

Translation and Cultural Adaptation of Symptom Outcome Measures in International CNS Trials: The Current Reality

Should We Be Doing Things Differently?

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Conflict of Interest Statement

- Employee of Quintiles Inc.
- Board of Directors, Cypress Biosciences
- Consultant to multiple pharmaceutical companies

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Symptom Outcome Measures Used in CNS Trials

Variability In Quality

- Conformance (meeting the needs of the purpose)/Features
 - Organic modifications to utility over time
e.g. HAM-D not originally designed to assess outpatients in clinical trials
 - Homogeneity of construct (focuses on the constructs of a disease)
e.g. Connors rating scale in ADHD v. MMPI II

Symptom Outcome Measures Used in CNS Trials

- Performance
 - Sensitivity to change (variability with HAM-D items)
- Reliability
 - Internal consistency, test-retest, inter-rater, intra-rater
- Validity
 - Face validity
 - Content validity (culture & relativity)

Types of Symptom Outcome Measures in CNS Trials

- **Diagnostic measures**

- Link to diagnostic criteria
- Clinician reports
- Advanced medical terminology

- **Outcome measures**

- Clinician reports
- Advanced medical terminology

- Patient reports (PROs)
- 3rd party observer reports



Gr. 8 reading level or lower

- **Different approach to translation and adaptation may be needed**

Terminology

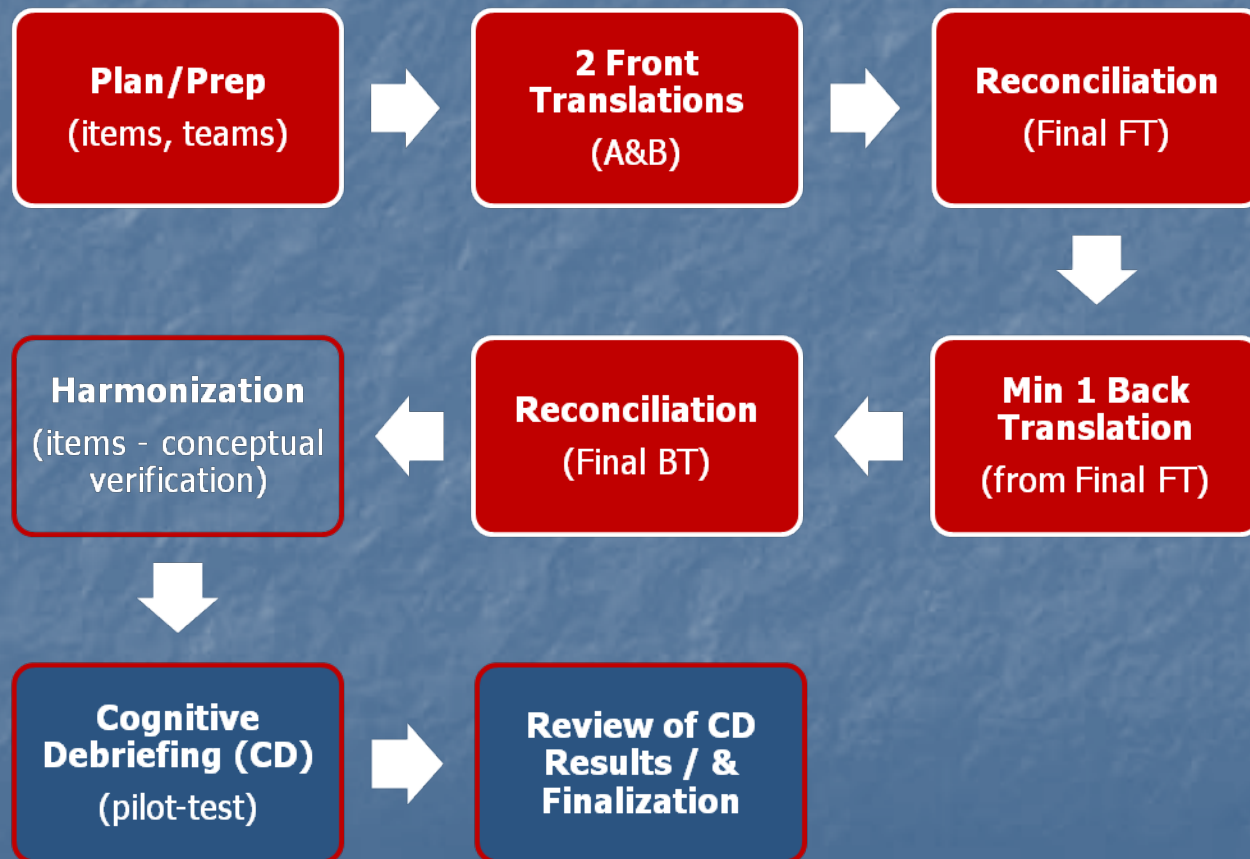
- **Translation**
 - Conceptually accurate conversion from Language A to Language B
- **Linguistic Validation**
 - Translation + pilot study = validated conceptual accuracy (includes cognitive debriefing)
- **Cultural Adaptation**
 - Linguistic validation + item customization + culture-specific statistical analysis of psychometric properties
- **Standardization**
 - Complete psychometric validation in a given culture/region/sample
 - Larger samples, normative data
 - Establishes gold standard scores

Current Recommended Practices For PROs

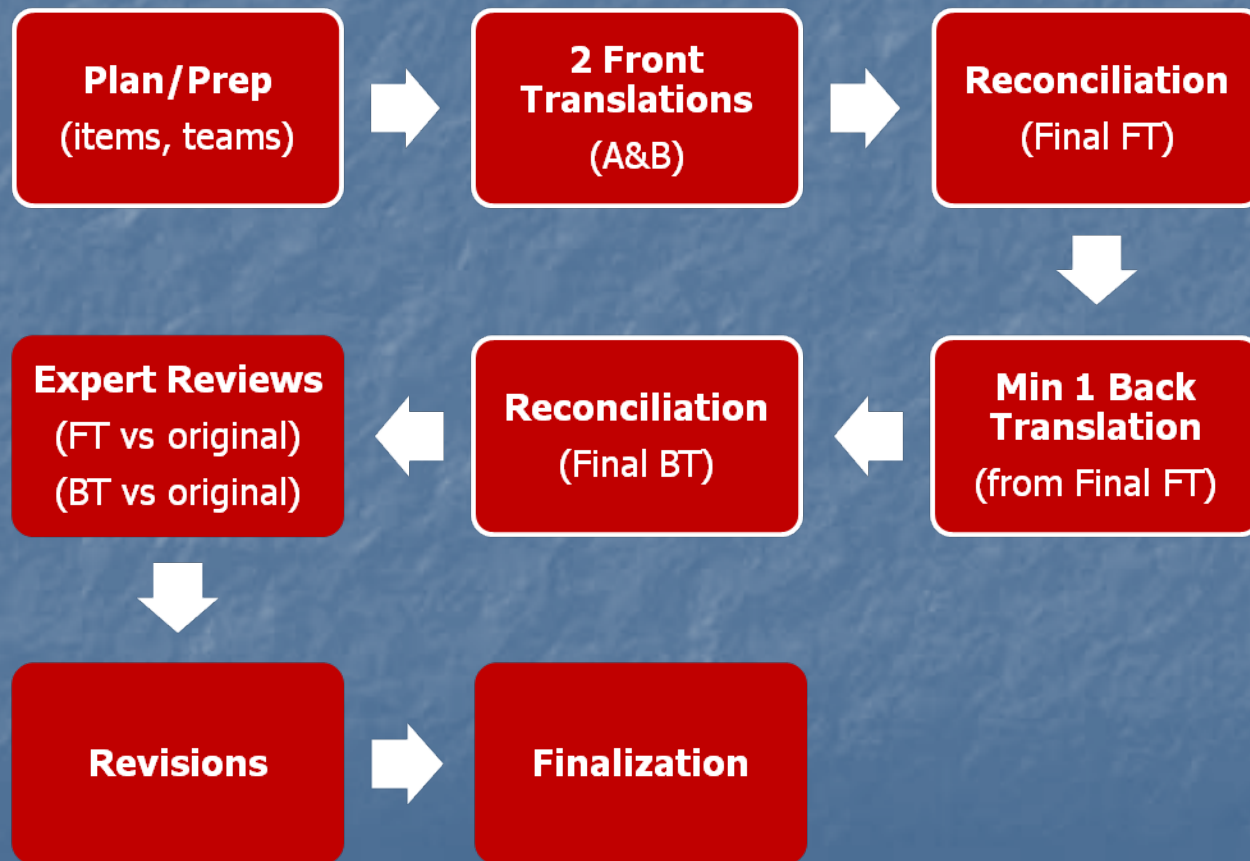
- **ISPOR Principles of Good Practice** (Wild et al, 2005)
- Only step-by-step guideline available in a single document
- Basic process for linguistic validation for PROs
- Translator qualifications undefined
 - PRO items = Grade 8 reading level or below
 - Translation not difficult
- May not necessary apply to clinician rated scales

ISPOR Methodology for PROs

Complete Process



Current Practices for Clinician-Reported Symptom Outcome Measures



Real World Practical Issues

- IP held by original test developer
- Budgets and Timelines
 - Always very short timelines before “first patient in”
 - Decreased R&D budgets restrict scope of work
 - Translation (8-12 weeks) - \$
 - Linguistic Validation (18-24 weeks) - \$\$
 - Cultural Adaptation (6-12 months) - \$\$\$\$
 - Common Practice: Translation only

Real World Practical Issues

- Existing Language Versions
- Unauthorized versions
 - Can be useful
 - May have been validated
- Test developers provide legally translated versions
 - Not always better than existing illegal versions

So What Happens Currently With Clinician-Reported Scales?

- Variability between study sponsors
- No consensus or agreement on what to translate
- No consensus on how to translate
- No cultural adaption done or felt to be necessary

Survey of Last 40 Studies in Major Psychiatric Indications

Indication	Number of Studies	Studies with Diagnostic Scales translated	Studies with Primary Efficacy Scales translated	Diagnostic Scales Translated	Primary Efficacy Scales Translated
BPD	10	6	7	60%	70%
MDD	11	7	8	64%	73%
Schizophrenia	19	9	14	47%	74%
	40	22	29	55%	73%

Should We Do Anything Differently?

Should We Do Anything Differently?

Clinician-reported symptom outcome measures:

- Should they be always translated?
- What about countries with multiple dialects like India?
- Should we be doing linguistic validation?
- Do we need to do cultural adaptation?
- Do psychiatric disease concepts vary by culture?
- Does it vary by diagnostic category e.g. schizophrenia/bipolar versus depression/anxiety

It Would be Useful if:

- The field developed consensus on these issues for Clinician-reported symptom outcome measures
- There could be official translated versions available to all
- More methodological research was conducted addressing these issues

Questions?
Comments?