Quality of Life-Nontuberculous Mycobacteria (NTM) Module

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Objectives

- **Nontuberculous mycobacteria (NTM) is a substantial cause of pulmonary infections and can affect those with chronic respiratory diseases, such as cystic fibrosis (CF) and bronchiectasis.**

- **NTM is rare, poorly understood, and difficult to treat, with few clear identified endpoints to evaluate new medications in randomized, controlled trials.**

- **We are developing a patient-reported outcomes (PROs) that identify key symptoms, tracks the progression of disease, and can serve as an important end-point in clinical trials of new therapies (FDA Guidance, 2009)**

- **The aim of this study was to develop an instrument for NTM symptoms; can be used with existing PROs measures for CF (CFQ-R) and bronchiectasis (QOL-B)**

Patient-Reported Outcomes: PROs

Both FDA & EMA now accept PROs as primary or secondary endpoints in clinical trials

Treatment Benefit = how a patient feels, functions and survives (FDA, 2009)

Begins with open-ended interviews with patients, experts; content analysis of key concepts; draft items and cognitive testing

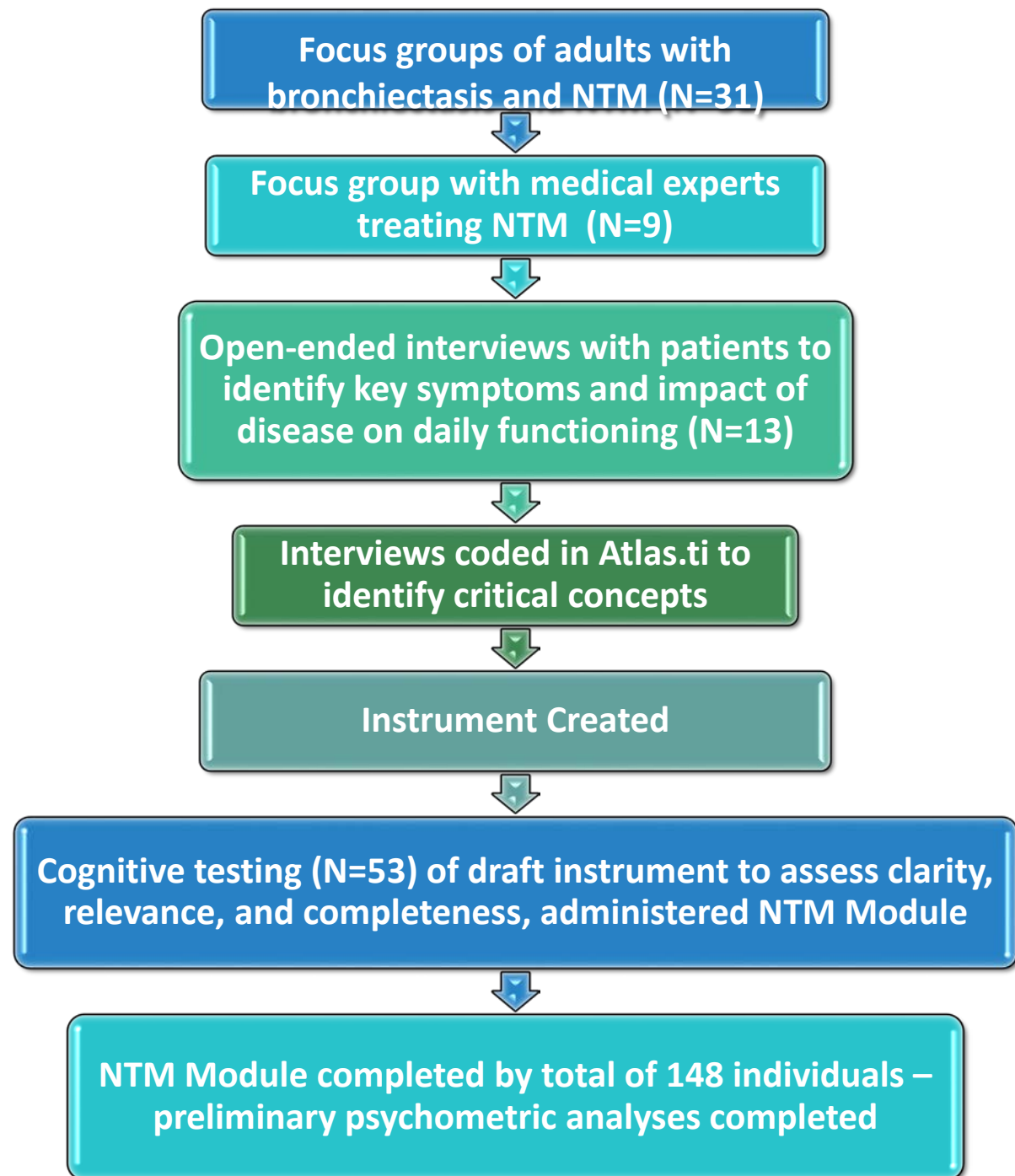Psychometric validation: reliability, validity, sensitivity to changes

Importantly: reflects the *"patient's voice"*

Methods

- We followed the FDA Guidance on PROs (2009)

- Reviewed published literature on NTM to identify critical symptoms and challenges of living with NTM

- Focus groups, moderated by a psychologist, were conducted with adults with NTM + bronchiectasis at 2 sites, N=31

- A consensus panel of 9 pulmonologists with expertise in NTM provided input on how NTM and its treatment affects their patients

- Open-ended interviews were conducted with 13 patients: how NTM affects daily functioning; frequent and difficult symptoms coded in Atlas.ti

- Cognitive testing, using a standard "think aloud" procedure conducted with 53 adults; input on preliminary items & rating scales

- We completed an initial psychometric validation of the module in 148 patients

Measurement Development Process

Focus groups of adults with bronchiectasis and NTM (N=31)

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Focus group with medical experts treating NTM (N=9)

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Open-ended interviews with patients to identify key symptoms and impact of disease on daily functioning (N=13)

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Interviews coded in Atlas.ti to identify critical concepts

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Instrument Created

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Cognitive testing (N=53) of draft instrument to assess clarity, relevance, and completeness, administered NTM Module

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NTM Module completed by total of 148 individuals – preliminary psychometric analyses completed

Key Themes

Main themes from Focus Groups (N=31)

- **Frequent pain (dull, aches, pressure in chest)**
  - **Metal taste in mouth**

  - **Fever**
  - **Lack of sleep**

Main themes from Open-Ended Interviews (N=13)

- **Fatigue**
- **Sensitivity to smell**

- **Sensitivity to cold/chills**
- **Hot flashes/sweats**

Main themes from Physician Panel (N=9)

- **Memory loss**
- **Body Image issues**

- **Side effects from medications: GI problems**
- **Weight loss with greater disease severity**

Results

- **Focus groups and open-ended interviews identified sleep quality, fever, and chills; physicians also identified body image as a concern**

- **The new NTM Module consists of eight unique symptoms; administered to 148 patients (α = .73); very good reliability**

Sample items from NTM module

"Bothered by cold weather?"

"Have you experienced problems with memory?"

NTM Symptoms

Indicate how you have been feeling during the past *week*:	A lot	A moderate amount	A little	Not at all
46. Have you had eating problems?	☐	☐	☐	☐
47. Have you had trouble gaining weight?	☐	☐	☐	☐
48. Have you felt feverish (sweating, chills)?	☐	☐	☐	☐
49. Have you had problems sleeping?	☐	☐	☐	☐
50. Have you had pain?	☐	☐	☐	☐
51. Have you felt bothered by cold weather?	☐	☐	☐	☐
52. Have you had sensitivity to smell?	☐	☐	☐	☐
53. Have you had sensitivity to taste?	☐	☐	☐	☐
54. Have you had a bad taste in your mouth due to sputum?	☐	☐	☐	☐
55. Have you experienced problems with memory?	☐	☐	☐	☐

Internal consistency of NTM module (N = 148)

Scale Name	Cronbach's Alpha
NTM Symptoms	0.73
Body Image	0.76
Eating Problems	0.89
Digestive Symptoms	0.75

Multitrait analysis of NTM module (N = 148)

Item	Abbreviated Item Content	*NTM Symptoms*
NTM48	Feverish (chills, sweating)	0.42[a]
NTM49	Problems sleeping	0.39[a,b]
NTM50	Pain	0.41[a]
NTM51	Bothered by cold weather	0.51[a]
NTM52	Sensitivity to smell	0.37[a,b]
NTM53	Sensitivity to taste	0.39[a]
NTM54	Bad taste in mouth	0.48[a]
NTM55	Memory problems	0.45[a]

[a]Item-scale correlation adjusted for overlap (item removed from its scale for correlation)
[b]Item-scale correlation is <.40

Algorithm for administering NTM module with QOL-B or CFQ-R

Individual with NTM

Bronchiectasis

CF

Completes QOL-B

NTM Module

Completes CFQ-R

NTM Module + Additional Scales

CFQ-R contains Body Image, Digestive Symptoms, & Eating Issues Scales

Digestive Symptoms

Eating Issues

Body Image

NTM Symptoms

Only fill out NTM Module
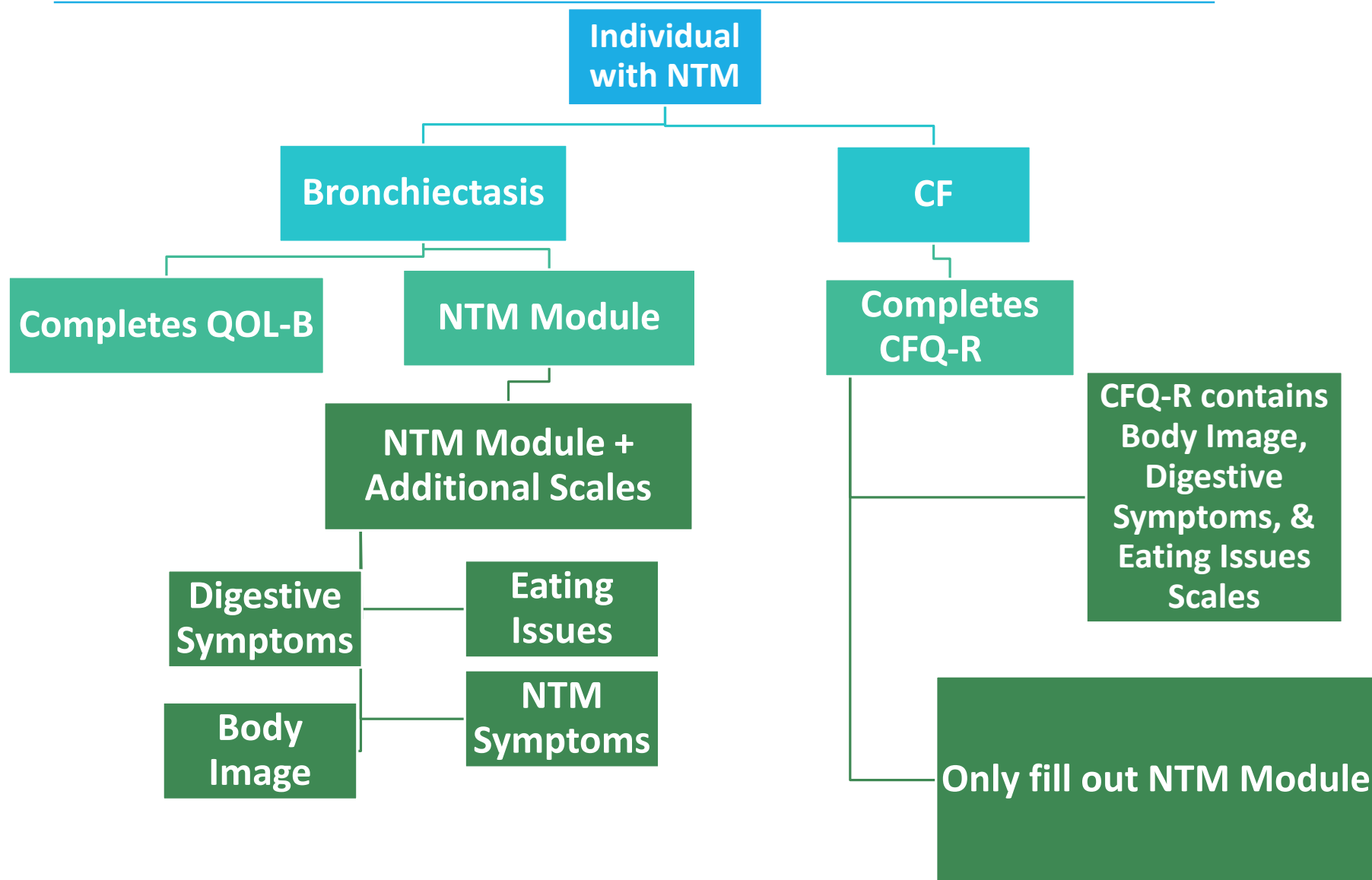
Summary & Future Directions

- **Cognitive testing indicated that the draft items were relevant, clear, and easy to understand**

- **Very good reliability**

- **When utilizing NTM module with bronchiectasis: use module + Body Image, Eating Issues, & Digestive Symptoms scale?**

- **Need more data!**

Summary & Future Directions

- **Next steps include additional psychometric testing, and identification of meaningful change**

- **Insmed has agreed to perform extensive psychometric analyses on their baseline clinical trial:**

  - **Reliability**

  - **Convergent validity: medical characteristics, microbiology, SGRQ, 6-minute walk**

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