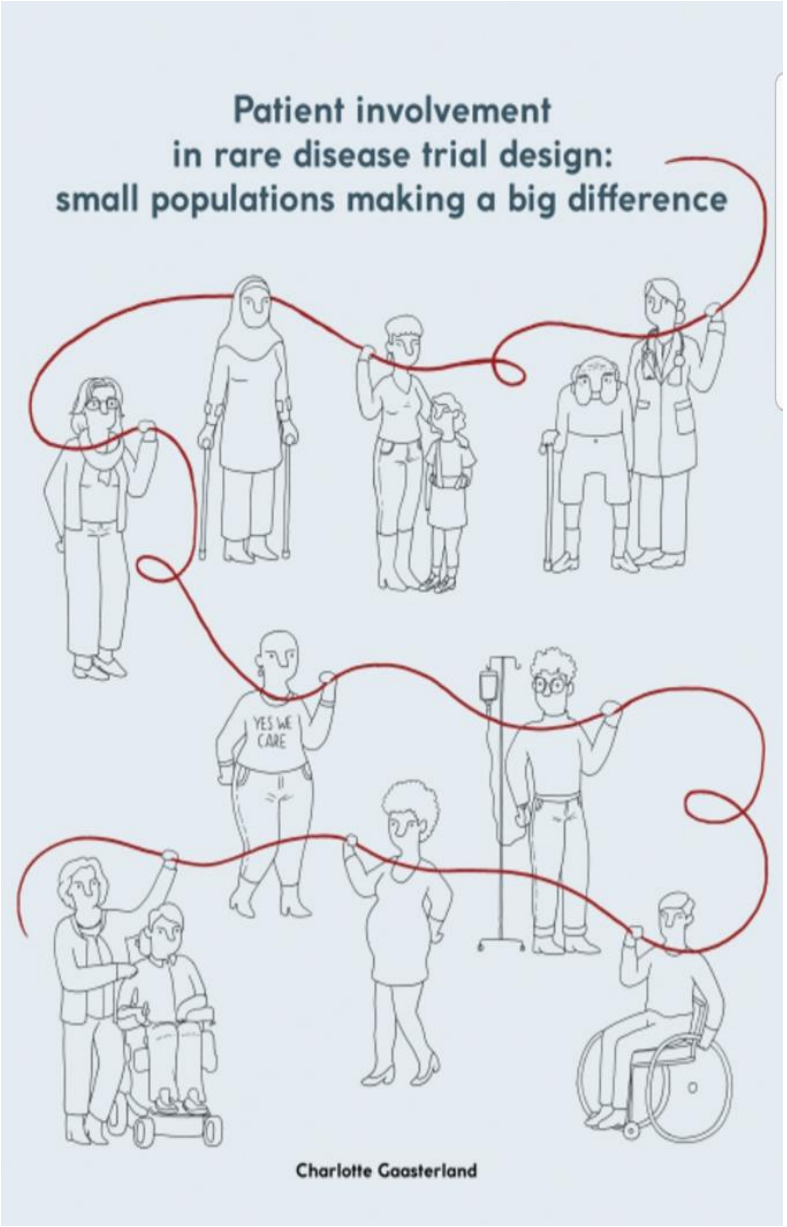
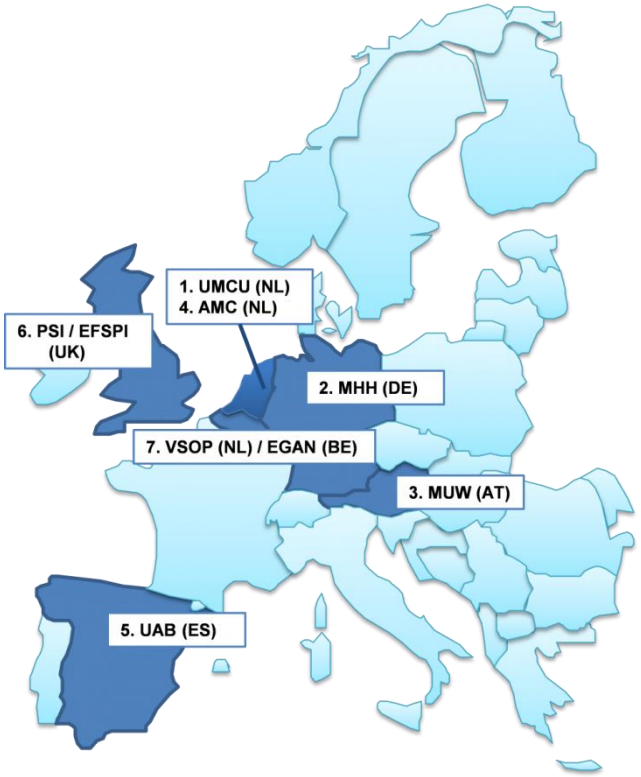


Goal Attainment Scaling: Validation & use for rare disease

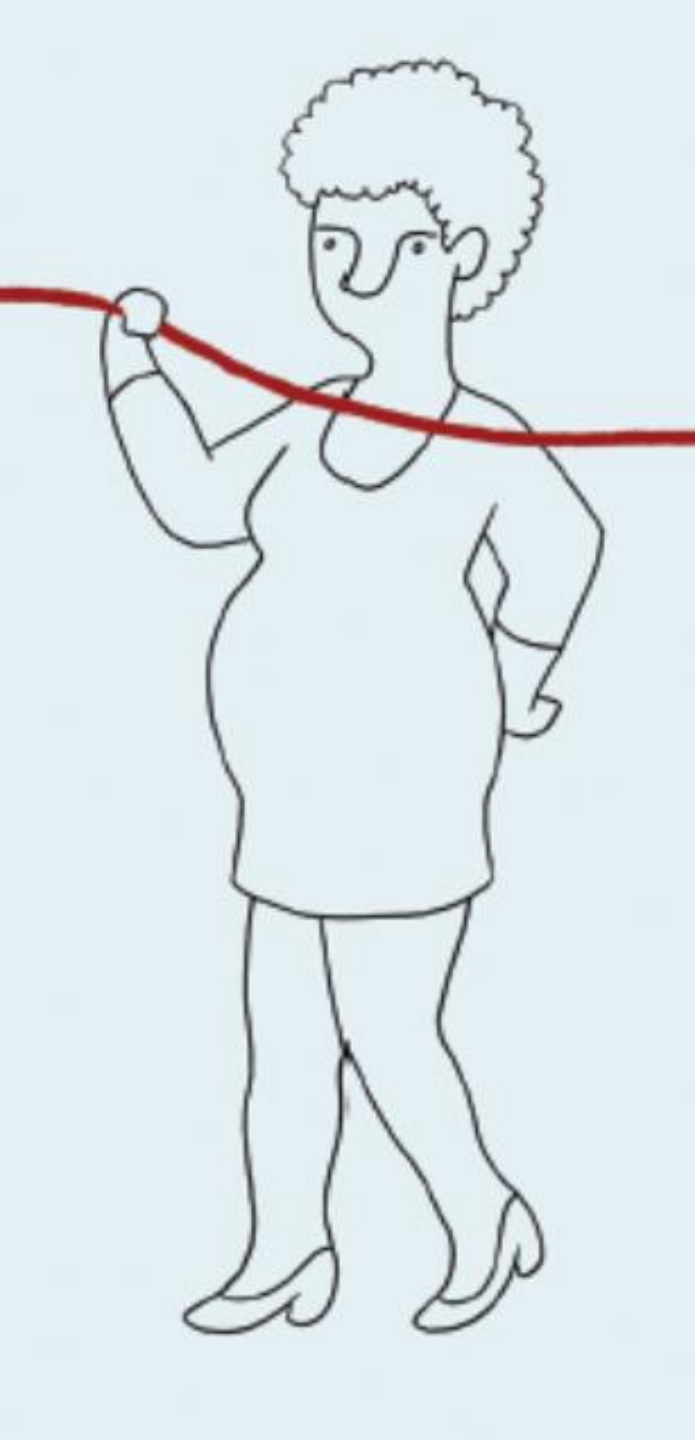
The Asterix project

Advances in Small Trials dEsign for Regulatory Innovation and eXcellence



Patient Think Tank

Ten patient representatives, from various disease groups



Goal Attainment Scaling

- **What is GAS?**
- When could GAS be used?
- Is GAS validated?
- How can GAS be further validated?

Imagine 3 boys with Duchenne disease:

‘I want to be able to walk’

‘I want to be able to eat independently’

‘I want to breathe independently’

Six minute walk test
Goal Attainment Scaling

-2 Adam is unable to walk

-1 Adam can take 3 steps

0 Adam is able to walk for 5 minutes

1 Adam can walk for 15 minutes

2 Adam can walk longer distances

-2 Chris is unable to breathe independently

-1 Chris can breathe for 10 minutes

0 Chris can breathe for one hour

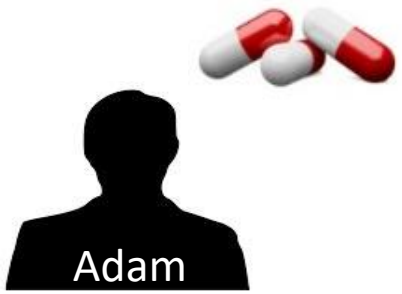
1 Chris can breathe for two hours

2 Chris can breathe for at least three hours

‘I want to be able to walk’
‘I want to be able to get dressed in the morning’
‘I want to be able to use my wheelchair without any help’
‘I want to be able to play with friends’

$$T = 50 + \frac{10\,\Sigma w_i x_i}{\sqrt{(1-\rho)\Sigma w_i^{\,2} + \rho(\Sigma w_i)^2}}$$

1. What are your goals, defined in 5 levels of attainment?
2. Which goals are most important to you?
3. *Intervention*
4. Have you attained your goals?



Goal Attainment Scaling

- What is GAS?
- **When could GAS be used?**
- Is GAS validated?
- How can GAS be further validated?

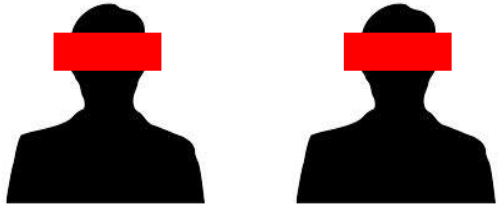
When can GAS be used?

Useful:

✓Chronic disease

✓Effect of intervention expected on behavioral ability, that can be assessed independently

✓Concurrent blinded controls



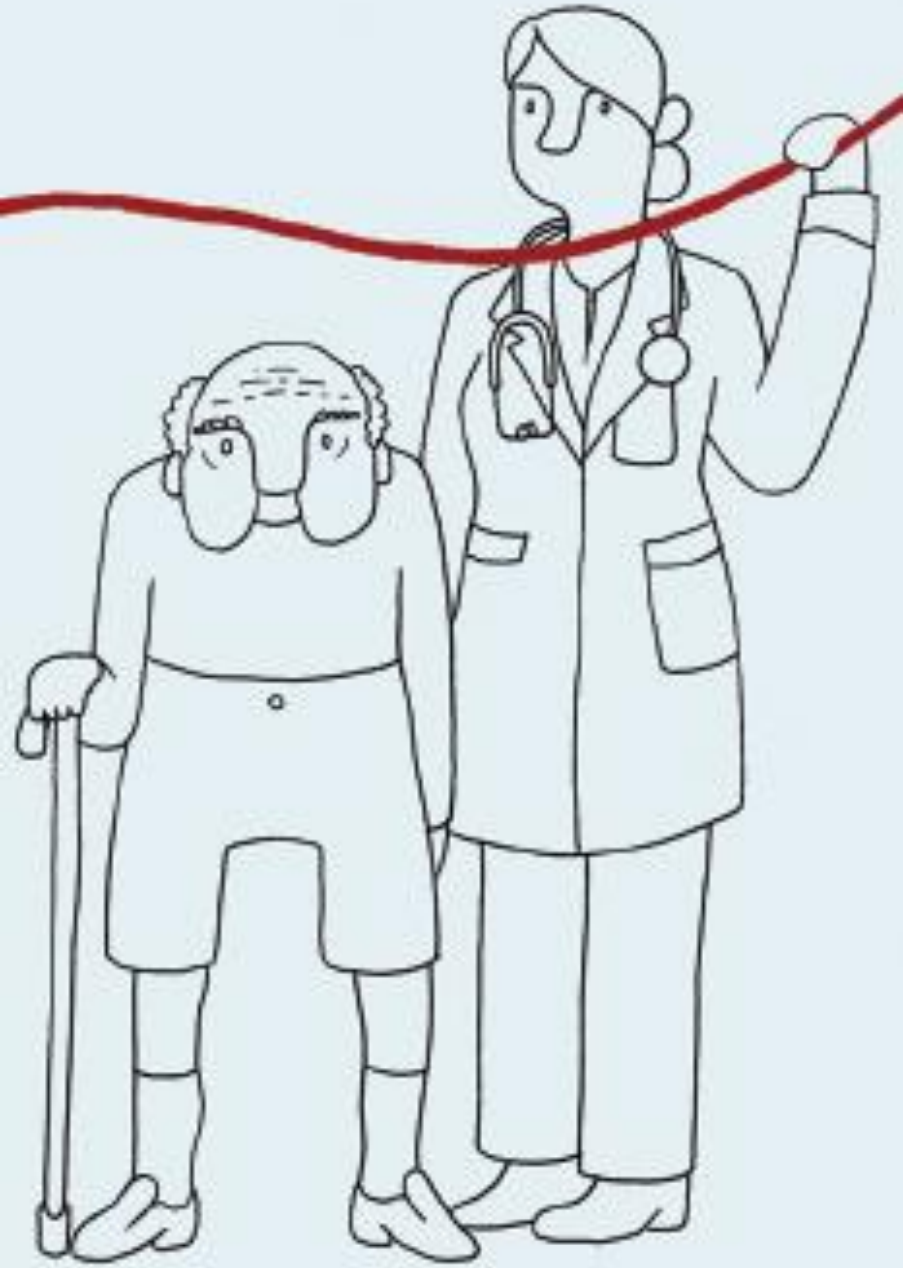
Not useful:

- Acute, episodic or unpredictable diseases

- Cross-over trials

Practical constraints

- Time
- Hawthorne effect
- Unknown or unpredictable disease course
- Lack of standardization
- Are the chosen goals realistic?



Goal Attainment Scaling

- What is GAS?
- When could GAS be used?
- **Is GAS validated?**
- How can GAS be further validated?

Systematic review

- Is GAS used in drug studies?
- Has GAS been validated in drug studies?
- Has GAS been validated in other studies?

Gaasterland *et al. BMC Medical Research Methodology* (2016) 16:99
DOI 10.1186/s12874-016-0205-4

BMC Medical Research Methodology

RESEARCH ARTICLE Open Access

A systematic review to investigate the measurement properties of goal attainment scaling, towards use in drug trials

Charlotte M. W. Gaasterland[1*], Marijke C. Jansen-van der Weide[1], Stephanie S. Weinreich[1,2] and Johanna H. van der Lee[1]

Abstract

Background: One of the main challenges for drug evaluation in rare diseases is the often heterogeneous course of these diseases. Traditional outcome measures may not be applicable for all patients, when they are in different stages of their disease. For instance, in Duchenne Muscular Dystrophy, the Six Minute Walk Test is often used to evaluate potential new treatments, whereas this outcome is irrelevant for patients who are already in a wheelchair. A measurement instrument such as Goal Attainment Scaling (GAS) can evaluate the effect of an intervention on an individual basis, and may be able to include patients even when they are in different stages of their disease. It allows patients to set individual goals, together with their treating professional. However, the validity of GAS as a measurement instrument in drug studies has never been systematically reviewed. Therefore, we have performed a systematic review to answer two questions: 1. Has GAS been used as a measurement instrument in drug studies? 2: What is known of the validity, responsiveness and inter- and intra-rater reliability of GAS, particularly in drug trials?

Methods: We set up a sensitive search that yielded 3818 abstracts. After careful screening, data-extraction was executed for 58 selected articles.

Results: Of the 58 selected articles, 38 articles described drug studies where GAS was used as an outcome measure, and 20 articles described measurement properties of GAS in other settings. The results show that validity, responsiveness and reliability of GAS in drug studies have hardly been investigated. The quality of the reporting of validity in studies in which GAS was used to evaluate a non-drug intervention also leaves much room for improvement.

Conclusions: We conclude that there is insufficient information to assess the validity of GAS, due to the poor quality of the validity studies. Therefore, we think that GAS needs further validation in drug studies, especially since GAS can be a potential solution when a small heterogeneous patient group is all there is to test a promising new drug.

Trial registration: The protocol has been registered in the PROSPERO international prospective register for systematic reviews, with registration number CRD42014010619. http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014010619.

Keywords: Rare diseases, Goal attainment scaling, Drug trials, Validation, Systematic review

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Full list of author information is available at the end of the article

Gaasterland et al., 2016

Results

Primary search: 5459 titles & abstracts

→ 1641 duplicates removed

3818 titles & abstracts assessed for eligibility

→ 3511 articles excluded based on title & abstract

307 full text articles assessed for eligibility

→ 249 articles excluded based on full text

58 articles included

Results

- Is GAS used in drug studies?

Yes, Cerebral Palsy (Botox) and Alzheimer Disease (Donezepil)

- Has GAS been validated in drug studies?

Hardly

- Has GAS been validated in other studies?

Yes, but often with low quality

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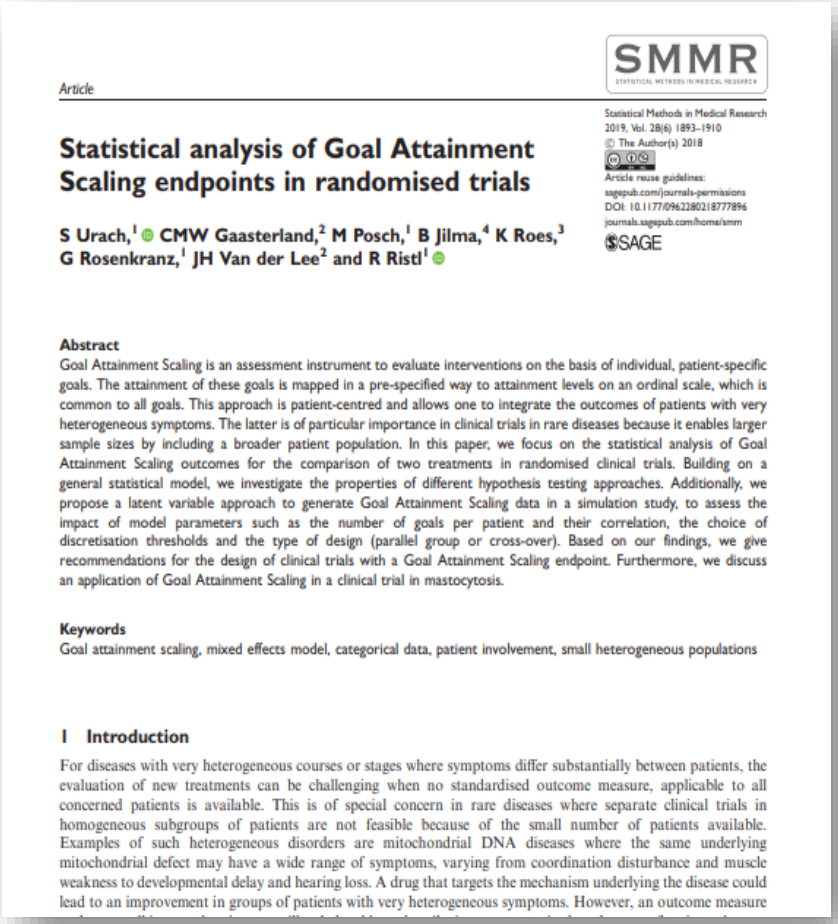
Gaasterland et al., 2016

How to use GAS: a simulation

- How should we use GAS?
- What model underlies its methodological properties?



Article

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2019, Vol. 28(6) 1893–1910

DOI: 10.1177/0962280218777896
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Statistical analysis of Goal Attainment Scaling endpoints in randomised trials

S Urach,[1] CMW Gaasterland,[2] M Posch,[1] B Jilma,[4] K Roes,[3] G Rosenkranz,[1] JH Van der Lee[2] and R Ristl[1]

Abstract

Goal Attainment Scaling is an assessment instrument to evaluate interventions on the basis of individual, patient-specific goals. The attainment of these goals is mapped in a pre-specified way to attainment levels on an ordinal scale, which is common to all goals. This approach is patient-centred and allows one to integrate the outcomes of patients with very heterogeneous symptoms. The latter is of particular importance in clinical trials in rare diseases because it enables larger sample sizes by including a broader patient population. In this paper, we focus on the statistical analysis of Goal Attainment Scaling outcomes for the comparison of two treatments in randomised clinical trials. Building on a general statistical model, we investigate the properties of different hypothesis testing approaches. Additionally, we propose a latent variable approach to generate Goal Attainment Scaling data in a simulation study, to assess the impact of model parameters such as the number of goals per patient and their correlation, the choice of discretisation thresholds and the type of design (parallel group or cross-over). Based on our findings, we give recommendations for the design of clinical trials with a Goal Attainment Scaling endpoint. Furthermore, we discuss an application of Goal Attainment Scaling in a clinical trial in mastocytosis.

Keywords

Goal attainment scaling, mixed effects model, categorical data, patient involvement, small heterogeneous populations

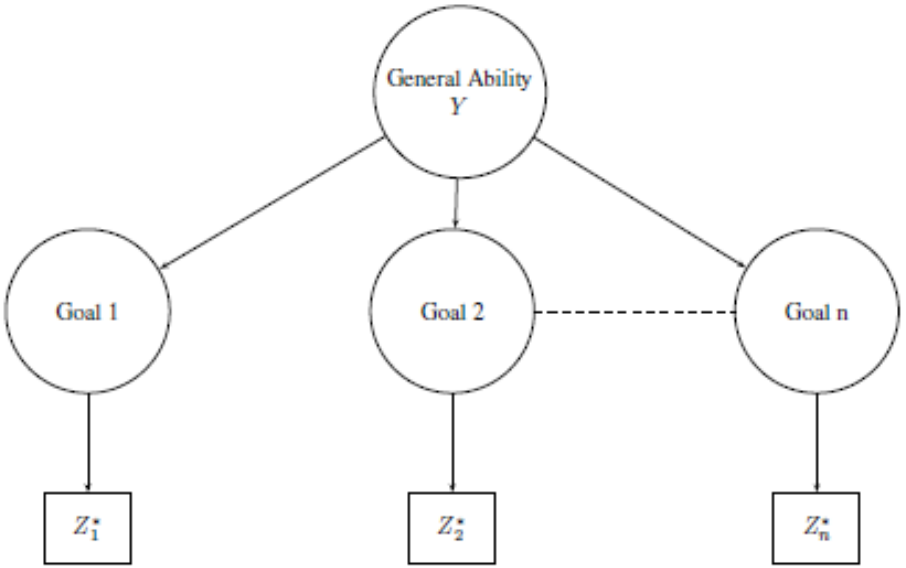
1 Introduction

For diseases with very heterogeneous courses or stages where symptoms differ substantially between patients, the evaluation of new treatments can be challenging when no standardised outcome measure, applicable to all concerned patients is available. This is of special concern in rare diseases where separate clinical trials in homogeneous subgroups of patients are not feasible because of the small number of patients available. Examples of such heterogeneous disorders are mitochondrial DNA diseases where the same underlying mitochondrial defect may have a wide range of symptoms, varying from coordination disturbance and muscle weakness to developmental delay and hearing loss. A drug that targets the mechanism underlying the disease could lead to an improvement in groups of patients with very heterogeneous symptoms. However, an outcome measure

Urach et al., 2019

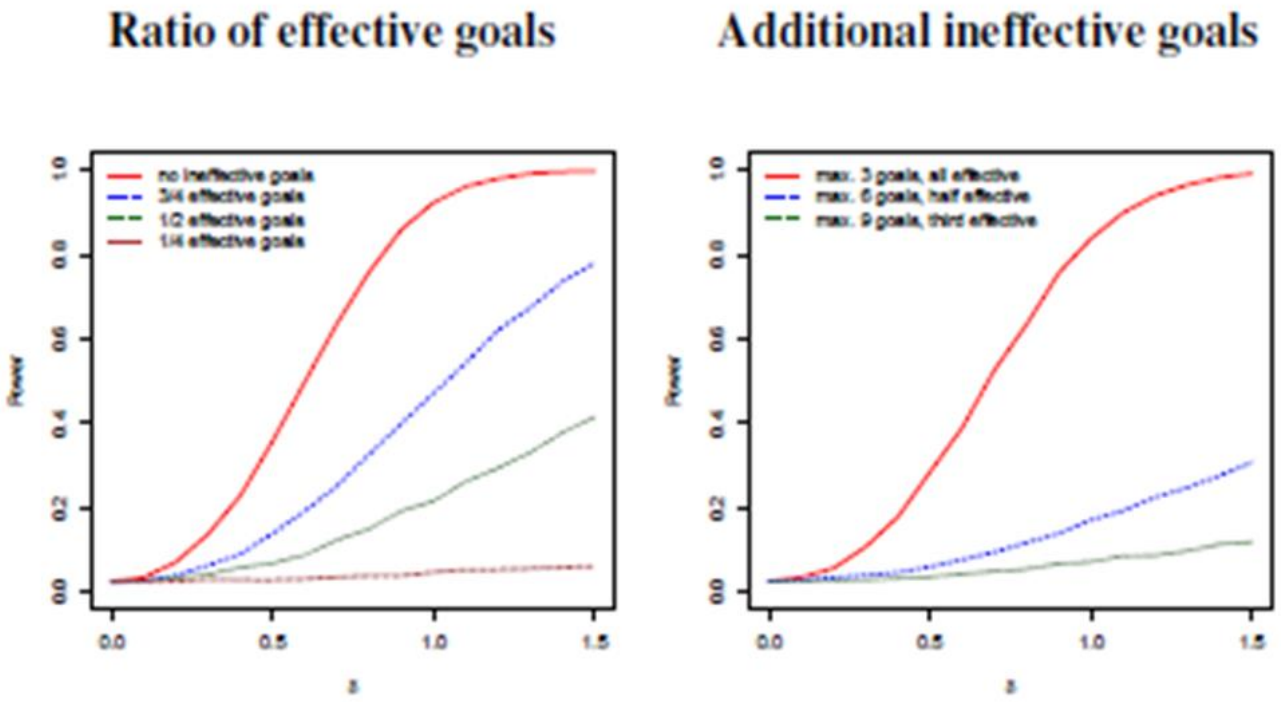
GAS simulation study

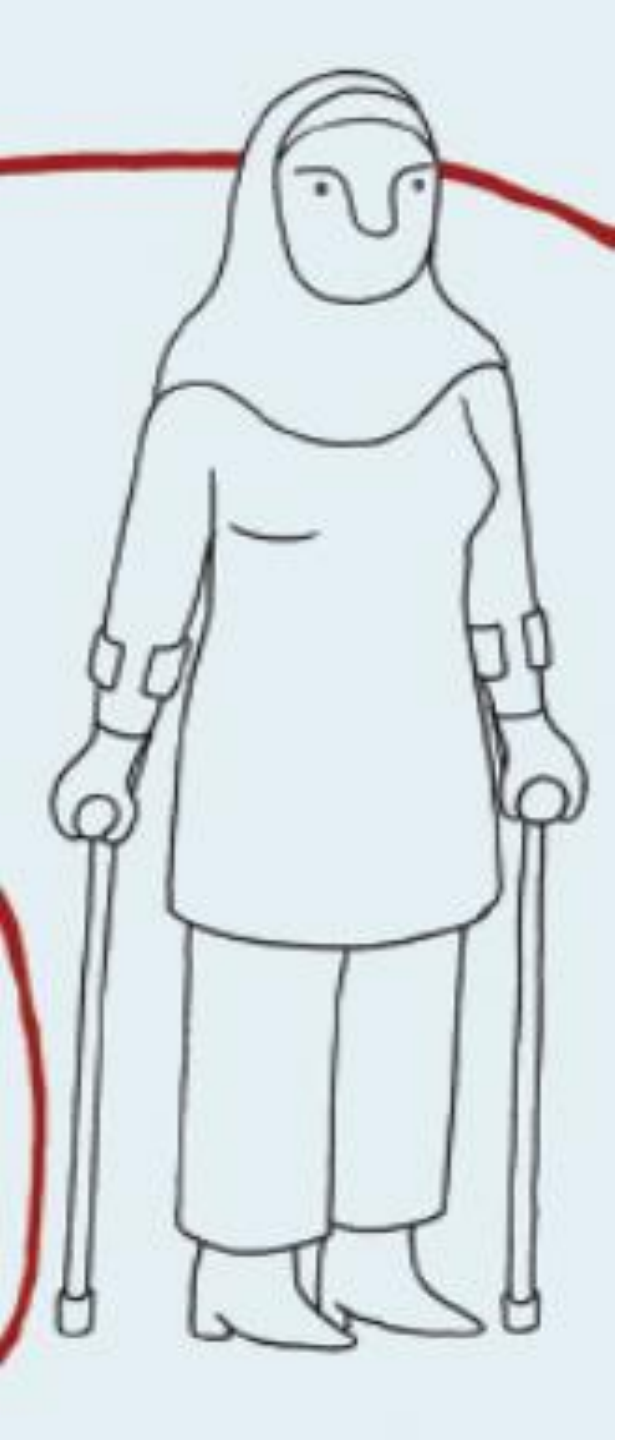
We modelled a latent variable model, where the 'General Ability' is the underlying disease..



..and there is a possible correlation between the goals

Adding extra goals is not always worthwhile





Goal Attainment Scaling

- What is GAS?
- When could GAS be used?
- Is GAS validated?
- **How can GAS be further validated?**

Underlying construct?

- Every goal is different
- Goals all correspond to different constructs and measurement instruments
- GAS is a change score

'I want to be able to walk'

'I want to be able to eat independently'

'I want to breathe independently'

Hypothetical trial: Mitochondrial disease

- Heterogeneous and rare population
- Underlying disease mechanism
- Effect of intervention expected on behavioural ability

Validation for use in in RCT

Content validity: assessed by therapist/physician

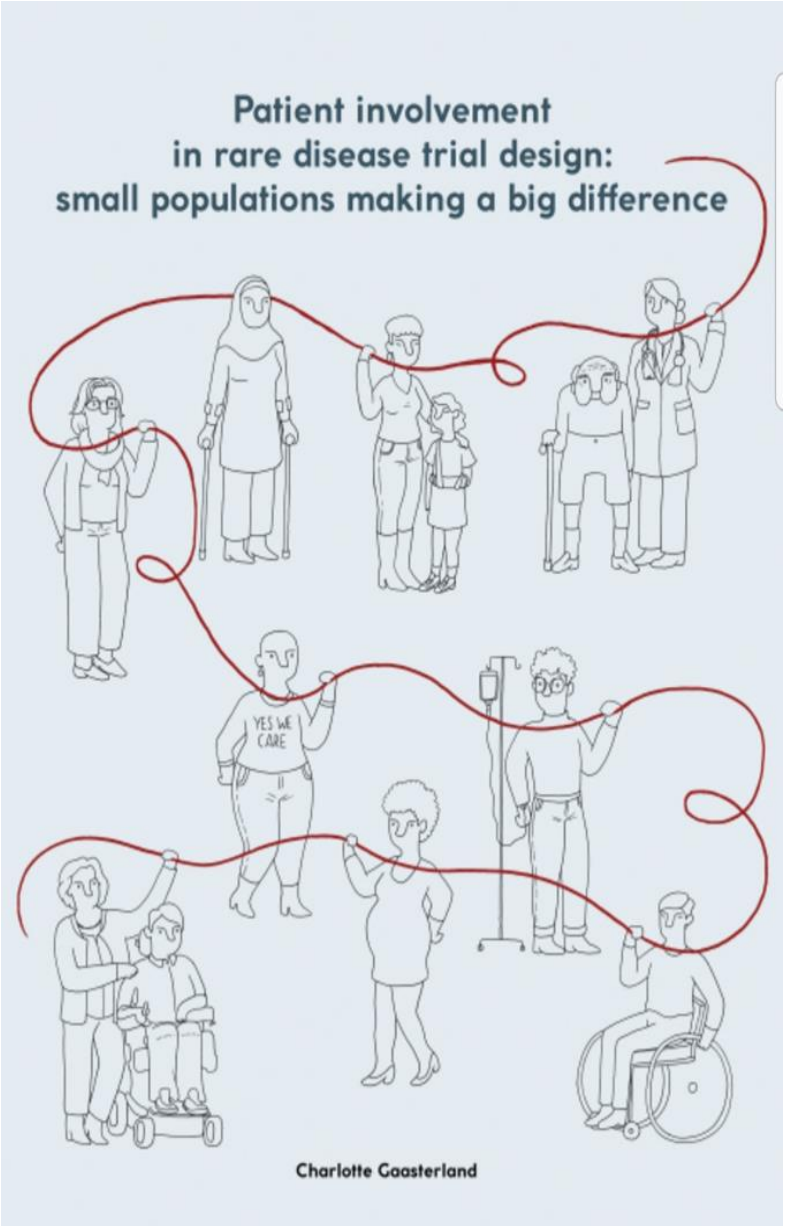
Construct validity: comparison with an instrument that measures a construct similar to constructs that are chosen as goals

Reliability: video-tapes of the goal choice

Validation on trial level

Construct validity: hypothesis testing between two groups with a different intervention (experimental vs control)

Inter-trial reliability: replication in similar trials



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