

Incorporating PROMS in PIBD Management

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Disclosures

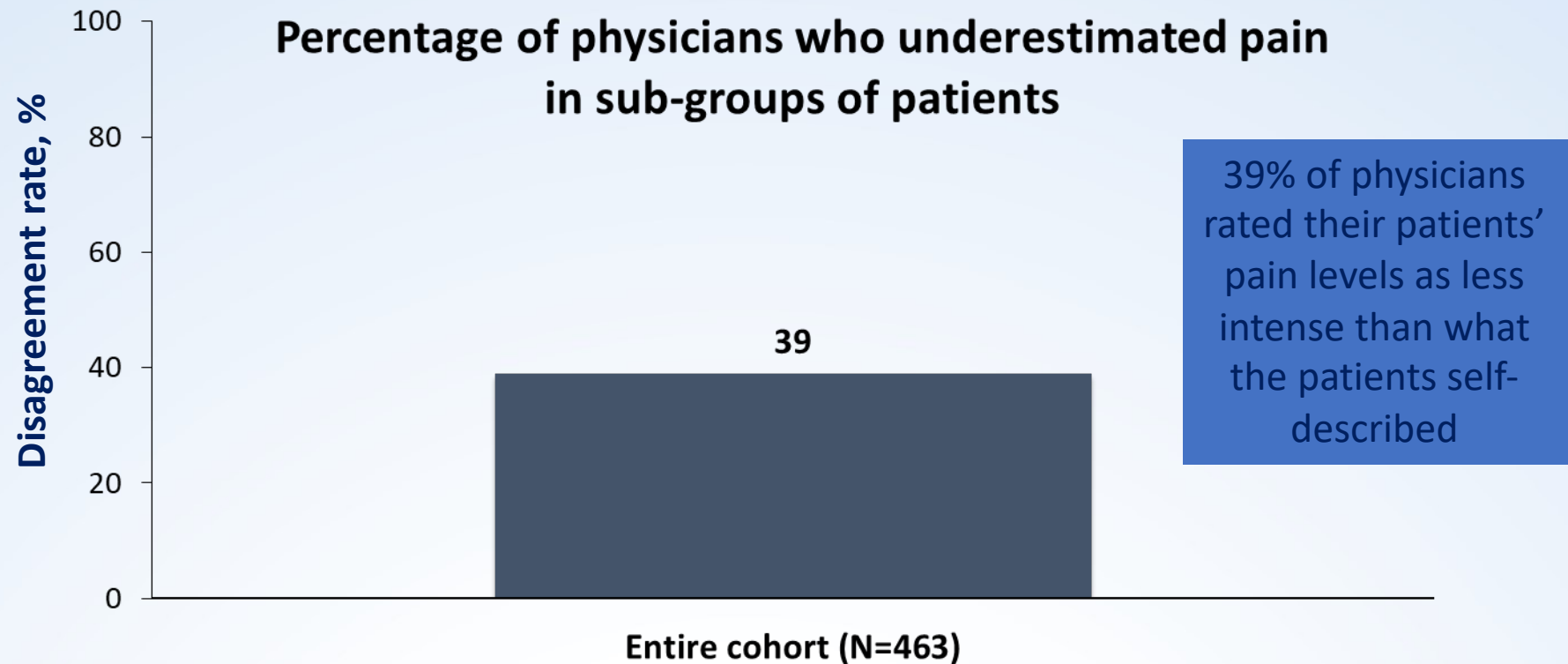
Conflict of interests

Last 3 years DT received consultation fee, research grant, royalties, or honorarium from: Janssen, Pfizer, Hospital for Sick Children, Shaare Zedek Medical Center, Ferring, Abbvie, Takeda, Atlantic Health, Shire, Celgene, Lilly, Roche, ThermoFisher, BMS

What goals do we dream about?

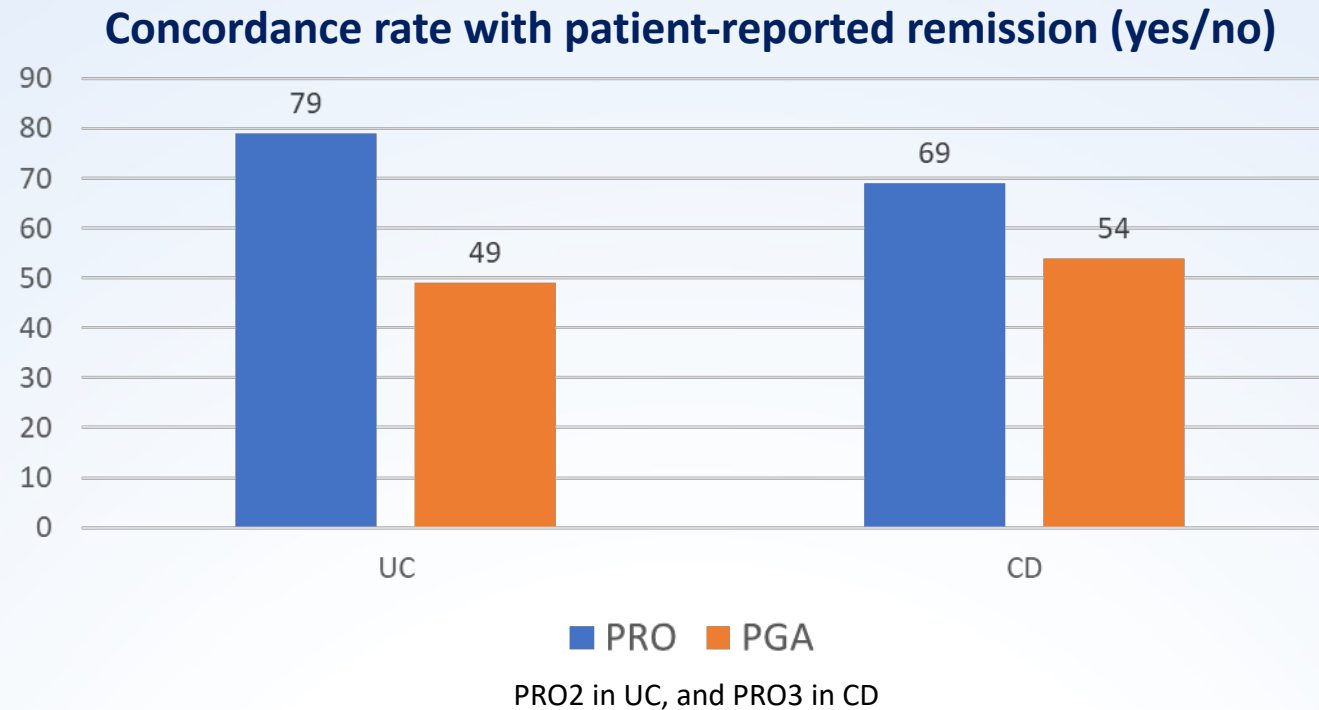


Disagreement in pain perception between patients and their physicians in primary care



Discrepancies in defining remission by patients (PRO) or their physicians (PGA)

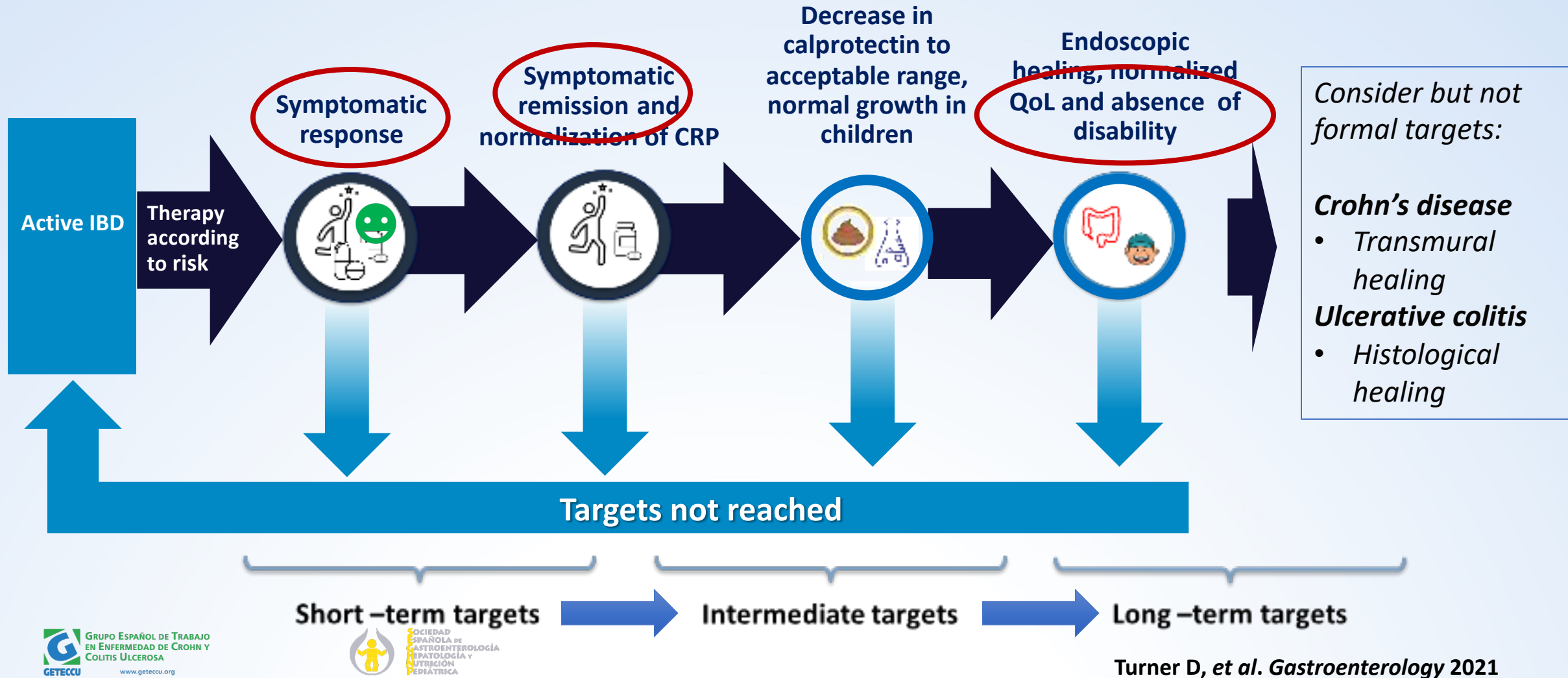
Retrospective analysis of 2004 IBD patients from the IBD Qorus Learning Health System



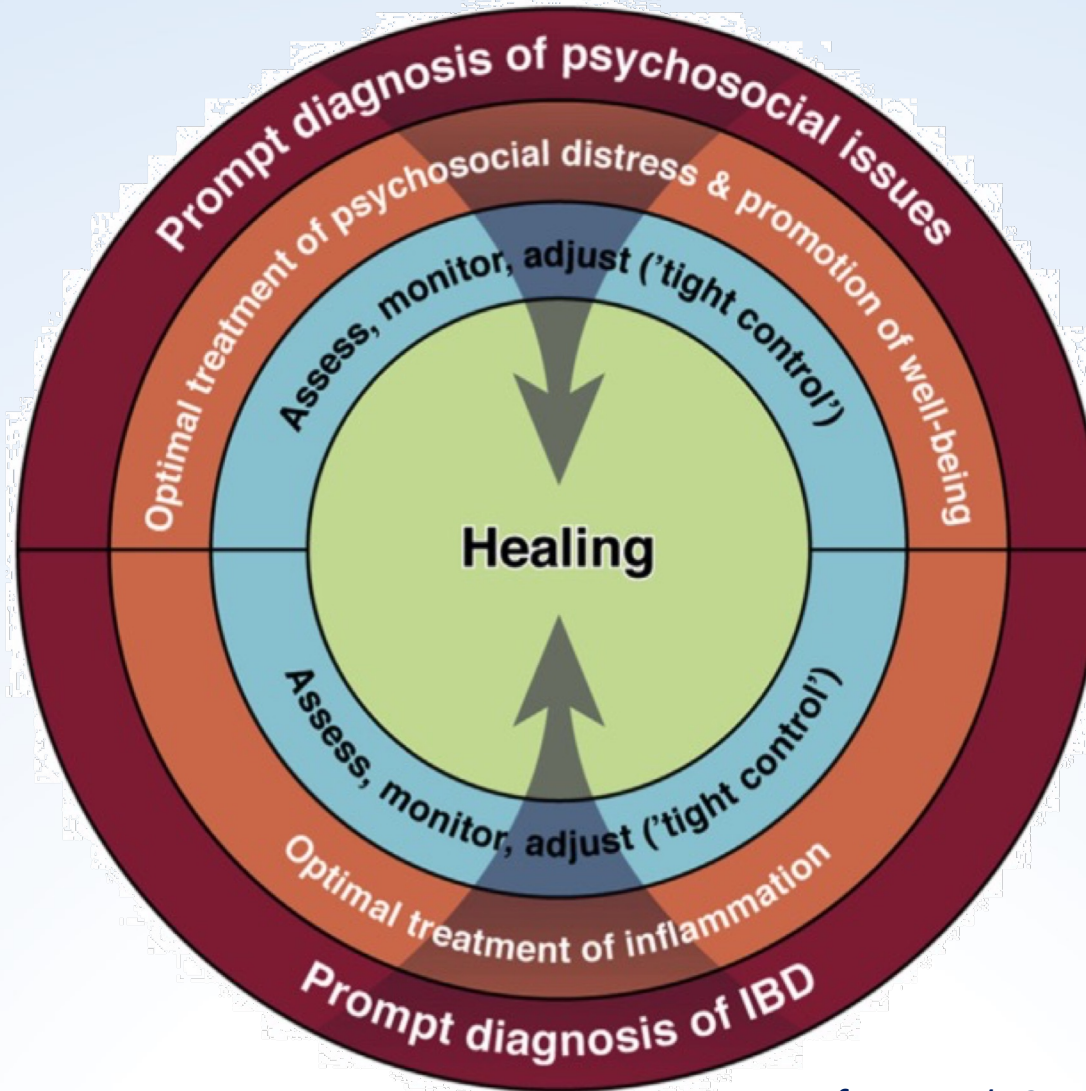


How can we reconcile??





Psychosocial support is an essential integrative part of the T2T scheme to ensure emotional wellness



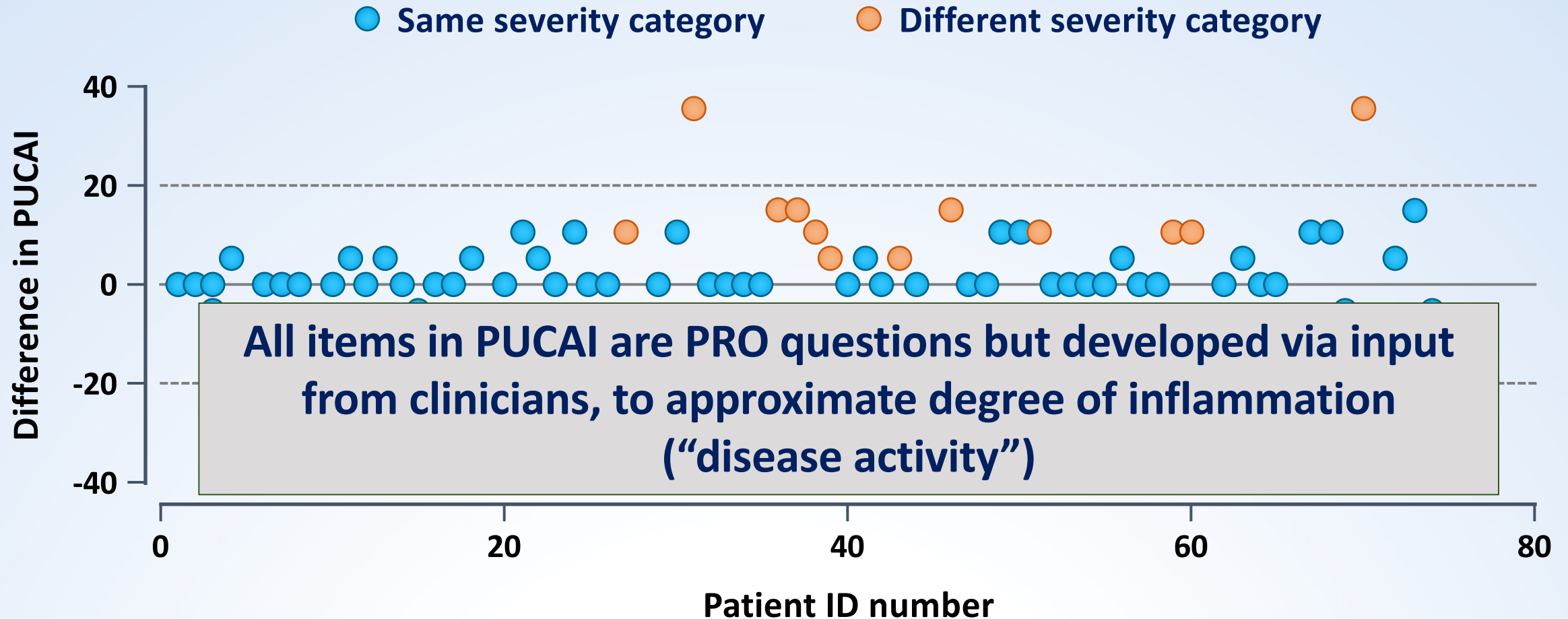
- **Disability**
- Fatigue
- Body image
- Sexuality
- Depression
- Eating disorders
- Anxiety
- Work/school

The PUCAI

Item		Points
1. Abdominal pain	No pain	0
	Pain can be ignored	5
	Pain cannot be ignored	10
2. Rectal bleeding	None	0
	Small amount only in <50% of stools	10
	Small amount with most stools	20
	Large amount (>50% of the stool content)	30
3. Stool consistency of most stools	Formed	0
	Partially formed	5
	Completely unformed	10
4. Number of stools per 24 hours	0–2	0
	3–5	5
	6–8	10
	>8	15
5. Nocturnal bowel movement (any diarrhoea episode causing wakening)	No	0
	Yes	10
6. Activity level	No limitation of activity	0
	Occasional limitation of activity	5
	Severe restricted activity	10
Sum of PUCAI (0–85)		

Turner D, et al. *Gastroenterology* 2007;133:423–32

Strong agreement between PUCAI scores obtained directly from patients and those completed by physicians



Lee JJ, et al. *JPGN* 2011;52:708–13

Development and psychometric evaluation of a PRO (TUMMY-UC)

Concept elicitation qualitative interviews – patients & caregivers

- Understand the terminology; Rank importance of items; Define age-groups; Start exploring response options; Define recall period

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Cognitive interviews – patients & caregivers

- To determine the exact wording of the items; Finalise the response options; Develop user's guide; Finalise weights

Evaluation and validation

- Construct and discriminant validity, reliability and responsiveness
- Developing a scoring system

Development and psychometric evaluation of a PRO (TUMMY-UC)

208 interviews in total with 127 children and 81 caregivers



Concept elicitation qualitative interviews – patients & caregivers

1, 2A: 79 interviews (46 children, 33 caregivers (of which 30 double)

Cognitive interviews – patients & caregivers

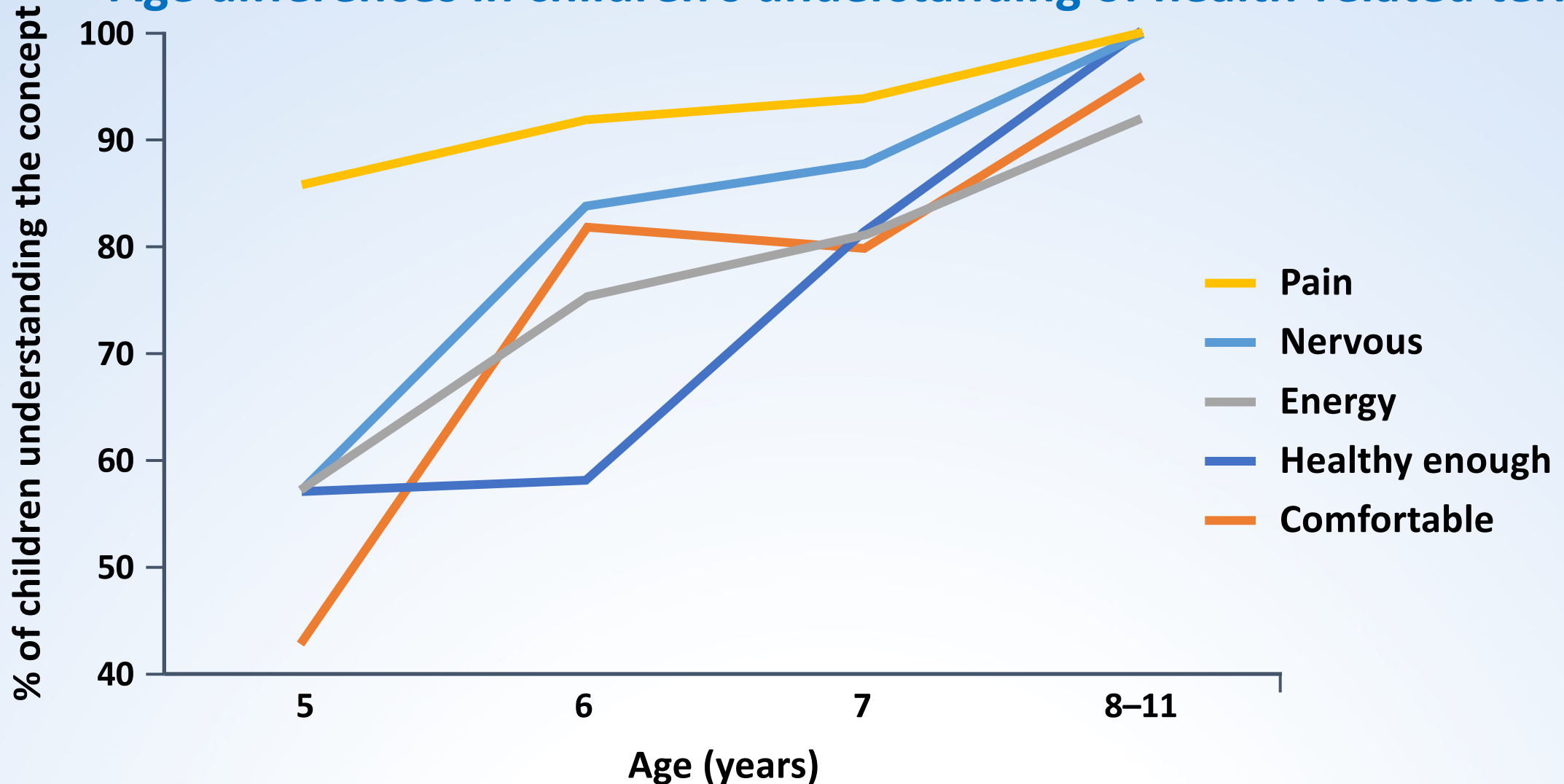
2B: 47 interviews (34 children, 13 caregivers)

2C: 82 interviews (47 children, 35 caregivers (of which 22 double)

Evaluation and validation

- Construct and discriminant validity, reliability and responsiveness
- Developing a scoring system

Age differences in children's understanding of health-related terms



Stage 2: cognitive interviews: children item example

II. Since yesterday at this time until now (last 24 hours), how much blood did you see in your worst poop?

Set number 1

1. There is no blood at all
2. There is more poop than blood
3. There is more blood than poop
4. There is only blood (without any poop)

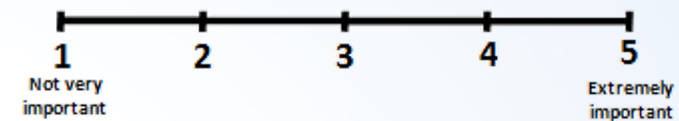
Set number 2

1. There is no blood at all
2. There are only small streaks of blood
3. There is quite a bit of blood
4. There is mostly blood

Set number 3

1. There is no blood at all
2. There are only small streaks of blood
3. There is quite a bit of blood but more poop than blood
4. There is more blood than poop
5. There is only blood (without any poop)

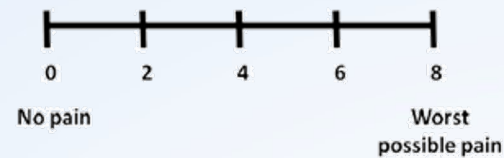
- A. Did you **understand the question**? Please explain in your own words what this question is asking you to do.
- B. Which **set of responses** do you think is easier to answer when you are trying to tell me what your worst poop had been like?
- C. Was it **easy to answer this set** of responses about blood in your poop? Explain why.
- D. Did you **understand the words used in all the responses** in the set that you chose as the easiest?
- E. Do you think some answers should be **changed or taken out** to make it easier to answer? Do any new responses need to be added?
- F. Do you have **another way** of describing the amount of blood in your poop that is easier for you to understand?
- G. Think about the things that **tell you when your colitis is starting to get bad** or acting up. How important is seeing blood in the stool in letting you know that your colitis is starting to get bad or acting up?



Caregivers item example

1. The following questions are behaviors that are sometime seen in children with tummy pain. Since this time yesterday (last 24 hours), how often did your child show any of the following behaviors:

1. The caregiver should be asked to get the child scoring the **FACES** scale by him/herself after oral explanation.
2. Please circle the number that matches with how much your child's tummy has hurt when it hurt at its worst Since this time yesterday (last 24 hours):



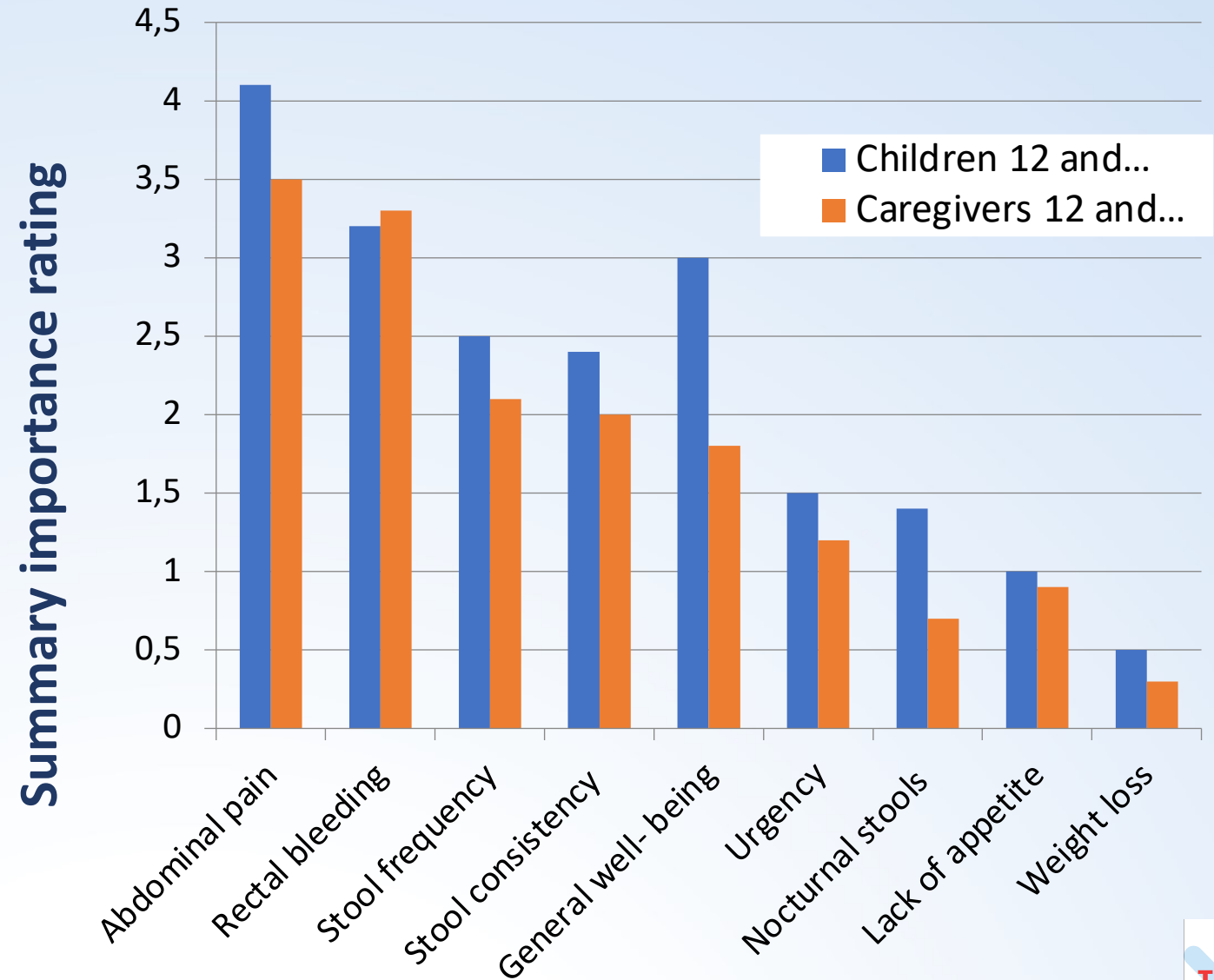
3. How does your **child typically behave** when you believe that he/she is not in pain? What about when you believe that he/she is in pain?
4. What observable behaviors make you believe that your child is in pain?
5. How often did you observe the following behaviors and verbalizations (what your child tell you) **Since this time yesterday (last 24 hours)**? Which of the following behaviors and verbalizations (what your child tells you) do you believe are important in showing that your child has tummy pain?

observable behaviors and verbalizations	Is it important in showing that your child is in pain?	How often did your child experience this symptom in the last 24 hours? Please circle one response.
Holding the stomach	Yes/No	Never/Rarely/Sometimes/Often/Very often
Crying	Yes/No	Never/Rarely/Sometimes/Often/Very often
Playing less than usual	Yes/No	Never/Rarely/Sometimes/Often/Very often
Lying down most of the time	Yes/No	Never/Rarely/Sometimes/Often/Very often
Not eating as usual	Yes/No	Never/Rarely/Sometimes/Often/Very often
Moodier than usual	Yes/No	Never/Rarely/Sometimes/Often/Very often
Quieter than usual	Yes/No	Never/Rarely/Sometimes/Often/Very often
Lying down with the legs folded towards the stomach/arching	Yes/No	Never/Rarely/Sometimes/Often/Very often
Complains of stomach cramping	Yes/No	Never/Rarely/Sometimes/Often/Very often
Complains of stomach ache/ pain/sore	Yes/No	Never/Rarely/Sometimes/Often/Very often
Looks weak	Yes/No	Never/Rarely/Sometimes/Often/Very often

6. Do you feel that any of these **behaviors or verbalizations are not applicable** or that any other behaviors should be added to this list?
7. Do you feel that **it easy for you to report** on how often you see the observable behavior or hearing verbalization made by your child?
8. Do you think some of the **possible responses should be changed** or taken out to make it easier to answer? Do any new responses need to be added?
9. When your child appears to have tummy pain, how much does it **tell you that your child's colitis is starting to get bad** or acting up?
10. Was it easy to answer these questions? Explain why. You can see that there are 2 ways to describe your child's tummy pain:
 - Which of the two options is preferable?
 - Do you think your **child is capable** to score the FACES reliably?

Children and caregivers agree on importance of TUMMY-UC items

Top three items may be *weighted 50% higher than other items*





TUMMY-UC Content

- Final 8 items selected based on previous stages:
abdominal pain, stool frequency, blood in stool (amount), blood in stool (frequency), urgency, weakness, stool consistency and nocturnal stool
- An ObsRO was determined to be required for children <8 years.

Observer TUMMY-UC (for children ≥ 2 but <8 years)

- These questions should be completed by the caregiver.
- We ask how your child has been doing because of the colitis since yesterday at this time (last 24 hours).
- It is important that the time the TUMMY-UC is completed each day is kept consistent; ideally at the end of the day, when your child goes to sleep.
- Please answer the questions based on behaviors that you have observed in your child and things that he/she may have said to you that indicate how he/she has been feeling.

Please mark the time you completed the TUMMY:

___ / ___ / ___
HH MM A.M.
P.M.

___ / ___ / ___
DD MMM YYYY

I. Which of the following best describes your child's behavior since yesterday at this time (last 24 hours)?

The list of behaviors may assist you.

My child behaves in a way that:

- No stomach pain- Acts and behaves normally, plays, eats, and sleeps.
- Minimal stomach pain- Complaints of pain, but behavior - acts normally, plays, eats, and sleeps.
- Mild stomach pain- Still acts normally, but may complain of stomach pain.
- Moderate stomach pain- Stays in bed or down from time to time, may complain of pain.
- Severe stomach pain- Holds himself/herself, complains of pain or may be inconsolable.

II. How many times did your child go to the bathroom since yesterday at this time (last 24 hours)? Count the number of all visits to the bathroom when you pooped, including accidents (e.g., in your underwear or pants). If he/she poops more than 8 times, count them as one time.

- 0-2 times
- 3-5 times
- 6-8 times
- More than 8 times

TUMMY-UC (PRO for children 8-18 years)

- These questions ask about how you have been feeling because of your colitis since yesterday at this time (last 24 hours).
- It is best that you complete the TUMMY-UC before you go to bed at night and report the time since you went to bed last night until now. However, this is not mandatory and it may be completed at any time during the day on condition that the time during the day remains the same.
- Please answer honestly. There are no right or wrong answers.

Please mark the time you completed the TUMMY:

___ / ___ / ___
HH MM A.M.
P.M.

___ / ___ / ___
DD MMM YYYY

I. What is the worst your tummy has hurt since yesterday at this time (last 24 hours)?



0

No pain



1



2



3



4

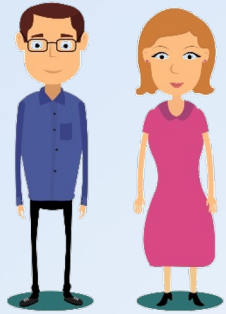
Worst Possible pain

II. How many times did you poop since yesterday at this time (last 24 hours)? Count the number of all visits to the bathroom when you pooped, including accidents (e.g., in your underwear or pants). If you poop a few times during one visit to the bathroom, count them as one time.

- 0-2 times
- 3-5 times
- 6-8 times
- More than 8 times

Conceptual equivalence of the TUMMY-UC (n=44)

22 completed obsRO



Ability of caregivers to reflect their children symptoms

22 completed PRO



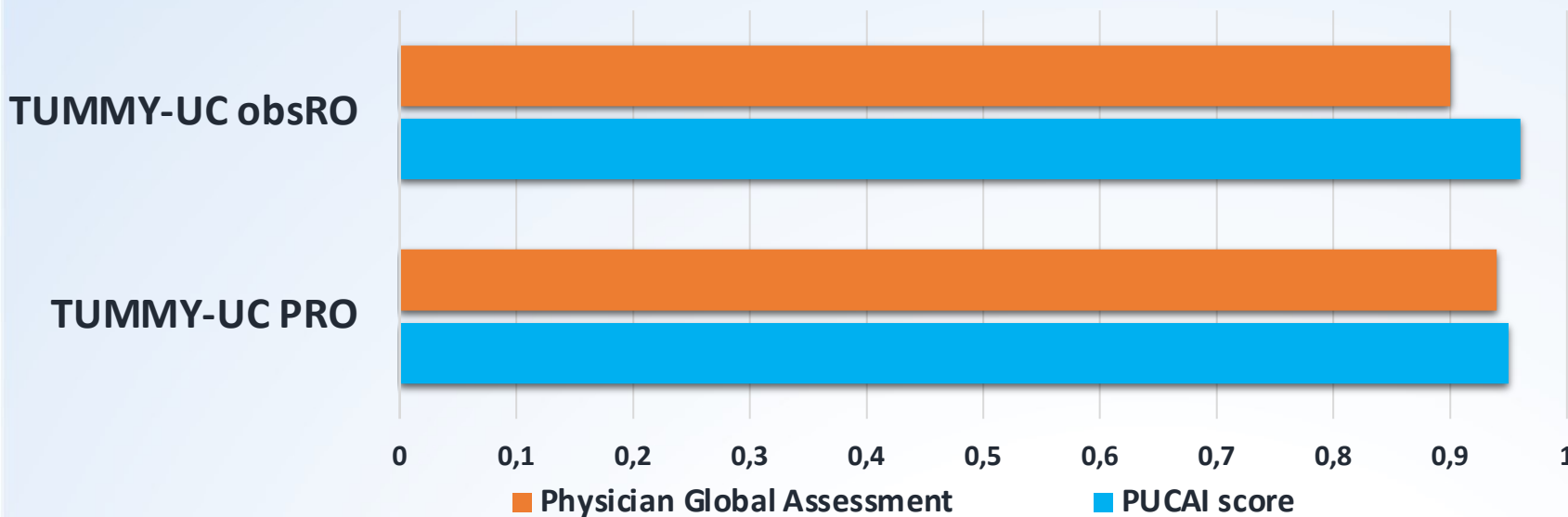
Ability of children to accurately score their symptoms



Range of overlapping age when conceptual equivalence can be broadly estimated

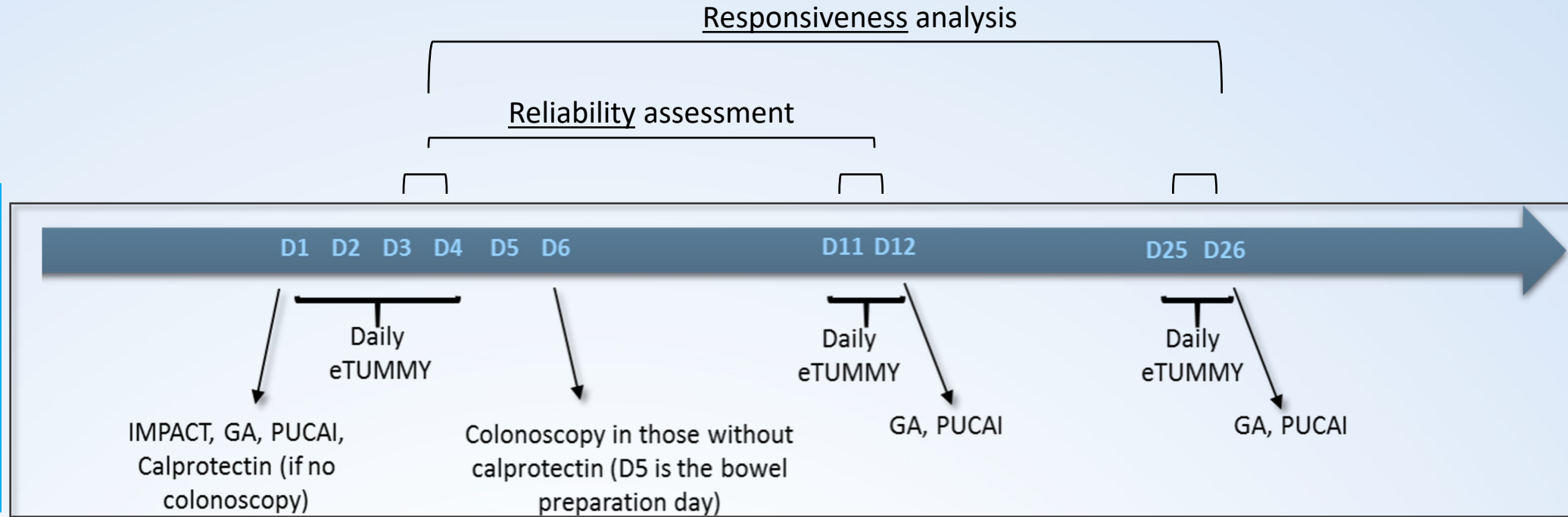
Conceptual equivalence of the TUMMY-UC (n=44)

- There was excellent agreement between the total TUMMY-UC PRO and obsRO scores (ICC=0.92 (95%CI 0.74-0.98)).
- The obsRO scores were always within the same disease-activity category as the corresponding PRO score (i.e. remission, mild and moderate-severe disease).



Validation Study Participants and Design

84 children (age 12.1 +/- 4.3 years; 48% males) were included: 52 undergoing colonoscopy, the remainder providing stool for calprotectin measurement.



Construct and discriminative validity were assessed by different measures of disease severity and quality of life.

Results



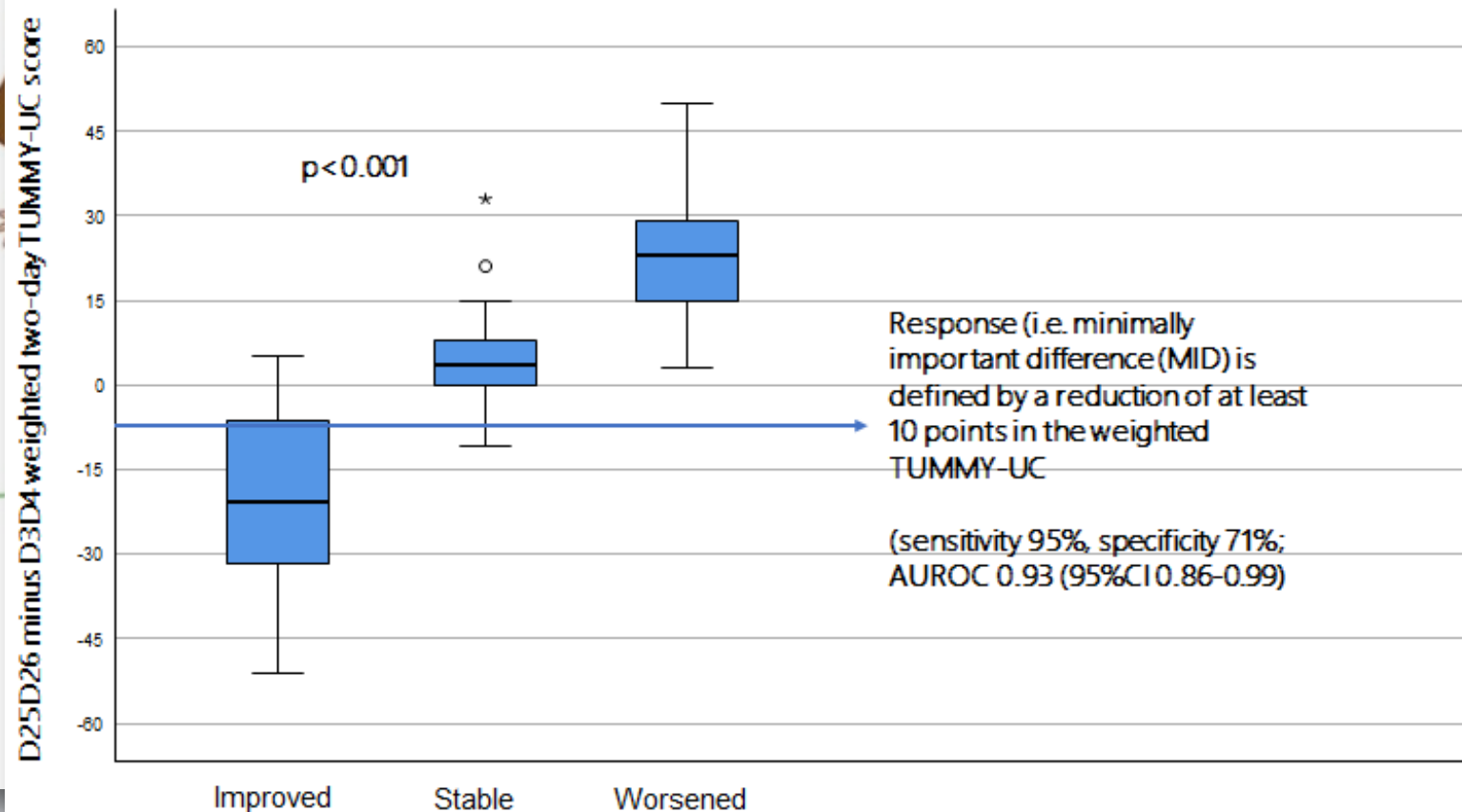
Figure 1: TUMMY-UC and endoscopic disease activity

Figure 2: TUMMY-UC to differentiate clinical remission

Figure 3: Discriminative validity of the TUMMY-UC version by the PUCAI disease activity categories

Figure 4: Reliability of the TUMMY-UC

Figure 5: Responsiveness to change from days 3-4 to days 24-25



Responsiveness

The TUMMY-UC differentiated well between children who improved, worsened or remained unchanged after 3 weeks

TUMMY-CD



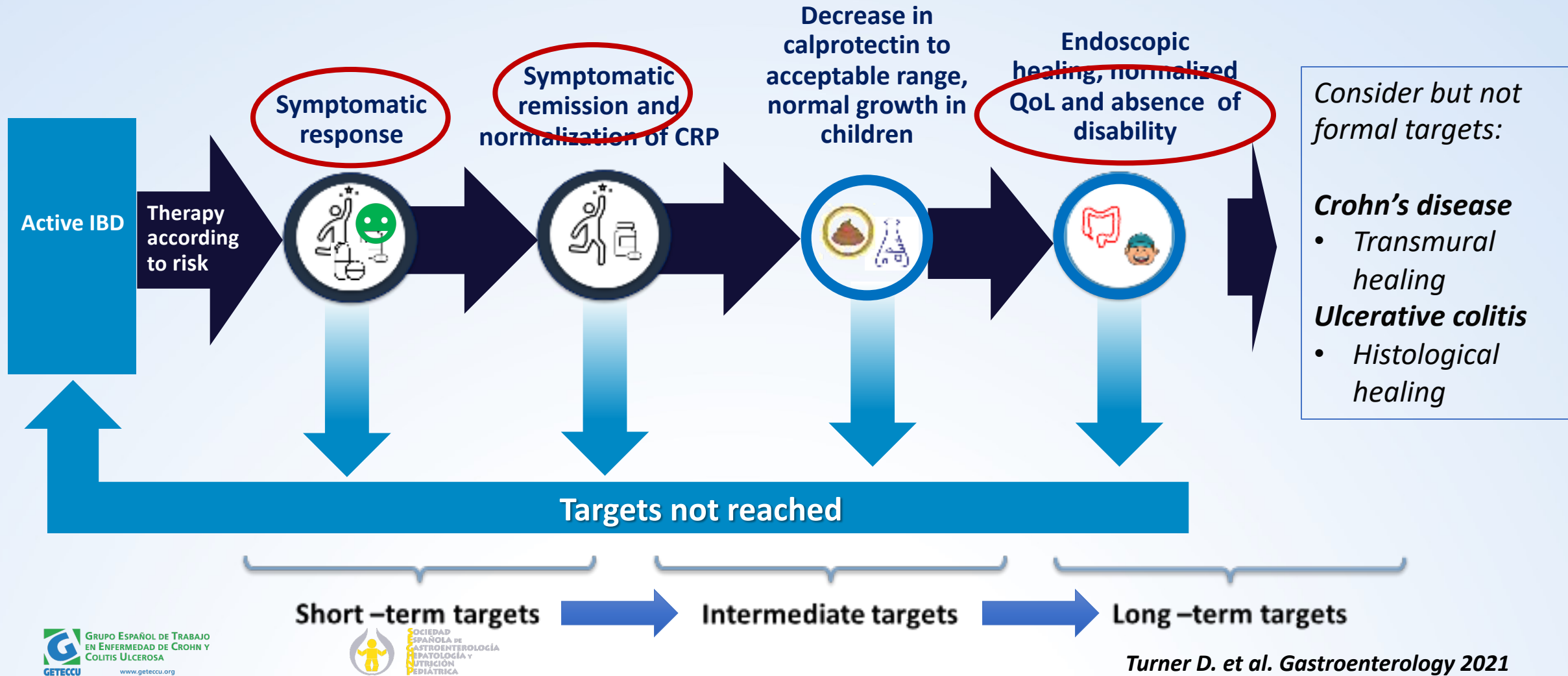
Concept elicitation qualitative interviews – patients & caregivers

- Rank importance of items and determine response options; Define age-groups

Cognitive interviews – patients & caregivers

- To determine the exact wording of the items and response options

MB Crane, et al. *Development of the TUMMY-CD, A symptoms-based disease activity patient reported outcome (PRO) for pediatric Crohn's disease. JCAG, Volume 1, Issue suppl 2, 1 March 2018, Pages 197–198.*



IMPACT-III disease-specific QOL scale

- 35 item
- 6 domains
 - Bowel symptoms
 - Body image
 - Functional / social impairment
 - Emotional impairment
 - Tests / treatments
 - Systemic impairment
- Scores
 - Range from 35 to 175 (higher score = higher HRQOL)

שאלה 1: באיזו עוצמה כאבה לך הבעון במשך השבועיים האחרונים?

☐ ככלל לא ☐ כמעט ולא ☐ כאבה קצת ☐ די כאבה ☐ כאבה מאוד

שאלה 2: נטילת תרופות או כדורים מטרידה אותי

☐ ככלל לא ☐ כמעט ולא ☐ מטרידה קצת ☐ די מטרידה ☐ מטרידה מאוד

שאלה 3: באיזו תדירות מחלת המעי הדלקתית מנעה ממך לאכול מה שרצית במשך השבועיים האחרונים?

☐ אף פעם ☐ לעיתים רחוקות ☐ לפעמים ☐ לעיתים קרובות ☐ לעיתים קרובות מאוד

שאלה 4: באיזו תדירות היית מוטרד מהתלקחות המחלה (עליה בסימפטומים) במהלך השבועיים האחרונים?

☐ אף פעם ☐ לעיתים רחוקות ☐ לפעמים ☐ לעיתים קרובות ☐ לעיתים קרובות מאוד

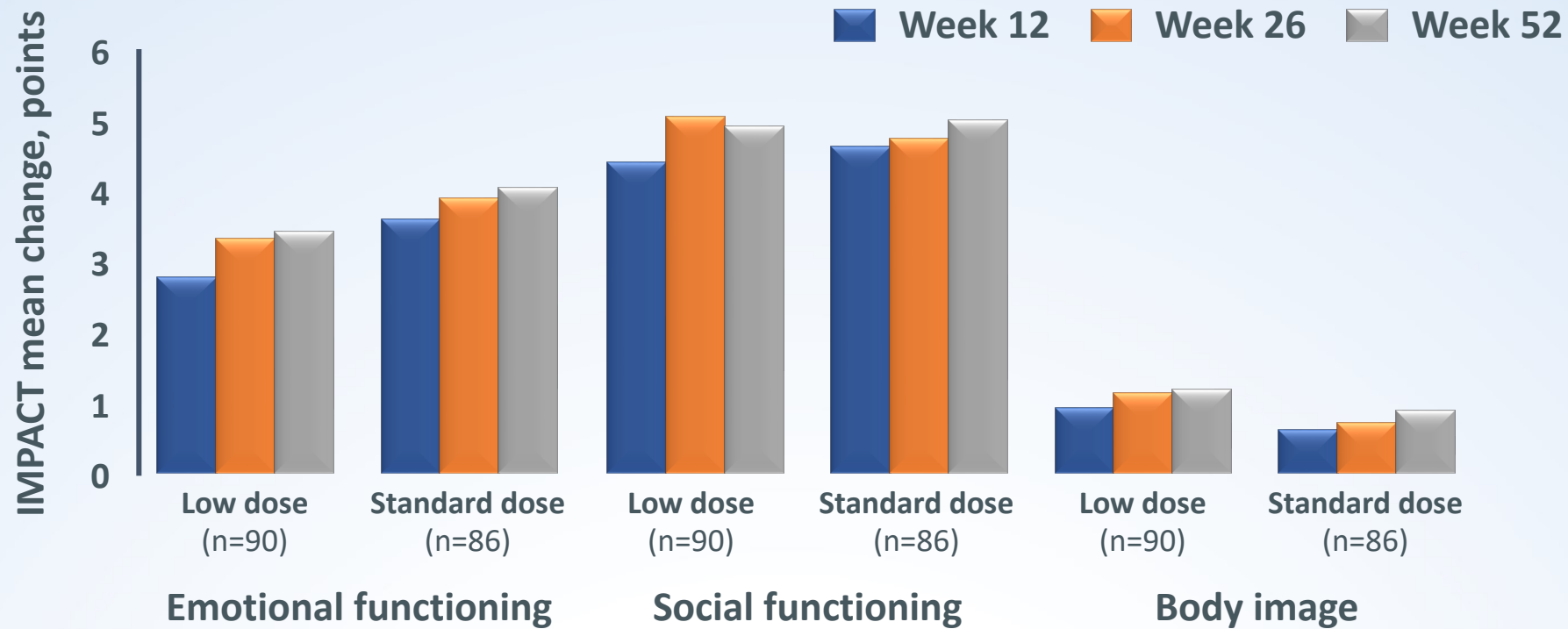
שאלה 5: עד כמה מטרידה אותך העובדה שיש לך מחלה שאינה חולפת?

☐ ככלל לא ☐ כמעט ולא ☐ מטרידה קצת ☐ די מטרידה ☐ מטרידה מאוד

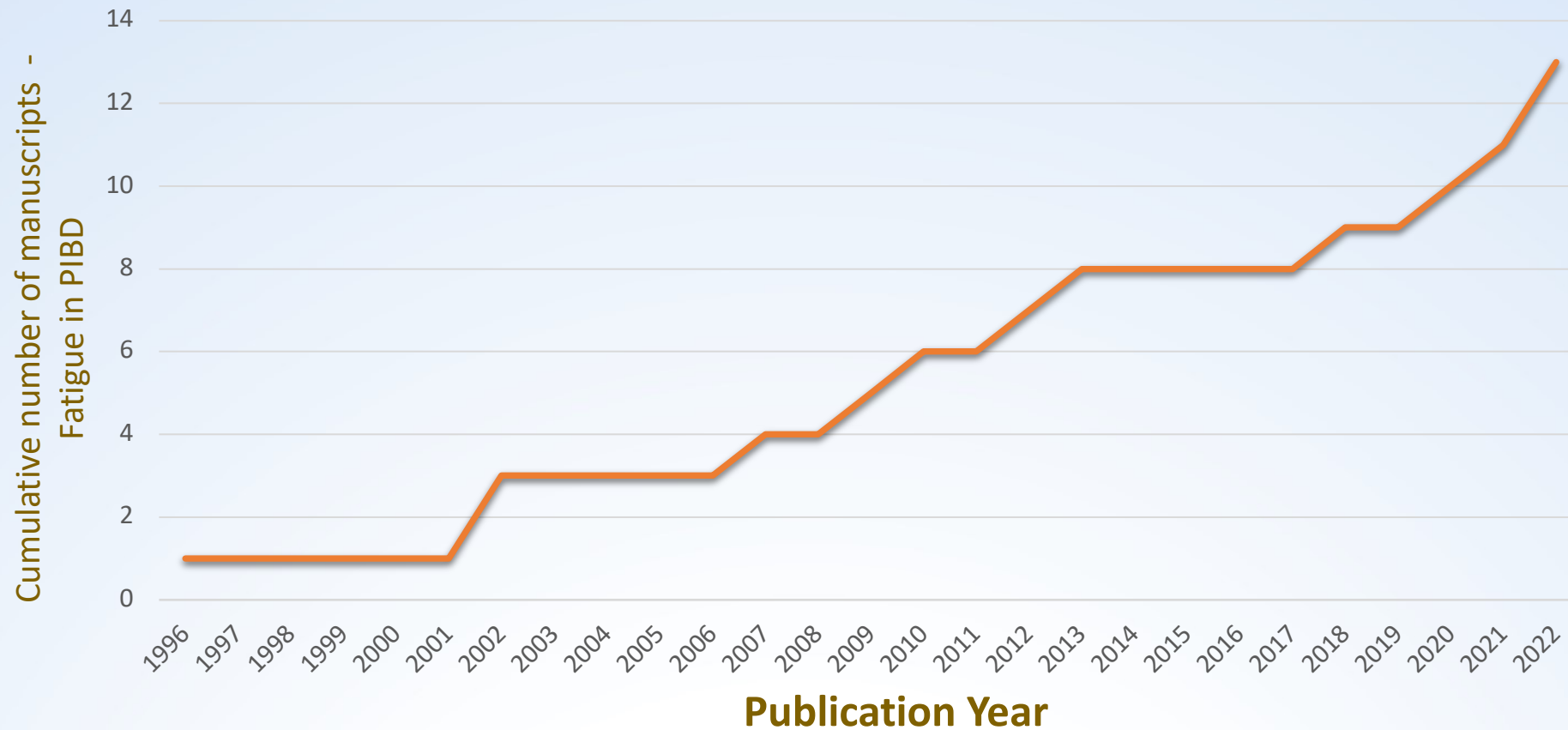
© זכויות היוצרים 2002, שמורות להפצת העבודה של מחלות מעי דלקתיות בילדים על איסוף חיים

IMAgINE-1: Mean change in IMPACT-III QOL questionnaire

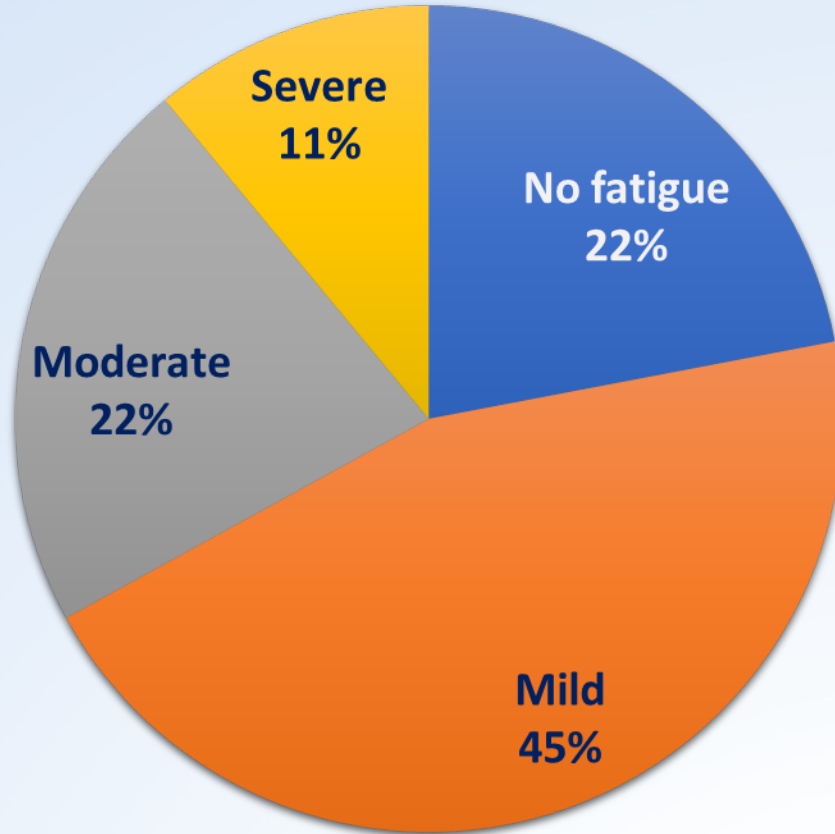
$p < 0.01$ for within-group change for all comparisons



Fatigue-related publications in patients with IBD

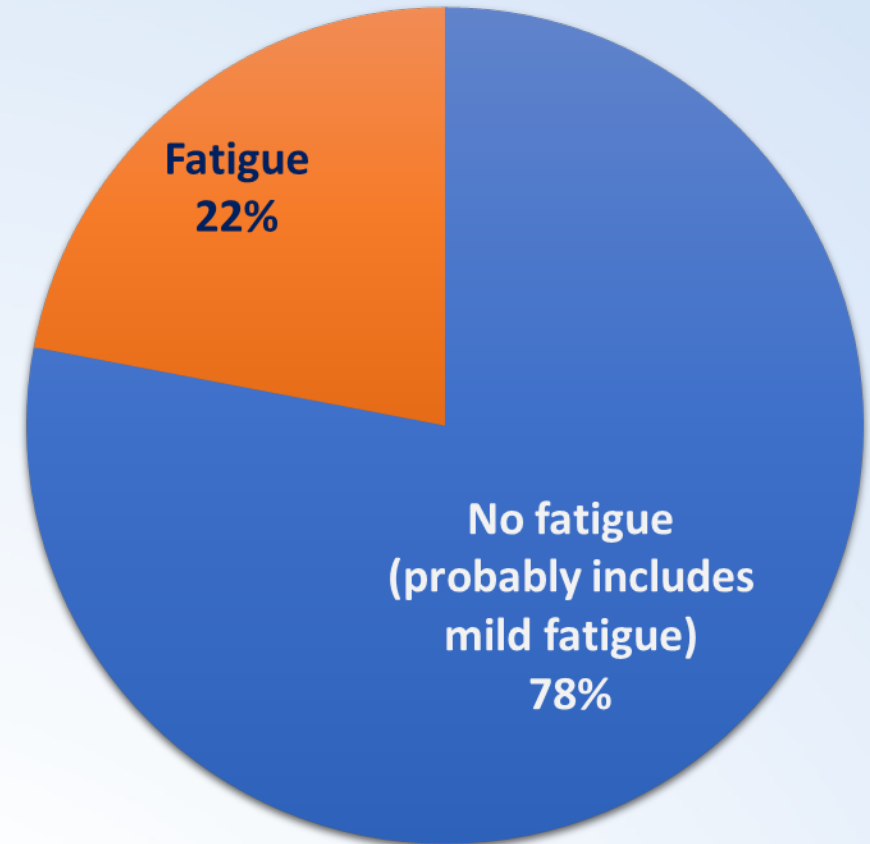


Fatigue is very common in pediatric IBD



N=80 children with IBD, measured at 4 months after diagnosis, Fatigue estimated from the two fatigue-related questions of IMPACT-III

Turner S and Focht G, *et al. JPGN 2023 in press*

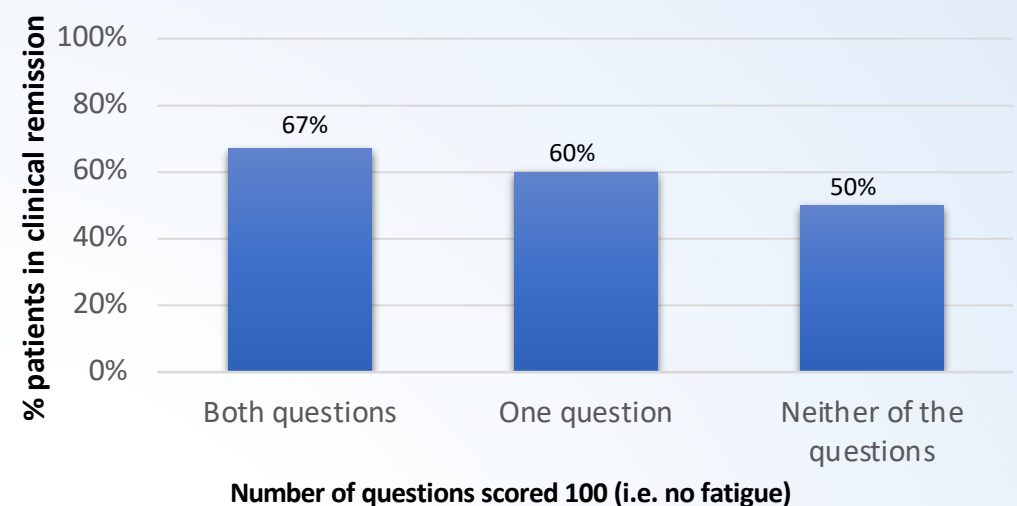
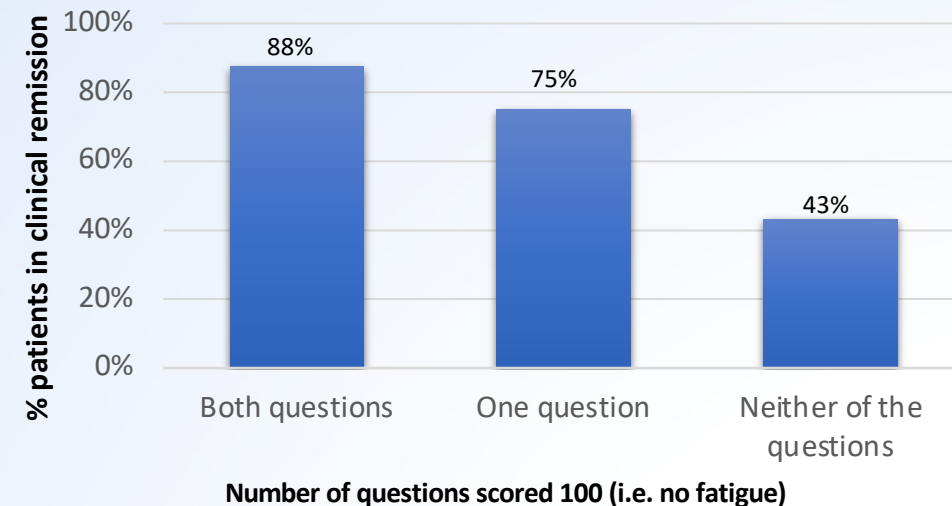
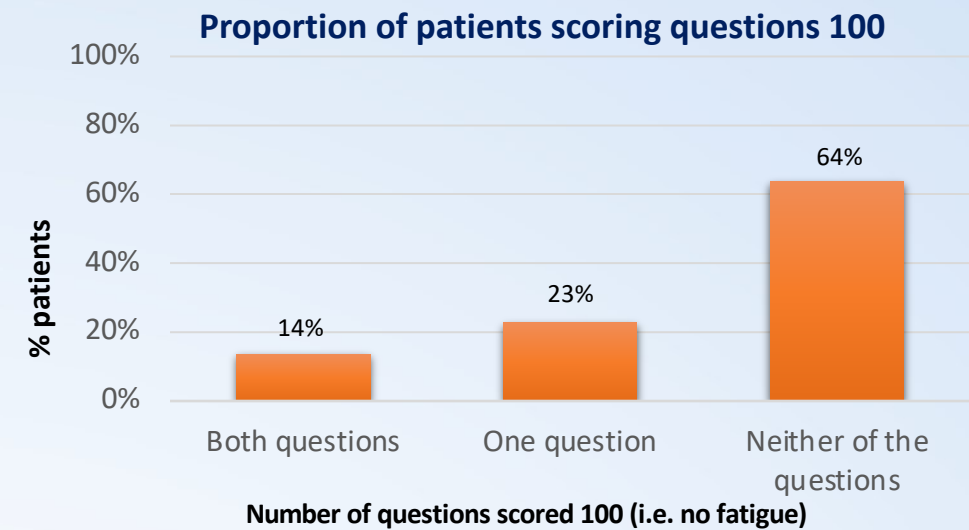
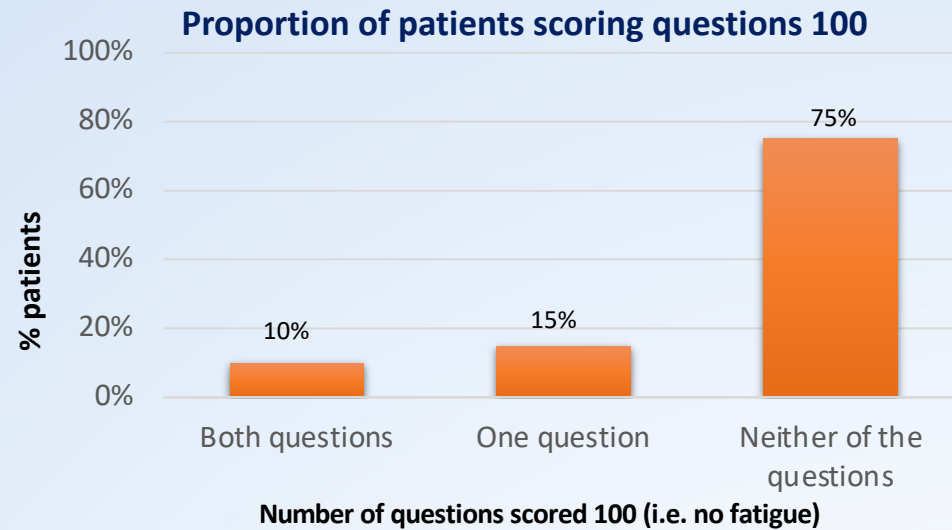


N=294 children with ,mostly active CD, from the COMBINE trial. Fatigue defined at 95TH centile in PROMIS-fatigue domain compared with US reference population

Chuchard J, *et al. Acad Pediatr 2022; 22:1520-8*

Rate of children (n=80, 9-18 yrs) scoring the two IMPACT-III related fatigue questions 100 (i.e. lack of fatigue) and clinical remission

Four months after diagnosis



Turner S and Focht G *et al.* JPGN 2023 in press

Development of PIFI and PIDI

Stage 1

Systematic literature review

Stage 2

Evaluation for disability in an inception cohort

Stage 3

**Development of a PRO and obsRO of
Disability and Fatigue in PIBD:
PIDI and PIFI**

Phase 1

Qualitative concept elicitation interviews
(CEI)

Phase 2

Cognitive debriefing interviews (CDI)

Phase 3

validation



Clinical Response

Clinical Activity



Endoscopic Healing

Endoscopy

Capsule
Endoscopy

Non-
invasive



Transmural Healing

MRI

Ultrasound



Patient-reported Wellbeing

QOL

Disability/
Fatigue

CROHN'S DISEASE

PCDAI/ wPCDAI
TUMMY-CD

CDEIS
SES-CD
SEMA-CD
UGI-SES-CD

LEWIS
SCORE
CECDAI

MINI index

MRE
PICMI
Pelvic MRI
PEMPAC
Van Assche score

International
Bowel Ultrasound
Group criteria

IMPACT-III

Missing

ULCERATIVE COLITIS

PUCAI
TUMMY-UC

UCEIS
Mayo
Endoscopic
Subscore

International
Bowel Ultrasound
Group criteria

IMPACT-III

Missing

“Scientific results inevitably involve functional relations among measured variables, and ...

...the science can progress no faster than the measurement of its key variables”

Nunnally 1994, pg 7

**We are
always
measuring
and
comparing....**





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ANNE & JOE TURNER
PEDIATRIC IBD CENTER
Shaare Zedek Medical center



המרכז הרפואי
שערי צדק
SHAARE ZEDEK
MEDICAL CENTER

