Natural history of RDEB: news from PEBLES

EB2017 & EB-CLINET
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Jemima Mellerio
Great Ormond Street and
St John's Institute of Dermatology
London
Natural history of EB

- Clinical trials need endpoints
- Need to know natural history of disease to know what to evaluate
Natural history of EB

Prospective Epidermolysis Bullosa Longitudinal Evaluation Study
Natural history of EB

Prospective Epidermolysis Bullosa Longitudinal Evaluation Study

Recessive dystrophic EB
- Type of RDEB and lab data
- Clinical aspects
- Laboratory results and investigations
- Disease severity scores
- Subjective scores
- Photographs of skin
- Economic costs
PEBLES

- Company employed to devise data capture tool
- Tablet device with questionnaires
- Up to 2000 possible data entry points per patient
PEBLES

- Moving to web-based data capture
- More robust to handle volume of data
- Retrieve data via a dashboard to interrogate different variables
PEBLES

- Data collection repeated
  - every 6 months (<10y age)
  - every 12 months (>10y age)
Patients/parents sent booklet of questionnaires to complete before review by researcher

- Age appropriate scores e.g. QOL, puberty, pain
- Blister count
- Dressings
- Also sent a camera for standard view photographs
PEBLES: background and clinical data

- Demographics
  - Name and DOB
  - Gender
  - Type of EB
  - IF and mutation results
  - Ethnicity
  - Family history
  - Social history
  - School/work

- Skin
  - Body map wounds etc
  - Blister count

- Photographs
  - Standard views on tablet or own camera

- Growth/development
  - Ht and Wt
  - BMI
  - Pubertal stage
PEBLES: background and clinical data

- **Dental**
  - Caries/missing teeth
  - Microstomia
  - Dental surgery

- **Hands**
  - Hand contracture/flexion
  - Splints
  - Previous surgery
PEBELES: background and clinical data

- Mobility
  - Fully mobile
  - Limited walking
  - Walking around the house
  - Wheelchair dependent

- ENT
  - Symptoms
  - Interventions

- Eyes
  - Symptoms
PEBLES: background and clinical data

- Gastrointestinal tract
  - Dysphagia
  - Aspiration
  - Previous ODs
  - Nutrition
  - Oral/tube feeding
  - Bowel habit
  - Colitis
PEBLES: background and clinical data

- **Cancer**
  - Age at first SCC
  - Numbers/sites of SCCs
  - Local/regional/distant spread
  - Therapies
  - Other cancers

- **Severity scores**
  - iSCOREB
  - BEBS
PEBLES: laboratory data

- **Haematology**
  - Hb
  - Iron
  - Ferritin

- **Renal**
  - Urinalysis
  - BP
  - Renal function

- **Inflammatory status**
  - CRP
  - ESR
  - Ferritin
  - Platelet count

- **Serum stored**
PEBLES: laboratory data

- **Endocrine/bone health**
  - Calcium
  - Vitamin D
  - Spine X-ray
  - DEXA scan

- **Nutritional**
  - Albumin
  - Vitamin D
  - Selenium
  - Zinc

- **Cardiology**
  - Echocardiogram
PEBLES: subjective data

- Pain questionnaire
  - Procedural pain
  - Background pain

- Itch questionnaire
  - Leuven itch score

- Quality of life score
  - PEDSQL
  - QOLEB
PEBLES: health economic data

- Hospital appointments
  - Numbers
  - Admissions
  - Length of stay

- Medication
  - Types and route
**PEBLES: health economic data**

- **Dressings**
  - Types
  - Sizes
  - Numbers used per week
  - Linked to costs

- **Dressing changes**
  - Who does them?
  - Paid?
  - Hours/week
### EB Natural History Project Medications

**How many PRN medications do you wish to list?**

- [ ] 1
- [ ] 2
- [ ] 3
- [ ] 4
- [ ] 5
- [ ] 6
- [ ] 7
- [ ] 8
- [ ] 9
- [ ] 10
- [ ] None

#### Regular Medication

- **Name:**
- **Dose:**
- **Unit:**

#### Route

- [ ] Oral
- [ ] Per gastrostomy
- [ ] Jejunostomy
- [ ] Naso-gastic tube
- [ ] Trans-dermal
- [ ] Nasal spray
- [ ] Injection

#### Frequency

- [ ] Weekly
- [ ] OD
- [ ] BD
- [ ] TDS
- [ ] QDS
- [ ] Continuous
- **Taken regularly?**
  - [ ] Yes
  - [ ] No

#### PRN Medication - frequency in 24 hours

- **Name:**
- **Dose:**
- **Unit:**

#### Average number of doses in 24 hours:

#### Total dose in 24 hours:
<table>
<thead>
<tr>
<th>Spinal fractures since last review?</th>
<th>Yes</th>
<th>No</th>
<th>How many spine fractures?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracic - Site(s) of fractures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>O</td>
<td></td>
<td>O</td>
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<tr>
<td>T2</td>
<td>O</td>
<td></td>
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<td>T3</td>
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<td>T4</td>
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<td>T5</td>
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<td>O</td>
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<td>T6</td>
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<td>T7</td>
<td>O</td>
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<td>T8</td>
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<td>T9</td>
<td>O</td>
<td></td>
<td>O</td>
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<td>T10</td>
<td>O</td>
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<td>O</td>
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<td>T11</td>
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<td>O</td>
</tr>
<tr>
<td>T12</td>
<td>O</td>
<td></td>
<td>O</td>
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<tr>
<td>Fractures - Thoracic - Date of diagnosis</td>
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<tr>
<td>DD/MM/YYYY</td>
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<td>Fractures - Thoracic - Source of information</td>
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<tr>
<td>○ Hospital EPR</td>
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<td></td>
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<tr>
<td>○ Hospital notes</td>
<td></td>
<td></td>
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<tr>
<td>○ GP</td>
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</tr>
</tbody>
</table>

| Lumbar - Site(s) of fractures   |     |    |                          |
| L1      | O   |    | O                        |
| L2      | O   |    | O                        |
| L3      | O   |    | O                        |
| L4      | O   |    | O                        |
| L5      | O   |    | O                        |
| Fractures - Lumbar - Date of diagnosis |
| DD/MM/YYYY |
| Date must be completed in (DD/MM/YYYY) format. Put hashes (#) where date info is not known |
| Fractures - Lumbar - Source of information |
| ○ Hospital EPR |
| ○ Hospital notes |
| ○ GP |

<table>
<thead>
<tr>
<th>Calcaneal fractures since last review?</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcaneal fractures since last review?</td>
<td></td>
<td></td>
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<tr>
<td>- Right?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Fractures - Calcaneal Right - Date of first diagnosis</td>
<td></td>
<td></td>
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<tr>
<td>DD/MM/YYYY</td>
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<td>Fracture - Calcaneal Right - Source of information</td>
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<td></td>
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<tr>
<td>○ GP</td>
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<td></td>
</tr>
</tbody>
</table>

| Fractures - Calcaneal Left - Date of first diagnosis |
| DD/MM/YYYY |
| Date must be completed in (DD/MM/YYYY) format. Put hashes (#) where date info is not known |
| Fracture - Calcaneal Right - Source of information |
| ○ Hospital EPR |
| ○ Hospital notes |
| ○ GP |
EB Natural History Project SCC

Squamous cell carcinoma (SCC) Skin cancer - Does the patient currently have; or has he/she had an SCC in the past?
- Yes
- No

SCC - Date of first diagnosis

Total Number of SCCs

Surgical treatment (SCC) - Total number of excisions

SCC - Date of diagnosis

SCC - Date of excision

SCC - Histology (differentiation)
- Well
- Moderate
- Poor

SCC - Type of excision
- WLE
- Mohs

Location of SCC

Size of SCC (length cm's)

Size of SCC (width cm's)

Was PET/CT performed?
- Yes
- No

SCC - PET/CT results

Was FNA performed?
- Yes
- No
- Positive
- Negative
- Inconclusive

SCC - FNA results details

SCC Were there any amputations for this case of SCC
- Yes
- No

Amputations LEFT

Thumb
- Index finger
- Middle finger
- 3rd finger (ring)
- Little finger
- Hand
- Arm below elbow
- Arm above elbow

Amputations RIGHT

Thumb
- Index finger
- Middle finger
- 3rd finger (ring)
- Little finger
- Hand
- Arm below elbow
- Arm above elbow
PEBLES: where are we now?

- 55 consented patients
- 11 children, 44 adults
- 2 withdrawn, 1 lost to follow-up
  - 52 completed data for 1st assessment
  - 46 completed 2nd assessment
  - 23 completed 3rd assessment
  - 5 completed 4th assessment
  - 3 completed 5th assessment
  - 1 completed 6th assessment
PEBLES: where are we now?

- 55 consented patients
- 11 children, 44 adults
- 2 withdrawn, 1 lost to follow-up

- 25 GS-RDEB
- 18 GI-RDEB
- 8 RDEB-I
- 1 RDEB-pru
Age by RDEB type
Itch distress all RDEB types

10. In the past month, how distressing was your itching? (0.0-10.0)
10. In the past month, how distressing was your itching? (0.0-10.0)
Height/weight/BMI by age all types RDEB
Average BMI by age group
Average BEBS score by age group
Average Hb by age group RDEB-SG

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Hb Value</th>
</tr>
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<tbody>
<tr>
<td>0-16</td>
<td>108.40</td>
</tr>
<tr>
<td>17-25</td>
<td>123.00</td>
</tr>
<tr>
<td>26-35</td>
<td>110.86</td>
</tr>
<tr>
<td>36-45</td>
<td>88.00</td>
</tr>
<tr>
<td>46-55</td>
<td>93.00</td>
</tr>
</tbody>
</table>

Legend:
- Q041 Sub-type_RDEB
- RDEB - Sev Gen

Age_Group_v3
Mobility by RDEB subtype

Q537 Mob.Child_Adults

0 - Unable to walk, tr...
1.00

1 - Household walke...
2.00

2 - Able to walk short...
1.00

3 - Independently mo...
4.00

4 - Independently mo...
5.00

Q041 Sub-type_RDEB
RDEB - I
RDEB - O
RDEB - Pr
RDEB - Sev Gen

16.00
7.00
Dressing costs per year all patients

Research_No

1  £53,398.80
3  £138.32
13 £104,952.12
5  £7,926.88
7  £3,900.00
8  £131.56
10 £4,375.28
12 £83,265.52
16 £167,644.36
18 £570.18
20 £2,507.44
21 £1,183.04
23 £724.36
26 £104,892.32
28 £95,752.28
31 £6,976.32
32 £523.38
33 £6,881.00
36 £671,693.44
38 £531,426.20
40 £8,137.74
41 £136,210.74
42 £32,900.60
44 £1,517.88
46 £12,906.40
48 £4,422.08
50 £2,073.24
52 £2,073.24

£542,543.04

0  200,000  400,000  600,000
Dressing costs per year GS-RDEB
Longitudinal care costs per week RDEB-SG

Dress Hours a Week x Care Cost Per Hour

- Research No 1: £187.25
- Research No 10: £449.40
- Research No 11: £29.96, £37.45
- Research No 16: £108.61, £104.86
- Research No 19: £224.70
- Research No 27: £52.43, £29.96, £41.20
- Research No 32: £209.72
- Research No 40: £213.47
- Research No 47: £1,700.16

Bar graph showing the longitudinal care costs for different research numbers and hours, with the care cost per hour varying for each.
Longitudinal iscor-EB physician scores RDEB-SG
Longitudinal iscor-EB patient scores RDEB-SG
PEBLES

- More detailed information about RDEB than previously collected
- Comprehensive picture of all aspects of well-characterised RDEB patients
- Will extend to other centres
- In time, for other types of EB

Identify meaningful endpoints for future clinical trials
Acknowledgements

- Liz Pillay
- Pankaj Patel and DCC
- Jennie Hon
- Manpret Lakhan
- Danielle Greenblatt
- Anna Martinez
- Susan Robertson
- Emma Batten
PEBLES: natural history of EB

Any questions or comments?