

11-12 December 2025

ERN-Skin Board Meeting

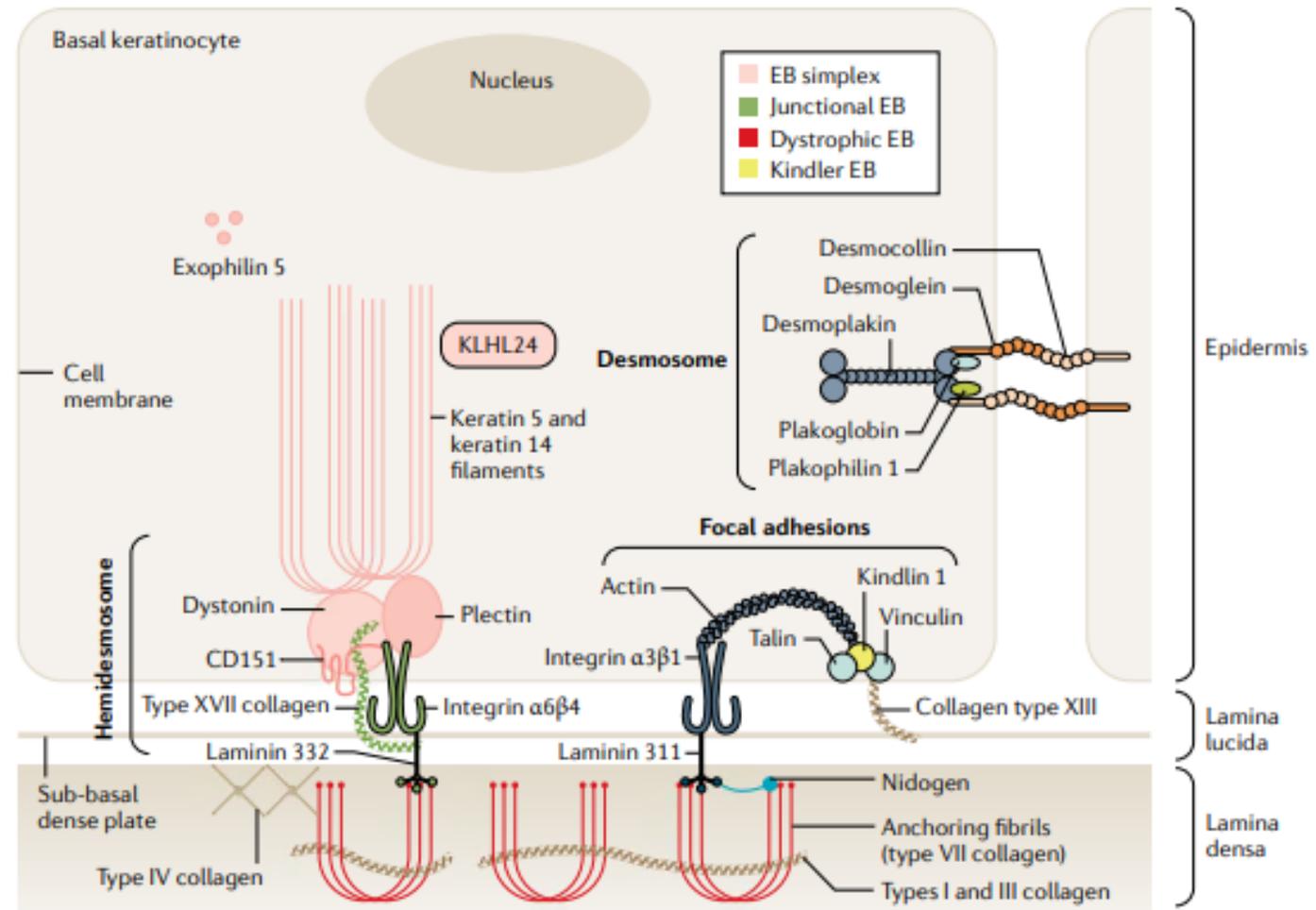
Update on



Development of core outcome sets for EB trials

Epidermolysis bullosa

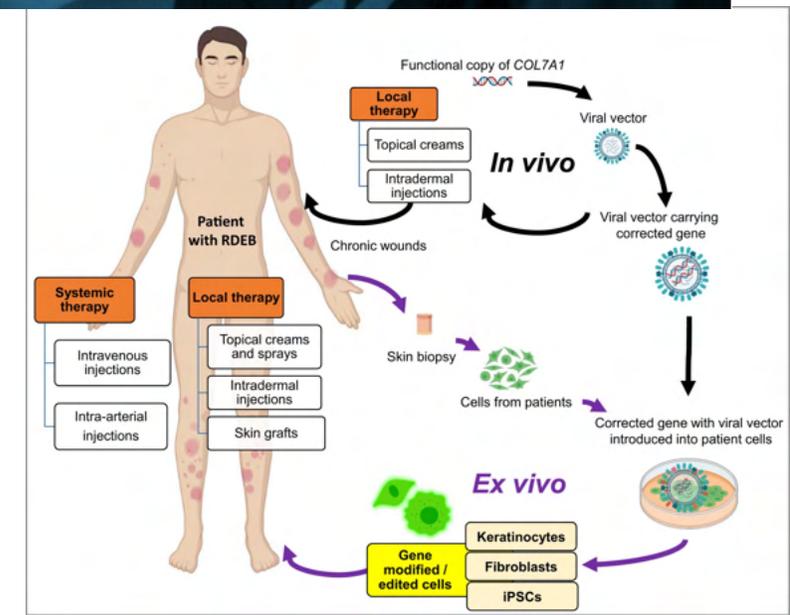
- **Heterogeneous** group of rare, **genetic blistering** disorders
- **Four main types** with **distinct clinical hallmarks**, >30 subtypes
- Epithelial **fragility**: genetic variants in genes encoding structural and functional components of DEJ



Treatment landscape

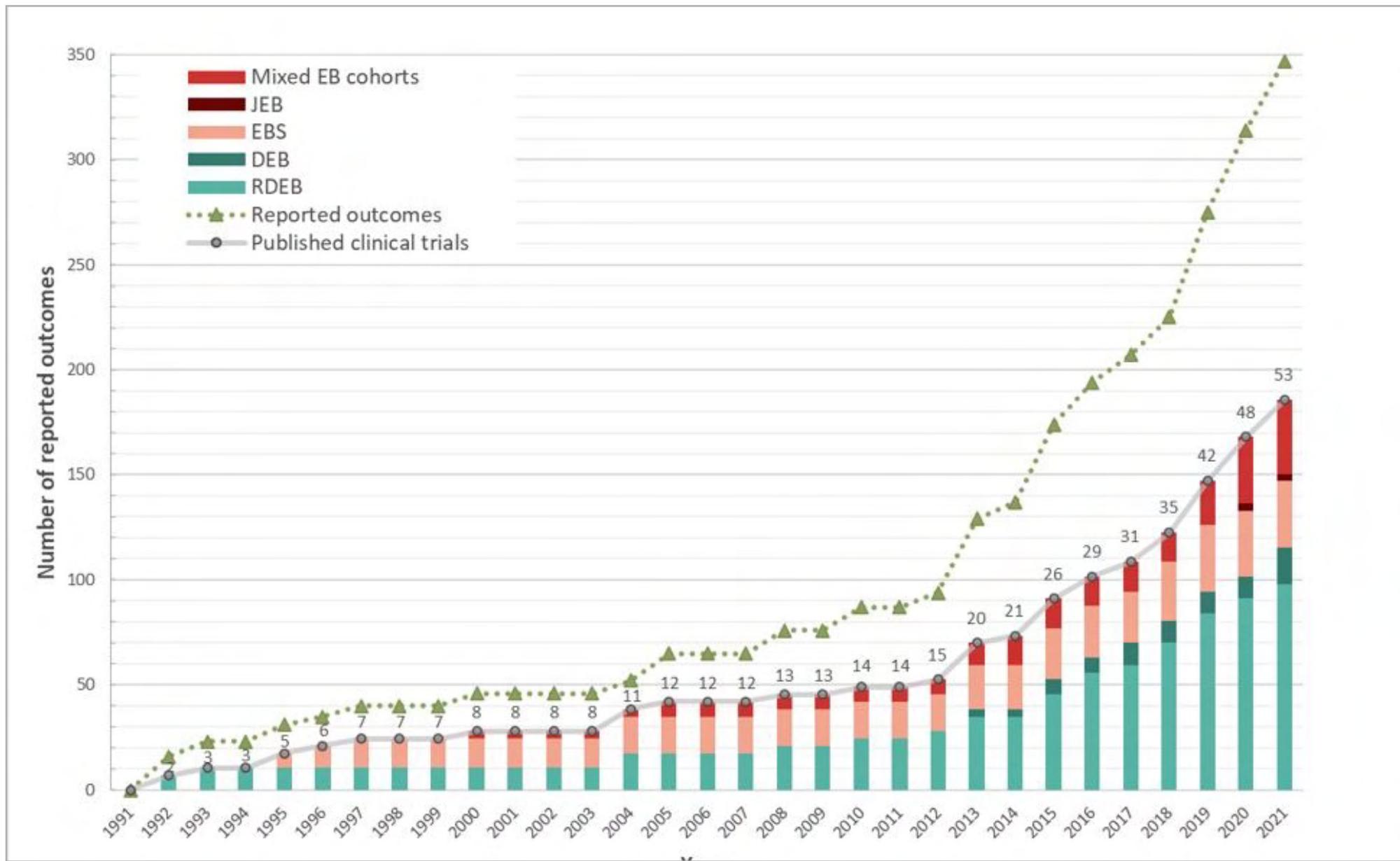
- Complex, multidisciplinary specialized care, expertise centers
- Translational advances: 3 recently approved topical therapies
 - Filsuvez
 - Vyjuvek
 - Zevaskyn
- Horizon: many trials ongoing for both novel and repurposed therapies

FDA approves first topical gene therapy



Therapeutic potential broadens

- More bench to bedside
- **Corrective** therapies
- **Symptom-relieving, disease modifying** therapies



Trials measure effect of treatment

Pain



Wound healing



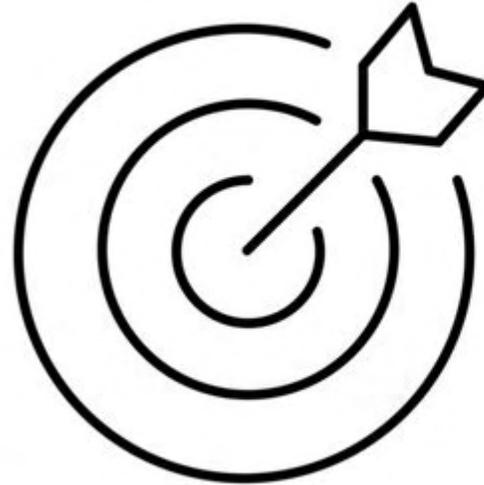
Sleep



Adverse effects



Hand function



Measurement terminology



Outcomes describe effect of health intervention

Epithelialisation rate

Similar outcomes grouped into **outcome domains**

Construct/concept of the what to measure to examine interventional effect

Wound healing

Similar outcome domains result in **outcome areas**

Cutaneous manifestations

Outcome measurement instruments

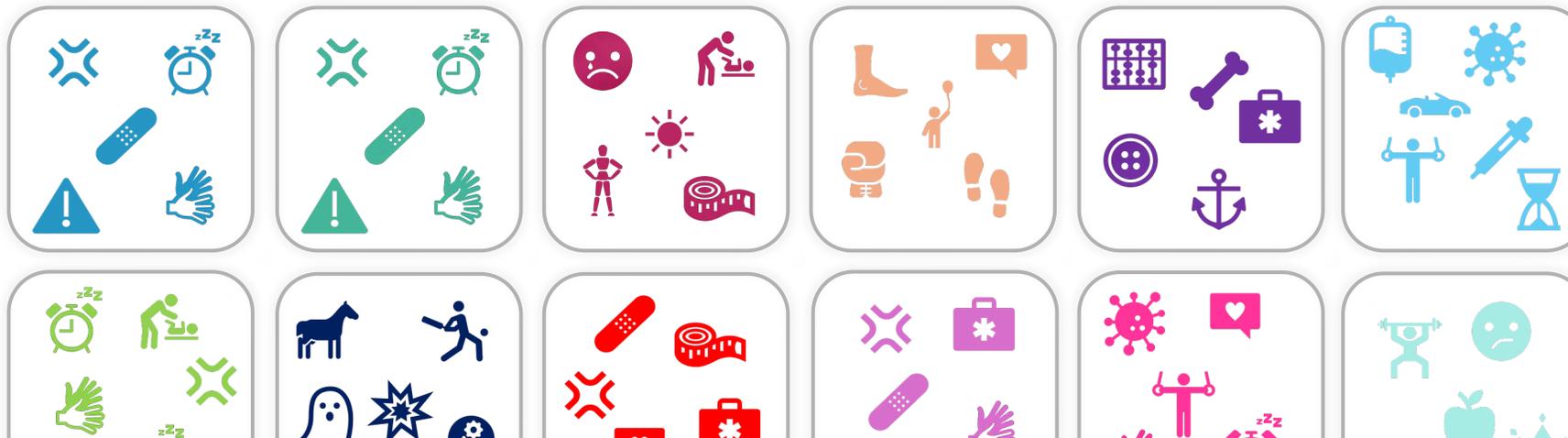
The how to measure quality/quantity of interventional effect

Serial digital photographs, score, questionnaire, laboratory measurement

EB outcome landscape 1991-2021

What to measure?

How to measure?



BJD Improving patient outcomes in skin disease worldwide

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British Journal of Dermatology



Volume 189, Issue 1
July 2023

JOURNAL ARTICLE

Heterogeneity of reported outcomes in epidermolysis bullosa clinical research: a scoping review as a first step towards outcome harmonization

Eva W H Korte, Tobias Welponer, Jan Kottner, Sjoukje van der Werf, Peter C van den Akker, Barbara Horváth, Dimitra Kiritsi, Martin Laimer, Anna M G Pasmooij, Verena Wally ... [Show more](#)

BJD Improving patient outcomes in skin disease worldwide

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British Journal of Dermatology



Volume 189, Issue 1
July 2023

JOURNAL ARTICLE

Epidermolysis bullosa: time to come together for better outcomes [Get access >](#)

Gabriela Petrof ✉, Anna E Martinez

British Journal of Dermatology, Volume 189, Issue 1, July 2023, Page 5,
<https://doi.org/10.1093/bjd/ljad123>

Published: 17 April 2023 **Article history** ▼

Considering...



Increasing number of **novel therapies** in development



Increasing number **interventional studies**



Variety of **outcomes and definitions**, many different **instruments**

- Even within stratified subgroups

... need for (more) harmonization



Scoping review

-  Increasing number of **novel therapies** in development
-  Increasing number **interventional studies**
-  Variety of **outcomes and definitions**, many different **instruments**
 - Even within stratified subgroups

standardization of
outcome
measurement

uniformity,
consistency in
outcome reporting

better **comparison** of
treatment outcomes

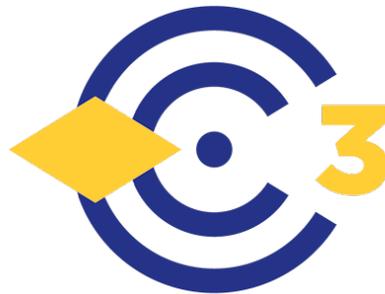
enhanced **efficacy** of
treatment
development

Reduced research waste, measuring **meaningful outcomes**



Development and implementation of core outcome sets for EB trials

launched in 2023



PERSPECTIVE

The Harmonizing Outcome Measures for Eczema (HOME) Roadmap: A Methodological Framework to Develop Core Sets of Outcome Measurements in Dermatology

Jochen Schmitt¹, Christian Apfelbacher², Phyllis I. Spuls³, Kim S. Thomas⁴, Eric L. Simpson⁵, Masutaka Furue⁶, Joanne Chalmers⁴ and Hywel C. Williams⁴

Kirkham et al. *Trials* (2019) 20:116
<https://doi.org/10.1186/s13063-019-3230-x>

Trials

RESEARCH

Open Access

Core Outcome Set-STandardised Protocol Items: the COS-STAP Statement

Jamie J. Kirkham¹, Sarah Gorst¹, Douglas G. Altman², Jane M. Blazeby³, Mike Clarke⁴, Sean Tunis⁵, Paula R. Williamson^{1*} and for the COS-STAP Group

Open Access



The COMET Handbook: version 1.0

Paula R. Williamson^{1*}, Douglas G. Altman², Heather Bagley¹, Karen L. Barnes¹, Jane M. Blazeby³, Sara T. Brookes³, Mike Clarke^{4,5}, Elizabeth Gargon¹, Sarah Gorst¹, Nicola Harman¹, Jamie J. Kirkham¹, Angus McNair³, Cecilia A. C. Prinsen⁶, Jochen Schmitt⁷, Caroline B. Terwee⁶ and Bridget Young¹

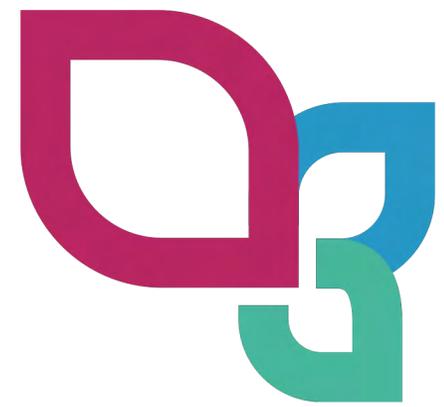
Aim



- Multi-stakeholder consensus-based agreement
- **Minimum set of outcome domains & measurement instruments** that should be measured & reported in all clinical trials of **each major EB type**
- **Meaningful enough** to be **assessed** in each trial

- What (outcome) and how (instrument)
- Current first step is *the what*

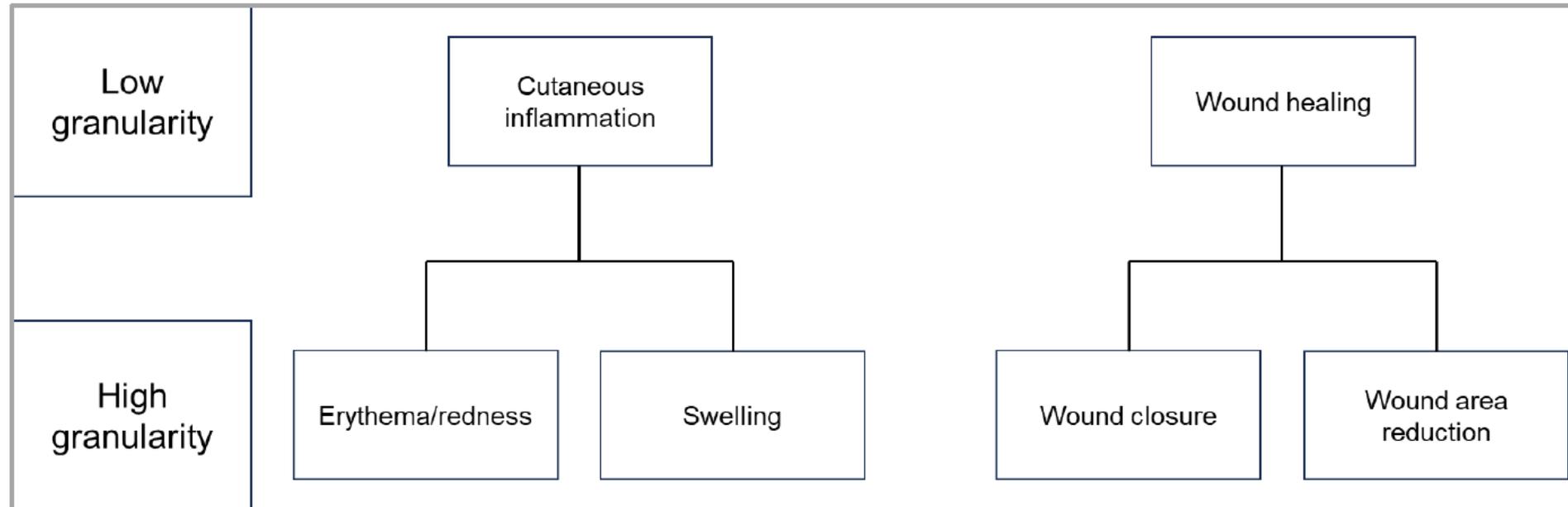
Goals



- **COSEB** is about...
 - ... domains, not specific outcomes
 - ... core domains, not harmonization of all outcomes
 - ... balancing granularity and specificity for usability

Specific enough
to be meaningful

General enough
to be practical



Non-goals



- **COSEB** is about...
 - ... domains, not specific outcomes
 - ... core domains, not harmonization of all outcomes
 - ... balancing granularity and specificity for usability

EB PASI 40

NOT:

- Dictating endpoints for each study > **measuring more is always possible** (i.e. to capture the EB subtype specific target of a therapy)
- Detailed outcome domains specific for a subtype

COSEB consortium

Steering committee



Tobias Welponer



Martin Laimer



Dimitra Kiritsi



Eva Korte



Verena Wally



Peter van den Akker



Marieke Bolling



Marjon Pasmooij

C3 methodologists



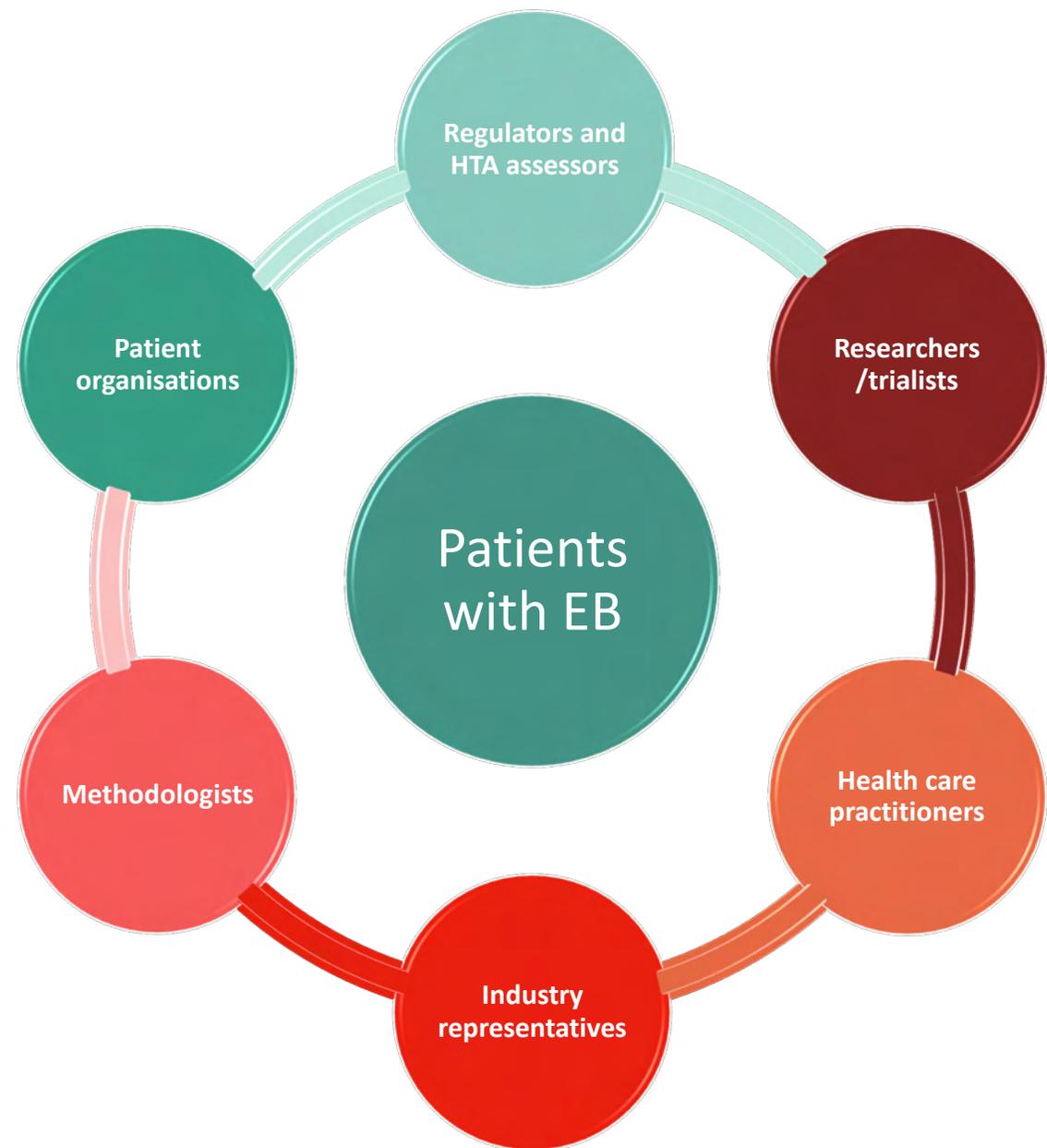
Phyllis Spuls



Jan Kottner



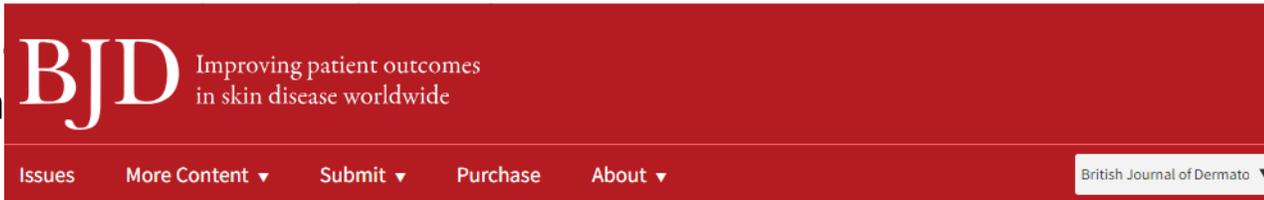
Sanna Prinsen



COSEB Kick-off

April, 2023 - Digital kick-off meeting

- 10 speakers and 104 participants (all stakeholder roles)
- 24 countries represented
 - Europe
 - Asia
 - North America
 - South America
 - Australia



- Education: E
- > Provide p
- Engagement:
- Gauge agree

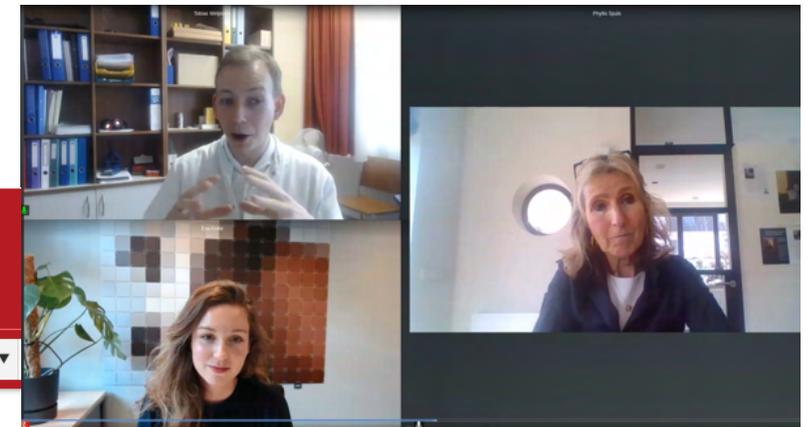
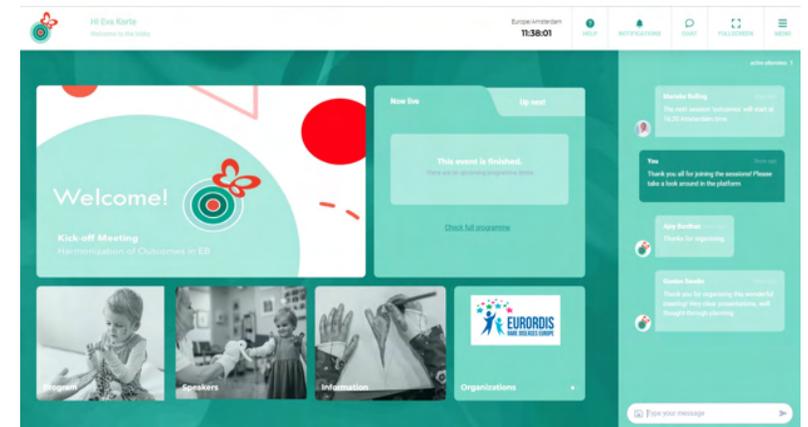
JOURNAL ARTICLE ACCEPTED MANUSCRIPT

Harmonization of outcomes in epidermolysis bullosa – report of the Core Outcome Sets for Epidermolysis Bullosa (COSEB) kick-off meeting

Eva W H Korte, Phyllis I Spuls, Peter C van den Akker, Dimitra Kiritsi, Martin Laimer, Anna M G Pasmooij, Rainer Riedl, Elizabeth Vroom, Verena Wally, Tobias Welpner ...
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British Journal of Dermatology, ljad361, <https://doi.org/10.1093/bjd/ljad361>
Published: 04 October 2023 [Article history](#)

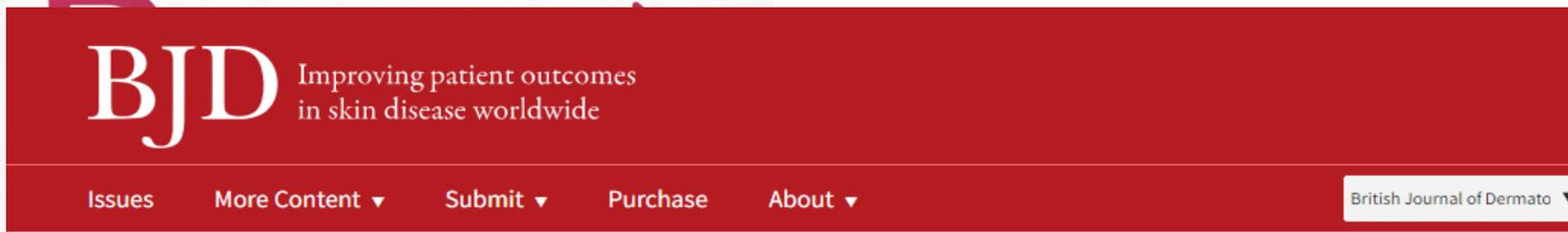
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COSEB Workshop

December, 2023, Hybrid workshop Amsterdam

- Start-up working groups
- Input funding plan
- Refinement protocol
- Patient participation



Volume 191, Issue 3
September 2024

JOURNAL ARTICLE

Towards a roadmap for COSEB: the next steps in harmonization of outcomes for epidermolysis bullosa

Eva W H Korte, Anna M G Pasmooij, Maria C Bolling, Sinéad Hickey, Sagair Hussain, Dimitra Kiritsi, Jan Kottner, Cecilia A C Prinsen, Angélique Sauvestre, Gaston Sendin ...

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[Author Notes](#)



COSEB Satellite meeting

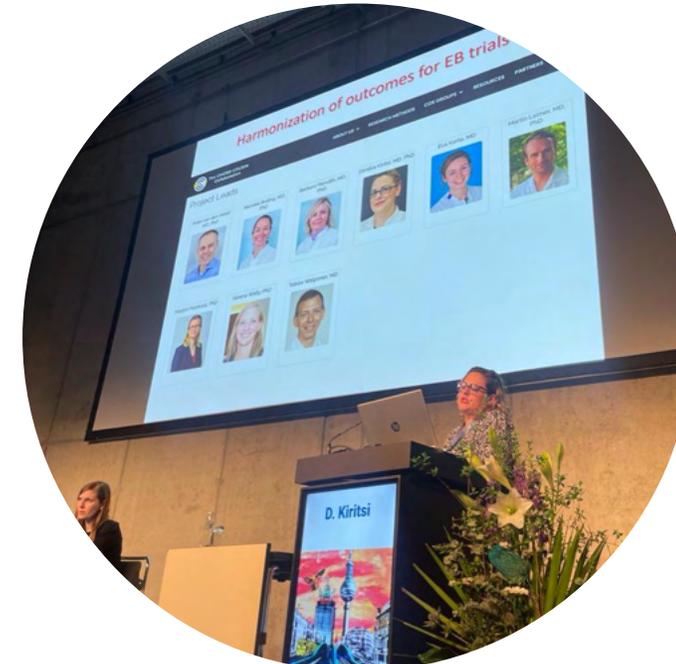


Working group progress
Refinement of protocol
Pitching and discussing interview studies



COSEB on the map

- Representation on EB congresses and workshops
- Worldwide initiative
- Together





COSEB methodology

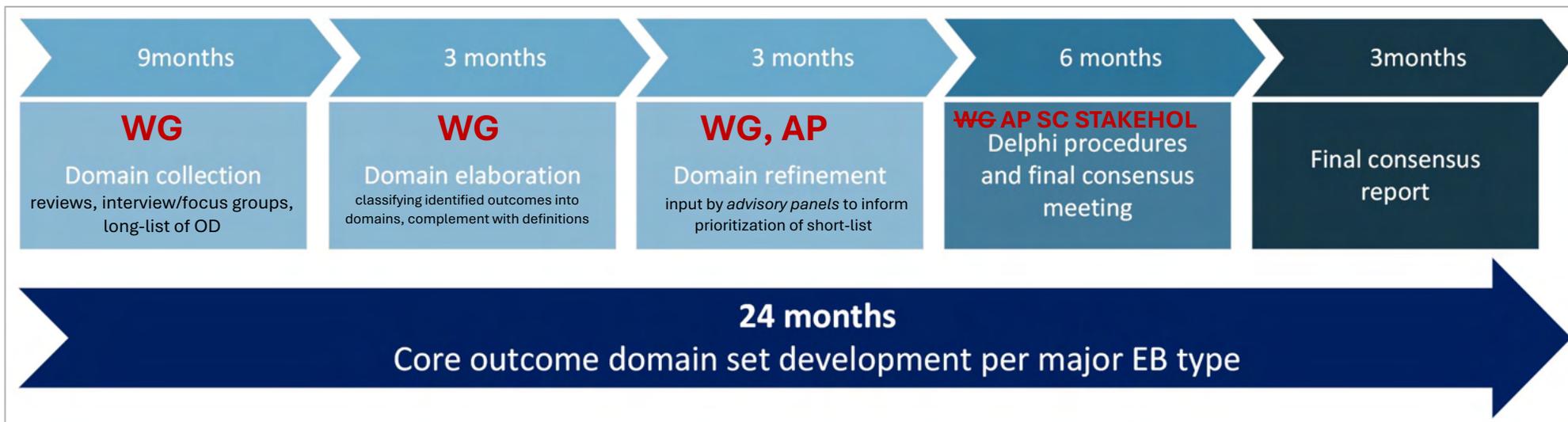
Working groups: **OD long list** >>>

Advisory panel: **consented feedback** >>>

Working groups: **refinement & (re) prioritization to OD short list** >>>

Delphi voting panel: **vote on provisional core OD set** >>>

Consensus meeting: **finalizing COD set**



- Patient(s) (representatives)
- Clinicians
- Researchers
- Methodologists
- Industry representatives
- Regulators
- HTA, payers

Status quo

Working groups are active

WG	WG Lead	Status
EBS	Ajoy Bardhan	Long List completed Definitions ongoing
JEB	Anne Lucky	Long List in preparation
DEB	Irene Lara-Corrales Amy Paller	Long List completed Definitions ongoing



EB simplex WG outcome domain list

Domain Set 1: Cutaneous manifestations

1. Wound healing
2. Blister formation
3. Lesion characteristics
4. Infection

Domain Set 2: Safety

5. Adverse effects
6. Toxicity
7. Tolerability

Domain Set 3: Symptoms

8. Pain
9. Pruritus

Domain Set 4: Physical functioning

10. Ability to chew and swallow
11. Intake
12. Appetite
13. Ability to move
14. Plantar characteristics
15. Fatigue
16. Hand function

Domain Set 5: Quality of life

17. EB-specific quality of life

Domain Set 6: Clinical assessment

18. Global assessment by investigator

Domain Set 7: Resource use

19. Medication usage
20. Dressing usage
21. Costs
22. Hospital attendance

Domain Set 8: Patient satisfaction

23. Patient reported satisfaction

Domain Set 9: Developmental status

24. Weight and height
25. Nutritional status
26. Pubertal status

Domain Set 10: Extracutaneous manifestations

27. Oesophageal stricture

Domain Set 11: Psychosocial status

28. Sleep
29. Psychological impact
30. Social functioning

Domain Set 12: Survival

31. Overall survival
32. Treatment related mortality

Dystrophic EB WG outcome domain list

Mucocutaneous manifestations

1. Total BSA of involvement
 - BSA of blisters erosions
 - BSA of wounds
 - BSA of prurigo lesions
2. Wound area reduction
3. Cancer formation
4. Infection (treated with systemic antibiotics)
5. Scarring
6. Lesion characteristics and appearance
7. Mucosal involvement

Safety

8. Adverse events

Symptoms

9. Pain
10. Itch

Physical functioning

11. Hand functioning
12. Ability to chew
13. Ability to swallow
14. Contractures
15. Daily functionality and disability
16. Ability to move
17. Fatigue
18. Sexual health

Quality of life

19. EB-specific quality of life

Clinical assessment

20. Global assessment
21. Patient/parent reported disease severity

Resource use

22. Cost
23. Lost days of work/school

Treatment characteristics

24. Treatment cost

Patient satisfaction

25. Patient reported satisfaction and benefit

Developmental status

26. Height and weight
27. Nutritional status
28. Pubertal status (for studies with adolescents)

Extracutaneous manifestations

29. Esophageal strictures

Psychosocial functioning

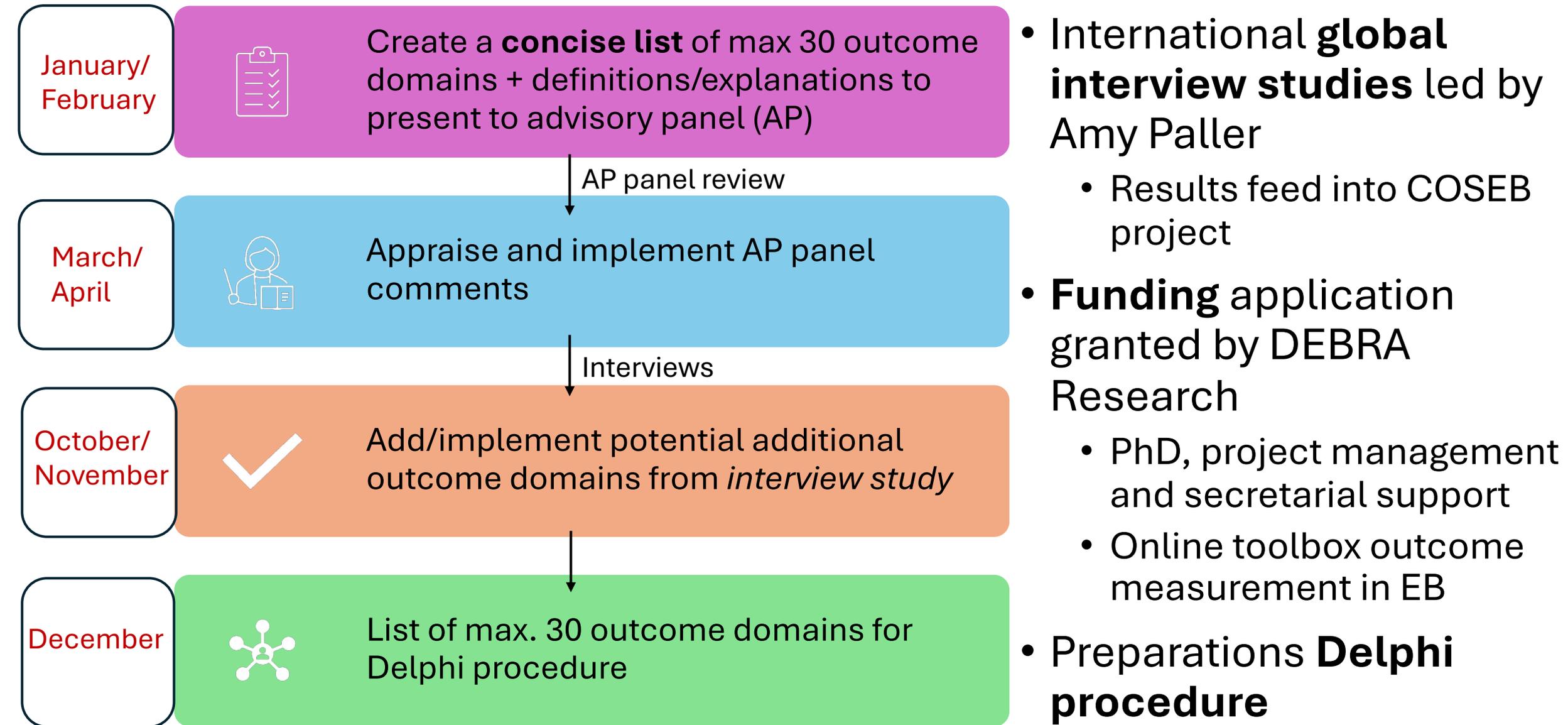
30. Mental health
31. Sleep
32. Social functioning

Death/survival

33. Overall survival
34. Treatment related mortality

Current standing and next steps 2026

Target time for delivery



Thank you

- COSEB websites
 - c3outcomes.org/coseb
 - comet-initiative.org/studies/details/1033
- COSEB publications: open access



Scoping review

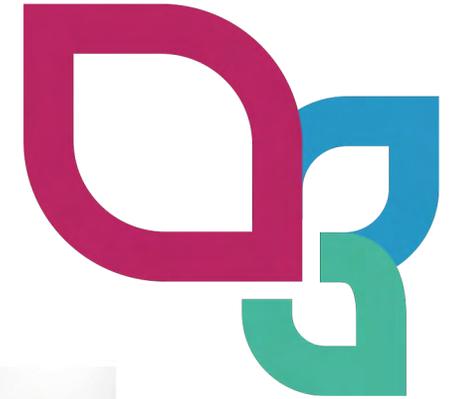


Kick-off meeting report



Workshop report

- Contact: coseb@umcg.nl



BMC
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Protocol
(accepted)