Universiteit
Leiden
The Netherlands

Paediatric health related quality of life : a European perspective : instrument development, validation, and use in clinical practice

Baars, R.M.

Citation
Baars, R. M. (2006, March 30). *Paediatric health related quality of life : a European perspective : instrument development, validation, and use in clinical practice*. Retrieved from https://hdl.handle.net/1887/18420

Version:	Corrected Publisher's Version
License:	Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden
Downloaded from:	https://hdl.handle.net/1887/18420

Note: To cite this publication please use the final published version (if applicable).

8

Implementation of the DISABKIDS instrument: general discussion

Thus, QoL, and its measurement, can seem nebulous or unscientific compared with traditional endpoints. However, the more elusive and subjective outcomes may, in the end, be more important (C. Eiser and R. Morse, 2001).

DISABKIDS's past

The aim of the DISABKIDS project was to develop, test and implement a new European health related quality of life (HRQoL) instrument for children and adolescents between the age of 4-16 with a chronic medical condition, and their parents [1]. The DISABKIDS instrument is the first paediatric measure that was developed cross-nationally in Europe, applied a patient-derived method and includes a chronic generic module and seven condition-specific modules.

The DISABKIDS project consisted of predefined work packages (WP) (Chapter 1). The literature review (WP 1) in Medline (1985-2000) identified 8233 abstracts concerning HRQoL assessment in children and adolescents with a chronic medical condition. Several HRQoL questionnaires were reviewed, and published HRQoL domains were considered for the DISABKIDS domain structure. A total of 154 children and adolescents participated in the focus groups or interviews, 142 family members and 26 health care professionals participated in either focus groups or interviews (WP 2). A total of 3515 statements were collected from the focus group transcripts. The item development steps led to a chronic generic module with 100 items and seven condition-specific modules with 26 to 44 items which made up the pilot study instrument (WP 3). The items were translated through a forward –backward –forward translation in each country (WP 4). A total of 360 children and adolescents with a chronic medical condition and 345 parents in seven European countries participated in the pilot study (WP 5). The analysis of the pilot study resulted in a field study instrument with 57 items in the chronic generic module and between 14 and 19 in each condition-specific module (WP 6). A total of 1152 families (including 405 children and adolescents with asthma), spread over 7 European countries, participated in the field study (WP 7). After the analysis of the field study data the final DISABKIDS instrument consisted of a 37-item chronic generic module with 6 domains and seven 10 to 12-item condition-specific modules consisting of 2 domains (WP 8). The implementation of the DISABKIDS instrument is still ongoing in several countries for the paper-pencil and computer versions (WP 9).

This thesis aimed to describe and discuss some of the steps taken within the European DISABKIDS project with a specific emphasis on the results obtained for asthma.

DISABKIDS at present

The two level modular DISABKIDS instrument is now available for children and adolescents between the age of 8 and 16 years with asthma, juvenile idiopathic arthritis (JIA), atopic dermatitis, cerebral palsy (CP), cystic fibrosis (CF), diabetes and epilepsy

(Chapter 6). A short 6-item smiley module is available for the 4-7 year old children with any chronic medical condition. The instrument has been psychometrically tested in Austria, France, Germany, Greece, the Netherlands, Sweden and the United Kingdom, and is available in each of these languages in a paper-pencil and computer version. The instrument is simple to administer, the modules are relatively short and it takes about 15 minutes to complete.

Advantages

The DISABKIDS instrument has several advantages above other instruments (Box 1). The main advantages are the modular build-up, the multiple language versions and the cross-national validation.

- Two modules
- Several languages
- Applicable cross-nationally
- Several chronic conditions
- Short and easy to use
- Paper and computer version
- Wide age range
- Proxy version

Box 1. Advantages of the DISABKIDS instrument.

A unique combination is created when combining the generic module from the KIDSCREEN project with the DISABKIDS chronic generic and condition-specific modules (Chapter 1). The combination of the generic, chronic generic and condition-specific modules allows for a comprehensive assessment of HRQoL. The generic module assesses the HRQoL of any child or adolescent, with or without a chronic medical condition while the chronic generic module focuses on issues related to living with a chronic medical condition. The chronic generic module offers the possibility of comparing the HRQoL score between different chronic medical conditions. By supplementing the chronic generic module with a condition-specific module the clinician or investigator are given additional information concerning a specific condition. It is suggested that collected information from a condition-specific module relates more closely to the treatment regime and is more responsive to clinically significant changes [2-5].

Before actual HRQoL assessment can take place a questionnaire has to meet certain standards (Box 2). These criteria have been established to achieve a certain level of international conformity and facilitate the chance of incorporation in future studies or clinical use [6]. The DISABKIDS project aimed to meet the necessary requirements, yet some aspects such as responsiveness and interpretation still need to be further assessed.

- Sound theoretical basis and definition of HRQoL
- Multidimensional measurement
- Suitable for study question
- Domains are described and scored separately
- Adequate psychometrics (reliability and validity)
- Sensitive to changes over time (responsiveness)
- Norm group data available (for disease and age)
- Practical in use (administration and interpretability)
- Accepted by patients
- Appropriate to culture and lifestyle

Box 2. Recommended criteria for HRQoL measures [2,3,6-11].

Limitations

Although the design and aim of the DISABKIDS instrument sounds promising there are still several limitations and methodological issues that need to be addressed. A recurring problem is the recruitment and inclusion of participants. Selection bias is a possibility as the participants who were willing to contribute may not be representative for the population. Recruitment may have been influenced by the attitude or interest towards HRQoL, individual confidence, the willingness to do something for the paediatrician, better coping mechanism or a higher experienced HRQoL [12]. Non-responders might have more severe asthma, may lack the energy to participate or have a different view on illness and the effect it has on their lives. However, there are also several aspects that help to strengthen the validity of the findings. Central is the fact that the respondents were recruited from several European locations and the severity distribution of the asthma group was similar to other reports [13]. If a selection bias has occurred in the DISABKIDS project the observed HRQoL would probably be higher with a narrower severity distribution, compared to the population of interest. Thus, our results may underestimate the real variation in HRQoL among the different severity states and underrate the discriminative properties of the DISABKIDS instrument.

A further limitation was that the number of respondents in some chronic condition groups, cerebral palsy and atopic dermatitis in particular, was relatively small in both the pilot and the field studies. So even though the total number of participants over all conditions and countries was acceptable, the results of the separate analyses of some chronic conditions should be interpreted with caution. Although the cross-national focus has been an explicit approach of the DISABKIDS project, lack of time and resources stood in the way of testing each chronic condition in each DISABKIDS country. Only the asthma specific module was tested adequately in all seven countries (Chapter 6 and 7). However, a comparison of the asthma outcome between countries is still problematic, as some countries have only tested around 30 or 40 children and adolescents. All modules will need to be tested further in larger groups and across countries in future studies.

Another critical note relates to the DISABKIDS project as a European consortium. Within the European project, all countries worked individually on each work package. Although care was taken to stress uniformity in the group (such as supplying a manual for the focus groups, planning regular DISABKIDS meetings and describing every work package in detail) each DISABKIDS member had a considerable amount of autonomy. There was no opportunity to monitor how investigators in each country completed the work packages and no way of checking aspects such as the method of recruitment or data collection. Several factors could have played a role, including personal interpretations and interests, hospital facilities, time constraints and earlier research experience. For example, focus groups were used in the DISABKIDS project to take into account the child and adolescent's own ideas and language (Chapter 3 and 4). The literal transcripts were available in each national language and the investigator was responsible for the selection of statements and the translation into English. As there was no official translation the quality of the supplied English statement could not be guaranteed. The meaning of the original statement may have been altered, which could influence the chance of being selected as final instrument item. A possible solution would have been to use expert or panel translators, supply training sessions or perform these tasks with an international group to facilitate European conformity [14,15]. We emphasise the importance of training, as the quality of the collected data is very much tied to the skills of the investigator (Box 3).

The bottom-up (patient-derived) methodology that was applied in the DISABKIDS project was another reason for debate. The collection of the HRQoL statements from the focus groups and interviews were the basis of the DISABKIDS instrument and were applied to secure that the child and adolescent's opinion was incorporated (Chapter 3 and 4). This patient-derived method was followed by the (top-down) investigator's judgement for the selection of the final items (Chapter 5). This top-down procedure conflicted with the aim of developing the DISABKIDS instrument through a bottom-up procedure (child and adolescent input). With a patient-derived method one would prefer to have the children and adolescents select the important items but the extensive statement pool (3515 statements) was thought to be too large for them [16-19]. To compensate for the top-down procedure the child and adolescent's opinion was again included into the pilot test when they were asked to approve the selected items and judge them on comprehension and applicability in the cognitive interview [20-22].

- Recruitment of the participants
- Moderating the focus groups
- Identifying the appropriate statements from the focus group transcripts
- Translation of the HRQoL statements and items
- Rewriting statements to items
- Data input
- Statistical analyses

Box 3. Situations in which specific guidelines, expert translators, training sessions or international working groups would be advised.

On the other hand, because most aspects identified in the DISABKIDS asthma focus groups had been discussed in earlier publications (Chapter 4), one might question whether it is still necessary to include the patient's opinion when developing a questionnaire. Despite the extensive research of certain conditions (i.e. asthma) we still advocate to include the patients' opinions. Information on some chronic conditions (i.e. cerebral palsy or atopic dermatitis) is still limited and new results and different viewpoints may be yielded through patient-derived methods. Furthermore, the main advantage of the focus groups in the DISABKIDS project was the cross-national recurrence of issues and the combination of patient, parent and clinician's data.

A further drawback in our method is that we cannot assume that all important issues were included in the DISABKIDS instrument. Not all relevant topics may have been discussed in the focus groups or some children may have found it difficult to talk about certain topics. It is also possible that some topics were removed in the item selection phase (Chapter 5). The cross-national developmental process disregarded some items that may have been important in certain countries (for instance items concerning pets or riding a bike to school). A possibility would have been to run focus groups till no new issues were presented [12,23,24]. This was not possible in the DISABKIDS project as each work package was set in a certain time frame.

In short, there where a number of methodological issues and limitations during the development of the DISABKIDS instrument. Even so, the initial psychometric results and the first implementation experiences by clinicians and investigators are promising. Future research will help to explore the implementation possibilities.

DISABKIDS's future

The DISABKIDS instrument can play an important part in the future of paediatric HRQoL assessment. The two level modular build-up and the multiple language versions of the DISABKIDS instrument makes it utilizable in several circumstances, including population studies, clinical trials and individual assessment.

- **HRQoL evaluation:** includes mainly the description of a population group or a comparison between patient groups [25-31,31,32]. It can give the clinician a fair description of a group but is of little use for the care of the individual patient. The availability of the different DISABKIDS language versions makes the instrument suitable for group and cross-national comparisons.
- **HRQoL in clinical trials:** is mainly used to compare the outcome of different treatments within a group or to evaluate therapeutic effectiveness between groups [2,33,34]. While the use of HRQoL is increasingly being implemented in adult clinical trials the inclusion of HRQoL in paediatric clinical trials is still limited [35-38]. In the future the DISABKIDS instrument can be of use in (cross-)national clinical trials. Results are of use to the clinician and the general patient group but have no role in the individual evaluation and treatment of the patient.

- **HRQoL in clinical practice:** is aimed at the care of the individual. Objective measures of disease or clinical judgement in for instance asthma only weakly correlate with how a patient feels and functions (Chapter 7) [39-42]. HRQoL assessment can therefore provide a broader picture of health and provide insight into the impact of a chronic medical condition on the daily life of an individual child or adolescent. Knowledge of the HRQoL status can improve medical guidance to the children and their parents, identify those that need particular attention, screen for psychosocial problems or monitor the patient's progress [43]. The children and adolescent's HRQoL can be assessed with the help of a paper-pencil or computer-assisted instrument. The use of the DISABKIDS instrument in clinical practice will still need to be tested.

While the first psychometric results of the DISABKIDS instrument sound promising and the design comes with several advantages it is still essential to further test the current instrument in several situations to judge where improvements are necessary (Box 4). For instance additional testing of the modules is necessary in each country and for each module in sufficiently large groups. The chronic generic module can also be tested for applicability in other chronic medical conditions, for example haemophilia, heart disease or obesity. There is also need for more evidence that the instrument can function as an individual screening tool, which includes higher levels of reliability (Cronbach's alpha ≥ 0.9)[6,44].

- Psychometric properties in each country with sufficiently large groups
- Psychometric properties for each chronic condition in larger groups
- Comparisons to existing condition-specific HRQoL questionnaires
- Comparisons to clinical outcome and physiologic assessment of disease severity
- Sensitivity and the responsiveness to change in individual patients
- Longitudinal data to assess long-term changes in measured HRQoL
- Use in comparing interventions, treatment changes or different medications
- Relevance to clinical practice
- Appropriateness for cultural background of the patient

Box 4. Aspects that need to be studied further.

However, continuation of the DISABKIDS project is not uncomplicated and depends on external factors as time and resources. Since the European funding of the DISABKIDS project has ended there is a danger of discontinuation. Nevertheless, we still aim to interest investigators and clinicians in the continuation of testing and implementing the DISABKIDS instrument. The current advantages of the DISABKIDS instrument, especially the possibility of working with an international consortium, should give the instrument a fair chance. The available DISABKIDS manual should also assist in the proceedings to look for cross-national collaborations in the future to further validate and implement the DISABKIDS instrument.

HRQoL assessment in clinical practice; implementation philosophy

Since the management of chronic medical conditions revolves more around care than cure and HRQoL has been recognised as important to the care of children and adolescents, the number of paediatric HRQoL questionnaires has grown over the last decades [45,46]. There is however, still little evidence of their relevance in and influence on adult and paediatric clinical practice and the current need is to discuss why HRQoL assessment is not systematically implemented (Chapter 2)[37,47-51].

Experienced barriers

One problem is that there are several definitions of quality of life (QoL). There is no gold standard as to what it represents or how it can be measured as it includes subjective issues and the concept depends on the applied perspective (social, economical, psychological) [2,7,45,52,53]. A similar problem concerns HRQoL [54]. One can question whether we are able to reliably assess a subjective concept as HRQoL. A person's perception of health and expectations are related to the individual and can vary over time [55]. Further complicating is that when HRQoL is assessed in children and adolescents there are even more practical aspects to consider as cognitive development, changing perspectives, disease knowledge and age related activities, all of which can influence HRQoL outcome [56]. There is no straightforward way of solving these aspects.

Another issue that needs to be considered is that clinicians may feel that identified problems lay outside the traditional area of medical care and may not see it as their task to discuss HRQoL issues with their patients [33,47,49,50]. Clinicians were found to focus on symptoms and physical functioning but rarely on emotional or social problems (Chapter 4)[47,57-60]. A dilemma is that if psychosocial problems are revealed and the clinician feels incapable of interfering with these problems, they may be reluctant to adopt HRQoL measures. This is one of the reasons why the clinicians' perspective also needs to be taken into account during the development of a HRQoL questionnaire for clinical use (Chapter 2). The clinician may contribute by suggesting which aspects to measure so that the questionnaire relates to issues he feels he can intervene in. Strategies can also be discussed on how a questionnaire is best implemented and experienced barriers can be avoided. The possibility of giving HRQoL feedback to other health care professionals such as (specialised) nurses or psychologists also need to be considered [48,49].

Although some patients do not feel comfortable about discussing certain issues with their clinicians, the majority of patients want their clinicians to assess HRQoL aspects and feel this is useful to clinical practice [47,48,57-59,61,62]. Communication is seen as a crucial element in the quality of health care and can positively influence patient health outcome [63-66].

In summary, there are still ample problems that need to be solved before HRQoL is regularly assessed in clinical practice. Fortunately, there is evidence that clinicians are interested in HRQoL outcome, especially when it concerns a chronic medical condition

(Chapter 2 and 4)[48-50,67]. It is now essential to identify and reduce experienced barriers (Chapter 2) to encourage the implementation of HRQoL assessment in clinical practice on a regular basis (Box 5).

- HRQoL not seen as a priority in clinical practice
- Unfamiliar with HRQoL questionnaires
- Insufficient training in and knowledge of HRQoL
- Unavailability of appropriate questionnaires
- Unsatisfactory psychometric properties
- No proof of clinical relevance
- Insufficient feasibility (ease of collection and use)
- Costs of implementation
- Limited time and resources
- No intervention guidelines

Box 5. Main barriers for the use of HRQoL questionnaires in clinical practice [47-49,68].

Requirements necessary before clinical implementation

A fundamental concern is whether a questionnaire, like the DISABKIDS instrument, can and will be used for individual patient assessment. Current studies inform us more about experienced barriers and lack of clinical impact than about required essentials for successful and meaningful use of HRQoL assessment in daily clinical practice [69]. Thus, if HRQoL questionnaires are to be used routinely and become an important part of clinical practice (especially paediatric health care) the given obstacles (Box 5) need to be dealt with and HRQoL assessment needs to be promoted. Requirements to achieve acceptance of HRQoL assessment include: informing clinicians about available questionnaires, proving clinical relevance and providing guidelines for interpretation of HRQoL outcome scores (Box 6). If the necessary requirements are achieved the HRQoL questionnaire is more likely to be accepted by clinicians and to be included as outcome in the care for the patient.

Promotional needs:
- Information: increase familiarity with HRQoL and publish data in clinical journals
- Training: in implementation possibilities and interpretation of HRQoL outcome
- Health care professionals: stimulate a multidisciplinary approach in HRQoL assessment

Questionnaire factors:
- Content: includes items regarding important aspects for the patient
- Design: short, practical, computerised
- Psychometrics: reliable, valid, sensitive to change and availability of norm data
- Outcome: clinical relevance

Practical requirements:
- Implementation: easily available, quick to complete and administer
- Scoring: simple, provided promptly and in a useful format
- Interpretation: guidelines available for easy interpretation
- Intervention: strategies to translate outcome into specific interventions

Box 6. Requirements to promote HRQoL assessment in clinical practice [9,33,43,47-50,53,70-72].

Is there proof of clinical relevance?

The importance of HRQoL assessment in clinical practice is stressed as it is assumed to provide meaningful clinical information. Various suggestions are provided of how HRQoL assessment may be of benefit to individual patient care (Box 7) but clinical relevance is not always clear-cut [48,61,62,73,74]. Greenhalgh et al. (2005) have described the mechanisms between HRQoL intervention and expected outcome in a model, demonstrating its complexity [47]. The challenge is to decide what outcome to measure as several processes (communication, treatment response, recognition of problems) can be influenced before the final outcome of improved HRQoL or patient satisfaction is realized [47,61].

- Identifying and prioritising problems
- Assess treatment efficiency
- Monitoring disease progression
- Assisting in informed treatment changes
- Facilitating clinician-patient communication
- Improving patient satisfaction
- Allocating health care resources

Box 7. Suggested use of HRQoL measures in clinical practice [9,48,51,61,72,75].

A number of studies have reported on the impact of HRQoL feedback to clinicians. In general there is limited proof of influence on medical decisions (referring to others, treatment changes, clinical tests), patient satisfaction or HRQoL outcome [47,61-63,73,75]. Feedback of HRQoL assessment to clinicians does affect the extent in which HRQoL issues are discussed in a consultation, improves identification of psychological and social problems and increases the clinicians' awareness of the patient's HRQoL [47,61,63,73,75,76]. Only a few studies demonstrated that this increased recognition of HRQoL problems is subsequently associated with clinical intervention (follow-up appointments, counselling or referral) [48,59,76]. Clinicians may not consider HRQoL issues to be important enough to adapt their treatment or referrals to it. The facilitated communication, resulting from the HRQoL feedback, may be sufficient for clinicians [47-49,62]. Disappointingly there are currently no implementation studies available that describe individual HRQoL assessment in paediatric care.

What do we gain through HRQoL assessment?

There is a growing awareness that the clinician, parent and child or adolescent differ in their perception of HRQoL, disease severity and treatment expectations (Chapter 4 and 7) [77-81]. These differences, together with insufficient clinician-patient communication can lead to misunderstandings and dissatisfied patients [65]. If HRQoL assessment can improve the clinician-patient communication and patient health outcome, this may well be a sufficient reason to implement HRQoL measures [63,65]. Although this has not been proven in paediatric care, common sense tells us that improved communication can facilitate the recognition and acknowledgment of problems and can enable clinicians to improve the quality of care of the child and adolescent.

Implementation in asthma care

The asthma focus groups and interviews illustrated that there is a considerable impact on the life of a child and adolescent with asthma (Chapter 4). Physical limitations, which were often linked to social issues, were a dominant theme and non-compliance seemed to be linked to insufficient knowledge or denial. Clinicians found it hard to recognise these important issues in the life of a child or adolescent with asthma and felt that awareness of and familiarity with these problems might assist them in improving the care for their patients (Chapter 2 and 4). If children or adolescents feel misunderstood by their clinician, or for that matter their parents, this can negatively influence their clinician-patient relationship and may even affect their adherence to treatment.

The DISABKIDS instrument can evaluate a patient's HRQoL and help the clinician to focus on areas of particular importance to the child and adolescent. A future prospective could be to ask patients to complete the DISABKIDS instrument before consultation, preferably on a computer. The computerised instrument can be easily administered, save time and supply the clinician with immediate feedback of the patient's HRQoL status [9,73,82,83]. If the DISABKIDS computer version is implemented this can give an instant readout of the 0-100 score on each domain and compare this to a previous assessment or to the population norm data. The 37-item chronic generic module can provide general data on the impact of living with asthma. The 11-item asthma specific module can supply the clinician with asthma-related issues by concentrating on specific limitations and fears related to asthma. Any conspicuous scores can then be discussed with the patient. For instance if a low score on the medication domain is discussed with the child this could make clear that the child is rebelling against the medication because he or she doesn't feel it is doing any good. Clinical parameters or regular consultations may not have identified this problem. Problematic issues can be discussed, problems can be dealt with or explained and if necessary the child or adolescent can be referred to the appropriate health care professional (social worker, psychologist).

Conclusion

While HRQoL may seem ill defined and its assessment unscientific, to the patient this subjective outcome may be more important than biomedical endpoints [45]. Although the inadequate proof of clinical relevance may currently be the main reason for the limited use of HRQoL assessment in clinical practice, the expectation is that in the future a growing number of clinicians will incorporate routine HRQoL assessment [62,72]. In the mean time considerable work needs to be done to prove the benefit of HRQoL assessment in clinical practice and to overcome experienced barriers.

The European DISABKIDS project has come a long way in the development of a new cross-national HRQoL instrument for children and adolescents with a chronic medical condition. The DISABKIDS instrument can play an important role in future paediatric HRQoL assessment. The modular build up and cross-national development

also offers advantages for assessment on a national and international level in HRQoL evaluation studies and clinical studies. However, further evaluation of the DISABKIDS instrument is needed to test its performance as individual measure in clinical practice and prove its relevance to clinicians. This refinement can only be achieved through future implementation, as understanding how current measures perform in practice facilitates improvements [84].

We may need to restrain our expectations of the impact of HRQoL assessment on clinical practice. As there is currently insufficient evidence that HRQoL assessment changes the treatment and referral plans of the clinician we might need to accept that an improved clinician-patient communication is sufficient reason to implement HRQoL questionnaires [47,63]. Improved communication can be an important component of the overall HRQoL assessment of a patient. Clinicians can benefit from the information presented to them and use it to facilitate communication and discuss problematic areas. Yet, one does need to keep in mind that HRQoL assessment will never address all issues that are important to the patient and that it can only supplement current clinical measures or communication and does not substitute them.

References

1. Bullinger M, Schmidt S, Petersen C. Assessing quality of life of children with chronic health conditions and disabilities: a European approach. Int.J.Rehabil.Res.2002; 25:197-206.
2. Fitzpatrick R, Davey C, Buxton MJ, Jones DR. Evaluating patient-based outcome measures for use in clinical trials. Health.Technol.Assess.1998; 2:i-74.
3. Eiser C, Morse R. Quality-of-life measures in chronic diseases of childhood. Health Technol.Assess.2001; 5:1-157.
4. Guyatt GH, King DR, Feeny DH, Stubbing D, Goldstein RS. Generic and specific measurement of health-related quality of life in a clinical trial of respiratory rehabilitation. J.Clin.Epidemiol.1999; 52:187-192.
5. McSweeny AJ, Creer TL. Health-related quality-of-life assessment in medical care. Dis.Mon.1995; 41:1-71.
6. Assessing health status and quality-of-life instruments: attributes and review criteria. Qual.Life.Res.2002; 11:193-205.
7. Spieth LE, Harris CV. Assessment of health-related quality of life in children and adolescents: an integrative review. J.Pediatr.Psychol.1996; 21:175-193.
8. Doward LC, Meads DM, Thorsen H. Requirements for quality of life instruments in clinical research. Value Health.2004; 7 Suppl 1:S13-S16.
9. Higginson IJ, Carr AJ. Measuring quality of life: using quality of life measures in the clinical setting. BMJ 2001; 322:1297-1300.
10. Cramer JA. Principles of health-related quality of life: assessment in clinical trials. Epilepsia.2002; 43:1084-1095.
11. Wallander JL, Schmitt M, Koot HM. Quality of life measurement in children and adolescents: issues, instruments, and applications. J.Clin.Psychol.2001; 57:571-585.
12. Sim J. Collecting and analysing qualitative data: issues raised by the focus group. J.Adv.Nurs.1998; 28:345-352.
13. Rosier MJ, Bishop J, Nolan T, Robertson CF, Carlin JB, Phelan PD. Measurement of functional severity of asthma in children. Am.J.Respir.Crit.Care Med.1994; 149:1434-1441.
14. Swaine-Verdier A, Doward LC, Hagell P, Thorsen H, McKenna SP. Adapting quality of life instruments. Value.Health.2004; 7 Suppl 1:S27-S30.
15. The World Health Organization Quality of Life assessment (WHOQOL): position paper from the World Health Organization. Soc.Sci.Med.1995; 41:1403-1409.
16. Townsend M, Feeny DH, Guyatt GH, Furlong WJ, Seip AE, Dolovich J. Evaluation of the burden of illness for pediatric asthmatic patients and their parents. Ann.Allergy 1991; 67:403-408.
17. Griffiths AM, Nicholas D, Smith C, Munk M, Stephens D, Durno C, Sherman PM. Development of a quality-of-life index for pediatric inflammatory bowel disease: dealing with differences related to age and IBD type. J.Pediatr.Gastroenterol.Nutr.1999; 28:S46-S52.

18. Richardson G, Griffiths AM, Miller V, Thomas AG. Quality of life in inflammatory bowel disease: a cross-cultural comparison of English and Canadian children. J.Pediatr. Gastroenterol.Nutr.2001; 32:573-578.
19. Rutishauser C, Sawyer SM, Bond L, Coffey C, Bowes G. Development and validation of the Adolescent Asthma Quality of Life Questionnaire (AAQOL). Eur.Respir.J. 2001; 17:52-58.
20. Petersen C, Schmidt S, Power M, Bullinger M, and the DISABKIDS group. Development and pilot-testing of a health-related quality of life chronic generic module for children and adolescents with chronic health conditions: a European per spective. Qual.Life.Res 2005. (In Press)
21. Quittner AL, Sweeny S, Watrous M, Munzenberger P, Bearss K, Gibson NA, Fisher LA, Henry B. Translation and linguistic validation of a disease-specific quality of life measure for cystic fibrosis. J.Pediatr.Psychol.2000; 25:403-414.
22. Barofsky I. Cognitive aspects of quality of life assessment. In Spilker B (ed). Quality of life and pharmacoeconomics in clinical trials. Philadelphia: Lippincott-Raven; 1996:107-115.
23. McEwan MJ, Espie CA, Metcalfe J, Brodie MJ, Wilson MT. Quality of life and psychosocial development in adolescents with epilepsy: a qualitative investigation using focus group methods. Seizure.2004; 13:15-31.
24. McLafferty I. Focus group interviews as a data collecting strategy. J.Adv.Nurs.2004; 48:187-194.
25. Brunner HI, Giannini EH. Health-related quality of life in children with rheumatic diseases. Curr.Opin.Rheumatol.2003; 15:602-612.
26. Kolsteren MM, Koopman HM, Schalekamp G, Mearin ML. Health-related quality of life in children with celiac disease. J.Pediatr.2001; 138:593-595.
27. Austin JK, Smith MS, Risinger MW, McNelis AM. Childhood epilepsy and asthma: comparison of quality of life. Epilepsia.1994; 35:608-615.
28. Hallstrand TS, Curtis JR, Aitken ML, Sullivan SD. Quality of life in adolescents with mild asthma. Pediatr.Pulmonol.2003; 36:536-543.
29. Austin JK, Huster GA, Dunn DW, Risinger MW. Adolescents with active or inactive epilepsy or asthma: a comparison of quality of life. Epilepsia.1996; 37:1228-1238.
30. Loonen HJ, Grootenhuis MA, Last BF, Koopman HM, Derkx HH. Quality of life in paediatric inflammatory bowel disease measured by a generic and a disease-specific questionnaire. Acta.Paediatr.2002; 91:348-354.
31. Sawyer MG, Reynolds KE, Couper JJ, French DJ, Kennedy D, Martin J, Staugas R, Ziaian T, Baghurst PA. Health-related quality of life of children and adolescents with chronic illness--a two year prospective study. Qual.Life.Res.2004; 13:1309-1319.
32. Okelo SO, Wu AW, Krishnan JA, Rand CS, Skinner EA, Diette GB. Emotional quality-of-life and outcomes in adolescents with asthma. J.Pediatr.2004; 145:523-529.
33. Wu AW, Cagney KA. The role of quality of life assessments in medical practice. In Spilker B (ed). Quality of life and pharmacoeconomics in clinical trails. Philadelphia: Lippincott-Raven; 1996:517-522.

34. Beenakker EA, Fock JM, Van Tol MJ, Maurits NM, Koopman HM, Brouwer OF, Van der Hoeven JH. Intermittent prednisone therapy in Duchenne muscular dystrophy: a randomized controlled trial. Arch.Neurol.2005; 62:128-132.
35. Quality of life and clinical trials. Lancet.1995; 346:1-2.
36. Sanders C, Egger M, Donovan J, Tallon D, Frankel S. Reporting on quality of life in randomised controlled trials: bibliographic study. BMJ 1998; 317:1191-1194.
37. Clarke SA, Eiser C. The measurement of health-related quality of life (QOL) in paediatric clinical trials: a systematic review. Health.Qual.Life Outcomes 2004; 2:66.
38. Bender BG. Measurement of quality of life in pediatric asthma clinical trials. Ann. Allergy Asthma Immunol.1996; 77:438-445.
39. Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. Qual.Life.Res.1996; 5:35-46.
40. van der MT, Postma DS, Schreurs AJ, Bosveld HE, Sears MR, Meyboom dJ. Discriminative aspects of two generic and two asthma-specific instruments: relation with symptoms, bronchodilator use and lung function in patients with mild asthma. Qual.Life Res.1997; 6:353-361.
41. Rowe BH, Oxman AD. Performance of an asthma quality of life questionnaire in an outpatient setting. Am.Rev.Respir.Dis.1993; 148:675-681.
42. Carranza R, Jr., Edwards L, Lincourt W, Dorinsky P, ZuWallack RL. The relationship between health-related quality of life, lung function and daily symptoms in patients with persistent asthma. Respir.Med.2004; 98:1157-1165.
43. Fitzpatrick R, Fletcher A, Gore S, Jones D, Spiegelhalter D, Cox D. Quality of life measures in health care. I: Applications and issues in assessment. BMJ 1992; 305:1074-1077.
44. Nunnally JC, Bernstein IH. Psychometric theory. New York: McGraw-Hill; 1994.
45. Eiser C, Morse R. The measurement of quality of life in children: past and future perspectives. J.Dev.Behav.Pediatr.2001; 22:248-256.
46. Andelman RB, Zima BT, Rosenblatt AB. Quality of life of children: toward conceptual clarity. In Maruish ME (ed). The use of psychological testing for treatment planning and outcomes assessment. Mahwah, NJ: Lawrence Erlbaum; 1999:1383-1413.
47. Greenhalgh J, Long AF, Flynn R. The use of patient reported outcome measures in routine clinical practice: lack of impact or lack of theory? Soc.Sci.Med.2005; 60:833-843.
48. Greenhalgh J, Meadows K. The effectiveness of the use of patient-based measures of health in routine practice in improving the process and outcomes of patient care: a literature review. J.Eval.Clin.Pract.1999; 5:401-416.
49. Baars RM, van der Pal SM, Koopman HM, Wit JM. Clinicians' perspective on quality of life assessment in paediatric clinical practice. Acta.Paediatr.2004; 93:1356-1362.
50. Taylor KM, Macdonald KG, Bezjak A, Ng P, DePetrillo AD. Physicians' perspective on quality of life: an exploratory study of oncologists. Qual.Life Res.1996; 5:5-14.

51. Gilbody SM, House AO, Sheldon T. Routine administration of Health Related Quality of Life (HRQoL) and needs assessment instruments to improve psychological outcome--a systematic review. Psychol.Med.2002; 32:1345-1356.
52. Anderson KL, Burckhardt CS. Conceptualization and measurement of quality of life as an outcome variable for health care intervention and research. J.Adv.Nurs.1999; 29:298-306.
53. Wood-Dauphinee S. Assessing quality of life in clinical research: from where have we come and where are we going? J.Clin.Epidemiol.1999; 52:355-363.
54. Doward LC, McKenna SP. Defining patient-reported outcomes. Value Health.2004; 7 Suppl 1:S4-S8.
55. Carr AJ, Gibson B, Robinson PG. Measuring quality of life: Is quality of life determined by expectations or experience? BMJ 2001; 322:1240-1243.
56. Harding L. Children's quality of life assessments: a review of generic and health related quality of life measures completed by children and adolescnets. Clin.Psychol. Psychother.2001; 8:79-96.
57. Schor EL, Lerner DJ, Malspeis S. Physicians' assessment of functional health status and well-being. The patient's perspective. Arch.Intern.Med.1995; 155:309-314.
58. Detmar SB, Aaronson NK, Wever LD, Muller M, Schornagel JH. How are you feeling? Who wants to know? Patients' and oncologists' preferences for discussing health-related quality-of-life issues. J.Clin.Oncol.2000; 18:3295-3301.
59. Jacobs JE, van de Lisdonk EH, Smeele I, van Weel C, Grol RP. Management of patients with asthma and COPD: monitoring quality of life and the relationship to subsequent GP interventions. Fam.Pract.2001; 18:574-580.
60. Rothwell PM, McDowell Z, Wong CK, Dorman PJ. Doctors and patients don't agree: cross sectional study of patients' and doctors' perceptions and assessments of disability in multiple sclerosis. BMJ 1997; 314:1580-1583.
61. Detmar SB, Muller MJ, Schornagel JH, Wever LD, Aaronson NK. Health-related quality-of-life assessments and patient-physician communication: a randomized controlled trial. JAMA 2002; 288:3027-3034.
62. Wagner AK, Ehrenberg BL, Tran TA, Bungay KM, Cynn DJ, Rogers WH. Patient-based health status measurement in clinical practice: a study of its impact on epilepsy patients' care. Qual.Life Res.1997; 6:329-341.
63. Velikova G, Booth L, Smith AB, Brown PM, Lynch P, Brown JM, Selby PJ. Measuring quality of life in routine oncology practice improves communication and patient wellbeing: a randomized controlled trial. J.Clin.Oncol.2004; 22:714-724.
64. Laine C, Davidoff F, Lewis CE, Nelson EC, Nelson E, Kessler RC, Delbanco TL. Important elements of outpatient care: a comparison of patients' and physicians' opinions. Ann.Intern.Med.1996; 125:640-645.
65. Stewart MA. Effective physician-patient communication and health outcomes: a review. CMAJ 1995; 152:1423-1433.
66. Detmar SB, Aaronson NK. Quality of life assessment in daily clinical oncology practice: a feasibility study. Eur.J.Cancer 1998; 34:1181-1186.

67. Walsh DL, Emrich LJ. Measuring cancer patients' quality of life. A look at physician attitudes. N.Y.State.J.Med.1988; 88:354-357.
68. Morris J, Perez D, McNoe B. The use of quality of life data in clinical practice. Qual. Life Res.1998; 7:85-91.
69. Thornicroft G, Slade M. Are routine outcome measures feasible in mental health? Qual.Health Care 2000; 9:84.
70. Guillemin F. Functional disability and quality-of-life assessment in clinical practice. Rheumatology (Oxford) 2000; 39 Suppl 1:17-23.
71. Bezjak A, Ng P, Skeel R, DePetrillo AD, Comis R, Taylor KM. Oncologists' use of quality of life information: results of a survey of Eastern Cooperative Oncology Group physicians. Qual.Life Res.2001; 10:1-13.
72. McHorney CA, Earl BD, Jr. A qualitative study of patients' and physicians' views about practice-based functional health assessment. Med.Care 2002; 40:1113-1125.
73. Taenzer P, Bultz BD, Carlson LE, Speca M, DeGagne T, Olson K, Doll R, Rosberger Z. Impact of computerized quality of life screening on physician behaviour and patient satisfaction in lung cancer outpatients. Psychooncology 2000; 9:203-213.
74. Kazis LE, Callahan LF, Meenan RF, Pincus T. Health status reports in the care of patients with rheumatoid arthritis. J.Clin.Epidemiol.1990; 43:1243-1253.
75. Espallargues M, Valderas JM, Alonso J. Provision of feedback on perceived health status to health care professionals: a systematic review of its impact. Med.Care 2000; 38:175-186.
76. Rubenstein LV, McCoy JM, Cope DW, Barrett PA, Hirsch SH, Messer KS, Young RT. Improving patient quality of life with feedback to physicians about functional status. J. Gen.Intern.Med.1995; 10:607-614.
77. Loonen HJ, Derkx BH, Griffiths AM. Pediatricians overestimate importance of physical symptoms upon children's health concerns. Med.Care.2002; 40:996-1001.
78. Janse AJ, Gemke RJ, Uiterwaal CS, van dT, I, Kimpen JL, Sinnema G. Quality of life: patients and doctors don't always agree: a meta-analysis. J.Clin.Epidemiol.2004; 57:653-661.
79. Theunissen NC, Vogels TG, Koopman HM, Verrips GH, Zwinderman KA, Verloove-Vanhorick SP, Wit JM. The proxy problem: child report versus parent report in health-related quality of life research. Qual.Life Res.1998; 7:387-397.
80. Eiser C, Morse R. Can parents rate their child's health-related quality of life? Results of a systematic review. Qual.Life Res.2001; 10:347-357.
81. Sung L, Young NL, Greenberg ML, McLimont M, Samanta T, Wong J, Rubenstein J, Ingber S, Doyle JJ, Feldman BM. Health-related quality of life (HRQL) scores reported from parents and their children with chronic illness differed depending on utility elicitation method. J.Clin.Epidemiol.2004; 57:1161-1166.
82. Velikova G, Wright EP, Smith AB, Cull A, Gould A, Forman D, Perren T, Stead M, Brown J, Selby PJ. Automated collection of quality-of-life data: a comparison of paper and computer touch-screen questionnaires. J.Clin.Oncol.1999; 17:998-1007.

83. Koopman HM, Baars RM, Segaar RW. The use of computer-aided health-related quality-of-life questionnaires for children with a chronic disease and their parents. The Ear Foundation. 33-44. 2003. Oxford, Hughes associates. Measuring the Immeasurable? Proceedings of a Conference on Quality of Life in Deaf Children. 17-5-2002.
84. Eiser C, Morse R. A review of measures of quality of life for children with chronic illness. Arch.Dis.Child.2001; 84:205-211.