

COSEB

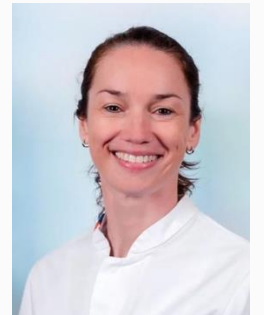
EB-Clinet meeting

October 17, 2024 Vienna

Marieke Bolling, MD PhD

Dermatologist, EB Expertise Center

University Medical Center Groningen, the Netherlands



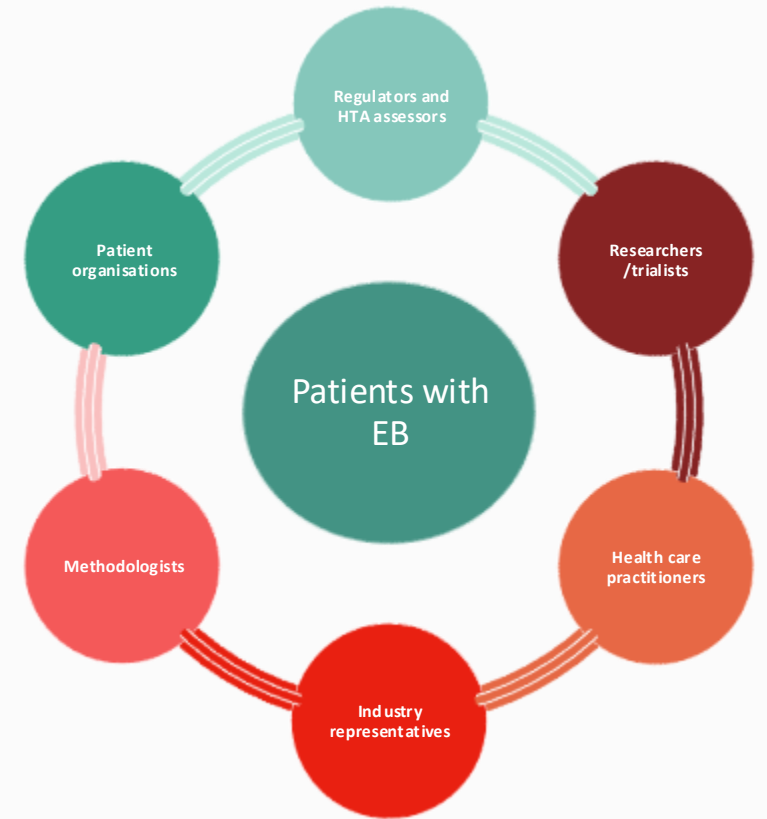
COSEB presentation

- What is COSEB?
- Why & objectives
- Roadmap
- Current status
- Future plans



What is COSEB?

- Consortium, multi-stakeholder
- Aim: harmonizing and optimizing outcome measurement in clinical trials in EB
- Why?



COSEB: why?



Increasing number of potential **novel therapies for EB** in development



Increasing number **interventional studies in EB**

The COSEB initiative



Scoping review
Korte *et al*
BJD 2023

Steering Committee



Tobias Welpner



Martin Laimer



Dimitra Kiritsi



Eva Korte



Verena Wally



Peter van den Akker



Marieke Bolling



Marjon Pasmooij

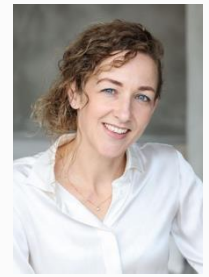
C3 methodologists



Phyllis Spuls



Jan Kottner



Sanna Prinsen

Scoping review outcome measurement in EB



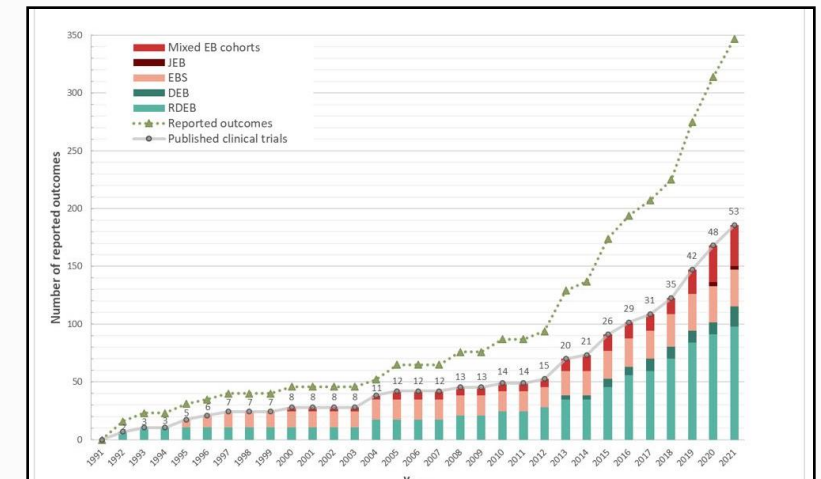
Increasing number of potential **novel therapies for EB** in development



Increasing number **interventional studies in EB**



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



Scoping review
Korte *et al*
BJD 2023



Needs

1. Uniform **definitions** of outcome domains
2. Uniform **use** of **outcome domains** (where possible)
3. Uniform **use** of the best **instruments** we have (fit for purpose)
4. Identify where we **lack** well-functioning instruments
 - improve trial/study protocol development and **meaningful outcome measurement**, comparability of studies and pooling of data in future (much needed in rare disease)
 - faster translation of novel therapeutic strategies into the clinic

COSEB: how?

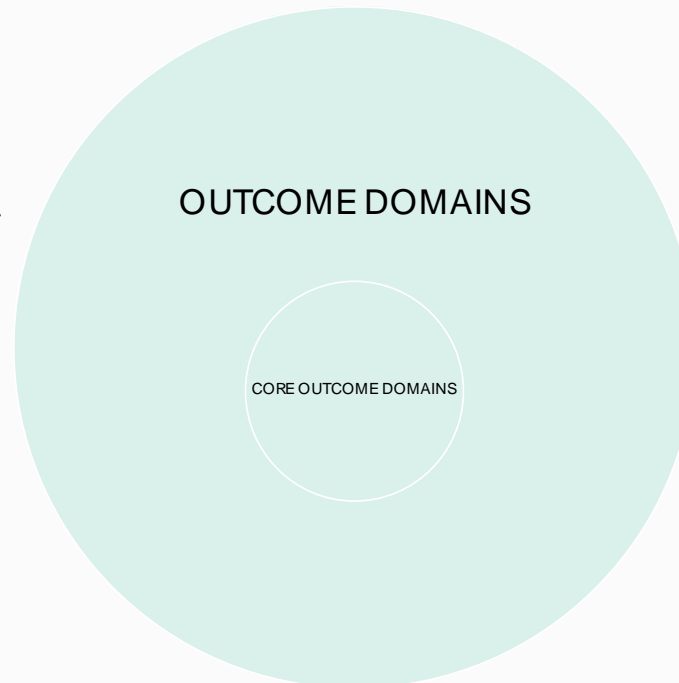
Development of a core outcome set (COS) for EB trials

'A (multi-stakeholder) consensus-based agreed **minimum set** of: **1. outcome domains** and **2. measurement instruments** that should be measured and reported in all clinical trials of a specific disease or trial population'

NB:

Not necessarily the primary endpoint of a trial.

Measuring more always possible!

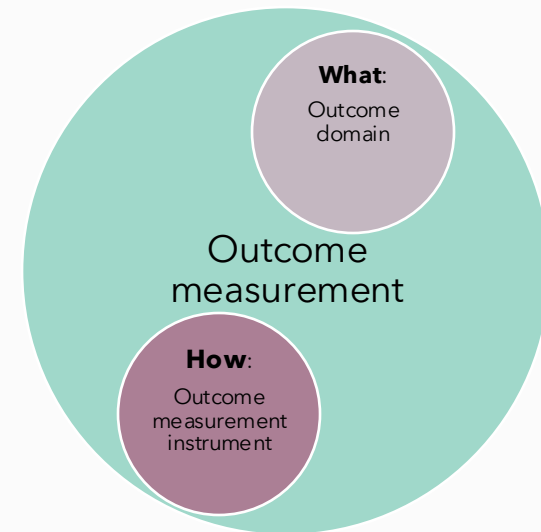


What (outcome) versus how (instrument)!

Main achievements, main tasks

1. **Outcome domains** (the *what*):

- uniform definitions
- consensus on core outcome domains > **core outcome domain set**



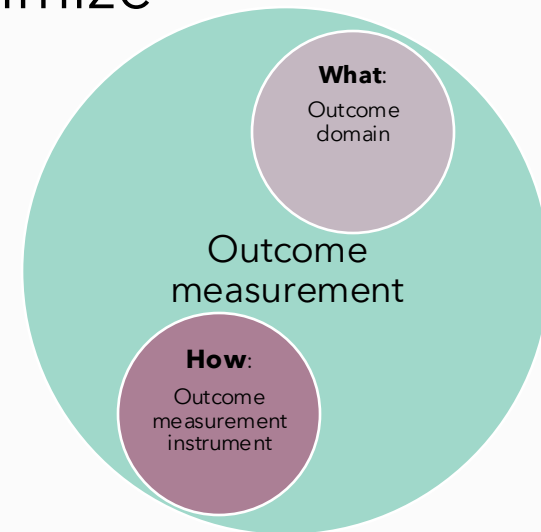
Main achievements, main steps/tasks

1. **Outcome domains** (the *what*):

- uniform definitions
- consensus on core outcome domains > core outcome domain set

2. **Instruments, fit for purpose** (the *how*):

- What do we have, how do they perform? > **core measurement set**
- If needed, development of novel instruments and/or optimize the existing



Main achievements, main steps/tasks

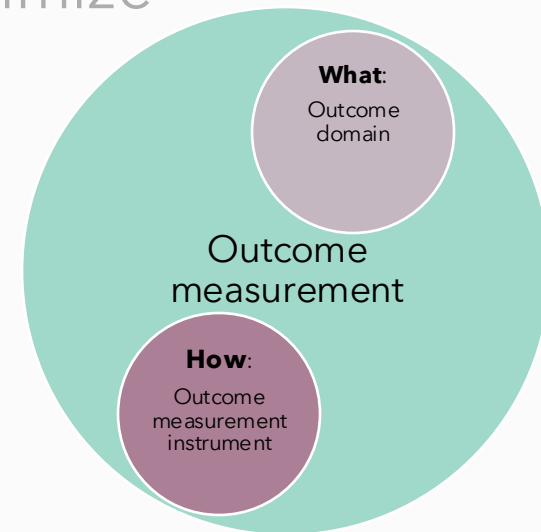
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- uniform definitions
- consensus on core outcome domains > core outcome domain set

2. **Instruments, fit for purpose** (the *how*):

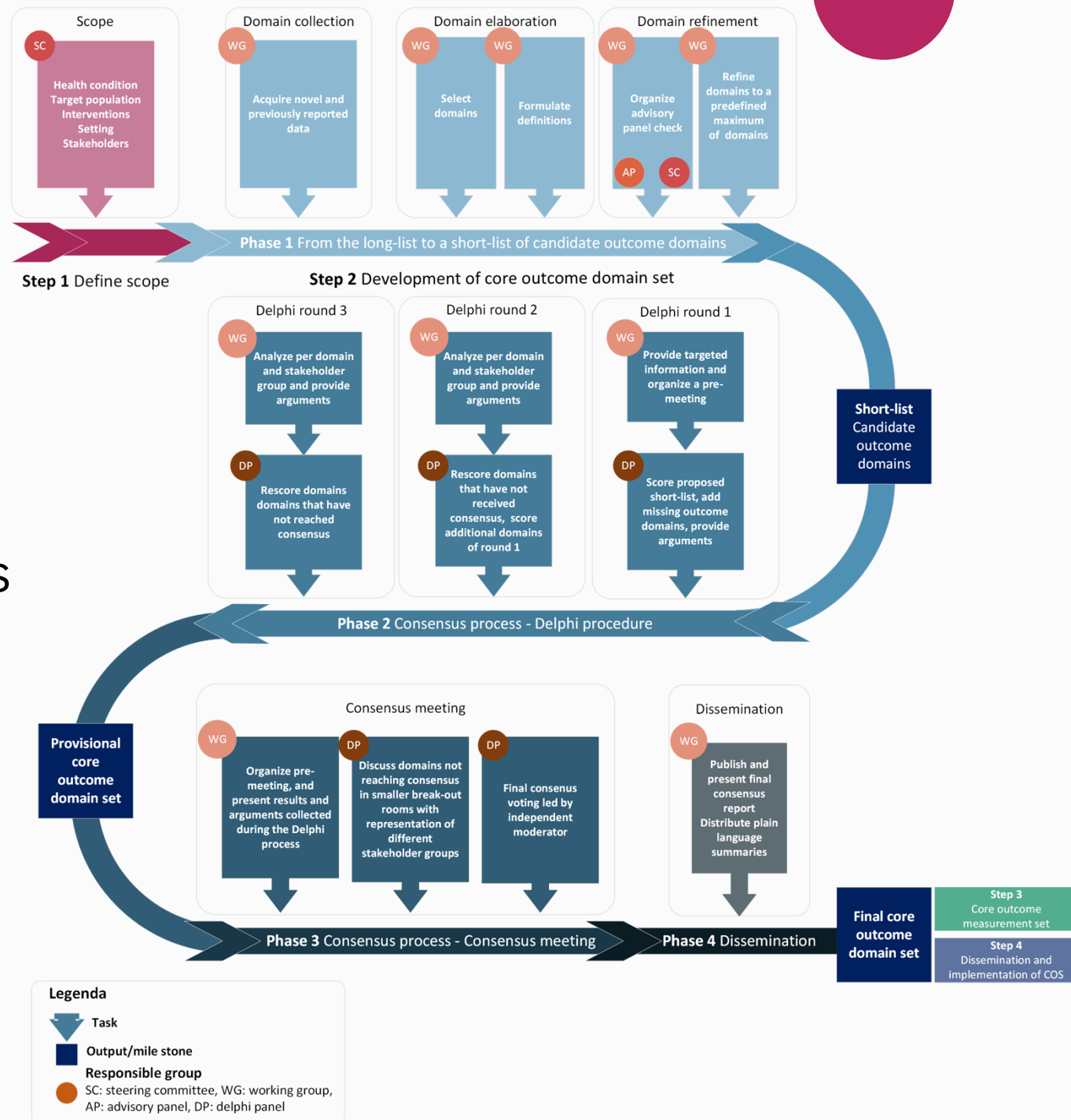
- What do we have, how do they perform? > core measurement set
- If needed, development of novel instruments and/or optimize the existing

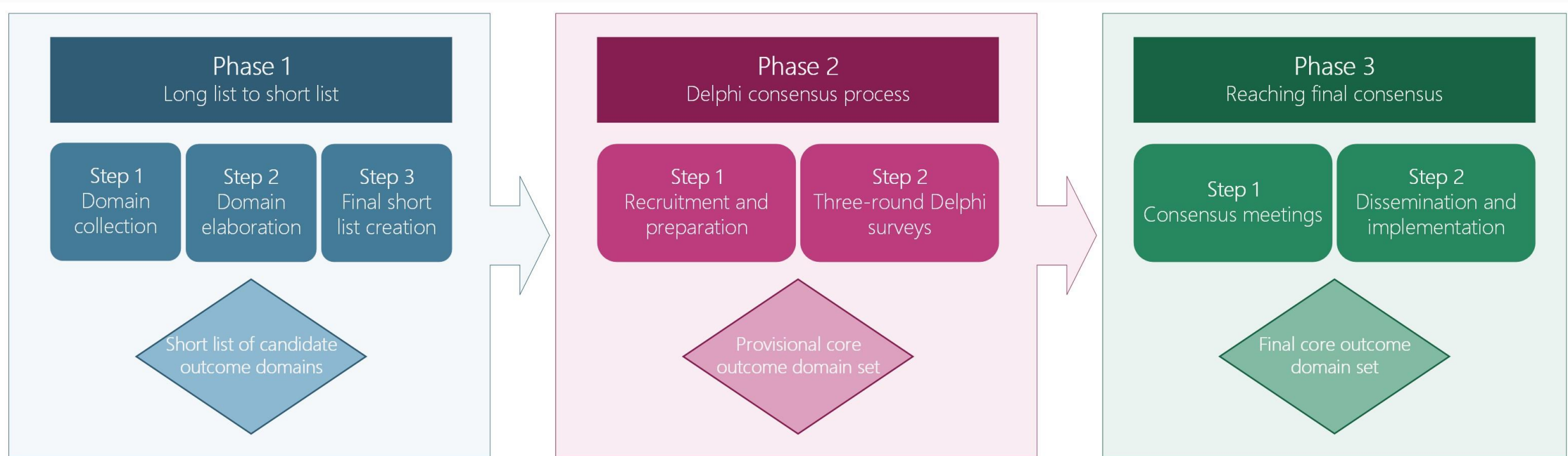
→ **Core outcome set (COS)**



COSEB: how?

- Scope: clinical trials in EB
- COS per main type of EB, WG for each type
- Worldwide, all stakeholders
- Patient voice





Then → Core outcome measurement (the 'how') set

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graph TD; A[DEBRA World Congress - Sep 2021] --> B[Scoping review published in BJD]; B --> C[Kick-off meeting - Apr 2023]; A --> D[Workshop on clinical outcomes in EB]; C --> E[Survey: agreement with];
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DEBRA World Congress - Sep 2021

Scoping review published in *BJD*

Kick-off meeting - Apr 2023

Workshop on clinical outcomes in EB

- Involved people
- What do we have?
- What do we need?

Survey: agreement with

- Problem statement
- Scope
- COS proces



Workshop on clinical outcomes in EB

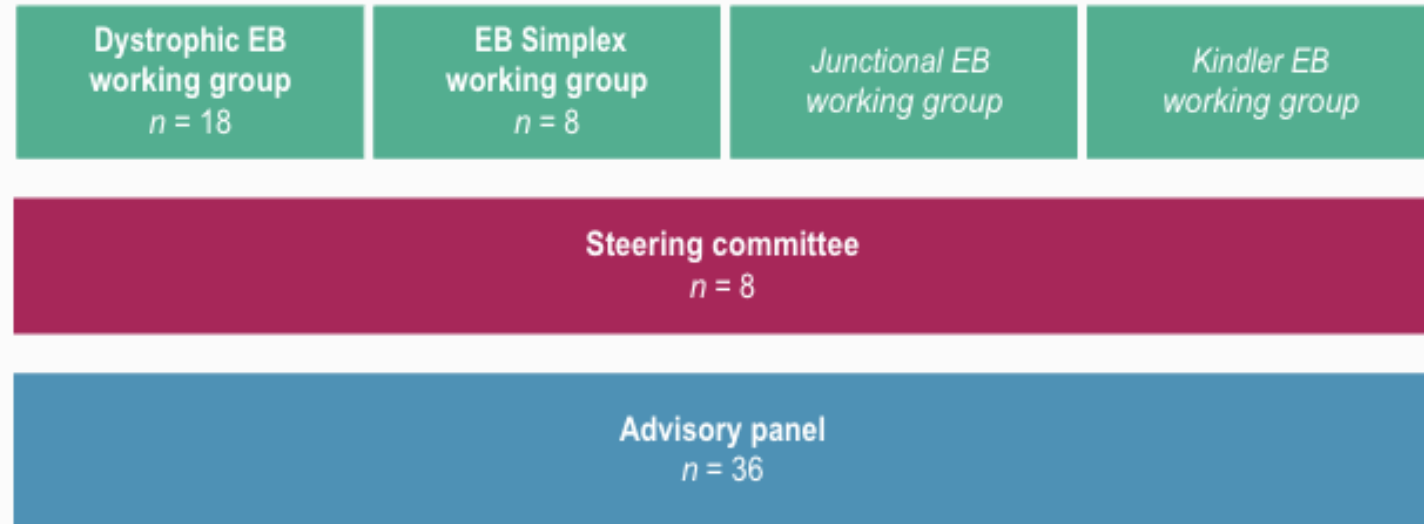
- Involved people
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- What do we need?

Survey: agreement with

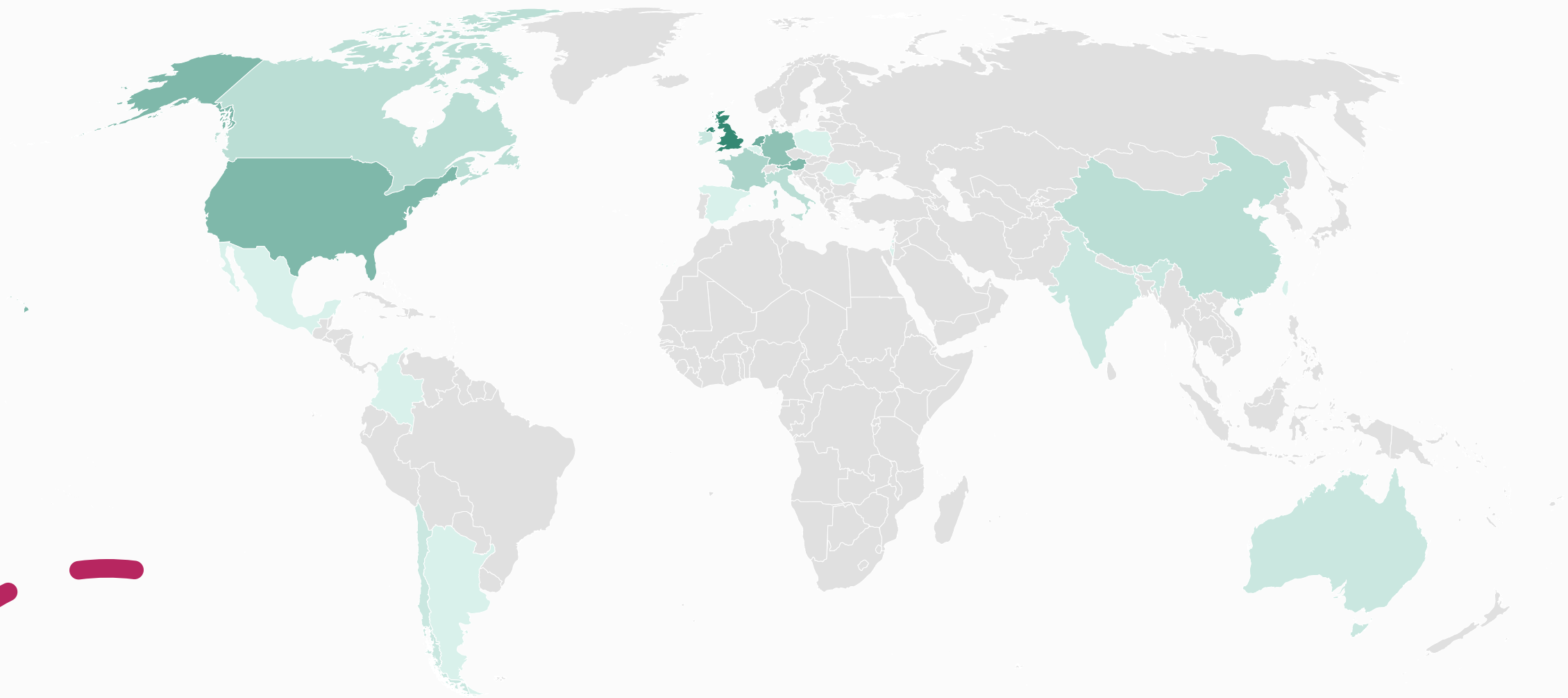
- Problem statement
- Scope
- COS proces

COSEB: where are we?

- Consortium installed (72 members)
- WGs EBS & DEB running
(leads: EBS Ajoy Bardhan; DEB Amy Paller/Irene Lara-Corrales)
- JEB will start (lead: Anne Lucky)

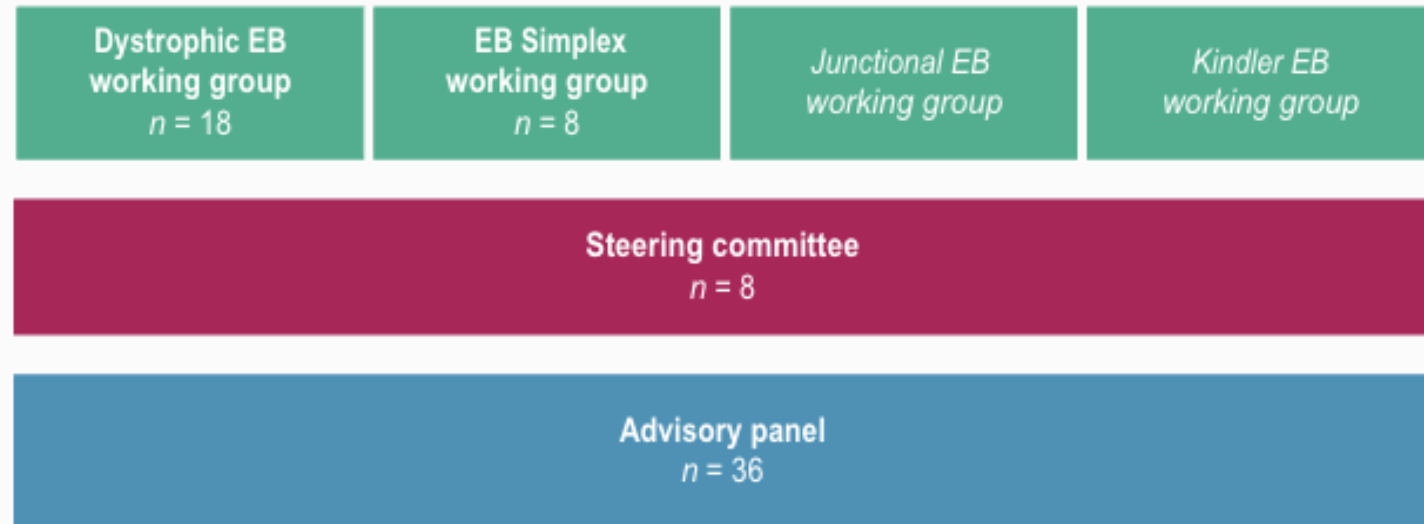


Multi-stakeholder, worldwide



COSEB: where are we?

- Consortium installed (72 members)
- WGs EBS & DEB running
- JEB will start)
- Protocol finalized > ethical approval > submitted
- Grant proposal, awaiting outcome
- Patient voice! > interview study protocol



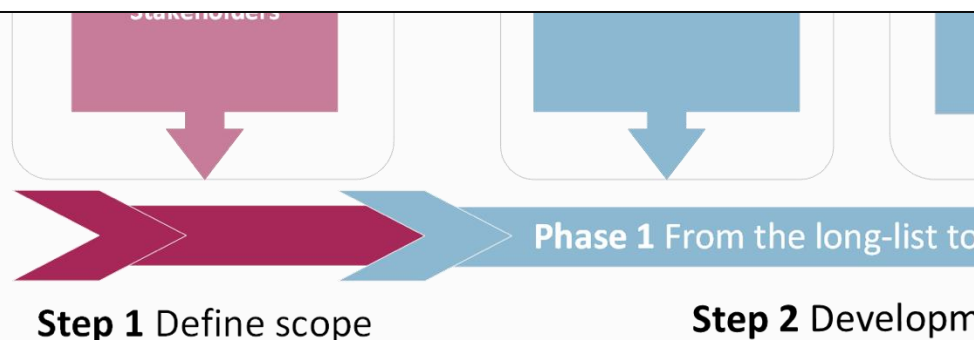
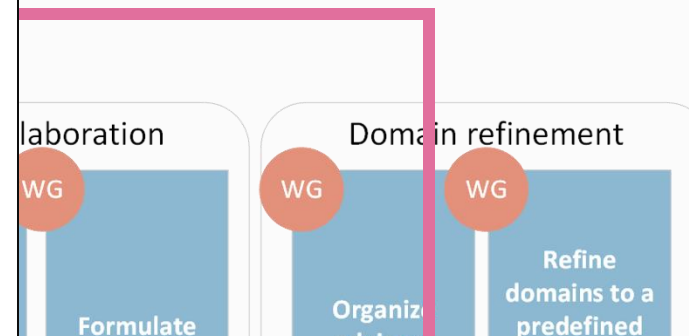


Step 4 – consolidation of survey/discussion

From 14 outcome areas and 80 outcome domains, now we have 13 outcome areas and 34 outcome domains

<u>Mucocutaneous manifestations</u>	<u>Quality of life</u>
1. Total BSA of involvement <ul style="list-style-type: none">• BSA of blisters erosions• BSA of wounds• BSA of prurigo lesions	19. EB-specific quality of life
2. Wound area reduction	<u>Clinical assessment</u>
3. Cancer formation	20. Global assessment
4. Infection (treated with systemic antibiotics)	21. Patient/parent reported disease severity
5. Scarring	<u>Resource use</u>
6. Lesion characteristics and appearance	22. Cost
7. Mucosal involvement	23. Lost days of work/school
<u>Safety</u>	<u>Treatment characteristics</u>
8. Adverse events	24. Treatment cost
<u>Symptoms</u>	<u>Patient satisfaction</u>
9. Pain	25. Patient reported satisfaction and benefit
10. Itch	<u>Developmental status</u>
<u>Physical functioning</u>	26. Height and weight
11. Hand functioning	27. Nutritional status
12. Ability to chew	28. Pubertal status (for studies with adolescents)
13. Ability to swallow	<u>Extracutaneous manifestations</u>
14. Contractures	29. Esophageal strictures
15. Daily functionality and disability	<u>Psychosocial functioning</u>
16. Ability to move	30. Mental health
17. Fatigue	31. Sleep
18. Sexual health	32. Social functioning
	<u>Death/survival</u>
	33. Overall survival
	34. Treatment related mortality

Implement patient voice



Step 6 – Outcome labels and definitions

Process:

1. Conor drafted initial definitions
2. Co-chairs revised
3. Distributed to working group
4. Discussed during Sept meeting
5. Feedback by email
6. Final definitions approved (67)

Definitions

Ability to chew - ability to bite/crush/grind food and make it into small pieces that are safe for swallowing.

Ability to move - ability to walk from place to place independently with or without assistive device.

Ability to swallow - safe and successful passage of fluids and/or solids from the mouth to the stomach.

Adverse event - Any untoward medical occurrence in a patient or clinical investigation subject administered an intervention during a research study, regardless of causation.

Blisters - raised, fluid-filled skin lesions without pus.

BSA of involvement - percentage of body surface with active skin disease. |

Body surface area (BSA) - total surface of the human body.

Cancer - a group of diseases characterized by the uncontrolled growth of abnormal cells.



COSEB satellite symposium program yesterday

17:30 – 18:00	Opening session COSEB aims and roadmap COSEB consortium standing Patient voice in COSEB	Peter van den Akker Marieke Bolling Martin Laimer Eva Korte
18:00 – 18:30	Working group session Progress, hurdles, expectations	Irene Lara-Correles (DEB) Ajoy Bardhan (EBS)
18:30 – 18:55	Discussion session Discussion points raised by working groups and consortium members	Irene Lara-Correles (DEB) Ajoy Bardhan (EBS) Steering Committee panel
18:55 – 19:00	Closing and path forwards	Marieke Bolling



What's next?

- Awaiting financial support
- Publication COSEB protocol
- Patients' voice: protocol interview studies; international, online
- EBS and DEB WGs:
 - Ask AP about short-list > comments > finalize short-list for voting
> Delphi procedures

What's next?

- JEB WG: lead Anne Lucky, membership: interested?
- KEB start-up?
- AP or consortium member?

→ coseb@umcg.nl

More information

- COSEB websites
 - c3outcomes.org/coseb
 - comet-initiative.org/studies/details/1033
- COSEB publications: PubMed
 - Scoping review: doi.org/10.1093/bjd/ljad077
 - BJD editorial: hdoi.org/10.1093/bjd/ljad123
 - Kick-off meeting report: doi.org/10.1093/bjd/ljad361
- Contact: coseb@umcg.nl

Steering Committee



Tobias Welponer



Martin Laimer



Dimitra Kiritsi



Eva Korte



Verena Wally



Peter van den Akker



Marieke Bolling



Marjon Pasmooij



Acknowledgments

DEBRAs of

- Austria
- France
- Ireland
- Spain
- United Kingdom



COSEB

Thank you!

