HOW SHOULD WE MEASURE QUALITY OF LIFE IMPACT IN RARE DISEASE? RECENT LEARNINGS IN SPINAL MUSCULAR ATROPHY

Biogen-01490. October 2018

Introduction of the symposium

Martina Garau

ISPOR Europe 2018. Sponsored symposium
11th November 2018

Office of Health Economics Research

Biogen

Challenges in measuring QoL in rare conditions (1)

- Measuring and collecting Quality of Life (QOL) is one of several major challenges when it comes to assessing treatments for rare diseases
- When a rare disease occurs in a pediatric population, there are further challenges including
  - the need to use proxy-reporting
  - hard to disentangle changes in QOL as a result of age-related, developmental changes and changes in QOL as a result of the condition and/or its treatment

Expert opinion

Challenges in measuring QoL in rare conditions (2)

- Conceptualising QOL in rare condition populations (when there is no alternative treatment)– how well do existing measures do?

- According to parents, very small (tiny) changes in function can be meaningful for them but these are unlikely to be reflected on QOL measures

Expert opinion

Structure of the symposium

Patient perspective
Huub van Rijswijck
Deputy board member
SMA Europe, PROMs

Moderator
Martina Garau

Payer perspective
Josie Godfrey
NICE Programmes

Academic researcher
Julio Lopez-Bastida
SMA BOI study in EU 4

Methods expert/ PRO researcher
Andrew Lloyd
Vignettes study

SMA: Spinal muscular atrophy
PROMs: Patient reported Outcomes Measures
BOI: Burden of illness
NICE: National Institute for Health and Care Excelence

ISPOR Europe 2018
Quality Of Life measurements in SMA
A caregivers perspective (n=1)

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11 november 2018

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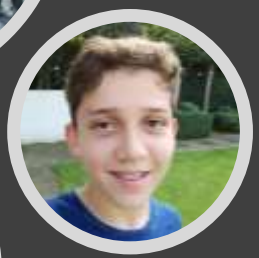
ISPOR: International Society of Pharmacoeconomics and Outcomes research
SMA: Spinal muscular atrophy



SMA Europe

Introduction

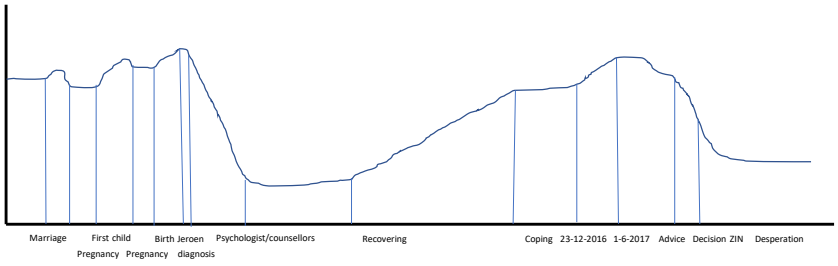
- Father of Jeroen 13 years old with SMA type 3a.
- ICT entrepreneur in the field of Digital Customer eXperience.
- Deputy board member of SMA Europe representing the Netherlands
- Organiser/manager of a yearly winter sport for disabled children and there families within a dutch organisation for disabled skiers (VGW).

ICT: Information and communication technology

Speaker experience

How are you doing ?

Qol-timeline caretakers Jeroen (me and my wife).

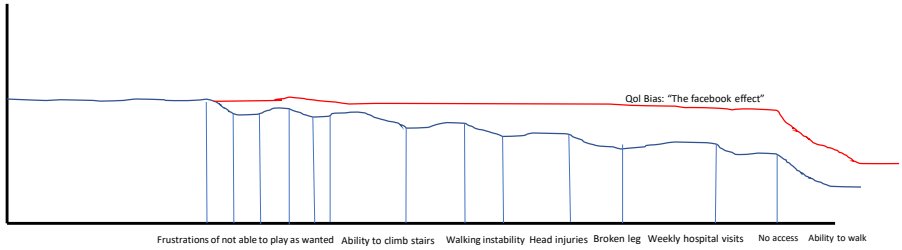


"Man suffers most from the suffering he fears" *Dutch proverb*

QoL: Quality of Life

Speaker experience

Qol timeline of Jeroen



Primary school
- Ambulant companion for specific classes
- Lunch support
- Adapted gymnastic
- Not being invited for parties
- First wheelchair

Secondary school
- Computer aided lessons
- Unreadable handwriting
- Learning problems
- No gymnastics
- Deprived for the first time for an external event
- More and more ill days with no specific reason
- Awareness about personal future

QoL: Quality of Life

Speaker experience

QoL: Quality of Life

Speaker experience

Personal opinion about Qol measurements

- Qol measures in progressive diseases should include the impact of the knowledge the natural future.
  - What does Qol with you today living the fact that within 2 years you will lose your ability to walk, within 4 years the ability to go independent to the toilet, within 6 years no able to turn yourself at night, and in twenty years not able to breath without respiration support.
- Qol measuring of children with a progressive disease should find a way to get rid of the "facebook" bias.
- Qol of children should include recognition of a valuable human being.
  - Being recognised as a valuable person that matters is the most deepest desire of humans.
  - Selective access of treatments to children caused by national HTA decisions touches the deepest fears of humans.
- Discussing about Qol measurement in progressive genetic rare diseases is a symptom of the limitations of evidence based science for rare progressive diseases.
  - Qol is not a subject for statisticians and accountants. It doesn't add up to a number.
  - From the working of Spinraza it can be reasoned that further deterioration of motor neurons is stopped. That should be enough.
  - Stopping the irreversible progressive of the disease burden should be the primary goal.
- Halting progressive diseases is a race against the clock, determining a great part of the Qol of SMA patients
  - The fast track privileges for orphan drugs is not effective if HTA's procedures slowing down or prevent access to treatments, frustrating/devastation Qol of thousands of patients and there caregivers.
- Giving false hope has a big impact on Qol of patients.
  - Broad labelling by FDA and EMA causes big impact on patients Qol when at the end there is no access to the treatment.

QoL: Quality of Life
SMA: Spinal muscular atrophy
HTA: Health technologies assessments
FDA: Food and drug administration
EMA: European medicine agency

Speaker experience

Questions for the experts.

QoL: Quality of Life
SMA: Spinal muscular atrophy
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Limitations of statistics and measurements in rare deseases/ orphan medicins.

- Thoughts about clinical trails duration issues in case of slowly progressive diseases.
- Qol for young children is only indirect and will therefore probably mainly focus on the gain of live expectancy.
- Phenotypes in SMA compete with each other.
- Natural history data as opposed to Natural future expected disease burden.
- Is life expectancy in years not overqualified in Qaly's that the improvements in Qol of patients with "normal" live time expectancy.

Thoughts about the "collateral damage" of the orphan drug legislation related to the Qol of patients.

- Pricing strategies of pharmaceuticals and the effect on Qol of patients.
- Labeling by EMA compared to the individual HTA reimbursement decisions and the impact on Qol of patients.
- HTA's becoming an unwanted purchase instrument for the national health ministries and the lobby by its insurance companies.
  - The effectiveness of a medicine is argued down on behalf of price negotiations and cost control preventing the majority of patients access to treatments.
  - The limitations of the outcome measurements and trail designs used as and argument: "not scientifically proven" so no access.

Speaker experience

Spinal Muscular Atrophy

Health-related Quality of Life in patients and Burden of informal care across Europe

Julio López-Bastida
University of Castilla-La Mancha

Biogen-01278, Octubre 2018

CONTEXT

- The "Social Economic Burden and Health-Related Quality of Life in Patients with Rare Diseases in Europe" (**BURQOL-RD**) project quantify the HRQOL of patients suffering from 10 rare diseases and their caregivers in 8 Countries in Europe. (1)
- SMA is the second most common severe hereditary disease of infancy and early childhood, with an incidence estimated of 1/5000 to 1/10000 births and a carrier frequency of 1/35 to 1/50. (2)
- SMA patients have significant medical expenditures due to the high utilization of health care services and social costs: average annual costs is estimated at € 33,722 in Spain (2).

1. López-Bastida J, Oliva Moreno J, Linertová R Serrano-Aguilar P. Social/economic costs and health-related quality of life in patients with rare diseases in Europe The European Journal of Health Economics 2016, 17, 1–5
2. López-Bastida et al. Social/economic costs and health-related quality of life in patients with spinal muscular atrophy (SMA) in Spain Orphanet Journal of Rare Diseases (2017) 12:141

RESEARCH QUESTIONS

- To define the HRQOL of SMA patients in four European countries (Germany, France, UK and Spain).
- To estimate the burden of informal care of SMA due to the high dependence of this disease

Experiencia del ponente.

DATA INFORMATION

- Observational study, enrolling caregivers through different patients associations of SMA across four European countries: France, Germany, Spain and the UK.
- Data were obtained from a questionnaire completed by the primary caregiver through a website specially developed for this study.

Experiencia del ponente.

DATA INFORMATION

The questionnaires included

- Socio-economic questions.
- The EQ-5D-3L proxy version questionnaire to measure Health-Related Quality Life of patients with SMA.
- Barthel Index to measure physical disability.
- Time of care provided on basic or instrumental activities of the daily living using the recall method.
- Zarit Caregiver Interview (subjective burden among caregivers).

Experiencia del ponente.

DATA INFORMATION

- Informal caregiver: any familiar, friend or another relative person who carried out the usual caregiving activities but he/she have not received some particular training/formation for caring.

- This person had to care in some of the Basic Activities of the Daily Living (BADL) and Instrumental Activities of the Daily Livings (IADL).

Experiencia del ponente.

Challenges in measuring quality of life in rare diseases

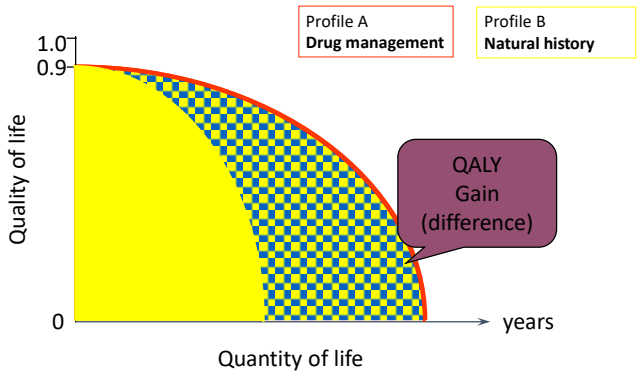
Andrew Lloyd

Health technology assessment

- Costs of new treatments
  - Drugs and administration costs
- Health benefit of new treatments
  - Improved length of life
  - Improved quality of life
  - Combined into Quality Adjusted Life Year – QALY
- In a fixed health care budget
  - If money is spent on a new treatment…..
    …..less must be spent on other treatments in other disease areas
- So these are very significant decisions

Expert opinion

Cost-effectiveness

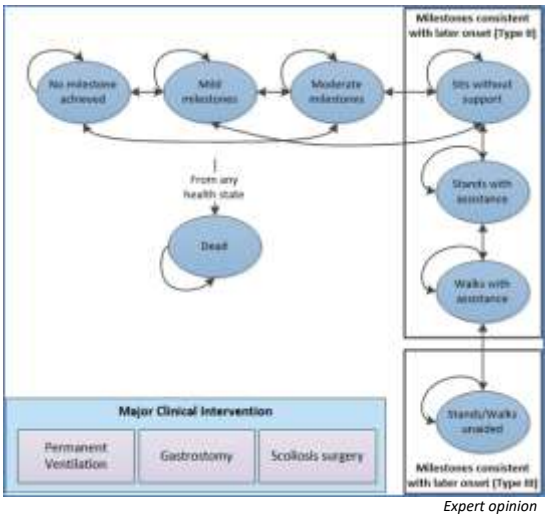


Expert opinion

Cost effectiveness estimated with models

- Example from Spinraza – but true for most disease areas
- Defined by discrete health states
  - Disease severity
  - Events
- Each health state has a QoL profile
- We need specific type of HRQL data for this purpose
  - Utilities – EQ-5D

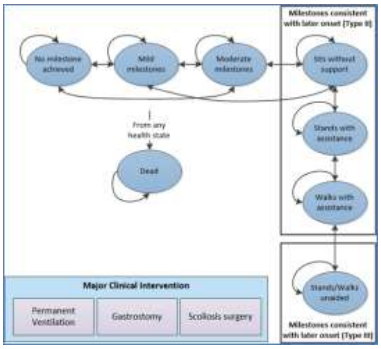
QoL: Quality of Life
HRQOL: health related quality of life
EQ-5D: Euroqol 5 dimensions



Expert opinion

Challenges

- Trials may capture some data on some states but not all
- Model requires representative 'quantitative' utility data for all states
- Many trials do not include utility measures
- Other sources of data challenging
  - No or very limited published literature
  - Observational studies – e.g. Lopez Bastida[1]

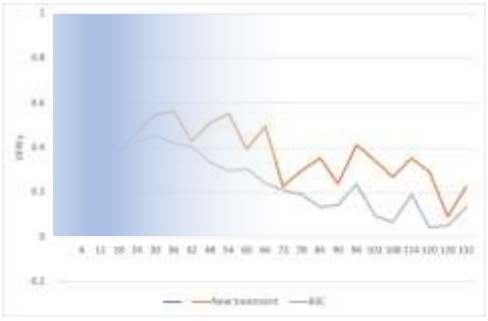


Lopez Bastida et al. Health-related Quality of Life in patients and Burden of informal care across Europe. ISPOR EU 2018.

Expert opinion

Other issues

- Measures not valid <6/7yrs
  - EQ-5D-Y
  - CHU-9D
- Must rely on proxy report
  - Work exploring validity
- PedsQL
  - Valid to 2ys
  - Mapping function has limitations
- Do we just assume HRQL for 8 year old fits all?

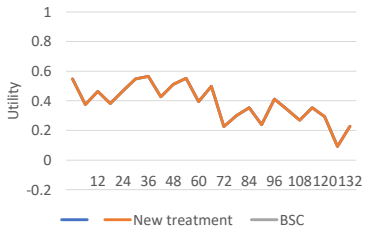


EQ-5D-Y: Euroqol 5 dimensions youth
CHU 9D: Children health utility 9D
PedsQL: pediatrics quality of life inventory
HRQL: Health related quality of life

Expert opinion

Trial designs for orphan drugs

- Trials often single arm
- Untreated profile poorly understood
  - Difficult to estimate net benefit



Expert opinion

Solutions

- Low prevalence makes recruitment extremely difficult
- Solutions
  - International research
  - Collaboration with advocacy groups & KOLs
  - Supported with technology
  - Planning
  - Multi company efforts
- Some data from patients or proxies should be captured
- Mapping studies from clinical endpoints

KOL: Key Opinion Leaders

Expert opinion

Solutions

- Simpler models
  - Models with less states will arguably need less data
- Encourage companies to capture more and better HRQL data
  - Early advice programs
  - Educational role for groups like ISPOR
- Establishment of routine data collection efforts
- Adoption of other methods
  - Vignette research – proxy ratings of health states
- Triangulation of methods

  Small survey ⇒ Mapping research with limitations ⇒ Vignette research

HRQL: Health related quality of life

Expert opinion