A systematic review of psychometric properties of health-related quality of life and symptom instruments in adult acute leukemia survivors

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Abstract

Background—Acute leukemia represents 4% of cancer cases in the United States (US) annually. There are over 302,000 people living with acute and chronic leukemia in the US. Treatment has been shown to have both positive and negative effects on health-related quality of life (HRQOL).

Objective—Examine psychometric properties of symptom and HRQOL instruments and to provide implications for the assessment in adults with acute leukemia relevant to clinical practice and future research.

Methods—Systematic literature search was conducted from 1990-2014 using electronic databases and manual searches. Psychometric studies were considered eligible for inclusion if 1) the psychometric paper was published using at least one HRQOL or symptom instrument and 2) adults with acute leukemia were included in the sample. Studies were excluded if the age groups were not adults, or if the instrument was in a language other than English.

Results—Review identified a total of 7 instruments (1 cancer generic HRQOL, 2 symptom-related, 3 HRQOL combined with symptom questions, and 1 disease- specific). The most commonly used instrument was the European Organization for Research and Treatment of Cancer (EORTC QLQ-C30), followed by the Functional Assessment of Cancer Therapy-Fatigue (FACT-F).

Conclusions—An acute leukemia diagnosis can have a significant impact on HRQOL. Our recommendations include using both a HRQOL and symptom instrument to capture patient experiences during and after treatment.

Implications for Practice—The availability of comprehensive, valid and reliable HRQOL and symptom instruments to capture the experiences of adults with acute leukemia during and posttreatment is limited.

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Keywords

Acute leukemia; acute leukemia survivors; health related quality of life; symptoms; instruments; psychometrics; cancer-related fatigue

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Introduction

It is estimated that 54, 270 individuals in the Unites States (US) will be diagnosed with leukemia in 2015 and an estimated 24,450 will die from the disease.[1] Of these new cases, 27,080 have acute lymphoblastic leukemia or acute myeloid leukemia, and 11, 910 will die with the disease, with the remaining being chronic leukemias[1]. Acute leukemia has a 5-year survival rate of 56% in the US.[2] Newly diagnosed acute leukemia is usually treated in a specialized care center with an average stay of 4-6 weeks. It is common for patients to have fluctuating symptoms associated with the disease and its treatment such as myelosuppression, stomatitis, and nausea throughout their hospitalization.[3,4]

There is the potential to advance acute leukemia science by systematically reviewing symptoms that occur, solely or concurrently, during and after treatment to determine how health-related quality of life (HRQOL) changes over time. It is important to understand patient-reported symptoms and HRQOL of adults with acute leukemia to better address their physical and psychosocial needs. In Bryant et al,[4] cancer related fatigue (CRF), depression, and anxiety were found to be the most prominent symptoms that interfered with HRQOL and activities of daily living. In that review, we found that acute leukemia and its treatment have a significant impact in all QOL domains; we concluded that there was a need for future studies focused on longitudinal research and increased minority representation[4].

One common way of assessing symptoms and HRQOL is through self-reported instruments, measuring the outcomes at one or more points. These instruments vary in the symptoms and HRQOL domains measured, the length of the questionnaire, the wording of questions and their response options, the reference or recall period, and the level of psychometric evidence in support of the validity and reliability of the measure.

The majority of the measures are not leukemia specific, except for the Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu), which was recently developed in 2002.[5]

This review examined the psychometric properties of instruments used in acute leukemia research, and provides clinical and research relevant implications of symptom and HRQOL instruments used in adults with acute leukemia.

Methods

Search strategy

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[6], a systematic literature search was conducted by the first (ALB) and third (JSK) authors. The search was completed in August 2014. The electronic databases

PubMed, PsychInfo, EMBASE, CINAHL, and HAPI were searched using the following text words and their combinations: leukemia or leukaemia and each individual instrument included in this study. In a previous acute leukemia literature review conducted by Bryant et al[4], 20 instruments were identified: Brief Fatigue Inventory (BFI), Center for Epidemiologic Studies Depression Scale (CES-D), Distress Thermometer, Edmonton Symptom Assessment Scale (ESAS), European Organization for Research and Treatment of Cancer (EORTC QLQ-C30), Fatigue Visual Analog Scale (F-VAS), Functional Assessment of Cancer Therapy-Fatigue (FACT-F), Functional Assessment of Cancer Therapy-General (FACT-G), Functional Assessment of Cancer Therapy-Spiritual (FACT-Sp), Functional Living Index-Cancer (FLIC), Geriatric Depression Scale (GDS), Hospital and Anxiety Scale (HADS), Life Ingredient Profile (LIP), Mental Adjustment to Cancer (MAC), the M.D. Anderson Symptom Inventory (MDASI), Psychosocial Adjustment to Illness Scale-Self report (PAIS-SR), Perceived Quality of Life (PQOL), Revised Piper Fatigue Scale (RPFS), Schedule for the Evaluation of Individual Quality of Life (SEIQOL), and Short-Form-36 (SF-36). Fifteen instruments were removed from the initial review of 20 instruments due to not being clearly defined as a symptom or HRQOL domain, lack of testing to determine psychometric properties, or the sample did not specifically include adults with acute leukemia. The five remaining instruments were BFI[7], FACT-F[8], FACT-G[9], MDASI[10], and EORTC QLQ-C30[11]. Two additional instruments were added based on the search strategy: Functional Assessment of Cancer Therapy-Anemia (FACT-An)[8] and Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu).[5] The final analysis included 7 instruments.

Inclusion and Exclusion Criteria

Studies were considered eligible for inclusion if 1) the psychometric paper was published using at least one HRQOL or symptom instrument and 2) adults with acute leukemia were included in the sample. Studies were excluded if the age groups were not adults, or if the instrument was in a language other than English. Other exclusions included case reviews, summary reports, clinical reviews, and literature and systematic reviews.

A total of 1,547 articles were identified through the 5 electronic databases and manual searches. Five hundred sixty-nine were duplicates articles, 324 were chronic leukemia, myelodysplastic syndrome (MDS), or hematopoietic stem cell transplant (HSCT), 309 were about cancer survivors and not acute leukemia, and 290 did not meet the criteria and were removed after initial review. Fifty-five full text articles were assessed for eligibility, and 10 of those were excluded because the studies used non-English instruments, 23 were review or case studies, and 11 focused on childhood cancers. Fourteen studies reported use of a HRQOL and/or symptom instrument [7,12-24] (Figure 1). Seven instruments were identified based on inclusion criteria: 1) Brief Fatigue Inventory (BFI)[7], 2) European Organization for Research and Treatment of Cancer (EORTC QLQ-C30)[11], 3) Functional Assessment of Cancer Therapy-Anemia (FACT-An)[8], 4) Functional Assessment of Cancer Therapy-Fatigue (FACT-F)[8], 5) Functional Assessment of Cancer Therapy-General (FACT-G)[9], 6) Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu)[5], and 7) M.D. Anderson Symptom Inventory (MDASI)[10].

Data Extraction

Both generic and disease-specific HRQOL aspects of leukemia were identified in this review. In addition, the review also yielded symptom instruments which were either solely symptom focused or multidimensional with HRQOL domains. The psychometric properties, reliability and validity, of each instrument were extracted using the Scientific Advisory Committee of the Medical Outcomes Trust criteria.[6] Reliability is "the degree to which an instrument is free from error" and validity is the "degree to which the instrument measures what it purports to measure"[6](pg. 3).

Data Synthesis

The findings from the review are in narrative and table form. The different measures identified in this review and their complete description such as number of items, scoring, domains, scaling, reliability, validity, and numbers of studies are provided in Table 1. The number of items and measured domains of all instruments ranged from 10-47 and 5-15, respectively. Four instruments measured both symptom and HRQOL domains (FACT-An, FACT-F, FACT-Leu and EORTC QLQ-C30). The 14 studies identified in the review are described in Table 2.

Validated HRQOL measures used in Adults with Acute Leukemia

A total of 7 instruments (1 cancer generic HRQOL, 2 symptom-related, 3 HRQOL combined with symptom questions, and 1 disease-specific) were identified and included in this review. The cancer generic HRQOL instrument was the FACT-G.[9] The two symptom-related instruments included the BFI[7] and MDASI[10]. The three HRQOL instruments with symptom questions included FACT-An[8], FACT-F[8], and EORTC-QLQ-C30[11]. The FACT-Leu was the only disease-specific instrument.[5]

Description of Symptom and HRQOL Instruments and their Psychometric Properties

The psychometric properties of the fourteen studies and their use of symptom and HRQOL instruments are presented in the Table 2. The symptom measure with the highest number of items was MDASI.[10] The most commonly used HRQOL measure was the EORTC-QLQ-C30 measures (physical, role, social and emotional function, cognitive, financial impact, and global QOL).

The number of items and domains in the symptom instruments ranged from 1-13 and 1-6. The BFI recall period was in the "past 24 hours,"[7] MDASI recall period was the "last 24 hours,"[10] and FACT instruments were in the "last 7 days"[5,8-9]. All the HRQOL instruments reviewed in this study report overall internal consistency reliability in the range of .54-.96 and test-retest reliability ranging from .77-96. Content and convergent validity were reported for all measures.

Description of Identified Studies

The fourteen studies included in this review were of several types: one was a prospective, cross-sectional study, two were tool validation studies, two were prospective observational studies, four were exercise interventions, and five were prospective longitudinal studies. Ten

of the studies included only patients with acute leukemia, one included patients with acute and chronic leukemia and the other three studies included patients of various cancer types. (Table 2). Stage of cancer treatment was not included because of the variety of cancer types and treatments patients were undergoing. The average number of patients in each of these studies was 104 (range 10-595). All studies were published between 1998-2012.

Discussion

This study reviewed the published psychometric literature and described 7 instruments that measured symptoms or HRQOL in adults with acute leukemia. There is no universally accepted definition of QOL/HRQOL, but various organizations and researchers have defined it as multidimensional in nature. In 2005, the World Health Organization (WHO)[25] defined QOL as "an individual's perception of their position in life, in the context of the culture and value systems in their life, and in relation to their goals, expectations, standards and concerns."[25] Cella's[26] definition of HRQOL refers to the extent to which one's usual or expected physical, emotional, and social well-being are affected by a medical condition or its treatment, whereas Ferrell's QOL framework[27] includes physical, psychological, social, and spiritual domains. Consideration of these QOL domains is necessary in understanding the impact of an acute leukemia treatment and the long term and late effects that accompany this diagnosis.

While using the Scientific Advisory Committee of the Medical Outcomes Trust guidelines[28], we assessed the HRQOL instruments using the attributes and criteria that focus on reliability, validity, cultural and language adaptations. We did assess cultural and language adaptations and noted many of these instruments had been translated and adapted in several languages. One challenge faced by researchers and clinicians is use of reliable and valid measures during and after treatment are responsive to clinical changes. Measures that can capture change over time (i.e., an instruments "responsiveness" to change) are ideal and allows for comparisons between time points. There are two types of HRQOL measures used in this analysis. First, the generic cancer HRQOL measure, FACT-G, is able to measure these domains across different cancers. Few instruments are available that measure HRQOL domains specific to acute leukemia survivors, with one exception, the FACT-Leu. Surprisingly, the FACT-F measure was used more often in these studies than FACT-G or FACT-Leu. This may be associated with emerging data on the impact that cancer related fatigue (CRF) has on adults with acute leukemia during inpatient treatment[12-15,17-18,29-30], and CRF being a persistent symptom during and after treatment.[3-4,31] The FACT-G and EORTC-QLQ-C30 have been validated in a number of cancer groups with a variety of translations, compared to the FACT-Leu, which was only recently developed and validated.

Limitations of this review include focus on adults with acute leukemia without searching grey literature for additional studies such as dissertation abstracts and letters to the editors. We did not focus on chronic leukemias or other hematological cancers, which limits our generalizability to other cancers. However, a systematic methodologic approach using PRISMA was a strength of this review.

Conclusions

Acute leukemia researchers, clinicians, and oncology nurses need to have comprehensive data to explore clinical changes in their patients' symptom or HRQOL responses. Oncology nurses are at the frontline of caring for these patients and it is essential for them to be aware of instruments and tools used in acute leukemia research. Their use of these instruments will allow for early recognition and identification of common symptoms and/or HRQOL changes in these adults. There are certain domains of HRQOL that may be more prominent in acute leukemia survivors, such as increased symptoms and decreased functionality.[4] To the authors' knowledge, this is the first review to explore the psychometric properties of instruments used with the acute leukemia adult population.

Our recommendations for clinical use and research are based on this review including a using both a HRQOL and symptom instrument to capture patient experiences during and after treatment. There are sound, reliable instruments that have been used in this population and we believe there are instruments that could adequately measure the patient's symptom and HRQOL experience throughout their illness trajectory. However, we question if these measures will be relevant over time with longer term survivors? The majority of measures have been tested in patients within 2 years of treatment; researchers lack data to support use of these measures in longer term survivors (>5 years or longer). Survivorship needs of these patients may need to be re-evaluated after 2 years since the late and long term effects may differ in each cancer population.

The HRQOL instruments vary in domains but the FACT-Leu has both general and specific leukemia questions. None of the current studies identified used the Patient-Reported Outcomes Measurement Information System (PROMIS), a promising new system designed to validly and reliably measure HRQOL domains in multiple populations; however no studies to date have examined the psychometric properties of PROMIS measures in acute adult leukemia. This review provides an overall synopsis of previous symptom and HRQOL literature in the acute leukemia population.

Acknowledgments

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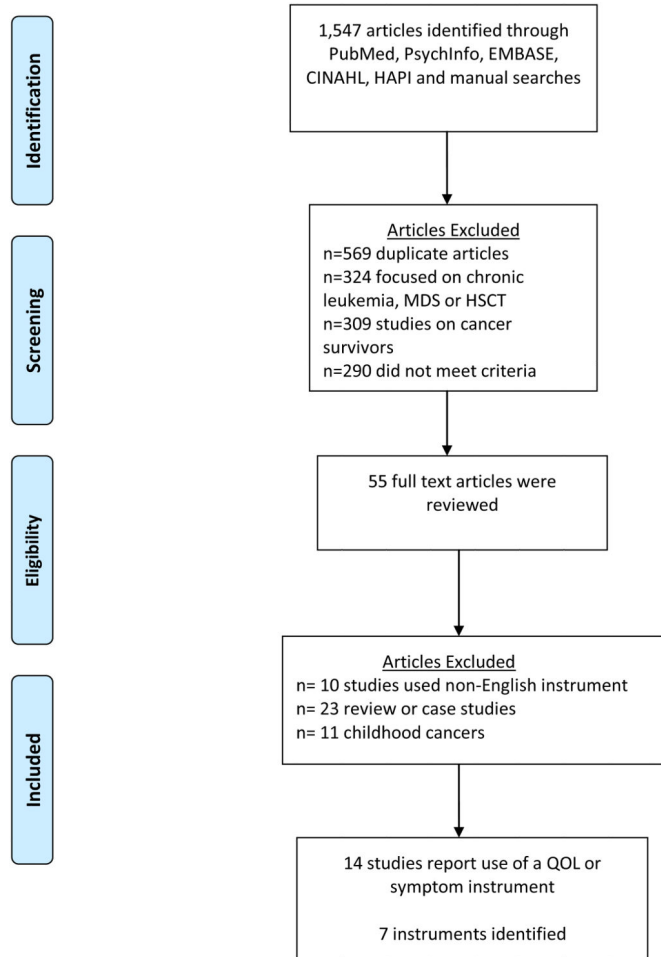
Figure 1. PRISMA Flow Diagram

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Table 1

Characteristics of Instruments Used to Measure Symptoms and HRQOL in Adults with Acute Leukemia

Instrument	# of items	Domains Measured	Scale	Recall Period	Were acute leukemia patients included in sample?	Reliability	Validity	Language/Cultural Adaptations
Brief Fatigue Inventory (BFI)[7]	10 items Higher score, more fatigue (intensity/ interference) patients perceived	Fatigue Intensity Average fatigue intensity Worst level of fatigue Least level of fatigue Fatigue interference with daily life (past week)	0-11 Likert 0=no fatigue (or no interference) at all to 10=worst fatigue (or interference) one can imagine	Past 24 hours	Yes n=17 (51%) acute leukemia	IC: 0.96 Test-retest: Nor reported in original study	Content Criterion related: concurrent Construct: Divergent	Psychometrically and linguistically validated in 8 languages Chinese (simplified and traditional) English Filipino German Greek Japanese Korean Russian
European Organization for Research and Treatment of Cancer (EORTC QLQ-C30)[11]	30 items Higher score poorer QOL	Fatigue Nausea Pain Dyspnea Sleep Disturbance Appetite Loss Constipation Diarrhea Physical function Role function Social function Emotional function Cognitive Financial Impact Global QOL	0-4 Likert 0=not at all to 4=very much	Past Week	Yes n=113 (100%) acute leukemia	Cronbach alpha: 0.54-0.89 Test-retest: Not reported in original study	Content Criterion related: Concurrent Predictive Construct: Convergent Divergent Known group	79 languages
Functional Assessment of Cancer Therapy-Anemia (FACT-An)[8]	47 items Higher the number, greater anemia symptoms	Physical Well-being Social Well-being Emotional Well-being Functional Well-being Anemia related questions	0-4 Likert 0=not at all to 4=very much	Past 7 days	Yes n=3 (6%) acute leukemia	IC: .96 Test retest: .96	Content Criterion-related: Concurrent Construct: Convergent Divergent Known group validity	60 languages
Functional Assessment of Cancer Therapy-Fatigue (FACT-F)[8]	40 items Higher the number, increased fatigue	Physical Well-being Social Well-being Emotional Well-being Functional Well-being Fatigue related questions	0-4 Likert 0=not at all to 4=very much	Past 7 days	Yes n=3 (6%) acute leukemia	IC: .93-.95 Test retest: .90	Content Criterion-related Concurrent Construct Convergent Divergent Known group validity	58 languages

Instrument	# of items	Domains Measured	Scale	Recall Period	Were acute leukemia patients included in sample?	Reliability	Validity	Language/Cultural Adaptations
Functional Assessment of Cancer Therapy-General (FACT-G)[9]	27 items Higher the number, poorer QOL	Physical Well-being Social/Family Well-being Emotional Well-being Functional Well-being	0-4 Likert 0=not at all to 4=very much	Past 7 days	Yes N=8% leukemia	Internal consistency .69-.82 Test-retest reliability .82-.92	Content Criterion-related: Concurrent Construct: Convergent Divergent Known group validity	60 languages
Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu)[5]	42 items Higher the number, greater leukemia symptoms	Physical Well-being Social Well-being Emotional Well-being Functional Well-being Leukemia related questions	0-4 Likert 0=not at all to 4=very much	Past 7 days	Yes N=35 (44%) acute leukemia	Internal consistency .75-.96 Test-retest reliability .765-.890	Content Criterion-related: Concurrent Construct: Convergent Divergent Known Group Validity	46 languages
M.D. Anderson Symptom Inventory (MDASI)[10]	13 items Higher the number, increase symptom distress	General activity Mood Work Relations with others, Walking Enjoyment of life	Symptom Severity 0=Not present to 10=As Bad as you can Imagine Symptom Interference 0=Did not interfere and 10=interfered completely	Last 24 hours	Yes n=29 acute leukemia	IC: 0.82-0.94 Test-retest: 0.83-0.84	Content Criterion-related: Concurrent Predictive Construct: Convergent Known group validity	Psychometrically and linguistically validated in 9 languages Arabic Chinese (Simplified and traditional) English Filipino French Greek Japanese Korean Russian

Table 2

Summary of the Studies using Symptoms and HRQOL Instruments in Adults with Acute Leukemia (n=14)

Author Purpose	Study Design	Sample Characteristics
Alibhai, Leach et al[14]	Prospective, longitudinal	Total n=65; n=65 acute leukemia
Alibhai, Leach, Kermalli et al[13]	Prospective, longitudinal	Total n=65; n=65 acute leukemia
Alibhai et al[12]	Non-randomized, prospective exercise intervention	Total n=35; n=35 acute leukemia
Battaglini et al[15]	Non-randomized exercise intervention	Total n=10; n=10 acute leukemia
Cella et al[24]	Tool validation	Total n=29 (item generation), 79 (validation); acute and chronic leukemia
Efficace et al[16]	Prospective, observational	Total n=119; mixed cancers
Jarden et al[17]	Prospective exercise and health counseling trial	Total n=17; n=17 acute leukemia
Oliva et al[20]	Prospective, observational	Total n=113; n=113 acute leukemia
Mendoza et al[7]	Tool validation	Total n=595; n=68 acute leukemia
Mohamedali et al[19]	Prospective, longitudinal cohort	Total n=103; n=103 acute leukemia
Pearce et al[21]	Prospective, cross-sectional	Total n=150; mixed cancers
Persson et al[22]	Prospective, longitudinal	Total n=16; mixed cancers
Shabbir et al[18]	Non-randomized prospective exercise intervention	Total n=35; n=35 acute leukemia
Schumacher et al[23]	Prospective, longitudinal	Total n=28; n=28 acute leukemia