Prospective Epidermolysis Bullosa Longitudinal Evaluation Study (PEBLES): development of an electronic data capture tool in recessive dystrophic epidermolysis bullosa.

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Introduction: In the last 5-10 years, novel translational therapies for the rare inherited skin fragility disease, epidermolysis bullosa (EB), have started to reach early phase clinical trials. However, the complexity and multisystem nature of the disease, as well as variable disease subtypes, mean that selection of meaningful endpoints for later phase trials is fraught with difficulty. To evaluate therapeutic outcomes, a clear understanding of the natural history of EB subtypes is essential to determine whether clinical variation is due to any intervention or just reflects underlying disease progression. Furthermore, current supportive treatments for EB, such as specialised dressings, are very expensive; clarification of the economic and social burden of disease may help justify the development of costly future treatments.

Methods: An electronic tablet-based questionnaire was developed in conjunction with an IT services company, Document Capture Co. Ltd. An iterative process was used amongst the study team, with input from EB patients, to capture comprehensive information about many aspects of recessive dystrophic EB (RDEB) from patients and/or their families and carers.

Specifically, the following details were sought (Fig. 1):

- Demographic details
- Subtype of RDEB including skin biopsy and mutational data
- Family history of disease
- Neonatal history
- Non-EB morbidities
- Cutaneous and extra-cutaneous EB-related problems
- Hospital appointments and inpatient episodes
- Standard view photographs
- Blister count
- Severity scores (Birmingham EB Severity Score and iSCOREB)
- Age appropriate quality of life score (EBQoL or PEDSQL)
- Procedural and background visual analogue pain scores
- Leuven Itch Score
- Medication history
- Dressings and topical therapy usage
- Paid or unpaid carer doing dressings and time spent
- Laboratory parameters including blood tests, echocardiograms, DEXA scans, radiographs and urinalysis

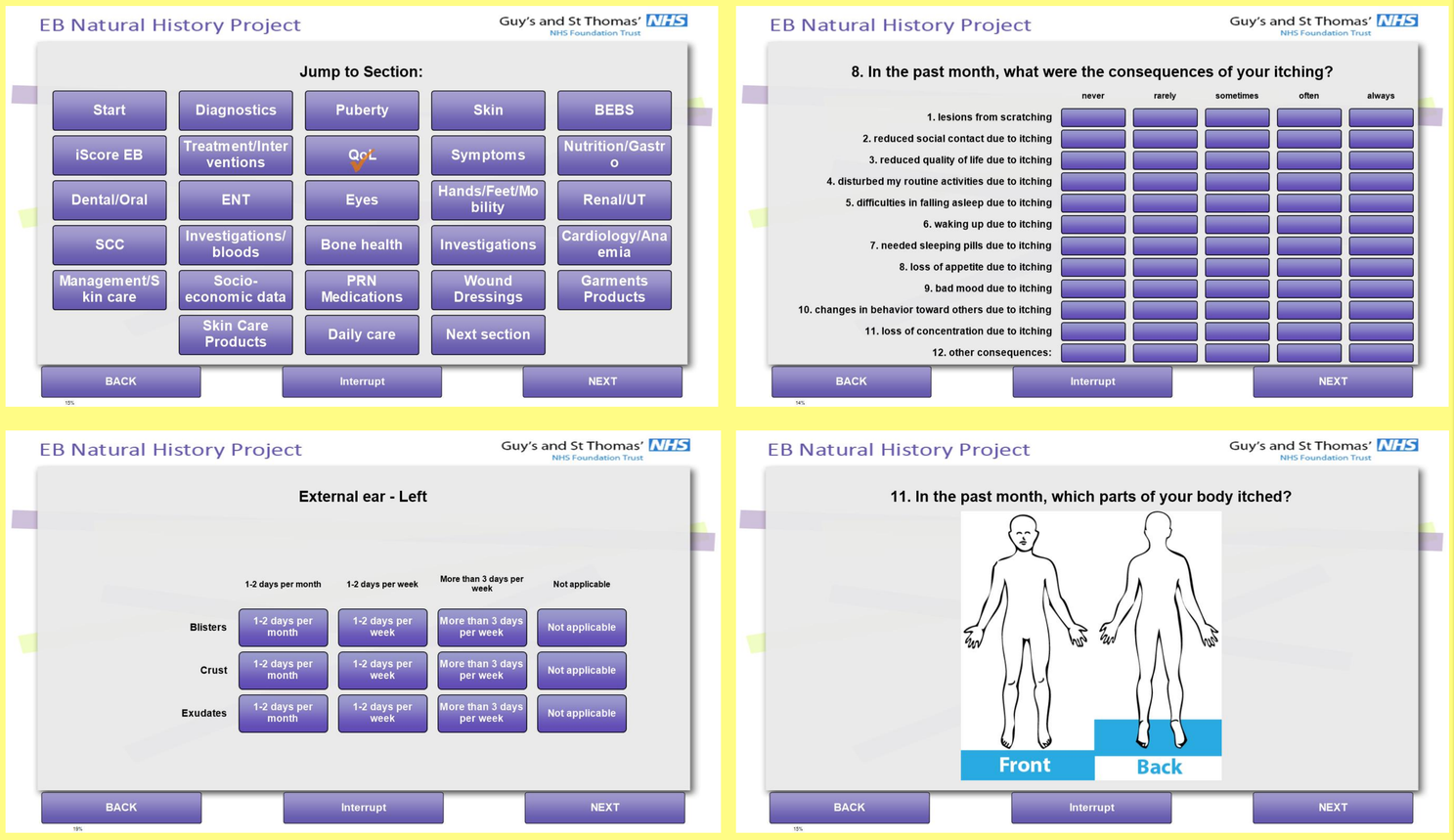
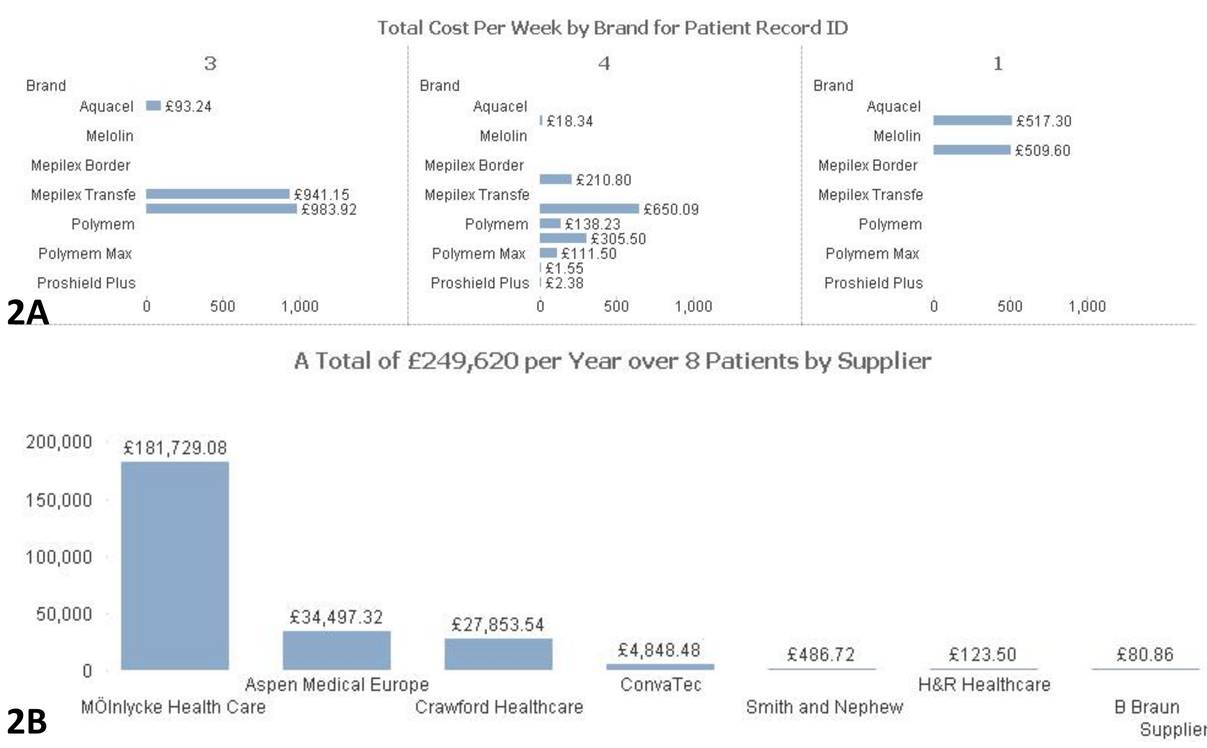


Fig.1. Sample screens from the data capture tool.

All patients with RDEB seen at our institutions and able to give informed consent (or with parent/carer able to give consent for children) will be eligible for inclusion in this study (N= approx 150). Information will be entered by a researcher onto the tool. Questionnaire data and photographs completed by the patient in advance of the visit will be entered at the same time. We plan to capture baseline data on patients at any age from birth and will re-evaluate every 6 months (under 10 years) or 12 months (above 10 years) to gather prospective information on disease progression with time. Importantly, mortality data will also be collected prospectively. This study has local R&D and REC approval.

Results: Patient interviews and data entry take around 1-3 hours and have been well-accepted by patients/families. The data capture tool can assimilate over 2,500 items per patient visit which is anonymised and uploaded to a secure server. Stored data from individuals or cohorts of patients can be interrogated to compare variables between different individuals, different subtypes of RDEB and at different ages. Preliminary data from initial patients shows that recall and analysis of data is robust and will provide a framework for future analysis of the natural history of EB.



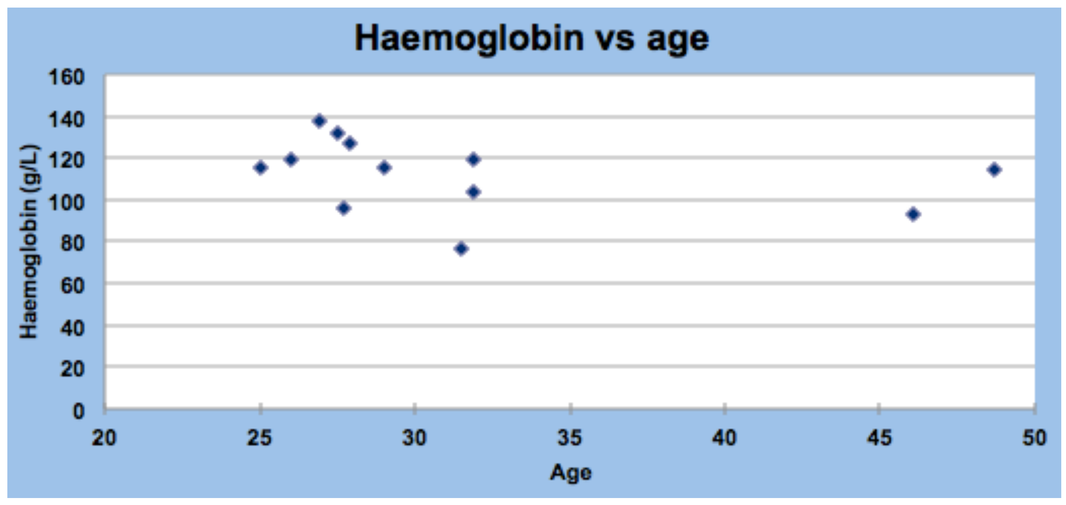


Fig.2. Preliminary data. A dressing costs per participant; B total dressing costs by supplier ; C haemoglobin levels by age

Discussion: The development of this data capture tool and the ability to retrieve and interrogate data is integral to PEBLES. Collection of detailed data will provide a level of granularity about the natural history of RDEB which has not been captured previously. It is hoped that PEBLES will give insight into the normal disease trajectory enabling definition of parameters which will be useful outcome measures for future clinical trials in RDEB. Currently, there exists very scant information about the health economics of EB, particularly regarding expenditure on specialised dressings and carer time needed to undertake dressing changes. Delineation of these costs should provide compelling support for investment into potentially expensive future innovative therapies for RDEB where cost-benefit ratios will be key.