



ERS

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every breath counts

Selecting outcomes that are relevant to patients and healthcare professionals for trials

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*Disclaimer: The views presented are the reflections of the presenter and may not necessarily reflect the views of or being endorsed by the ERS.

Objectives

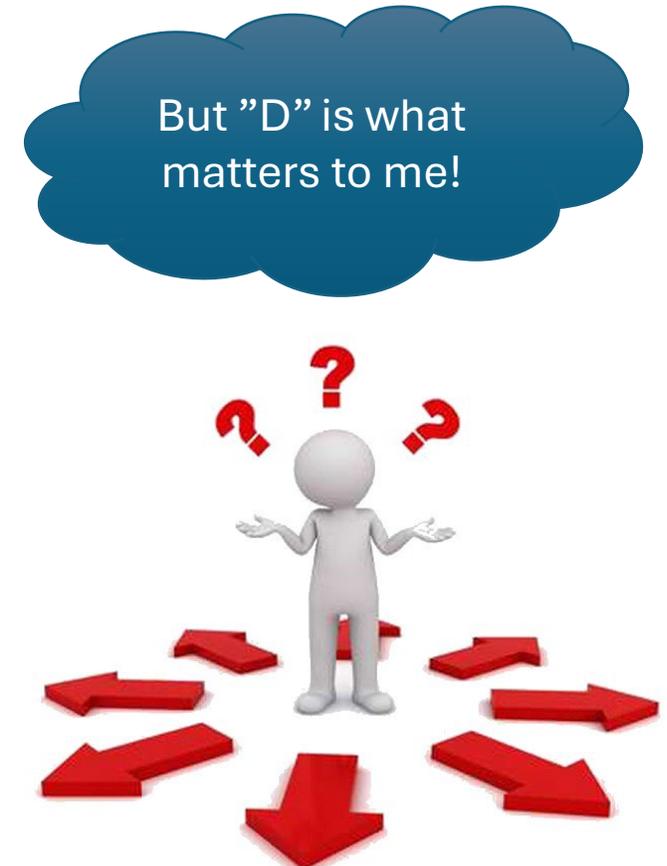
This presentation addresses four questions:

- **Why does trial outcome selection matter for patients, clinicians, and regulators?**
- What are core outcome sets (COS), and how are they developed?
- What has been the ERS experience in COS development?
- How could COS better support EMA regulatory assessments?

Why does trial outcome selection matter?

- Outcome selection determines what trials can -and cannot- tell us.

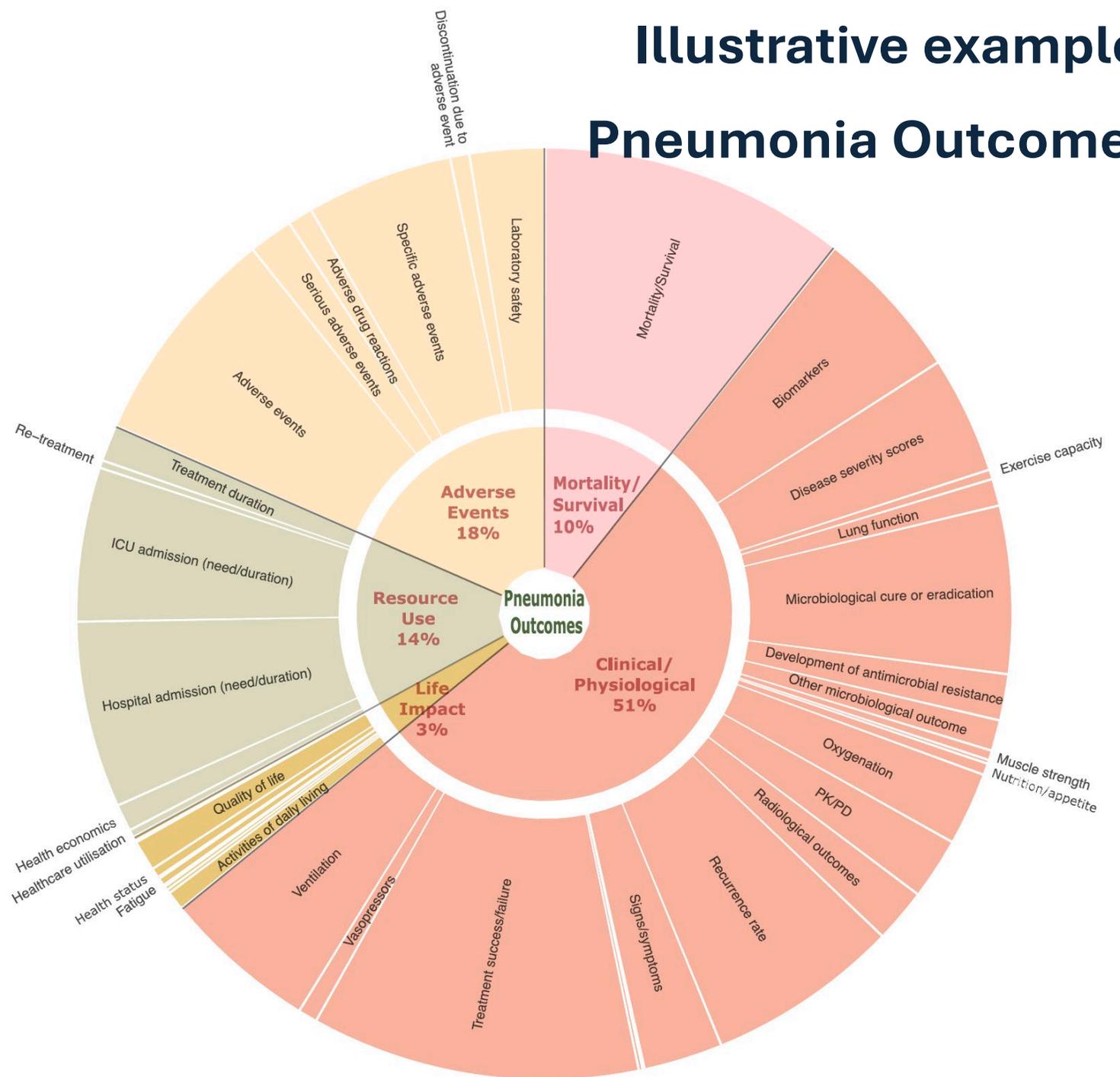
| | Outcomes | | | |
|---------|----------|---|---|---|
| | A | B | C | D |
| Trial 1 | ✓ | ✓ | | |
| Trial 2 | | ✓ | | |
| Trial 3 | | | ✓ | |
| Trial 4 | ✓ | | | |
| | | | | |
| Trial N | | ✓ | | ✓ |



Trials assess diverse outcomes using different instruments

Across disease areas, only three to four outcomes are assessed consistently in more than 50% of trials

Illustrative example: Pneumonia Outcomes



Outcomes that are important to patients and healthcare professionals are often omitted.

- Outcomes may not reflect symptom burden or daily functioning
- Inconsistent use of patient-reported outcomes
- Challenges translating trial results into practice



Eating



Dressing



Bathing



Toileting



Transferring



Mobility

Implications for Regulators & HTA

- Reduced interpretability of treatment effects
- Difficulty comparing development programmes
- Increased uncertainty in benefit-risk assessment
- Reliance on post-hoc justification of outcomes

**How can we ensure consistency and relevance without
constraining innovation?**

Objectives

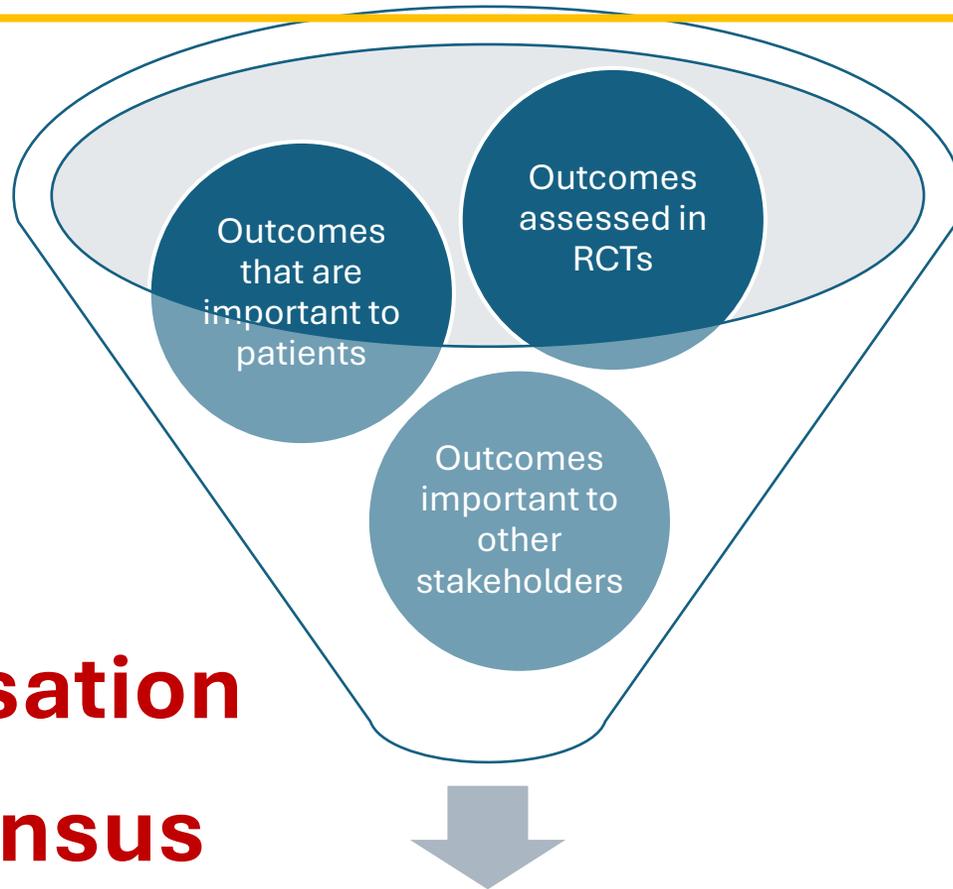
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A core outcome set (COS) is an agreed standardised set of outcomes that should be measured and reported, as a minimum, in all clinical trials in specific areas of health or health care.

Core Outcome Sets



Prioritisation

Consensus

Core Outcome Set

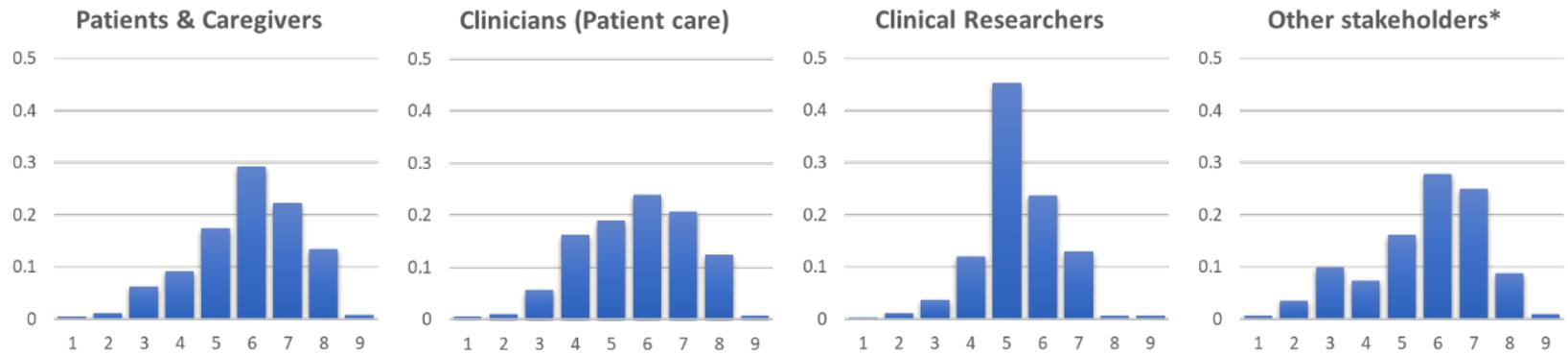
Outcome Measurement Instruments



Core Outcome Measures
in Effectiveness Trials

- ✓ Evidence informed
- ✓ Global
- ✓ Multistakeholder
- ✓ Consensus

Delphi Survey: Multistakeholder Consensus



*Guideline developers, regulators, policy makers, funders, etc

| Outcome | Score | | | | | | | | | |
|------------|--------------------|---|---|--------------------------|---|---|----------|---|---|-----------------|
| | Limited importance | | | Important – Not critical | | | Critical | | | Unable to score |
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | |
| Outcome #1 | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

Core Outcome Sets

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COPD Exacerbations Core Outcome Set

- An illustrative example

TABLE 2 Frequency that different outcome measures were reported in the 123 randomised controlled trials (RCTs) and 38 systematic reviews (SRs) included in this methodological review

| Outcomes | Frequency of reporting | |
|---|------------------------|----------|
| | RCTs | SRs |
| Patient-important outcomes | | |
| Mortality | 101 (82%) | 29 (76%) |
| Treatment success or failure | 77 (63%) | 29 (76%) |
| Adverse effects | 73 (59%) | 26 (68%) |
| Health status, symptoms and quality of life | 73 (59%) | 17 (45%) |
| Duration of exacerbations | 42 (34%) | 20 (53%) |
| Re-exacerbation, re-hospitalisation | 33 (27%) | 16 (42%) |
| Exercise capacity | 14 (11%) | 1 (3%) |
| Anxiety and depression | 6 (5%) | 1 (3%) |
| Surrogate, physiological and laboratory outcomes | | |
| Lung function | 58 (47%) | 18 (47%) |
| Arterial blood gases and oxygen saturation | 40 (33%) | 5 (13%) |
| Microbiological response | 16 (13%) | 7 (18%) |
| Biomarkers | 32 (26%) | 2 (5%) |
| Medication use | 18 (15%) | 3 (8%) |

Identification of COPD exacerbation outcomes

Systematic review



What outcomes are tested and reported in clinical research studies?

What outcomes are important to patients?

- ✓ 123 Clinical trials
- ✓ 38 Systematic reviews of clinical trials
- ✓ 4 primary studies and one systematic review evaluating patients preferences

Qualitative research



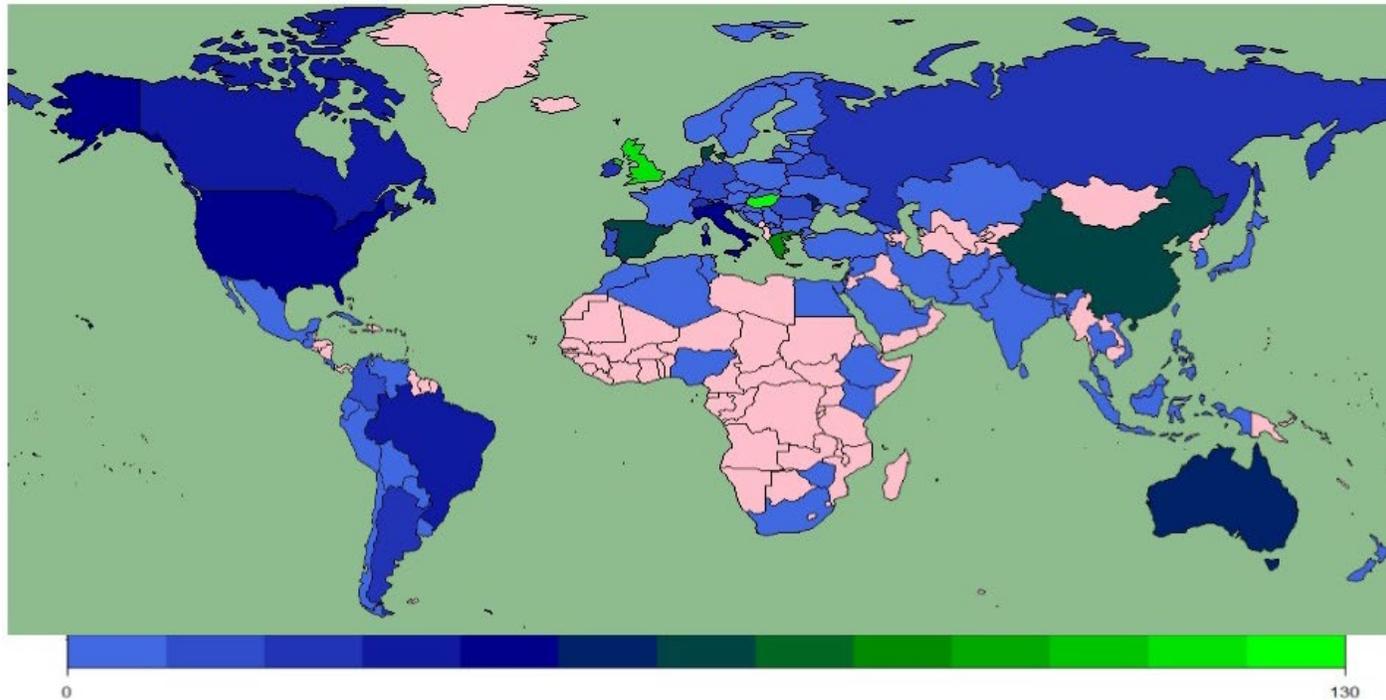
- ✓ Focus group(s) and individual interviews with 86 patients.
- ✓ 11 countries globally

What outcomes are important to patients all-over the world?



Global multistakeholder consensus (>1,000 contributors, including >250 patients)

Responders by Country of Residence



Explicit prioritisation of outcomes that matter to patients and health professionals

(to ensure relevance, interpretability, and comparability across trials)



The ERS COPD Exacerbations Core Outcome Set

BOX 1 Core outcome set for clinical trials evaluating the management of COPD exacerbations. Detailed descriptions of the outcomes are available in the text and appendix 6 (supplementary material)

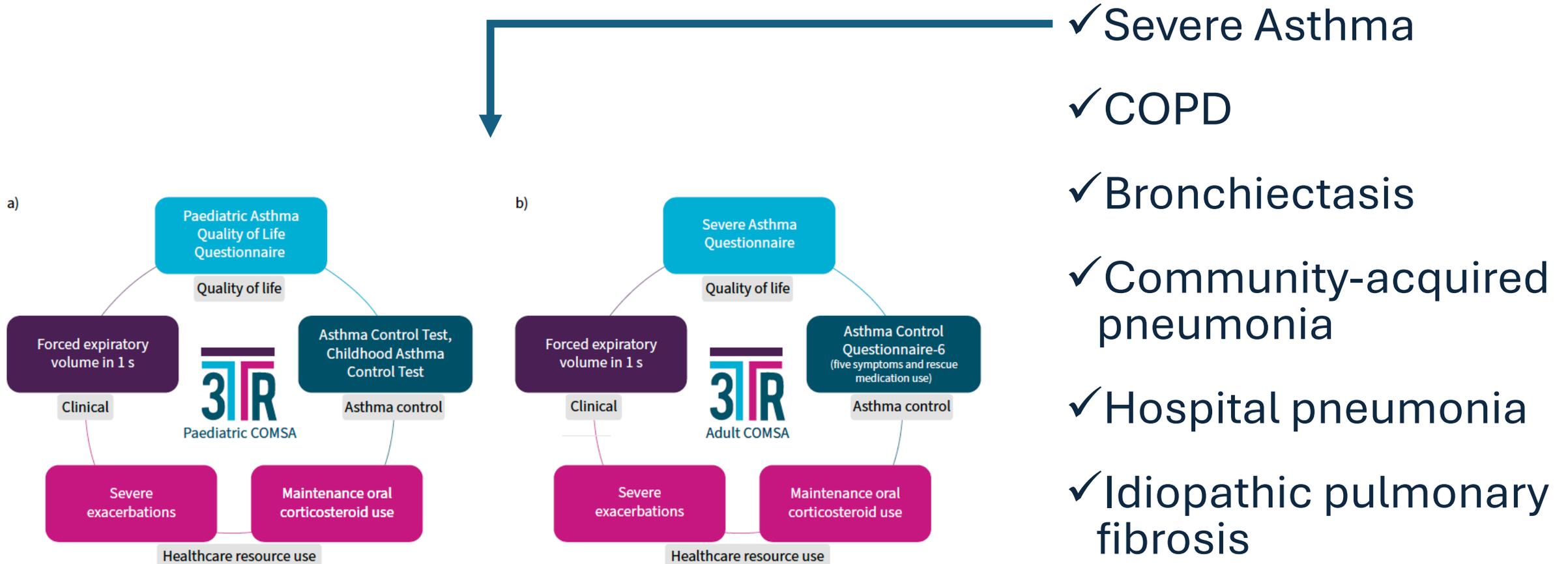
- 1) Death
 - a) Death from any cause
 - b) Death from a COPD exacerbation
- 2) Treatment success
- 3) Need for higher level of care
 - a) Need for hospital admission for the presenting exacerbation
 - b) Need for admission to the intensive care unit for the exacerbation
- 4) Levels of oxygen and carbon dioxide in the blood (arterial blood gases)
- 5) Patient-reported outcomes
 - a) Breathlessness
 - b) Health-related quality of life
 - c) Activities of daily living
 - d) Worsening of symptoms after the initial treatment
- 6) Future impact
 - a) Disease progression
 - b) Future exacerbations
 - c) Future hospital admissions
- 7) Safety
 - a) Serious adverse events from treatments
 - b) Development of resistant bacteria
 - c) Development of pneumonia
- 8) Treatment adherence

+

**Measurement
Instruments**

Mathioudakis et al. Eur Respir J 2022

Emerging Respiratory Core Outcome Sets



Khaleva et al. Eur Respir J 2023

Classified as public by the European Medicines Agency

Close Collaboration with COMET

- Ensuring methodological rigour in the development of respiratory core outcome sets.
- Contributing to COS methods and the wider COMET community, including guideline and patient-facing perspectives.
- Supporting awareness and appropriate uptake of COS across trials, guidelines, and research programmes.



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- **How could COS better support EMA regulatory assessments?**

What do core outcome sets bring to the table?

- **A globally informed, multi-stakeholder agreement**

Including strong patient involvement – on the minimum outcomes that should be measured in trials addressing a specific disease

- **An enabling framework, not a fixed endpoint strategy**

COS define a common minimum while allowing developers to retain flexibility for innovation, mechanism-specific, or programme-specific outcomes

- **Potential to reduce avoidable uncertainty**

By ensuring that development trials consistently generate outcomes relevant for regulatory and HTA decision-making

Where regulatory input could strengthen COS development

- Views on **COS methods** that would ensure robustness and regulatory acceptability
- Regulatory input into **COS development** processes, including scope and timing
- Advice on **balancing consistency with flexibility**, particularly for innovative therapies



Importance of potential regulatory alignment

- Potential **alignment** between EMA-recommended outcomes and high-quality COS, where appropriate
- Understanding how regulatory signals could support appropriate **uptake** of COS, without constraining innovation



Take home messages

- **Outcome selection matters:** Heterogeneity in trial outcomes limits comparability, interpretability and regulatory decision-making.
- **Core outcome sets provide a solution:** They establish a shared, patient-centred minimum while preserving flexibility and innovation.
- **ERS leadership:** A transparent, patient-partnered framework to develop and endorse high-quality core outcome sets for respiratory trials.
- **Alignment with regulators is key:** Early dialogue could enhance the regulatory relevance and uptake of core outcome sets.

Thank you!

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