

A systematic review of studies that determine which outcomes should be measured in clinical trials in children

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Background

- Interventions are assessed in RCTs by measuring change in outcomes
- Selection of appropriate outcomes is crucial –

“Clinical trials are only as credible as their outcomes”¹

What should be measured in clinical trials involving children?

- Illness can affect children in a variety of ways, each of which could potentially be measured as an outcome
- Children are not small adults - it may be inappropriate to use outcomes measured in adults in children
- Some outcomes are unique to children (eg linear growth, developmental milestones)

Core outcomes

- Are a disease-specific minimum set of outcomes that should be measured and reported in all clinical trials
- Advantages of using core outcomes:

- Less heterogeneity between trials
- Easier to design/interpret trials
- Reduced selective reporting

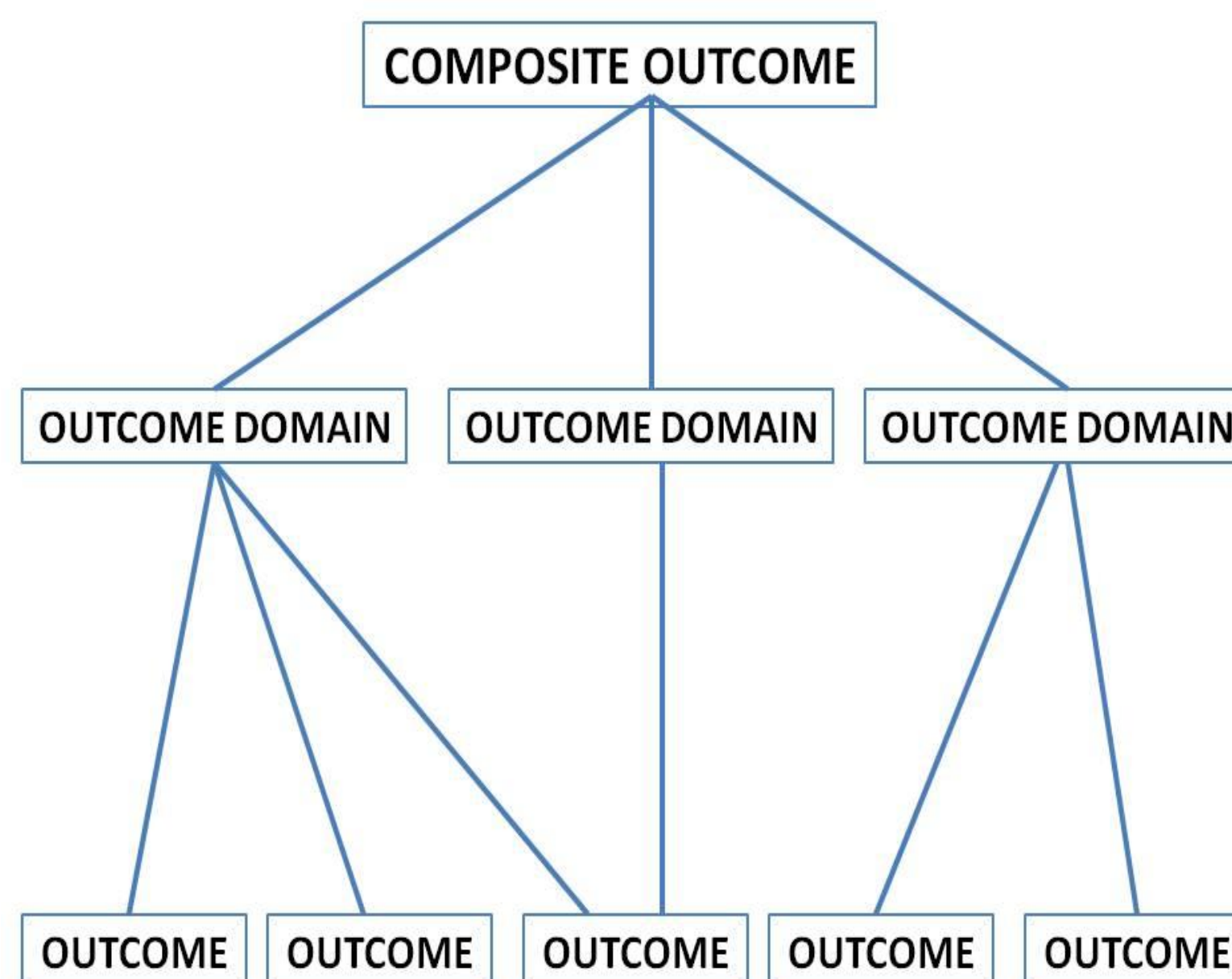
Definitions used in the review

Outcome domain: Broad aspect of the effect of illness on a child’s life

Outcome: Measurable variable within an outcome domain

Composite outcome: Outcome spanning more than one domain

Outcome measure: Tool or scoring system used to measure outcome



Aim

To systematically review studies that address the process of determining which outcomes should be measured in clinical trials in children

Methods

•Included studies:

Studies using methodology for selecting outcome domains or outcomes for use in clinical trials in children

•Identification of studies:

1) Databases : MEDLINE, SCOPUS, Cochrane

Search strategy: Clinical trial + methods + outcomes + children

2) Communication with paediatricians with interest in clinical trials

•Data extraction:

Methods used to determine appropriate outcomes

The outcomes which were selected

Quality of the description of the methods used

Results

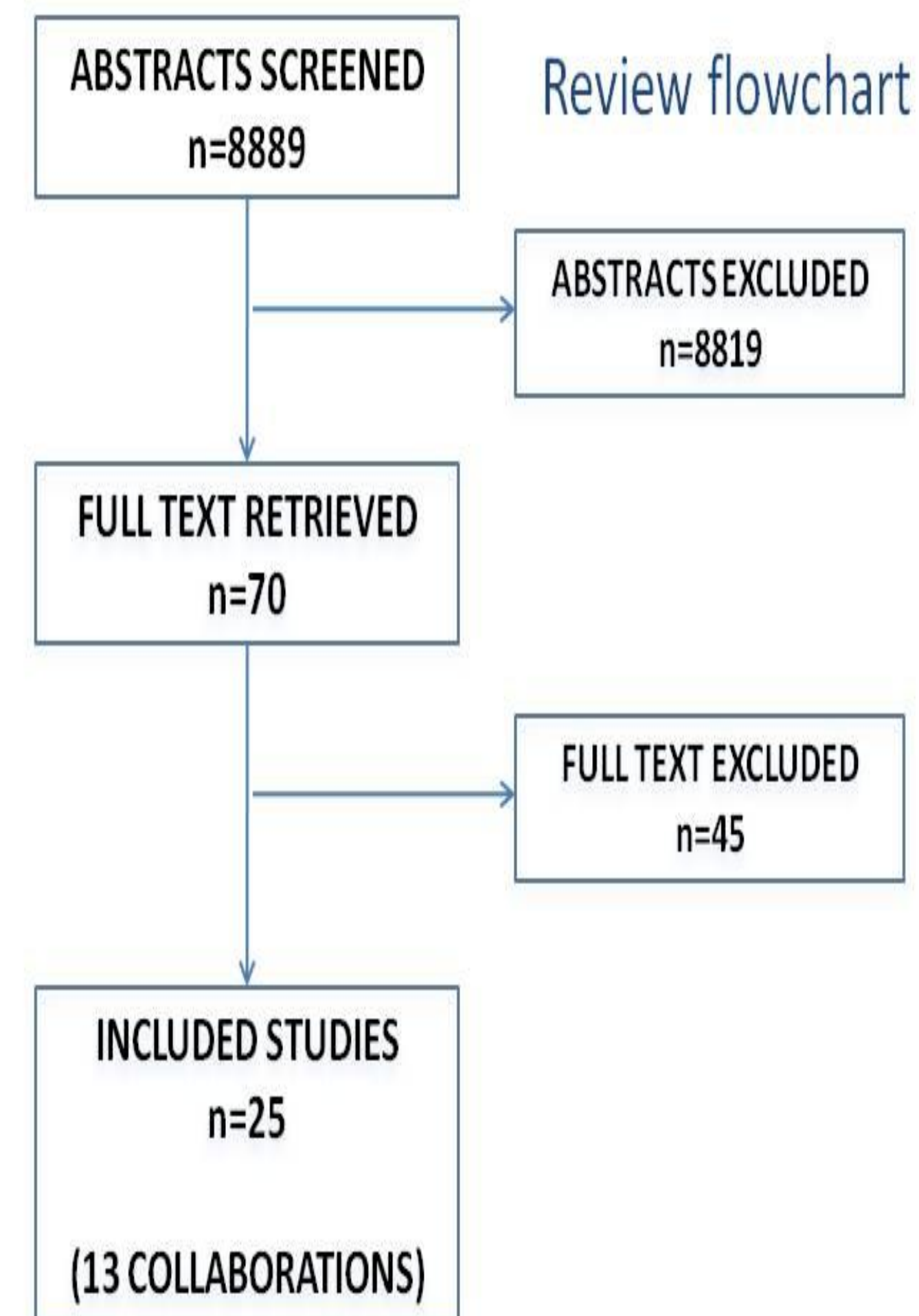
25 studies representing 13 collaborations

Methods used:

- 4/13 structured consensus (Delphi/NGT)
- 8/13 semi-structured discussion
- 1/13 questionnaire

People involved:

- Clinical and research experts
- Industry/drug regulatory representatives
- 3 groups involved parents
- No groups involved children



Specialities for which outcomes were selected

Speciality	Conditions
Critical care	Sepsis
Dentistry	Dental restoration
Gastroenterology	Crohn’s disease
Haematology	Graft Versus Host Disease
Neonatology	Apnoea, seizures, cardiac dysfunction,pain
Neurology	Infantile spasms
Psychiatry	Bipolar disorder Non-epileptic seizures
Respiratory	Asthma Cystic Fibrosis
Rheumatology	Idiopathic myopathy Juvenile arthritis SLE

Example core set : Idiopathic Inflammatory Myopathy²

Domain	Outcomes
Disease activity	Global assessment (parent) Global assessment (physician) Muscle strength Muscle enzymes (CK, LD etc)
Disease damage	Global damage assessment Other organ system assessment
Functional ability	Child Health Assessment Questionnaire
QoL	SF36



Conclusions

- Methodological work relating to outcome selection has been conducted for very few paediatric conditions
- The quality of this work is variable
- Patient/parent involvement has been minimal

Sinha I, Jones L, Smyth RL, Williamson PR (2008) A systematic review of studies that aim to determine which outcomes to measure in clinical trials in children. PLoS Med 5(4): e96

1 Tugwell P (1993) OMERACT conference on outcome measures in rheumatoid arthritis clinical trials: J Rheum 528–530.

2 Miller F et al (2001) Proposed preliminary core set measures for disease outcome assessment in adult and juvenile idiopathic inflammatory myopathies. Rheum 40: 1262–1273