observed on admission or subsequently developed were grade 1 (65% in 1, 74% in 2) or grade 2 (29% in 1, 20% in 2), with a small proportion of grade 3 ulcers (5% in 1 and 7% in 2). According to Waterlow score, 50% of patients in group 1 were at high risk of pressure ulceration and 50% at very high risk. In group 2, 57% of patients were at high risk and the remaining 43% at very high risk. However, it is not known how well the Waterlow score adequately categorises risk of pressure ulcers. Schoonhoven (2002) suggests that the Waterlow score does not satisfactorily predict development of pressure ulcers, with a low positive predictive value of 6.7%, but Anthony (2003) suggests that it is a good predictor of subsequent pressure ulceration.

The population in this study seems to broadly fit the population defined in the scope. The scope did not state a method of classifying risk and components of the Waterlow score do match the groups identified as at-risk. Of those admitted with a pressure ulcer, the majority were grade 1 or 2, although a small proportion of ulcers were grade 3.

4.7.2 Technology

The technology is Parafricta Bootees and Undergarments as an adjunct to other pressure-reducing devices currently used in standard NHS clinical practice.

4.7.3 Comparator(s)

The comparators are other pressure-reducing devices currently used in standard NHS clinical practice (i.e without Parafricta).

4.7.4 Model structure

4.7.4.1 Hospital model

The Sponsor's chosen model structure reflected the Smith (2010) data, with five potential pathways (or health states) for at-risk patients. Patients may have had an incidence of a pressure ulcer, whether existing on admission or developed during the hospital stay. Patients admitted with a pressure ulcer may have had an improvement or deterioration of their pressure ulcer, or have developed an additional pressure ulcer whilst in hospital.

The five pathways considered in the model were:

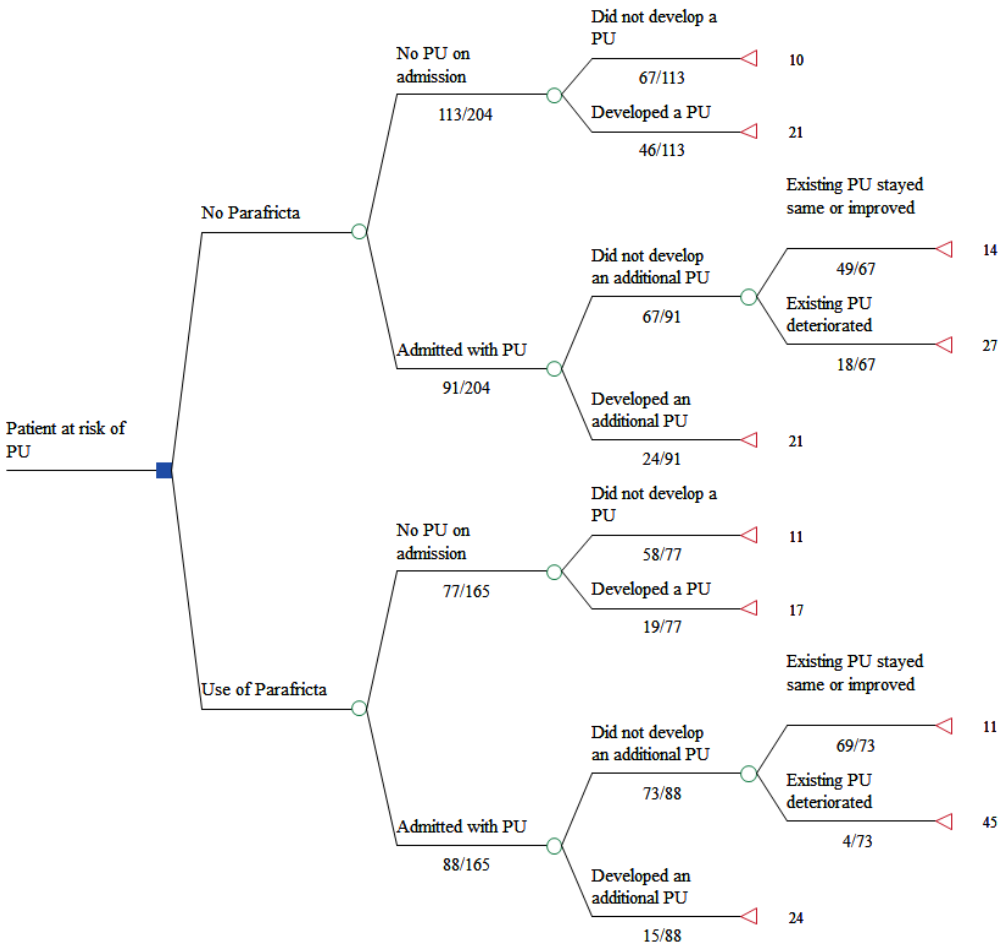
1. Admitted without pressure ulcer(s) and remained without
2. Admitted without a pressure ulcer(s), but developed a pressure ulcer in hospital
3. Admitted with a pressure ulcer(s) which did not deteriorate
4. Admitted with a pressure ulcer(s) which deteriorated
5. Admitted with a pressure ulcer(s) and developed an additional pressure ulcer in hospital

The sponsors included a flowchart diagram showing the patient pathways, but this has been redrawn by the EAC and presented as a decision tree to aid clarity (see Figure 2). It shows the possible pathways of a patient at risk of a pressure ulcer, with the corresponding proportion of patients in the Smith (2010) study that moved into each pathway. Decision nodes are shown by a blue square, chance nodes are shown as green circles, and terminal nodes as red triangles. The only decision node in the model reflects the decision to use Parafricta or not use Parafricta. At each chance node the probabilities of a patient experiencing an outcome are reflected by the Smith (2010) data, with the numbers that inform probabilities below each branch. They are also detailed in Table 8 and discussed further in section 4.7.5 of this report. Each observed median length of stay for the relevant pathway is shown. The model then uses the median length of stay and proportions in each pathway to

compute a weighted length of stay for the Parafricta group and the no Parafricta group.

Costs for each group are estimated based on cost per day of hospital stay (including pressure relieving mattresses) and other associated pressure ulcer dressing costs.

Figure 2. Redrawn diagram of Sponsor's model – Patient pathways



The model inherently assumed that if a patient developed a pressure ulcer, this would require an extended hospital stay. There is some limited evidence to suggest that this assumption may be justified (Smith 2010, Dealey 2012).

Smith (2010) did not report any statistically significant differences in length of stay, but EAC reanalysis showed a small, important but not statistically significant difference in length of stay between the cohort using Parafricta and the cohort no using Parafricta (see Appendix 3 - Reanalysis of Smith (2010) data). These results are still subject to potential bias as the study was non-randomised and patient characteristics were not available to account for in the analysis. Confounders may well have biased the results.

In the absence of many data sources to populate a new model, it is understandable why the model structure was chosen. Use of median length of stay was not appropriate. The EAC also notes that the costs associated with the pathways reflecting change in pressure ulcer condition do not incur different costs. Given each pathway is based on Smith (2010), the more differentiated the pathways become, the more diluted the data on length of stay becomes, increasing the uncertainty. This is however, likely to have a small effect on results.

4.7.4.2 Community model

The Smith (2010) study was based in a hospital setting (an NHS orthopaedic ward and two general medicine wards). The community model uses this data to infer potential reductions in prevalence in the community from the addition of Parafricta to standard clinical practice. The estimation was not very well described in the sponsor submission, with the supplied flowchart extremely hard to follow. The EAC has provided a narrative description of this model and used the input data from the base case model to illustrate how the community model works.

The community model constitutes a steady-state comparison of costs with and without the use of Parafricta. It uses data from the hospital model to estimate point prevalence for pressure ulcers in the community with and without the use of Parafricta. Results are calculated assuming that without Parafricta, for every patient in the community with a pressure ulcer, there will be two other at-risk patients without a pressure ulcer. The sponsor stated that this was consistent with published audits of prevalence (Stevens, 2000; NICE,2005).

The relative point prevalence (with Parafricta versus without Parafricta) is estimated from the following data:

- The time from incidence of a pressure ulcer, for those not admitted with a pressure ulcer (for each group), to discharge. This is used as a proxy for the duration of a pressure ulcer.

- The incidence per at-risk patient (0.25 in the Parafricta group and 0.41 in the standard care group) and duration of a pressure ulcer in each group respectively is used to calculate the point prevalence for each group.

- The ratio of these point prevalence gives an estimate of the relative point prevalence of Parafricta versus no Parafricta.

Costs without Parafricta are then estimated based on the cost of nurse visits related to prevalent pressure ulcer cases over a year of resource use. Costs of implementing Parafricta in the community are estimated by multiplying the

annual costs of Parafricta garments per patient (£80) by the number of at-risk patients (at-risk to prevalence ratio; 3 per person with a pressure ulcer in base case) given Parafricta garments. Savings associated with Parafricta garments in the same community are then estimated by multiplying the cost of nurse visits per case (1.86 visits per week @ £61 a visit) by the estimated number of pressure ulcers avoided (1-0.37 per pressure ulcer in base case).

The Sponsor acknowledges the community model lacked data collected from that setting and relied on hospital data. It is difficult to interpret the meaning of the absolute cost for the Parafricta group and the no Parafricta group, but the sponsor presented a total annual cost per prevalent case and associated cost saving. It also had the same problems as in the hospital model with regard to the quality of study design in Smith (2010). None of the data used in the Sponsor's community model were adjusted for case mix, which could largely explain variation in length of stay and/or incidence. The use of time from incidence of a pressure ulcer to discharge also relies on an assumption that either all ulcers have healed on discharge (which is not the case) or that the distribution of ulceration is the same between groups on discharge.

A more intuitive model using incidence data to calculate a relative risk and charting progression of pressure ulcers in the community and time to healing (taken from a study such as Dealey(2012)) might have offered a more easily interpretable model.

4.7.5 Clinical parameters and variables

4.7.5.1 Hospital model

As stated previously, the model was populated largely with data from Smith (2010). This case series study with historical controls gathered data on two successive 3 month groups, one without use of Parafricta (July to September 2009) and another group subsequently using Parafricta Bootees and Undergarments as an adjunct to standard care (October to December 2009). Standard care included the use of pressure relieving mattresses (Invacare/ MSS Softform premier glide or Huntleigh Healthcare Nimbus 3), with at-risk patients being repositioned two hourly. Smith (2010) stated that all other interventions (e.g. nutrition) were the same across both groups, although no further details were provided. The same group of nurses (due to low staff turnover) cared for both groups. The mix of use of Undergarments and/or Bootees per patient was not known in the study.

The Table 8 below comes directly from the sponsor's model and shows the median length of stay for each pathway and the number of patients in each pathway, which is used to weight the length of stay.

Table 8 Patient pathways and median length of stay

	[group/PU status on admission/PU status during stay	Length of stay (median days)	Number of patients
Group 1	group1/withoutPU/ withoutPU	10	67
No Parafricta	group1/withoutPU/ withPU	21	46
	time taken to develop PU	5.5	
	group1/withPU/no deterioration	14	49
	group1/withPU/ deterioration	27	18
	group1/withPU/ &additionalPU	21	24
total			204
Group 2			
Use of Parafricta	group2/withoutPU/ withoutPU	11	58
	group2/withoutPU/ withPU	17	19
	time to develop PU	7.5	
	group2/withPU/no deterioration	11	69
	group2/withPU/ deterioration	45	4
	group2/withPU/& additionalPU	24	15
total			165

It can be seen that median length of stay was lowest in both groups for those patients at risk of a pressure ulcer, but that did not have one on admission and did not develop one during their stay (10 days in group 1, 11 days in group 2). Longer length of stay was observed for those who were admitted without a pressure ulcer but subsequently developed one in hospital (21 days in group 1, 17 days in group 2). The median time taken to develop a pressure ulcer for this group of patients was 5.5 days in group 1 and 7.5 days in group 2.

For those admitted with a pressure ulcer that did not subsequently deteriorate the respective median length of stay for groups 1 and 2 were 14 days and 11 days respectively. The length of stay was substantially higher for those admitted with a pressure ulcer which deteriorated in hospital (27 days in group 1, 45 days in group 2). The final pathway related to those admitted with a pressure ulcer that went on to develop an additional pressure ulcer during their stay (21 days in group 1, 24 days in group 2). There was a slight discrepancy between the number of patients in group 1 without a pressure ulcer on admission and who subsequently developed one. The Sponsor used the published figure of 46 but the actual number was 48 (personal communication from G.Smith via the Sponsor) but the discrepancy did not make much difference. In the Smith (2010) paper it is stated that the between group differences in median length of stay for each pathway were not significant. This was checked by the EAC and found to be true.

In the model, relevant per day costs were then applied to relevant proportions of weighted stay. These differ for those days spent without a pressure ulcer, where only general hospital costs were incurred, and days with a pressure ulcer. Per-day unit costs for hospital stay are detailed in the next section of this report.

The submission stated that the time horizon was one year, however because of the use of the Smith (2010) data, the model time horizon is thus limited to the inpatient stay of an at risk patient. Costs were estimated on a per patient basis. This was not explicitly represented as potential cost savings over a longer fixed period of time.

There are some limitations to the parameters used in the model, which are a reflection of the quality of data and its use:

- Although length of stay data may be skewed, the EAC would question the validity of using median length of stay in a modelling exercise of this kind. This skew reflects the nature of length of stay as observed in NHS practice; some patients require significantly longer time in hospital. It is hard to assume that these longer lengths of stay constitute outliers. For modelling purposes, an

arithmetic mean would better represent the average length of stay experienced for each of these groups.

- In some instances, the number of patients in each pathway is very low (e.g group2/withPU/ deterioration). The resulting length of stay is likely to be highly uncertain. Whilst it may be important to note the subsequent pathways that patients moved into after developing a pressure ulcer (in terms of deterioration or improvement) from a quality of life perspective, the EAC does not feel there is enough data to use this approach for calculating length of stay and hence costs. Furthermore, there is no distinction in costs made dependent on the condition of the ulcer on discharge, meaning this approach only serves to dilute the length of stay data. A truncated version of the model, removing the branches relating to improving or deteriorating ulcers is presented in section 4.12 and incorporates adjusted mean values to determine effect sizes.

- The EAC would draw particular attention to the quality of the Smith (2010) study, which whilst of illustrative use, does not provide good quality and robust evidence for differences in incidence or length of stay when using Parafricta Bootees and Undergarments. This has been discussed in more detail in section 4.12. The EAC has tried to mitigate for some of the limitations of the case series study design by producing estimates of length of stay adjusting for some of the baseline patient characteristics and then used these in the EAC version of the model.

4.7.5.2 Community model

Input parameters in the community models were extrapolated from the hospital data, based on Smith (2010), to estimate the prevalence of pressure ulcers in the community. The difference between median length of stay when a pressure ulcer has developed and time to develop a pressure ulcer were used as a proxy for pressure ulcer duration. The incidence per at-risk patient (0.25 in the Parafricta group and 0.41 in the standard care group), and the duration, are used to calculate a point prevalence as discussed in the previous section 4.7.4.2.

able 9 Clinical data used in community model

	No Parafricta	Parafricta
Time to develop PU (median)	21	7.5
LOS if developed PU (median)	5.5	17
Duration of PU	15.5	9.5
Incidence per at-risk patient	0.41	0.25
Point prevalence†	6.63	2.38
Prevalence ratio*	0.37	
†(Duration of PU x incidence per at-risk), *(Parafricta prevalence/ no Parafricta prevalence)		

Costs were then estimated based on the cost of a prevalent case for one year and the associated nurse visit resource use. The relative prevalence ratio was then applied to this cost of a year of intervention to estimate the cost when using Parafricta in the community.

The EAC has reproduced the community model using the re-analysed Smith (2010) data in section 4.12.

4.7.6 Resource identification, measurement and valuation

The sponsor did not detail any additional searches to help identify potentially relevant resource use. They highlighted several potential cost savings that have not been estimated in the model: pharmaceuticals usage, complication costs (including infections), which may increase the potential cost savings from avoiding pressure ulcers. They note the involvement of a tissue viability nurse and involvement of health economist in the design of the Smith (2010) study to identify relevant resource use.

The sponsor consulted relevant national tariffs and NHS reference costs.

4.7.6.1 Hospital model

The sponsor stated that treatment episodes for pressure ulcers or damage to frail skin often do not generate a specific reference cost, as the patient has been admitted for another reason. According to the submission, a 2013/14 tariff for a non-severe pressure ulcer requiring day case treatment or admission may be coded as HRG JD03A, B, or C with associated tariffs of £2,622, £1,569 and £908 (NHS 2014).

Consultation with clinical experts by the EAC did suggest that in some instances where a more severe pressure ulcer has developed, it might lead to an admission. We however do not know how many, if any, of the admissions in Smith (2010) were directly attributable to pressure ulcers.

The identification of resource use came from Smith (2010), with some associated unit costs also taken from this study. This included the cost of a bed day (and associated care), dressings and the use of pressure relieving mattresses. Unit costs used in the hospital model are shown in Table 10.

Table 10 Hospital model unit costs

Unit cost	Per day cost	Source
Bed day	£325.00	Sponsor assumption
General dressing	£0.74	Smith (2010)
Average Mattress cost	£0.59†	Smith (2010)
General hospital costs	**£326.33**	(£325 +£0.74 +0.59)
Average PU dressing	**£0.74‡**	Smith (2010)
† (86% mattress @ £0.30, 14% Nimbus @ £2.37), ‡ (70% cat 1 dressing @ £0.48, 25% cat 2 dressing @ 1.11, 5% cat 3 dressing @ £2.59)		

The EAC notes that cost for dressings were taken from 2009 dressing catalogues, but that these were not adjusted for general healthcare inflation. The EAC has updated for inflation (2013/14 prices), but this did not have a substantial effect on cost savings. The cost base for the mattresses was not clear, but assuming it is also from 2009, this had been adjusted for general healthcare inflation to 2013/14 prices. In the submission the sponsor included details of operating procedure codes associated with the reconstruction of a non-healing grade 4 pressure ulcer of the heel (W04.8 and W04.9), and stated that there were other relevant codes for similar procedures of other sites. However, the modelling did not account for potential savings from the avoidance of these procedures. There might be some resource use that has been neglected. (Notably, there are more resource use items in the Dealey (2012) study).

The EAC notes that it appears that dressing costs were being double counted as a general cost and a pressure ulcer specific cost. This is very minor, but had a small impact on cost savings. This has been rectified in the EAC version of the model.

The cost of a bed day was the biggest cost component in the hospital model. The original Smith (2010) study had estimated the cost of a bed day to be £350, which was supplied to the authors by the PCT. Further details of how this cost was estimated are not given in the paper. The Sponsor suggests that NHS reference costs may give an indication of the likely cost associated with an additional day in hospital. The reference cost (2012/13) for an elective excess bed stay was £349 and non-elective excess bed stay £265. A weighted average gives a cost of an excess bed day as £273. The Sponsor stated that the cost per excess bed day in trauma and orthopaedic wards was £277. The Sponsor used £325 as a central assumption, stating that “patients

with pressure ulcers are likely to be more costly because of the time that will be spent assessing and treating the patient's pressure ulcer".

The EAC sought clarification for the justification of the central assumption. The Sponsor specified that an excess bed day would "normally mean a day too long spent in hospital awaiting discharge and hence requiring little nurse intervention time", but that a pressure ulcer would require significantly more nurse intervention.

However, this is not how the EAC understands the definition of an excess bed day. For most interventions, reference costs reflect the total expected costs per episode, fully loaded (staff time, overheads, bed stay). In some instances a patient may however have an extended length of stay, which is sufficiently large that the cost would not be captured by the main HRG. Excess bed days are applicable after a certain trim point. The trim point is defined as the upper quartile length of stay for the HRG plus 1.5 times the inter-quartile range of length of stay. Excess bed days are able to reflect the potential for skew for particular long length of stays. It is therefore very hard to make a judgement about whether or not the average excess bed stay cost would constitute less resource use. If it applies to patients who have been in hospital for a long time, it could reflect the seriousness of their condition and hence be higher. It is not possible to make an assumption about the likely resource use included in excess bed day estimates. The EAC feel that the central assumption of £325 may not be very robust. Alternative costs are presented in section 4.12.

4.7.6.2 Community model

The community model was based solely on the cost of Parafricta garments and potential savings associated with reduced nurse/care visits. The model made the assumption that the patient included in the model had sufficient pressure ulceration to justify a costed time for a specialist nurse or carer. No other resource use was identified as relevant and included in the model.

The unit cost of nurse/carer interventions = £61 (PSSRU, 2013).

In the modelling the cost in the community was a factor of three components:

1. The unit cost of nurse/ carer interventions,
2. The number of interventions that occur per week,
3. The number of weeks these interventions persist.

The model assumed that a prevalent case required 1.86 visits a week for 52 weeks. The 1.86 visits is based on data from Isle of Wight district nursing audit.

Cost savings are therefore a reflection of a prevalent case for a whole year, and do not take account of ulcers healing or time taken to heal.

4.7.7 Technology and comparator costs

4.7.7.1 Hospital model

Parafricta garment = **£35.14**

It was assumed that at any time a patient would have access to six different Parafricta garments in rotation. In the base case it was assumed the six garments can be washed and used by a total of three different successive patients. This may be a conservative estimate, based on experience of users.. These means that, over the product lifetime, garments are being washed twice for re-use. Laundry costs were assumed to be £0.50 /unit. Therefore additional laundry costs were estimated to be £1 per garment.

This led to an effective per patient cost of using Parafricta to be:

Cost of garments per patient = (£35.14 + (0.5*2))*(6/3) = £72.28

4.7.7.2 Community model

Parafricta garments per year = **£80**

It is not clear why this differs from the hospital cost.

4.7.8 Sensitivity analysis

The potential impact of structural uncertainty was not investigated explicitly in the submission. However, the Sponsor stated that face validity had been sought through their clinical advisors, and this was implied by the peer-reviewed nature of the original Smith (2010) modelling, on which the sponsors cost analysis was based. In relation to the community model, the submission indicated that it had been received favourably by reviewers and that the assumptions erred on the conservative side with regards to savings.

The Sponsor conducted a series of probabilistic and deterministic sensitivity analyses to assess the impact of the remaining uncertainty in the models.

4.7.8.1 Hospital model (deterministic sensitivity analysis)

The following parameters were combined in a series of multi way deterministic sensitivity analyses to produce 26 different scenarios (excluding base case):

Table 11. Deterministic sensitivity analysis – Hospital model

Variable	Base case	Sensitivity	Sensitivity range
Hospital general costs	£326	± 25%	244.75- 407.91
Cost of Parafricta	£72.28	±25%	54.21- 90.35
Weighted length of stay no Parafricta	16.2 days	±25%	14.8 - 17.7
Weighted length of stay with Parafricta	13.7 days	±25%	12.5 - 14.9

4.7.8.2 Community model (deterministic sensitivity analysis)

The following parameters were combined in a series of multi-way deterministic sensitivity analysis to produce 20 different scenarios (excluding base case):

Table 12 Deterministic sensitivity analysis – community model

Variable	Base case	Sensitivity	Sensitivity range
Cost of Parafricta	£80	±£40	40-120
At risk to prevalence ratio	3	±1	2-4
Cost of nurse/carer intervention	1.86 * £61 = £113.46	±25%	85.10 – 141.83

An additional six scenarios were run assuming that Parafricta was 50% less effective than assumed in the base case, with the range of cost of Parafricta incorporated:

Prevalence ratio: Base case 0.37 - 50% (0.685)

Given that the submission presented probabilistic sensitivity analysis as well, largely based on arbitrarily assigned confidence intervals, it may have been more useful to present a series on one-way deterministic analysis to see the impact the uncertainty of each individual component may have had.

Whilst the ranges used around the base case values presented a wide array of combinations, the values chosen were all arbitrary and no justification was provided in the Sponsor's submission.

4.7.8.3 Hospital model (probabilistic sensitivity analysis)

Table 13 Probabilistic parameters, CI and distribution – Hospital model

Variable	Mean	99.9% CI	Distribution
Hospital general costs	£326	251.33 – 401.33	Normal
Cost of Parafricta	£72.28	57.28 - 87.28	Normal
Weighted length of stay no Parafricta	16.2	15.4- 17.0	Normal
Weighted length of stay with Parafricta	13.7	13.0 – 14.4	Normal

4.7.8.4 Community model (probabilistic sensitivity analysis)

Table 14 Probabilistic parameters, CI and distribution – community model

Variable	Mean	99.9% CI	Distribution
Cost of Parafricta	£80	40 - 120	Normal
Intervention savings (=1.86*61*52*0.37)	£3,695	2,956-4,434	Normal
Ratio of at-risk to prevalence	3	2-4	Normal

In the probabilistic sensitivity analysis distributions were attached to input parameters. For each of the 500 iterations in the analysis, values were drawn for input parameters from each defined distribution. The calculation of costs for each of the 500 iterations gave a distribution of savings, from which the underlying stochastic uncertainty could be characterised. The submission did not give full details of the distributions attached to each input parameter, but they were presented using information in the computerised model and were as follows:

The submission states that the nurse/ carer unit cost was attached a normal distribution, though this is not strictly what the EAC was able to observe in the model. A normal distribution was attached to the intervention saving per year (which was dependent on both the cost of nurse/carer intervention and the prevalence ratio). The EAC found it hard to disentangle how this had been done.

It is unclear to the EAC what the sponsor's probabilistic sensitivity analysis added to the understanding of uncertainty. Given that all of the distributions were arbitrarily assigned, either based on absolute deviations from a mean value or based on a percentage of the mean value, this analysis only constituted a sophisticated multi-way sensitivity analysis. It incorporated no

information on true stochastic uncertainty associated with input parameters, even for the main parameter of interest for which we do hold information (length of stay). Distributions were also assigned to deterministic cost components for which we hold relatively good information (e.g the cost of a Parafricta garment), which only served to create imposed levels of uncertainty.

The EAC has presented an alternative analysis later in this report (section 4.12), which uses available information on mean length of stay and associated confidence intervals in a more meaningful manner.

4.8 Results of de novo cost analysis

Results are presented separately for the two models in the hospital setting and community setting. The cost saving is relevant per at risk patient (cost of inpatient stay) for the hospital model and per prevalence (annual cost) for the community model.

4.8.1 Base-case analysis results

4.8.1.1 Hospital model

Without Parafricta	= £5,306.76	per at risk patient
With Parafricta	= £4,549.65	per at risk patient
Cost saving	= £757.11	per at risk patient

4.8.1.2 Community model

Without Parafricta	= £5,899.92	per prevalence
With Parafricta	= £2,444.93	per prevalence
Cost saving	= £3,454.99	per prevalence

4.8.2 Sensitivity analysis results

4.8.2.1 Deterministic sensitivity analysis

Over the range of multi-way sensitivity analyses presented by the sponsor model for the hospital setting, Parafricta was cost saving in all cases, except when the median length of stay without Parafricta was reduced by 25% and the median length of stay with Parafricta was increased by 25%. In this scenario of length of stay this was the case across all variations of the hospital costs (£245-£407) and Parafricta costs (£54.21- £90.35), because the median length of stay was slightly higher in the Parafricta group. In these scenarios, use of Parafricta cost approximately £82 to £138 more than not using Parafricta.

The cost savings were greatest when the median length of stay without Parafricta was increased by 25% and the median length of stay with Parafricta was reduced by 25%. Savings were up to £2,000 when combined with the highest hospital costs per day and lowest Parafricta cost. The full range of these scenarios is shown in Figure 3.

This confirms that the modelled cost savings were most sensitive to the length of stay values used.

For the community model the cost savings ranged from approximately £1,500 to £4,500 over the multi-way sensitivity analyses and always favoured the use of Parafricta. This was still the case even when the effectiveness of Parafricta (relative prevalence ratio) was reduced by 50%. The full range of scenarios is shown in Figure 4.

Figure 3. Deterministic sensitivity analysis results - Hospital model

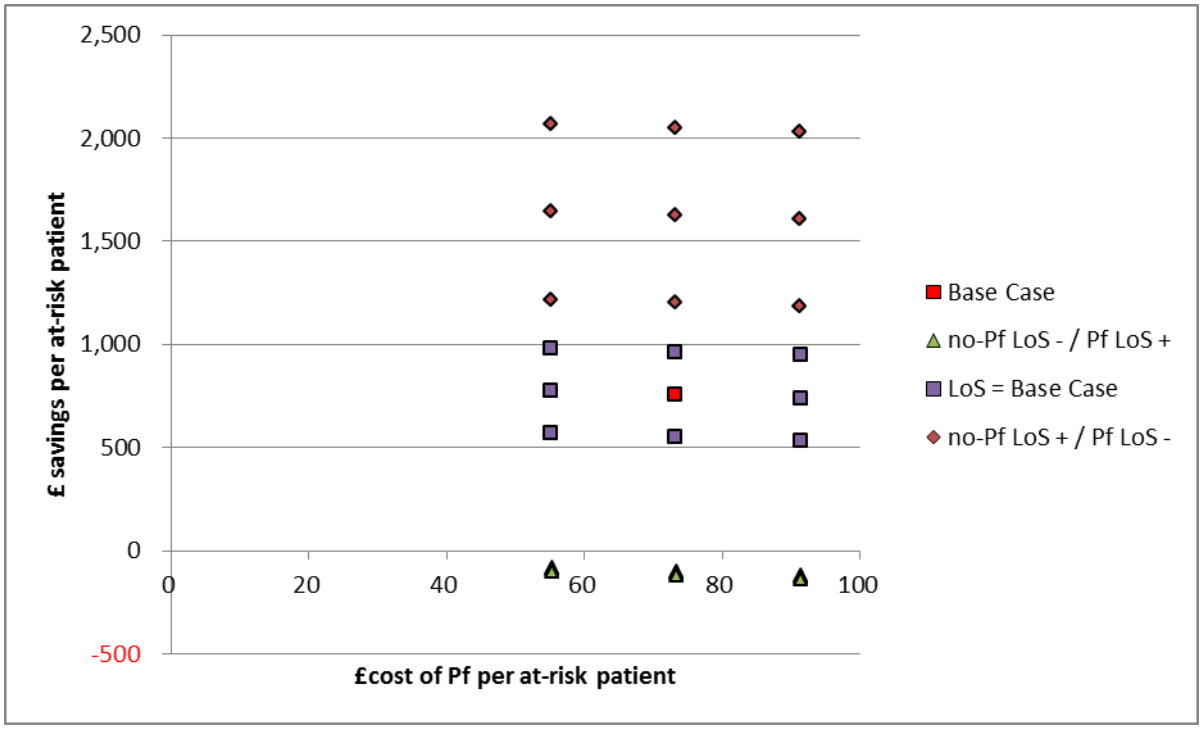
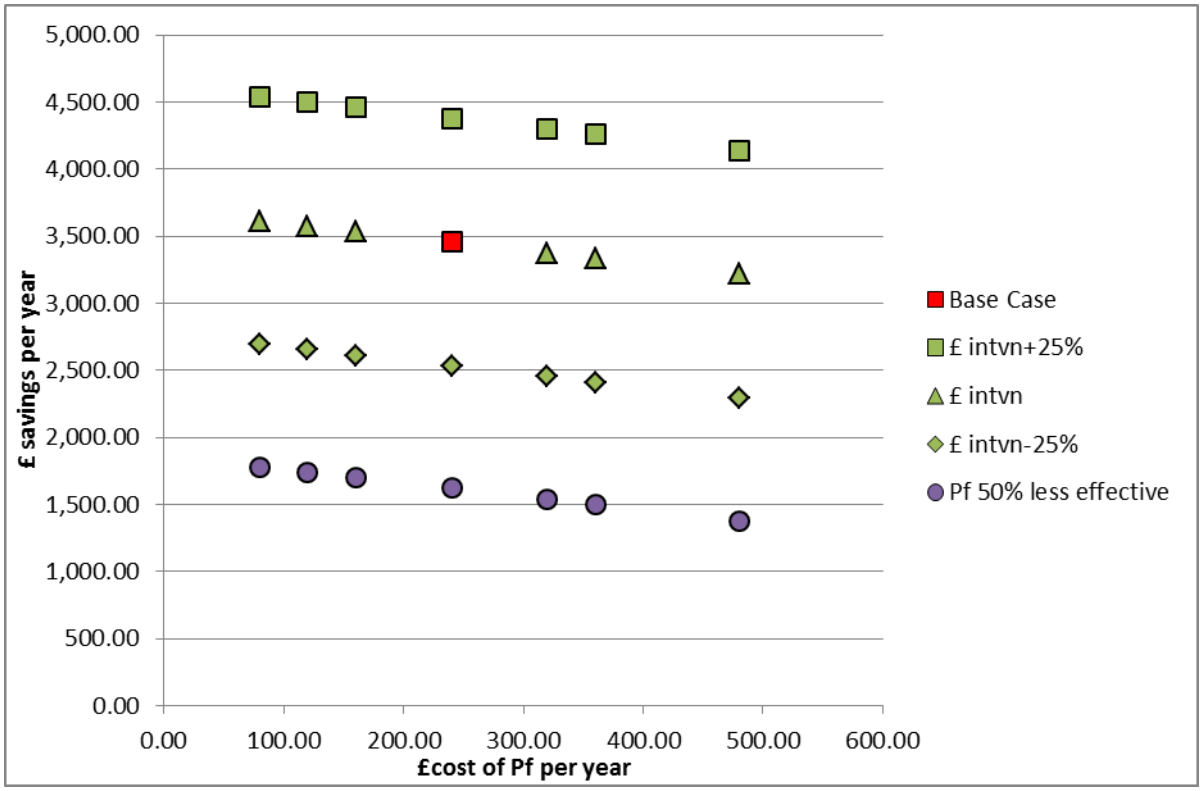


Figure 4. Deterministic sensitivity analysis results - Community model



4.8.2.2 Probabilistic sensitivity analysis

The probabilistic sensitivity analysis produced 500 iterations of cost savings based on sampling from each distributition assigned to input parameters, represented by the clouds in Figure 5 and Figure 6. In the hosptial model , this analysis suggests that there was very little uncertainty, with Parafricta always being cost saving. The same is the case for the community model. It should be noted that the lack of uncertainty is largely down to the imposition of confidence intervals, not based on observed variation in input parameters to define any stochastic uncertainty. Hence this lack of uncertainty in cost savings is not surprising and may not be accurate.

Figure 5. Probabilistic sensitivity analysis results (500 iterations) - Hospital model

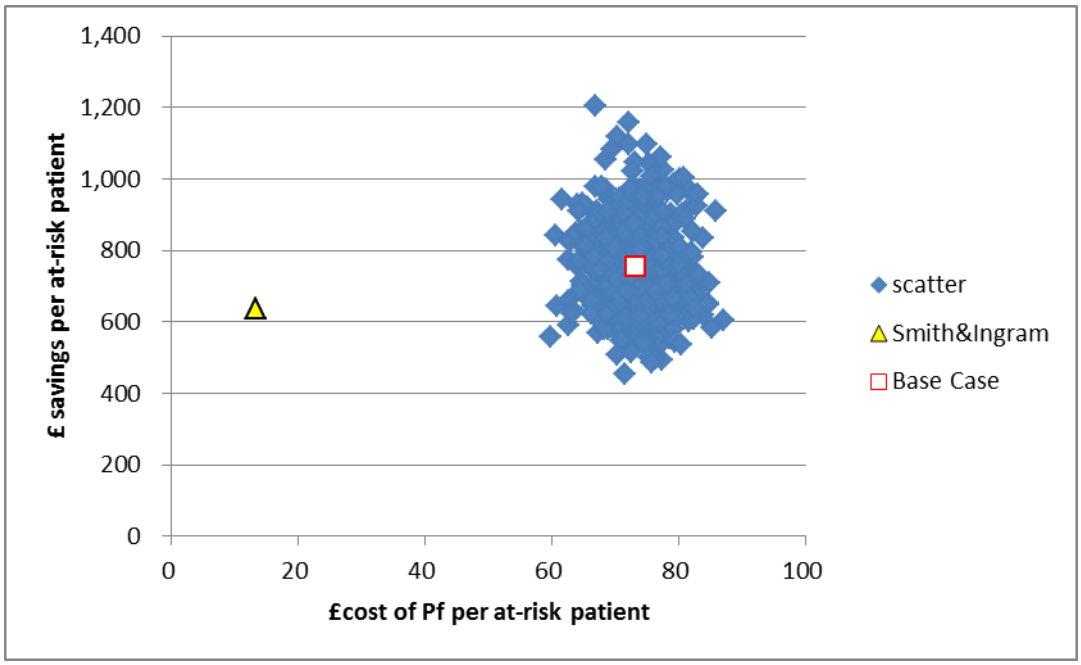
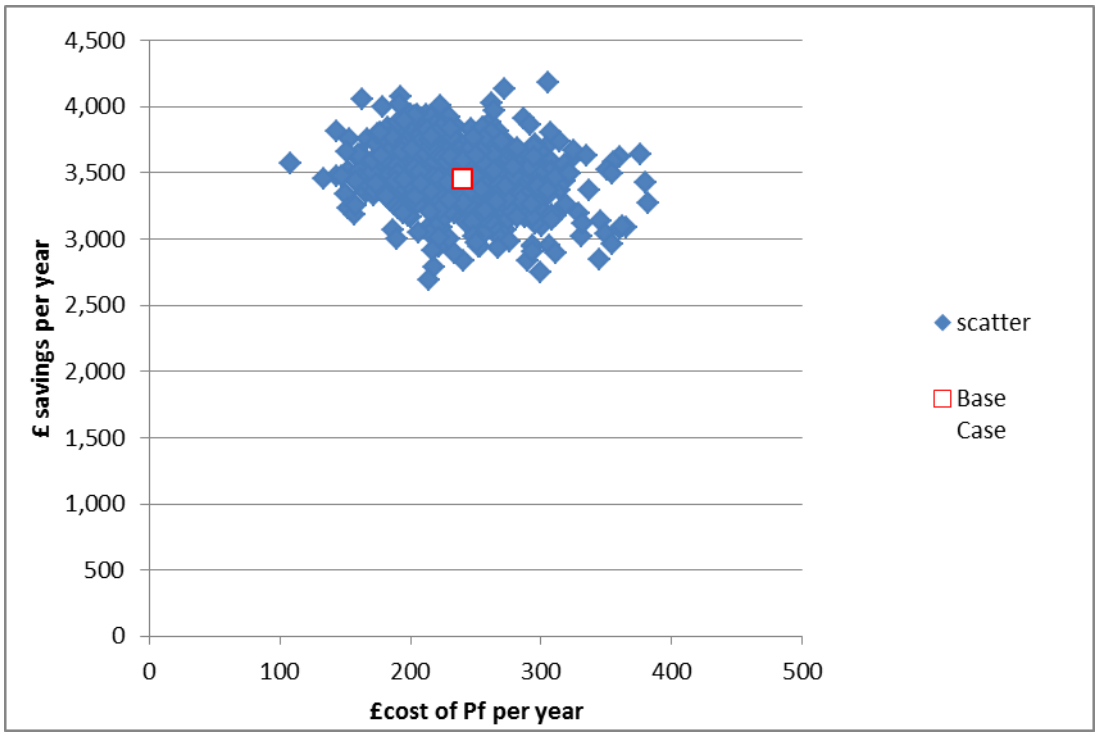


Figure 6. Probabilistic sensitivity analysis results (500 iterations) - Community model



4.9 Subgroup analysis

No subgroup analysis was undertaken. The sponsor noted the relevance of Parafricta use to a wide range of patients who exhibit fragile skin, limited mobility or neurological issues that cause skin breakdown due to repetitive motion or movement. However there is no relevant data sub-dividing this larger population into groups or differentiating the level of benefit from Parafricta use.

4.10 Model validation

The sponsor verified that they were able to reproduce the Smith (2010) cost analysis results with their computerised version of this work. The modelling was operationalised in MS Excel and all cells containing variables were named to facilitate checking.

All code in the modelling was checked independently by the EAC. The EAC ran a series of simple verification checks to assess the model for errors. This involved manipulating parameters and observing the outcomes of modelling, to ensure the model behaved in line with expectations. The series of checks confirmed the computational consistency of the models and showed no specific errors. The following checks were conducted:

Hospital model

- All costs were set to £0 except Parafricta garments and ensured additional costs were equal to cost of Parafricta garments.

- With all other costs set to £0 the number of garments was increased by multiples to ensure consistency.

- The length of stay and incidence data in group 1 was replicated in group 2, to ensure that there were no differences in cost except the use of Parafricta garments, under these parameter inputs.

- Using the same length of stay and incidence data in groups 1 and 2, Parafricta garment and laundry costs were set to £0. The cost of a bed days were increased and equal costs observed.

Community model

- The length of stay and incidence data in group 1 was replicated in group 2, to ensure that there were no differences in cost except the use of Parafricta garments, under these parameter inputs.

- The number of nurse interventions needed for pressure ulcer management was set to 0 and ensured that cost were equal to additional Parafricta garment costs.

Reassured by these simple checks, the EAC then conducted a thorough investigation of each worksheet and cells, to ensure calculations were accurate, and found no errors.

4.11 Interpretation of economic evidence

The Sponsor noted that their results were in line with those published in Smith (2010), the only relevant economic study. One would obviously expect this given the reliance on data form this study. They stated that the cost analysis was generalisable to all NHS setting, given the nature of the data and the two separate models presented. They cautioned that the community model may be less robust than the hospital model, given the lack of data based on this setting. The Sponsors interpreted the results from both hospital and community models to conclude that use of Parafricta was cost-saving.

4.12 Additional work undertaken by the External Assessment Centre in relation to economic evidence

The EAC verified the sponsor's search strategies for economic studies. The EAC produced its own critical appraisal of the Smith (2010) paper on which the sponsor's submission is based (Appendix 3). The EAC validated the sponsor's economic model (section 4.10) and reconstructed decision tree for clarity as well as validity check (Fig 1).

It was necessary for the EAC to reanalyse the Smith data to generate more robust effect sizes that the Sponsors have used. This reanalysis and the results are presented in Appendix 4.

The bed-day costs were revisited. The EAC acknowledges that it is difficult to identify an appropriate per day cost of "hotel stay" alone. Given that the use of Parafricta is intended to reduce length of stay at the margins, excess bed days may be a reasonable proxy. Although the reason for primary admission may be widely heterogeneous, the true cost is that associated with pressure ulcers. As stated by the sponsor there is no specific HRG for pressure ulcers, however other skin disorders do have appropriate codes. Although the exact resource use may differ between skin conditions, this will be more closely aligned with the necessary resource use (nurse time for dressings and assessment) than other conditions contained in the reference costs schedule. The Smith (2010) paper identified that the wards that this at-risk population were treated on were general medical wards and trauma and orthopaedics wards. The EAC therefore used excess bed days, for general medicine ward

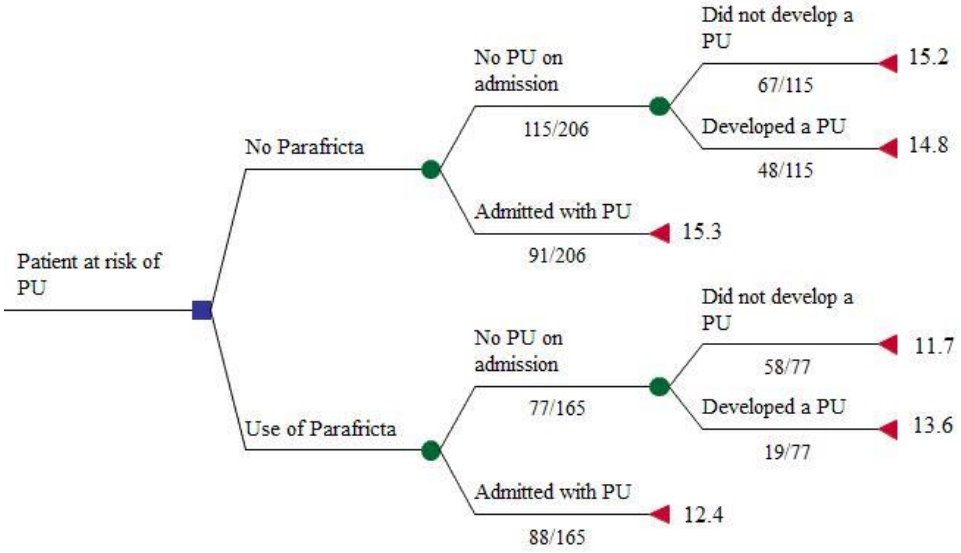
and Trauma and orthopaedic wards, specifically for the gamut of skin disorders (with and without intervention and the whole range of severity) to calculate a weighted cost. The weighted costs are shown in Table 15. It can be seen that the sponsor estimate of £325 may be at the higher end of the bed day cost. The sponsor model did however conduct some sensitivity analysis around this component of the model and in correspondence did acknowledge the uncertain nature of the input. The EAC model uses £234 as the base case and ran a sensitivity analysis of £328 as an upper limit.

Table 15 Excess bed day cost estimates from National reference costs 2012/13

	Type of admission		
Ward	Elective	Non-elective	Weighted
General Medicine	254.2	225.9	226.3
Skin disorders only	510.2†	222.8	225.7
Trauma and Orthopaedics	310.1	265.2	274.7
Skin disorders only	241.2	274.5	271.3
Combined GM and T&O	302.5	236.1	241.1
Skin disorders only	327.5	231.4	**233.9**
†based on a small numbers of cases (281)			

Finally, the EAC version of the economic model was produced by addressing a few issues with sponsor model raised in the previous sections. In particular, unit costs were inflated where relevant, double counting of dressing removed, more robust estimates of cost of bed day used, and a refined version of the treatment pathway that is sensible for data availability used. Most importantly, the refined model used means and confidence intervals adjusted for a few baseline patient characteristics to reflect more robust evidence base. The EAC decision tree is depicted below.

Figure 7 EAC adapted structure of the hospital model



In this model, the following input parameters were used:

- Unit cost bed stay = £234 (£325 in sponsor model)
- Other unit costs (dressing and mattress costs inflated 2012/13 prices)
- Double count of dressing cost removed
- Adjusted means used for all length of stay data (except time to develop) as shown in Appendix 4, with a gamma distribution fitted based on mean and standard error
- Mean time to develop an ulcer used, as estimated in Appendix 4

Results of EAC version of the hospital model

The EAC version of the model estimates the base-case cost savings to be £595, as opposed to the sponsor's estimate of £757 as shown in Table 16. For the one way sensitivity analysis with a bed day costing £328 the costs saving were £863. The probabilistic sensitivity analysis suggested that in nearly 8 out of 10 occasions the use of Parafricta resulted in cost-savings

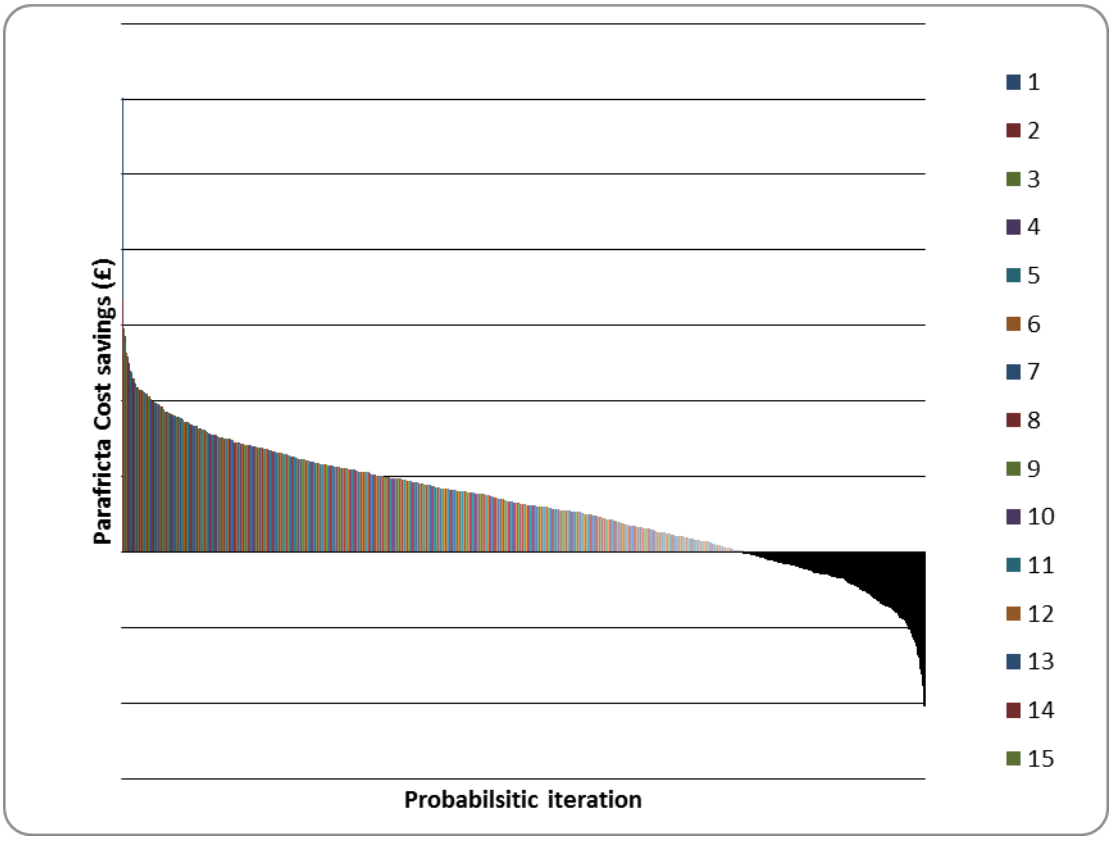
Figure 8 shows the distribution of cost savings from 1000 iterations of the probabilistic model. It shows that the majority of iterations show Parafricta to be cost saving, with the maximum savings around £6,000. However this analysis also shows that the results become more uncertain and there are some iterations where Parafricta adds costs, reflecting the uncertainty in length of stay data from Smith (2010).

Table 16 EAC results of hospital model

Base case cost of bed day = £234	Deterministic	Probabilistic
Without Parafricta	£3,556	£3,818
With Parafricta	£2,960	£3,191
Cost saving	£595	£627
P (Cost saving)	N/A	0.77
Sensitivity analysis with cost of bed day = £328		
Without Parafricta	£4,977	£5,293
With Parafricta	£4,115	£4,373
Cost saving	£863	£920

P (Cost saving)	N/A	0.78

Figure 8 EAC probabilistic sensitivity analyses results (1000 iterations) – Hospital model



Results of EAC community model

The use of adjusted mean length of stay data as shown in Appendix 4 feeds into the community model, in the estimation of a prevalence ratio. No other changes have been made to this modelling. A truly probabilistic analysis incorporating distributions around the time to develop a pressure ulcer and the length of stay was not possible, because a negative value of the duration of ulcer could be encountered during distribution draws. Hence as an illustrative sensitivity analysis the upper and lower limits that have been estimates in Appendix 4 have been used to re-estimate cost savings.

Table 17 EAC community model results

	Cost per prevalent case
Without Parafricta	£5,900
With Parafricta	£3,390
Cost saving	£2,510

The EAC version estimated the cost savings in the community as £2,510per prevalence case, as opposed to £3,455 per prevalence case. The deterministic sensitivity analysis, varying length of stay data based on lower and upper limits of 95% confidence intervals suggested that the cost-savings could be between £2,295 and £2,799.

Table 18 EAC deterministic sensitivity analyses results- community model

	Lower limits	Upper limits
Without Parafricta	£5,900	£5,900
With Parafricta	£3,101	£3,604
Cost saving	£2,799	£2,295

As the EAC work has provided different results, see the 'Impact on the cost difference between the technology and comparator of additional clinical and economic analyses undertaken by the EAC' section.

4.13 Conclusions on the economic evidence

The sponsor's submission relied on a poorly designed (non-randomised) case series study with results unadjusted for confounding, therefore uncertainty in reported effect size is likely as it is not clear whether the intervention and the control groups were similar in the baseline. Unfortunately, this is the only available data available to assess the cost-effectiveness of Parafricta Bootees and Undergarments.

In addition to relying on the use of a poor evidence base, the sponsor model assumptions were not always robust. The use of £325 as the cost for a bed day, use of additional pathways not sensitive to the available data, extrapolation of hospital data to estimate prevalence of pressure ulcers in the community are a few examples.

Despite limitations and use of less robust data, the EAC confirms that the sponsor's conclusion that Parafricta may be cost saving is unaltered- the scale of savings is lower though. However, as the best available data under which such an evaluation can be carried out is subject to significant uncertainty, any estimate based on such data will also risk the same level of uncertainty.

5. Impact on the cost difference between the technology and comparator of additional clinical and economic analyses undertaken by the External Assessment Centre

The difference in the estimates of cost savings between sponsor's submission and the EAC version is reported in Table 19. The EAC models scale the savings down from the sponsor's, both in the hospital and community settings. This reflects the smaller effect size (i.e. length of stays) as well as the lower bed-day costs used in the EAC models.

However, the sponsor's conclusion that Parafricta is cost-saving is unchanged. In the hospital model, probabilistic sensitivity analysis showed that there is nearly an 8 in 10 chance that cost-savings are achievable. In the community model, deterministic sensitivity analysis showed that the cost-savings could be as low as £2,295and as high as £2,799 per prevalent case (per year).

Table 19. Variation in Sponsor and EAC estimates

	Sponsor base case estimate	EAC deterministic estimate	EAC probabilistic estimate
Hospital model	Cost per at risk patient	Cost per at risk patient	Cost per at risk patient
Without Parafricta	£5,307	£3,556	
With Parafricta	£4,550	£2,960	
Cost saving	£757	£595	£627
P (Cost saving)	N/A	N/A	0.77
	Sponsor's base case estimate	EAC base case estimate	EAC sensitivity estimates
Community model	Cost per prevalent case	Cost per prevalent case	Cost per prevalent case (lower-upper)
Without Parafricta	£5,900	£5,900	£5,900-£5900
With Parafricta	£2,445	£3,390	£3,101 - £3,604
Cost saving	£3,455	£2,510	£2,295- £2,799

6. Conclusions

Seven studies were submitted by the sponsor and one clinical audit was also assessed in this report. None of the studies were of high quality – the best evidence being a relatively large case series with historical controls. Parafricta Bootees and Undergarments were compared to UK clinical practice without Parafricta Bootees and Undergarments. There was no evidence submitted where the comparator was sheepskin or other pressure relieving bootees.

There is insufficient evidence to demonstrate that Parafricta Bootees and Undergarments are associated with a decreased incidence, improvement, deterioration or better healing of pressure ulcers compared to no Parafricta, and no information on Parafricta compared to sheepskin or pressure-relieving bootees.

The main development of Parafricta is the material having less friction and shear than standard materials such as bed linen and cotton. However, the evidence suggests that only a small proportion of pressure ulcers are due to this (7.5% to 13.9%) so it in small case series, any differential effects are unlikely to be demonstrated. The largest case series evaluated patients who were unable to reposition so again was unlikely to show any difference. We do not know whether confounding factors, rather than clinical effectiveness of Parafricta Bootees and Undergarments are responsible for any differences observed.

The economic evidence on which the sponsor's submission is based (Smith 2010) is less robust due to non-randomised design and inability to account for confounders. Unfortunately, this remains the only study that can provide data needed to evaluate cost-effectiveness of Parafricta Bootees and Undergarments. While the best use of available low quality evidence suggests that Parafricta Bootees and Undergarments is cost saving, because the evidence base itself is subject to significant uncertainty, the cost-effectiveness modelling is not free from such a problem also. However, the EAC work suggests that there may be nearly an 8 in 10 chance that Parafricta Bootees and Undergarments are cost-saving, at least in the hospital settings.

7. Implications for research

A number of future studies will improve our understanding of the cost-effectiveness of Parafricta garments. First, and most importantly, two good quality randomised controlled trials should be conducted, one on the use of Parafricta Bootees and one on the use of Parafricta Undergarments. For each, the participants should be patients at risk of pressure ulcers caused predominantly by friction and shear. The comparators should be normal NHS hospital practice without Parafricta garments. Outcomes measured should

include pressure ulceration, acceptability, quality of life and costs. These should then be repeated in community care.

Secondly, good quality cohort studies should be conducted in wards where Parafricta Bootees and Undergarments are being used, to check for cross-infection due to the garments being worn by more than one patient and inadequate washing, that has been known to occur in the NHS.

Thirdly, future studies need to ascertain true cost of a hospital bed-day applicable in pressure ulcer care by grade of pressure ulcer.

Fourthly, more good quality research is needed to estimate the prevalence of pressure ulcers in hospital and in the community.

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9. Appendices

Appendix 1. Study designs in clinical research and what they can tell us about effectiveness of interventions.

1. Case series. This follows up a group of patients over time. This can tell us what happens to these patients. If they have had a treatment, it cannot tell us whether any recovery was caused by the treatment because it could have happened anyway. For example if a group of patients had a particular wound dressing and were followed up, this study design cannot be used to tell whether the wound dressing was linked to wound healing.

2. Case-control study. This selects a group of patients with a condition and compares them with controls without the condition and looks back to see whether there are any factors that occurred more or less frequently in the cases compared to the controls. For example, elderly women with hip fractures compared to those not having hip fractures, comparing the rate of taking Hormone Replacement Therapy in the past in cases versus controls, to determine whether taking HRT is linked to fewer hip fractures.

3. Cohort study. This selects a group of individuals, some of whom are exposed to a risk factor for a disease, or a treatment for a disease, and some of whom are not (the control group). Both groups are followed up over time to see whether the exposed group have a higher rate of healing (if it's a treatment) than the non-exposed group. As this study has a control group it can be inferred that the exposure to treatment might be beneficial if the exposed group have a higher rate of healing than the unexposed group. For example in a group of patients, some have a wound dressing and some do not and at follow up the patients exposed to the wound dressing have a higher rate of healing.

4. Randomised controlled trial. This selects a group of individuals, some of whom are randomised to a treatment for a disease (intervention group) and some of whom are not (the control group). The control group may be given a placebo instead or have sham treatment or an alternative treatment. Both groups are followed up over time to see whether the intervention group have a higher rate of healing than the control group. As this study has randomisation and a control group it can be inferred that the exposure to treatment is more likely to be beneficial if the intervention group have a higher rate of healing than the unexposed group. For example if a group of patients are randomised to a wound dressing or not and at follow up the patients with the wound dressing have a higher rate of healing.

Appendix 2. Waterlow scores

The Waterlow pressure ulcer risk assessment/prevention policy tool is the most frequently used system in the UK and is understood and used by nurses dealing directly with patients in hospitals, care homes and residential nursing homes. All assessments and, just as importantly, reassessments must be documented and the plan of care adjusted as necessary, particularly as patients move from one care provider to another. It is however a simplistic tool, and it is the responsibility of assessors to use the risk assessment system and the advice on the selection of preventative aids, in conjunction with their own expertise and their own area of care's specific constraints. One side of the score card illustrates the risk assessment scoring system. The reverse side provides guidance on nursing care, types of preventative aids associated with the three levels of risk status, wound assessment and dressings.

Both sides of the score card are reproduced below.

(NB this scorecard is freely available on the internet at http://www.judy-waterlow.co.uk/the-waterlow-score-card.htm)

WATERLOW PRESSURE ULCER PREVENTION/TREATMENT POLICY

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

BUILD/WEIGHT FOR HEIGHT	◆
AVERAGE BMI = 20-24.9	0
ABOVE AVERAGE BMI = 25-29.9	1
OBESE BMI > 30	2
BELOW AVERAGE BMI < 20	3
BMI=Wt(Kg)/Ht (m)^2	

SKIN TYPE VISUAL RISK AREAS	◆
HEALTHY	0
TISSUE PAPER	1
DRY	1
OEDEMATOUS	1
CLAMMY, PYREXIA	1
DISCOLOURED GRADE 1	2
BROKEN/SPOTS GRADE 2-4	3

SEX AGE	◆
MALE	1
FEMALE	2
14 - 49	1
50 - 64	2
65 - 74	3
75 - 80	4
81 +	5

MALNUTRITION SCREENING TOOL (MST) (Nutrition Vol.15, No.6 1999 - Australia

A - HAS PATIENT LOST WEIGHT RECENTLY
- YES - GO TO B
- NO - GO TO C
- UNSURE - GO TO C AND SCORE 2

B - WEIGHT LOSS SCORE

0.5 - 5kg	= 1
5 - 10kg	= 2
10 - 15kg	= 3
> 15kg	= 4
unsure	= 2

C - PATIENT EATING POORLY OR LACK OF APPETITE
'NO' = 0; 'YES' SCORE = 1

NUTRITION SCORE
If > 2 refer for nutrition assessment / intervention

CONTINENCE	◆
COMPLETE/ CATHETERISED	0
URINE INCONT.	1
FAECAL INCONT.	2
URINARY + FAECAL INCONTINENCE	3

MOBILITY	◆
FULLY	0
RESTLESS/FIDGETY	1
APATHETIC	2
RESTRICTED	3
BEDBOUND e.g. TRACTION	4
CHAIRBOUND e.g. WHEELCHAIR	5

SPECIAL RISKS

TISSUE MALNUTRITION	◆
TERMINAL CACHEXIA	8
MULTIPLE ORGAN FAILURE	8
SINGLE ORGAN FAILURE (RESP, RENAL, CARDIAC,)	5
PERIPHERAL VASCULAR DISEASE	5
ANAEMIA (Hb < 8)	2
SMOKING	1

NEUROLOGICAL DEFICIT	◆
DIABETES, MS, CVA	4-6
MOTOR/SENSORY	4-6
PARAPLEGIA (MAX OF 6)	4-6

MAJOR SURGERY or TRAUMA	
ORTHOPAEDIC/SPINAL	5
ON TABLE > 2 HR#	5
ON TABLE > 6 HR#	8

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

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

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

© J Waterlow 1985 Revised 2005*
Obtainable from the Nook, Stoke Road, Henlade TAUNTON TA3 5LX
* The 2005 revision incorporates the research undertaken by Queensland Health.

www.judy-waterlow.co.uk

REMEMBER TISSUE DAMAGE MAY START PRIOR TO ADMISSION, IN CASUALTY. A SEATED PATIENT IS AT RISK
ASSESSMENT (See Over) IF THE PATIENT FALLS INTO ANY OF THE RISK CATEGORIES, THEN PREVENTATIVE NURSING IS REQUIRED A COMBINATION OF GOOD NURSING TECHNIQUES AND PREVENTATIVE AIDS WILL BE NECESSARY
ALL ACTIONS MUST BE DOCUMENTED

PREVENTION

PRESSURE REDUCING AIDS

Special Mattress/beds:	10+ Overlays or specialist foam mattresses. 15+ Alternating pressure overlays, mattresses and bed systems 20+ Bed systems: Fluidised bead, low air loss and alternating pressure mattresses Note: Preventative aids cover a wide spectrum of specialist features. Efficacy should be judged, if possible, on the basis of independent evidence.
Cushions:	No person should sit in a wheelchair without some form of cushioning. If nothing else is available - use the person's own pillow. (Consider infection risk) 10+ 100mm foam cushion 15+ Specialist Gell and/or foam cushion 20+ Specialised cushion, adjustable to individual person.
Bed clothing:	Avoid plastic draw sheets, inco pads and tightly tucked in sheet/sheet covers, especially when using specialist bed and mattress overlay systems Use duvet - plus vapour permeable membrane.

NURSING CARE

General	HAND WASHING, frequent changes of position, lying, sitting. Use of pillows
Pain	Appropriate pain control
Nutrition	High protein, vitamins and minerals
Patient Handling	Correct lifting technique - hoists - monkey poles Transfer devices
Patient Comfort Aids	Real Sheepskin - bed cradle
Operating Table Theatre/A&E Trolley	100mm(4ins) cover plus adequate protection
Skin Care	General hygene, NO rubbing, cover with an appropriate dressing

WOUND GUIDELINES

Assessment	odour, exudate, measure/photograph position

WOUND CLASSIFICATION - EPUAP

GRADE 1	Discolouration of intact skin not affected by light finger pressure (non-blanching erythema) This may be difficult to identify in darkly pigmented skin
GRADE 2	Partial thickness skin loss or damage involving epidermis and/or dermis The pressure ulcer is superficial and presents clinically as an abrasion, blister or shallow crater
GRADE 3	Full thickness skin loss involving damage of subcutaneous tissue but not extending to the underlying fascia The pressure ulcer presents clinically as a deep crater with or without undermining of adjacent tissue
GRADE 4	Full thickness skin loss with extensive destruction and necrosis extending to underlying tissue.
Dressing Guide	Use Local dressings formulary and/or www.worldwidewounds

IF TREATMENT IS REQUIRED, FIRST REMOVE PRESSURE

Appendix 3. EAC's Critical Appraisal – Smith (2010)

The paper aimed to estimate the effectiveness of Parafricta Bootees and Undergarment in reducing the incidence and prevalence of pressure ulceration for patients at risk of developing a pressure ulcer (defined as those with a Waterlow score of ≥15). This study is a cost-consequence analysis and the main economic metric reported is the cost-savings attributable to the use of Parafricta garments.

The design is a case-series in which 165 patients who wore Parafricta Bootees and Undergarments were compared with a historical cohort of 204 patients who did not wear them. Both groups of patients received the same standard care (i.e use of pressure reducing devices), except that the group with 165 patients also used Parafricta garments. On admission, the patients might or might not have had one or more pressure ulcers but importantly they were unable to reposition themselves independently. It is not clear however that the two groups of patients were similar enough to be able to detect the true effect of the use of Parafricta garments.

The cost-consequence analysis used the data from 6-month follow up (3 months each for each group). The authors do not report perspectives but the cost-ingredients used in the estimates suggest that the perspectives are from the NHS.

The main assumption underlying the cost-consequence analysis is that developing a new or deterioration of an existing pressure ulcer will result in longer hospital stay. The groups of patients considered in the treatment pathways are: patients with pressure ulcers at hospital admission, who developed additional ulcers or did not develop one and those without pressure ulcer on admission, who did not develop any or developed new ulcers. The analysis uses median, instead of mean, length of stay in each treatment pathway.

Three main cost categories- bed stay, dressings, and pressure reducing devices – are reported. The data were sourced from the finance department of Isle of Wight Primary Care Trust. The average cost of stay was used as the basis of bed day costs. The 2009 dressing audit data was used to estimate dressing costs and the cost of the most common high specification foam mattress was used for costs of pressure reducing devices.

Uncertainty was assessed by using 95% confidence intervals around incidence rates and length of stay.

The paper estimated a statistically significant 16% difference in the incidence of pressure ulcers between the two groups. Costs were calculated for each treatment pathway and it was estimated that Parafricta Bootees and Undergarments could save more than £63,000 per 100 at-risk patients.

The authors concluded that the Parafricta garments appeared to produce better patient outcomes and cost savings.

ERC critique:

This is a non-randomised study and therefore the comparability of the groups at baseline is questionable, given that no supporting evidence is presented. It is not clear if any adjustments were made for confounding between the two group of patients. Not accounting for any confounders makes the effectiveness estimate comparisons subject to significant uncertainty. The use of weighted median, instead of mean, length of stay in the cost model is not convincing. No quality of life effect was taken into consideration, given that the patients were unable to reposition themselves independently. Very little information was provided as to how the unit costs data were estimated and they all came from one Primary Care Trust, making it hard to justify their generalisability. The paper does not adequately report the methods of the economic evaluation; neither does it attempt to combine costs and effectiveness, ending up as a cost-consequence analysis. The sensitivity analysis is limited. A major weakness of the study is that the authors did not control for differences between the groups before and during the treatment period (which they acknowledge as a limitation of the study).

Therefore, the authors conclusion that Parafricta Bootees and Undergarments are cost-savings need to be interpreted with caution, as the estimates are subject to significant uncertainty. Any further work based on this evidence will need to address uncertainty fully.

Appendix 4: Reanalysis of Smith data

Reanalysis of Smith (2010) data

The sponsor had access to the original data from Smith (2010) paper and this was provided to the EAC. The EAC reanalysed this data to estimate some additional input parameters for the EAC version of the costing model. The data had a limited number of confounders: patient's gender, Waterlow score and the ward that the patient was admitted to. These variables are used to estimate an adjusted effect size. The effect size was defined as the difference in length of stay between those using Parafricta plus standard care and those using standard care only.

Table 20: Reanalysis of Smith (2010) data by the EAC

Waterlow score	Para	No-Para
15-19	103 (50.0)	94 (57.3)
20-24	82 (39.8)	51 (31.1)
25+	21 (10.2)	19 (11.6)
Total	206 (100)	164 (100)

1 missing value. Chi2 (2)=3.0079, p-value=0.22

The bivariate reanalysis suggests that waterlow scores did not differ between the Parafricta and no-Parafricta group. The evidence is “indicative” of the risk profile being comparable between the two groups (indicative because it is based on just the bivariate relationship). However, for the economic model, it is important to consider the main outcome (length of stay) and whether the group’s waterlow score profile would have any impact on the outcome, allowing for other potential confounders. We still lack full information to adequately adjust for all potential confounders.

The length of stay data was skewed. Therefore, they were transformed to logarithmic scale before regressing length of stay on Parafricta (1/0), gender (male/female), Waterlow score (medium/high risk) and location (medical1/medical2/orthopaedic ward). This model was subject to rigorous diagnostic tests. The model coefficients were then used to predict the log of length of stays for all branches in the decision tree. These log-values were then converted to length of stay values.

The results are as follows:

Variables	Coefficient	Std. Err.	t	P>t	[95% Conf.	Interval]
Parafricta	-.180816	.085926	-2.10	0.036	-.3498089	-.0118231
Male	.0275794	.0910947	0.30	0.762	-.151579	.2067378
Medical2	-.0962274	.0962211	-1.00	0.318	-.2854679	.0930131
Orthopaedic	.4834872	.2059539	2.35	0.019	.0784322	.8885421
Waterlow 20+	.1945194	.0861253	2.26	0.025	.0251345	.3639043
Constant	2.632679	.0995199	26.45	0.000	2.43695	2.828407

Number of obs = 358; F(5, 352) = 3.68; Prob > F = 0.0029; Adjusted R-squared = 0.0362. The model passes normality test, specification test and heteroskedasticity test.

Based on this model, the effect size (i.e. different in average lengths of stay) is: 2.47 days (14.935 days minus 12.465 days as obtained by predicting log of LOS for parafricta and non-parafricta groups to attain the difference in log (LOS) of 0.1808 (= coefficient value). The coefficient is significant at 5% level.

The EAC used this model to predict lengths of stay for the branches in the decision tree for economic modelling, to better reflect differences in length of stay in Parafricta and no Parafricta groups.

Table 21 Effect size based on re-analysis

Group	Raw values						Predicted values *			
	Mean LOS	sd LOS	se LOS	median LOS			Mean (LOS)	se	LL	UL
No Para	20.31	18.95	1.34	14			14.94	1.06	13.34	16.72
Para	16.27	12.5	0.98	13			12.47	1.07	10.99	14.13
Difference	**4.05**		**1.72**	**1**			**2.47**			
p-value	0.019			0.076						
LOS- Length of stay; sd= standard deviation; se=standard error; LL =95% lower confidence limit; UL= 95% upper confidence limit										

Table 22 Summary values for all branches in the decision tree

						n	Probability (pathway)	effective n (non-missing LOS)	mean LOS	Standard deviation LOS	median LOS
Patient at risk of PU						**371**					
	No Parafricta					206	0.56	201	20.31	18.95	14
		No PU on admissions				115	0.56	110	19.46	20.05	12.5
			Did not develop PU			67	0.58	63	12.98	11.78	10
			Developed PU			48	0.42	47	28.13	25.13	21
				PU improved		16	0.33	16	32.41	31.44	23
				PU stayed same or deteriorated		32	0.67	26	25.65	22.19	16
		Admitted with PU				91	0.44	91	21.35	17.57	18
			Did not develop additional PU			67	0.74	67	20.18	19.42	15
				Existing PU stayed same or improved		49	0.73	49	15.33	10.49	14
				Existing PU deteriorated		18	0.27	18	33.39	30.01	25.5
			Developed additional PU			24	0.26	24	24.63	10.53	20.5
	Parafricta					165	0.44	164	16.27	12.5	13
		No PU on admissions				77	0.47	76	15.37	10.84	14
			Did not develop PU			58	0.75	57	13.14	10.02	11
			Developed PU			19	0.25	19	22.05	10.68	17
				PU improved		14	0.74	14	24.36	11.44	20
				PU stayed same or deteriorated		5	0.26	3	15.33	5.77	12

		Admitted with PU				88	0.53	88	17.05	13.79	12
			Did not develop additional PU			73	0.83	73	15.25	12.8	11
				Existing PU stayed same or improved		69	0.95	69	13.9	10.9	11
				Existing PU deteriorated		4	0.05	4	38.5	21.89	45
			Developed additional PU			15	0.17	15	25.8	15.46	24
LOS=length of stay, PU = pressure ulcer											

Table 23 Adjusted effect size for all branches in the decision tree

Patient at risk of PU (total n=371)						N		Predicted values: Log of LoS					Predicted values: LoS			
							N (non missing LOS)	mean	se	LL	UL		mean	se	LL	UL
	No Parafricta					206	201	2.7037	0.05736	2.59093	2.81656		14.93549	1.059037	13.34217	16.719
		No PU on admissions				115	110	2.70948	0.059868	2.59174	2.82723		15.02146	1.061696	13.35299	16.898
			Did not develop PU			67	63	2.72154	0.06066	2.60224	2.84084		15.20372	1.062538	13.49393	17.130
			Developed PU			48	47	2.69265	0.062724	2.56929	2.81601		14.77077	1.064733	13.05655	16.710
				PU improved		16	16	2.67079	0.061269	2.55029	2.79129		14.45138	1.063185	12.81082	16.302
				PU stayed same or deteriorated		32	26	2.69132	0.062186	2.56902	2.81363		14.75113	1.06416	13.05303	16.670
		Admitted with PU				91	91	2.72482	0.059945	2.60693	2.84272		15.25367	1.061778	13.55737	17.162
			Did not develop additional PU			67	67	2.71898	0.058788	2.60336	2.8346		15.16485	1.06055	13.50905	17.023
				Existing PU stayed same or improved		49	49	2.70555	0.060001	2.58754	2.82355		14.96254	1.061838	13.29702	16.836

				Existing PU deteriorated		18	18	2.75555	0.059228	2.63906	2.87203		15.72969	1.061017	14.00004	17.672
			Developed additional PU			24	24	2.74114	0.070427	2.60263	2.87965		15.50465	1.072966	13.49919	17.808
	Parafricta					165	164	2.52293	0.063872	2.39731	2.64855		12.46507	1.065956	10.99356	14.133
		No PU on admissions				77	76	2.49519	0.065565	2.36624	2.62414		12.12404	1.067762	10.65725	13.792
			Did not develop PU			58	57	2.45755	0.066021	2.3277	2.58739		11.67617	1.068249	10.25433	13.295
			Developed PU			19	19	2.60811	0.076859	2.45695	2.75928		13.57337	1.07989	11.66917	15.788
				PU improved		14	14	2.62993	0.08877	2.45534	2.80451		13.8728	1.092829	11.65039	16.518
				PU stayed same or deteriorated		5	3	2.57773	0.098716	2.38359	2.77188		13.16721	1.103753	10.84376	15.988
		Admitted with PU				88	88	2.51759	0.065154	2.38945	2.64573		12.39868	1.067323	10.90749	14.093
			Did not develop additional PU			73	73	2.51235	0.064726	2.38505	2.63965		12.33388	1.066867	10.85961	14.008
				Existing PU stayed same or improved		69	69	2.50136	0.064921	2.37367	2.62904		12.19907	1.067075	10.73672	13.860
				Existing PU deteriorated		4	4	2.70198	0.095765	2.51363	2.89032		14.90922	1.1005	12.34968	17.999
			Developed additional PU			15	15	2.54309	0.069075	2.40724	2.67894		12.71891	1.071517	11.10327	14.569

LOS- Length of stay; sd= standard deviation; se=standard error; LL =95% lower confidence limit; UL= 95% upper confidence limit