Where should research be directed to?
An example of priority setting
Background

DEB is a rare disease and the research budget is limited.

As a rare disease, the number of unanswered questions in EB is large.

A recently updated review of therapies for inherited forms of EB identified, up to December 2011, seven randomized clinical trials evaluating seven different interventions for decreasing number of skin lesions. None of the studied medications showed a significant effect.

Therefore, prioritizing the most important unanswered questions is essential to research in EB.

UNANSWERED QUESTIONS = UNCERTAINTIES
The traditional way of setting the research agenda is usually led by researchers, academia and pharmaceutical industry, but these groups might not have the same research priorities as patients, carers and healthcare professionals (HCP’s).

The James Lind Alliance, funded by the UK National Institute for Health Research, has developed a method to identify and prioritize the unanswered questions / uncertainties, that patients, carers and clinicians agree as the most important.

There are few examples of the use of this method in dermatology and it has not been applied to very rare disorders, where prioritization might be especially important.

METHOD TO PRIORITIZE UNCERTAINTIES RELEVANT TO PATIENTS, CLINICIANS…

= PRIORITY SETTING PARTNERSHIPS
How do “Priority Setting Partnerships” work?
STAGE 1: INITIATION
Choose stakeholders: patients and carers of children with EB (DEBRA Spain), physicians involved in EB care (Dermatology Academy) and other professionals involved in the treatment and care of people with DEB. Nov – Dec 2011

STAGE 2: CONSULTATION SURVEY
Identify uncertainties by asking: “What question(s) about DEB treatment would you like to be answered by research?” Additional uncertainties were identified from existing evidence (guidelines, DEBRA, NHS evidence, etc). Dec – Feb 2012 (Survey-Monkey). 154 surveys sent (29 professionals and 125 patients & carers). 58 replies and 323 uncertainties.

STAGE 3: COLLATION
Add 50 uncertainties from evidence, and review treatment uncertainties, removing the duplicates, the ones not related with therapy and combining where possible. Result: 77 final treatment uncertainties. Feb – May 2012.

STAGE 4: RANKING EXERCISE
Repeat survey to identify the favourite topics from the list of uncertainties and create a “top uncertainties”. 46 people voted, result: 24 top uncertainties. May – Sept 2012.
STAGE 5: FINAL PRIORITIZATION WORKSHOP

Half-day workshop where the aim of this final stage was to identify the top 10 most relevant uncertainties for DEB, obtained by consensus between a group of patients, carers and HCP’s.
Results
Which **wound care** method obtains better outcomes (improved healing, decrease pain, improve quality of life, decrease smell, prevent infection)? Interventions include types of dressings (polyethylene, polyester plus petrolatum, hydrocolloid, collagen, hydrofiber, hydrogel, silicone…), topical antibacterial treatment (chlorhexidine, bleach bath, vinegar bath, honey, antibiotics, silver dressings) and frequency of cure (daily or alternate days?).
What is the best treatment to control itch in DEB patients (sedating antihistaminics, non-sedating antihistaminics, topical menthol, topical corticosteroids, moisturizers, doxepin, gabapentine, cylosporine, dronabinol, ondansetron)?
What is the best pain control strategy (analgesics, sedative drugs, addition of NaCl into the water) to decrease pain during wound care and bath in DEB patients?
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How much does management in reference centres help patients with DEB (in terms of quality of life, avoiding complications and disability, cost-effectiveness)?
How effective is an “early tumour diagnosis” protocol in patients with EB to decrease mortality, amputations and disability?
What are the long-term results of **syndactyly surgery**? Which is the best technique? How often should it be performed?
Which is the most effective method in avoiding or delaying syndactyly in patients with DEB? Including different types of bandages, dressings, gloves and splints, physiotherapy and occupational therapy?
What role might tissue engineering have in treating wounds in patients with DEB?
What role might stem cell therapy and bone marrow transplantation play in treating DEB?
What role might *growth hormone* play in decreasing growth and puberty delay in DEB patients?
Priority Setting Partnerships has showed that people with EB, carers and healthcare professionals have many questions / uncertainties.

A later search was conducted (24th of April 2013) using the International Clinical Trials Registry Platform (World Health Organization) and the Clinical Trials.gov (US National Institute of Health) to assess how many of the current registered clinical trials for DEB match the ten prioritized uncertainties

= 25 registered studies cover 4 of the 10 uncertainties


Updated systematic review of randomized controlled trials of treatments for inherited forms of epidermolysis bullosa.

Garcia-Doval I, Davile-Seijo P, Lengan SM.

PMID: 22731863 [PubMed - in process]
The mismatch between the research needs perceived by people with EB and clinicians and research could encourage the funding of research to study the other priorities which follow patients needs. This is very important when research is difficult and resources are limited.

Limitations of our research are:
- Uncertainties are sometimes broad and not specific questions (but specific questions can be extracted for research purposes)
- Not all people with EB and clinicians might agree on the priorities described
- Some research might be ongoing but not included in registries
Prioritization of therapy uncertainties in Dystrophic Epidermolysis Bullosa: where should research direct to? an example of priority setting partnership in very rare disorders

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Abstract (provisional)

Background

Dystrophic Epidermolysis Bullosa (DEB) is a rare genodermatosis (7 cases per million) that causes blisters and erosions with minor trauma in skin and mucosa, and other systemic complications. A recently updated systematic review showed that the research evidence about DEB therapies is poor. As new trials in DEB are difficult and expensive, it is important to prioritizise research that patients and clinicians consider more relevant.
Thank you!

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