Patient involvement in rare disease trial design: small populations making a big difference

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:

- *Adam*: ‘I want to be able to walk’
- *Brian*: ‘I want to be able to eat independently’
- *Chris*: ‘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
Adam

‘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’

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

Primary search: 5459 titles & abstracts

3818 titles & abstracts assessed for eligibility

307 full text articles assessed for eligibility

58 articles included

1641 duplicates removed

3511 articles excluded based on title & abstract

249 articles excluded based on full text
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

Gaasterland et al., 2016
How to use GAS: a simulation

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

Urach et al., 2019
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

Adam
‘I want to be able to walk’

Brian
‘I want to be able to eat independently’

Chris
‘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 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
Thank you for your attention & please take a copy