Chapter 11 from Theunissen, N.C.M. (1999). Health related quality of life in children. Ph.D. Thesis Leiden University Medical Center. Ridderkerk, The Netherlands: Ridderprint. ISBN: 90-9013294-5
Referred to at http://www.ntheunissen.nl

11 General discussion

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In this thesis, we investigated Health related Quality of Life (HRQoL) in children. As a generally accepted definition or theoretical framework is missing, we defined HRQoL as: the individual's perception of problems in health status, combined with the affective responses to such problems. In this definition Health Status (HS) is the assessment by a person of his or her own health. The 'health' component in HRQoL refers to quality of life as a result of a certain state of health, which involves physical, psychological as well as social functioning. The definition of HRQoL incorporates individual and culturally determined differences in coping with HS problems and reflects internal standards about HRQoL, factors which are emphasised by several authors.[1-5] Furthermore, we subscribe to the notion that HRQoL is multi-factorial (physical, psychological and social well-being), patient self-administered, subjective and variable over time.[6,7] Although the studies described in the previous chapters served various purposes, four themes arose repeatedly: the difference between HRQoL and HS, measuring HRQoL in children, the choice of an informant on the child's HRQoL, and the ideas about how much HRQoL is related to health. In the next paragraphs these themes are discussed.

11.1 HRQoL versus HS

Throughout the thesis it was stated that HRQoL differs from HS. In both constructs the person gives a subjective assessment, but in HS he or she describes the *quantity* of problems, and in HRQoL the person describes the *emotional impact* that the problems have on the person's life. When we started studying HRQoL in children in 1994, most available instruments measuring "quality of life" used a HS approach. This is illustrated by the review in Chapter 7, in which half of the longitudinal studies used a HS approach in defining HRQoL as was described in Table 2. This could be explained by the fact that HRQoL is a construct originating from the medical tradition. In that tradition it is unusual to incorporate subjective opinions, which are viewed as unscientific.[8] A construct in which affective evaluations of the patients

themselves are included, is therefore even more unusual. As long as children with severe disorders were studied, for instance with cancer, it was considered obvious that the HRQoL of these children was low. When the HRQoL concept became more popular, children with less severe disorders were studied as well. In these situations it was recognised that children with a minor disorder could live a happy life. This recognition probably created an opening for the study of subjective and individual differences in dealing with HS. Nowadays, scientists operating in the medical tradition have started to recognise that even children with severe disorders can be happy and can have a high HRQoL. According to the psychological tradition, subjective opinions can be studied as long as the measurement method itself is objective and reproducible. The co-operation of psychologists and paediatricians in our research group, resulted in instruments that allowed for HRQoL as well as HS scores. Therefore we could compare these two constructs in this thesis, which produced some interesting results.

Firstly, it was found that sometimes the HRQoL score was better than the HS score, and sometimes poorer. For instance, it was shown in samples from the general population, that only half of the reported HS problems were combined with negative affective responses to those problems (Chapters 2 and 5). As a result, HRQoL is often reported as much better than HS. Furthermore, according to the parents of pre-school children born very preterm, motor functioning including affective responses (=HRQoL) was better than motor functioning excluding affective responses (= HS). In contrast, lungs, stomach and sleeping scores including affective responses were poorer than lungs, stomach and sleeping scores excluding affective responses (Chapter 6). In a group of children with idiopathic short stature the standard deviations of the mean HS scores were in general somewhat lower than that of the HRQoL scores. This means that the differences between children became larger when the affective evaluations were taken into account. (Chapter 10).

Secondly, the relationship between HRQoL and physical health can differ from the relationship between HS and physical health, which was shown in a group of pre-school children with problems with respect to the neonatal period (Chapter 6). Correlations between perinatal factors and motor functioning including affective responses (=HRQoL) were lower and less often significant than between perinatal factors and motor functioning excluding affective responses (=HS).

Finally, agreement between informants was sometimes different for HRQoL and HS. For instance, the global judgement of a neonatologist correlated with HS, but not with HRQoL (both estimated by the parent). It was concluded that the neonatologists did not include the affective evaluation of HS problems in her judgement which the parents did (Chapter 6). Moreover, conceptualisation of HRQoL as a combination of HS and affective evaluation had consequences for agreement between parent and child as well (Chapter 3). Children may wish to incorporate the fact that they do not feel bad about a certain HS problem by rating their HS problem as more or less severe than a proxy informant such as a parent, or a doctor would. According to previous studies, agreement seemed to be relatively good for observable measures.[9-11] Affective evaluations are probably less observable for parents than HS. Therefore, agreement between parent and child on HRQoL could be expected to be lower than agreement on HS. Indeed, HRQoL agreement on motor functioning and autonomy was significantly lower than HS agreement. However, HRQoL agreement matched HS agreement on the other scales, which indicates that adding affective evaluation does not influence observability. Perhaps these HS scales already have a strong subjective component: when children or parents report about the quantity of problems in, for instance, social functioning, there subjective evaluation might influence the counting of these problems. By adding affective evaluation to HRQoL, agreement on motor functioning and autonomy became poor, but the level of subjectiveness became probably distributed more even among the HRQoL scales. The possibility that patients have a health problem but do not feel bad about it may bias patient's self-reporting in typical HS questionnaires.

Conclusions and recommendations

In this thesis it was shown that the distinction between HRQoL and HS is justified. Consequently, the HS of a cohort of children born preterm (Chapter 9) cannot be equated to the HRQoL of these children. If it matters how children feel about their functioning rather than how they are functioning, measuring HS alone does not provide all relevant information. Children as well as parents distinguish between the HS problems they observe, and the emotional evaluation of these problems incorporated in HRQoL.

11.2 Measuring HRQoL in children

Instruments that measure HRQoL in children should be multi-factorial (physical, psychological and social well-being), self-administered and subjective. In this thesis four generic HRQoL questionnaires were used that met these requirements. Two instruments were exhaustively described, the TACQOL designed for children age 6 to 15 years (Chapters 2 and 3) and the TAPQOL designed for children 1 to 5 years (Chapter 5). Two other generic instruments were added for comparison, DUCATQOL (Chapter 10) and KINDL (Chapter 2). The multi-factorial structure of the TACQOL and the TAPQOL was confirmed by statistical analyses. The instruments had good reliability and validity (Chapters 2, 3 and 5). Validity was extensively tested by Multi-Trait Multi-Method modelling on the TACQOL scores of 8-11 year olds and their parents (Chapter 3). The multi-factorial structure was not only confirmed by statistical analyses, it appeared useful as well. Children reported different HRQoL at different scales. For instance, children born very preterm had a low HRQoL in different scales to children with other problems in the neonatal period (Chapter 6). Furthermore, children with idiopathic short stature had the same HRQoL as children from a reference group, except for social functioning in which the HRQoL was lower (Chapter 10).

The life of 6 to 15 year old children differs from that of 1 to 5 year olds, which has to be reflected in the content of HRQoL instruments (Chapter 7). The TACQOL contains scales which are different to those of the TAPQOL, both in objective and in items. For instance, the TACQOL contained items like 'riding a bicycle ' and 'reading' (Chapter 2), which are irrelevant to pre-schoolers. Instead, the sleeping scale in the TAPQOL appeared relevant for children age 1 to 5 years (Chapter 2). The TACQOL's cognitive functioning scale contains schoolability items, the TAPQOL's communication scale measures cognitive skills that are considered relevant for pre-school children. Within the TAPQOL, some scales are suitable for children of at least one-year-and-a-half (Chapters 2 and 3). Within the TACQOL age range, there were minor differences between scores of various age groups (Chapters 3 and 10).

Although the items from the TACQOL and TAPQOL appeared relevant, the fact remains that the construction followed a top-down procedure. The items were selected by adult investigators. Children's knowledge about health and disease is age- and experience-related and therefore different from

the knowledge of adults.[12,13]
A bottom-up procedure in which the items are derived from the children themselves perhaps would give a different result.

The feasibility of instruments for self administering HRQoL by the child is limited by the cognitive skills of the child.[14] Therefore the TAPQOL uses the parent as informant. The TACQOL has a parent form to inquire about the HRQoL of children age 6-15 years old, and a child form which can be filled in by the child hem/herself at age 8-15 years. As child and parent have different views on the child's HRQoL (see next paragraph), switching between informants is advised against. Consequently, when conducting a longitudinal study from 1 to 12 years of age, the parent should be main informant. But even when the same informant is used throughout the study, the content of the instruments changes with age, which may hamper longitudinal studies. However, in this thesis a strategy was presented that could overcome the problem of changing measurement instruments between time points (Chapter 8).

Conclusions and recommendations

In the thesis it was shown, that one-third of the publications that studied longitudinal HRQoL in children, used instruments without clear-cut measurement properties (Chapter 7). This should not be necessary in future research, because currently there are many good generic HRQoL instruments for children that can be used [15-19], and four are presented in this thesis. Most HRQoL instruments are paper and pencil questionnaires. As the use of these questionnaires is limited in young children, it would be interesting to develop other instruments like observation systems or interviews. Nevertheless, it can be concluded that the scientific tools are available to measure HRQoL in children. As stated before, the results have shown that 'subjectivity can be made scientific'.[20]

11.3 Informant of HRQoL

Although HRQoL aims for the individual's perception, children cannot always serve as informant. They may lack the cognitive skills or could be too ill to fill in questionnaires. In that case someone has to act as a proxy, for instance the parent or the physician.[9-11,21-25] Proxies may not have the same

knowledge and internal standard as the child him or herself, which can influence their reports.[26] For instance, the HRQoL that parents reported about their pre-school children, related to the feelings that the parent had towards their child (Chapter 6). It is not clear if the reported HRQoL of the pre-school child was the result or the cause of the parent's feelings towards this child. Unfortunately we do not have instruments to obtain the child's HRQoL from the pre-school children themselves. We could, however, get an impression of the differences between child and parent report, in a sample of children 8 to 11 years of age and their parents.

Parent reports were only moderately correlated to child reports in the general population (Chapters 2 and 3). Yet, both child- and parent reports proved to be valid, as was described in the previous paragraph. The mean differences between the TACQOL scores of children and parents differed between studies. In the open population, children reported significantly lower HRQoL than their parents on the physical complaints, motor functioning, autonomy, cognitive functioning and positive emotions scales (Chapter 3). In a group of children with a chronic disorder, children reported significantly lower HRQoL on physical complaints, motor functioning and positive emotions, but higher HRQoL than their parents on social functioning and negative emotions (Chapter 4). In a group of children with idiopathic short stature, the children reported significantly lower HRQoL than their parents on physical complaints at time 2, higher HRQoL on cognitive and social functioning at time 2 and time 3 and higher HRQoL on negative emotions (=less negative emotions reported) at time 3 (Chapter 10). Since the differences between parent and child at group level depend on the sample, it is not possible to give a formula for 'translating' parent scores into child scores. In two samples (Chapters 3 and 4) we found that agreement relates to height of the HRQoL scores. Child scores appear to be less extreme than parent scores. When parents are very pessimistic, children seem to say "it isn't so bad", and when parents are very optimistic, children seem to say "it isn't that good". One might consider parents failing as informants about the child and children as lacking a time perspective, but still, both child and parent reports proved to be valid.

As the parent is close to the child, the parent is the preferable proxy. In a clinical situation, however, the treatment program is established in concordance between physician and parent, if possible in consultation with the

child. Therefore it is important to study the agreement between the physician and the parent, and between the physician and the child. This agreement cannot be estimated during a regular consultation. Developmental psychology has shown that children are used to treating adults as their tutors; when a question is asked they will refer to an adult to learn if their answer is correct.[27] As a result the opinion of the child is highly influenced by the presence of a parent or a physician. However, even parents can be highly influenced by the social status of the physician during the consultation.[28] This may give the impression to the physician that agreement with the parent is higher than it is in reality, which could have consequences for parental satisfaction with the consultation.

In this thesis HRQoL information is obtained from physicians, independently of the information obtained from parents and children. In a study about the HRQoL of pre-school children born preterm, it was found that parents noticed many motor problems(=HS). However, the parents considered these problems not to be of great emotional impact (=HRQoL). The judgement of the neonatologist related to the HS but not to the HRQoL as obtained by the parents. As a result, in a clinical situation the neonatologist is surprised that a parent does not want to have full treatment for the child's motor functioning problems. The parent simply does not consider the motor problems to be as serious as the neonatologist does. In reverse, parents evaluated problems with lungs, stomach and sleeping as being more of an emotional burden than the neonatologist does. The parent therefore does not understand why these problems in their child receive less attention from the neonatologist.

Child, parent and physician's perception on the child's HRQoL was studied in a group of children with idiopathic short stature. Half of the group was treated with growth hormone, the other half acted as a control group (Chapter 10). It was found that the pattern of longitudinal changes differed between child, parent and physician. The physician reported an improvement of HRQoL in the children treated for short stature, the parents reported no change, whereas according to the children themselves the treatment group had the same or sometimes even poorer HRQoL than the control group.

Conclusions and recommendations

It appeared that in healthy as well as chronically ill children, the children and their proxies assessed HRQoL differently. It would be interesting to investigate what the effect is of feedback to the informants about their

disagreement. Furthermore, if the observability is influencing agreement, studies are needed in future about what exactly children and their proxies observe. As no gold standard exists and both child's and parent's opinion were valid, it seems best to obtain both parent's and children's evaluations whenever possible. The judgement of the physician should be obtained in addition to help clinical communication and decision making.

11.4 Is HRQoL health related or not?

As is indicated by the term *Health Related* Quality of Life, a relation is implied between health and HRQoL. This relation can be studied in a cross-sectional design by testing the hypothesis that children with a health problem had poorer HRQoL than healthy children. In a longitudinal design the hypothesis could be formulated as: changes in the child's health can result in changes in HRQoL, or, improved health will give improved HRQoL. In the introduction, health is defined as 'a state of complete physical, mental, and social well being, and not merely the absence of disease or infirmity' (WHO,1948)[29]. This implies that children with a physical, mental or social health problems could be subject of study. In this thesis we limited ourselves to studies in children with a physical health problem. Partly because the three kinds of health problems each require different knowledge and approaches, partly because HRQoL is a construct that is specifically popular in the medical world where people with a physical health condition are studied. In this thesis some support was found for the hypothesis that children with a physical health problem had poorer HRQoL than healthy children. In a group of 6 to 11 year old children from the open population, children with a chronic illness, children who had undergone medical treatment, and even children who had a common illness (a cold or influenza) had significantly lower HRQoL than healthy children (Chapter 2). In a group of 1 to 5 year old children from the open population again it was found that children with a chronic illness (mostly children with respiratory problems) had poorer HRQoL than healthy children (Chapter 5). Furthermore, children born preterm had lower HRQoL than a healthy reference group (Chapters 5 and 6).

Even if studies are limited to children with a physical health problem, as a rule, changes in HRQoL can be the result of physical, psychological as well as social changes (Chapter 7). Investigations that endorse the importance of this

rule, use a biopsychosocial model of change in HRQoL.[30] This model recognises that health and HRQoL are determined by psychological and social as well as physical factors, all of which interact to produce the current HRQoL. To study these changes the research design must allow for collecting psychological and social variables along with physical parameters. Furthermore, medical treatments as well as psychological interventions could be beneficial in changing HRQoL. Even if a medical treatment is the objective, assessment of HRQoL has to be planned not only in relation to the physical effects of this medical intervention, but also in relation to the psychosocial effect. For instance, in addition to side effects of medications, also school absenteeism or not being able to see friends are considered important factors that could elicit changes in HRQoL. Five out of the 32 longitudinal studies reviewed in Chapter 7, used a biopsychosocial model of change.[31-35] One of the studies in this thesis described the HRQoL of children with idiopathic short stature (ISS), which is short stature without an underlying disease or deficiency (Chapter 10). By treating these children with growth hormone, it is not their physical health which is changed but rather their physical appearance. It was hoped that increasing height would give more age appropriate reactions to the children, which in turn would improve their HRQoL. In other words, not physical health but psychological or social health was object of study, and therefore the psychological variable 'self-esteem' was measured in addition. At start the HRQoL of children with ISS was not lower than the HRQoL of a reference group, except for social functioning. Self-esteem did not differ from the reference group. This could indicate that ISS is more a social than a physical or psychological problem. Although the physician reported an improvement in HRQoL in the children treated for short stature, the parents reported no change, and the children in the treatment group reported the same or sometimes even poorer HRQoL than the control group. Furthermore, it was found that changes in HRQoL of these children did hardly relate to growth (objectively measured or as perceived by the child). Instead, changes in some HRQoL and self-esteem scales were related to the height appreciation by the child her/him self. The appreciation of height did not differ between groups, which is an indication of a psychological phenomenon called coping, the ability to adjust to difficult situations.

In the foregoing paragraphs, the ability of children to change in HRQoL over time is stressed, and changes in physical, psychological or social health are

seen as the motor of change. We call this the plasticity approach of change in HRQoL. Another possible approach to change in HRQoL is the predictability approach. This is change defined as the maintenance of relative position on particular characteristics over time, which can denote both stability (absolute levels of HRQoL remain stable over time), as well as continuity (consistency in relative rank over time on HRQoL). Both approaches are extensively discussed in Chapter 7.

The thesis contains a study illustrating the predictability approach as well. It involved a longitudinal study in children born preterm between 5 and 10 years of age (Chapter 9). Problems in basic functioning decreased while negative moods increased, and concentration problems increased slightly. The changes in HS found in this study were mainly age-related instead of health-related. The most remarkable HS change was the decrease in basic functioning problems in children with more than one handicap. The results of this study support the idea of continuity in change, in which a consistency in relative rank over time could be found. The normal development of children at a certain age was reflected in the type of problems that the parents reported. Basic functioning is important from early childhood onwards. At 'kindergarten age', concentration problems become more important. When children grow older they start to communicate more about their moods. Therefore, parents could successively detect problems in basic functioning, concentration problems and negative moods. As a result, at the age of 10 years the parents could have grown accustomed to the first, less to the second, but not to the last kind of HS problems. In this study changing parental standards appeared to be the motor of change. Although these results are about HS, these probably would have been found in HRQoL as well. It appeared that the priorities and goals of the parents changed with time and were modified by the age of the child and experience with the child. These changes narrow Calman's Gap[7,36], the gap that Calman positioned between the patient's expectations and achievements or possibilities. The better the gap is closed the higher the QoL should be.

A review in 32 longitudinal studies about HRQoL in children -- half of the time defined like we defined HS -- revealed the presumption that stable physical health gives stable HRQoL and that changes in physical health change the HRQoL (Chapter 7). This presumption appeared so strong that most investigators did not feel the need to prove it. However, as shown above, not only changes in physical health, but also changes in psychological and social

health, and changing internal standards of the informant could influence changes in HRQoL.

Conclusions and recommendations

The two terms HRQoL and QoL are often intermingled in publications, even in a standard work such as Spilker's 'Quality of Life and pharmacoeconomics in clinical trials'.[37] To avoid the impression that the terms HRQoL and QoL describe different constructs, it might be better to choose between these terms in the future. It is important to realise that when the term *health related* QoL is used, psychological and social health should be considered as well as physical health. All three kinds of health should be considered when studying differences in HRQoL between groups, or seeking the cause of changes in HRQoL. The notion that not only physical health is relevant in HRQoL, requires more research about processes that influence psychosocial health like coping and adaptation. This implies that when changes in physical health cannot be realised in children with a chronic illness, changes in psychological and social health may be able to improve the HRQoL of children.

11.5 Reference List

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