EB CLINICAL PRACTICE GUIDELINE PROJECT

SCOPING PROJECT REPORT, 2016

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The purpose of clinical practice guidelines (CPGs) is to support and improve decision-making in patient care. They guide medical professionals in their care of people with EB and also guide patients as they participate in their own care. The recommendations the guidelines provide are based on scientific evidence and, when no evidence exists, on expert opinion.

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Background

DEBRA International is undertaking a long-term initiative to develop clinical practice guidelines for EB, in order to improve the clinical care of people with the condition. It is unusual for the development of clinical guidelines to be led by a patient organisation but, in the case of a rare disease such as EB, it is unlikely that guidelines would be developed without the drive of patients. Despite being well-placed to lead such an initiative, there are some major challenges for DEBRA to address in order to ensure its future success. A scoping project was undertaken during the period Feb-July 2016, in order to assess the needs of the initiative and to make recommendations for future steps. The project far exceeded its initial goals and, over its course, considerable steps were taken to progress and strengthen plans for many guidelines in varied aspects of EB clinical care.

Objectives and purpose of the project

- To reassess the priorities of the EB community for future EB guidelines
- To assess the availability of experts to participate in the guideline development, through discussion with international clinicians and patients on their willingness to lead or participate in the development of guidelines
- To consider the requirements to develop guidelines in each of the possible clinical areas for which there is a need

Methods employed

The following were undertaken over the course of the project:

- An international survey of clinicians, patients and care-givers (n=90 up to Aug 20th, 2016 and ongoing) to better understand which clinical areas the EB community prioritises for guideline development and to identify people who would be willing to contribute their time and expertise to the initiative
- Discussions (through email and conference call) with all individuals involved in EB guideline development to date and all new possible participants (engagement with approx. 220 individuals).
- Interviews with all leaders of completed or in-progress guidelines.
- Engagement with external experts (primarily through the RARE-Bestpractices project) to understand best practices in guideline development for both common and rare diseases

Key findings and outcomes

Priorities of the community

- **EB guidelines are proposed for at least 20 clinical topics** (see Table 1 for a list of confirmed and possible guidelines and Table 3 for the status of currently planned guidelines).
- The **clinical topics identified as the top priorities for guidelines** (as identified through the survey) are the ones previously identified as priority and have already been undertaken or are in development.
- Although interpretation is limited by small numbers of patient respondents, some **differences between the priorities of patients and other survey respondents** were identified (see note under Table 1).

Acknowledging the challenges

- Many **challenges for EB guideline developers** were identified, including
  - lack of time
  - lack of funding
  - lack of expertise in different aspects of methodology, including systematic literature reviews, systematic appraisal of papers, formulating recommendations etc.
  - lack of experience in building a development panel and retaining the commitment of its members
  - lack of knowledge on how to include patients or patient representatives in the process
  - difficulties with aspects the publication process.
- While individually excellent, **no standard development or publication format** has been adopted by previously completed guidelines. A summary of the approach used in the development in each of these guidelines is provided in Table 2.

Supporting the next steps

- A **database** of all potential participants in guideline development, with details of their interests, areas of expertise and contact details was created.
- Over the course of the scoping project, **9 new guidelines were initiated** or progressed from an early stage (see Table 3). This was achieved through the establishment of panels of experts (including patients) and through support for the leaders/potential leaders of each guideline.
- The **various possible future EB guidelines are each likely to require a tailor-made solution to support their development**. For some, that might include employing or contracting a dedicated person with the expertise to develop guidelines. For others, where a strong potential lead has emerged, there will still be the need for on-going support to help reduce or eliminate the challenges listed above.

Recommendations

Over-arching recommendation

The major recommendation of the project is to employ an **EB Guideline Coordinator** (on a part-time basis) to facilitate the translation of the goodwill and commitment of the many volunteers involved into actual results, in the form of EB clinical practice guidelines. The EB guideline coordinator, with the support of the DEBRA International Project Lead, could implement many of the subsequent recommendations[1].

Other recommendations

Maximising the value of the network

- **Maintenance of a network database**: The database of all participants and possible participants in the initiative (clinicians, patient representatives and others who can add value) should be maintained. Among other things, this will continue to facilitate the assembly of development panels. Ideally this would be linked to a DEBRA International database.
- **A network of guideline leaders**: Such a network should be established to allow leads to provide mutual support to each other, to improve dissemination of knowledge gained from training and to facilitate communication across guideline topics (which frequently overlap). It will also facilitate the EB Guideline Coordinator and Project Lead to share pertinent information with all leaders easily and efficiently. *Note: this network has already been established.*

Making guideline development better and quicker

- **A DEBRA Guideline Development Standard**: The creation of a DEBRA Guideline Development Standard is strongly recommended to support leaders and panel members in all aspects of EB guideline development. This standard should adopt best practice from widely used approaches to guideline development and adapt them for the EB context. It should be a dynamic document which can be updated to reflect changes in practice over time. *Note, a first version of this standard has already been developed - see Table 4.*
- **Providing training**: Providing leads and other panel members with training in best practice in guideline development has already proven beneficial and should be continued. Training sessions in standard guideline methodologies such as those employed by GRADE or SIGN could potentially be linked to DEBRA conferences and would ideally happen annually. Training in the appraisal of guidelines is also of value in supporting clinicians to implement guideline recommendations.

[1] This recommendation has already been implemented and Dr. Kattya Mayre Chilton has been employed in the role one day a week for 18 months.

- **The use of project managers**: In cases where there is no obvious clinical lead or the clinical lead needs additional support, the possibility of employing a project manager with expertise in clinical practice guideline development, is encouraged (funding permitting).[2]
- **Narrow scope guidelines**: Due to time and funding restrictions, the development of narrow scope guidelines, addressing one aspect of a larger clinical area, should be considered. Such smaller guidelines are more likely to be possible to realise in a timely manner and are in-keeping with international trends.

Reaching the audience

- **Translation of guidelines**: As this is an international initiative, the translation of guidelines into languages other than English should be considered. This requires investigation into how best to overcome the potential risk of misinterpretation of clinical recommendations.
- **Patient versions**: While the guidelines have always been intended for patient use as well as clinician use, patients are not currently accessing the guidelines to the degree hoped for. The development of a patient version for each guideline is recommended.
- **Communicating updates**: Up-to-date information on the status of various guidelines and guidance documents for developers should be maintained on the DEBRA International and EB-CLINET websites. All DEBRA social media channels should be used to promote the dissemination of published guidelines and information about the initiative.
- **Use of a single journal for all guidelines**: The possibility of using one scientific journal to publish all DEBRA guidelines (and reviews) should be investigated. This would be of value in facilitating a standard format, ensuring the guidelines are fully accessible to the EB community and may help reduce publishing costs.

Acknowledgements

Kattya and Avril would like to thank the members of the DEBRA International Executive Committee, the EB-CLINET leadership and Dr. Francis Palisson for their commitment to this project. We would also like to sincerely thank all who gave their time and knowledge to facilitate its successful undertaking. Many of you remain involved and it is your commitment to developing guidelines that will allow us to make a difference to the care of people with EB. It is our hope that the EB clinical practice guidelines will routinely be a first port of call for clinicians and patients alike who are in need of guidance for the management of EB.

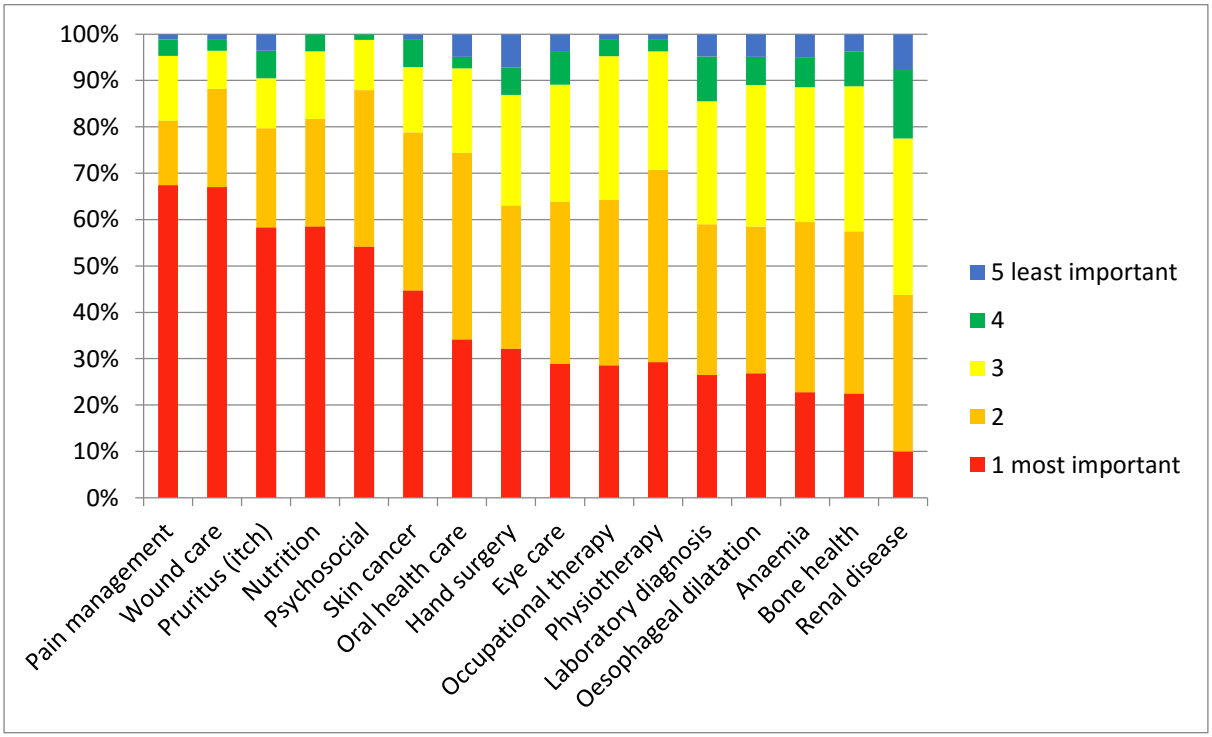
Note: A more in-depth report exists for those who would like more information. Please get in touch with us for a copy of this.

[2] With generous funding from DEBRA Norway, Dr. Kattya-Mayre Chilton has been employed to project manage the development of a psychosocial guideline, one day a week for 24 months.

Supporting Tables

Table 1. Priorities of the EB community for clinical practice guidelines

Responses to survey question: "Please rank the degree to which you think guidelines are important for these aspects of EB clinical care (rank even those for which guidelines already exist)." N=87/90 (collected 20th Aug 2016)



**Note 1: A number of additional clinical topics were proposed over the course of the project, including podiatry and women's health and childbirth*

**Note 2: Of the small numbers of people with EB that responded to the survey (n=7), the top priorities were psychosocial, wound care, hand surgery and itch.*

Table 2. Profile of EB guidelines published between 2012-2015 (n=4)

Summary	Cancer (Skin)	Pain (& Pruritus)	Oral Health Care	Wound Care
Date published	2015	2014	2012	2012
Lead(s)	Mellerio *et. al.*	Goldschneider *et. al.*	Krämer *et. al.*	Denyer & Pillay *et. al.*
Primary site	UK	USA	Chile	UK
Journal	BJD	BMC Medicine	Int. J. of Paediatric Dentistry	Wounds International
Funding	Publication funded by DEBRA Belgium. No other funding requested	Funded by DEBRA of America	Funded by DEBRA UK	Educational grant from the Urgo Foundation (non-profit-making)
Panel number	20	8	13	12
PPI number	3	3	2	Reviewed by a small group of patients and carers
Reviewer number	Unclear		12	International peer review by recognised experts in the field of EB
No. of centres	11	6	5	6
No. of countries	9	2	3	5
Literature search	Medline, CINAHL, British Nursing Index, Embase, Allied & Com. Med. Database and PsychINFO. Search limited to articles in English and French	MEDLINE, Cinhal, PsychInfo, The Cochrane Library (Trials) Search limited to articles in English	MEDLINE, EMBASE, CINAHL, The Cochrane Library and trials registered, DARE & hand searching etc. English, Spanish, French, German, or Italian articles were included	British Nursing Index, Cochrane Library, Embase, Google, Google scholar, Medline, Science Direct, Scopus, NICE, SIGN and the DH,
Methodology	SIGN	GRADE / LEGEND	SIGN	SIGN

Table 3. Stages in development for new EB guidelines initiated between 2014 and 2016 (n=9)

Topic area	Stage of development				
	1	2	3	4	5
Occupational therapy	Amber	Red			
Hand surgery and rehab	Amber				
Psychosocial	Green	Red			
Laboratory diagnosis	Amber				
Nutrition: constipation	Green				Amber
Physiotherapy	Red				
Anaemia	Amber	Red			
Podiatry	Green	Red			
Women's health & child birth	Red				

Key: ■ (Green) completed; ■ (Amber) in progress; ■ (Red) not yet initiated

Development stages (see Table 4 for more detailed information)

1. Establishment of panel and determination of clinical questions
2. Systematic literature searches
3. Systematic appraisal of papers identified in the search
4. Formulation of recommendations
5. Writing and publication of guideline

Table 4. DEBRA Guideline Development Standard

Steps	EB Clinical Practice Guidelines
1	**Establishment of panel and determination of clinical questions** 1. Select the clinical **topic** to focus on 2. Identify a clinical expert to be the **lead/chair** of the CPG (or engage a **project manager**) 3. Build the guideline development **panel**. The panel should: • Include 8-12 individuals • Include 2-3 patient representatives who should be involved in all steps of the guideline development and included as authors on the final publication. • Be multidisciplinary, including experts in the clinical topic and experts in overlapping areas of clinical care. • Include at least 3 different centres (and ideally countries) and more if possible. • Ideally meet in person at least once (coordination with a DEBRA or EB-CLINET meeting might facilitate this). Online conferencing tools should be used for other meetings. **Note**: people with valuable expertise, who are unable to be panellists can still be included through being asked to review the draft guideline. Any suggestions they make would need to be considered and agreed on by the panel, in a transparent fashion. 4. **Undertake preliminary literature search** and/or **audit of current practice** (this can support completion of the DEBRA application form and provide background information for the first panel meeting meeting) 5. Complete and **submit application form** to DEBRA international 6. **Scope out the population (patient) priorities** (this feeds into the first meeting and if completed prior to making the application it can be used as evidence here). 7. **Plan first panel meeting** • Minimum of 6 members must be physically present for good group dynamics • Other members can be linked through online conferencing tools • Minutes should be taken and feedback requested from all panel members. 8. **Meeting plan:** group introductions (brief); panel ground rules (relating to communication, deadlines, responsibilities etc.); background on methodology to be adopted; presentation of preliminary data, presentation of patient priorities, determination of main clinical question(s) through use of the PICO (population, intervention, comparison and outcomes) framework; summary of meeting and allocation of jobs. 9. Rate clinical questions by importance and narrow down to 5-7 • Clinical Questions should be determined by **practice** (what do we need to know) and **NOT** evidence driven • Outcomes should be determined by **importance** to patients and **NOT** evidence driven
2	**Systematic literature searches** The literature search should: 1. Assess guidelines (in the area or related area)

	2. Be based on the prioritised 5-7 clinical outcomes 3. Follow a systemic system to ensure compatibility (in the case of more than one searcher) and that no data is missed 4. Involve sifting, selecting and removal of duplicates 5. Use more than 3 search engines 6. Possibly include trials registrations, conference abstracts, hospital protocols, other related guidelines 7. Be undertaken in different languages (other than just English). 8. Go as far back in date as possible in the case of a new guideline or back to date from when the last searches were conducted (or engines not previously used) in the case of a review. 9. Use separate searches for each clinical question
3	**Systematic appraisal of papers identified in the search** The appraisal of papers should: 1. Assess the quality of the papers 2. Assess potential bias in the papers 3. Follow a systemic system to ensure compatibility (in the case of more than one appraiser) and that no data is missed 4. Involve each paper being appraised by at least 2 panel members to ensure consistency rating. 5. Involve a third member (lead, chair or project manager), where there is less than 50% consistency between appraisers. 6. Include all group study types for rare diseases: systemic reviews, meta-analysis, RCTs, cohorts studies, case control studies, observational studies and lastly expert opinions 7. Summarise the appraisal results by compiling an evidence profile for each question and study type
4	**Formulation of recommendations** **Plan final panel meeting** • Minimum of 6 members must be physically present for good group dynamics • Other members can be linked through online conferencing tools • Minutes should be taken and feedback requested from all panel members. **Meeting plan:** group introductions (brief); panel ground rules (relating to communication, deadlines, responsibilities etc.); overview of plan for the meeting and decision framework to be adopted; report on literature search/appraisal; considered judgement of evidence, formulation of recommendations; drafting of recommendations (together with transparent explanations of how arrived at); summary of meeting and allocation of jobs. Recommendations should be clear, transparent and actionable and use standard wording. They should include the: • Direction of the recommendation (i.e. for or against) • The strength of the recommendation • The quality of the recommendation
5	**Writing and publication of guideline** The final guideline should: • Include a recommendations summary table where recommendations are clearly linked to evidence and transparency.

	• Include all relevant information, according to the AGREE II tool • Provide clear recommendations for further research in areas for which no evidence was identified • Be sent for review by clinical and patient representatives who were not part of the panel (in order to bring fresh perspectives.) • Incorporate reviewer feedback on the basis of agreement by the whole panel (with inclusion of footnotes where necessary for transparency) • Be formatted as per journal instructions • Be submitted for publication in an open access journal which permits a link to the full publication on the DEBRA international website