1. **FDA:** It may be useful to include definitions for the terms child and adolescent. This seems obvious but one of the main points from this paper revolves around the significance of age groups to determine what the optimal instrument is, I think a level setting on the definition of terms is important.

2. I do agree with the idea to develop the instruments by age group but have another thought about "literacy" issue. There are some differences among the children within same age or grade. We should consider this subtle difference. Also I would like to emphasize cultural difference. Some culture force not to express the pain and endure it until they cannot stand. There must be different way to rate the degree of pain as well depending on their culture and languages, too.

3. It might be useful to have a summary table, chart or box listing the validated instruments - after a quick read of the document I couldn't easily tell whether validated instruments are available, for what age groups, conditions, etc.

4. I would also like to see more work with interactive electronic media. This might fall under research needs, rather than best practices, but the black and white paper visuals are so out of date for today's children! I imagine a time when children just are so puzzled by black and white paper visuals that they cannot respond!! And it may be sooner than we think.

5. The only improvement I would suggest is the replacement of the textual 'In sum,' paragraph at the conclusion of each section with a bulleted 'Key Points' summary of the main recommendations made in that section.

6. Digital technology opens up an array of opportunities not previously available for helping young children understand issues. It may be worth noting that more research in this area may be fruitful.

7. I did not see any guidance on analytical approach. If the goal ultimately is a PRO claim and if there are trials with different age group of patients. For example if the trial has combination of ages and used a pictoral version for one age group and non-pictoral version for the older age group. What would be the best approach for analysis to get aggregate data that can support label or promotional claim?

8. Overlap - each of the issues is presented as discrete criterion and yet there is overlap between them (e.g., age, ethnicity and gender – as well as other characteristics - play a role in how people respond to pictorial representations as well as the language used to describe a particular illness). Thus, the issue of cofounding and overlap among the criterion is a point worth mentioning.

9. Gender in addition to age/ethnicity plays a role and yet this is not mentioned in the paper (see book chapter). Also young adults – those between18-24 might be worth mentioning. As I mentioned, we have a call for papers in International Journal of Peds and have included them because they are “forgotten” in many ways – lost in the middle – not kids and yet not adults and most measures are not applicable. There is a journal Emerging Adulthood (Sage) that might be of interest as well.

10. Mode of administration and its impact is not mentioned but plays a role as well – especially with regard to the pediatric/adolescent field

11. Regarding “qualitative" work – cognitive debriefing only scratches the surface and is on the peripheral of true ethno-grounded research. There is a tacit understanding that anyone can be a good interviewer but this is not the case. The output is only going to be as useful and informative as the input and it is more than just “asking questions” – the linguistic and non verbal style, gender, background, experience and type of training of the interviewer play a significant role in this regard yet these aspects are rarely identified. I think this is a topic for a book chapter in and of itself. The field could be greatly informed by the work of Beach and others in the field of communications and discourse analysis.
12. Regarding parent/child – too often we present the respondent issue as either/or and that concordance is key and yet I have discussed and still believe that both perspectives are important. More work needs to be done in this area of proxy reporting because (despite FDA PRO guidance in autism for example) it is not going to go away and has impact beyond the pediatric realm – e.g., stroke patients, Alzheimer’s etc).

13. Regarding readability – how is “understanding” defined – there needs to be a standard set of criteria and definitions that are used in the field because this is one area that is lacking. The Flesch-Kincaid statistic is readily available but rarely cited for most available measures. Many do not understand how it’s is derived and its true interpretation. As I mention in the book chapter factors such as font, layout etc impact readability and the field could greatly benefit from the Reading/Education literature in this area. Mode of administration will overlap in this area.

14. Regarding Pictures – the COOP Charts took an early lead in this area with both adult and adolescent charts and McHorney et al reported in Med Care on the impact of pictures with adults (see section in book chapter and related citations)

15. Regarding future directions - we often stop short in addressing issues and I have come to believe that there is life beyond the criteria identified -- interpretation of scores and identifying meaningful differences is quite important – even with disease or condition specific measures but it does not get addressed – I didn’t mention it back in 1996 because the field was so new but added it to my 2005 book chapter. The issue with dx specific is that often everyone creates their own measure and it gets used in one or two studies but if the field is to truly evolve we need to think beyond measurement construction.

16. There needs to be some discussion of how the parent/caregiver can prepare the child for the survey or interview. Leaving this to chance may have some unintended (and probably unknown) consequences.

17. Younger children may be every bit as susceptible to peer pressure as teens are, and they also may have as much capacity for embarrassment. I think there are general assumptions about teens vs. younger kids that need careful consideration rather than blanket acceptance.

18. It would have been nice to see more discussion of how to frame the task of completing a PRO so that children can understand what is required of them and the purpose of the questions they will be asked, as well as what will be done with the answers they give, what to do if they get tired, don't want to answer a question, want to stop, etc.

19. This document is positioned as guidance on the use of PRO instruments for clinical trials of medical products. However, I believe this application is too limiting. Indeed the document has value for any research, academic or industrial, that involves the use of PRO instruments. I suggest replacing “medical product” with “health technology” throughout the document and clearly stating the broad applicability of this guidance beyond clinical trials for product registration.

20. The issues of cost and benefit of customized PRO instrument suitable for a particular age and health condition, or a universal one should be considered.

21. As the proposed guidelines highlight the importance of inclusion of qualitative data from children, parent, clinician and expert, it is a good step towards assessment, but the bias cannot be negated.

22. It is very good to have age cut offs and to include pictograms for assessment among younger groups Informant reported outcome should be used to assess observable content as much as possible.

23. To consider cross cultural issues it is necessary to reassess the age is appropriate or not in each country.
24. Guidelines are good based on the present knowledge available. There is further need of research to modify the existing instruments. Overall the report is useful and good.

25. How the PRO instrument delivered to children’s, environment plays a very important role. It should be delivered in presence or absence of parents or only the treating physicians as some children's are very sensitive and of shy nature and will not easily mix up and response will vary.

26. Handling of Bias in PRO Instrument is a very important area to be considered.

27. The issues of validity, universal content for a specific age group and across cultures, and ease of administering of PROs in children and adolescent are crucial before determining the benefit of PROs.

28. Whether the PRO instruments will be universal, or could be standardized for any therapeutic treatment in case of children and adolescent?

29. Developing a customized PRO instrument for kids and adolescent for accurate reporting will be crucial, but the feasibility and practicality of PRO instrument for kids and adolescent will be questionable for the time being.

30. Objectives / research questions are clearly stated and objectives are addressed. Needed to be tested globally.

Specific Comments

Background to the Task Force (Lines 1-25)

Introduction (Lines 26-78)

1. 

2. Line 35-37: FDA says is there an example to cite for this use?

3. Line 42: What about adapting instruments for other populations?

4. Line 53-54: FDA says to add "There is limited available guidance for research involving pediatric PRO assessment related to medical product development."

5. Line 57-58: FDA says to delete “In sum, there is limited available guidance for research involving pediatric PRO assessment related to medical product development”

6. Line 59: FDA says seems strong; should it be recommendations? can it be best practices

7. Line 59: Replace ‘effectiveness’ with ‘efficacy’ as you are specifically considering their use in RCTs to support product approval/authorization.

Good Practices in Developing and Implementing Pediatric Pro Instruments (Lines 79-723)

Good Practice 1 (Lines 81-260)

8. Line 81: FDA says Previous citation was best

9. Line 83: FDA - Consider making this Good Practice 2
10. *Page 8:* suggest discussing the role of clinician interviews earlier. In adult research, we often start with a literature review and clinician interviews to understand the concepts before conducting the qualitative work. This may not be clear to someone reading this paper who is not involved in PRO development.


12. *Line 93-95:* FDA says to add "This qualitative work, which has previously been described in detail, generally proceeds in two sequential steps, concept elicitation and cognitive interviews (Brod et al. 2009; FDA 2009; Leidy & Vernon 2008)."

13. *Lines 95-97:* As above, I perceive the narrow focus on medical product development and labeling as an unnecessary limitation.


15. *Line 120:* FDA says “cognitively able” needs a definition

16. *Lines 122-123:* When it comes to children, it must be recognized not only that they use a different word vocabulary, but that they also exhibit a "vocabulary" of behaviours that are distinctive. While the concept of behavioural observation is mentioned in the section on GP3, there is inadequate recognition in the rest of the document that children communicate mood as well as symptoms with the use of behavioural cues. These are often cross-referenced such that children who complain of a “tummy ache” may actually be experiencing other types of pain. Similarly fidgeting, listlessness, crankiness, and tiredness, are examples of important behavioural cues that a trained interviewer will be able to perceive, record and pursue for deeper meaning.

   The topic of interviewer training has not been adequately addressed. Unlike adult PROs, interviewer-administered child and adolescent PROs require special training to teach the interviewer how to communicate with a child and how to read behavioural cues. This is critical to the success of the data collection process.

17. *Line 125 - would suggest to replace " whenever possible " by " and to provide a justification if this has not been done " (rationale: children even some of those belonging to the age group 1 (line 282) may be able to reflect on and to articulate basic personal needs and there is no reason not to include them into pediatric PRO research

18. *Line 142:* use of term “disabled” in this instance may need to be clarified as one is able to elicit meaningful feedback from some disabled children depending on the type and level of disability (e.g., functional vs. cognitive, mild vs. moderate).

19. *Line 148:* Clarify most relevant perspective

20. *Lines 156, 158 and 165 - replace “clinicians” by "clinicians and nurses" (rationale: especially in hospital care nurses may be much closer to the individual pediatric patient than any other person besides the parents; NB, is there a reasons not to explicitly mention pediatricians and pediatric nurses?)

21. *Line 161.* IQWiG: Children are embedded … This is true for anybody around this world. Any person's social contexts include the family, a peer group, the job, the community …. So this is not unique for children.

22. *Line 163:* IQWiG: The impact of disease … Same as above. This also holds for adults. I often hear that certain aspects only pertain to children. But even though I am a pediatrician by training and know that there are unique aspects of child health I think we should be very critical of when and how we implement the criterion of uniqueness. Adults can likewise not participate in (daily) peer group activities (line 166f) because of an impairment.
23. Line 163: impact of symptoms on social and academic activities?

24. Line 165: suggest further subsequent discussion of how best to obtain information from clinicians, teachers, parents that can be used in instrument development.

25. Line 170: suggest the use of creative activities when eliciting concepts from children in order to keep them engaged - e.g., drawing, play doh modeling

26. Line 178-181: FDA - While I think this is true, are there any data to support this statement [and can it be cited] is this any different from a diverse set of adults in a focus group?

27. Line 179: This can also be the case with younger children.

28. line 184 - replace "parents" by "parents and other adults" (rationale: researchers may think about including parents especially in the higher age groups)

29. Line 186: what if a parent wants to listen in? If this is done through a two way mirror, should this be disclosed to the patient? Should this be taken into account when evaluating the qualitative data?

30. Line 188: and kids!

31. Line 190: Not only are the perspectives of other informants (parents, teachers, clinicians) important, but obtaining these perspectives in mixed groups is also important. Focus groups that combine children and parents or parents and clinicians may provide richer and more valid data than among a sole type of informant alone. Furthermore, the cross-informant discussion may allow for increased stability and validity of responses.

32. Line 190: Add ‘carers’ after ‘parents’

33. Line 194ff: IQWiG: Same could hold for adults. Topics such as sexual dysfunction, partnership problems because of a disease, mental illness might not be addressed in focus groups, but in individual interviews. So again I am not sure whether this is really a unique aspect for children and adolescents—though I admit that it is often very problematic for adolescents.

34. Line 196: IQWiG: May … There are many mays in this section. If there are mays, what does that mean. What are the real differences and the may would hold for any group of interviewees.

35. Line 201: IQWiG: become distracted. I find this a typically adult way of looking at children. When I was a child I remembered that many adults were much less focused and concentrating than I could. So my message: Many adults are similarly distracted in (large) focus groups and will follow an opinion leader. So again: Is this truly a unique aspect in interview with children and adolescents or does it only vary in degree etc. Even professors are often very distracted in meetings … Also many adults are influenced by their peer groups, for instance perspectives on gay and lesbian people or on handicapped are much more influenced by what is socially wanted and you might gather totally different results in anonymous individual interviews over (larger) focus groups. So be aware: This is not unique to children.

36. Line 204: I think it is very important to frame the reason for the interview in a way that the child understands why he/she is there and what is expected of them, especially younger kids. While it is a great strategy for the interviewer to begin with general questions and proceed to the more specific line of inquiry, unless there is a clear notion of the interview's purpose, the child can be confused by these introductory questions or become frightened when the conversation shifts to the questions about their health. Can you please address strategies for framing interviews and focus groups in pediatric populations?
37. **Lines 206-213:** It may be helpful to provide information on ethical and legal guidance when interviews are done in the absence of parents. There could be differences in laws and IRB requirements that need to be followed.

38. **Line 208:** the actual act of item generation is skipped over. suggest mentioning it and providing some sources for where information about this process can be found.

39. **Line 209-210:** It is ill advised to recommend that child interviews should be performed without parents whenever possible, particularly for young children. This issue was explored directly in my study of a dyad approach to quality of life assessment (Ungar WJ et al. A parent-child dyad approach to the assessment of health status and health-related quality of life in children with asthma. In press, *PharmacoEconomics*, 2012.) Young children who are interviewed alone are more likely to exhibit various forms of response bias as well as respond with set/patterned responses or missing answers. These problems can be mitigated in the presence of a parent and an interviewer who is trained to moderate the communication between parent and child. In our study, there was 20% less missing data when the child was interviewed with a parent. Again, training of the interviewer is key to ensuring that responses are valid.

The document focuses mainly on questionnaire items, response options, structure and formatting. There is no mention of the development of the preamble/instructions for completion. Although seemingly pedantic, this is almost as important as the questionnaire itself in ensuring comprehension and completeness of data, especially for self-administered questionnaires.

Similarly, the physical setting, lighting, physical comfort, rest and play breaks, how the interviewer is seated and positioned with respect to the child and parent, are all critical to successful implementation of a PRO measure and should be discussed.

The subject of the use of electronic aids is important. Some children, especially adolescents, may be more adept at completing tasks on a smart phone or tablet than the researcher. The use of electronic devices to explain concepts as well collect data is worth mentioning.

40. **Line 213:** IQWiG: For example, adults may resist discussing their difficulties with obesity in the presence of peers. I understand what you want to explain, but I could easily replace adolescents by adults and it would be equally true.

41. **Line 230:** suggest moving discussion to age to next section

42. **Line 232:** suggest mentioning that age groups may be considered during concept elicitation as well. I have seen researchers set quotas for recruitment of relevant age groups and then see if saturation is reached within each age group in order to ensure that there is sufficient coverage within each age group

43. **Line 234:** Consider noting that it is really the level of cognitive development of the child rather than age since this varies considerably among individuals

44. **Line 250:** What about assessing patient motivation to complete the questionnaire and burden? May be worth mentioning that some new e-PRO tools may provide more of a "game like" setting that motivates children and adolescents to complete their questionnaires.

45. **Line 251:** It is also important to train the parent/caregiver on how to introduce the child to the interview process, including what will happen, what is required of the child, what the interviewer will do with the child's answers, and what to do if she/he wants to stop, rest, or doesn't want to answer a question. There should also be some discussion between the parent and child about the confidentiality of the child's answers. I know the interviewer will go through all this, but it is advisable to provide the parent with what to say and ways to say it so the properly child will be prepared at the time of the interview.

46. **Line 257:** IQWiG: I know you point it out later, but I think the problem is not so much that you should conduct interviews within a narrow age grouping, but there is—as you point out later—a huge variety within each age group (line 304ff).
47. IQWiG: Section on Cognitive Interviews: Just out of personal interest: Why did you not include behavior coding for testing as well?

48. There may be too much differentiation between adolescents and children when it comes to peer pressure and feelings of shame or embarrassment. For example, Lines 178 - 179: "Furthermore, due to the complex social pressures of adolescence, some respondents in this [adolescent] age group may be reluctant to speak openly in the presence of peers". Lines 186 - 188: "Researchers should also consider whether the medical condition of interest may cause shame or embarrassment which would be more inhibiting for adolescents than for adults."

49. Apply the global health competency of conducting a situation analysis across a range of cultural, economic, and health contexts in Section title Good Practice 1: Establishing Content Validity of Pediatric PROs (Children as content experts).

50. Apply the global health competency of fundamental principles of international standards for the protection of human research subjects in diverse cultural settings; analyzing ethical and professional issues that arise in responding to public health emergencies; explaining the mechanisms used to hold international organizations accountable for public health practice standards in Section title Good Practice 1: Establishing Content Validity of Pediatric PROs (The Central Role of Children’s context).

51. Apply the global health competency of applying scientific evidence throughout program planning, implementation, and evaluation; planning evidence-based interventions to meet internationally established health targets; developing context-specific implementation strategies for scaling up best-practice interventions in Section title Good Practice 1: Establishing Content Validity of Pediatric PROs (Concept elicitation and Item Generation).

Good Practice 2 (Lines 261-401)

52. FDA - Consider making this Good Practice 1

53. Related to this, consider making 'Good Practice 2' the first Good Practice. It is important to establish the significance of the age groupings for the subsequent points.

54. The discussion regarding proxy outcomes should state up front (rather than at the end of the section) that the proxy measures should be discouraged due to frequent discrepancy between informant and child perspectives. The discussion (as written) still has statements that seem to support the use of proxy measures

55. Line 262: Consider integrating lines 228 - 244 into this section?

56. Line 275: As above, the interviewer should simply be trained in how to communicate with a child. It is not really reasonable to expect that children should be reoriented
The section on GP3 is really excellent and the best description I have seen anywhere about the subtle but important differences in proxy and observer reporting. The discussion of observational measures begs the question of the availability of instruments that focus on behavior. Are there any? One topic that is not addressed directly but explains some observed discordance between parent proxy and child reports is adaptation. A child with a disability’s sense of “normal” and their frame of reference is inherently different than a parent’s. The differences in their perceptions are not a source of error as both perspectives are valid.

57. The following statement (line 329) might be too strong, because we already have products approved on the basis of self-report in children younger than age 8.

58. Line 329: Therefore, while we encourage further research in children younger than 8 years old, self-report measures are unlikely to yield results that will be acceptable for regulatory decision-making. Line 330: Not sure everyone would agree with this comment. If the concept is simple, e.g., pain, then reliability and understanding may be greater than a complex concept
59. Line 333: I think you meant to say Group 2

60. Line 334: Reference in bracket is mentioned as “Cremeens et al” but in reference there two such studies. It is 2006a or 2006b? Kindly clarify.

61. Line 341: Here and above, I am not certain whether you are referring to children self-completing a questionnaire without assistance or whether you are also considering a different mode of administration which would be more appropriate for the young children. Perhaps this could be clarified.

62. Line 344: “in this age range” should show that it clearly refers to “under 5”

63. Line 356: suggest saying age 8-12 instead of 8 and above - the latter overlaps with the next age group

64. Line 356: The basis for the following statement is unclear. Qualitative research would be needed, but the reason (self reports in this age group are not commonly used as primary or secondary endpoints) should not be the basis. Additionally, the qualitative research need not be "extensive" it just needs to be sufficient to demonstrate the children understand the PRO as intended, just as in any other age group.

65. Line 356: However, given that self-reports of this age group are not commonly used as primary or secondary endpoints, extensive qualitative research will likely be required to convincingly demonstrate that the children truly understand the PRO measure as intended.

66. Line 382: aren’t most adult studies 18 years and up - what do we do if this 18-20 group is included in our study? Also - what do we do for studies like in asthma where studies are typically conducted in patients 12 and up? Should a different measure be used for patients 12-18/20?

67. Line 382 - The age limit of the 20s seems to be artificial and too much driven by a cultural thinking that persons aged younger than 21 may not have obtained full personal rights before the age of 21. If you think about not fully allowing persons aged 18 to the 20s being recognized similar to other adults for the sake of equally treating all adults you may want to at least discuss other age groups, e.g., the elderly, who also may have needs differing from general adulthood.

68. Line 400: when doing quantitative assessments - how do you tell between an item that responds poorly because it is not understood by children and an item that responds poorly to internal consistency because it doesn’t fit well with the other concepts measured?

69. Apply the global health competency of implementing strategies to engage marginalized and vulnerable populations in making decisions that affect their health and well-being; analyzing distribution of resources to meet the health needs of marginalized and vulnerable groups in Section title Good Practice 2: Consider Developmental Differences and Determine Age-Based Cut-offs.

Good Practice 3 (Lines 402-487)

70. Lines 407-415: The guidance on the need for separate PROs or validation in ‘young adults’ i.e., early 20’s seems to be an area that requires further discussion and perhaps a separate report. We suggest considering taking this section out of the report until there is more evidence to support this recommendation or perhaps provide clarification around the statement and highlighted phrase, “However, we recommend caution when using previously validated instruments with young adults, who may have some developmental characteristics similar to those of adolescents.” Are you implying that this age group may be immature or demonstrate developmental delays or disability depending on their condition? There is also the instance of adolescents who are gifted or advanced for their age.
IQWiG: Adults similarly encounter age-specific unique challenges with regard to level of independence (with vs. without children, with young vs. with older children etc.), personal identity career development (phases of unemployment, early stages in one’s career etc.), and relationships.

line 421- some research suggests.... may have a stronger correlation with actual patient reports.....

line 423- proxy items often yield useful data..... parent's perspective is important

Line 448 – FDA says to delete “However” from the sentence as this is a critical edit, from FDA perspective

Line 453: suggest moving this paragraph above the one previous.

Line 453- proxy reported measures have yielded impt info.....
Perhaps these could be rephrased-- e.g., although parent's perspective is important, observable measures are strongly recommended

Lines 473-479: FDA says implies FDA concordance and to date the IGERQR has not been found acceptable to my knowledge

Line 485: FDA says regarding “an informant-report measure” - would use current propsoed language of PRO and ORO

Apply the global health competency of analyzing the impact of transnational movements on population health in Section title Good Practice 3: Determine Whether an Informed-Reported Outcome Instrument is Necessary.

Good Practice 4 (Lines 488-699)
Line 488: “such as pain and emotional issues” . since emotional issues often result in observable behavioral changes, perhaps use only pain as an example.

Line 526: As noted above, there sometimes seems to be an assumption that alternative modes of administration cannot be used. It might be useful to clarify this point.

Line 556: “conducting concept elicitation research”. Provide a reference

Line 563: The following text (to line 570) basically is an expansion of lines 310 - 313. Suggest deleting the latter.

Line 568: What is a reasonable guideline for percent of extreme responses? If an age group provides a high number of extreme responses, what is recommended to address this while still keeping the instrument similar to the one administered to other age groups?

Line 589: is there such a thing as too short of a recall period? For instance, is a twice daily diary ok in children or will they not be able to accurately report on first vs. second half of the day?

Line 591ff: IQWiG: The reduction of percentage in extreme answers may not necessarily reflect that older children are able to rate their emotions better, but could also reflect a process of socialization, that is oexf adaption to the societally wanted reduced spectrum of how oneself should control their temper. Therefore, I do not fully agree with the consequences you draw.

Line 602: Not sure what "reasonable results" means.

Line 604 - I would suggest to discuss the recall period "today" separately as such a short recall period may be sufficient for many questions (e.g., symptoms report) with little bias risk.
IQWiG: When do adults mix up extended periods of time? Do they mix up experiences from different years that children could sort out much better for they experience every year as very different from the others, while many adults do not perceive a difference when year after year the same happens.

Line 618: Please change to “….by linking the timeframe to specific events…” so the reader does not mistakenly think that the health-related difficulties should be linked to specific events.

Lines 629-633: The use of shorter recall periods has consequences, such as a requirement for more frequent measurement, which may be infeasible. These consequences should be discussed as some are threats to validity.

FDA says for “never, sometimes, often, and always” of the sentence - These response options require the child to average their experience over time in addition to evaluating their experience with respect to the item content. I hope you say something to point out the complicated nature and discourage this type of response option.

Line 649: May be worth including a discussion of the power of on-line graphics and videos as instrument presentation tools. The world of PRO is poised to be dramatically overhauled (and hopefully improved) as we migrate our data collection efforts onto the web and use social media to engage and retain research subjects. These tools may be especially powerful for children and adolescents who often respond better to electronic media than adults.

IQWiG: Strengthen that pictures can be distracting. You only state that many researchers believe … I agree that pictures can help, but when I looked at figure 3 I felt I did not like that person and could not relate my experience to that person’s so this may happen in any person who has to answer this question.

IQWiG: Even as a child I found the smiley faces kind of ridiculous. So maybe we should think of other ways of expressing positive and negative feelings with regard to an item.

FDA says for “Independently” of the sentence - Say something about the need for caution when pooling these forms.

Apply the global health competency of planning evidence-based interventions to meet internationally established health targets in Section title Good Practice 4: Ensure that the Instrument is Designed and Formatted Appropriately for the Target Age Group.

Good Practice 5 (Lines 700-723)

I very much enjoyed reading this extremely interesting Task Force Report. I have only one item that I think bears adding. In Good Practice #5 :Cross-Cultural Issues (beginning at line 700), I would recommend adding a mention that if pictorials are used in the instrument they may need to be modified for each country/culture in which they will be used in order to be understandable to a child and/or informant.

FDA says in regards to “may be” – shouldn’t this be is?

Consider adding a bulleted list of the key recommendations to this section.

Apply the global health competency of applying social justice and human rights principles implementing strategies to engage marginalized and vulnerable populations in making decisions that affect their health and well-being; critiquing policies with respect to impact on health equity and social justice; analyzing distribution of resources to meet the health needs of marginalized and vulnerable groups; describing the roles and relationships of the entities influencing global health; analyzing the impact of transnational movements on population health; analyzing context-specific policy making processes that impact health; designing health advocacy strategies; describing multi-agency policy-
making in response to complex health emergencies; describing the interrelationship of foreign policy and health diplomacy in Section title Good Practice 5: Consider Cross-Cultural Issues.

Conclusions and recommendations for future research (Line 724-766)

102. Conclusions and Recommendations for Future Research (Page 32): Glad to see that a comment on “interpretation” of PRO data in the pediatric population and data from multiple raters was included as I was looking for a mention of this in the paper although I knew it probably would not be addressed as per the title of the report.

103. line 724 onwards - I do miss a short recommendation regarding optimal recall period research.

104. Line 743: suggest including that if sponsors companies conduct this type of work that it be published in order to advance the field.

105. Line 753: FDA says in regards to “informant-reported outcomes” - would recommend use of observer based be used throughout paper

106. Apply the global health competency of promoting inclusion of representatives of diverse constituencies in partnerships; communicating lessons learned to community partners and global constituencies in Section title Conclusions and Recommendations for Future Research.

References

107. Line 928: Kincaid et al. study is not mentioned anywhere in the running text of the manuscript?

108. As you may know, Pharmaco Economics will be publishing a special supplement on Child Health in 2012. I do not know how their publication schedule dovetails with your timetable for producing the ISPOR Task Force report, but it's likely that the supplement will include articles of relevance to the report (besides my own). You might want to contact Lisa Prosser (lisapros@med.umich.edu) who is the Editor of the supplement for more information.

109. Indeed a number of renown child health researchers have recognized the value of multiple perspectives in the elucidation of a child’s health status. See:
Saigal S, Rosenbaum PL, Feeny D et al. (2000). Parental perspectives of the health status and health-related quality of life of teen-aged children who were extremely low birth weight and term controls, Pediatrics, 105(3), 569–74

110. I enjoyed reading your draft ISPOR report, it will be a valuable resource for the field. You may remember I contacted you some time ago when I was writing this report for the DH in the UK http://phi.uhce.ox.ac.uk/pdf/PROMs_WithChildren_Oxford_2009.pdf
Given the discussion in your report about qualitative research with children you may be interested [or even want to reference] a paper we wrote about running focus groups with children with foot and ankle problems to generate issues/items for a PRO, see attached. Some of the methods might be considered innovative and are potentially helpful to others.

Figures and Tables
Compliments

113. The task force did a great job in considering various aspects, different viewpoints and analysis of previously published knowledge on the subjects.

114. This is an excellent and very engaging document. Although my experience has been in developing and implementing QOL tools in adult populations, I appreciate that these guidelines succinctly yet comprehensively cover those issues that are unique to children and provide an approach to each issue within each age group.

It is clear that developing and implementing PRO instruments for assessment of children and adolescents requires many more considerations than for PRO instruments used in adult populations in the context of medical product development and labeling, acceptable to the FDA or related European bodies. This task force seems to have done a valiant job in providing guidelines for each of the delineated age groups (substantiated by research in each age group), emphasizing developmental appropriateness of PROs in each age group, and stressing the importance of the pediatric patient being able to understand the differences of particular items essential for content validity.

All of the 5 Good Practice Recommendations cover the global concept and objectives of these guidelines. Each individual Good Practice Recommendation discusses not only recommendations but alerts the would-be developer to specific caveats and suggestions for further research in particular categories and strongly advocates the use of cognitive interviews to determine appropriate response options in each age group. The document succeeds as non-prescriptive, but rather a set of useful, well-researched and tried guidelines, encouraging future researchers to use them as a basis to explore and develop pediatric PRO instruments for disease states in which such tools are lacking and for which there might be new indications for drug therapy.

Excellent bibliography and examples of pediatric renderings of Likert scales.