Patient Reported Outcomes and Clinical Research Databases

Nathalie Jetté MD, MSc, FRCPC
Professor Neurology and Population Health Science & Policy
Vice Chair Neurology Clinical Research
Chief Division Health Outcomes and Knowledge Translation Research
Icahn School of Medicine at Mount Sinai

CLAE Meeting
September 22, 2019
Faculty/Presenter Disclosure

• **Faculty:** Nathalie Jette

• **Relationships with financial sponsors:**
  – Grants/Research Support: NIH (NINDS) and PCORI
  – Speakers Bureau/Honoraria: n/a
  – Consulting Fees: n/a
  – Patents: Widget n/a
  – Other: n/a
Disclosure of Financial Support

• This program has not received financial or in-kind support

• Potential for conflict(s) of interest:
  – Not applicable
Mitigating Potential Bias

• n/a
Objectives

1. Understand the application and types of patient reported outcomes (PROs) used in clinical practice and for research

2. Learn about the tools and methods available to develop, identify, analyze and use PROs for clinical care and research, with a focus on depression in epilepsy

3. Be able to discuss approaches used to facilitate the implementation of PROs in clinical practice and for clinical research
Why Consider Patient Views?

1. Most healthcare aims to reduce symptoms, minimize disability, and improve quality of life (QoL) – which only patients can assess.

2. Patients welcome being involved.

3. Patients’ response rates are invariably better than clinicians’.

4. Avoids observer bias.

5. Increases public accountability of health services and healthcare professionals.

Black N, BMJ 2013
Patient reported outcome measures could help transform healthcare

Nick Black professor of health services research
Can Patient-Reported Outcomes Combat Physician Burnout?

Bridget M. Kuehn
October 05, 2017

Implementing routine use of patient-reported outcomes (PROs) at Partners HealthCare in Boston, Massachusetts, has boosted physician and patient satisfaction, according to a perspective article published today in the New England Journal of Medicine (NEJM).
As comfort with PROs has grown, feedback has increasingly underscored that clinicians find collecting PROs to be beneficial rather than burdensome. Evidence from experienced users suggests PRO collection may even enhance physician satisfaction and prevent burnout.

Making Patients and Doctors Happier — The Potential of Patient-Reported Outcomes

“PROs can enhance workflow efficiency and save time when they’re used regularly. One primary care physician noted that using electronic surveys that included a screening questionnaire, risk assessments and a review of systems enabled her to be a doctor again. Because patients had already answered screening questions electronically while in her clinic’s waiting room, she was no longer forced to wade through verbal checklists during visits. Instead, she examined and communicated, focusing on the issues that most required her attention. She saved about 10 minutes on each annual physical exam – and for the first time in years, her practice ran on schedule.
# Definitions

<table>
<thead>
<tr>
<th>Concept</th>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-Reported Outcome</td>
<td>PRO</td>
<td>The concept of any report of the status of a patient’s health condition that comes directly from the patient (or in some cases a caregiver or surrogate) without interpretation of the patient’s perspective by a clinician or anyone else. (i.e. Concept of depression)</td>
</tr>
<tr>
<td>PRO Measure</td>
<td>PROM</td>
<td>An instrument, scale or single-item measure used to assess the PRO concept as perceived by the patient, obtained by directly asking the patient (or in some cases a caregiver or surrogate) to self-report (i.e. Patient Health Questionnaire = PHQ-9)</td>
</tr>
<tr>
<td>PRO-Based Performance Measure</td>
<td>PRO-PM</td>
<td>A performance measure that is based on PROM data aggregated for a health care entity. (i.e. % of patients with depression and an initial PHQ-9 score &gt;9 who after 6 months of mental health management have a PHQ-9 score &lt;5 at follow-up)</td>
</tr>
</tbody>
</table>

Application of PRO Data

1. To inform routine clinical care
2. As part of clinical research
3. To support a label claim
4. To support reimbursement decisions

Box 1: Uses of PROMs

Health system
- Performance assessment
- Value for money

Healthcare provider organisation
- Benchmarking
- Quality improvement

Clinical trials
- Screening
- Treatment outcomes

Clinical practice
- Diagnosis
- Monitoring progress

Information for patients or clinicians
- Choice of provider
- Choice of treatment

Types of PROs

- **Generic**
  - Psychological General Well Being Index (PGWBI)
- **Disease specific**
  - Seizure severity questionnaire (SSQ)
- **Dimension specific**
  - Physical activity index (PAI)
- **Region/site specific**
  - Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR)
    Individualized
- **Utility measures**
  - Utility measure for major, unipolar depression (McSad)
- **Summary items**
  - General Household Survey

Patient Reported Outcome (PRO) assessment in epilepsy: a review of epilepsy-specific PROs according to the Food and Drug Administration (FDA) regulatory requirements

Annabel Nixon*, Cicely Kerr, Katie Breheny and Diane Wild

- None of the 26 PRO identified have the full evidence required by the FDA to support a label claim.

- All require further research to support their use as an endpoint.

- The Subjective Handicap of Epilepsy (SHE) and the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) → fewest gaps, although NDDI-E was designed as a screening tool and is therefore unlikely to be suitable as an instrument for capturing change in a clinical trial and the SHE lacks the conceptual focus on signs and symptoms favored by the FDA.
Important PRO for those living with epilepsy: Depression

“Having epilepsy does not mean you have to expect and cope with depression. You have as much right to help and support as anyone else.” Anonymous
Why Screen for Depression in Epilepsy?

- Depression is the most common psychiatric disorder in people with epilepsy with a lifetime prevalence ~30-35%.

- Impact of depression in epilepsy
  - Poorer response to AEDs and more side effects
  - Higher risk of premature mortality
  - Strong predictor of quality of life in epilepsy
  - Higher health resource utilization

Depression in Epilepsy

70% of those with epilepsy in Calgary study who had depression were not being treated for it.

This has been consistently reported in other studies.

50% of those with epilepsy who had depression in the Calgary study also endorsed suicidal ideation.

Impact on Clinical Care and Practice

“Because it is associated with the risk of suicide, depression must be considered a life-threatening disease.” – Gus A. Baker 2006

- Important for clinicians taking care of people with epilepsy to be able to identify and manage psychiatric diseases, especially mood disorders, and to be familiar with risk factors for suicide in epilepsy and screen for these.
How to Select the Right Depression Screening Tool (PRO)?

1. Relevant
2. Good psychometric properties
   – Reliable, valid, responsive
3. Inexpensive/availability
   – Copyrighted vs. in public domain
4. Ease of administration
5. Quick to complete
6. Easy to score/interpret
7. Available in multiple languages

Regardless of the PRO you use, it must be developed, implemented analyzed and reported rigorously & systematically...
A PRACTICAL GUIDE ON INCORPORATING AND EVALUATING PATIENT-REPORTED OUTCOMES IN CLINICAL TRIALS

Xuemei Luo
Joseph C. Cappelleri

Step 1  Formulating study objectives
Step 2  Developing or selecting an instrument
Step 3  Developing data collection strategies
Step 4  Analyzing data
Step 5  Reporting data
Step 6  Interpreting study findings
FIGURE 1  Key steps for evaluating patient-reported outcomes in clinical trials.

Luo and Cappelleri, Clin Res and Regulatory Affairs 2008
Checklist to operationalize measurement characteristics of patient-reported outcome measures

David O. Francis¹,²,³*, Melissa L. McPheeters³,⁴,⁵, Meaghan Noud¹, David F. Penson²,⁴,⁶,⁷ and Irene D. Feurer²,⁸

• Checklist to evaluate the properties and applicability of PROs
• 18 item checklist with six domains
  – See next page...
**CONCEPTUAL MODEL**

1. Has the PRO construct to be measured been specifically defined?  
2. Has the intended respondent population been described?  
3. Does the conceptual model address whether a single construct/scale or multiple subscales are expected?

**CONTENT VALIDITY**

4. Is there evidence that members of the intended respondent population were involved in the PRO measure's development?  
5. Is there evidence that content experts were involved in the PRO measure's development?  
6. Is there a description of the methodology by which items/questions were determined (e.g., focus groups, interviews)?

**RELIABILITY**

7. Is there evidence that the PRO measure's reliability was tested (e.g., test-retest, internal consistency)?)  
8. Are reported indices of reliability adequate (e.g., ideal: $r \geq 0.80$, adequate: $r \geq 0.70$, or otherwise justified)?

**CONSTRUCT VALIDITY**

9. Is there reported quantitative justification that single scale or multiple subscales exist in the PRO measure (e.g., factor analysis, item response theory)?  
10. Are there findings supporting expected associations with existing PRO measures or with other relevant data?  
11. Are there findings supporting expected differences in scores between relevant known groups?  
12. Is the PRO measure intended to measure change over time? If YES, is there evidence of both test-retest reliability AND responsiveness to change? Otherwise, award 1 point if there is an explicit statement that the PRO measure is NOT intended to measure change over time.

**SCORING & INTERPRETATION**

13. Is there documentation how to score the PRO measure (e.g., scoring method such as summing or an algorithm)?  
14. Has a plan for managing and/or interpreting missing responses been described (i.e., how to score incomplete surveys)?  
15. Is information provided about how to interpret the PRO measure scores (e.g., scaling/anchors (what high and low scores represent), normative data, and/or a definition of severity (mild → severe))?  

**RESPONDENT BURDEN & PRESENTATION**

16. Is the time to complete reported and reasonable? OR, if it is NOT reported, is the number of questions appropriate for the intended application?  
17. Is there a description of the literacy level of the PRO measure?  
18. Is the entire PRO measure available for public viewing (e.g., published with the citation, or information provided about how to access a copy)?

---

*Fig. 1* Checklist to operationalize developmental characteristics and applicability of patient-reported outcome measures
Other online databases of instruments:
1. Patient-Reported Outcome and Quality of Life Instruments Database (http://www.proqolid.org)
2. Quality of Life Instruments Database (http://www.OLGA-QoL.com)
Depression screening tools in persons with epilepsy: A systematic review of validated tools

*†Stephanie J. Gill, *†Sara Lukmanji, †‡Kirsten M. Fiest, †§Scott B. Patten, *††Samuel Wiebe, and *††Nathalie Jetté

*Epilepsia, **(*): 1–11, 2017
doi: 10.1111/epi.13651

SUMMARY

Objective: Depression affects approximately 25% of epilepsy patients. However, the optimal tool to screen for depression in epilepsy has not been definitively established. The purpose of this study was to systematically review the literature on the validity of depression-screening tools in epilepsy.

Methods: MEDLINE, EMBASE, and PsycINFO were searched until April 4, 2016 with no restriction on dates. Abstract, full-text review and data abstraction were conducted in duplicate. We included studies that evaluated the validity of depression-screening tools and reported measures of diagnostic accuracy (e.g., sensitivity, specificity, and negative and positive predictive values) in epilepsy. Study quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies Version 2. Medians and ranges for estimates of diagnostic accuracy were calculated when appropriate.

Results: A total of 16,070 abstracts were screened, and 38 articles met eligibility criteria. Sixteen screening tools were validated in 13 languages. The most commonly validated screening tool was the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) (n = 26). The Mini International Neuropsychiatric Interview (MINI) (n = 19) was the most common reference standard used. At the most common cutpoint of >15 (n = 12 studies), the NDDI-E had a median sensitivity of 80.5% (range 64.0–100.0) and specificity of 86.2 (range 81.0–95.6). Meta-analyses were not possible due to variability in cutpoints assessed, reference standards used, and lack of confidence intervals reported.

Significance: A number of studies validated depression screening tools; however, estimates of diagnostic accuracy were inconsistently reported. The validity of scales in practice may have been overestimated, as cutpoints were often selected post hoc based on the study sample. The NDDI-E, which performed well, was the most commonly validated screening tool, is free to the public, and is validated in multiple languages and is easy to administer, although selection of the best tool may vary depending on the setting and available resources.
Number of Validation Studies in Epilepsy per Depression Screening Tool

Depression Screening Tools

- **NDDI-E**: Neurological Disorders Depression Inventory for Epilepsy
- **BDI**: Beck’s Depression Inventory
- **HADS**: Hospital Anxiety and Depression Scale
- **PHQ**: Patient Health Questionnaire
- **ET**: Emotional Thermometer
- **HAM-D**: Hamilton Depression Rating Scale
- **CES-D**: Center for Epidemiologic Studies Depression Scale
- **Other Tools Include**: Mbewe et al. 10 Item Screening Tool, Young Adult Questionnaire for Psychiatric Disorders, Adult Self Report from the Achenbach System of Empirically-Based Assessment, Child Behavior Checklist, Parent Questionnaire for Psychiatric Disorders

Gill et al, *Epilepsia* 2017
Rapid detection of major depression in epilepsy: a multicentre study

Frank G Gilliam, John J Barry, Bruce P Hermann, Kimford J Meador, Victoria Vahle, Andres M Kanner

<table>
<thead>
<tr>
<th></th>
<th>Always or often</th>
<th>Sometimes</th>
<th>Rarely</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>Everything is a struggle</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Nothing I do is right</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Feel guilty</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>I’d be better off dead</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Frustrated</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Difficulty finding pleasure</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

For the statements in the table, patients are asked to circle the number that best describes them over the past 2 weeks including the day of the assessment.

Major depression in epilepsy if score >15
## Summary Statistics for Validation of the NDDI-E

<table>
<thead>
<tr>
<th>NDDI-E Cut point</th>
<th>Number of Validations</th>
<th>Sensitivity (Median (Range))</th>
<th>Specificity (Median (Range))</th>
<th>PPV (Median (Range))</th>
<th>NPV (Median (Range))</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;11</td>
<td>4</td>
<td>93.6 (84.6-100) n=4</td>
<td>66.0 (0-85.3) n=4</td>
<td>55.56 (44.8-61.1) n=3</td>
<td>95.3 (0-98.2) n=3</td>
</tr>
<tr>
<td>&gt;12</td>
<td>7</td>
<td>94.0 (84.0-100) n=7</td>
<td>58.8 (0-86.8) n=7</td>
<td>45.15 (28.8-65.22) n=6</td>
<td>96.3 (0-98.6) n=6</td>
</tr>
<tr>
<td>&gt;13</td>
<td>8</td>
<td>84.0 (65.4-93.3) n=8</td>
<td>84.17 (69.6-94.7) n=8</td>
<td>61.0 (38.5-77.3) n=8</td>
<td>95.1 (90.9-97.0) n=8</td>
</tr>
<tr>
<td>&gt;14</td>
<td>8</td>
<td>83.45 (77.5-93.33) n=8</td>
<td>83.53 (78.0-94.5) n=8</td>
<td>63.3 (43.2-77.78) n=7</td>
<td>94.0(89.9-97.0) n=7</td>
</tr>
<tr>
<td>&gt;15</td>
<td>14</td>
<td>80.5 (64.0-100) n=14</td>
<td>87.9 (81.7-95.6) n=14</td>
<td>59.95 (33.0-87.5) n=11</td>
<td>96.0 (88.1-100) n=11</td>
</tr>
<tr>
<td>&gt;16</td>
<td>4</td>
<td>68.0 (0-92.0) n= 4</td>
<td>89.9 (89.0-100) n=4</td>
<td>49.8 (0-68.7) n=4</td>
<td>93.87 (83.6-99.0) n=4</td>
</tr>
<tr>
<td>&gt;17</td>
<td>3</td>
<td>42.5 (0-60.0) n=3</td>
<td>95.1 (95.0-100) n=3</td>
<td>71.4 (0-73.3) n=3</td>
<td>90.0 (80.8-91.9) n=3</td>
</tr>
<tr>
<td>&gt;18</td>
<td>6</td>
<td>44.0 (35.0-58.0) n=6</td>
<td>97.0 (94.4-98.0) n=6</td>
<td>73.5(64.0-90.0) n=6</td>
<td>88.05 (78.9-97.0) n=6</td>
</tr>
</tbody>
</table>

Gill et al, *Epilepsia* 2017
NDDI-E

**Advantages**
- Free
- In public domain
- Fast
- Most validated tool in epilepsy
- Available in many languages
- Does not include symptoms that overlap with epilepsy cognitive symptoms or AED side effects
- Depression yes vs. no
- Can also identify major vs. minor depression and suicide risk

**Disadvantages**
- Not validated in non epilepsy population
- Others?

Discussion

• Most depression screening tools performed similarly regardless of whether they include symptoms that overlap with AED side effects/cognitive symptoms or not.
  – Sn and Sp most often ~0.8-0.9
  – NPV almost always >0.9
  – PPV usually ~0.4-0.7

• NDDI-E was the most commonly validated (26 studies) in epilepsy

• The best tool depends on the setting and available resources
  – The NDDI-E and the PHQ-9 are good choices to consider as they are fast, easy to interpret, free and in the public domain; the NDDI-E in particular has been validated in many languages.

Mitchell et al, J Affect Disord 2013; Fiest et al, Neurol Clinics (2016); Gill et al, Epilepsia 2017
Other Issues to Consider when Collecting PROs such as Depression
Data Collection Strategy

• How often will you measure the PROs?
  – Based on disease progression, treatment response, drug side effects, duration of trial and number of questionnaires
  – At a minimum, consider baseline and at end of study

• Mode of administration
  – In person (paper, tablet, computer, etc.)
  – Mail, telephone, etc.

• Eligibility criteria
  – Cognitive delay, language barrier, etc.

• Standardizing data collection

Luo and Cappelleri, Clin Res and Regulatory Affairs 2008
Missing PRO Data

• How to address this?
  1. Remove patients with missing forms
     • Not recommended
     • Can reduce sample size
     • May produce bias if missing data are not missing completely at random (MCAR)
  2. Impute missing data
     • Regression imputation, hot deck imputation, cold deck imputation (preferably with multiple imputation)
  3. Application of likelihood-based approach that mixed-effects models incorporate
  4. Other approaches...

Consider involving a biostatistician

Luo & Cappelleri, Clin Res and Regulatory Affairs 2008
117 sources met eligibility criteria

- Design and methodological strategies to minimize proportion of missing data included (but were not limited to):
  - Minimizing patient burden
  - Appointing a PRO coordinator
  - PRO specific training for staff
  - Ensuring PRO studies are adequately resourced

- This article provides great information on many strategies to minimize missing data
Reporting of Patient-Reported Outcomes in Randomized Trials

The CONSORT PRO Extension

Melanie Calvert, PhD
Jane Blazeby, MD
Douglas G. Altman, DSc
Dennis A. Revicki, PhD
David Moher, PhD
Michael D. Brundage, MD
for the CONSORT PRO Group

The CONSORT (Consolidated Standards of Reporting Trials) Statement aims to improve the reporting of randomized controlled trials (RCTs); however, it lacks guidance on the reporting of patient-reported outcomes (PROs), which are often inadequately reported in trials, thus limiting the value of these data. In this article, we describe the development of the CONSORT PRO extension based on the methodological framework for guideline development proposed by the Enhancing the Quality and Transparency of Health Research (EQUATOR) Network. Five CONSORT PRO checklist items are recom-
CONSORT-PRO Extension

• **Abstract**
  – Item 1b – The PRO should be *identified in the abstract as a primary or secondary outcome*

• **Introduction**
  – Item 2b – The *PROs hypothesis* should be stated and relevant domains identified, if applicable.

• **Methods**
  – Item 6a – Evidence of PRO *instrument validity and reliability* should be provided or cited if available including the *person completing the PRO* and *methods of data collection* (paper, telephone, electronic, other)
  – Item 12a – Statistical approaches for dealing with *missing data* are explicitly cited

• **Discussion**
  – Item 21 – PRO-specific *limitations and implications* for generalizability and clinical practice

Calvert et al, *JAMA* 2013
Framework and guidance for implementing patient-reported outcomes in clinical practice: evidence, challenges and opportunities

Box 3. Framework for the successful implementation of patient-reported outcomes in clinical practice.

- Clinical activity:
  - Screening
  - Diagnosis
  - Risk stratification and prognosis
  - Prioritization
  - Goal setting
  - Indication for treatment (medical/surgical)
  - Monitoring of:
  - General health status
  - Response to treatment/management
  - Facilitating communication:
    - Between patients and health professionals
    - Within teams and between professionals (along care pathways)
- PROM:
  - Simple (low burden of administration)
  - Valid
  - Reliable
  - Responsive
  - Interpretable (explicit link between PROMs outputs and clinical activity)
  - Tailored to the particular setting and clinical activity
- Setting:
  - Questionnaire-friendly environment
- Feedback system:
  - Integrated in clinical information systems
  - Structured, with explicit interpretation of the individual scores
  - Targeting both all relevant healthcare professionals and patients
  - Frequent and timely
- Support to the implementation:
  - Training of patients and health professionals on the interpretation of scores and outputs
  - Additional resources

In addition, the effectiveness of the implementation can be maximized by targeting specific groups most likely to benefit from this approach

- Patients:
  - Male
  - Those previously unknown to the clinician
  - Those with perceived borderline status of measurement in relation to the clinical activity
- Health professionals with low familiarity/degree of confidence in the clinical activity
Ethical and logistical considerations

- Increased concerns about risks to patients and potential legal liability when PRO information is not reviewed until later on in a study.

- No clear consensus on how to deal with “PRO alerts”

- Could lead to suboptimal care, or could lead to variations between sites in the management of symptoms that could affect study results

Kyte D et al, *JAMA* 2013
Patient-Reported Outcome Alerts
Ethical and Logistical Considerations in Clinical Trials

<table>
<thead>
<tr>
<th>Approach</th>
<th>Trial-Level Considerations</th>
<th>Participant-Level Considerations</th>
</tr>
</thead>
</table>
| Research personnel blinded to PRO data | Simple to implement; low cost
Hinders monitoring/prevention of missing data by research staff
No capacity to capture data on cointerventions | Ethically questionable; trial participants “in need” may receive suboptimal care |
| 2-Part disclaimer                | Low cost; no alert monitoring resources required
Allows monitoring/prevention of missing data by research nurses
Potentially lessens burden on research staff
Dissuades patients from tailoring questionnaire responses to influence care
No capacity to capture data on cointerventions | Requires participants to identify their own needs and respond accordingly if they require assistance
Participants may lack insight or frame of reference to determine if their problem warrants intervention |
| 24-Hour help line                | Allows monitoring/prevention of missing data by research nurses
Discharges researcher obligation to protect trial participants by ensuring availability of personalized advice
Ability to capture data on cointerventions (in-house help line only)
Help line staff require suitable training and support
Resource implications | Immediate response available
Requires participants to identify their own needs and respond accordingly
Participants may lack frame of reference to determine if their problem warrants intervention |
| Active PRO alert monitoring       | Allows monitoring/prevention of missing data by research personnel
Satisfies researcher obligation to protect trial participants
Ability to capture data on cointerventions
Requires predefined thresholds for alert generation
Requires prespecified tailored response list/action plan and timely entry of PRO data into trial systems
Research staff require suitable training and support
Resource implications | Does not depend on participants having insight into the extent of their problems |

Abbreviation: PRO, patient-reported outcome.
There was a shortage of the Level I critical antiepileptic drug (AED) clobazam (a.k.a. Onfi) in Calgary from May to October 2016.

Therefore, we aimed to study the impact of the clobazam shortage on patients with epilepsy from their perspective, while it was occurring.
Methods

• All adult CEP REDCap registry patients who were taking clobazam and agreed to be contacted for future studies were approached to participate in this study.

• Baseline data included clinical variables and pre-survey patient-reported outcomes (PROs) from the CEP REDCap registry.

• A mixed methods cross-sectional questionnaire was administered via telephone.

• We analyzed quantitative data using descriptive methods and qualitative data using a phenomenological approach.
Participant Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Participants (n=71)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>42 (59.2)</td>
</tr>
<tr>
<td><strong>Age in years</strong></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>18-78</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>39.7 (16.9)</td>
</tr>
<tr>
<td><strong>Highest Level of Education</strong></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>6 (8.5)</td>
</tr>
<tr>
<td>Grade School</td>
<td>3 (4.2)</td>
</tr>
<tr>
<td>High School</td>
<td>33 (46.5)</td>
</tr>
<tr>
<td>University/College</td>
<td>28 (39.4)</td>
</tr>
<tr>
<td><strong>Employed</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27 (38.0)</td>
</tr>
<tr>
<td><strong>Epilepsy Duration in years</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>24.1 (13.9)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>21 (13.0)</td>
</tr>
<tr>
<td><strong>Caregiver participants</strong></td>
<td>15 (21.1)</td>
</tr>
</tbody>
</table>

- 84% of eligible patients agreed to participate
- >70% had a medication change
- Quantitative PRO did not change pre and post shortage
Qualitative Results

Physical Impact of the Shortage

Seizure frequency change
(n=5, reference=6)

No seizure frequency change
(n=13, references=13)

Side effects
(n=11, references=15)

Psychological Impact of the Shortage

Fear and anxiety about the future
(n=42, references=93)

No fear or anxiety about the future
(n=15, references=18)

Frustration
(n=5, references=6)

“Two years ago there was a shortage of Frisium and I had to go on a generic one and I took that for 3 months until I had a seizure.”

“When I first found out about the shortage I panicked and I immediately worried that I was going to run out of my pills and thought far ahead - I have a problem with catastrophic thinking - I thought far ahead about if I run out of Frisium and if I have a seizure and worried about losing my license and house and then losing AISH. When it got to that point I thought about killing myself. The anxiety got that bad.”
Conclusions

• PROs such as depression *should* be considered as primary or secondary outcomes in epilepsy clinical database research, and should be collected as part of routine clinical care.

• PRO has to be:
  – Carefully selected (relevant domains)
  – Valid & reliable
  – Systematically implemented and analyzed
  – Minimize burden for patient
  – In clinical settings, should not impact flow of clinical care

• It is important to involve patients, health care providers and other key stakeholders if you are planning to implement PROs in clinical practice and for clinical research.

• There is not a one size fits all approach - the implementation of PROs for clinical care and research must be adapted to the local context.
Thank you to my students, research team members and funding agencies who have supported me over the years...

Key faculty research collaborators/mentors for some of the work presented today:
Samuel Wiebe MD, MSc
Colin Josephson MD MSc
Scott Patten MD PhD
Hude Quan MD PhD
Jose Tellez-Zenteno MD PhD
Thank you

nathalie.jette@mssm.edu