Goal Attainment Scaling, an individualized instrument with potential for outcome measurement in rare diseases

Hanneke van der Lee
AMC Emma Kinderziekenhuis
Amsterdam

RSNN
Regulatory Science Netwerk Nederland

asterix

amc
Academisch Medisch Centrum
Universiteit van Amsterdam

Rare diseases outcome measures

- Generic outcome measures usually not responsive
- Development and validation of disease-specific outcome measures in rare diseases problematic
- Heterogeneity among rare disease trial participants
- Looking for an individual outcome measure: Goal Attainment Scaling (GAS)

RSNN
Regulatory Science Netwerk Nederland

asterix

Goal Attainment Scaling: A General Method for Evaluating Comprehensive Community Mental Health Programs

Thomas J. Kiresuk, Ph.D.
Robert E. Sherman, M.S.

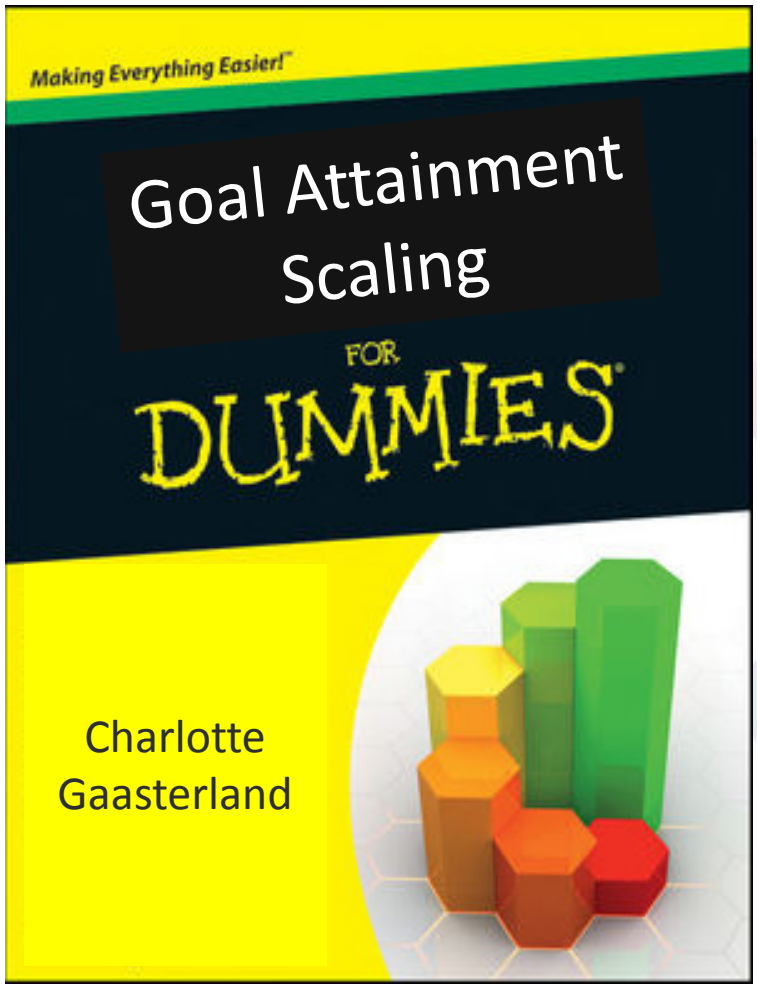
Community Mental Health Journal, Vol. 4 (6), 1968

443

RSNN
Regulatory Science Netwerk Nederland

asterix

GAS…?



RSNN
Regulatory Science Netwerk Nederland

Imagine 3 boys with Duchenne disease:

‘I want to walk’

‘I want to eat independently’

‘I want to breathe independently’

How do we measure improvement?

RSNN
Regulatory Science Netwerk Nederland

-2 Adam is unable to walk

-1 Adam can take 3 steps

0 Adam can 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

RSNN
Regulatory Science Netwerk Nederland

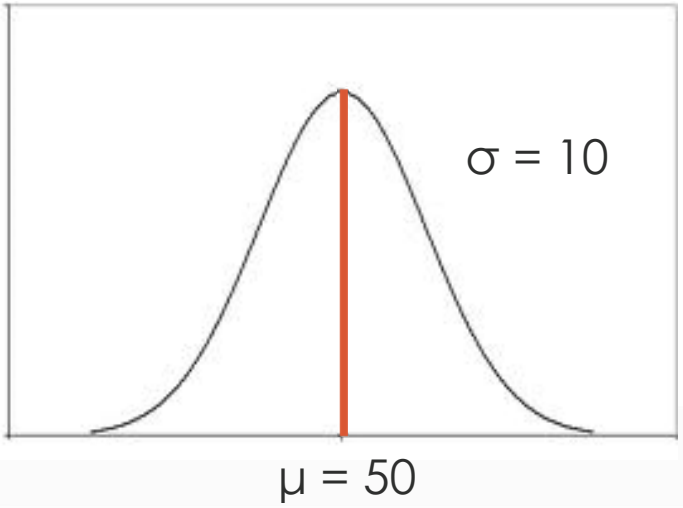
‘I want to be able to walk’
‘I want to be able to get dressed in the morning’
‘I want to be able to use my wheelchair without any help’
‘I want to be able to play with friends’

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

RSNN
Regulatory Science Netwerk Nederland

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

T	=	*GAS score*
x_i	=	*Original score*
w_i	=	*Weight given to the original score*
ρ	=	*Intercorrelation among goal scores (estimated at 0.3)*



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?

RSNN
Regulatory Science Netwerk Nederland

Methods

- Systematic review of the literature
  - Is GAS used in drug trials?
  - What are the measurement properties of GAS?
- Simulation study
  - How many goals?
  - Effect of weighing of goals

RSNN
Regulatory Science Netwerk Nederland

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

Results SR

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

RSNN
Regulatory Science Netwerk Nederland

Drug trials n=38

- Mostly investigated:
  - Botox and Baclofen in patients with Cerebral Palsy
  - Donepezil and Galantamine in Alzheimer Disease patients
- Measurement properties investigated in 7 drug studies

RSNN
Regulatory Science Netwerk Nederland

Data extraction

Face validity

Content validity

Construct validity

Intra-rater reliability

Inter-rater reliability

Responsiveness

RSNN
Regulatory Science Netwerk Nederland

Data extraction

Face validity

Content validity

Construct validity

~~Intra-rater reliability~~

Inter-rater reliability

Responsiveness

RSNN
Regulatory Science Netwerk Nederland

Face validity

In drug studies: 1

In GAS validity studies: 0

- *Therapists and intakers evaluated the relevance of the goal area for a patient on a 5-point scale.*
- *'Goal areas were suitably chosen'*

RSNN
Regulatory Science Netwerk Nederland

Content validity

In drug studies: 0

In validity studies: 3

- *Different methods were used*

- *'Goals were grouped in major categories, and reviewed by clinicians'*

RSNN
Regulatory Science Netwerk Nederland

Construct validity

In drug studies: 6

In validity studies: 11

- *Mainly correlations with other relevant measurement instruments*

RSNN
Regulatory Science Netwerk Nederland

Inter-rater reliability

In drug studies: 2

In validity studies: 10

- *Overall: Good inter-rater reliability (ICC > 0.9, κ >0.5)*

- *Only in one study the ICC calculation was reported*

RSNN
Regulatory Science Netwerk Nederland

Responsiveness

In drug studies: 3

In validity studies: 11

- *Responsiveness is usually good to very good: ES > 1*

RSNN
Regulatory Science Netwerk Nederland

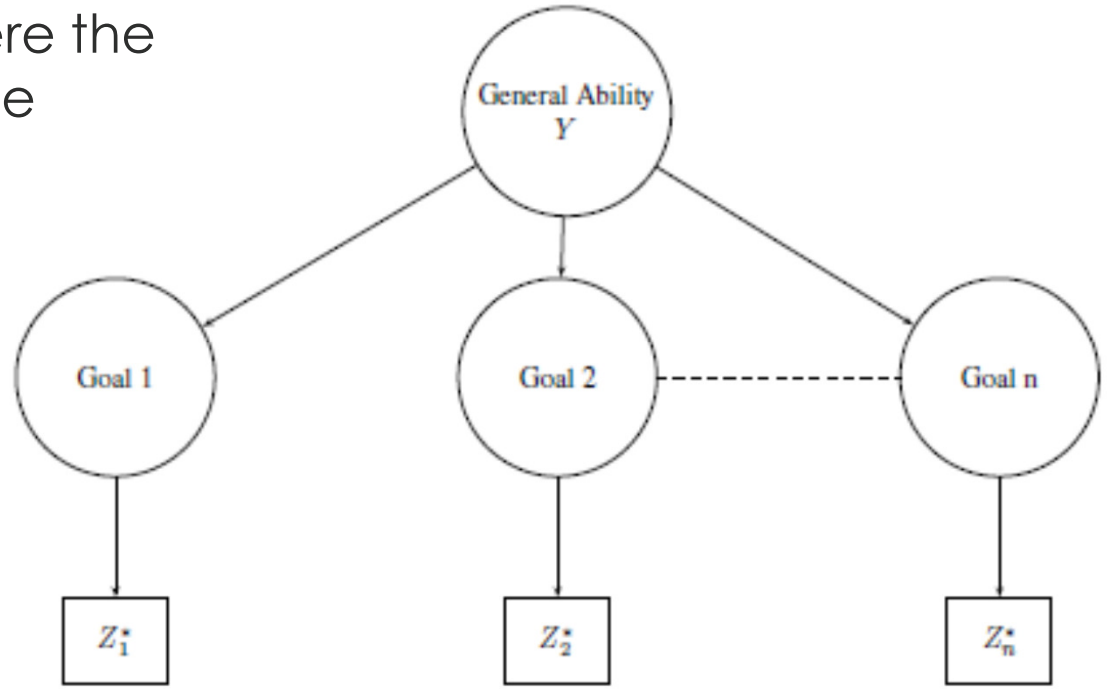
Conclusions SR

- Validation is mainly done in geriatrics/rehabilitation
- Usually in non-drug trials
- Insufficient information about validity

RSNN
Regulatory Science Netwerk Nederland

Simulation study: Latent variable model

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

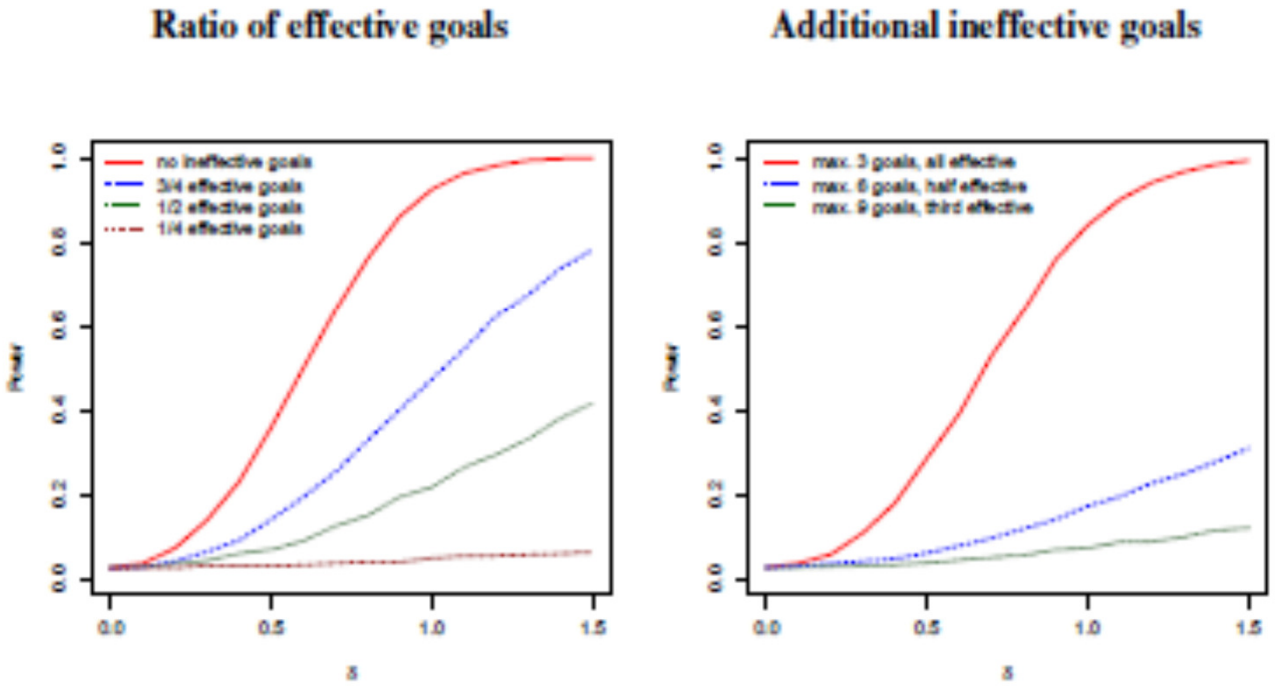


..and there is a possible correlation between the goals

RSNN
Regulatory Science Netwerk Nederland

Results: number of goals

More goals is not necessarily better. It is more important that the goals are chosen well, and are a good reflection of the underlying disease



RSNN
Regulatory Science Netwerk Nederland

More results: weighing of goals and which statistical test to use

- To increase power, weighing of goals can best be based on how well the goal reflects the underlying disease
- Weighing based on difficulty only decreases power
- We are still researching which test is the best test to evaluate the difference between two groups

RSNN
Regulatory Science Netwerk Nederland

Conclusions

GAS is a promising measurement instrument for heterogenous patient groups

Validation of GAS in drug trials needs more research

The theoretical assumptions are met in simulation studies

RSNN
Regulatory Science Netwerk Nederland

asterix

Next steps

- Apply GAS as an additional outcome measure in a phase III rare disease trial
- Investigation of measurement properties during the trial
- Submit to EMA for endorsement as a PRO in selected orphan drug trials

RSNN
Regulatory Science Netwerk Nederland

asterix

Thanks to …

- Charlotte Gaasterland
- Martine Jansen-van der Weide
- Stephanie Weinreich
- Susanne Urach
- Robin Ristl
- Martin Posch
- Kit Roes

RSNN
Regulatory Science Netwerk Nederland

asterix