Exploring the Financial Burden Associated with the Management of Dystrophic Epidermolysis Bullosa (DEB): A Systematic Literature Review (SLR) with Database Review of Future Disease-Modifying Therapies (DMTs)

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Introduction and Objective

- DEB is a rare, inherited, progressive dermatological condition that results in the formation of extensive skin blisters and wounds[1].
- Until recently, DEB management primarily focused on symptomatic relief[1]. Wound care is an essential part of this management, necessitating specialized bandages that facilitate healing[1].
- Wound care can be time consuming and expensive[3], with the necessity of daily dressing changes following cleansing making treatment burdensome to both patients and caregivers[1].
- However, promising new treatment options including the first topical gene therapy have recently been approved[2] that have the potential to be disease-modifying for patients with DEB.
- In this context it is important to fully understand the current economic burden of DEB. Therefore, this study aims to investigate the healthcare resource use cost drivers associated with DEB and explores potential future DMTs that may impact these costs.

Methods

- A broad SLR was conducted in Embase in March 2023 to evaluate the direct and indirect costs associated with six rare diseases.
- Studies of interest were full text papers published 2008-2023 or conference proceedings published 2020-2023 presenting data on healthcare resource utilization or disease-related direct or indirect costs. This sub-analysis focused on direct cost data for DEB.
- Studies were screened by two reviewers and reconciled by a third. Data was extracted by a single reviewer, with data number-checked by a second reviewer.

Embase hits: 63

↓

Included economic publications: 14

↓

Direct costs: 6

- Costs were converted from the published currency into United States Dollar (USD) using April 2024 currency rates via https://www.google.com/finance/ where 1 Euro = 1.09 USD, and where 1 Great British Pound (GBP) = 1.26 USD.
- A clinicaltrials.gov search was then conducted in January 2024 using the search term DEB to identify potential future treatments.
- Clinical trials of interest were those registered as Phase 2 or Phase 3, with a status of completed, active not recruiting, recruiting, or enrolling by invitation.

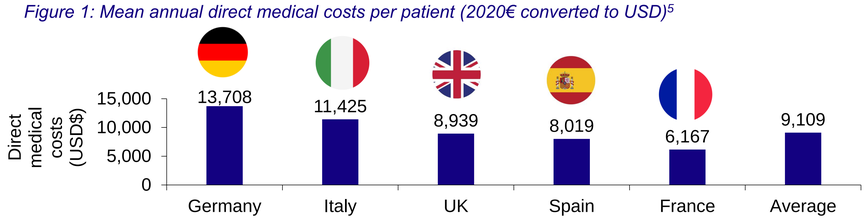
Results

The SLR yielded 6 papers presenting data on direct costs in DEB, 3 for the US and 3 for Europe.

Direct healthcare costs

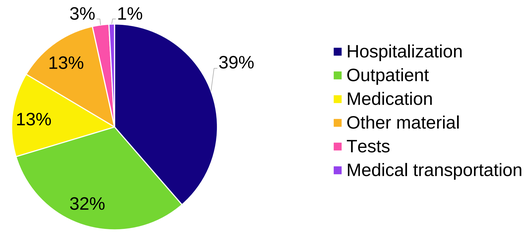
- The direct medical costs associated with DEB per patient per year (PPPY) were higher in the US ($32,352)[4] compared with Europe ($9,109 [€8,357])[5]. In Europe, direct costs were highest in Germany ($13,708 [€12,576]) and lowest in France ($6,167 [€5,658]) (Figure 1).

Figure 1: Mean annual direct medical costs per patient (2020€ converted to USD)[5]



- In one European study, hospitalizations corresponded to 39% ($3,519) of direct medical costs, outpatient visits to 32% ($2,890), and medication to 13% ($1,203) (Figure 2)[5]. No breakdown for the US costs was identified.

Figure 2: Proportion of direct medical costs by category of healthcare resource use[4]



Wound care

- In the UK, average wound care costs PPPY ranged from $3,413 (£2,709, 2017) to $103,141 (£81,858, 2017), increasing with disease severity[6]. Annual costs of dressings and retention garments also increased with disease severity in the UK, ranging from $2,141 (£1,699, year not reported) to $107,297 (£85,156, year not reported)[7].
- In the US, annual mean costs for bandages were $4,705 (USD 2019)[8].

Clinical Trials.gov search

The clinicaltrials.gov database search identified 9 trials in Phase 2 or 3 for patients with DEB:

- 6 trials were completed, 2 were recruiting, and 1 was active, not recruiting (Table 1).
- 6 trials investigated advanced therapies (EB-101, B-VEC, ALLO-ASC-SHEET, FCX-007), 2 trials investigated protein-replacement therapies (PTR-01), and 1 trial investigated a proteinase inhibitor (Polyphenon E).

Negative news

- A Phase 1/2 study for QR-313, an antisense oligonucleotide, was terminated due to low enrollment in 2021 (NCT03605069)[9].

Positive News

- The topical gene therapy Vyjuvek (B-VEC) received FDA approval in May 2023[2] and orphan drug designation in Japan in January 2024[10].
- EB-101 was granted both Breakthrough Therapy (Aug 2017)[11] and Rare Pediatric designation (January 2018) by the FDA[12]. If Priority Review is accepted, approval of EB-101 is expected in the second quarter of 2024[13].
- FCX-007 was granted Orphan Drug, Rare Pediatric Disease, Fast Track and Regenerative Advanced Therapy designations by the FDA in October 2021[14].

Table 1: Registered clinical trials investigating disease modifying treatments in DEB

Status	Intervention	Phase	Sponsor	Completion Date	Study Location	NCT Number
Completed	B-VEC	3	Krystal Biotech	Jul 2023	US	NCT04917874
	EB-101	3	Abeona Therapeutics	Oct 2022	US	NCT04227106
	PTR-01	2	Phoenix Tissue Repair	Aug 2022	US	NCT05143190
	B-VEC	3	Krystal Biotech	Jan 2022	US	NCT04491604
	PTR-01	2	Phoenix Tissue Repair	Sep 2021	US	NCT04599881
	Polyphenon E	2	Centre Hospitalier Universitaire de Nice	Jul 2013	France	NCT00951964
Recruiting	ALLO-ASC-SHEET	2	Anterogen Co.	Feb 2025	US	NCT05157958
	EB-101	3	Abeona Therapeutics	Dec 2024	US	NCT05725018
Active, not recruiting	FCX-007	3	Castle Creek Biosciences	Jul 2037	US	NCT04213261

Conclusions

- Direct medical costs appear to be substantially greater in the US compared to in Europe, potentially resulting from frequent ambulatory visits in the US (13.9 visits per patient over a 6-month period)[4].
- In Europe, hospitalizations and outpatient visits are the key cost drivers for direct medical costs in DEB, although medication costs and wound care play an important role. Since historically there were no DMTs available for DEB, disease management focused on symptomatic relief only, which naturally increased in cost as disease severity increased.
- The launch of new DMTs will change this economic landscape, moving from expenditure only on the symptomatic treatment of wounds to preventative interventions that aim to reduce or remove the need for wound care completely, as well as reduce the wound complications that require outpatient treatment or hospitalization.
- Future DMTs will need to be able to demonstrate a reduction in wounds that translates into economic benefits, which will primarily be achieved through a reduction in hospitalization, outpatient visits, and wound care costs.

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3. Bodke, A., (2023) Value in Health 26(12):S126-127.
4. Roman, J., et al, L16 ACMP 2022.
5. Angelis, A., et al. Orphanet J Rare Dis, 2022. 17(1): p. 346.
6. Pillay, E.J., et al. 1st World Congress on Epidermolysis Bullosa. 2020. EB2020
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Nexus Values