IP14: PATIENT-CENTERED DECISION MAKING

HOW DO YOU GENERATE RELEVANT PATIENT-REPORTED OUTCOMES EVIDENCE FOR CHRONIC DISEASE MANAGEMENT AND MARKET-ACCESS DECISION MAKING?

ISPOR 20th Annual European Congress, November 7, 2017

Presenters

- **Finn Børlum Kristensen, MD, PhD,** Professor, University of Southern Denmark, Odense, Denmark (Moderator)
- **Katharine Barnard, PhD CPsychol AFBPsS,** Visiting Professor, Bournemouth University, Poole, UK
- **Simon O'Neill, REG.N.,** Director of Health Intelligence and Professional Liaison, Diabetes UK, London, UK
- **Francois Meyer, PhD,** Advisor to the President, International Affairs, Haute Autorité de Santé (HAS), Saint-Denis, France

Katharine Barnard, PhD CPsychol AFBPsS
Visiting Professor, Bournemouth University, Poole, UK

Key Points

- Role of PROs and critical appraisal alongside safety and medical outcomes
- How best to inform decision-making and reimbursement
- Measurement and reporting of PROs – the challenges identified in the evidence base
- A uniformed approach by academia, FDA, NIH, Industry and Non-profit funders (Helmsley & JDRF)

BHR Limited
Health Psychology Research

Role of PROs in Patient-Centred Decision Making

Expectation by patients that devices are safe, efficacious and reliable

- PROs assess the IMPACT of device/therapy/intervention on lived experience
- PROs robust assessment of acceptability and implementation in everyday life
- PROs rarely effectively evaluated to sufficient rigour for critical appraisal by regulatory approvals bodies

BHR Limited
Health Psychology Research

The Problem

PROs crucial to policy decision-making, reimbursement and patient care

BUT

- They are often poorly reported secondary outcomes in clinical trials
- There is a wide range of PROs assessing different aspects of psychosocial functioning and quality of life
- Data is often poorly reported and of poor quality, making synthesis difficult

BHR Limited
Health Psychology Research

Example of the Evidence

Systematic literature search of diabetes device studies 2016

- Qualitative research – semi-structured interviews, focus groups)
- Quantitative research – questionnaires, pre / post studies, RCTs, controlled trials, observational studies

BHR Limited
Health Psychology Research

Types of Outcomes

Psychosocial aspects, from all study designs, including:

- Quality of life / Well-being / treatment satisfaction
- Diabetes distress / hypo fear / depression
- Psychosocial functioning / Change in psychosocial status
- Change in self-management activities eg SMBG, self-exam or increased clinic attendance

BHR Limited
Health Psychology Research

Results of Review

- 4554 records identified in initial search
- 723 eligible for full text asssessment
- 232 met inclusion criteria and were included in review
  - 137 studies (Artificial pancreas=9; CGM=32; CSII=96)
  - 74 commentaries
  - 16 health economic articles
  - 5 policy papers

BHR Limited
Health Psychology Research

Published Literature: Clinical Relevance

- **Insufficient data** to demonstrate direct **causal link** between **psychosocial outcomes and clinical outcomes** reported in the literature
- Improved QoL associated with CSII, however **inconsistent** A1c benefit
- **Mixed psych benefits / downsides** associated with CGM
- Improved psychosocial functioning associated with AP however prototype / **early technology fraught with difficulties** but rapid development of devices means this early data is meaningless in real life

BHR Limited
Health Psychology Research

Patient-Reported Facilitators for Device Use

- Reduced mental burden / Improved QoL due to less diabetes-related distress
- Improved glycemic control, fewer highs/lows, reduced variability associated with device
- Reduced risk of long-term complications
- Less user input – less chance for human error
- Accuracy / reliability (esp in hypo and hyper range)
- Latest generation devices more acceptable due to technology improvements and functionality
- Size – smaller and more discreet
- Perceived QoL benefits eg convenience, lifestyle flexibility

BHR Limited
Health Psychology Research

Patient-Reported Barriers to Device Use

- Unacceptable tasks: wearing multiple pumps/sensors/devices; too many tubes/wires; devices too large; too many tasks
- Site changes more frequently than every 3 days
- Painful insertions
- No health insurance
- Lack of accuracy and reliability
- Adolescents don't like wearing / using it / visibility of disease state
- Over-reliance on the device, potential to forget basic MDI skills

BHR Limited
Health Psychology Research

Views, Attitudes and Experiences of Patient, HCP and Payers

- Patients: tech will improve A1c &QoL, reduce diabetes burden and reduce risk of long-term complications but burden of tech includes alarms, lack of reliability, increased visibility of disease state and cost **EXPERIENCE**
- HCPs: believe new technologies optimize diabetes control in people with T1D however insufficient time to effectively implement and manage them **MEDICAL OUTCOMES**
- It is **not possible [currently]** to pre-judge those who will 'do best' on technology (REPOSE trial)
- Payers: no information on payers

BHR Limited
Health Psychology Research

Frameworks, Models or Theories Used to Explain Effect and Relevance

- **None identified in the review – rarely reported!**
- No direct causal links, in any literature on devices between mechanisms of psychosocial factors to clinical outcomes
- Fear of hypoglycaemia and treatment satisfaction were the only PRO measures that correlate with clinical outcomes

BHR Limited
Health Psychology Research

What PROs Add to Question of Relevance and Comparative Effectiveness?

NOT ENOUGH!

- Contribution is mixed. Positive and negative impact on psych functioning widely published for CGM and CSII, less so for AP due to novelty of technology
- It is widely acknowledged by regulatory approvals bodies such as FDA, NICE etc that PROs are crucial to critical appraisal of health technologies
- Inconsistent assessment: timing, measures, outcomes and links to clinical outcomes makes it impossible to effectively make sense out of them
- Consistent, evidence-based theory-driven psychosocial measurement is required (INSPIRE)

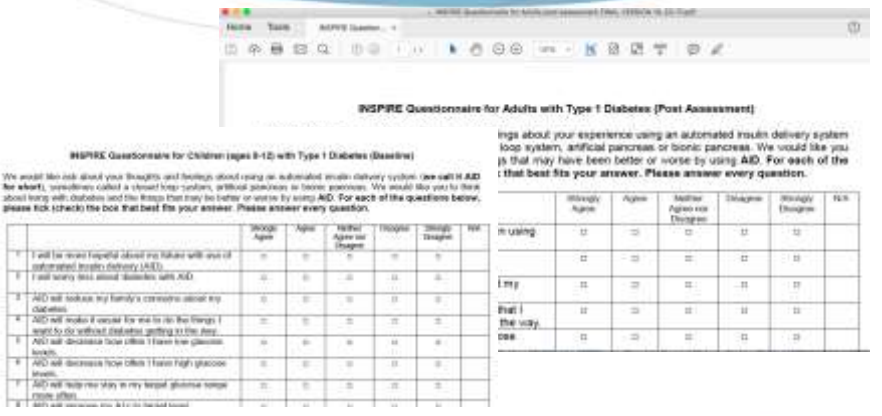
BHR Limited
Health Psychology Research

Harmonisation of PROs in Clinical Trials - INSPIRE

- INSPIRE patient preference measures used as basis for **harmonisation** across ALL clinical trials
- Matrix of psychological constructs with all validated and reliable measures mapped to each construct
- **All clinical triallists** are **using harmonised measures** to ensure **consistent, comprehensive and robust PRO assessment**
- Regulatory approvals bodies and payers **WILL** be able to **meaningfully critically appraise PROs** alongside safety and efficacy data

BHR Limited
Health Psychology Research

INSPIRE Examples


INSPIRE Questionnaire for Adults with Type 1 Diabetes (Post Assessment)

INSPIRE Questionnaire for Children (ages 9-12) with Type 1 Diabetes (Baseline)

BHR Limited
Health Psychology Research

Conclusions

- PRO benefits associated with diabetes devices but evidence is mixed for earlier and newer generations (making assessment difficult)
- PRO evidence is currently insufficiently robust to be considered equally with clinical outcomes
- No direct link to clinical outcomes a result of poor reporting (what is meaningful difference?). PRO often a 'bolt on' rather than integral to clinical outcomes assessment
- Standardised measures, assessed at standardised timepoints in clinical trials crucial for effective PRO assessment in HTA TARs eg INSPIRE

BHR Limited
Health Psychology Research

Thanks for Listening

For further information

contact:

katharinebarnard@bhrltd.com

Tel: 0044 (0)7590 532866

www: bhrltd.com

BHR Limited
Health Psychology Research

Simon O'Neill, REG.N.

Director of Health Intelligence and Professional Liaison,

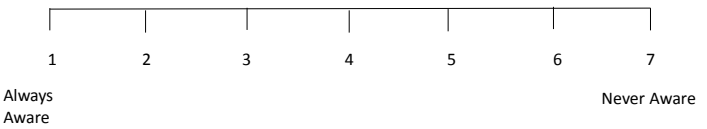
Diabetes UK, London, UK

"There is no bigger stakeholder. Involving the patient in the decision making process is essential, to both better the patient outcome and improve patient experience."

Kevin Pho

Gold Score for Hypos

"Do you know when your hypos are commencing?"



- I'm so scared of hypos, I won't leave the house
- I run my blood sugars high to avoid hypos at all costs – even though I know that puts me at risk of complications
- I'm frightened my son might die during the night – so I have to check his blood sugars at least twice
- I gave up sports because I couldn't bear the hypos

DIABETES UK
KNOW DIABETES. FIGHT DIABETES.

DIABETES UK
KNOW DIABETES. FIGHT DIABETES.

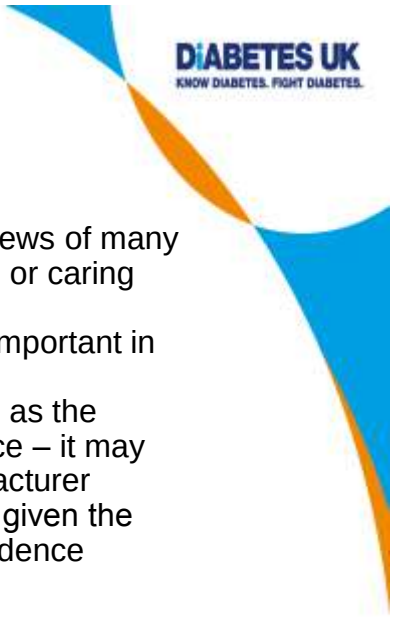
- Painful
- Inconvenient
- Messy
- Worried about testing in public
- Extra information makes me feel more in control
- I can test my child while he's asleep
- I feel much safer wearing this
- This device has given me my life back

DIABETES UK
KNOW DIABETES. FIGHT DIABETES.

Getting patient's views

- Tokenistic
- The voice of one person doesn't reflect the views of many
- Do we ask the right questions?
- Do we weight patient experience as highly as clinical evidence?

DIABETES UK
KNOW DIABETES. FIGHT DIABETES.



Getting patient's views

- Ask patient groups to gather views of many people living with the condition or caring for them
- Ask people what they think is important in their care
- Ask people what they perceive as the benefits of a treatment or device – it may not be the same as the manufacturer
- Ensure that the user's voice is given the same weight as the clinical evidence

Francois Meyer, PhD

Advisor to the President, International Affairs,

Haute Autorité de Santé (HAS), Saint-Denis, France

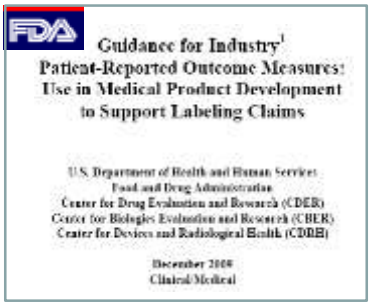
HAS
HAUTE AUTORITÉ DE SANTÉ

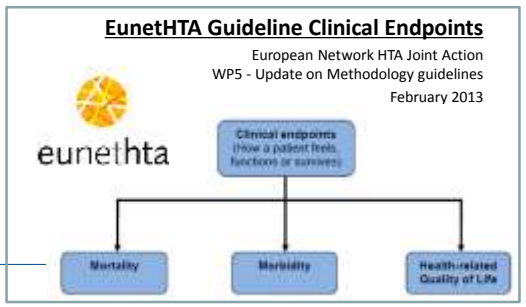
Patient Reported Outcomes: what impact on the evaluation of health technologies

François Meyer MD
ISPOR Europe 2017
Glasgow

Place of PRO in the assessment of new treatments

From neglected to recognised





Example: Chronic pulmonary infections due to Pseudomonas aeruginosa in cystic fibrosis (CF)

Colobreathe, colistimethate sodium : polymyxin antibiotic
Non-inferiority hypothesis vs Tobramycin (TOBI)

Clinical data

- Single pivotal trial **without** blinding (powder inhalation vs nebuliser solution)
- **Initial analysis** for non-inferiority was **negative**

QoL, PROs:

- QoL significant differences seen **only** at 4-wk
- Clear patient preference for Colobreathe : Patient ease of use/preference assessment 'very easy to use' 52% (Colobreathe) vs 10% (TOBI) p<0.001

Conclusions:

- Positive B/R ratio (EMA)
- Positive assessment from HAS: reimbursed, second-line use

HAS

European public assessment report (EPAR) - http://www.ema.europa.eu

EUROPEAN MEDICINES AGENCY

Psoriasis : EMA Note for Guidance
CPMP/EWP/2454/02 (Nov. 2003)

EUROPEAN MEDICINES AGENCY

4.1.2. Patient's assessed outcome measures

Efficacy of a new drug evaluated by patient is important when … even relatively limited extent of skin psoriasis may severely socially and psychologically disable the patient.

The assessment of HRQL scales specific for psoriasis may represent an added value for a new drug in comparative clinical trials, in addition to classical efficacy/safety measures. Patient-assessed drug efficacy may be a secondary or tertiary endpoint in pivotal clinical trial.

Quality of life and clinical severity of psoriasis often do not correlate and focus on different type of information.

HAS

Moderate to severe plaque psoriasis

DERMATOLOGY
New medicinal product
October 2016

- Ixekizumab : Marketing Authorisation in the treatment of moderate to severe plaque psoriasis in adults who require systemic therapy**.**

- Substantial improvement after treatment with ixekizumab was demonstrated compared with the placebo and etanercept in terms of reduction of the severity and extent of lesions (PASI scores 75 and PGA clear or almost clear: > 80% of responders versus < 8% with placebo and versus 35 to 50% with etanercept) and **improvement of symptoms (itching) and quality of life**.

HAS

HAS
HAUTE AUTORITÉ DE SANTÉ

HAS' request for post launch RWD collection

HAS
HAUTE AUTORITÉ DE SANTÉ

The Committee wishes data of a representative cohort of patients treated in France in order to specify:

- Exact profile of the population to be prescribed for treatment
- Evaluation of the benefit: follow-up of the cohort at least five years must make it possible to better understand the patient's experience and the interest of treatments in the "real life" on the following 4 elements:
  - Maintenance of the benefit after several cures and the occurrence of a rebound effect
  - Therapeutic strategy
  - Long-term toxicity (including carcinological, cardiovascular, cutaneous, and infectious)
  - **Quality of life perceived by the subject by means of multidimensional indicators (the consequences of treatment that could affect different areas of patients' quality of life than could not be reflected in a global or generic questionnaire).**

HAS

Development and validation of PRO questionnaires
Each step needs patients' input

Before

Now

1. Qualitative research : patients interviews to generate important and relevant concepts (10-50 patients depending of the complexity)

2. Psychometric validation study on a larger sample size (100-300)

3. Linguistic validation and **cultural adaptation**

Generic instruments for HRQL may fail to capture relevant concepts for patients

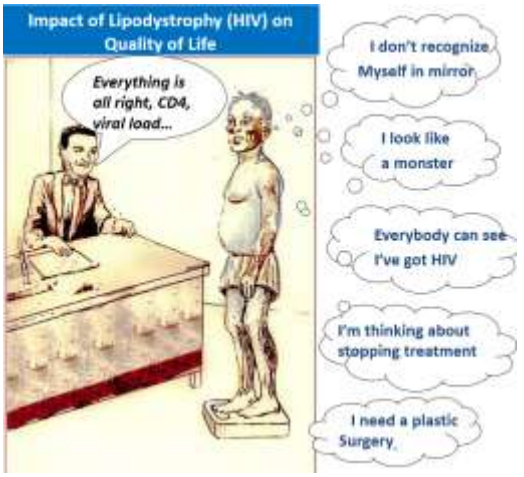
84 patients with lipodystrophy **(LD)**

HRQL measure : Spanish version of the Profil des Lebensqualität Chronichkranker (PLC)

- 40 items
- 6 dimensions : Physical Capacity, Psychological functioning, positive mood, social functioning, social well-being
- Self-administered, but **interviewer** supervised to ensure that the questions were correctly understood and answered

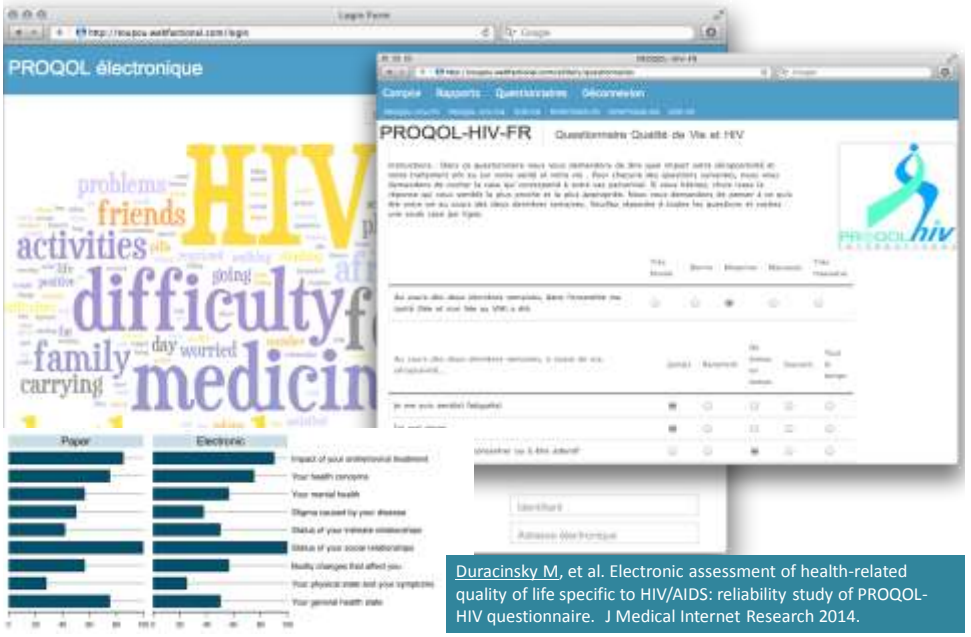
Conclusion : LD had no influence on overall quality of life !

Blanch J et al. Impact of lipodystrophy on the quality of life of HIV-1 infected patients. JAIDS 2002.



Duracinsky M, et al. The development of PROQOL-HIV: an international instrument to assess the HRQL of persons living with HIV/AIDS. J AIDS 2012;59:498-505.

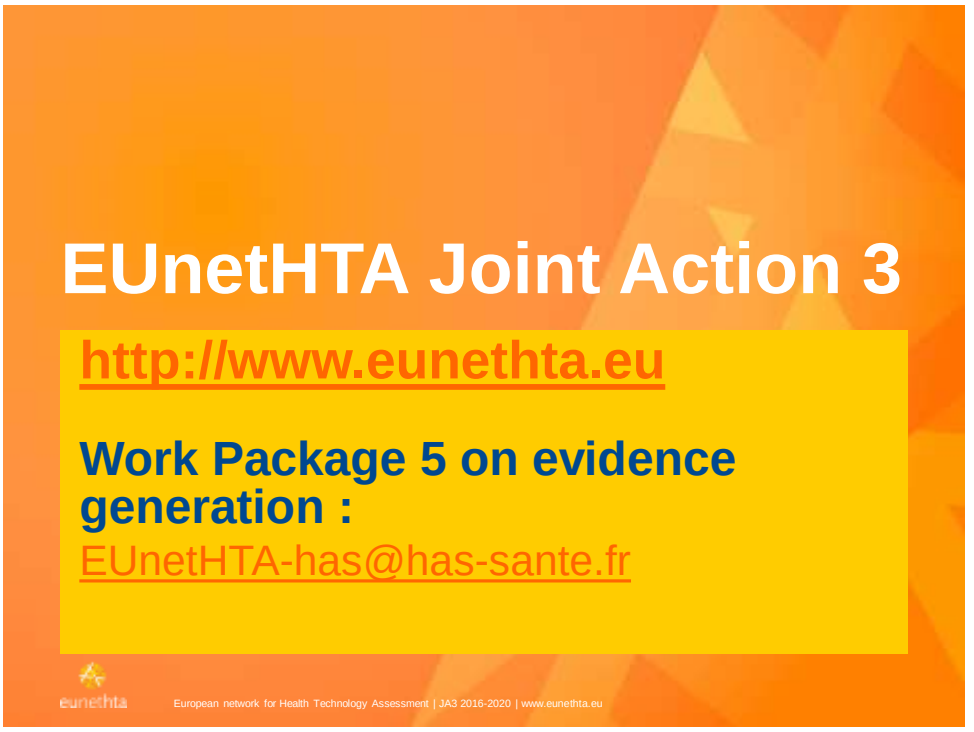
Electronic assessment (ePRO)



Duracinsky M, et al. Electronic assessment of health-related quality of life specific to HIV/AIDS: reliability study of PROQOL-HIV questionnaire. J Medical Internet Research 2014.

The way forward

- **New tools**
  - Development of e-reporting by patients
  - Self-reported websites databases
- **Dialogues and interactions**
  - Between sponsors of new technologies, regulators, patients
  - At an early stage to discuss initial studies
  - Later on Post Launch RWD collection
- **Debate?**
  - Generic vs disease specific HRQL scales


EUnetHTA Joint Action 3
http://www.eunethta.eu
Work Package 5 on evidence generation :
EUnetHTA-has@has-sante.fr
eunethta
European network for Health Technology Assessment | JA3 2016-2020 | www.eunethta.eu

Discussion