NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical Technologies Evaluation Programme

Sponsor submission of evidence:

Evaluation title: Debrisoft monofilament debridement pad for the debridement of acute and chronic wounds

Sponsor: Activa Healthcare Ltd

Date sections A and B submitted: 26rd July 2013

Date section C submitted: 19th August 2013

August 2011

Contents

Instructions for sponsors

This is the template for submission of evidence to the National Institute for Health and Care Excellence (NICE) as part of the Medical Technologies Evaluation Programme process for developing NICE medical technologies guidance. Use of the submission template is mandatory.

The purpose of the submission is for the sponsor to collate, analyse and present all relevant evidence that supports the case for adoption of the technology into the NHS in England, within the scope defined by NICE. Failure to comply with the submission template and instructions could mean that the NICE cannot issue recommendations on use of the technology.

The submission should be completed after reading the 'Medical Technologies Evaluation Programme Methods guide' and the 'Medical Technologies Evaluation Programme Process guide' available at www.nice.org.uk/mt. After submission to, and acceptance by, NICE, the submission will be critically appraised by an External Assessment Centre appointed by NICE.

Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence'). When data are 'commercial in confidence' or 'academic in confidence', it is the sponsor's responsibility to highlight such data clearly. For further information on disclosure of information, submitting cost models and equality issues, users should see section 11 of this document 'Related procedures for evidence submission'.

The submission should be concise and informative. The main body of the submission should not exceed 100 pages (excluding the pages covered by the template and appendices). The submission should be sent to NICE electronically in Word or a compatible format, not as a PDF file.

The submission must be a stand-alone document. Additional appendices may only be used for supplementary explanatory information that exceeds the level

of detail requested, but that is considered to be relevant to the case for adoption. Appendices will not normally be presented to the Medical Technologies Advisory Committee when developing its recommendations. Any additional appendices should be clearly referenced in the body of the submission. Appendices should not be used for core information that has been requested in the specification. For example, it is not acceptable to attach a key study as an appendix and to complete the economic evidence section with 'see appendix X'.

All studies and data included in the submission must be referenced. Identify studies by the first author or trial ID, rather than by relying on numerical referencing alone (for example, 'Trial 123/Jones et al.[126], rather than 'one trial[126]').Please use a recognised referencing style, such as Harvard or Vancouver.

The sponsor should provide a PDF copy of all studies included in the submission. For unpublished studies for which a manuscript is not available, provide a structured abstract about future journal publication. If a structured abstract is not available, the sponsor must provide a statement from the authors to verify the data provided.

If a submission is based on preliminary regulatory recommendations, the sponsor must advise NICE immediately of any variation between the preliminary and final approval.

Document key

Boxed text with a grey background provides specific and/or important guidance for that section. This should not be removed.

The user should enter text at the point marked 'Response' or in the tables as appropriate. 'Response' text may be deleted.

List of tables and figures

Please include a list of all tables and figures here with page references.

Glossary of terms

If a glossary of terms is required to inform the submission of evidence include in the table. Delete if not required.

Term	Definition
Hyperkeratosis	A build up of dead epithelial cells, wound debris and product residue
Necrosis	Dead blackened tissue also termed devitalised tissue and may exist as hard black eschar or fragmented areas
Slough	Devitalised tissue consisting of dead tissue and bacteria. This may present as yellow, grey or green tissue of varying consistency and fluid content. It may be fixed or free floating.
Debridement	The removal of devitalised tissue

Section A – Decision problem

Section A describes the decision problem, the technology and its clinical context. There is also information about ongoing studies, regulatory information and equality issues.

Sponsors should submit section A before the full submission (for details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

1 Statement of the decision problem

The decision problem is specified in the final scope issued by NICE. The decision problem states the key parameters that should be addressed by the information in the evidence submission. All statements should be evidence based and directly relevant to the decision problem.

Table A1 Statement of the decision problem

	Scope issued by NICE	Variation from scope	Rationale for variation
Population	People (adults or children of any age) requiring debridement of an acute or chronic wound by a healthcare professional in a community-based setting. The chronic or acute wounds could be open (non-intact skin) or closed (intact skin). Wound types are likely to include: - Chronic - lymphoedema - pressure ulcers - leg ulcers - diabetic foot ulcers - Acute (and subacute) – surgical or trauma - burns - dehisced - haematomas (in acute wounds)	The healthcare professional could include a podiatrist or a doctor	Clinical evidence shows that debridement is carried out by members of the multi-disciplinary team and not just nurses.
Intervention	Debrisoft single use pad	Debrisoft monofilament for debridement pad for debridement of acute and chronic wounds	To use the correct name and standardise terminology in all documents
Comparator(s)	The comparator is likely to vary by wound type and is expected to include irrigating the wound with saline and : - using hydrogel or other autolytic dressing or - cleansing with gauze (see also 'Cost analysis' below)	Add larvae to the list of comparators	Clinical evidence for Debrisoft shows effective use of Debrisoft compared with larvae

Outcomes	The outcome measures to consider include: □ quality of life □ pain and discomfort for the patient when debriding the wound □ wound malodour □ time-to-complete debridement (not necessarily complete healing) □ time-to-healing □ wound infection/cellulitis □ the number of healthcare professional (nurse) visits for each patient □ the frequency of healthcare professional (nurse) visits for each patient □ the duration of each visit by the healthcare professional (nurse) for each patient □ the number of debridements required □ the number of dressings required to dress the wound □ the type of dressings required to dress the wound □ the need to refer to a Tissue Viability Nurse or Hospital specialist clinic □ the need to escalate to other debridement methods. E.g. surgical debridement □ device-related adverse events including non-selective trauma to healthy surrounding tissue or bleeding.	Any healthcare professional to be included as care giver	The healthcare professional may not necessarily be a nurse
Cost analysis	Comparator(s): Complete debridement of all the different types of wound (including open and closed chronic and acute wounds) should be considered. The individual comparators are likely to vary by wound type and are expected to include irrigating the wound with saline and - using hydrogel or other autolytic dressing or - cleansing with gauze Costs will be considered from an NHS and personal social services perspective.	To be updated when the cost analysis is due	Cost analysis to be submitted later

	The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.		
Subgroups to be considered	People (adults or children - with no age limit) with closed acute or chronic wounds where the skin is intact (including people with lymphoedema and hyperkeratotic skin). □ People (adults or children - with no age limit) with open acute or chronic wounds where the skin is non-intact (including haematoma).		
Special considerations, including issues related to equality	It should be noted that people with chronic wounds 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 and 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.		

2 Description of technology under assessment

2.1 Give the brand name, approved name and details of any different versions of the same device.

Debrisoft monofilament debridement pad for the debridement of acute and chronic wounds

All different versions/prototypes of the technology listed here must be CE marked or have equivalent UK regulatory approval.

2.2 What is the principal mechanism of action of the technology?

The moistened pad is applied to the skin and / or wound using gentle pressure and a circular motion or strokes. The specially cut fibres effectively and rapidly remove devitalised tissue (slough, necrosis and hyperkeratosis), keeping the debris in the fibres and away from the skin and / or wound. The process takes on average 2-4 minutes and analgesia should not normally be required before, during and after the procedure (Haemerle et al 2011[1]).However the process may take longer and require several episodes depending on the type and extent of devitalised tissue.

3 Clinical context

3.1 Provide a brief overview of the disease or condition for which the technology is being considered in the scope issued by NICE.

Until May 2013, no guidelines existed on debridement and the condition was ill-defined with no data available. Methods of debridement are varied with no standardised practice.

The European Wound Management Association published a document on debridement and recommended that as debridement is a central part of wound management all wound types should be debrided. There are no data on the numbers of wounds with devitalised tissue. (Strohal R, Apelquist J, Dissemond J, et al

2013[47]). *However, some wounds should not be debrided by any mechanism and this is explained later.*

The disease or condition for which the technology is being considered in the scope must include an estimate of prevalence and/or incidence for the benefitting population. All estimates must be referenced.

3.2 Give details of any relevant NICE or other national guidance or expert guidelines for the condition for which the technology is being used. Specify whether the guidance identifies specific subgroups and make any recommendations for their treatment. If available, these should be UK based guidelines.

The EWMA Debridement Document referred to in 3.1 was authored by international experts and the monofilament pad is listed in a separate section on Page 12. The monofilament pad is positioned as quick and easy to use causing little to no pain to the patient.

The UK Consensus Document on Debridement provides guidelines for practice in a changing NHS and included multidisciplinary experts from across the UK. (Effective debridement 2013[48] available from www.wounds-uk.com). The document recommends that debridement is an integral part of all wound care. Autolytic debridement with dressings is described as overused and it is suggested that other more active forms may be needed to speed up the process and optimise wound healing. The document states that non-viable tissue can impede healing, reduce the effectiveness of topical treatments, mask the signs of infection, promote septic inflammation, obscure assessment by the practitioner and lead to excess exudate that may be harmful to wound healing. Therefore devitalised tissue should be removed as quickly as possible. Whilst chronic wounds are most likely to develop necrotic and sloughy tissue and would benefit from debridement, acute wounds may also need debridement to remove foreign matter and debris. Both might need initial and maintenance debridement if full debridement is not

achieved in one treatment episode. This would depend on the clinical situation.

The debridement method should be selected based on the amount and type of devitalised tissue, type of wound and speed with which impediments to wound healing need to be removed. It is also recommended that the debridement should consider patient choice. Debrisoft is positioned as a selective, easy to use, quick and effective method of debridement that can even be used by patients under supervision and involving patients in their care. Debridement is contraindicated by any method on wounds and digits in the presence of critical ischemia.

3.3 Describe the clinical pathway of care that includes the proposed use of the technology.

The clinical pathway as described in the above mentioned UK Consensus Document should begin by assessing the wound and the patient, decision on debridement and treatment goals, discussion with the patient, consultation with or referral to the multidisciplinary team, debridement if indicated using the most appropriate method for the wound, skin, condition and the patient. Reassessment is an important stage to determine effectiveness of the intervention and decide follow on care.

The consensus document lists all debridement methods including autolytic debridement, Debrisoft and larvae that may be used by generalist nurses. Other methods of debridement such as hydrosurgery, sharp and surgical debridement are listed for use by specialists. Debrisoft may also be used by specialists in conjunction with or instead of specialist methods (Green M 2011[9]; Stoffels I et al 2012[38]). Where surgical debridement may be too painful even under local anaesthesia and general anaesthesia is not advised, Debrisoft has been used with minimal pain to the patient (Weindorf and Dissemond 2012[29]).

If a relevant NICE clinical guideline has been published, the clinical pathway of care should be consistent with the NICE guideline and described. If relevant, this should include comparator technologies.

3.4 Describe any issues relating to current clinical practice, including any uncertainty about best practice.

As the consensus documents highlight, there have been no guidelines until 2013 and debridement practices vary according to tradition, ritualistic practice, levels of knowledge and training. Autolytic debridement can be slow and larvae treatment requires forward planning and delays whilst waiting for despatch (Johnson S et al 2012[44]). In many cases there has been no debridement as previous practice as debridement was not common practice, hence the lack of comparators in the literature. No debridement would have been standard practice.

If the clinical pathway of care described in response to question 3.3 is not consistent with the relevant NICE clinical guideline, this should be explained in response to question 3.4.

3.5 Describe the new pathway of care incorporating the new technology that would exist if the technology was adopted by the NHS in England.

The new pathway:

Assessment of the skin, wound and patient

Offer the patient a choice of debridement following discussion of treatment options

Debridement using Debrisoft with no or minimal analgesia required. Debridement should be completed within minutes in a single episode. This is quicker in other forms of debridement such as larvae (Hawkins K 2012[19]).

However subsequent debridement episodes may be required for more persistent devitalised tissue.

Referral and / or follow on treatment as the wound, skin and condition require

Reassessment to evaluate the effectiveness of treatment.

3.6 Describe any changes to the way current services are organised or delivered as a result of introducing the technology.

The new pathway would be a simpler and more rapid treatment than autolytic or larval debridement (Hawkins 2012[19]) and could be implemented by generalists and in some cases, patients under supervision in the community, involving patients in their own care (Whitaker J 2012[10])

3.7 Describe any additional tests or investigations needed for selecting or monitoring patients, or particular administration requirements, associated with using this technology that are over and above usual clinical practice.

No extra tests would be required.

3.8 Describe any additional facilities, technologies or infrastructure that need to be used alongside the technology under evaluation for the claimed benefits to be realised.

No additional facilities are required with the technology (Stephen-Haynes and Callaghan 2012[3]).Training in the use of the product is based on the simple instructions for use. Follow on treatment of the skin and wound may include the use of emollients, dressings and compression therapy as the condition requires to take the wound to full healing.

3.9 Describe any tests, investigations, interventions, facilities or technologies that would no longer be needed with using this technology.

Additional dressing facilities associated with autolytic debridement, or additional training associated with larval therapy may no longer be required for use by generalist nurses in the community.

Describe how the NHS in England can disinvest from tests, investigations, interventions, facilities or technologies described in section 3.9 that would no longer be needed with using this technology.

Debridement episodes may be reduced as result of using Debrisoft and referrals to specialists could be minimised (Johnson et al 2012[44]). It is possible that the use of specialist community treatments such as sharp debridement may be reduced. In some cases referrals to specialist hospital services for treatments such as surgical debridement or hydrotherapy may be reduced as a result of using Debrisoft in the first instance.

4 Regulatory information

4.1 Provide PDF copies of the following documents:

- Instructions for use
- CE mark certificate or equivalent UK regulatory approval such as EC declaration of conformity
- Quality systems (ISO 13485) certificate (if required).

PDF copies of these documents should be submitted at the same time as section A.

4.2 Does the technology have CE mark for the indication(s) specified in the scope issued by NICE? If so, give the date that authorisation was received. If not, state current UK regulatory status, with

relevant dates (for example, date of application and/or expected approval dates).

Yes 09.12.09

4.3 Does the technology have regulatory approval outside the UK? If so, please provide details.

Yes, the technology has regulatory approval in Germany, the Netherlands, and Austria. In Austria, reimbursement for Debrisoft is limited until 31st December 2013 for specific conditions such as:

- *Venous and arterial leg ulcers greater than 5 cm diameter*
- *Pressure ulcers grade 2 with a VAS Score greater than 4*

In 2014, an evaluation will be conducted to determine the future reimbursement of Debrisoft in Austria.

4.4 If the technology has not been launched in the UK provide the anticipated date of availability in the UK

The technology has been launched and is available in the UK

4.5 If the technology has been launched in the UK provide information on the use in England.

The technology is used mostly in the community by nurses and podiatrists for chronic wounds such as diabetic foot ulcers, leg ulcers and pressure ulcers. It is also used for chronic wounds in hospitals and acute wounds such as trauma wounds and haematomas.

5 Ongoing studies

5.1 Provide details of all completed and ongoing studies on the technology from which additional evidence relevant to the decision problem is likely to be available in the next 12 months.

Clark M, Young T. A prospective, randomised controlled exploratory study comparing the debridement of sloughy venous leg ulcers undertaking either with a novel debriding agent (monofilament fibre pad) or autolytic debridement using wound dressings. On-going study (ISRCTN47349949).

5.2 If the technology is, or is planned to be, subject to any other form of assessment in the UK, please give details of the assessment, organisation and expected timescale.

6 Equality

NICE is committed to promoting equality of opportunity and eliminating unlawful discrimination on the grounds of age, disability, gender reassignment, race, religion or belief, sex, and sexual orientation, and to comply fully with legal obligations on equality and human rights.

Equality issues require special attention because of NICE's duties to have due regard to the need to eliminate unlawful discrimination, promote equality and foster good relations between people with a characteristic protected by the equalities legislation and others.

Any issues relating to equality that are relevant to the technology under assessment should be described. This section should identify issues described in the scope and also any equality issues not captured in the final scope.

Further details on equality may be found in section 11.3 of this document.

6.1.1 Describe any equality issues relating to the patient population and condition for which the technology is being used.

There are no equality issues relating to the population for which Debrisoft is intended.

Describe any equality issues relating to the assessment of the technology that may require special attention.

There are no equality issues relating to the assessment of the technology

6.1.2 How will the submission address these issues and any equality issues raised in the scope?

6.1.3 Section B – Clinical evidence

7 Published and unpublished clinical evidence

Section B requires sponsors to present published and unpublished clinical evidence for their technology.

Sponsors should read section 6 of the Medical Technologies Evaluation Programme methods guide on published and unpublished evidence, available from www.nice.org.uk/mt

All statements should be evidence-based and directly relevant to the scope. Reasons for deviating from the scope should be clearly stated and explained in table A1.

Sponsors are required to submit section B in advance of the full submission (for details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

7.1 Identification of studies

Published studies

7.1.1 Describe the strategies used to retrieve relevant clinical data from the published literature. Exact details of the search strategy used should be provided in section 10, appendix 1.

This review was commissioned by the manufacturer (Activa Healthcare Ltd) and no review protocol was developed or made available for comment. The review was undertaken following the guidance contained within the PRISMA statement and from the Centre for Reviews and Dissemination, York.

The search strategy comprised the following main elements:

A search of six electronic bibliographic databases (Medline, Embase®, CINAHL Plus, Cochrane Library, Medline® (R) In-process and PubMed) was performed upon the OVID platform on June 6th 2013 for studies that met the inclusion criteria. The databases were searched from inception to the date of the search with no limitation upon publication date or language of publication. The search strategy used in CINAHL Plus is described in section 10, appendix 1.

Bibliographies of included studies were searched for further relevant studies. References were managed using EndNote version 17 (Thomson Reuters USA). Further internet searches were performed on June 7th 2013 using Google and entering Debrisoft or monofilament fibre pad as search terms. Additional publications were sought from the product manufacturer (in the UK, Activa Healthcare Ltd; in the rest of the EU, Lohmann and Rauscher GmbH & Co).

A full review of the retrieved studies is provided in Appendix 1.

Unpublished studies

7.1.2 Describe the strategies used to retrieve relevant clinical data from unpublished sources.

No unpublished sources were identified through a Google search, where separately Debrisoft and monofilament fibre pad were used as search terms. No unpublished studies were identified by the product manufacturer.

7.2 Study selection

Published studies

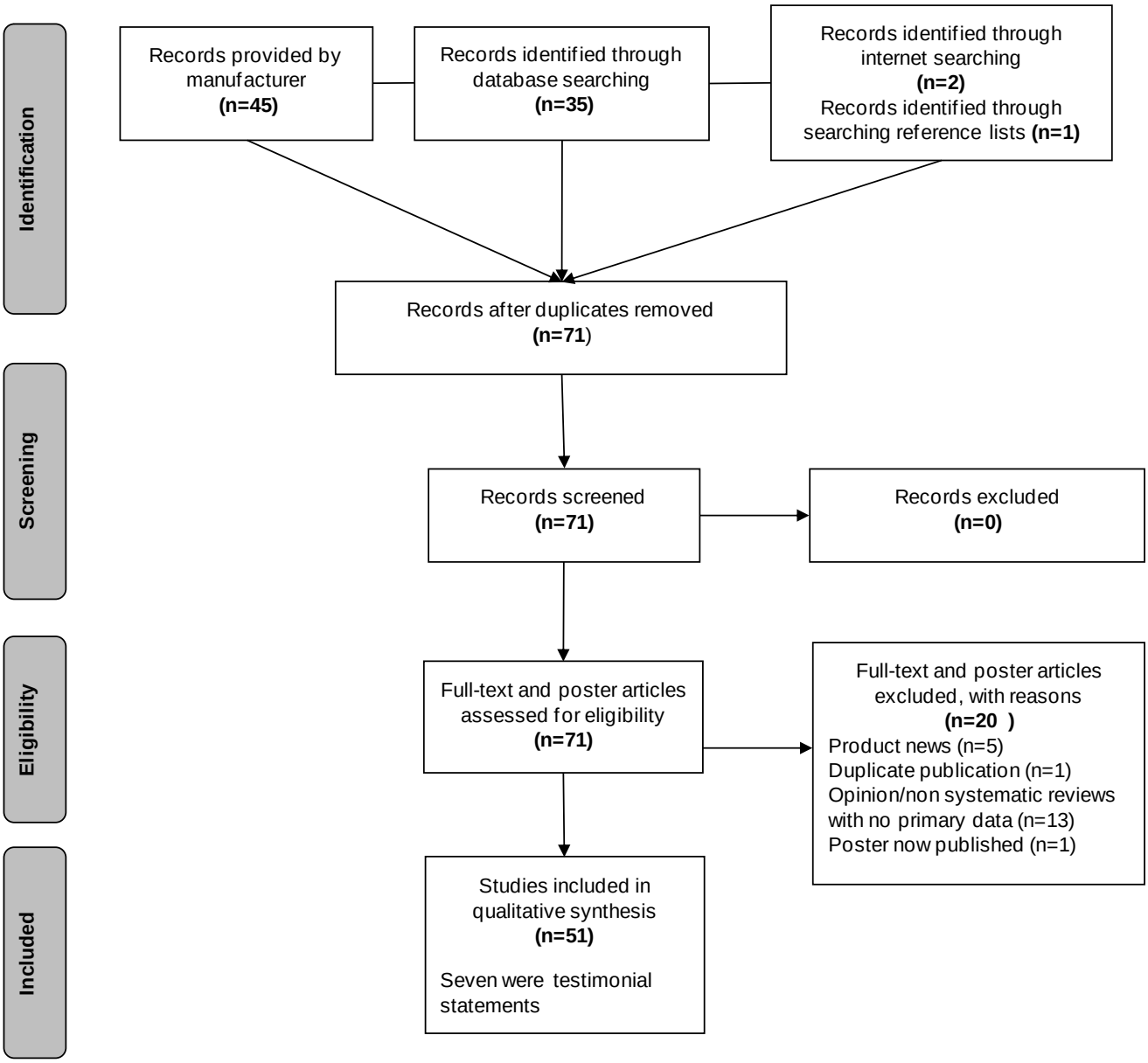
7.2.1 Complete table B1 to describe the inclusion and exclusion criteria used to select studies from the published literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table B1 Selection criteria used for published studies

Inclusion criteria	
Population	People with a wound (any aetiology) requiring debridement located in any case setting
Interventions	Intervention: Debrisoft Comparators: Autolytic debridement, mechanical debridement, or larval therapy
Outcomes	Complete debridement, pain, time to debridement
Study design	Systematic reviews, randomised, nonrandomised, cohort, case-series and case studies, observational and qualitative studies and testimonials
Language restrictions	None
Search dates	From inception of the databases
Exclusion criteria	
Population	None
Interventions	Surgical debridement
Outcomes	None
Study design	Reports describing product news , non-systematic reviews containing no primary data
Language restrictions	None
Search dates	None

7.2.2 Report the numbers of published studies included and excluded at each stage in an appropriate format.

Flow chart showing records identified, screened and included in the synthesis.



Unpublished studies

7.2.3 Complete table B2 to describe the inclusion and exclusion criteria used to select studies from the unpublished literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

No unpublished sources

Table B2 Selection criteria used for unpublished studies

Inclusion criteria	
Population	
Interventions	
Outcomes	
Study design	
Language restrictions	
Search dates	
Exclusion criteria	
Population	
Interventions	
Outcomes	
Study design	
Language restrictions	
Search dates	

7.2.4 Report the numbers of unpublished studies included and excluded at each stage in an appropriate format.

No unpublished source

7.3 Complete list of relevant studies

The sponsor should provide a PDF copy of all studies included in the submission. For unpublished studies for which a manuscript is not available, provide a structured abstract about future journal publication. If a structured abstract is not available, the sponsor must provide a statement from the authors to verify the data provided.

7.3.1 Provide details of all published and unpublished studies identified using the selection criteria described in tables B1 and B2.

No studies were identified from the literature search that had concurrent comparators. All retrieved studies were either case series or single case reports, with 29 available only as poster presentations which were supplied by the product manufacturer.

There were five case series with multiple patients, published in peer-reviewed journals, which are summarised in Table B6. A further eleven published case series, each reporting a single case-study, were retrieved during the evidence search and are summarised in Table B6A. However, no quality assessment of these studies was undertaken, given that their focus was upon the fate of single patients undergoing debridement and/or removal of peri-wound debris. Table B6B details the poster presentations that reported the use of Debrisoft among multiple subjects or in single case studies. No quality assessment checklists were completed for poster presentations, due to the anticipated incompleteness of the reporting of each study, imposed by the limitations of the poster format. Two of the poster presentations (Westgate 2012[42] and Wiegand 2012[43] reported in-vitro studies into the mode of action of the Debrisoft product.

Historical comparators to the use of Debrisoft in wound debridement were available in 18 of the retrieved studies, although details of the specific comparator intervention, the frequency of use of the comparator and the outcomes achieved were often unreported. In Table B3, the column concurrent/historical comparator gives data upon specific debridement methods, other than Debrisoft. Where specified, 'none' indicates there was no mention made of previous debridement regimes, and 'unspecified indicates a prior mention of debridement was made, but no details were provided.

Table B3 List of relevant published studies

Primary study reference	Study name (acronym)	Population	Intervention	Concurrent/ Historical Comparator
Haemmerle 2011[1]		Acute care	Debrisoft	None
Bahr 2010[2]		Community care	Debrisoft	Hydrogel/wet gauze
Stephen-Haynes 2012[3]		Community	Debrisoft	None
Gray 2011[4]		Unspecified	Debrisoft	None
Johnson 2012[5]		Acute and community care	Debrisoft	Unspecified
Whitaker 2011[6]		Community	Debrisoft	None
Simon 2011[7]		Community	Debrisoft	Removal of dry skin using forceps
Sharpe 2011[8]		Community	Debrisoft	None
Green 2011[9]		Community	Debrisoft	Bi daily dressings - Activon, Tegaderm and Tubifast. Sharp debridement
Whitaker 2012[10]		Unspecified	Debrisoft	Unspecified
Shepherd 2011[11]		Community	Debrisoft	None
McGrath 2013[12]		Community	Debrisoft	None
Fumarola 2012[13]		Acute care	Debrisoft	None
Pritchard 2012[14]		Acute care	Debrisoft	Non-adherent dressing, padding and bandage
Young 2012[15]		Community	Debrisoft	None
Cook 2012[16]		Unspecified	Debrisoft	None
Callaghan 2012[17]	Poster	Acute	Debrisoft	Unspecified
Sewell 2012[18]	Poster	Acute	Debrisoft	None
Hawkins 2012[19]	Poster	Acute	Debrisoft	Larval therapy
Fumarola 2012[20]	Poster	Acute	Debrisoft	Saline irrigation, gauze swabs, surgical scrubbing
Collarte 2011[21]	Poster	Community	Debrisoft	None

Primary study reference	Study name (acronym)	Population	Intervention	Concurrent/ Historical Comparator
Alblas 2012[22]	Poster	Acute	Debrisoft	None
Van Dam 2012[23]	Poster	Community	Debrisoft	Saline soaks 4 times a day
Dam 2012[24]	Poster	Unspecified	Debrisoft	None
Prouvost 2012[25]	Poster	Unspecified	Debrisoft	None
Wiser 2012[26]	Poster	Unspecified	Debrisoft	Saline soaks
Rieke 2012[27]	Poster	Unspecified	Debrisoft	None
Skovgaard-Holm 2012[28]	Poster	Community	Debrisoft	None
Weindorf 2012[29]	Poster	Acute	Debrisoft	None
Mustafi 2011[30]	Poster	Acute and community	Debrisoft	None
Alblas 2012[31]	Poster	Acute	Debrisoft	Unspecified
Renato 2012[32]	Poster	Acute	Debrisoft	Autolytic debridement
Lloyd-Jones 2012[33]	Poster	Community	Debrisoft	Unspecified
Flinton 2011[34]	Poster	Community	Debrisoft	None
Wilson 2013[35]	Poster	Acute	Debrisoft	Hydrogel/alginate dresssings
Denyer 2013[36]	Poster	Community	Debrisoft	Gauze
Makanin 2012[37]	Poster	Acute	Debrisoft	None
Stoffels 2012[38]	Poster	Acute	Debrisoft	None
Van Zweeden 2012[39]	Poster	Community	Debrisoft	Unspecified
Van Dam 2012[40]	Poster	Community	Debrisoft	None
Amesz 2012[41]	Poster	Community	Debrisoft	None
Westgate 2012[42]	Poster	In-vitro	Debrisoft	None
Wiegand 2012[43]	Poster	In-vitro	Debrisoft	None
Johnson 2011[44]	Poster	Acute	Debrisoft	Sharp debridement, autolysis, larval therapy, high pressure water
Stephen-Haynes 2012[45]	Poster	Community	Debrisoft	Unspecified

Table B4 List of relevant unpublished studies - None

Data source	Study name (acronym)	Population	Intervention	Comparator

7.3.2 State the rationale behind excluding any of the published studies listed in tables B3 and B4.

Studies that reported the fate of either one or two subjects and poster presentations, were excluded from quality review, given either their focus upon the experience of individual patients, or where the poster format precludes full reporting of the study data. All single case series and poster presentations are summarised in Tables B6A and B6B. Table B6C gives data extracted from case series and poster presentations, where historical comparators were reported.

7.4 Summary of methodology of relevant studies

7.4.1 Describe the study design and methodology for each of the published and unpublished studies using tables B5 and B6 as appropriate. A separate table should be completed for each study.

Table B5 Summary of methodology for randomised controlled trials - None retrieved

Study name
Objectives
Location
Design
Duration of study
Sample size
Inclusion criteria
Exclusion criteria
Method of randomisation
Method of blinding
Intervention(s) (n =) and comparator(s) (n =)

Baseline differences	
Duration of follow-up, lost to follow-up information	
Statistical tests	
Primary outcomes (including scoring methods and timings of assessments)	
Secondary outcomes (including scoring methods and timings of assessments)	

Table B6 Summary of methodology for observational studies

Study name	**Haemmerle 2011[1]**
Objective	Wound debridement
Location	Acute care
Design	Case series
Duration of study	Unreported
Patient population	Venous leg ulcers, mixed aetiology ulcers, arterial ulcers, diabetic ulcers
Sample size	11
Inclusion criteria	Unreported
Exclusion criteria	Unreported
Intervention(s) (n =) and comparator(s) (n =)	Intervention n=11, no comparator stated
Baseline differences	Not applicable
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	Single debridement using Debrisoft
Statistical tests	None
Primary outcomes (including scoring methods and timings of assessments)	Unmasked visual assessment of wound, Masked assessment of wound images by second clinician to assess need for surgical debridement of the wound
Secondary outcomes (including scoring methods and timings of	Pain (no scoring) Scanning electron images of the debrider pad pre and post use.

assessments)

Table B6 Summary of methodology for observational studies

Study name	Bahr 2010[2]
Objective	Wound debridement
Location	Community care settings in Germany, Italy and Austria
Design	Case series
Duration of study	Unreported, debridement performed at four day intervals up to day 8
Patient population	Unspecified
Sample size	60
Inclusion criteria	Wounds coated with slough and/or yellow fibrinous tissue Wounds with both serous crusts and healthy tissue Wounds with hyperkeratotic debris and/or dried exudate on the peri-wound skin Wounds suspected of containing biofilms
Exclusion criteria	Symptoms and signs of systemic and/or spreading wound infection Severe pain (7 or higher on VAS scale) or hyperaesthesia in wound Aged under 18 or over 85 Allergy to test materials Pregnant or lactating
Intervention(s) (n =) and comparator(s) (n =)	Intervention n=60, historical comparator for time to debride per episode of debridement (gauze and hydrogel). Number of comparator cases unreported.
Baseline differences	Not applicable
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	Unspecified follow-up method No report of loss to follow-up
Statistical tests	None
Primary outcomes (including scoring methods and timings of assessments)	Unmasked visual assessment of wound, masked assessment of wound images by clinician pre and post debridement, wound condition reported Condition of wound bed at day 0, 4 and 8 – time required to debride (<2 minutes, 2-4 minutes, 5-7 minutes, >7 minutes); removal of visible debris/slough/necrosis from wound bed, was debris/slough/necrosis absorbed by debrider.

	Clinicians (nonmasked) rated wounds pre and post debridement as A (wound bed covered with slough and some black necrotic plaques, periwound skin covered with scales, dried exudate and hyperkeratotic tissue B wound bed covered with slough (no black necrotic tissue) and some scales and dried exudate on peri-wound skin C peri-wound skin is clean less than 20% slough in wound bed. Subjective comments upon debrider and other debridement methods used in study centres
Secondary outcomes (including scoring methods and timings of assessments)	Safety and tolerance of technique by subjects. Tolerability. Questionnaire to assess discomfort, pain, pressure, burning sensation, bleeding, irritation of the periwound skin, swelling, redness and adverse reactions User satisfaction – comparison of clinician view of debrider against other techniques (excellent/very good/good/poor/very poor/inadequate)

Table B6 Summary of methodology for observational studies

Study name	**Stephen-Haynes 2012[3]**
Objective	Wound debridement
Location	UK community care
Design	Case series
Duration of study	Unreported
Patient population	Community care, supplemented by interviews with 40 nurses upon their experience of the Debrisoft intervention. 2 reported case studies - a) Category III heel pressure ulcer (size 9 x 6cm) b) Sacral pressure ulcer (size 4 x 3 cm), category unreported No reporting of concurrent care (pressure redistribution)

	simply stated to be 'appropriate'
Sample size	2 subjects, 40 nurses interviewed
Inclusion criteria	Nurses - qualified nurses undertaken an accredited tissue viability course and received tissue viability and supplementary debridement training during the six months prior to interview. Subjects - unreported
Exclusion criteria	Unreported
Intervention(s) (n = 2) and comparator(s) (n = 2)	Intervention n=2, historical comparator hydrogel and honey dressing
Baseline differences	Not applicable
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	Unspecified follow-up method No report of loss to follow-up
Statistical tests	None
Primary outcomes (including scoring methods and timings of assessments)	Wound debridement (visual assessment of wound) Time to debride (as reported by the interviewed nurses) Skin condition after product use (as reported by interviewed nurses) Ease of planning future care after debridement (as reported by the interviewed nurses)
Secondary outcomes (including scoring methods and timings of assessments)	None specified

Table B6 Summary of methodology for observational studies

Study name	**Gray 2011[4]**
Objective	Wound debridement
Location	UK - unspecified care settings
Design	Case series
Duration of study	Unreported
Patient population	Wounds unspecified
Sample size	18 (9 cases unreported in publication)
Inclusion criteria	Unreported
Exclusion criteria	Unreported

Intervention(s) (n =) and comparator(s) (n =)	Intervention n=18, no comparator
Baseline differences	Not applicable
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	Single use of Debrisoft to debride wounds
Statistical tests	None
Primary outcomes (including scoring methods and timings of assessments)	Visual assessment of wounds pre and post debridement.
Secondary outcomes (including scoring methods and timings of assessments)	None specified

Table B6 Summary of methodology for observational studies

Study name	**Johnson 2012[5]**
Objective	Wound debridement
Location	UK - hospital based wound clinic, community based leg ulcer clinic
Design	Case series
Duration of study	Unreported
Patient population	Leg ulcers (n=10) community, acute - ischaemic ulcers, diabetic ulcers and leg ulcers (number unspecified)
Sample size	20
Inclusion criteria	Chronic wound with soft slough Chronic wound with necrotic tissue Hyperkeratosis requiring debridement
Exclusion criteria	Unreported
Intervention(s) (n =) and comparator(s) (n =)	Intervention n=20, no comparator stated
Baseline differences	Not applicable
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of	Single use of Debrisoft to debride wounds

follow-up, participants lost to follow-up	
Statistical tests	None
Primary outcomes (including scoring methods and timings of assessments)	Pain (VAS scale) Time to debride (in minutes) Removal of hyperkeratosis (Good, very good, much better) Debridement compared with previous method (Good, much better, very good)
Secondary outcomes (including scoring methods and timings of assessments)	None specified

Given the widespread lack of detail in the reports of single case series and poster presentations data extraction from these sources has been summarised in table B6A (single subject case studies) and B6B Poster presentations).

Table B6A. Summary characteristics of included case series with single subjects and published in peer reviewed journals.

Reference	Type of Study	Sample	Intervention(s)	Outcome measures and length of follow-up	Results	Limitations
Whitaker 2011[6]	Case series	Single case study Leg ulcer (unspecified aetiology)	Removal of hyperkeratosis using Debrisoft Single application	Change in appearance of leg after two weeks.	Photograph showing appearance of the leg after Debrisoft use (before application image shows different aspect of the lower leg)	Single case series
Simon 2011[7]	Case series	Single patient case study Bilateral ulceration on	Debridement using Debrisoft moistened with water	Single application of Debrisoft Visual appearance of	Less pain reported using Debrisoft than prior attempts to remove dry skin	Single case series, no objective measurements

Reference	Type of Study	Sample	Intervention(s)	Outcome measures and length of follow-up	Results	Limitations
		upper shins, diagnosis unconfirmed, Right leg reported in case study – areas of lesions (n=12) and 8x4cm area of dry skin with minimal exudate	Duration under 2 minutes	leg, self-reported pain	using forceps No bleeding upon removal	
Sharpe 2011[8]	Case series	Single case study Right plantar pressure ulcer 945 x 10mm,	Debridement using Debrisoft Mid-foot one	Subjective visual assessment.	Able to clean the wound bed No reported	Single case study

Reference	Type of Study	Sample	Intervention(s)	Outcome measures and length of follow-up	Results	Limitations
		stated to be moderate to deep. Sloughy wound base moderate to high exudate Right mid-foot pressure ulcer (10 x 15mm, shallow to moderate depth), moderate exudate, sloughy wound base	application Plantar two applications,		discomfort	
Green 2011[9]	Case series	Single case study	Debridement using Debrisoft	Visual assessment of the	First application	Single case study

Reference	Type of Study	Sample	Intervention(s)	Outcome measures and length of follow-up	Results	Limitations
		Left heel pressure ulcer, wound bed 80% thick yellow slough	moistened with saline and applied for 4 minutes Two applications 7 days apart	wound	No reported pain Wound bled 'slightly' Second application No pain Wound bled	
Whitaker 2012[10]	Case series	Single case study	Removal of hyperkeratosis	Visual assessment of	Hyperkeratosis	Single case study

Reference	Type of Study	Sample	Intervention(s)	Outcome measures and length of follow-up	Results	Limitations
		Bilateral full leg chronic lymphoedema Bilateral hyperkeratosis gaiter area	using Debrisoft, single application 10 minutes duration.	skin changes	reduced No discomfort Relief from 'itching'	
Shepherd 2011[11]	Case series	Single case study Bilateral leg	Removal of hyperkeratosis using Debrisoft moistened with warm tap water,	Visible assessment of skin changes	Hyperkeratosis removed Patient comfortable	Single case study

Reference	Type of Study	Sample	Intervention(s)	Outcome measures and length of follow-up	Results	Limitations
		lymphoedema, large areas of hyperkeratosis on feet and lower legs	duration of treatment approximately 12 minutes Single application		throughout No trauma to healthy skin	
McGrath 2013[12]	Case series	Single case study Bilateral leg lymphoedema Hyperkeratosis, Papillomatosis,	Debrisoft mentioned as part of the range of interventions used to manage the individual. No details on	General overall report of patient management; no specific outcomes	No specific outcomes of Debrisoft use reported	Single case study

Reference	Type of Study	Sample	Intervention(s)	Outcome measures and length of follow-up	Results	Limitations
		Lymphangiomas Obesity Restricted mobility	frequency of application or specific outcomes			
Fumarola 2012[13]	Case series	Single case study Necrotising infection of lower leg with circumferential loss of tissue from knee to ankle. Extensive slough present with contamination	Debridement with Debrisoft moistened with sterile saline Application repeated at each dressing change (2-3 times per week)	Visual subjective assessment of debridement and ability to apply skin graft. Length of follow up unreported	Skin graft applied successfully	Single case study

Reference	Type of Study	Sample	Intervention(s)	Outcome measures and length of follow-up	Results	Limitations
		with *P. aeruginosa*				
Pritchard 2012[14]	Case series	Single case study Superficial wounds to lower leg Cellulitis Lack of concordance to treatment – wound deteriorated covered in thick	Debridement with Debrisoft moistened with warm water Single application of Debrisoft (? Unclear from report) with time to perform debridement unreported	Visual appearance of wound (nonmasked)	Wound healed within 4 weeks of discharge from hospital Patient 'overwhelmed at the sight of the slough being removed'	Single case study

Reference	Type of Study	Sample	Intervention(s)	Outcome measures and length of follow-up	Results	Limitations
		slough with bright green exudate				
Young 2012[15]	Case series	Two case studies (one used with permission from Collarte et al 2011), second from Callaghan (described below) Haematoma on oedematous leg Attempt to avoid cost of transfer to	Debridement with Debrisoft Number of applications unreported	Visual assessment of the wound	Haematoma debrided in under 10 minutes No pain for patient No bleeding during debridement	Single case study

Reference	Type of Study	Sample	Intervention(s)	Outcome measures and length of follow-up	Results	Limitations
		A&E for debridement				
Cook 2012[16]	Case series	Single case study Mixed aetiology leg ulcer, thin layer of slough thicker towards the wound edges	Debridement using Debrisoft moistened (fluid unspecified) Time of application 5 minutes	Visible appearance of the wound	After two weeks wound reduced in size, healthy granulation tissue visible and no evidence of slough returning	Single case study

Table B6B. Summary characteristics of included poster presentations.

Study ID	Number of subjects	Wound aetiology	Number of Debrisoft treatments provided	Duration of Debrisoft treatment (mins)	Outcomes
Callaghan 2012[17]	12	Pressure ulcers at heel (n=6), sacrum (n=2), foot (n=3) and hip (n=1)	Single	0-5 minutes	11/12 improved ability to see wound bed Pain before debridement VAS (? Unspecified) Score 7 (n=1), score 1 (n=2), score 0 (n=9) Pain during debridement (0 n=8), 1 (n=2), 4 (n=1), 6 (n=1)) Pain after debridement (0 n=12)
Sewell 2012[18]	11	Gravel rash or abrasions	Single	0-5	Pain scores (unspecified when taken) 7/11 VAS <=2 3/11 VAS 3-4

					1/11 VAS 6
Hawkins 2012[19]	5	Unspecified	Unspecified	3-10	Mean cost treatment £6.19 compared with historical data of £465 for larvae therapy (treatment duration 5 – 15 days)
Fumarola 2012[20]	8	Unspecified	Unspecified	Unspecified	All 8 would choose Debrisoft over saline irrigation, gauze swabs or surgical scrubbing
Collarte 2011[21]	10 (2 described in poster)	a) Venous leg ulcer, present for 3 years debrided for 2 years using autolytic or larval therapy b) Thick hyperkeratosis	Single Single ?	4 Unspecified	No pain during debridement No pain during removal of hyperkeratotic debris
Alblas 2012[22]	10 (4 described in detail in	Crush injury shin (n=1), soft tissue trauma lower leg (n=5), lost fingertip (n=1), bite wounds	1-3 applications to gain clean wound bed – 1 application	2.57 (SD 0.04) range 2-4	Slight discomfort 35% cases mean duration 2 mins. Some discrepancy in detailed cases

	poster)	(dogs; lost fingertip (n=1), lower leg bites (n=2))	(n=3), mean number of applications 2.1 (SD 0.83)		from summary? 1 head injury VAS pain before and during 4. 1 received 4 debridement sessions 1 fingertip injury VAS pain 5 unchanged during debridement
Van Dam 2012[23]	10 (2 cases presented)	a) Haematoma removal, Debrisoft moistened with PMHB, 5 weeks treatment wound 'almost closed' b) Mixed aetiology leg ulcer covered with necrotic tissue. Surgical debridement to remove hard necrotic tissue than Debrisoft.	Unspecified Unspecified	Unspecified Unspecified	Wound almost closed. Reported that all wounds closed within 12 weeks of treatment Unspecified
Dam 2012[24]	29	33 wounds (21 venous leg ulcers, 3 mixed aetiology leg ulcers, 3	Single	2-4 minutes	Soft fibrin cover within the wound bed reduced by 30%

		arterial leg ulcers, pyoderma gangrenosum (n=2), vasculitis and traumatic wounds (1 each)			Not able to remove fibrin firmly adherent to wound bed 11 debrided with topical analgesia 8 reported unchanged pain during debridement 10 reported increased (unspecified) pain during debridement 21 presented with keratosis around wound removed in all cases
Prouvost 2012[25]	4	a) Venous leg ulcer critically colonized with *P aeruginosa* b) Recurrent ulcers at right external malleolus, hyperkeratosis and papillomatosis in peri-wound skin c) Malleolus critically colonized with *P*	Unspecified Unspecified Twice, three	Unspecified Unspecified	Clean wound bed and peri-wound skin achieved in one or two debridements

		aeruginosa, hyperkeratosis d) Left leg venous leg ulcer covered with slough. Hyperkeratosis.	days apart Single	Unspecified Unspecified	
Wiser 2012[26]	15	Venous leg ulcers Diabetic foot ulcers both with sloughy wound beds Number of each wound type unspecified	Unspecified	Unspecified	'effective and fast debridement' Product rigid when used on toes and cavity wounds Less pain reported (no quantification) where Debrisoft used compared with prior use of saline soaks No damage to peri-wound skin
Rieke 2012[27]	25	Diabetic foot ulcers	Weekly	2.59 (SD 0.06)	18/25 healed in 12 weeks 2 closed with surgery 5/25 unhealed 8/25 also required surgical debridement

					to remove thick callus at ulcer edges
Skovgaard-Holm 2012[28]	10	Unspecified	Three times in 14 days	Unspecified	Reduced area of thin slough by 24% (3 subjects) N=6 with adherent slough reduction of 7% (mean) Thick slough reduced in area by 10% (N=1) 8/10 removed hyperkeratotic debris Pain increased during debridement in 8/10 cases (maximum increase VAS before=3, VAS during=7) Mean VAS before 2.3 mean during debridement 4.2 After debridement pain scores fell to pre debridement levels in 7/10 cases
Weindorf	5	Painful lower leg chronic wounds (epidemolysis bullosa, pyoderma	Single	Unspecified	Almost complete removal of fibrin slough achieved without need for

2012[29]		gangrenosum dystrophica, hypertensive leg ulcer, metabolic leg ulcer and gram-negative foot infection			general anaesthetic and surgical debridement Mean pain score VAS before debridement 9, mean VAS pain score during debridement 3.2, all subjects showed reduced pain during debridement
Mustafi 2011[30]	60	Unspecified	3 times over 12 days	Unspecified	97.4% of subjects reported no adverse events Mean ease and convenience level of the debridement process scored mean 2.29 points (scale and its range unspecified)
Alblas 2012[31]	10	Partial thickness burn injury	Single	Unspecified	8/10 time to healing 10.5 (range 7-12) days. 2 full thickness foot burns referred for surgery Mean pain score day 0 9.7 (SD 0.02),

					mean pain score after dressing application 3.4 and after 3 days mean VAS=0) Fewer dressing changes compared to previous debridement and dressing regime (data not provided)
Renato 2012[32]	27 compared with retrospective review of 25 subjects	Unspecified but all with fibrin and slough in wound bed, hyperkeratosis in peri-wound skin and maximum size under 60cm^2.	Single	13 minutes including preparation time (single case reported)	In single case provided single use of Debrisoft reduced wound bed slough by 92%, 2 applications autolytic debridement (historical data) gave 38.4% reduction in area of slough Cost reported for Debrisoft €35.54, cost reported for 5 times use of autolytic debridement €151.46
Lloyd-Jones 2012[33]	16	Unspecified	Unspecified	Unspecified	16 evaluations of Debrisoft use evaluated with nurses commenting that the technique had a role in wound care as rapid removal of non-viable tissue allowed better visualization of the

					wound bed, more accurate classification of pressure ulcers leading to better decisions in the next stages of wound management
Flinton 2011[34]	1	Venous leg ulcer and varicose eczema, hyperkeratotic debris	5 treatments with Debrisoft over 14 day period	2-10	No reported pain during and after treatment Wound and varicose eczema healed after the two weeks of treatment
Wilson 2013[35]	1	Mixed aetiology leg ulcer, hard black necrotic tissue and very dry flaky peri-wound skin	Single	20	Bottom edge of hard necrotic tissue lifted facilitating sharp debridement No analgesia required during Debrisoft treatment
Denyer 2013[36]	1	Hertz junctional epidermolysis bullosa, nail beds build-up of antimicrobial products and powders.	Unspecified	Unspecified	Previous attempts to clean nail bed using solutions and soft gauze gave Neonatal and Infant pain score (NIPS) of 6 (severe pain) despite analgesia. Parents shown how to use Debrisoft

					and when used NIPS was 3 (mild pain)
Makanin 2012[37]	1	Severe electrical burn to skull with osteonecrosis	Unspecified	Unspecified	Wound closure achieved within 14 days. No data upon wound debridement.
Stoffels 2012[38]	1	Firework burn (First and second degree) to face with explosive residues embedded in the facial skin	Single	Unspecified	Almost all of the embedded residues removed under local anaesthesia
Van Zweeden 2012[39]	1	Venous, arterial and lymphatic leg ulcer ($28.6cm^2$), 95% slough and unhealthy looking granulation tissue in wound bed	Unspecified	Unspecified	Use of Debrisoft within wider treatment plan and no specific data on debridement provided. Over 8 months wound reduced from $28.6cm^2$ to $19.1cm^2$ with a healthy looking wound bed Leg saved from amputation.
Van Dam 2012[40]	1	Sacral pressure ulcer, category IV copiously exuding and covered with slough. Macerated	Unspecified	Unspecified	Description of general preventive and treatment interventions applied to the

		peri-wound skin			wound No specific mention of Debrisoft?
Amesz 2012[41]	1	Radiation burn after vulvar carcinoma treatment	Unspecified	Unspecified	General treatment of the burn described with no specific data upon wound debridement
Westgate 2012[42]	In-vitro	Removal of single bacterial species from microtitre plates and pin lids Removal of 'biofilm' created upon polystyrene coupons	N/A	N/A	Bacterial species presented with Debrisoft, NA gauze, untreated (positive control) and incubated in sterile TSB only (negative control). Use of Debrisoft and NA gauze reduced bacterial attachment compared with positive control Significant reductions in bacterial loads recovered from coupons using Debrisoft compared with NA gauze or where left untreated Assumption that biofilms had been created in each experiment?

Wiegand 2012[43]	In-vitro	Glass plates coated with thick protein crust. Debrisoft and cotton gauze used to clean plates (moved over plate at constant speed of 1.6cm/s)	N/A	N/A	Debrisoft removed more protein 'slough' (70%) from glass plate than did the gauze (10%) Could use one Debrisoft pad to clean 4 glass plates, gauze single plate cleaning only.
Johnson 2011[44]	10	2 venous leg ulcers, 3 neuro-ischaemic foot ulcers, 2 mixed aetiology leg ulcers, 1 neuropathic foot ulcer, 1 digital amputation, 1 skin preparation prior to amputation	Single	Mean 4 minutes (range 2 - 10)	6 wounds healed within 6 weeks 1 patient died 1 amputation with no wound complications 2 wounds on-going Pain scores (unreported) remained low Quick and easy debridement of the wound Historical comparator - autolysis, sharp debridement, larval therapy, high

					pressure water - no data provided
Stephen-Haynes 2012[45]	2	Bilateral skin haemtaoma in diabetic patient Heel pressure ulcer	Unspecified Unspecified	6-10 minutes 3-5 minutes	Pain score during treatment 0 Treatment prevented admission to hospital Pain score during treatment = 0

Table B6C. Reported data showing historical comparators and Debrisoft from twelve studies where the historical comparator was identified.

Study	Comparison
Bahr 2010[2]	Time to debride in minutes. Hydrogel and gauze time measurements are not specified as to how many patients were timed during debridement? Debrisoft 2.51 (+/- 0.57) Hydrogel 7 +/- 2.08

Study	Comparison
	Wet gauze 5 +/- 1.6 Debridement efficacy (user comments), this self-reported measure could range from 1=excellent to 6=inadequate Debrisoft 1.98 (+/- 0.68) Hydrogel (2.54 (+/- 0.72), it is unclear how many reported their views upon the hydrogel comparator
Simon 2011[7]	Less pain reported using Debrisoft than prior attempts to remove dry skin using forceps
Green 2011[9]	Previous regime - Activon, Tegaderm and Tubifast changed every two days. Sharp debridement stated to be painful. Immediate improvement after single use of Debrisoft for 4 minutes.
Pritchard 2012[14]	Wound cleaned in single application of Debrisoft Wound healed within 4 weeks of discharge from hospital
Posters	
Denyer 2013[36]	Previous attempts to clean nail bed using solutions and soft gauze gave Neonatal and Infant pain score (NIPS) of 6 (severe pain) despite analgesia.

Study	Comparison
	Parents shown how to use Debrisoft and when used NIPS was 3 (mild pain)
Wilson 2013[35]	Typical regime - hydrogels/alginate dressings. Stay in hospital estimated to have been 21 days hydrogel debridement; 8 days Debrisoft debridement
Fumarola 2012[20]	All 8 patients asked would choose Debrisoft over saline irrigation, gauze swabs or surgical scrubbing
Hawkins 2012[19]	Mean cost treatment £6.19 compared with historical data of £465 for larvae therapy (treatment duration 5 – 15 days), 5 patients care priced in Debrisoft and larval arm
Wiser 2012[26]	Less pain reported (no quantification) where Debrisoft used compared with prior use of saline soaks
Renato 2012 [32]	In single case provided single use of Debrisoft reduced wound bed slough by 92%, 2 applications autolytic debridement (historical data) gave 38.4% reduction in area of slough Cost reported for Debrisoft €35.54, cost reported for 5 times use of autolytic debridement €151.46
Van Dam 2012[23]	Previous treatment was saline soaks changed 4 times a day. Wound healing achieved in 12 weeks.
Johnson 2011[44]	Historical comparator - autolysis, sharp debridement, larval therapy, high pressure water - no data provided upon effect of

Study	Comparison
	these interventions Debrisoft - Quick and easy debridement of the wound

7.4.2 Provide details on data from any single study that have been drawn from more than one source (for example a poster and unpublished report) and/or when trials are linked this should be made clear (for example, an open-label extension to randomised controlled trial).

No study drawn from multiple sources

7.4.3 Highlight any differences between patient populations and methodology in all included studies.

There are substantial differences between the five studies described in Table B6, with regard to the delivery of the intervention (single application or multiple debridements) and care settings (acute and community). Baseline characteristics of subjects were weakly reported, limiting comparison between studies.

7.4.4 Provide details of any subgroup analyses that were undertaken in the studies included in section 7.4.1. Specify the rationale and state whether these analyses were pre-planned or post-hoc.

No sub-group analyses

7.4.5 If applicable, provide details of the numbers of patients who were eligible to enter the study(s), randomised, and allocated to each treatment in an appropriate format.

No randomised controlled studies retrieved

7.4.6 If applicable provide details of and the rationale for, patients that were lost to follow-up or withdrew from the studies.

Loss to follow-up either did not occur (single occasions where the wounds were debrided) or was unreported.

7.5 Critical appraisal of relevant studies

7.5.1 Complete a separate quality assessment table for each study. A suggested format for the quality assessment results is shown in tables B7 and B8.

The quality of the five studies, included in Table B6, was assessed using the checklist developed by Moga et al[46], which measures the quality of case series studies. Table B7 illustrates that all five studies were of generally low quality, often failing to report whether subjects had been recruited consecutively or at a similar point in their wound history. Co-interventions were often not reported and little use occurred of either statistical tests or reporting of random variation, within the collected outcome measures.

Table B7. Summary of key quality indicators of the published case-series with multiple subjects.

Checklist	Haemmerle [1]	Bahr [2]	Stephen-Haynes [3]	Gray [4]	Johnson [5]
Study Objective					
1. Is the hypothesis/aim/objective stated clearly in the abstract, introduction or methods section?	Y	Y	Y	Y	Y
Study population					
2. Are the characteristics of the participants included in the study described?	Y	N	Y	N	Y
3. Were the cases collected in more than one centre?	Y	Y	N	N	Y
4. Are the eligibility criteria (inclusion and exclusion criteria) for entry into the study explicit and appropriate?	Y	Y	Y	N	Y
5. Were participants recruited consecutively?	N	N	N	N	N
6. Did participants enter the study at a similar point in the disease?	N	N	N	N	N

Checklist	Haemmerle [1]	Bahr [2]	Stephen-Haynes [3]	Gray [4]	Johnson [5]
Intervention and co-intervention					
7. Was the intervention clearly described in the study?	Y	Y	Y	Y	Y
8. Were additional interventions (co-interventions) clearly reported in the study?	N	N	Y	N	N
Outcome measure					
9. Are the outcome measures clearly defined in the introduction or methods section?	Y	Y	Y	N	Y
10. Were relevant outcomes appropriately measured with objective and/or subjective methods?	Y	Y	N	Y	Y
11. Were outcomes measured before and after intervention?	N	N	N	N	N
Statistical analysis					
12. Were the statistical tests used to assess the relevant outcomes	N	N	N	N	N

Checklist	Haemmerle [1]	Bahr [2]	Stephen-Haynes [3]	Gray [4]	Johnson [5]
appropriate?					
Results and conclusions					
13. Was the length of follow-up reported?	Y	Y	N	Y	Y
14. Was the loss to follow-up reported?	Y	Y	N	N	Y
15. Does the study provide estimates of the random variability in the data analysis of relevant outcomes?	N	Y	N	N	N
16. Are adverse events reported?	N	Y	Y	N	N
17. Are the conclusions of the study supported by results?	Y	Y	Y	N	Y
Competing interests and sources of support					
18. Are both competing interests and sources of support for the study reported?	Y	Y	N	N	N

7.6 Results of the relevant studies

7.6.1 Complete a results table for each study with all relevant outcome measures pertinent to the decision problem. A suggested format is given in table B9.

No statistical tests were performed in the five studies illustrated in Table B6. Accordingly, table B9 provides narrative comments upon the outcomes reported in each study.

Table B9 Outcomes from published studies

Study name	**Hammerle 2011**[1]
Comments	Wounds reported by appearance rather than aetiology Exudating, seropurulent wounds (n=3) Dry wounds with serocrusts (n=3) Wounds with necrotic layers, hyperkeratotic debris and crusts of dried exudate (n=5) Data reported in selected images rather than comprehensive data reporting. Subjective view from health professional (use of the debrider was easy, fast and efficient) Masked assessment by surgeon. 8/9 before debridement no indication for surgical debridement. After debridement, all wounds had no indication for surgical debridement with debridement of all wounds rated as 'very good' Visual assessment of wounds post debridement showed 'removal of almost all debris leaving healthy granulation tissue intact, including small epithelialized islands of vital tissue' No adverse reports of pain associated with the procedure Scanning electron images showed debris held within the texture of the debrider

Study name	**Bahr 2010[2]**
Comments	After first debridement visual appearance of the wounds were Type A 60% (n=34) Type B 28% (n=16) Type C 12% (n=7) After third debridement 47% (n=27) A 25% (n=14) B 7% (n=4) C 21% (n=12) healed Duration of debridement Mean duration 2.51 minutes (+/-2.64 SD, range 1.8 to 3.1 minutes) Historical comparison suggested this was faster than time to use hydrogel, wet gauze or surgical debridement Visible debris removed in 142/152 (93.4% of debridements) Safety. Debrider remained intact in 145/152 sessions (95.4%) Tolerability 45% (n=26) reported no pain during debridement N=29 (50.4%) reported slight discomfort and 4.6% (n=2) reported moderate pain of short duration (mean 2.4 minutes)
Study name	**Stephen-Haynes 2012[3]**
Comments	Overall performance of the debridement product (as reported by the interviewed nurses) 38/40 nurses considered skin condition had improved after Debrisoft use.

	34/40 reported that after debridement able to identify clearer objectives for the management of the wound based on clearer visibility of wound bed. Time to debride. 0-2 minutes (n=8) 3-5 (n=21) minutes 6-10 minutes (n=9) Numbers stated to be by patient but are these the reported time to use product given by nurses? Overall performance N=24, 60% (very good) N=10 (25%) (good) N=5 (12.5%) (fairly good) N=1 (2.5%) (poor) Case studies – debridement stated to be effective in both cases
Study name	**Gray 2011[4]**
Comments	Time to debridement Removal of hyperkeratosis (2 cases reported) Haematoma debridement (3 cases reported) Removal of soft slough (heel pressure ulcer, 2 cases reported) Hyperkeratosis 5-10 minute treatment to remove hyperkeratotic debris Haematoma debridement Less than 5 minutes treatment required Removal of soft slough Only data presented indicated 10 minute treatment to debride a sloughy leg ulcer
Study name	**Johnson 2012[5]**

Comments	Pain 16/20 no reported pain, 3 VAS =1, n=1, VAS = 7 Time to debride (mins) N=10; 2-4 minutes N=5; 5-7 minutes N=5; >7 minutes Removal of hyperkeratosis Good n=1 Very good n=1 Much better n=6 N/A n=12 Debridement compared with previous method Good n=5 Very good n=3 Much better n=8 N/A n=4

7.6.2 Justify the inclusion of outcomes in table B9 from any analyses other than intention-to-treat.

No analyses were performed (intention to treat or otherwise) within the five studies detailed in Table B9.

7.7 Adverse events

In section 7.7 the sponsor is required to provide information on the adverse events experienced with the technology being evaluated in relation to the scope.

For example, post-marketing surveillance data may demonstrate that the technology shows a relative lack of adverse events commonly associated with the comparator.

7.7.1 Using the previous instructions in sections 7.1 to 7.6, provide details of the identification of studies on adverse events, study selection, study methodologies, critical appraisal and results.

Adverse events were identified from the studies retrieved and appraised in sections 7.1 to 7.6.

7.7.2 Provide details of all important adverse events reported for each study. A suggested format is shown in table B10.

Only two studies, Bahr 2010[2] and Johnson 2012[5], collected data upon adverse events (pain) associated with the intervention. Neither study had a comparison group, limiting interpretation of the adverse event data presented. Table B10 provides narrative comments upon the occurrence of pain during debridement.

Table B10 Adverse events across patient groups

Study name	**Bahr 2010**
Comments	45% (n=26) reported no pain during debridement N=29 (50.4%) reported slight discomfort and 4.6% (n=2) reported moderate pain of short duration (mean 2.4 minutes)
Study name	**Johnson 2012**
Comments	Pain 16/20 no reported pain, 3 VAS =1, n=1, VAS = 7

7.7.3 Describe all adverse events and outcomes associated with the technology in national regulatory databases such as those maintained by the MHRA and FDA (Maude).

No adverse incidents are registered with the national databases

7.7.4 Provide a brief overview of the safety of the technology in relation to the scope.

In 4 cases (Callaghan 2012[17], Johnson 2012[44], Sewell 2012[18]), a moderate degree of discomfort was reported, and this related directly to the condition of the patients, rather than the technology. Occasionally, mild discomfort was recorded with the use of the technology, but this lasted only minutes following the procedure (Bahr et al 2011[2], Green 2011[9], Stephen-Haynes 2012[45], Wiser 201[26], Gray 201[4],Weindorf 2012[29]).

Safety v Risk

Bleeding and trauma to healthy tissue

All debridement carries a risk of some bleeding when the devitalised tissue is removed, exposing healthy tissue in preparation for healing. Clinical skills and experience inform the practitioner on the point at which to stop the debridement procedure. In the case of vascular conditions such haematomas, slight bleeding is inevitable and assessment of the patient and the local area enables the clinician to make the correct and safe choice of follow on care.

Debrisoft is less likely to cause bleeding than surgical debridement (Weindorf, Dissemond 2012[29]). Where slight bleeding has occurred, this has not been detrimental to the patient (Fumarola 2011[13]). At risk structures such as tendons that may have been obscured by devitalised tissue have remained undamaged when the wound was debrided with Debrisoft. This has the additional benefit of providing clearer assessment to enable safe and appropriate care (Fumarola

2011[13]). Although this procedure was conducted by a specialist nurse, it could have been performed safely by a general nurse. Studies have shown the removal of devitalised tissue without damage to healthy epithelialising tissue, when examined under an electron microscope (Haemmerle 2011[1]).

Ischaemic limbs

Debridement is contraindicated on critically ischaemic limbs and digits, as the infrastructure is not in place to remove remaining products of debridement, thereby increasing the risk of local and even systemic infection. Additionally, the presence of moisture created by dressings or the debridement process could lead to osteomyelitis, an infection of the bone. In these cases the digit should be allowed to auto amputate (UK Debridement Consensus Document 2013[48]).

We have no experience with Debrisoft on these patients and limbs. For this reason, Debrisoft is not recommended on these limbs even though invitro studies show that the debris is safely held in the fibres (Wiegand 2013[43], Westgate 2012[42]).

Pain or discomfort

Removal of devitalised tissue by any means may cause discomfort or pain to the patient. Surgical debridement may be painful, requiring local or even general anesthesia. Debrisoft has been used as an alternative, where surgical debridement even under local anesthesia caused pain (Weindorf and Dissemond 2013[29]).

Some dressings used for autolytic debridement may cause a drawing sensation.

Debrisoft has been used safely even on children (Sewell 2012 [18], Denyer 2012[36]).

Patient anxiety

Anticipated pain often prevents full debridement in the anxious patient, and some treatments such as larvae may be abhorrent to patients. Debridement on children, and restless or confused patients, may be difficult when using methods that could cause trauma, if patients change position suddenly.

Debrisoft has been used safely and successfully with the full consent of patients or guardians following discussion about treatment (Collarte 2011[21], Denyer 2013[36]).

Patients have been encouraged to use Debrisoft in their own care (Stoffels 2012[38]).

These aspects of treatment with the NHS domains of care advocate safety, clinical effectiveness and a positive patient experience (NHS White Paper 2010[49]).

7.8 Evidence synthesis and meta-analysis

When more than one study is available and the methodology is comparable, a meta-analysis should be considered.

Section 7.8 should be read in conjunction with the 'Medical Technologies Evaluation Programme Methods Guide', available from www.nice.org.uk/mt

7.8.1 Describe the technique used for evidence synthesis and/or meta-analysis. Include a rationale for the studies selected, details of the methodology used and the results of the analysis.

No synthesis of the case series studies was performed.

7.8.2 If evidence synthesis is not considered appropriate, give a rationale and provide a qualitative review. The review should summarise the overall results of the individual studies with reference to their critical appraisal.

Given that there were no comparative studies identified in the literature search, only case-series studies, there was no data upon which to build a synthesis of the evidence. This was compounded by the heterogeneity between case series, with regard to the frequency of intervention use, patient population, and the trend towards subjective unmasked assessment of change in the wounds debrided. The quality of the case series studies was generally low, although this assessment may be harsh given three reasons; (i) the check-list developed by Moga 2012[46] has not yet been subjected to peer review, (ii) many of the case series were conducted/reported prior to the publication of the quality checklist and (iii) the case series author(s) were clinicians seeking to share initial information upon the new mechanical debridement technique, rather than academics who might have been anticipated to focus more upon the quality of their case series report.

The 18 studies with information upon historical comparators, contrasted the fate of patients whose wounds were debrided with Debrisoft, and where debridement took place in acute and community care using hydrogels, larval therapy, gauze, saline soaks, and sharp debridement. Single applications of Debrisoft, appeared to be effective in cases where wounds (and the need for debridement) had previously existed for considerable periods of time. The time to undertake debridement using Debrisoft was

shorter than if gauze or hydrogels were used (Bahr 2010[2]). When asked, both nursing staff and patients rated their experience of Debrisoft highly, preferring this technique to others previously encountered. The simplicity of Debrisoft use may allow debridement to be undertaken in community settings, with reduced admission to hospital for wound debridement.

7.9 Interpretation of clinical evidence

7.9.1 Provide a statement of principal findings from the clinical evidence highlighting the clinical benefit and any risks relating to adverse events from the technology.

Although firm conclusions cannot be drawn regarding Debrisoft there are a number of trends that emerge from the available evidence, all of which require exploration in future controlled studies.

a) *Debrisoft has been used in both acute and non-acute care settings, and does not appear to require the intervention of specialist wound care practitioners.*

b) *Debrisoft has been used on a wide variety of chronic and acute wounds.*

c) *The ability of Debrisoft to remove slough from the wound bed with a single application, appears to depend upon the strength of the attachment of the slough to the wound bed, with thin slough removed* with a single application, *whereas tenacious slough and necrotic eschar may not.*

d) *Debrisoft appeared to remove hyperkeratotic debris within one to two applications.*

e) *The time to debride a wound ranged from under 2 minutes to a maximum of 20 minutes. Most reports cited single*

applications to achieve their outcomes, with 16 reports failing to specify the number of applications provided.

The effect of Debrisoft upon patients' experience of pain during debridement appears contradictory, although this may represent the weak evidence available.

7.9.2 Provide a summary of the strengths and limitations of the clinical-evidence base of the technology.

The strengths of the evidence base primarily relate to the growing volume of clinical evaluations, since the product was launched in 2011. However, given that there are no concurrent controlled studies and limited data where historical comparators were used, this limits the strength that can be placed upon the interpretation of the role of Debrisoft in wound debridement.

Provide a brief statement on the relevance of the evidence base to the scope. This should focus on the claimed patient- and system-benefits described in the scope.

The limited clinical evidence, indicates that wound debridement may be quickly performed using the intervention, and that this process may be achieved in a single session. Pain is reported during the intervention, although the limited data prohibits any generalisation as to its duration or intensity. The limited clinical data, does not allow any estimation of the overall time to healing, of wounds that have been debrided using the intervention.

7.9.3 Identify any factors that may influence the external validity of study results to patients in routine clinical practice.

The lack of controlled studies limits understanding of whether the benefits of the intervention seen in the case series can be extrapolated to other patient populations.

7.9.4 Based on external validity factors identified in 7.9.4 describe any criteria that would be used in clinical practice to select patients for whom the technology would be suitable.

From the limited case series, studies the technology may be best suitable for use in wounds with lightly adhering slough, where traditional debridement techniques are painful, and where the peri-wound skin has hyperkeratotic debris.

Section C – Economic evidence

Section C requires sponsors to present economic evidence for their technology.

All statements should be evidence-based and directly relevant to the decision problem.

The approach to the de novo cost analysis expected to be appropriate for most technologies is cost-consequence analysis. Sponsors should read section 7 of the Medical Technologies Evaluation Programme Methods guide on cost-consequences analysis, available from www.nice.org.uk/mt

Sponsors are requested to submit section C with the full submission. For details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

8 Existing economic evaluations

Identification of studies

8.1.1 Describe the strategies used to retrieve relevant health economics studies from the published literature and to identify all unpublished data. The search strategy used should be provided as in section 10, appendix 3.

The key biomedical literature databases, (Medical Literature Analysis and Retrieval System Online [MEDLINE®], Excerpta

Medica Database [Embase®]), National Health Service Economic Evaluation Database (NHSEED), and EconLIT® were searched. This is in accordance with the list of databases suggested by the HTA agencies, such as NICE. MEDLINE® In-Process was searched to ensure that non-indexed citations are retrieved.

Embase® and MEDLINE® were searched using the Embase.com interface, while NHSEED and MEDLINE® In-Process were searched using Wiley Cochrane library and PubMed platforms, respectively. EconLit® was searched via AEAweb.org interface.

All databases were searched from database start to 16th July 2013 in order to retrieve the latest evidence. The search strategy used has been provided in section 10, appendix 3.

8.1.2 Describe the inclusion and exclusion criteria used to select studies from the published and unpublished literature.

Citations identified were initially assessed based on title and abstract. Each citation was screened by a single reviewer, and validated by an independent reviewer. Any discrepancy was resolved by consensus amongst the reviewers. Citations that did not match the eligibility criteria were excluded. Eligibility criteria were then applied to full text citations to yield the final data set for inclusion. The final included data set consisted of studies for Debrisoft® and those for comparator treatments. Inclusion and exclusion selection criteria are presented in Table C1.

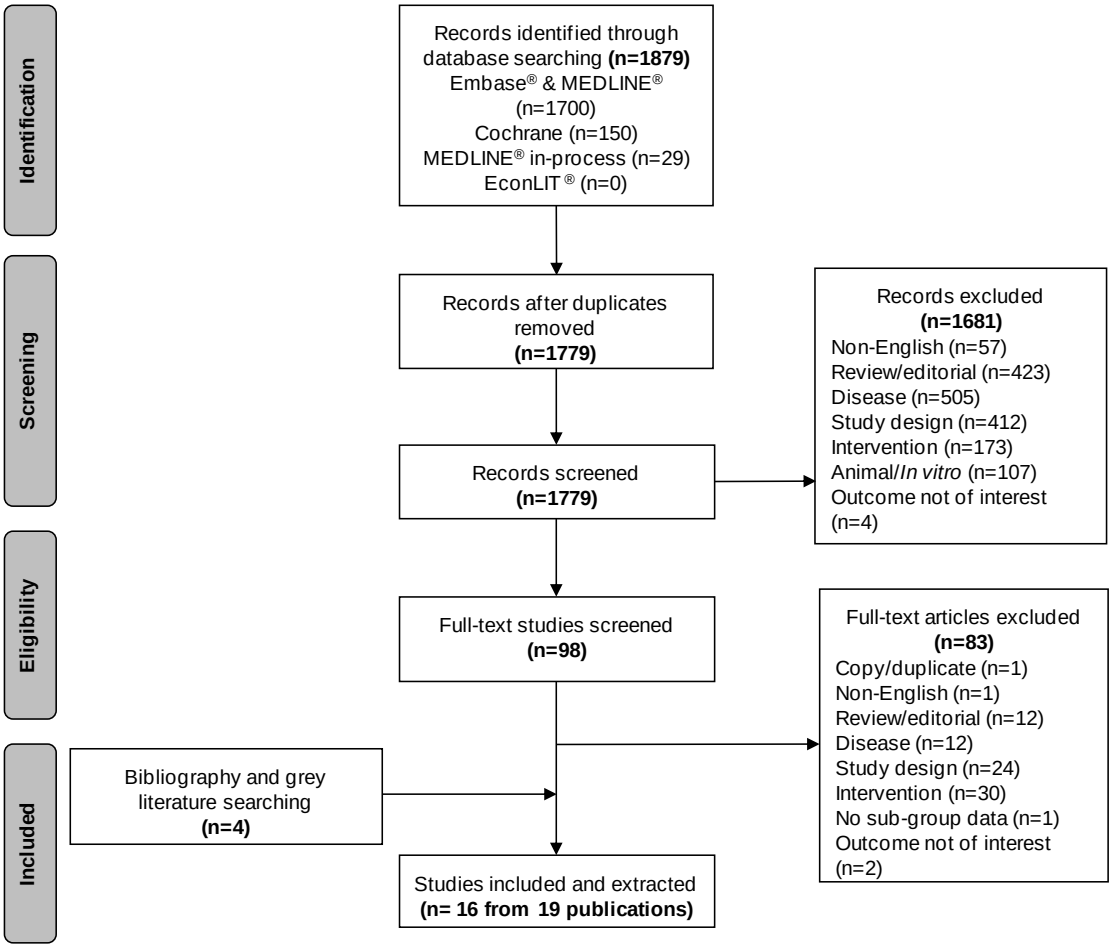
Table C1 Selection criteria used for health economic studies

Inclusion criteria	
Population	Age: Any Gender: any Race: any Condition: Wounds associated with any condition (i.e. disease, surgery, infection, etc.)
Interventions	Autolytic debridement (hydrogel, hydrocolloid) Larval debridement (biosurgery or maggot therapy) Mechanical debridement (gauze swabs)
Outcomes	Type of wound (e.g. leg ulcer, pressure ulcer) Wound bed condition (dry/necrotic; wet/sloughy with low/moderate exudate or heavily exuding) Mean time to debridement (in days); or % debrided in the study period Number of applications of debridement method required (e.g. how many times are maggots applied, how many times is hydrogel applied) Frequency of dressing change during debridement (e.g. every 2-3 days) Number of dressing changes during the time to debridement Cost (total, direct, indirect associated with wound debridement)
Study design	Burden of illness/cost of illness/cost evaluation studies Database studies collecting cost data (e.g. claims databases and hospital records) Prospective/retrospective/case-control/single-arm studies/case report evaluating costs Modelling studies (cost-effectiveness/cost-consequence/cost-utility/cost-minimisation analysis) reporting costs related to wound debridement
Language restrictions	English language only
Search dates	Database start to present
Exclusion criteria	
Population	Burn wounds or other wounds requiring surgical debridement
Interventions	Surgical/sharp debridement (using scalpel or scissors) Mechanical debridement (pressurised wound irrigation, using jets of water) Enzymatic debridement (proteolytics, fibrinolytics, collagenase)
Language restrictions	Non-English
Search dates	No restriction on database search timeframe

8.1.3 Report the numbers of published studies included and excluded at each stage in an appropriate format.

Figure 1 presents the flow of studies through the systematic review process. Following assessment and exclusion of studies based on title, abstract and full text articles, 16 studies from 19 publications were considered to meet the inclusion criteria, and were included in the final data set.

Figure 1: PRISMA flow diagram



Embase: Excerpta Medica Database; MEDLINE: Medical Literature Analysis and Retrieval System Online

8.2 Description of identified studies

8.2.1 Provide a brief review of each study, stating the methods, results and relevance to the scope.

Table C2 (A) summarises disease burden associated with wound debridement, which was reported in eight of the included studies. The disease burden was reported in terms of mean cost of treatment incurred due to medication and nursing costs.

Table C2 (A): Summary of studies showing disease burden associated with wound debridement

Study name	Study country	Patient population	Intervention/control	Type of cost	Cost item	Units/time-frame	N	Total cost Mean (SD)	Comment
Wayman 2000[50]	United Kingdom	Patients having a sloughy venous ulcer	Control group (hydrogel dressing)	Direct cost	Nursing cost	-	-	£53.85*	-
			Larval debridement therapy		Nursing cost	-	-	£10.77*	-
			Control group (hydrogel dressing)		Dressing materials excluding larvae	-	-	£89.55*	-
			Larval debridement therapy		Dressing materials excluding larvae	-	-	£9.87*	-
			Control group (hydrogel dressing)		Cost of treatment	-	-	£136.23	-
			Larval debridement therapy		Cost of treatment	-	-	£78.64*	-
			Control group (hydrogel dressing)		Total cost of one month treatment time	-	-	£1054	-

Study name	Study country	Patient population	Intervention/control	Type of cost	Cost item	Units/time-frame	N	Total cost Mean (SD)	Comment
			Larval debridement therapy		Total cost of one month treatment time	-	-	£492	-
Harding 2000[51]	United Kingdom	Patients with pressure ulcer and venous leg ulcers	Pressure ulcers Gauze	Direct costs	Dressing	-	-	£115	-
					Nurse time	-	-	£2548	-
			Pressure ulcer Granuflex		Dressing	-	-	£124	-
					Nurse time	-	-	£298	-
			Pressure ulcer; Comfeel		Dressing	-	-	£189	-
					Nurse time	-	-	£453	-
			Venous ulcer; Gauze		Dressing	-	-	£48	-
					Nurse time	-	-	£327	-
			Venous ulcer; Granuflex		Dressing	-	-	£124	-
					Nurse time	-	-	£97	-
			Venous ulcer; Apligraf		Dressing	-	-	£6526	-
					Nurse time	-	-	£70	-

Study name	Study country	Patient population	Intervention/control	Type of cost	Cost item	Units/time-frame	N	Total cost Mean (SD)	Comment
Thomas 2006[52]	United Kingdom	Patients with chronic wounds	Maggots: Pressure ulcer	Direct cost	Treatment cost	Per day	1 00 000[#]	£13 325 000	Includes treatment cost of maggots of £28.30 per day plus daily baseline treatment costs of £25 per day
			Maggots: Diabetic ulcer		Treatment cost		84 000[#]	£6 715 800	Includes treatment cost of maggots of £28.30 per day plus daily baseline treatment costs of £25 per day

Study name	Study country	Patient population	Intervention/control	Type of cost	Cost item	Units/time-frame	N	Total cost Mean (SD)	Comment
			Maggots: Leg ulcer		Treatment cost		1 50 000[#]	£1 998 750	Includes treatment cost of maggots of £28.30 per day plus daily baseline treatment costs of £25 per day
Mulder 1995[53]	United States	Patients with dry eschar	Hydrogel/ Polyurethane secondary dressing foam	Direct cost	Dressing cost	cost/day	9	US$ 12.47	-
					Nursing time	cost/day	9	US$ 5.34	-
					Total cost	cost/day	9	US$ 17.81	-
					Dressing cost to debridement	-	9	US$ 135.78 (62.06)	Debridement was defined as 50% removal of eschar
					Total cost to debridement	-	9	US$ 193.93 (88.63)	Debridement was defined as 50% removal of eschar
			Saline moistened		Dressing cost	cost/day	7	US$ 8.1	-

Study name	Study country	Patient population	Intervention/control	Type of cost	Cost item	Units/time-frame	N	Total cost Mean (SD)	Comment
			gauze		Nursing time	cost/day	7	US$ 8	-
					Total cost	cost/day	7	US$ 16.1	-
					Dressing cost to debridement	-	3	US$ 91.8 (76.99)	Median; 89.1; Range: 16.2-170.1; Calculated from individual patient data
					Total cost to debridement	-	3	US$ 182.47 (153.02)	Median; 177.1; Range: 32.2-338.1; Calculated from individual patient data
Woo 2013[54]	Canada	Patients with chronic wounds	Autolytic debridement	Total costs (Direct costs + Indirect costs)	Debridement cost	-	-	Canadian $ 1504	Base case costs were reported
			Mechanical debridement		Debridement cost			Canadian $ 1840	
			Biologic debridement		Debridement cost			Canadian $ 2150	
Mosher 1999[55]	-	A hypothetical	Autolytic debridement	Direct costs	Medication & Supply Cost	Cost for 28 days	-	US$ 247	-

Study name	Study country	Patient population	Intervention/control	Type of cost	Cost item	Units/time-frame	N	Total cost Mean (SD)	Comment
		elderly female (78 year old) resident having pressure-ulcer	Autolytic debridement		Medication & Supply Cost	Cost/day	-	US$ 8.82	
			Autolytic debridement		Total treatment cost	Cost for 28 days	-	US$ 920.73	
			Autolytic debridement		Total treatment cost	Cost/day	-	US$ 32.88	
			Mechanical debridement (Wet-to dry saline dressing)		Medication & Supply Cost	Cost for 28 days	-	US$ 249	
			Mechanical debridement (Wet-to dry saline dressing)		Medication & Supply Cost	Cost/day	-	US$ 8.89	
			Mechanical debridement (Wet-to dry saline dressing)		Total treatment cost	Cost for 28 days	-	US$ 1008.72	
			Mechanical debridement (Wet-to dry saline dressing)		Total treatment cost	Cost/day	-	US$ 36.03	

Study name	Study country	Patient population	Intervention/control	Type of cost	Cost item	Units/time-frame	N	Total cost Mean (SD)	Comment
VENUS II trial[57]	United Kingdom	Patients with venous or mixed venous and arterial leg ulcers	Loose larva	Direct costs	Total unadjusted costs	-	78	£1833 (1978)	Median (range): 1195 (139 to 9821); Base case costs were reported
			Bagged larvae		Total unadjusted costs		71	£1696 (1948)	Median (range): 868 (29 to 10 135); Base case costs were reported
			Hydrogel		Total unadjusted costs		75	£1596 (1861)	Median (range): 1123 (0 to 9989); Base case costs were reported
Waycaster 2013[60]	United States	Patients with Stage 3 and stage 4 pressure ulcers	Hydrogel	Direct costs	Hydrogel (Solosite gel), 90g	1 tube/42 days	-	US$ 17.4	-
					Nursing time	1 min/day	-	US$ 9.3	-
					Cover dressing (CovRSite)	1 dressing/day	-	US$ 2.21	-

Study name	Study country	Patient population	Intervention/control	Type of cost	Cost item	Units/time-frame	N	Total cost Mean (SD)	Comment
					Wound irrigation system (Irrimax)	1 irrigation/day	-	US$ 21.39	-
					Wound care kit	1 kit/day	-	US$ 4.17	-

*: Median cost reported; #: Number of wounds; $: Dollar; £: Sterling (pound)

Table C2 (B) summarises resource utilisation associated with wound debridement, which was reported in six of the included studies. Resource utilised for wound debridement was reported in terms of number of visits for dressing, and number of visits by consultants and nurses.

Table C2 (B): Summary of studies showing resource use associated with wound debridement

Study name	Study country	Patient population	Intervention/Control	Resource use item	Units/timeframe	N	Mean (SD)
Wayman 2000[50]	United Kingdom	Patients with sloughy venous ulcer	Control (hydrogel dressing)	Number of visits	-	6	19*
			Larval debridement therapy	Number of visits	-	6	3*
			Control (hydrogel dressing)	Nursing time	Hours	-	375*
			Larval debridement therapy	Nursing time	Hours	-	75*
Gilead 2012[61]	Israel	Patients with leg ulcers	Maggot debridement therapy	Number of treatments	-	435	2.9; 2*
Mulder 1995[53]	United States	Patients with dry eschar	Hydrogel/ Polyurethane secondary dressing foam	Number of dressings changed	per day	9	1
			Saline moistened gauze	Number of dressings changed	per day	7	2
Milne 2012[62]	United States	Patients aged >18 years having pressure ulcers	Hydrogel	Dressings change	per week	14	9.01*
			Hydrogel	Number of tubes used	-	14	1.07 (20 g)*

Study name	Study country	Patient population	Intervention/Control	Resource use item	Units/timeframe	N	Mean (SD)
VENUS II trial[57]	United Kingdom	Patients with venous or mixed venous and arterial leg ulcers	Loose larvae	Number of applications of trial treatment	-	89	1.44 (1.22)
			Bagged larvae	Number of applications of trial treatment	-	82	1.46 (1.06)
			Hydrogel	Number of applications of trial treatment	-	82	9.2 (27.78)
			Loose larvae	Nurse consultations	-	88	37 (40)
			Bagged larvae	Nurse consultations	-	82	36 (41)
			Hydrogel	Nurse consultations	-	82	39 (45)
			Loose larvae	Doctor consultations	-	88	2 (4)
			Bagged larvae	Doctor consultations	-	82	4 (5)
			Hydrogel	Doctor consultations	-	82	4 (9)
			Loose larvae	Hospital visits	-	88	10 (20)
			Bagged larvae	Hospital visits	-	82	7 (15)
			Hydrogel	Hospital visits	-	82	5 (12)

Study name	Study country	Patient population	Intervention/Control	Resource use item	Units/timeframe	N	Mean (SD)
Lok 1999[63]	France	Patients with venous leg ulcers	Mechanical debridement: EMLA cream	Number of debridement	-	36	11.5*
			Placebo	Number of debridement	-	33	>15*

*: Median reported

Table C2 (C) summarises studies reporting the "time to debridement" or "percentage slough remaining" associated with wound debridement. Time to debridement was reported in eight studies while percentage of slough remaining after wound debridement was reported in one study.

Table C2 (C): Summary of studies showing time to debridement/percent slough remaining associated with wound debridement

Study name	Study country	Patient population	Intervention/Control	N	Mean	SD	Comments
Time to debridement							
Groenewald 1980[64]	South Africa	Patients with post-phlebitic stasis ulcer	Debrisan®	50	5.9	-	Reported in days
			Control	50	15.4	-	Reported in days
			Debrisan; Investigator A	50	6.9	3.8	Reported in days
			Control; Investigator A	50	15.7	5.9	Reported in days
			Debrisan; Investigator B	50	5.8	3.2	Reported in days
			Control; Investigator B	50	16.7	5.3	Reported in days
			Debrisan; Photographic analysis	50	5.88	2.9	Reported in days
			Control; Photographic analysis	50	15.4	6.4	Reported in days

Study name	Study country	Patient population	Intervention/Control	N	Mean	SD	Comments
Bahr 2010[2]	Germany, Italy, Austria	Specific inclusion criteria were: • Wounds coated with slough and/or yellow fibrinous tissue • Wounds with both serous crusts and healthy tissue • Wounds with hyperkeratotic debris and/or dried exudate on the periwound skin • Wounds suspected of containing biofilm	Debrisoft®	57	2.51	-	Reported in minutes per procedure
Jiang 2013[65]	China	A 51-year-old man with type II diabetes, hypertension, and dilated cardiomyopathy; with a painful ulcer in the middle of second finger of his right hand	Maggot debridement therapy	1	3	-	MDT showed complete debridement after three days, with redness and swelling around the ulcer gradually subsiding.
Thomas 2006[52]	United Kingdom	Patients with chronic wounds	Maggots	1 00 000#	2 50 000	-	Reported in days; Based on an average treatment duration of five days

Study name	Study country	Patient population	Intervention/Control	N	Mean	SD	Comments
			Maggots	84 000[#]	1 26 000	-	Reported in days; Based on an average treatment duration of five days
			Maggots	1 50 000[#]	37 500	-	Reported in days; Based on an average treatment duration of five days
Mulder 1995[53]	United States	Patients with dry eschar	Hydrogel/ Polyurethane secondary dressing foam	9	10.9	5	Reported in days
			Saline moistened gauze	3	11.3	9.5	Reported in days; Calculated from individual patient data
VENUS II trial[57]	United kingdom	Patients with venous or mixed venous and arterial leg ulcers	Loose larvae	94	14*	-	Reported in days
			Bagged larvae	86	28*	-	Reported in days
			Hydrogel	87	72*	-	Reported in days
Lok 1999[63]	France	Patients with venous leg ulcers	Mechanical debridement: EMLA cream	36	4*	-	Reported in minutes
			Placebo	33	3*	-	Reported in minutes

Study name	Study country	Patient population	Intervention/Control	N	Mean	SD	Comments
Sherman 2002[66]	United States	Patients with pressure ulcers	Maggot debridement therapy	43[#]	1.4	-	Reported in weeks until half the necrotic tissue was debrided; Percentage of necrotic wounds completely debrided was reported in the grid
				43[#]	8	-	Reported in weeks until total debridement of necrotic wounds
Percentage of slough remaining							
Opletalova 2012[67]	France	Patients with non-healing, sloughing wound on the lower limb	Maggot debridement therapy; day 1	51	79.7	22.3	Reported as percentage of slough remaining reported
			Maggot debridement therapy; day 8	51	54.5	31.6	Reported as percentage of slough remaining reported
			Maggot debridement therapy; day 15	51	55.4	30	Reported as percentage of slough remaining reported

Study name	Study country	Patient population	Intervention/Control	N	Mean	SD	Comments
			Maggot debridement therapy; day 30	48	55.4	30.4	Reported as percentage of slough remaining reported

*: Median reported; #: Number of wounds

8.2.2 Provide a complete quality assessment for each health economic study identified

The quality assessment of included health economic studies is presented in details in Table C3. The quality assessment was performed only for eight included studies, which reported the cost of wound debridement (e.g. time-to-debridement).

Table C3 Quality assessment of health economic studies

Study question	Wayman 2000[50]	Harding 2000[51]	Thomas 2006[52]	Mulder 1995[53]	Woo 2013[54]	Mosher 1999[55]	VENUS II trial[57]	Waycaster 2013[60]
1. Was the research question stated?	Yes; the research question was stated clearly	Yes; the research question was stated	Yes; the research question was stated clearly	Yes; the research question was stated clearly	Yes; the research question was stated clearly	Yes; the research question was stated	Yes; the research question was stated	Yes; the research question was stated
2. Was the economic importance of the research question stated?	Yes; the economic importance of the research question was stated	Yes; the economic importance of the research question was stated	Yes; cost benefit analysis was conducted	Yes; the economic importance of the research question was stated	Yes; the economic importance of the research question was stated	Yes; the economic importance of the research question was stated	Yes; the economic importance of the research question was stated	Yes; the economic importance of the research question was stated

Study question	Wayman 2000[50]	Harding 2000[51]	Thomas 2006[52]	Mulder 1995[53]	Woo 2013[54]	Mosher 1999[55]	VENUS II trial[57]	Waycaster 2013[60]
3. Was/were the viewpoint of the analysis clearly stated and justified?	No; the view-point of the analysis was not stated	No; the view point of the analysis was not reported	Yes; the study was carried out with cost benefit to the NHS	No; the view-point of the analysis was not stated	Yes; the view-point of the analysis was Canadian Health care system	Yes; the study has been conducted from payer's perspective	Yes; the study has been conducted from payer's perspective	Yes; the study has been conducted from payer's perspective
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?	Yes; rationale was reported for the choice of alternatives compared	Yes; the rationale was reported for the choice of the alternative programmes or interventions compared	Yes; rationale was reported for the choice of alternatives compared	Yes; rationale was reported for the choice of alternatives compared	Yes; rationale was reported for the choice of alternatives compared	Yes; the rationale was reported for the choice of the alternative programmes or interventions compared	Yes; the rationale was reported for the choice of the alternative programmes or interventions compared	Yes; the rationale was reported for the choice of the alternative programmes or interventions compared
5. Were the alternatives being compared clearly described?	Yes; the alternatives compared were described	Yes; the alternatives compared were clearly described	Yes; the study compared maggot debridement therapy with conventional therapy	Yes; the alternatives compared were described	Yes; alternatives were compared and described	Yes; the alternatives compared were clearly described	Yes; the alternatives compared were clearly described	Yes; the alternatives compared were clearly described

Study question	Wayman 2000[50]	Harding 2000[51]	Thomas 2006[52]	Mulder 1995[53]	Woo 2013[54]	Mosher 1999[55]	VENUS II trial[57]	Waycaster 2013[60]
6. Was the form of economic evaluation stated?	Yes; this was a randomised-controlled trial in which cost-effectiveness of the debridement methods was compared	Yes; cost effectiveness evaluation was performed	No; the form of economic evaluation was not stated although cost savings of maggot debridement therapy to the NHS were calculated	Yes; this was a cost-effectiveness analysis study	Yes; cost-effectiveness analysis was carried out	Yes; cost effectiveness evaluation was performed	Yes; cost effectiveness evaluation was performed	Yes; cost effectiveness evaluation was performed
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?	Yes; it was justified	Yes; the CEA was justified	No; the form of economic evaluation was not stated although cost savings of maggot debridement therapy to the NHS were calculated	Yes; the choice of the form of economic evaluation was justified in relation to the question addressed	Yes; the choice of economic evaluation was justified in relation to the questions addressed	Yes; the CEA was justified	Yes; CEA was justified	Yes; CEA was justified

Study question	Wayman 2000[50]	Harding 2000[51]	Thomas 2006[52]	Mulder 1995[53]	Woo 2013[54]	Mosher 1999[55]	VENUS II trial[57]	Waycaster 2013[60]
8. Was/were the source(s) of effectiveness estimates used stated?	Yes; this was a randomised-controlled trial in which cost-effectiveness of the debridement methods was compared	Yes; the source of effectiveness parameter was defined	Yes; published data were used	Yes; the effectiveness estimates were used from the a published study	Yes; published data were used	Yes; the source of effectiveness parameter was defined	Yes; the source of effectiveness parameter was defined	Yes; the source of effectiveness parameter was defined
9. Were details of the design and results of the effectiveness study given (if based on a single study)?	Yes; this was a RCT in which cost-effectiveness of the debridement methods was compared	Yes; the effectiveness parameters were based on the pooled analysis of the published clinical reports	Yes; details of the published data were reported	Not clear; the details of the design and results of the effectiveness were not reported	Not clear; the details of the design and results of the effectiveness were not reported	Yes; model assumes the effectiveness parameter on single patient	Yes; the effectiveness parameters were based on a single randomized trial i.e. VENUS II	Yes; the effectiveness parameters were based on a single randomized trial

Study question	Wayman 2000[50]	Harding 2000[51]	Thomas 2006[52]	Mulder 1995[53]	Woo 2013[54]	Mosher 1999[55]	VENUS II trial[57]	Waycaster 2013[60]
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	N/A	Yes; the method of meta-analysis of estimates was defined	No; details of the methods of synthesis were not described	No; details of the methods of synthesis were not described	No; details of the methods of synthesis were not described	Yes; T=the method of synthesis of estimates was defined	Yes; the method of synthesis of estimates was defined	N/A
11. Were the primary outcome measure(s) for the economic evaluation clearly stated?	Yes; the primary outcome of the economic evaluation was stated	Yes; the primary outcome was clearly specified	No; the primary outcome was not stated	Yes; the primary outcome of the economic evaluation was stated	Yes; the primary outcome was stated	Yes; the primary outcome was clearly specified	Yes; the primary outcome was clearly specified	Yes; the primary outcome was clearly specified
12. Were the methods used to value health states and other benefits stated?	No; methods used to value health states and other benefits were not stated.	Yes; the methodology was clearly defined	No; methods used to value health states and other benefits were not stated	No; methods used to value health states and other benefits were not stated	No; methods used to value health states and other benefits were not stated	Yes; the methodology was clearly defined	Yes; the methodology was clearly defined	Yes; the methodology was clearly defined

Study question	Wayman 2000[50]	Harding 2000[51]	Thomas 2006[52]	Mulder 1995[53]	Woo 2013[54]	Mosher 1999[55]	VENUS II trial[57]	Waycaster 2013[60]
13. Were the details of the subjects from whom valuations were obtained given	Yes; details of the subjects were reported	Yes; the details were given	Yes; details of the subjects were reported	Yes; the details were provided	Yes; details of the subjects were reported	No; no such details were reported	Yes; the details were given	No; no such details were reported
14. Were productivity changes (if included) reported separately?	No; productivity changes were not reported	No; no such details were reported	Yes; cost savings were calculated	No; productivity changes were not reported	No; productivity changes were not reported	No; no such details were reported	No; no such details were reported	No; no such details were reported
15. Was the relevance of productivity changes to the study question discussed?	N/A	No; no such details were reported	Yes; the study was carried out to determine the cost benefit to the NHS	N/A	N/A	No; no such details were reported	No; no such details were reported	No; no such details were reported
16. Were quantities of resources reported separately from their unit cost?	No; details were not reported	No; the quantities of resources were not specified	No; details were not reported	No; details were not reported	No; details were not reported	No; the quantities of resources were not specified	Yes; the quantity of resources were reported	Yes; the quantity of resources were reported

Study question	Wayman 2000[50]	Harding 2000[51]	Thomas 2006[52]	Mulder 1995[53]	Woo 2013[54]	Mosher 1999[55]	VENUS II trial[57]	Waycaster 2013[60]
17. Were the methods for the estimation of quantities and unit costs described?	Yes; the methods of estimation of quantities and unit costs were not reported	Yes; methods for the estimation of quantities and unit costs were described	No; details were not reported	No; details were not reported	Yes; methods for estimation of quantities and unit costs were not reported	Yes; methods for estimation of quantities and unit costs were described	Yes; methods for estimation of quantities and unit costs were described	Yes; methods for estimation of quantities and unit costs were described
18. Were currency and price data recorded?	Yes; currency and price data were recorded	Yes; the currency and price data were recorded	Yes; currency and price data were recorded	Yes; currency and price data were recorded	Yes; currency and price data were reported	Yes; the currency and price data were recorded	Yes; the currency and price data were recorded	Yes; the currency and price data were recorded
19. Were details of price adjustments for inflation or currency conversion given?	No; details were not described	No; no such details were reported	No; details were not described	No; details were not described	No; details were not described	No; no such details were reported	Yes; the costs were adjusted according to 2006 cost year	Yes; the costs were adjusted according to 2012 cost year

Study question	Wayman 2000[50]	Harding 2000[51]	Thomas 2006[52]	Mulder 1995[53]	Woo 2013[54]	Mosher 1999[55]	VENUS II trial[57]	Waycaster 2013[60]
20. Were details of any model used given?	No; no model was used	Yes; the details of the decision tree model was given	No; details of any model used was not described though sensitivity analysis was carried out along with key assumption	No; details of any model used was not described.	No; details of any model used was not described though sensitivity analysis was carried out along with key assumption	Yes; the details of the decision tree model was given	Yes; the details were given	Yes; the details of the Markov model was specified
21. Was there a justification for the choice of model used and the key parameters on which it was based?	N/A	No; no such details were reported	No; no such details were reported	N/A	No; no such details were reported	No; no such details were reported	No; no such details were reported	Yes; the justification is provided
22. Was the time horizon of cost and benefits stated?	No; no such details were reported	No; no such details were reported	No; no such details were reported	No; no such details were reported	No; no such details were reported	No; no such details were reported	Yes; the time horizon of 1 year was employed	Yes; the time horizon of 1 year was being employed
23. Was the discount rate stated?	No; no such details were reported	No; no such details were reported	No; no such details were reported	No; no such details were reported	No; no such details were reported	No; no such details were reported	No; discounting has not been employed	No; discounting has not been employed

Study question	Wayman 2000[50]	Harding 2000[51]	Thomas 2006[52]	Mulder 1995[53]	Woo 2013[54]	Mosher 1999[55]	VENUS II trial[57]	Waycaster 2013[60]
24. Was the choice of rate justified?	N/A	No; no such details were reported	No; no such details were reported	N/A	N/A	No; no such details were reported	No; justification for not employing discounting has been provided	No; justification for not employing discounting has been provided
25. Was an explanation given if cost or benefits were not discounted?	N/A	No; no such details were reported	No; no such details were reported	No; no information around discount rate was reported	No; no information around discount rate was reported	No; no such details were reported	No; justification for not employing discounting has been provided	No; justification for not employing discounting has been provided
26. Were the details of statistical test(s) and confidence intervals given for stochastic data?	No; no such details were reported	No; no such details were reported	No; no such details were reported	No; no such details were reported	No; no such details were reported.	No; no such details were reported	Yes; Bayesian approach is employed	No; no such details were reported
27. Was the approach to sensitivity analysis described?	No; no such details were reported	No; no such details were reported	Yes; the approach was described	No; sensitivity analysis was no reported	Yes; the approach was described	Yes; the approach was described	Yes; the approach was described	Yes; the approach was described

Study question	Wayman 2000[50]	Harding 2000[51]	Thomas 2006[52]	Mulder 1995[53]	Woo 2013[54]	Mosher 1999[55]	VENUS II trial[57]	Waycaster 2013[60]
28. Was the choice of variables for sensitivity analysis justified?	N/A	No; no such details were reported	Yes; choice of variables was justified	N/A	No; no justification was provided for variable in sensitivity analysis	Yes; the choice of variables for sensitivity analysis was justified	Yes; the choice of variables for sensitivity analysis was justified	Yes; the choice of variables for sensitivity analysis was justified
29. Were the ranges over which the parameters were varied stated?	N/A	No; no such details were reported	Yes; the ranges were stated	N/A	No; no information regarding the ranges was provided	Yes; the parameter varied were stated	Yes; the parameter varied were stated	Yes; the parameter varied were stated
30. Were relevant alternatives compared? (That is, were appropriate comparisons made when conducting the incremental analysis?)	Yes; relevant alternatives were compared	Yes; the alternatives were compared	Yes; maggot debridement therapy was compared with conventional therapy	Yes; relevant alternatives were compared	Yes; relevant alternatives were compared	Yes; the comparisons were made between the four debridement methods: Collagenase, autolysis, wet to dry, fibrinolysin	Yes; the alternatives were compared (loose larvae vs. bagged larvae vs. hydrogel)	Yes; the alternatives were compared (Hydrocolloid versus collagenase)
31. Was an incremental analysis reported?	No; an incremental analysis was not reported	Yes; CE ratio was reported	Yes; cost savings were calculated	No; this was a cost-analysis study	No; an incremental analysis was not reported	Yes; CE ratio was reported	Yes; CU ratio was reported	Yes; CE ratio was reported

Study question	Wayman 2000[50]	Harding 2000[51]	Thomas 2006[52]	Mulder 1995[53]	Woo 2013[54]	Mosher 1999[55]	VENUS II trial[57]	Waycaster 2013[60]
32. Were major outcomes presented in a disaggregated as well as aggregated form?	Yes; total cost and individual costs were reported	Yes; the major outcomes were presented in a disaggregated as well as aggregated form	Yes; total cost and individual costs were reported	No; unit costs were not reported	Yes; total cost and individual costs were reported	Yes; the major outcomes were presented in a disaggregated as well as aggregated form	Yes; the major outcomes were presented in a disaggregated as well as aggregated form	Yes; the major outcomes were presented in a disaggregated as well as aggregated form
33. Was the answer to the study question given?	Yes; the answer was clearly described	Yes; the answer to the study question was clearly described	Yes; the answer was clearly described.	Yes; the answer was clearly described.	Yes; the answer was clearly described	Yes; the answer to the study question was clearly described	Yes; the answer to the study question was clearly described	Yes; the answer to the study question was clearly described
34. Did conclusions follow from the data reported?	Yes; conclusions followed the data reported	Yes; conclusions followed from the data reported	Yes; conclusions followed the data reported	Yes; conclusions followed the data reported	Yes; conclusions followed the data reported	Yes; conclusions followed from the data reported	Yes; conclusions followed from the data reported	Yes; conclusions followed from the data reported
35. Were conclusions accompanied by the appropriate caveats?	Yes; conclusions were accompanied by the appropriate caveats	Yes; conclusions were accompanied by the appropriate caveats	Yes; conclusions were accompanied by the appropriate caveats	Yes; conclusions were accompanied by the appropriate caveats.	Yes; conclusions were accompanied by the appropriate caveats	Yes; conclusions were accompanied by the appropriate caveats	Yes; conclusions were accompanied by the appropriate caveats	Yes; conclusions were accompanied by the appropriate caveats

Study question	Wayman 2000[50]	Harding 2000[51]	Thomas 2006[52]	Mulder 1995[53]	Woo 2013[54]	Mosher 1999[55]	VENUS II trial[57]	Waycaster 2013[60]
36. Were generalisability issues addressed?	No; the generalisability issues were not discussed	No; no such issues were addressed	No; no such issues were addressed	No; the generalisability issues were not discussed	No; the generalisability issues were not discussed	No; no such issues were addressed	No; no such issues were addressed	Yes; the generalisability issue was discussed and the results cannot be generalized to other hydrogel dressings
Adapted from Drummond MF, Jefferson TO (1996) Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. British Medical Journal 313 (7052): 275–83. Cited in Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination								

CEA: Cost-effectiveness analysis; CUA: Cost-utility analysis; NHS: National Health Service; N/A: Not applicable; RCT: Randomised controlled trial

9 De novo cost analysis

Section 9 requires the sponsor to provide information on the de novo cost analysis.

The de novo cost analysis developed should be relevant to the scope.

All costs resulting from or associated with the use of the technology should be estimated using processes relevant to the NHS and personal social services.

Note that NICE cites the price of the product used in the model in the Medical Technology guidance.

9.1 Description of the de novo cost analysis

9.1.1 Provide the rationale for undertaking further cost analysis in relation to the scope.

The search of published economic literature, identified only one study involving Debrisoft (Bahr, 2010), and this was a non-comparative evaluation. Other literature on Debrisoft (Section 6) is non-comparative, and typically does not include an assessment of economic outcomes. The scope requires an evaluation of the costs and resource consequences to the NHS, associated with the use of Debrisoft and comparators in a community setting. Due to the absence of good quality economic evidence, a de novo cost analysis has been developed.

Patients

9.1.2 What patient group(s) is (are) included in the cost analysis?

In line with the scope, the patient groups included in the cost analysis are adults and children requiring debridement of an acute or chronic wound, by a healthcare professional in a community setting. A community setting includes patients treated by a district nurse at home (including residential or nursing home), or in a

community-based clinic. It does not include patients treated in a hospital.

Technology and comparator

9.1.3 Provide a justification if the comparator used in the cost analysis is different from the scope.

The comparators are the methods of debridement most commonly used by nurses in a community setting. The scope includes irrigating the wound with saline and:

- *Using a hydrogel or other autolytic dressing, or*
- *Cleansing with gauze*

The analysis also includes biosurgical (larvae) debridement, because this is an appropriate comparator for Debrisoft for sloughy wounds, and because it is used in the UK by nurses in the community. Most of the published literature identified in the search of economic studies relates to biosurgical debridement.

Model structure

9.1.4 Provide a diagram of the model structure you have chosen.

The model is a cost-consequences analysis, which evaluates the costs and resource consequences for the NHS, resulting from the use of Debrisoft and comparators in a community setting. The time horizon of the analysis, is the time to complete debridement of the wound, defined as the time from first assessment of the wound as requiring debridement, to the final assessment of complete debridement. The focus on costs and resource use is justified by the assumption, that the clinical outcomes associated with different methods of debridement are approximately the same.

9.1.5 Justify the chosen structure in line with the clinical pathway of care identified in response to question 3.3.

The clinical pathway involves:

- *First assessment of the skin, wound and patient by a district nurse, and a decision on the appropriate method of debridement. Nurse contacts may take place at the patient's home or at a community-based clinic.*
- *Depending on the choice of method of debridement, and the location of the nurse contact, the first assessment may involve ordering and/or prescribing product.*
- *First application of chosen method of debridement (Debrisoft, saline & gauze, hydrogel or larvae).*
- *Regular district nurse contacts to re-evaluate the condition of the wound, in order to determine if further debridement is required. Further applications of debridement product (if required) until debridement is judged to be complete.*

The cost model covers the pathway from first assessment of the wound as requiring debridement, to assessment that debridement is complete.

9.1.6 Provide a list of all assumptions in the cost model and a justification for each assumption.

<u>Cost to complete debridement.</u> The cost analysis estimates the total cost to achieve complete debridement for each of the comparators. This cost is defined as:

> *Number of applications (of debridement product) x cost per application + Number of nurse contacts x cost per nurse contact*

Number of applications. The number of applications required to completely debride a wound in the base case model, was derived wherever possible from the published literature. The most appropriate sources were selected from the studies identified in the searches of economic and clinical studies. In all cases, base case estimates are the most conservative estimates available in the literature. What this means in practice is, that estimates of the costs of comparators are likely to be at the lower end of the range, and estimates of the costs of Debrisoft are likely to be at the higher end of the range. Uncertainties are tested in sensitivity analysis.

- *Larvae. The mean number of applications of larvae, required to achieve complete debridement in the base case cost model, is taken from Soares M (2009)[56]. Soares reports the results of a cost-effectiveness analysis of larval therapy based on results of the VenUS II[57] study. VenUS II[57] was a randomised controlled trial, which compared the clinical effectiveness of larval therapy with a standard debridement technique (hydrogel dressings), as a means to debride sloughy or necrotic leg ulcers (n= 267 patients). In the larvae arm, the mean number of treatment applications was 1.45 per wound, and the mean duration of treatment was 11.95-12.84 days (for loose and bagged larvae, respectively). Other studies with relevant information on larval debridement, identified in the literature search (Gilead, L (2012)[61]; and Sherman R, (2002)[66]) report a mean of 2.9 applications (median = 2); and 9.6 applications (4.8 weeks of treatment at 2 applications per week), respectively.*

- *Hydrogel. Hydrogel debridement was the comparator in the VenUS II[57] trial, and this is the source of the value in the base case cost model. In the hydrogel arm the mean number of treatment applications was 9.2, and the mean duration of*

treatment was 43.17 days. No better sources were identified in the literature search.

- *Debrisoft. The base case value is taken from a prospective non-comparative evaluation of 57 patients treated with Debrisoft (Bahr S (2011[2]). The authors report that 77% of wounds were completely debrided after three applications of Debrisoft. The mean procedure time was 2.51 minutes. The cost model assumes that patients not completely debrided after three applications of Debrisoft will be switched to a hydrogel dressing and will incur the total cost of hydrogel debridement. No other studies on Debrisoft were identified in the search of economic literature. Clinical evidence (summarised in Section 6) suggests that in a substantial proportion of cases, Debrisoft may achieve complete debridement with a single application.*

- *Saline and gauze. No relevant sources were found for the number of applications required to completely debride a wound. The base case cost model makes the conservative assumption, that cleansing with saline and gauze can achieve debridement in 12 applications (4 weeks at 3 applications per week). This is very conservative in light of the evidence from VenUS II[57], that the mean time to debridement with hydrogel dressings was 43 days, and in light of the fact that daily (or more frequent) dressing changes are likely to be required with saline and gauze.*

Cost per application. The cost per application covers the cost of the debriding product, assuming a 10cm x 10cm wound, at one piece/dressing per application. Unit costs for Debrisoft, hydrogels and saline & gauze were obtained from British National Formulary (http://www.bnf.org/bnf/index.htm), accessed on-line 7th August 2013. The unit cost of larvae were provided by Biomonde (http://biomonde.com/homeUK.html) on 7th August 2013.

Number of nurse contacts (nurse visits). The number of nurse visits per application depends on the product, and on whether or not it is necessary to order product in advance. This in turn depends on whether the patient is seen at home, or in a community-based clinic.

- *Larvae. Larvae have a short life-span and will typically need to be ordered at the first assessment visit, applied at the second visit, and removed at the third visit when the wound is reassessed and additional larvae ordered if required. The base case cost model assumes that the first application requires 3 nurse visits, and each subsequent application requires 2 visits (apply and reassess). There is no difference depending on whether visits take place at the patient's home or in a clinic.*

- *Gauze. The model assumes that gauze is available immediately and does not need to be ordered. The first application requires 2 visits (assessment and application, and a subsequent visit to reassess the wound/apply a new dressing if required), and each subsequent application requires 1 visit to reassess the wound.*

- *Hydrogel dressings and secondary (cover) dressings are assumed to be immediately available, if the patient is seen at a community-based clinic. In this case, the first application requires 2 visits (apply and reassess/apply a new dressing if required) and each subsequent application requires 1 visit. The base case assumes that these products have to be ordered (prescribed and dispensed), if the patient is seen at home. Only one prescription is required at the first assessment to cover the planned treatment course. The first application requires 3 visits (assess and order, apply, reassess/apply new dressing if required) and each*

subsequent application requires 1 visit (to reassess the wound).

- *Debrisoft does not require a cover dressing and the wound can be treated and reassessed at the same visit. The base case assumes that Debrisoft is available in a clinic, and each application requires 1 visit. In a home setting, the model assumes that Debrisoft needs to be ordered on the first visit. In this case, the first application requires 2 visits, and each subsequent application requires 1 visit.*

Cost per nurse contact (nurse visit). The cost per nurse visit includes the cost of nurse time, secondary (cover) dressings where required and the cost of a dressing pack.

- *The cost of a district nurse visit is taken from PSSRU Unit Costs of Health and Social Care (http://www.pssru.ac.uk/project-pages/unit-costs/2012/) accessed on-line on 7th August 2013, assuming a 15-minute appointment. A home visit includes an additional cost for travel time.*

- *Secondary dressings are either an absorbent dressing pad, or semi-permeable adhesive film. Unit costs were obtained from British National Formulary (http://www.bnf.org/bnf/index.htm), accessed on-line 7th August 2013.*

- *One non-drug tariff specification sterile dressing pack includes vitrex gloves, large apron, disposable bag, paper towel, softswabs, adsorbent pad, sterile field. Unit costs were obtained from British National Formulary (http://www.bnf.org/bnf/index.htm), accessed on-line 7th August 2013.*

9.1.7 Define what the model's health states are intended to capture.

Not applicable

9.1.8 Describe any key features of the cost model not previously reported.

Table C4 describes key features of the cost model not previously reported.

Table C4 Key features of model not previously reported

Factor	Chosen values	Justification	Reference
Time horizon of model	Time to complete debridement of the wound	Consistent with the scope of the analysis	
Discount of 3.5% for costs	Costs are not discounted	Because of the short term nature of the analysis (<1 year)	
Perspective (NHS/PSS)	NHS only	There are not expected to be any differences in PSS costs depending on methods of wound debridement	
Cycle length	Not applicable	Not applicable	
NHS, National Health Service; PSS, Personal Social Services			

9.2 Clinical parameters and variables

9.2.1 Describe how the data from the clinical evidence were used in the cost analysis.

Data on the number of applications required to debride a wound, were drawn from the review of clinical literature (Section 6), and the review of economic studies (Section 7). Details of the sources of parameter estimates are given in Section 8.1.6 above.

9.2.2 Are costs and clinical outcomes extrapolated beyond the study follow-up period(s)? If so, what are the assumptions that underpin this extrapolation and how are they justified?

No extrapolations have been undertaken

9.2.3 Were intermediate outcome measures linked to final outcomes (for example, was a change in a surrogate outcome linked to a final clinical outcome)? If so, how was this relationship estimated, what sources of evidence were used and what other evidence is there to support it?

No

9.2.4 Were adverse events such as those described in section 7.7 included in the cost analysis? If appropriate, provide a rationale for the calculation of the risk of each adverse event.

Adverse events have not been included.

9.2.5 Provide details of the process used when the sponsor's clinical advisers assessed the applicability of available or estimated clinical model parameter and inputs used in the analysis.

The parameters in the model were derived from searches of clinical and economic literature, taken in conjunction with EWMA guidance and the UK Consensus Document on debridement (Section 3.2). Face to face and/or telephone interviews, were carried out with four experienced tissue viability nurses in the UK, with experience of Debrisoft and other methods of debridement, used in a community setting in the NHS.

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Sylvie Hampton
Tissue Viability Consultant
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Eastbourne

Agnes Collarte
Viability Nurse Team Lead
Central London Community Healthcare NHS Trust (CLCH)

Trudie Young

Tissue viability nurse
Director of Education and Training
Welsh Wound Innovation Centre,
Aneurin Bevan Health Board

9.2.6 Summarise all the variables included in the cost analysis. Provide cross-references to other parts of the submission. A suggested format is provided in table C5 below.

Table C5 shows the resources included in the cost model, with unit costs and data sources.

Table C5 Summary of variables applied in the cost model

Variable	Unit	Cost	Source
Nurse time	Home visit Clinic visit	£24.25 £12.75	PSSRU (2012) Table 10.1 District nurse, per 15-minute home visit including travel PSSRU (2012) Table 10.1 District nurse, per 15-minutes of patient-related activity, excluding travel
Debrider Gauze	Per pack of 5	£0.39	Gauze swab BP 1988. Sterile, 7.5cm x 7.5cm. BNF, A5.7.2
Debrider Hydrogel	Per dressing	£2.03	Median price of hydrogel sheets and amorphous hydrogels, 10cm x 10cm. BNF, A5.2.1 (hydrogel dressings)
Debrider Larvae	Bagged Loose	£295.00 £175.00	Biomonde, personal communication (August 2013). Min 400 maggots, suitable for 10cm x 10cm wound Biomonde, personal communication (August 2013). Min 300, suitable for a 10cm x 10cm wound
Debrider Debrisoft	Per piece	£6.19	BNF, A5.5.3 (physical debridement pads),

Variable	Unit	Cost	Source
			Debrisoft , 10cm x10 cm
Cover dressing	Film Per piece Absorbent dressing pad Per piece	£1.02 £0.17	Median price of semi-permeable adhesive film, 12cm x 10cm. BNF, A5.2.1 Median price of absorbent dressing pads, 20cm x 10cm. BNF,
Dressing pack	Per pack	£0.60	Non-drug tariff specification sterile dressing pack. BNF, A5.7.1

Table C6 shows values of the two key parameters in the cost model: number of applications required to achieve complete debridement, and the number of nurse visits to achieve complete debridement. These two variables drive differences in cost between Debrisoft and comparators. A justification of parameter values is given in the table and also in Section 8.1.6

Table C6: Model parameters

Parameter	Value	Source
No. applications to complete debridement		
Larvae	1.45	Soares M (2009)
Hydrogel	9.20	Soares M (2009)
Debrisoft	3.00 (to debride 77% of wounds)	Bahr S (2010)
Gauze	12.0	Conservative assumption based on clinical opinion
No. Nurse visits per application		
Larvae	1st application = 3 Subsequent = 2	Based on the need to order the product for delivery next day
Hydrogel -home	1st application = 3 Subsequent = 1	Based on the assumption that dressings need to be prescribed and dispensed (one prescription for the whole treatment course)
Hydrogel - clinic	1st application = 2 Subsequent = 1	Based on the assumption that dressings are immediately available in the clinic
Gauze	1st application =2 Subsequent = 1	Assumes gauze is immediately available for home and clinic visits
Debrisoft-home	1st application = 2 Subsequent = 1	Assumes Debrisoft has to be prescribed and dispensed
Debrisoft-clinic	1st application = 1 Subsequent = 1	Assumes Debrisoft is immediately available in the clinic

9.3 Resource identification, measurement and valuation

NHS costs

9.3.1 Describe how the clinical management of the condition is currently costed in the NHS in terms of reference costs and the payment by results (PbR) tariff.

District nursing services are not within the PbR framework, and there is no separate fee for wound debridement carried out by a district nurse.

NHS Reference Costs for 2010-11 (https://www.gov.uk/government/publications/nhs-reference-costs-financial-year-2011-to-2012) show a mean cost for district nursing services, adult face to face (service code CN301AF) of £37 (lower

and upper quartile £31 and £42 respectively). The mean cost for tissue viability nursing (code CN213 AF) is £61 (lower and upper quartiles £36 and £76 respectively).

9.3.2 State the Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS) codes for the operations, procedures and interventions relevant to the use of the technology for the clinical management of the condition.

There is no OPCS code for wound debridement, except for debridement carried out in a hospital setting.

Resource identification, measurement and valuation studies

9.3.3 Provide a systematic search of relevant resource data for the NHS in England. Include a search strategy and inclusion criteria, and consider published and unpublished studies.

Studies reporting resource use or costs of debridement, were included in the search of economic studies reported in Section 8 above.

9.3.4 Provide details of the process used when clinical advisers assessed the applicability of the resources used in the model[1].

See answer to 8.2.5 above

Technology and comparators' costs

9.3.5 Provide the list price for the technology.

Debrisoft price is £6.19 for a 10cm x 10 cm pad (BNF online accessed online 7th August, 2013)

[1] Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee.

(http://www.medicinescomplete.com/mc/bnf/current/PHP18673-debrisoft.htm)

9.3.6 If the list price is not used in the de novo cost model, provide the alternative price and a justification.

Not applicable

9.3.7 Summarise the annual costs associated with the technology and the comparator technology (if applicable) applied in the cost model.

The following tables (Table C7 (A) to C7(H),) show estimates of the expected cost to complete debridement for Debrisoft, and comparators, in the home and clinic setting. Information on parameter values used in the cost models is discussed in Section 8.2.6.

In the case of Debrisoft, because the best available information from the literature does not quote the number of applications to completely debride all wounds (77% of wounds), the cost model assumes that 23% of patients are switched from Debrisoft after 3 applications to a hydrogel. These patients incur the full cost of debridement with a hydrogel.

Table C7 (A) Expected cost to complete debridement: Debrisoft (home visit)

Resources	Units	Cost
DN home visit Secondary dressing Dressing pack	1 0 1	£24.25 - £0.60
Cost per DN visit		£24.85
No. of DN visits = 4	Cost of DN visits	£99.40
Debrisoft	1	£6.19
No. of applications = 3	Cost of Debrisoft	£18.57
Cost to debride with Debrisoft	77% of patients	£117.97
Cost to debride with Hydrogel	23% of patients	£308.42
Expected cost to complete debridement		£161.77

Table C7 (B) Expected cost to complete debridement: Debrisoft (clinic visit)

Resources	Units	Cost
DN clinic visit Secondary dressing Dressing pack	1 0 1	£12.75 - £0.60
Cost per DN visit		£13.35
No. of DN visits = 3	Cost of DN visits	£40.05
Debrisoft	1	£6.19
No. of applications = 3	Cost of Debrisoft	£18.57
Cost to debride with Debrisoft	77% of patients	£58.62
Cost to debride with Hydrogel	23% of patients	£165.25
Expected cost to complete debridement		£83.14

Table C7 (C) Expected cost to complete debridement: Hydrogel (home visit)

Resources	Units	Cost
DN home visit	1	£24.25
Secondary dressing	1	£1.02
Dressing pack	1	£0.60
Cost per DN visit		£25.87
No. of DN visits = 11.2	Cost of DN visits	£289.74
Hydrogel	1	£2.03
No. of applications = 9.2	Cost of hydrogel	£18.68
Expected cost to complete debridement		£308.42

Table C7 (D) Expected cost to complete debridement: Hydrogel (clinic visit)

Resources	Units	Cost
DN clinic visit	1	£12.75
Secondary dressing	1	£1.02
Dressing pack	1	£0.60
Cost per DN visit		£14.37
No. of DN visits = 10.2	Cost of DN visits	£146.57
Hydrogel	1	£2.03
No. of applications = 9.2	Cost of hydrogel	£18.68
Expected cost to complete debridement		£165.25

Table C7 (E) Expected cost to complete debridement: Gauze (home visit)

Resources	Units	Cost
DN home visit	1	£24.25
Secondary dressing	1	£0.17
Dressing pack	1	£0.60
Cost per DN visit		£25.02
No. of DN visits = 13	Cost of DN visits	£325.26
Gauze	1 application = 5 pieces	£0.39
No. of applications = 12	Cost of gauze	£4.68
Expected cost to complete debridement		£329.94

Table C7 (F) Expected cost to complete debridement: Gauze (clinic visit)

Resources	Units	Cost
DN clinic visit	1	£12.75
Secondary dressing	1	£0.17
Dressing pack	1	£0.60
Cost per DN visit		£13.52
No. of DN visits = 13	Cost of DN visits	£175.76
Gauze	1 application = 5 pieces	£0.39
No. of applications = 12	Cost of gauze	£4.68
Expected cost to complete debridement		£180.44

Table C7 (G) Expected cost to complete debridement: Larvae (home visit)

Resources	Units	Cost
DN home visit	1	£24.25
Secondary dressing	1	£0.17
Dressing pack	1	£0.60
Cost per DN visit		£25.02
No. of DN visits = 3.9	Cost of DN visits	£97.58
Larvae (loose)	Per pot	£175.00
No. of applications = 1.45	Cost of larvae	£253.75
Expected cost to complete debridement		£351.33

Table C7 (H) Expected cost to complete debridement: Larvae (clinic visit)

Resources	Units	Cost
DN clinic visit	1	£12.75
Secondary dressing	1	£0.17
Dressing pack	1	£0.60
Cost per DN visit		£13.52
No. of DN visits = 3.9	Cost of DN visits	£52.73
Larvae (loose)	Per pot	£175.00
No. of applications = 1.45	Cost of larvae	£253.75
Expected cost to complete debridement		£306.48

Health-state costs

9.3.8 If the cost model presents health states, the costs related to each health state should be presented in table C8. The health states should refer to the states in section 9.1.7. Provide a rationale for the choice of values used in the cost model.

Not applicable

Adverse-event costs

9.3.9 Complete table C9 with details of the costs associated with each adverse event referred to in 9.2.4 included in the cost model. Include all adverse events and complication costs, both during and after longer-term use of the technology.

Not applicable

Miscellaneous costs

9.3.10 Describe any additional costs and cost savings that have not been covered anywhere else (for example, PSS costs, and patient and carer costs). If none, please state.

No differences in PSS costs have been identified. Costs to patients and carers are not included in the analysis.

9.3.11 Are there any other opportunities for resource savings or redirection of resources that it has not been possible to quantify?

None

9.4 Approach to sensitivity analysis

Section 9.4 requires the sponsor to carry out sensitivity analyses to explore uncertainty around the structural assumptions and parameters used in the analysis. All inputs used in the analysis will be estimated with a degree of imprecision. For technologies whose final price/acquisition cost has not been confirmed, sensitivity analysis should be conducted over a plausible range of prices.

Analysis of a representative range of plausible scenarios should be presented and each alternative analysis should present separate results.

9.4.1 Has the uncertainty around structural assumptions been carried out in the cost analysis.

Uncertainty around model parameters has been modelled in a one-way sensitivity analysis and in scenario analysis.

9.4.2 Was a deterministic and/or probabilistic sensitivity analysis undertaken? If not, why not? How were variables varied and what was the rationale for this? If relevant, the distributions and their sources should be clearly stated.

Deterministic sensitivity analysis was undertaken. The main cost drivers are the number of debridement applications, and the number of district nurse visits. In the absence of consistent information about the likely variation about mean values, both parameters were varied by +/- 20%. Costs are also sensitive to whether patients are seen at home or in a community-based clinic. Additional sensitivity analysis has been carried out on unit costs and product prices.

9.4.3 Complete table C8, C9 and/or C10 as appropriate to summarise the variables used in the sensitivity analysis.

Table C8 summarises the variables used in the sensitivity analysis.

Table C8 Variables used in one-way scenario-based deterministic sensitivity analysis

Variable	Base-case value	Range of values	
		-20%	+20%
Number of applications Larvae	1.45	1.16	1.74
Number of applications Hydrogel	9.20	7.36	11.04
Number of applications Debrisoft	3.00	2.4	3.6
Number of applications Gauze	12.0	9.6	14.4
Total number of nurse visits Larvae	3.9	3.12	4.68
Total number of nurse visits Hydrogel -home	11.2	8.96	13.44
Total number of nurse visits Hydrogel - clinic	10.2	8.16	12.24
Total number of visits nurse Gauze	13	10.4	15.6
Total number of nurse visits Debrisoft-home	4	3.2	4.8
Total number of nurse visits Debrisoft-clinic	3	2.4	3.6
Nurse time - home visit	£24.25	19.4	29.1
Nurse time – clinic	£12.75	10.2	15.3
Debrider Larvae (Loose)	£175.00	£140.00	£210.00
Debrider Debrisoft	£6.19	£4.95	£7.43

Table C9 summarises the variables used in the multi-way scenario analysis.

Table C9 Variables used in multi-way scenario-based sensitivity analysis

Variable	***Probability Debrisoft will debride wound***	***Number of nurse visits Hydrogel - clinic***
Base case	77%	10.2
Scenario 1	50%	5
Scenario 2	90%	12

No parameters were used in probabilistic sensitivity analysis.

Table C10 Variable values used in probabilistic sensitivity analysis
Not applicable

If any parameters or variables listed in section 9.2.6 were omitted from the sensitivity analysis, provide the rationale.

The parameters omitted from the sensitivity analysis include the cost of debrider gauze, debrider hydrogel, cover dressing, and dressing pack. These costs were omitted from the sensitivity analysis as the costs are marginal and would not have significant impacts on the results of the model.

9.5 Results of de novo cost analysis

Section 9.5 requires the sponsor to report the de novo cost analysis results. These should include the following:

- costs
- disaggregated results such as costs associated with treatment, costs associated with adverse events, and costs associated with follow-up/subsequent treatment
- a tabulation of the mean cost results
- results of the sensitivity analysis.

Base-case analysis

9.5.1 Report the total costs associated with use of the technology and the comparator(s) in the base-case analysis.

Table C11 provides a summary of the base case results.

Table C11 Base-case results

	Debrisoft		**Gauze**		**Hydrogel**		**Larvae**	
	Home	**Clinic**	**Home**	**Clinic**	**Home**	**Clinic**	**Home**	**Clinic**
Total cost	£162	£83	£330	£180	£308	£165	£351	£306
			+£168	*+£97*	*+£147*	*+£82*	*+£190*	*+£223*
Consumables (cost)	£25	£24	£15	£14	£37	£35	£256	£256
			-£10	*-£10*	*+£12*	*+£11*	*+£231*	*£232*
Nurse time (cost)	£137	£59	£315	£166	£271	£130	£95	£50
			+£178	*+£107*	*+£134*	*+£71*	*-£42*	*-£9*
Nurse time (minutes)	85.5	70.5	195	195	168	153	58.5	58.5
			+109.5	*+124.5*	*+82.5*	*+82.5*	*-27.0*	*-12.0*
Home/clinic Appointments	5.7	4.7	13.0	13.0	11.2	10.2	3.9	3.9
			+7.3	*+8.3*	*+5.5*	*+5.5*	*-1.8*	*-0.8*

9.5.2 Report the total difference in costs between the technology and comparator(s).

See Table C11 (Section 8.5.1)

9.5.3 Provide details of the costs for the technology and its comparator by category of cost. A suggested format is presented in table C12.

See Table C11 (Section 8.5.1)

9.5.4 If appropriate, provide details of the costs for the technology and its comparator by health state. A suggested format is presented in table C13.

Not applicable

9.5.5 If appropriate, provide details of the costs for the technology and its comparator by adverse event. A suggested format is provided in table C14.

Not applicable

Sensitivity analysis results

9.5.6 Present results of deterministic one-way sensitivity analysis of the variables described in table C10.1.

Table C12 provides a summary of the one way deterministic sensitivity analysis based on the parameters and values outlined in Table C8.

Table C12 Summary of one way deterministic sensitivity analysis

Variable	Incremental cost of comparator using (-20% of base case values)						Incremental cost of comparator using (+20% of base case values)					
	Saline & gauze		Hydrogel		Larvae		Saline & gauze		Hydrogel		Larvae	
	Home	Clinic	Home	Clinic	Home	Clinic	Home	Clinic	Home	Clinic	Home	Clinic
Number of applications Larvae	-£168.2	-£97.3	-£146.6	-£82.1	-£138.8	-£172.6	-£168.2	-£97.3	-£146.6	-£82.1	-£240.3	-£274.1
Number of applications Hydrogel	-£169.0	-£98.2	-£143.8	-£79.2	-£190.4	-£224.2	-£167.3	-£96.4	-£149.5	-£85.0	-£188.7	-£222.5
Number of applications Debrisoft	-£171.0	-£100.2	-£149.5	-£85.0	-£192.4	-£226.2	-£165.3	-£94.4	-£143.8	-£79.2	-£186.7	-£220.5
Number of applications Gauze	-£167.2	-£96.4	-£146.6	-£82.1	-£189.6	-£223.3	-£169.1	-£98.2	-£146.6	-£82.1	-£189.6	-£223.3
Total number of nurse visits Larvae	-£168.2	-£97.3	-£146.6	-£82.1	-£170.0	-£212.8	-£168.2	-£97.3	-£146.6	-£82.1	-£209.1	-£233.9
Total number of nurse Hydrogel - home	-£181.5	-£97.3	-£102.0	-£82.1	-£202.9	-£223.3	-£154.8	-£97.3	-£191.3	-£82.1	-£176.2	-£223.3
Total number of nurse Hydrogel - clinic	-£168.2	-£104.0	-£146.6	-£59.5	-£189.6	-£230.1	-£168.2	-£90.6	-£146.6	-£104.7	-£189.6	-£216.6
Total number of	-£103.1	-£62.1	-£146.6	-£82.1	-£189.6	-£223.3	-£233.2	-	-£146.6	-£82.1	-£189.6	-£223.3

Variable	Incremental cost of comparator using (-20% of base case values)						Incremental cost of comparator using (+20% of base case values)					
	Saline & gauze		Hydrogel		Larvae		Saline & gauze		Hydrogel		Larvae	
	Home	Clinic	Home	Clinic	Home	Clinic	Home	Clinic	Home	Clinic	Home	Clinic
nurse Gauze								£132.4				
Total number of nurse Debrisoft-home	-£183.5	-£97.3	-£162.0	-£82.1	-£204.9	-£223.3	-£152.9	-£97.3	-£131.3	-£82.1	-£174.2	-£223.3
Total number of nurse Debrisoft-clinic	-£168.2	-£103.5	-£146.6	-£88.3	-£189.6	-£229.5	-£168.2	-£91.1	-£146.6	-£75.9	-£189.6	-£217.2
Nurse time – home	-£132.5	-£97.3	-£119.8	-£82.1	-£198.1	-£223.3	-£203.8	-£97.3	-£173.5	-£82.1	-£181.0	-£223.3
Nurse time - clinic	-£168.2	-£76.0	-£146.6	-£68.0	-£189.6	-£225.3	-£168.2	-£118.6	-£146.6	-£96.2	-£189.6	-£221.4
Debrider Larvae (Loose)	-£168.2	-£97.3	-£146.6	-£82.1	-£138.8	-£172.6	-£168.2	-£97.3	-£146.6	-£82.1	-£240.3	-£274.1
Debrider Debrisoft	-£171.0	-£100.2	-£149.5	-£85.0	-£192.4	-£226.2	-£165.3	-£94.4	-£143.8	-£79.2	-£186.7	-£220.5

9.5.7 Present results of deterministic multi-way scenario sensitivity analysis described in table C10.2.

The multi-way scenario sensitivity analysis, focused on the setting in which Debrisoft generates the most limited savings (hydrogel clinic), in order to analyse if changes in key parameters would change the results of the cost model. Table C13 provides a summary of the multi-way scenario analysis.

Table C13 Summary of multi-way scenario analysis

Variable	***Probability Debrisoft will debride wound***	***Number of nurse visits Hydrogel - clinic***	**Saline & gauze**		**Hydrogel**		**Larvae**	
			Home	**Clinic**	**Home**	**Clinic**	**Home**	**Clinic**
Base case	77%	10.2	-£168.2	-£97.3	-£146.6	-£82.1	-£189.6	-£223.3
Scenario 1	50%	5	-£116.7	-£105.9	-£95.2	-£16.0	-£138.1	-£231.9
Scenario 2	90%	12	-£192.9	-£108.6	-£171.4	-£119.2	-£214.3	-£234.6

9.5.8 Present results of the probabilistic sensitivity analysis described in table C10.3.

Not applicable

9.5.9 What were the main findings of each of the sensitivity analyses?

The sensitivity analysis indicates that in all scenarios, Debrisoft remains cost saving in comparison to gauze, hydrogel, and larvae.

9.5.10 What are the key drivers of the cost results?

The key drivers of the cost results include the number of nurse visits, and cost per nurse visit. Even with significant changes to these variables, Debrisoft remains cost saving (Table C12).

Miscellaneous results

9.5.11 Describe any additional results that have not been specifically requested in this template. If none, please state.

Not applicable

9.6 Subgroup analysis

For many technologies, the capacity to benefit from treatment will differ for patients with differing characteristics. Sponsors are required to complete section 9.6 in accordance with the subgroups identified in the scope and for any additional subgroups considered relevant.

Types of subgroups that are not considered relevant are those based solely on the following factors.

- Subgroups based solely on differential treatment costs for individuals according to their social characteristics.
- Subgroups specified in relation to the costs of providing treatment in different geographical locations within the UK (for example, if the costs of facilities available for providing the technology vary according to location).

9.6.1 Specify whether analysis of subgroups was undertaken and how these subgroups were identified. Cross-reference the response to the decision problem in table A1 and sections 3.2 and 7.4.4.

No subgroup analysis

9.6.2 Define the characteristics of patients in the subgroup(s).

Not applicable

9.6.3 Describe how the subgroups were included in the cost analysis.

Not applicable

9.6.4 What were the results of the subgroup analysis/analyses, if conducted? The results should be presented in a table similar to that in section 9.5.1 (base-case analysis).

Not applicable

9.6.5 Were any subgroups not included in the submission? If so, which ones, and why were they not considered?

Not applicable

9.7 Validation

9.7.1 Describe the methods used to validate and cross-validate (for example with external evidence sources) and quality-assure the model. Provide references to the results produced and cross-reference to evidence identified in the clinical and resources sections.

The model structure and inputs were validated with the clinical experts outlined in Section 8.2.5.

The technical validity of the model was quality assured by undertaking the following tests:

- *Function testing – test whether all sheets and other items in the model are in working order*
- *Input testing – changing all inputs to determine whether they function as expected*
- *Extreme value testing – using very large and small numbers for all values used in the model, to review whether the model behaves as expected*
- *Nothing testing – Setting all input values alternately to 0, e.g. setting all costs to 0 should yield a total cost of 0*
- *Scenario testing – setting the two different scenarios in the model the same, yielding a difference of 0*

9.8 Interpretation of economic evidence

9.8.1 Are the results from this cost analysis consistent with the published economic literature? If not, why do the results from this evaluation differ, and why should the results in the submission be given more credence than those in the published literature?

We did not find any comparable analysis in the published literature

9.8.2 Is the cost analysis relevant to all groups of patients and NHS settings in England that could potentially use the technology as identified in the scope?

Yes

9.8.3 What are the main strengths and weaknesses of the analysis? How might these affect the interpretation of the results?

Strengths: The analysis provides a simple cost comparison analysis reflecting clinical practice for wound debridement. The analysis utilises the best available data within the published literature. In addition, the analysis has been validated by clinical experts outlined in Section 8.2.5.

Weaknesses: The lack of data directly comparing gauze, hydrogel, larvae and Debrisoft within the same population group, in terms of cost to debridement, is a limitation of the analysis. The lack of direct comparison data, measuring the cost to debridement, required the analysis to use the best available data from multiple different sources. However, the sensitivity analysis outlined in Section 8.5.6, shows variation in parameters does not significantly change the results.

9.8.4 What further analyses could be undertaken to enhance the robustness/completeness of the results?

A randomised clinical trial, comparing cost to debridement and cost to healing with Debrisoft and comparators, may produce better

quality evidence. As mentioned in Section 5.1 a randomised controlled trial comparing Debrisoft to wound dressing is currently being undertaken. A prospective study (or a retrospective study of a representative sample of clinical records) of wound patients debrided in a community setting, would provide information on actual clinical practice (e.g. method of debridement, wound condition, frequency of nurse contacts, time to debridement, time to healing) ,which could be used to inform the relative cost-effectiveness of different debridement methods, including Debrisoft.

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25. Prouvost L (2012) A monofilament product as an alternative to mechanical debridement of the wound bed and periwound skin, Poster presentation, EWMA Conference, Vienna - May 2012
26. Wiser M (2012) A monofilament debridement product - Is it a new support for debridement?, Poster presentation, EWMA Conference, Vienna - May 2012

27. Rieke F (2012) A cohort study on the treatment of diabetic foot ulcer patients using a monofilament debrider and a collagen dressing, Poster presentation, EWMA Conference, Vienna - May 2012
28. Skovgaard-Holm H, Simonsen H (2012) Evaluation of a new polyester monofilament debridement pad* from both patients and homecare nurses point of view, Poster presentation, EWMA Conference, Vienna - May 2012
29. Weindorf M, Dissemond J, (2012) Wound debridement with a new debrider: A case report series about dermatologic patients with chronic painful ulcerations of differing aetiology, Poster presentation, EWMA Conference, Vienna - May 2012
30. Mustafi N et al, (2011) Clinical efficacy of a monofilament fibre containing wound debridement product evaluated in a multicentre real life study, CPC, January 2011
31. Alblas J, Klicks R.J. Andriessen A, (2012) A polyhexanide containing bio-cellulose dressing in the treatment of partial-thickness dermal burns, Poster presentation, EWMA Conference, Vienna - May 2012
32. Renato P, Ivano C, Raffaele D N, Paolo M, Gonzalez M, Ermollis P (2012) Economical comparison between three different types of debridement (autolytic and enzymatic vs mechanical debridement with polyester fibres) Poster presentation, Wounds UK, Harrogate November 2012
33. Lloyd-Jones M, Parry-Ellis R (2012) An evaluation of the role of an active debridement* system within a First Dressing Initiative, Poster Presentation, Wounds UK Conference, Harrogate - November 2012
34. Flinton R, (2011) A new solution to an old problem - an innovative active debridement system, Poster Presentation, Wounds UK Conference, Harrogate - November 2011
35. Wilson N (2013) Reducing the cost of debridement – a case study, Poster Presentation at TVS Conference, Kettering. April 2013
36. Denyer J (2013) The use of debridement pads in the management of children with severe Epidermolysis Bullosa, Poster presentation EWMA 2013 (NOT YET PUBLISHED)

37. Makanin AJ, Slavnika IA, Rubanov LN, Chernov AA (2012) Early surgical intervention for a patient with a severe electric burn of the skull, Poster presentation, EWMA Conference, Vienna - May 2012
38. Stoffels I , Dissemond J, Klode J (2012) Fireworks with after effects - Successful use of a polyester monofilament fibre product for the removal of embedded explosive residue, Poster presentation, EWMA Conference, Vienna - May 2012
39. van Zweeden J M, (2012) A special case: How lower limb amputation was prevented, Poster presentation, EWMA Conference, Vienna - May 2012
40. van Dam R (2012) The effective management of a patient with a grade four sacral pressure ulcer, Poster presentation, Wounds UK, Harrogate November 2012
41. Amesz S, Alice van den Wijngaard, Palliative care of a critically ill patient after vulvar carcinoma radiation treatment – a case study, Poster presentation, Wounds UK, Harrogate November 2012
42. Westgate, S.J. And Cutting, K.F (2012) A novel treatment method for the removal of biofilm material, Poster presentation, EWMA Conference, Vienna - May 2012
43. Wiegand C, Reddersen K, Abel M, Ruth P, Hipler U.-C (2012) Poster Presentation, Wounds UK Conference, Harrogate - November 2012
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10 Appendices

10.1 Appendix 1: Search strategy for clinical evidence (section 7.1.1)

The following information should be provided:

10.1.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- The Cochrane Library.

A search of six electronic bibliographic databases (Medline, Embase, CINAHL Plus, Cochrane Library, Medline (R) In-process and PubMed) was performed upon the OVID platform

10.1.2 The date on which the search was conducted.

June 6th 2013

10.1.3 The date span of the search.

From inception to June 6th 2013

10.1.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

S1TX Wound Healing

S2TX Wound

S3MH “Wounds and Injuries+”

S4TX Chronic wounds

S5S1 OR S2 OR S3 OR S4

S6TX monofilament fibre pad

S7TX Debrisoft

S8S6 OR S7

S9S5 AND S8

10.1.5 Details of any additional searches, such as searches of company or professional organisation databases (include a description of each database).

Bibliographies of included studies were searched for further relevant studies. References were managed using EndNote version 17 (Thomson Reuters USA). Further internet searches were performed on June 7th 2013 using Google, and entering Debrisoft or monofilament fibre pad as search terms. Additional publications were sought from the product manufacturer (in the UK, Activa Healthcare Ltd;in the rest of the EU, Lohmann and Rauscher GmbH & Co).

10.1.6 The inclusion and exclusion criteria.

The inclusion criteria is summarised in the table below. No exclusion criteria regarding study design was used. Reports describing product news were excluded from the final review along with non-systematic reviews containing no primary data.

Inclusion criteria for systematic review of clinical evidence

Criteria	Specification	Notes
Population	People with a wound (any aetiology) requiring debridement	

Intervention	Use of Debrisoft to debride wounds	Other forms of mechanical wound debridement were not be considered in this review except as comparators to Debrisoft
Comparator	Use of other wound debridement techniques	Limited to autolytic or mechanical debridement or larval therapy as these were most likely to be used by generalist practitioners
Outcome	Complete debridement	Review sought specific measures of debridement rather than wound healing or reductions in wound size
Outcome	Pain	Self-reported pain scores gathered using validated pain scales
Setting	Primary and secondary care	No restriction on geographical location
Study design	Systematic reviews, randomised, nonrandomised, cohort, case-series and case studies, observational and qualitative studies and testimonials	No restrictions on study type or limitation on publication status (published studies, in print manuscripts and poster presentations were included)

Length of follow up	Until debridement was achieved or 24 weeks whichever occurred first	
Language	No restriction on publication language	

10.1.7 The data abstraction strategy.

Data were extracted from included studies by one reviewer using standardised data extraction forms made available by SIGN (Scottish Intercollegiate Guidelines Network) (http://www.sign.ac.uk/methodology/checklists.html) and checked by a second reviewer. Data were gathered on the design, participants, methods, outcomes, baseline characteristics and results of the studies. No evidence tables were constructed for testimonial statements.

10.2 Appendix 2: Search strategy for adverse events (section 7.7.1)

The following information should be provided.

10.2.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- The Cochrane Library.

Not applicable

10.2.2 The date on which the search was conducted.

Not applicable

10.2.3 The date span of the search.

Not applicable

10.2.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

Not applicable

10.2.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

Not applicable

10.2.6 The inclusion and exclusion criteria.

Not applicable

10.2.7 The data abstraction strategy.

Not applicable

10.3 Appendix 3: Search strategy for economic evidence (section 8.1.1)

The following information should be provided.

10.3.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- EconLIT
- NHS EED.

The following databases were searched:

- *MEDLINE® (Embase.com interface)*
- *Embase® (Embase.com interface)*
- *EconLIT® (AEAweb.org interface)*
- *MEDLINE® In-Process (PubMed platform)*
- *NHS EED (Wiley Cochrane library platform)*

10.3.2 The date on which the search was conducted.

The searches were conducted on 16th July 2013.

10.3.3 The date span of the search.

MEDLINE®: From database start up to 16th July 2013

Embase®: From database start up to 16th July 2013

NHS EED: From database start up to 16th July 2013

10.3.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

Searches run in Embase® and MEDLINE® for comprehensive literature review (searched through Embase.com on 16 July 2013)

#	Search term	Hits
1	'debridement'/syn	30 874
2	debridement	30 739
3	debrid*	32 038
4	wound NEAR/2 clean* OR (necrot* OR devitali?e OR dead) NEAR/2 tissue	4982
5	wound* NEAR/2 irrigat*	1496
6	maggot'/syn	1029
7	maggot therapy'/syn	375
8	biosurg* OR biosurgery OR 'bio surgery'	1006
9	bio* NEAR/2 debri*	207
10	whirlpool	470
11	mechanic* NEAR/2 debri*	401
12	'hydro therapy' OR hydrotherapy	3792
13	'kneipp therapy' OR 'kneipp treatment' OR 'water immersion therapy'	52
14	dextranomer* OR cadexomer OR xerogel OR eusol OR debrisan	1578
15	polysacch* NEAR/1 (bead* OR paste)	15

#	Search term	Hits
16	intrasite NEXT/1 gel OR intrasitgel OR sterigel OR granugel OR nugel OR purilon NEXT/1 gel OR purilon OR vigilon	223
17	iodoflex OR iodosorb	122
18	(gauze OR adherent OR absorbent OR tulle OR polysaccharide OR hydrofibre) NEAR/2 dress* OR 'wet to dry dressing' OR 'wet to dry dressings'	1456
19	hydrocolloid* OR granuflex OR tegasorb OR aquacel OR hydrocoll OR combiderm OR duoderm	2825
20	alginate NEXT/1 dressing* OR foam NEXT/1 dressing* OR hydrogel* OR saline NEXT/1 gauze	19 930
21	'bioclusive of cutifilm' OR 'epiview of mefilm' OR 'opsite flexigrid' OR tegaderm	480
22	sorbsan OR tegagel OR kaltostat OR kaltogel OR 'comfeel seasorb' OR algisite OR algosteril OR megisorb OR 'cutinova cavity' OR 'seasorb filler'	252
23	jelonet OR bactigras OR chlorhexitulle OR serotulle OR 'fucidin intertulle' OR 'sofra tulle'	194
24	sharp NEAR/2 debride* OR autolytic NEAR/2 debride*	134
25	debrisoft	4
26	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25	67 364
27	'economics'/de OR 'economic aspect'/de OR 'cost'/de OR 'health care cost'/de OR 'drug cost'/de OR 'hospital cost'/de OR 'socioeconomics'/de OR 'health economics'/de OR 'pharmacoeconomics'/de OR 'fee'/exp OR 'budget'/exp OR 'economic evaluation'/exp OR 'hospital finance'/de OR 'financial management'/de OR 'health care financing'/de OR 'low cost' OR 'high cost' OR health*care NEXT/1 cost* OR 'health care' NEXT/1 cost* OR fiscal OR funding OR financial OR finance OR cost NEXT/1 estimate* OR 'cost variable' OR unit NEXT/1 cost* OR economic*:ab,ti OR pharmacoeconomic*:ab,ti OR price*:ab,ti OR pricing:ab,ti OR health*care NEXT/1 (utilisation OR utilization) OR 'health care' NEXT/1 (utilisation OR utilization) OR resource NEXT/1 (utilisation OR utilization OR use) OR (cost* NEAR/3 (treat* OR therap*)):ab,ti	1 050 130
28	(time OR duration) NEAR/4 (debrid* OR clean*)	1098
29	#26 AND #27	2224
30	#26 AND #28	297
31	#29 OR #30	2505
32	#29 OR #30 AND ([article]/lim OR [article in press]/lim OR [conference abstract]/lim OR [conference paper]/lim OR [erratum]/lim OR [short survey]/lim)	1697

Searches run in Cochrane for comprehensive literature review (searched through Cochrane library interface on 16 July 2013)

#	Search term	Hits
1	MeSH descriptor: [Debridement] explode all trees	423
2	debridement	1239
3	debrid*	1317

#	Search term	Hits
4	MeSH descriptor: [Larva] explode all trees	30
5	maggot	17
6	wound near/2 clean* or (necrot* or devitali?e or dead) near/2 tissue	261
7	biosurg* or biosurgery or "bio surgery"	23
8	bio* near/2 debri*	20
9	whirlpool	38
10	mechanic* near/2 debri*	115
11	wound* near/2 irrigat*	115
12	hydro therapy or hydrotherapy	285
13	kneipp therapy or "kneipp treatment" or "water immersion therapy"	5
14	dextranomer* or cadexomer or xerogel or eusol or debrisan	121
15	polysacch* near/1 (bead* or paste)	7
16	intrasite next/1 gel or intrasitgel or sterigel or granugel or nugel or purilon next/1 gel or purilon or vigilon	29
17	iodoflex or iodosorb	27
18	(gauze or adherent or absorbent or tulle or polysaccharide or hydrofibre) near/2 dress* or "wet to dry dressing" or "wet to dry dressings"	321
19	hydrocolloid* or granuflex or tegasorb or aquacel or hydrocoll or combiderm or duoderm	496
20	alginate next/1 dressing* or foam next/1 dressing* or hydrogel* or saline next/1 gauze	1002
21	bioclusive of cutifilm or "epiview of mefilm" or "opsite flexigrid" or tegaderm	76
22	sorbsan or tegagel or kaltostat or kaltogel or "comfeel seasorb" or algisite or algosteril or megisorb or "cutinova cavity" or "seasorb filler"	71
23	jelonet or bactigras or chlorhexitulle or serotulle or "fucidin intertulle" or "sofra tulle"	49
24	sharp near/2 debride* or autolytic near/2 debride*	41
25	debrisoft	0
26	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25	3493
27	(Time OR duration) near/4 (debrid* OR clean)	121
28	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 in Economic Evaluations	94
29	#26 and #27	60
30	#28 OR #29	150

Searches run in MEDLINE® In-process for comprehensive literature review (searched through Pubmed.com interface on 16 July 2013)

#	Search term	Hits
1	"Debridement"[Mesh]	11 333
2	debridement	21 189
3	debrid*	22 412

#	Search term	Hits
4	"Larva"[Mesh]	41 576
5	"Larva debridement" OR "Larval debridement" OR "Larva debridement" OR "Larval debridement"	262
6	(biosurg* OR biosurgery OR "bio surgery")	522
7	whirlpool	309
8	("hydro therapy" OR hydrotherapy)	17 076
9	("kneipp therapy" OR "kneipp treatment" OR "water immersion therapy")	104
10	(dextranomer* OR cadexomer OR xerogel OR eusol OR debrisan)	906
11	(iodoflex OR iodosorb)	67
12	("wet to dry dressing" OR "wet to dry dressings")	40
13	(hydrocolloid* OR granuflex OR tegasorb OR aquacel OR hydrocoll OR combiderm OR duoderm)	3928
14	"bioclusive of cutifilm" OR "epiview of mefilm" OR "opsite flexigrid" OR tegaderm	133
15	sorbsan OR tegagel OR kaltostat OR kaltogel OR "comfeel seasorb" OR algisite OR algosteril OR megisorb OR "cutinova cavity" OR "seasorb filler"	3949
16	jelonet OR bactigras OR chlorhexitulle OR serotulle OR "fucidin intertulle" OR "sofra tulle"	227
17	debrisoft	1
18	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17	89 428
19	economics	580 538
20	cost	553 643
21	socioeconomics	329 575
22	(fee) OR budget	38 158
23	(“cost-effectiveness” OR “cost-utility” OR “cost utility” OR “Cost benefit” OR “Cost minimisation” OR “Cost minimization” OR “budget impact” OR “cost consequence”)	75 319
24	"health care cost"	1297
25	"drug cost"	708
26	"hospital cost"	1553
27	"economic evaluation"	4832
28	"health economics"	8528
29	"health care financing"	2545
30	"low cost" OR "high cost"	29 892
31	"cost estimate"	146
32	"cost variable"	24
33	"unit cost"	577
34	economic* or pharmacoeconomic* or price* or pricing	550 539
35	"hospital finance" OR "financial management"	20 906
36	"health care utilization" or "health care utilisation"	3828
37	"resource use" or "resource utilisation" or "resource utilization"	8968

#	Search term	Hits
38	#19 OR #20 OR #21 OR #22 OR #23 OR #24 #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38	1 072 738
39	#18 AND #38	2342
40	#39 AND ((inprocess[sb] OR pubstatusaheadofprint))	30

Searches run in Econlit® In-process for comprehensive literature review (searched through AEAweb.org interface on 16 July 2013)

#	Search term	Hits
1	Debridement	0
2	Debrisoft	0

10.3.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

Additional searches included bibliographic and grey literature search.

10.4 Appendix 4: Resource identification, measurement and valuation (section 9.3.2)

The following information should be provided.

10.4.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- NHS EED
- EconLIT.

Not applicable

10.4.2 The date on which the search was conducted.

Not applicable

10.4.3 The date span of the search.

Not applicable

10.4.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

Not applicable

10.4.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

Not applicable

10.4.6 The inclusion and exclusion criteria.

Not applicable

10.4.7 The data abstraction strategy.

Not applicable

11 Related procedures for evidence submission

11.1 Cost models

An electronic executable version of the cost model should be submitted to NICE with the full submission.

NICE accepts executable cost models using standard software – that is, Excel, TreeAge Pro, R or WinBUGs. If you plan to submit a model in a non-standard package, NICE should be informed in advance. NICE, in association with the External Assessment Centre, will investigate whether the requested software is acceptable, and establish if you need to provide NICE and the External Assessment Centre with temporary licences for the non-standard software for the duration of the assessment. NICE reserves the right to reject cost models in non-standard software. A fully executable electronic copy of the model must be submitted to NICE with full access to the programming code. Care should be taken to ensure that the submitted versions of the model programme and the written content of the evidence submission match.

NICE may distribute the executable version of the cost model to a consultee if they request it. If a request is received, NICE will release the model as long as it does not contain information that was designated confidential by the model owner, or the confidential material can be redacted by the model owner without producing severe limitations on the functionality of the model. The consultee will be advised that the model is protected by intellectual property rights, and can be used only for the purposes of commenting on the model's reliability and informing comments on the medical technology consultation document.

Sponsors must ensure that all relevant material pertinent to the decision problem has been disclosed to NICE at the time of submission. NICE may request additional information not submitted in the original submission of evidence. Any other information will be accepted at NICE's discretion.

When making a full submission, sponsors should check that:

- an electronic copy of the submission has been given to NICE with all confidential information highlighted and underlined
- a copy of the instructions for use, regulatory documentation and quality systems certificate have been submitted
- an executable electronic copy of the cost model has been submitted
- the checklist of confidential information provided by NICE has been completed and submitted.

- A PDF version of all studies (or other appropriate format for unpublished data, for example, a structured abstract) included in the submission have been submitted

11.2 Disclosure of information

To ensure that the assessment process is as transparent as possible, NICE considers it highly desirable that evidence pivotal to the Medical Technologies Advisory Committee's decisions should be publicly available at the point of issuing the medical technology consultation document and medical technology guidance.

Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence').

When data are 'commercial in confidence' or 'academic in confidence', it is the sponsor's responsibility to highlight such data clearly, and to provide reasons why they are confidential and the timescale within which they will remain confidential. The checklist of confidential information should be completed: if it is not provided, NICE will assume that there is no confidential information in the submission. It is the responsibility of the manufacturer or sponsor to ensure that the confidential information checklist is kept up to date.

It is the responsibility of the sponsor to ensure that any confidential information in their evidence submission is clearly underlined and highlighted

correctly. NICE is assured that information marked ‘academic in confidence’ can be presented and discussed during the public part of the Medical Technologies Advisory Committee meeting. NICE is confident that such public presentation does not affect the subsequent publication of the information, which is the prerequisite allowing for the marking of information as ‘academic in confidence’.

Please therefore underline all confidential information, and highlight information that is submitted under ‘commercial in confidence’ in blue and information submitted under ‘academic in confidence’ in yellow.

NICE will ask sponsors to reconsider restrictions on the release of data if there appears to be no obvious reason for the restrictions, or if such restrictions would make it difficult or impossible for NICE to show the evidential basis for its guidance. Information that has been put into the public domain, anywhere in the world, cannot be marked as confidential.

Confidential information submitted will be made available for review by the External Assessment Centre and the Medical Technologies Advisory Committee. NICE will at all times seek to protect the confidentiality of the information submitted, but nothing will restrict the disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

The Freedom of Information Act 2000, which came into force on 1 January 2005, enables any person to obtain information from public authorities such as NICE. The Act obliges NICE to respond to requests about the recorded information it holds, and it gives people a right of access to that information. This obligation extends to submissions made to NICE. Information that is designated as ‘commercial in confidence’ may be exempt under the Act. On receipt of a request for information, the NICE secretariat will make every effort to contact the designated company representative to confirm the status of any information previously deemed ‘commercial in confidence’ before making any decision on disclosure.

11.3 Equality

NICE is committed to promoting equality and eliminating unlawful discrimination, including paying particular attention to groups protected by equalities legislation. The scoping process is designed to identify groups who are relevant to the evaluation of the technology, and to reflect the diversity of the population. NICE consults on whether there are any issues relevant to equalities within the scope of the evaluation, or if there is information that could be included in the evidence presented to the Medical Technologies Advisory Committee to enable them to take account of equalities issues when developing guidance.

Evidence submitters are asked to consider whether the chosen decision problem could be impacted by NICE's responsibility in this respect, including when considering subgroups and access to recommendations that use a clinical or biological criterion.

For further information, please see the NICE website (www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp).