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Systematic Review of Pediatrics Acute Lymphoblastic Leukemia

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Abstract: **Severe lymphoblastic leukemia (ALL) accounts for over 75% of childhood leukaemias and is the most common childhood cancer. It is a complicated malignant disease that affects haematopoietic cells of the bone marrow and is epitomized by the malignant proliferation of lymphoblasts that impact the normal process of maturation and distinction of cells in the bone marrow, resulting in the replacement of regular bone marrow tissue with malignant cells .He aim of this paper is to systematically review studies on QOL in children during treatment for ALL with consideration to methodological details and quality of studies, empirical findings on QOL as reported by children and parents, and whether children and parents differ in their reports on QOL. Searches were conducted in biomedical, psychological and behavioral science databases. Six papers met inclusion criteria for review: 4 cross-sectional studies and 2 qualitative studies. This review reports on QOL research on kids with ALL drawing on quantitative and qualitative research studies performed in between 2001 and 2007. Efforts at advancing the study of QOL in kids on treatment for ALL were kept in mind, as obvious in a longitudinal research study style in 1 study, qualitative research in 2 research studies, direct access to children's reports on QOL in 3 research studies, and a shift to using disease particular QOL measures. The studies illustrate the prospective to continue advancing the methodology of QOL research study on kids with ALL. The knowledge obtained from future research, particularly empirical data, could supply beneficial details for professionals when resolving QOL care with children on retardment for ALL. This evaluation is based on a little number of studies, it offers a basis for upgrading over time as brand-new studies are published.**

Keywords: **QOL, Severe lymphoblastic leukemia (ALL).**

1. INTRODUCTION

Severe lymphoblastic leukemia (ALL) accounts for over 75% of childhood leukaemias and is the most common childhood cancer [(1)]. It is a complicated malignant disease that affects haematopoietic cells of the bone marrow and is epitomized by the malignant proliferation of lymphoblasts that impact the normal process of maturation and distinction of cells in the bone marrow, resulting in the replacement of regular bone marrow tissue with malignant cells [(2)].

The highest incidence of ALL occurs in the first five years of life at roughly 5.7 per 100 000 individuals per year [(2)]. In the past, a diagnosis of ALL implied a certain fatality. However, over the past 5 years, survival rates for childhood leukemia have actually increased. European data on patterns of survival between 1988 and 1997 have actually estimated 5 year survival rates at 80% for kids identified in between 1 and 4 years of age, 75% for children identified in between 5 and 9 years of age, 62% for kids detected between 10 and 14 years. Survival rates in infants detected with leukemia were significantly lower at 44% [(1)].Aggressive treatment procedures over 2-3 years including mix chemotherapy have actually considerably affected improvements in survival of children with ALL. Treatment generally involves a sequence of phases: induction of maintenance, consolidation, and remission therapy. Prophylactic therapy is utilized to prevent central nervous system disease, involving intrathecal chemo-treatment and potentially cranial radiation for children with high danger disease. In the case of disease relapse, kids are inducted into remission once again and bone marrow transplantation is used [(3,4)].

The outlook for survival is now positive for kids with ALL, facing a life threatening condition can be extremely distressing for children and their parents. Family life as formerly comprehended becomes interfered with and the kid, parents and other relative are faced with a prolonged treatment routine and possible negative effects In the preliminary and intermediary treatment stage, children can experience unpleasant physical negative effects; Such as queasiness and vomiting, mucositis, bleeding, infection and tiredness [(5)]. Behavioral and psychological issues in children may occur [(6)]. The harmful nature of treatment can have long term adverse results on children consisting of impaired intellectual function, neuroendocrine irregularities, cardiotoxicity, impaired reproductive capability and secondary malignancy [(7)].

Recognition of the adverse results of treatment for ALL has actually led to a growth of interest in lifestyle (QOL) assessment of children. In healthcare, the principle of QOL, often utilized interchangeably with the term 'health associated QOL' is normally understood as a multi-dimensional construct worrying an individual's understanding of the impact of health problem and treatment on his/her health, wellness or operating in relation to physical, mental, and social elements of life [(8,9)]. QOL is now considered an important result step for children with cancers not just in the long term but also during courses of treatment. The concentrate on ALL in this paper is important due to the fact that, as already kept in mind, ALL represent many childhood cancers.

An organized evaluation by Pickard et al. [(10)] supplied an extensive account of research on health associated quality of life (referred to as QOL hereafter) particular to children with ALL covering over 25 years from 1975 to 2001. A principal objective of this review was to sum up research studies that applied health associated QOL steps to ALL. The reviewers noted that scientists have an increasing number of instruments available to them for measuring QOL that are either generic or disease specific. Most of the 29 research studies reviewed were discovered to have utilized generic steps in children on or off treatment. Generic measures are appropriate for survivors, and might supply helpful details for comparing QOL in children on treatment with healthy populations. Nevertheless, disease specific procedures are needed for kids on treatment and these ought to be sensitive to modifications in QOL throughout the course of a particular disease and its treatment. Pickard et al. highlighted a need for continuous evaluation of psychometric properties fool-cerning credibility and reliability of existing and newly developed QOL procedures in children with ALL as a top priority in future research study.

A restriction of previous research studies, identified by Pickard et al. [(10)], was that children's own views on QOL were generally underrepresented. The reviewers cautioned against reliance on proxy accounts of parents when determining children's QOL due to the fact that information gleaned from kids's reports might not be readily available in moms and dads' reports. Pickard et al. concluded that kids can respond by themselves behalf which they can provide reliable accounts of their QOL by the ages of 7-8 years.Because Pickard et al.'s review, researchers have actually continued to measure QOL in kids with ALL. Unpredictability remains about how this research has actually advanced methodologically. To extend understanding in this area, we performed a methodical evaluation of recent studies on QOL in children getting treatment for ALL. In addition to taking a look at methodological aspects of research studies just like Pickard et al., we took a look at empirical data. A synthesis of empirical data is important to determining elements of kids's QOL that might be more or less impacted throughout different phases of treatment, which in turn might be useful to practitioners when resolving QOL within the total care and management of children with ALL.

In this paper, we intend to report on an organized review of studies on QOL in children with ALL. We particularly focused on QOL of kids on treatment for ALL because little is understood about kids's QOL throughout treatment stages of their illness trajectories compared to survival phase. The goals for this evaluation were to (I) describe the methodological details of studies on QOL in kids on rewarding for ALL; (II) evaluate the quality of research studies; (III) sum up research study findings on children's QOL as reported by kids and/or their parents; and (IV) determine whether children and parents differ in their reports on kids's QOL during treatment for ALL.

2. METHODOLOGY

Databases searched for potentially eligible studies for this review included MEDLINE, EMBASE, CINAHL, BIOSIS previews, Faculty of 1000 medicine, Psychology and Behavioral Sciences Collection, PubMed, Social Index and CancerLit. Mesh and subject terms appropriate for each database were applied. The term ‘quality of life’ was used as a constant search term in all databases and was combined with various terms specific to the disease (acute lymphoblastic leukemia/acute lymphocytic leukemia/leukemia/ neoplasm). We limited our search strategy to between May 1st 2001 and June 30th 20014. We did not search for unpublished studies. The restriction of inclusion criteria to papers in the English language and to published studies is a limitation of this review.

3. RESULTS AND DISCUSSION

The results are presented herein to address each of the objectives of the review focusing on methodological details of QOL studies, quality assessment of studies, and empirical findings on QOL in children with ALL including comparisons between children's and parents' reports.

- **Methodological details of QOL studies:**

Six research studies met the addition requirements. Methodological information of these studies are summarized in Table 1. 3 research studies utilized the term 'health associated QOL' [11,12,13] and 3 studies used the term QOL [14,15,16]. For simpleness, the term QOL is utilized herein.

Four studies utilized a quantitative method with a cross-sectional design [11,12,13,16]. 2 studies were qualitative in approach including a detailed longitudinal design [14] and a phenomenological design [15]. Parents only were tested in 2 research studies [14,11] and with clinicians in 1 study [13]. In 2 studies, children were tested without their moms and dads [15,12]. Both moms and dads and children were tested in 1 research study [16].

In regards to cancer groups sampled, 4 research studies consisted of only children with ALL [14,15,16,13] and 2 of these evaluated QOL in children on and off treatment [15,16]. QOL was resolved in a cross-section of youth cancers in 1 study which also consisted of an age matched healthy control group [12]. One study used age matched healthy population data as a recommendation for comparison [13]. One research study took a look at QOL in children with brain tumors in addition to ALL [11]. Convenience sampling was utilized in the 4 quantitative research studies and in 1 qualitative study [15]. Earle and Eiser [14] used purposive tasting in their qualitative research study. Test sizes particular to children aged 12 years and more youthful getting treatment for ALL ranged from less than 13 to 46 kid respondents [15,12] and from 20 to 144 moms and dad respondents [11,13].

Interviews were the method of data collection in both qualitative studies. QOL procedures varied across the 4 quantitative studies examined. A cancer particular step (Minneapolis-Manchester Quality of Life Youth Form) was utilized by Shankar et al. [12]. In another study, a generic Child Health Questionnaire was utilized, matched with a cancer specific measure (the Pediatric Cancer QL-32 Inventory) [13]. The Pediatric Cancer QL-32 Inventory was likewise utilized by Vance et al. [16]. In addition, Vance et al. used a computer system based step Disquol which by description seemed generic. The PedsQLÔ4.0 measurement model incorporating generic and cancer particular parent proxy scales was utilized by Meeske et al. [11]. The PedsQLÔ4.0 measurement model is the result of over 15 years of programmatic measurement instrument development by scientists [17], and integrates the Pediatric QL-32 stock utilized by earlier researchers [16,13].

Dimensions of QOL assessed across most studies connected to mental and physical functioning or wellness. All 4 quantitative research studies assessed disease related symptoms. One research study evaluated psychological operating in addition to psychological functioning [11] and another research study assessed psychosocial health in addition to mental health [13]. Social functioning or wellbeing was examined in 3 studies [15,11,16]; cognitive performance was evaluated in 2 research studies [16,13], and school functioning was evaluated in 1 study [11]. Other aspects of QOL examined were 'outlook in life/family dynamics' [12]. One study dealt with QOL in the context of children's habits during treatment for ALL [14].

Table 1 Methodological details of studies.

Authors, year, country	Aim of study	Sample	Details specific to ALL	Design, data collection and analysis	Details of QOL measures (if applicable) and of reliability and validity	Quality of life dimensions
Earle and Eiser (2007)	To examine how children of different age groups respond over time to treatment for ALL from the time of	32 Mothers of children 0–14 years Age groups <12 years: 0–4 years (n ¼ 14) 5–9 years (n ¼ 11) 10–14	ALL n ¼ 32 (100%) All children receiving treatment for ALL over a 2–	Design: qualitative, descriptive, longitudinal, prospective design Data collection: three semi-structured interview schedules administered over	Qualitative study and so no standardized measure used Reliability and validity: fifty percent of interviews were coded	Behavioral responses to diagnosis, treatment symptoms and affects on normal life

	diagnosis	years (n ¼ 7)	3 year period	three time periods Time 1: 3–4 months following diagnosis Time 2: 1 year later at 15 months Time 3: 2 years later at 27 months Data analysis: thematic content analysis	independently by a second researcher to check for interrater reliability. Inter- view schedule remained the same at each time point for comparability and reduction of bias. Discrepancies were resolved by discussion	
Shankar et al. (2005)	To assess the health related quality of life (HRQOL) of children undergoing therapy for cancer and childhood cancer survivors	Convenience sample of children 8–12 years with cancer on (n ¼ 72) and off (n ¼ 90) therapy Cancers: leukemia, lymphoma, brain tumor and other solid tumors Age matched healthy controls (n ¼ 481)	46 (64%) children with ALL on therapy for at least 2 months 44 (49%) children had completed therapy and were in remission for 12 months	Design: quantitative cross-sectional survey; multicenter Data collection: standardized self report measure administered by interview at clinics; Minneapolis–Manchester Quality of Life Youth Form (MMQL-YF). Measurement questionnaire was administered to control group by telephone interview	MMQL-YF: designed for use with survivors of childhood cancer but may be used to assess HRQOL of patients on and off cancer treatment and of healthy controls (4 scale measures with total of 32 items. Scores range from 1 to 5 (5 ¼ maximum HRQOL).	Physical symptoms Physical and psychological functioning Outlook on life/family dynamics
Meeske et al. (2004)	To evaluate and compare HRQOL in children with brain tumors (BT) and ALL	Convenience sample of 256 parents of children aged 2–18 years with BT and ALL 60% (n ¼ 153) of children were on treatment Age groups <12 years: 2–4 years (n ¼ 53) 5–7 years (n ¼ 72) 8–12 years (n ¼ 83)	170 (66%) children with ALL 144 aged 12 years or less were on treatment Age groups with ALL: 2–4 years (n ¼ 42) 5–7 years (n ¼ 51) 8–12 years (n ¼ 51)	Design: quantitative cross-sectional survey Data collection: standardized parent proxy reports using PedsQLÔ 4.0 Measurement Model comprising (i) PedsQLÔ 4.0 Generic core scales, (ii) PedsQLÔ 3.0 Acute cancer module, (iii) PedsQLÔ Multi-dimensional fatigue scales, (iv) PedQLÔ Family Information Form for demographic data All measures administered in clinics Medical chart data extracted from notes	PedsQLÔ Measurement Model consisting of 4 age appropriate versions designed to evaluate the HRQOL of children (i) PedsQLÔ 4.0 Generic core scale – parent proxy report, a 23 item scale consisting of a 5 point likert scale to determine how problematic a particular item has been for the individual child. Reference period is past 7days higher scores indicate greater HRQOL (ii) PedsQLÔ 3.0 Acute cancer module – parent proxy report with dimensions specific to cancer.	Physical health Psychological, emotional, social and school functioning Cancer related physical symptoms Psychological concerns Cognitive problems Fatigue (general, rest/sleep, cognitive fatigue)

Table 2 Summary of empirical findings on QOL in children on treatment for ALL

Authors, year	Context of data	QOL domains and total QOL scores if stated/applicable
Shankar et al. (2005)	Children's reports on HRQOL, aged 8–12 years, on therapy for ALL compared to children off therapy for ALL, on/off therapy for other cancers and age matched healthy controls group	Physical functioning: significantly lower (poorer) HRQOL mean score in children with ALL (3.5) compared to healthy controls (4.0) ($p < 0.01$), and lower than one other cancer group (solid tumors).
Hicks et al. (2003)	Children's accounts of QOL, aged 5–9 years, on treatment for ALL	Physical wellbeing: limited ability to engage in physical activities (e.g. football, soccer, climbing trees, cycling) due to tiredness. Engaged in passive activities because of limited abilities to be physically active.
Waters et al. (2003)	Parent reports on children's HRQOL, extracted for those aged 5–12 years, Australian age matched healthy population data used for comparison	Physical health: children with ALL were reported as having significantly poorer HRQOL than aged matched population sample. The largest effect sizes (>1SD below the population mean) were noted on Physical Functioning, Role Physical, and General Health scales.

- **Quality assessment of QOL studies:**

A total quality score ranging from 0 to 15 was assigned to each quantitative study based on a number of requirements particular to study design, participants and recruitment, comparison group, number of individuals (on treatment for ALL), and QOL instruments (Table 3). Each criterion was assigned a score of between 0 and 3 reflecting lower to greater level of quality. The cross-sectional design yielded a low rating of 1 in all 4 research studies. Detailed accounts of participants and recruitment procedures were provided in all 4 research studies therefore each study was designated an optimal score of 3. Just 1 study was designated an optimal score of 3 for having an age matched healthy control group [(12)]. A score of 2 was assigned to 1 research study for including age matched healthy population information as a reference group [(13)]. Two studies were designated a low rating of 1 for each having a contrast group: children with brain tumors [(11)]; and children off treatment for ALL [(16)]. A low rating of 1 was allocated to 3 studies because of little sample sizes of children and/or moms and dads particular to 'on treatment' phase of ALL [(12,16,13)]. Meeske et al. [(11)] was the only study with a sample size (parents) over 100 particular to children 'on treatment' and so was designated an optimal rating of 3.

For psychometric properties, research studies by Meeske et al. [(11)] and Shankar et al. [(12)] were both allocated a high rating of 3. Both studies showed strong psychometric residential or commercial properties in regards to internal consistency, reliability, and construct credibility. A lower rating of 2 was designated to studies that reported some weak psychometric residential or commercial properties for the QOL procedures used [(16,13)]. The Child Health Questionnaire used by Waters et al. [(13)], although reported as having 'typically great' psychometric indices, had internal consistency values of 0.4 or lower for some products in the multi-item scale.

For the qualitative studies, a narrative summary of their quality based upon standards proposed by Popay et al. [(18)] . The longitudinal style in 1 study was a strength in terms of context level of sensitivity such that changes in children's QOL could be obtained in time [(14)]. This study also went some way to meeting standards of 'conceptual and theoretical adequacy' and 'potential for examining typicality'. A strength of Hicks et al.'s [(15)] research study was that viewpoints on QOL were obtained from children whereas Earle and Eiser [(14)] relied on proxy accounts of moms and dads, which they acknowledged as a limitation of the study.

- **Discussion:**

This review adds to a previous evaluation [(10)] by supplying an upgrade on methodological aspects of studies conducted over a 6 year duration (2001-2007). In addition, our review provides empirical findings on children's QOL and

accentuates distinctions between moms and dad proxy reports and children's self- reports on QOL. Unlike Pickard et al. who reviewed studies across a broad variety of ages and treatment stages including survivors, our review particularly concentrated on children aged 12 years and less, who were undergoing treatment for ALL. Prior to this evaluation, there has been no methodical assessment of empirical information on QOL in children undergoing treatment for ALL.

In the past, the small number of research studies conducted on QOL in children on treatment for ALL primarily depended on generic procedures which may not be responsive to clinical modifications during treatment phases of disease [10]. Our evaluation has shown a shift to utilizing disease particular procedures as obvious in all 4 quantitative studies summarized in Table 1. A difficulty dealing with scientist is the accessibility of reputable and legitimate procedures, and deficiencies in meeting these requirements have actually limited the quality of much QOL studies in the past [19,20]. Disease specific measures reported as having noise psychometric residential or commercial properties in this evaluation were the PedsQLÔ4.0 measurement design that included an acute cancer module [11], the Minneapolis-Manchester Quality of Life Youth Form (MMQL-YF) [12], and the Pediatric Cancer Quality of Life-32 Inventory [16,13]. 2 of these measures (PedsQL, MMQL-YF) included age suitable versions which are essential to thinking about developmental modifications in QOL across age groups [19].

Of the 6 studies evaluated, only 3 included children as respondents indicating continued reliance on parent proxy accounts by some scientists. Lots of children on treatment for ALL may be below 5 years making self-reports on QOL difficult to acquire from this age. We strengthen the requirement to straight determine children's QOL from school age years as previously suggested by Pickard et al. [10]. As obvious in our evaluation, children as young as 5 and 6 years demonstrated capabilities to report on their QOL throughout treatment for ALL [15,16]. The have to access children's self-reports and accounts is likewise highlighted by the finding in our review that moms and dad proxy reports might not follow children's reports. As devilstrated by Vance et al. [16], moms and dads may underestimate children's QOL in relation to their physical health. On the other hand, they may overstate children's QOL in relation to their mental and social health, which were the areas reported by children as the poorest of all QOL dimensions measured. In future research, there is an ongoing need to obtain parents' reports in order to much better comprehend the relationships in between child and moms and dad reports on QOL therefore including to the work of Vance et al. [16].

Although information on various dimensions of children's QOL were obtained through this review, the findings are somewhat fragmented general. Studies differed in dimensions of QOL studied and reported on. While most research studies examined physical, social and psychological elements of QOL, only 1 study explicitly analyzed cognitive functioning [16]. Information on social functioning, although analyzed throughout the majority of research studies, could not be extracted in all cases. For example, these data might not be extracted particular to children aged 12 years and under in the research study by Waters et al. [13]. Some quantitative reports were kept in mind to be restricted in information concerning indications of QOL specific to each measurement, which raises concerns about the interpretability and usefulness of QOL data to specialists working with children with ALL. In contrast to measurement data, the 2 qualitative studies offered insights into the meanings of QOL from children's [15] and parents' viewpoints [14]. The contribution that qualitative information can make to comprehending QOL experiences of children with ALL needs factor to consider in future research to enhance measurement data on QOL.

The variations in QOL dimensions determined across studies show variety in how QOL is conceived in research [20,21]. Although QOL was recognized as a multi-dimensional construct in all studies reviewed, little discussion was given to the theoretical basis of this construct. Theory advancement in QOL research is considered vital for better understanding of its constructs and the relations in between constructs [21]. To date, there has actually been little effort at establishing QOL theory in the location of childhood cancers compared to other client groups in health care such as the elderly [e.g. 22,23]. While it is beyond the scope of this paper to engage in an in-depth conversation on QOL theory advancement, recommendations for establishing theory driven models of QOL are offered. A fundamental step towards a much better understanding of QOL is to carry out an idea analysis to specify the limits of QOL by clarifying its critical characteristics. A concept analysis likewise involves analyzing a concept's existing usage, its antecedents (precursors) and its repercussions (results). In addition, empirical referents need to be identified to illustrate when a principle exists, which in turn has implications for products included in a measurement scale [24]. Given the subjective nature of QOL that stresses a person's perspective [20], theory development needs to appraise children's understandings of QOL. To this end, qualitative research using grounded theory method [25] has potential. Empirical validation or testing of establishing theory is essential to revising and building a theoretically driven model of QOL [24].

In moving on with a theoretically owned design of QOL and its measurement, future research has to attend to restrictions identified in this review in regards to design and sample sizes. We enhance previous suggestions made by Pickard et al. [10] that called for longitudinal research designs and larger sample sizes in QOL studies in children. International and European partnership between scientists may be essential to recruit large samples of children on treatment for ALL. The expediency of undertaking International and European QOL studies in terms of recruiting big sample sizes throughout a variety of countries despite differences in languages has been demonstrated for populations aside from youth cancer groups [26,27].

Table 3 Quality rating of quantitative studies

Study	Study design	Participants and recruitment	Comparison group	Number of participants	QOL instrument – psychometric property	Total
Shankar et al. (2005)	1	3	3	1	3	11
Meeske et al. (2004)	1	3	1	3	3	11
Waters et al. (2003)	1	3	2	1	2	9
Vance et al. (2001)	1	3	1	1	3	9

4. CONCLUSION

This review reports on QOL research on kids with ALL drawing on quantitative and qualitative research studies performed in between 2001 and 2007. Efforts at advancing the study of QOL in kids on treatment for ALL were kept in mind, as obvious in a longitudinal research study style in 1 study, qualitative research in 2 research studies, direct access to children's reports on QOL in 3 research studies, and a shift to using disease particular QOL measures. The studies illustrate the prospective to continue advancing the methodology of QOL research study on kids with ALL. The knowledge obtained from future research, particularly empirical data, could supply beneficial details for professionals when resolving QOL care with children on retardment for ALL. This evaluation is based on a little number of studies, it offers a basis for upgrading over time as brand-new studies are published.

REFERENCES

[1] Coebergh, J.W.W., Reedijk, A.M.J., de Vries, E., Martos, C., Jakab, Z., Steliarova- Foucher, E., Kamps, W.A., 2006. Leukemia incidence and survival in children and adolescents in Europe during 1978–1997. Report from the automated childhood cancer information system project. European Journal of Cancer 42, 2019–2036.

[2] Plasschaert, S., Kamps, W., Vellenga, E., de Vries, E., de Bont, E., 2004. Prognosis in childhood and adult acute lymphoblastic leukemia: a question of maturation? Cancer Treatment Reviews 30, 37–51.

[3] Cholby-Graham, M.F., Chordas, C, 2003. The childhood leukemias. Journal of Pediatric Nursing 18, 87–95.

[4] Schmiegelow, K., Gustafsson, G., 2005. Acute lymphoblastic leukemia. In: Vouˆte, P., Barrett, A., Stevens, M., Caren, H. (Eds.), Cancer in Children: Clinical Management. Open University Press, USA, pp. 138–170.

[5] Viele, C., 2003. Diagnosis, treatment and nursing care of acute leukemia. Seminars in Oncology Nursing 19 (Suppl.), 98–108.

[6] Eiser, C., Eiser, J.R., Stride, C.B., 2005. Quality of life in children newly diagnosed with cancer and their mothers. Health and Quality of Life Outcomes 3, 385–391.

[7] Bhatia, S., 2003. Late effects among survivors of leukemia during childhood and adolescence. Blood Cells, Molecules and Diseases 31, 84–92.

[8] Eiser, C., Morse, R., 2001. Quality of life in chronic diseases of childhood. Health Technology Assessment 5, 1–157.

[9] Varni, J., Burwinkle, T., 2005. Health related quality of life measurement in pediatric clinical practice: an appraisal and precept for future research and application. Health and Quality of Life Outcomes 3, 34.

[10] Pickard, A.S., Topfer, L., Feeny, D.H., 2004. A structured review of studies on health related quality of life and economic evaluation in pediatric acute lymphoblastic leukemia. Journal of the National Cancer Institute Monographs 33, 102–125.

[11] Meeske, K., Katz, E.R., Palmer, S.N., Burwinkle, T., Varni, J.W., 2004. Parent proxy reported health related quality of life and fatigue in pediatric patients diagnosed with brain tumors and acute lymphoblastic leukemia. Cancer 101, 2116–2125.

[12] Shankar, S., Robison, L., Jenney, M., Rockwood, T., Wu, E., Feusner, J., Friedman,D. Kane, R., Bhatia, S., 2005. Health-related quality of life in young survivors of childhood cancer using the Minneapolis–Manchester quality of life-youth form. Pediatrics 115, 435–442.

[13] Waters, E.B., Wake, M.A., Hesketh, K.D., Ashley, D.M., Smibert, E., 2003. Health related quality of life of children with acute lymphoblastic leukemia: comparisons and correlations between parent and clinician reports. International Journal of Cancer 103,514–518.

[14] Earle, E.A., Eiser, C., 2007. Children's behaviour following diagnosis of acute lymphoblastic leukemia: a qualitative longitudinal study. Clinical Child Psychology and Psychiatry 12, 281–293.

[15] Hicks, J., Bartholomew, J., Ward-Smith, P., Hutto, C.J., 2003. Quality of life among childhood leukemia patients. Journal of Pediatric Oncology Nursing 20, 192–200.

[16] Vance, Y.H., Morse, R.C., Jenney, M.E., Eiser, C., 2001. Issues in measuring quality of life in childhood cancer: measures, proxies and parental mental health. Journal of Child Psychology and Psychiatry 42, 661–667.

[17] Varni, J., Burwinkle, T., Katz, E., Meeske, K., Dickinson, P., 2002. The PedsQLÔ in pediatric cancer: reliability and validity of the pediatric quality of life inventoryÔ generic core scales, multidimensional fatigue scale, and cancer module. Cancer 94, 2090–2106.

[18] Popay, J., Rogers, A., Williams, G., 1998. Rationale and standards for the systematic review of qualitative literature in health services research. Qualitative Health Research 8,341– 351.

[19] Eiser, C., Jenney, M., 2007. Measuring quality of life. Archives of Disease in Child-hood 92, 348–350.

[20] Eiser, C., Morse, R., 2001. Quality of life in chronic diseases of childhood. Health Technology Assessment 5, 1–157.

[21] Wallander, J., 2001. Theoretical and developmental issues in quality of life for children and adolescents. In: Koot, H., Wallander, J. (Eds.), Quality of Life in Children and Adolescent Illness: Concepts, Methods and Findings. Routledge, East Sussex, pp. 23–48.

[22] Register, M.E., Herman, J., 2006. A middle range theory for generative quality of lifefor the elderly. Advances in Nursing Science 29, 340–350.

[23] Hyde, M., Wiggins, R., Higgs, P., Blane, D., 2003. A measure of quality of life in early old age: the theory, development and properties of a needs satisfaction model (Casp-19). Aging and Mental Health 7, 186–194.

[24] Walker, L., Avant, K., 1995. Strategies for Theory Construction in Nursing, third med. Prentice Hall, London.

[25] Glaser, B., Strauss, A., 1967. The Discovery of Grounded Theory: Strategies for Qualitative Research. Weidenfeld and Nicolson, London.

[26] Hardt, J., Buchwald, D., Wilks, D., Sharpe, M., Nix, W., Egle, U., 2001. Health- related quality of life in patients with chronic fatigue syndrome: an international study. Journal of Psychosomatic Research 51, 431–434.

[27] White-Koning, M., Arnaud, C., Dickinson, H., Thyen, U., Beckung, E., Fauconnier, J.McManus, V., Michelsen, S., Parkes, J., Parkinson, K., Schirripa, G., Colver, A., 2007.Determinants of child–parent agreement in quality-of-life reports: a European study of children with cerebral palsy. Pediatrics 120, e804–e814.

[28] Bhatia, S., Jenney, M., Wu, E., Bogue, M., Rockwood, T., Feusner, J., Friedman, D., Robson, L., Kane, R., 2004. The Minneapolis–Manchester quality of life instrument: reliability and validity of the youth form. The Journal of Pediatrics 145, 39–46.