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Adherence to Oral Chemotherapy in Childhood Acute Lymphoblastic Leukemia: An Evolutionary Concept Analysis

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Purpose/Objectives: To clarify the concept of adherence to daily oral chemotherapy in children with acute lymphoblastic leukemia (ALL), to examine its implications for clinical practice, and to provide a foundation for further research and knowledge development.

Data Sources: Published literature identified through the MEDLINE®, CINAHL®, PsycINFO, and ERIC databases.

Data Synthesis: Identified attributes of adherence to oral chemotherapy in childhood ALL included motivation, persistence, collaboration, mindfulness, cognitive capacity, flexibility, active participation, and identification of key participants in the process. Identified antecedents included a diagnosis of leukemia, the perceived value of adherence, and patient, family, and healthcare system-related factors. Identified consequences included the potential for maintaining optimal drug levels and improving disease outcome, as well as increased patient and caregiver esteem through active participation in the process. Adherence in the context of childhood ALL is defined as the active self-care behavior of taking (or having the responsibility for administering) daily oral chemotherapy, in collaboration with and according to the instructions of the healthcare provider over a defined, prolonged treatment period.

Conclusions: Adherence to oral chemotherapy in childhood ALL is a complex, multidimensional behavior that involves not only a willingness to follow the prescribed regimen over a prolonged period, but also the cognitive capacity and psychomotor skills to carry out the process.

Implications for Nursing: Nurses should recognize the importance of clear communication of medication instructions, reinforcement of adherence-related behaviors, and assistance with common issues such as pill-swallowing skills and reminder systems in caring for children with ALL.

Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy, affecting one in four children and adolescents younger than age 15 who are diagnosed with cancer in the United States (Horner et al., 2009). Although survival rates for childhood ALL have improved significantly over the past 50 years, such that the current five-year survival rate exceeds 85% (Jemal, Siegel, Xu, & Ward, 2010), a substantial number of children and adolescents continue to suffer relapse of the disease, greatly increasing the risk of mortality. Treatment for childhood ALL requires a prolonged maintenance phase that relies on self- or parent-administered daily oral antimetabolite chemotherapy given over a period of about two years (Gale & Butturini, 1991; Stanulla & Schrappe, 2009). Systemic exposure to 6-mercaptopurine (6MP), an oral antimetabolite chemotherapy agent, during the maintenance phase of therapy is a critical component of curative regimens for ALL (Koren et al., 1990; Relling, Hancock, Boyett, Pui, & Evans, 1999). Potential determinants of adequate systemic 6MP exposure include pharmacogenetics (Aplenc & Lange, 2004; Lennard, Lilleyman, Van Loon, & Weinshilboum, 1990; Relling et al., 1999), bioavailability (de Lemos, Hamata, Jennings, & Leduc, 2007; Rivard, Lin, Leclerc, & David, 1989; Schmidt & Dalhoff, 2002; Sofianou-Katsoulis, Khakoo, & Kaczmarski, 2006), and adherence to daily oral administration (de Oliveira, Viana, Zani, & Romanha, 2004; Lau, Matsui, Greenberg, & Koren, 1998; Lennard, Welch, & Lilleyman, 1995).

Adherence to oral chemotherapy in childhood ALL can be measured directly and indirectly. Direct measurements of adherence include red blood cell assays of the 6MP metabolites, thioguanine nucleotide, methylated mercaptopurine, and 6-methylthioinosine monophosphate (Dervieux et al., 2002; Lennard et al., 1990; Lennard & Singleton, 1992), which are metabolized from 6MP via competing pathways and may have differing patterns of concentration in adherent versus nonadherent patients (Lennard et al., 1995). Surrogate measures, such as white blood count or neutrophil count (de Oliveira et al., 2004), as well as behavioral observations,

such as pill counts and electronic medication-monitoring devices (Lau et al., 1998; Pritchard, Butow, Stevens, & Duley, 2006) also have been used to assess adherence in children and adolescents with ALL. Indirect measurements of adherence include patient and/or parent self-report, such as through questionnaires, interviews, and diaries (Davies, Lennard, & Lilleyman, 1993; Pritchard et al., 2006; Tebbi et al., 1986). Adding to the complexity and challenge of adherence to oral chemotherapy for childhood ALL is the fact that multiple chemotherapy agents are administered on differing schedules with differing administration parameters (Landier, 2001; Pui & Evans, 1998), and frequent dose adjustments may be required (Davies & Lilleyman, 1995).

Nonadherence to prescribed oral 6MP chemotherapy in children and adolescents with ALL has been observed in 10% (Lennard et al., 1995) to more than 50% of patients (de Oliveira et al., 2004; Festa, Tamaroff, Chasalow, & Lanzkowsky, 1992). Because nonadherence during the maintenance phase of treatment is a potential cause of low systemic exposure to 6MP, clarification of the concept of adherence to daily oral chemotherapy in children and adolescents with ALL has important implications for clinical practice and research.

Purpose

The purpose of the current analysis is to clarify the concept of adherence to daily oral chemotherapy in children and adolescents with ALL, to examine its implications for clinical practice, and to provide a foundation for further research and knowledge development. Rodgers' (2000) evolutionary method of concept analysis was selected because of its basis in the philosophy that concepts are dynamic, ever-changing over time, and affected by contextual factors. The evolutionary method employs an inductive approach to inquiry that incorporates a multidisciplinary literature review with rigorous data analysis to identify the attributes, antecedents, consequences, associated expressions, surrogate terms, and interdisciplinary and sociocultural contextual variations of the concept (see Table 1). The results, therefore, do not specifically determine what the concept is or is not but, rather, provide the necessary clarity to serve as a strong heuristic for further inquiry and development of the concept in research and practice (Rodgers, 2000).

This concept analysis will address the following questions through its review of the literature: (a) What are the attributes, antecedents, and consequences of adherence to oral chemotherapy in childhood ALL? (b) What are the surrogate terms and associated expressions used for adherence in childhood ALL? (c) What is a suggested definition of adherence to oral chemotherapy in childhood ALL? and (d) What are the implications for research and practice?

Table 1. Components of the Evolutionary Method of Concept Analysis

Component	Explanation
Identification of the concept of interest and associated expressions and surrogate terms	Allows the researcher to select the concept and terminology that are the focus of the study
Identification of setting and sample for data collection	Allows the researcher to identify the time period to be examined and the domains to be included that are consistent with the purpose of the study
Identify attributes of concept.	The primary focus of inquiry; attributes are the real or contextual (as opposed to a dictionary) definition of the concept.
Identify antecedents and consequences of the concept.	What is happening before and what happens after or as a result of the concept
Identify the interdisciplinary and sociocultural contextual variations of the concept.	The situational, sociocultural, and disciplinary contexts for application of the concept to understand how the concept is used in various situations by people from varying perspectives
Perform thematic analysis of each category of data (e.g., attributes, antecedents, consequences).	Thematic descriptors generated from the data
Identification of an exemplar (if possible)	A practical demonstration of the concept as identified in (not constructed from) the data. The ideal exemplar is generic and illustrates the concept clearly in a variety of instances.
Interpretation of results and identification of implications for further development of the concept	Provides a guide and foundation for further inquiry by delineating the current status of the concept and identifying gaps in current knowledge

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Methods

The concept of adherence is closely related to compliance, and in some cases, the terms are used interchangeably. Compliance often is associated with paternalistic or authoritarian healthcare provider behavior and lack of autonomy on the part of the patient (Evangelista, 1999), whereas adherence more commonly is associated with shared decision making between the patient and healthcare provider (Duncan, Cloutier, & Bailey, 2007). Associated expressions and surrogate terms include *mutuality, therapeutic alliance, maintenance, concordance, cooperation,* and *self-care* (Duncan et al., 2007; Kyngäs, Duffy, & Kroll, 2000; Pritchard et al., 2006; Shay, 2008). For the purpose of data gathering, the terms *adherence* and *compliance* both were included in the literature search strategy.

Setting and Sample

A search of the literature was conducted with the OvidSP search interface in the MEDLINE®, CINAHL®, and PsycINFO databases. An additional search was carried out in the ERIC database, because ERIC was not accessible through the OvidSP search interface. The search was limited to peer-reviewed published articles, and the search strategy employed the following parameters: (a) having *patient compliance* or *medication compliance* (or, in the case of PsycINFO, *treatment compliance)* as a subject heading, (b) having the key words a*dherence, child* or *adolescent*, and *chronic disease*, (c) limited to the English language, and (d) published from 1978–2008 (1982–2008 for CINAHL). The search was narrowed to this 30-year time frame beginning in 1978 because it spans the period from two years prior to the publication of the first articles on adherence to oral chemotherapy in childhood cancer and one year prior to publication of Haynes, Taylor, and Sackett's (1979) seminal work on compliance, through the present time. The search in CINAHL was initiated in 1982 because of constraints within the CINAHL database structure. Subject headings were not available in ERIC; therefore, the search strategy for this database included the key words *adherence* and *medication*. An enriched subset of articles specific to pediatric cancer and leukemia was identified through an additional search of MEDLINE using the above OvidSP search strategy and substituting the terms *cancer* and *leukemia* for *chronic disease* to yield more specific information regarding adherence in childhood ALL.

The database search strategies resulted in 349 citations retrieved from MEDLINE, 104 from CINAHL, 115 from PsycINFO, and 24 from ERIC. The cancer or leukemia-enriched subset yielded 17 additional articles from MEDLINE. After reviewing the retrieved citations for relevance, a total of 28 articles were sampled from MEDLINE, 22 from CINAHL, 16 from PsycINFO, 4 from ERIC, and 9 from the enriched cancer or leukemia subset, for a total sample size of 79 articles. Additional relevant articles were included in the data sample from the reference lists of the articles as the analysis proceeded, yielding a total of 83 articles in the final sample.

Data Analysis

Each article was coded by discipline (e.g., nursing, medicine, pharmacology, psychology, epidemiology), which was determined by the department affiliation or credentials listed for the first author. The findings then were summarized by completing a data abstraction form for each article. Data elements collected included citation, publication year, discipline, surrogate terms, and associated expressions, attributes, antecedents, consequences, interdisciplinary and sociocultural contextual variations, context, definition, and exemplar, in accordance with the evolutionary method of concept analysis (Rodgers, 2000). Not all articles contained all data elements, but all available data were entered onto an abstraction form for each article. Attributes, antecedents, and consequences then were coded for thematic analysis, and themes were identified inductively and compared across disciplines prior to combining data for the final analysis.

Findings

Definitions From the Literature

Given the overlapping definitions and use of surrogate terms in the context of oral chemotherapy for childhood ALL, the terms *adherence* and *compliance* can and have been used interchangeably to represent different attributes of this multifaceted and complex concept. Review of the evolution of these terms in the literature reveals that *adherence* more commonly is used in recent and current literature and, in some cases, is used in place of compliance. However, *compliance* was the more dominant term in the literature throughout the 1970s and 1980s.

Compliance: Evangelista (1999) described the five defining attributes of compliance as the "ability to complete or perform what is due, flexibility, adaptability, malleability, and subordinate behaviors" (p. 7). Additional definitions of compliance in the literature include those with a paternalistic connotation, such as "the extent to which a patient's behavior coincides with advice and therapy prescribed by the medical provider" (Festa et al., 1992, p. 808), and "following directions or following a prescribed regimen" (Evangelista, 1999, p. 7), as well as those with an aspect of participation and mutuality, such as "the extent to which an individual chooses behaviors that coincide with a clinical prescription" (Dracup & Meleis, 1982, p. 31), and "the patient's active, intentional, and responsible process of self-care, in which the patient works to maintain his or her health in close collaboration with healthcare staff" (Kyngäs, Duffy, et al., 2000, p. 7). Similar to compliance, definitions for noncompliance vary and range from "behaviors that vary from the consensual regimen" (Dracup & Meleis, 1982, p. 31) that form "a continuum from the occasional lapse to total refusal" (Lilleyman & Lennard, 1996, p. 1220) to the original definition of noncompliance used at the North American Nursing Diagnosis Association's first national conference in 1973: "A person's informed decision not to adhere to a therapeutic recommendation" (Kim & Moritz, 1982, p. 299). The essential characteristics described within the definitions can be summarized by the observation that "the complexity of noncompliance cannot be reduced to, and adequately reflected in, the labeling of the individual as being either compliant or noncompliant" (Kyngäs, Duffy, et al., 2000, p. 11).

Adherence: Dracup and Meleis (1982) defined adherence as "a willingness on the part of the patient to participate with the prescribed regimen" (p. 31). Shay (2008) described adherence as "one's ability to maintain the behaviors associated with a plan of care. This often involves taking medications, keeping appointments, or changing health behaviors" (p. 42). Nonadherence with oral medication occurs "when the failure to comply is sufficient to interfere appreciably with achieving the therapeutic goal" (O'Hanrahan & O'Malley, 1981, p. 291) and "can range from a complete failure to take the prescribed medication to the patient's altering of either dose or duration of therapy" (Festa et al., 1992, pp. 808–809).

Attributes

Identified attributes of adherence to oral chemotherapy in childhood ALL include (a) motivation or willingness to stick to the prescribed treatment, (b) persistence over a prolonged, defined treatment period that usually lasts two to three years, (c) collaboration with a healthcare provider, (d) mindfulness of dose requirements and administration parameters, including instructions regarding time of administration for each agent and restrictions relating to concomitant administration with or without food or dairy products, (e) the cognitive capacity to correctly follow instructions, (f) flexibility to adapt and conform to ongoing changes in the regimen, (g) active participation in the process of oral chemotherapy administration (e.g., development of concrete solutions to issues with pill swallowing, forgetfulness), and (h) identification of key participants in the adherence process, including the person responsible for home medication administration (parent, caregiver, or patient) and the healthcare provider who closely supervises the parent, caregiver, or patient (see Table 2).

Antecedents and Consequences

Identified antecedents to adherence to oral chemotherapy in childhood ALL include (a) the diagnosis of leukemia, which is a threat to well-being and a directing force through which susceptibility and vulnerability are perceived by the patient and/or family, (b) patient and family factors, including knowledge and understanding of the diagnosis and treatment, adaptation to the illness, ability or willingness to learn pill-swallowing skills, the child's age and developmental stage, family functioning, social support, a sense of normality, health beliefs, culture or ethnicity, and socioeconomic indicators, (c) healthcare system factors, including clear healthcare provider communication and supportive presence; the complexity, duration, and side effects of treatment; and healthcare access and costs of care; and (d) the perceived value of adherence by the patient and family and the healthcare team (i.e., a belief that long-term survival or cure of leukemia is achievable and related to adherence to oral chemotherapy) (see Table 3).

Identified consequences of adherence to oral chemotherapy in childhood ALL include (a) the potential for maintaining optimal levels of chemotherapy metabolites (e.g., thioguanine nucleotide, methylated

Table 2. Literature Support for Attributes

Attribute	Discipline[a] and References
Active participation	**Medicine:** Osterberg & Blaschke, 2005; **Nursing:** Goode et al., 2004; Kyngäs, 2007; Kyngäs, Kroll, et al., 2000; Malbasa et al., 2007
Cognitive capacity	**Medicine:** Cromer & Tarnowski, 1989; Friedman & Litt, 1987; **Nursing:** Malbasa et al., 2007; **Psychology:** Babbitt et al., 1991
Collaboration with a healthcare provider	**Medicine:** Cromer & Tarnowski, 1989; de Oliveira et al., 2004; Tebbi et al., 1986; **Nursing:** Kyngäs, 2007; Kyngäs, Kroll,et al., 2000; Kyngäs, Skaar-Chandler, et al., 2000; Malbasa et al., 2007; **Psychology:** Fielding & Duff, 1999; Lemanek, 1990
Dose requirements and administration parameters	**Medicine:** Cromer & Tarnowski, 1989; de Oliveira et al., 2004; Gaynon, 2006; Lau et al., 1998; **Pharmacology:** Lennard et al., 1995; Relling et al., 1999
Flexibility to adapt to changes	**Nursing:** Betz, 2006; Kyngäs, Skaar-Chandler, et al., 2000; **Psychology:** Roberts, 2005
Identification of key participants in the adherence process	
• Person responsible for home medication administration (parent, caregiver, or patient)	**Medicine:** de Oliveira et al., 2004; Mears et al., 2006; Tebbi et al., 1988, 1989; **Nursing:** Magyary & Brandt, 1996; Malbasa et al., 2007; **Psychology:** Martin et al., 2007; Pritchard et al., 2006
• Healthcare provider who supervises person responsible for home medication administration	**Medicine:** Lau et al., 1998; Sawyer & Aroni, 2003; **Nursing:** Betz, 2006; Malbasa et al., 2007; **Psychology:** Lemanek, 1990; Pritchard et al., 2006
Motivation	**Medicine:** Friedman & Litt, 1987; Lansky et al., 1983; **Nursing:** Kyngäs, 2000a, 2000b, 2007; Kyngäs & Rissanen, 2001; **Psychology:** Lask, 2003
Prolonged, defined treatment period	**Medicine:** Davies & Lilleyman, 1995; Hale & Lilleyman, 1991; **Nursing:** Malbasa et al., 2007; **Pharmacology:** Relling et al., 1999; **Psychology:** Pritchard et al., 2006

[a] Discipline was determined by departmental affiliation and/or credentials listed for first author of each article.

mercaptopurine, 6-methylthioinosine monophosphate), (b) the potential for improved disease outcome (i.e., decreased likelihood of leukemia relapse), and (c) increased patient and/or caregiver self-esteem, pride, and accomplishment related to active participation in care resulting in positive outcomes (see Table 4).

Contextual Variations

Interdisciplinary: Common attributes of adherence identified by the disciplines of nursing, medicine, pharmacology, and psychology included the importance of taking the medication exactly as prescribed, according to the instructions of the healthcare provider, over a prolonged, defined period (Davies & Lilleyman, 1995; Kyngäs, Duffy, et al., 2000; Malbasa, Kodish, & Santacroce, 2007; Pritchard et al., 2006; Relling et al., 1999; Tebbi et al., 1986). The importance of correct dosing and administration of the oral chemotherapy, including medication-specific restrictions such as time of day and timing of administration in relation to food intake, was identified by medicine and pharmacology (Gaynon, 2006; Lau et al., 1998; Lennard et al., 1995). The unique role of the child's age and developmental stage, the family's cultural and health beliefs, and the availability of social support in regard to medication adherence were emphasized by epidemiology (Hovell, Sipan, et al., 2003; Rogers, Miller, Murphy, Tanney, & Fortune, 2001; Salabarría-Peña et al., 2001). The importance of identifying a person responsible for medication administration within the family, such as a parent or caregiver, was identified by medicine, nursing, and psychology (Baker et al., 1993; de Oliveira et al., 2004; Malbasa et al., 2007; Pritchard et al., 2006). Willingness to stick to the prescribed therapy was identified as important by nursing and psychology (Kyngäs, 2000a, 2000b; Kyngäs & Rissanen, 2001; Lask, 2003), and nursing also emphasized the importance of adaptability and active participation in the process of oral chemotherapy administration (Evangelista, 1999; Goode, Harrod, Wales, & Crisp, 2004; Kyngäs, 2007; Kyngäs, Duffy, et al., 2000; Malbasa et al., 2007). A multidisciplinary view of adherence is multifaceted and incorporates precise administration, persistence, adaptability, active participation, and self- or parental responsibility for medication administration.

Sociocultural: Lower socioeconomic status was associated with decreased adherence in some studies, particularly in regard to income, access to care, and nutritional status (de Oliveira et al., 2004). Language barriers also were observed to be potential sources of impaired adherence (Tebbi et al., 1986). Consequently, socioeconomic and linguistic barriers may play an important role in adherence in this population.

References: References to the concept of adherence to oral chemotherapy were made in the context of children and adolescents with leukemia in the maintenance phase of treatment (Davies et al., 1993; Festa et al., 1992; Relling et al., 1999). In addition, the literature relevant to the concept of adherence to oral medication was reviewed in the context of children and adolescents with other chronic illnesses, including asthma (Knight, 2005), Hodgkin lymphoma, other cancers (Festa et al., 1992; Tamaroff, Festa, Adesman, & Walco, 1992), insulin-dependent diabetes mellitus (Kyngäs, 1999; Palardy, Greening, Ott, Holderby, & Atchison, 1998), HIV (Singh et al., 1999), rheumatoid arthritis (Kyngäs & Rissanen, 2001), and tuberculosis (Hovell, Sipan, et al., 2003). Therefore, although some considerations may be unique to oral chemotherapy, issues relevant to adherence to oral medications in children and adolescents with other chronic illnesses may contribute to the understanding of adherence behaviors among children and adolescents with ALL.

Clarifying and Defining the Concept

Based on the thematic analysis of the literature reviewed, a suggested definition for adherence to oral chemotherapy in childhood ALL is as follows: Adherence to oral chemotherapy in childhood ALL is a complex, multidimensional, context-bound concept that can be defined as the active self-care behavior of taking (or having the responsibility for administering) daily oral chemotherapy, in collaboration with and according to the instructions of the healthcare provider over a defined, prolonged treatment period. Inherent in this definition are the following themes: (a) the motivation or willingness to adhere to or follow a plan (Shay, 2008), (b) intention, capacity, responsibility, and collaboration (Kyngäs, Duffy, et al., 2000), (c) adaptation to change (Evangelista, 1999), (d) willingness to carefully follow the instructions of a healthcare provider (de Oliveira et al., 2004), and (e) active participation in the process of daily oral chemotherapy administration (Malbasa et al., 2007). The author's definition differs from other proposed definitions of adherence in the literature because the author's is context-bound to current treatment regimens for childhood ALL that incorporate daily oral chemotherapy as the mainstay of maintenance treatment.

Strengths and Limitations

Strengths of the evolutionary method used in the current analysis include the breadth of the literature reviewed, the systematic and rigorous approach, and the emphasis on current use of the concept. A limitation of the evolutionary method is that the sampling design for selecting literature for review did not include complete analysis of all retrieved articles but, rather, relied on the investigator performing a brief

review for relevance in choosing the final articles for review. That may have resulted in overlooked articles containing important information regarding the topic under study and could have resulted in missed themes or lack of corroboration of thematic elements by additional investigators. In addition, the analysis would have been strengthened by field work to identify relevant exemplars.

Table 3. Literature Support for Antecedents

Antecedent	Discipline and References
Diagnosis	
Threat to health; perceived susceptibility	**Epidemiology:** Zindani et al., 2006; **Medicine:** Cromer & Tarnowski, 1989; Friedman & Litt, 1987; Rianthavorn & Ettenger, 2005; Tebbi et al., 1986; **Nursing:** Deatrick, 1990; Kyngas, 2000a, 2000b; Kyngäs, Skaar-Chandler, et al., 2000; Wichowski & Kubsch, 1997; **Psychology:** Van Sciver et al., 1995
Diagnosis: Patient and Family Factors	
Adaptation	**Nursing:** Kyngäs, 2000b; Malbasa et al., 2007; Stewart & Dearmun, 2001
Age and developmental stage	**Epidemiology:** Hovell, Blumberg, et al., 2003; Hovell, Sipan, et al., 2003; **Nursing:** Betz, 2006; Deatrick, 1990; Malbasa et al., 2007; Stewart & Dearmun, 2001; **Medicine:** Festa et al., 1992; Rianthavorn & Ettenger, 2005; Smith et al., 1979; Tebbi, 1993; **Psychology:** Anderson & Collier, 1999; Fiese & Everhart, 2006; Logan et al., 2003; Manne et al., 1993; McQuaid et al., 2003
Culture	**Epidemiology:** Hovell, Blumberg, et al., 2003; Hovell, Sipan, et al., 2003; Salabarría-Peña et al., 2001
Family functioning	**Epidemiology:** Salabarría-Peña et al., 2001; Zindani et al., 2006; **Medicine:** Cromer & Tarnowski, 1989; Shemesh et al., 2007; Tebbi, 1993; **Nursing:** Deatrick, 1990; Kyngäs & Rissanen, 2001; Magyary & Brandt, 1996; Malbasa et al., 2007; **Pharmacology:** Costello et al., 2004; **Psychology:** Anderson & Collier, 1999; Fiese & Everhart, 2006; Fiese & Wamboldt, 2003; Hauser et al., 1990; La Greca, 1990; Pritchard et al., 2006; Wysocki & Gavin, 2006
Health beliefs	**Medicine:** Cromer & Tarnowski, 1989; Friedman & Litt, 1987; Sveum, 2005; Tebbi, 1993; **Nursing:** Goode et al., 2004; **Psychology:** Charron-Prochownik et al., 1993; Pritchard et al., 2006;
Knowledge	**Epidemiology:** Hovell, Blumberg, et al., 2003; **Medicine:** Nicholson et al., 2006; Osterberg & Blaschke, 2005; Rich et al., 2000; Smith & Shuchman, 2005; Tebbi et al., 1986; **Nursing:** Green & Ray, 2006; Magyary & Brandt, 1996; Schäfer-Keller et al., 2006; **Psychology:** Cunningham et al., 2006; Lemanek, 1990; Maikranz et al., 2007; Martin et al., 2007; Putnam et al., 1994; Rapoff, 2006
Pill-swallowing skills	**Psychology:** Babbitt et al., 1991; Cunningham et al., 2006; Garvie et al., 2007; Roberts, 2005
Sense of normality	**Nursing:** Kyngäs, 2000a, 2000b, 2007; Malbasa et al., 2007
Social support	**Epidemiology:** Hovell, Blumberg, et al., 2003; Rogers et al., 2001; **Nursing:** Kyngäs, 2007; Kyngäs & Rissanen, 2001; Kyngäs, Skaar-Chandler, et al., 2000
Healthcare System Factors	
Access to care	**Epidemiology:** Rogers et al., 2001; **Medicine:** de Oliveira, 2004; Osterberg & Blaschke, 2005
Communication	**Medicine:** de Oliveira, 2004; Osterberg & Blaschke, 2005; **Nursing:** Butz, 2006; Goode et al., 2004; **Pharmacology:** Costello et al., 2004; **Psychology:** Dimatteo, 2004
Costs	**Medicine:** Osterberg & Blaschke, 2005; **Nursing:** Schäfer-Keller et al., 2006
Perceived value of adherence	**Medicine:** Cromer & Tarnowski, 1989; **Psychology:** Van Sciver et al., 1995
Quality of relationship	**Medicine:** Cromer & Tarnowski, 1989; Osterberg & Blaschke, 2005; Puccio et al., 2006; Rich et al., 2000; Tebbi, 1993; Tebbi et al., 1986; **Nursing:** Klopovich, 1983; Kyngäs, 2000a, 2000b; Kyngäs & Rissanen, 2001; **Psychology:** Last & Grootenhuis, 2007; Pritchard et al., 2006
Treatment complexity	**Medicine:** Osterberg & Blaschke, 2005; Smith & Shuchman, 2005; Sveum, 2005; **Nursing:** Butz, 2006; Klopovich, 1983; Rosina et al., 2003; **Psychology:** Anderson & Collier, 1999; Lemanek, 1990; Martin et al., 2007
Treatment duration	**Medicine:** Davies & Lilleyman, 1995; Osterberg & Blaschke, 2005; **Psychology:** Marhefka et al., 2006
Treatment side effects	**Medicine:** Smith & Shuchman, 2005; **Nursing:** Green & Ray, 2006; Schäfer-Keller et al., 2006; **Psychology:** Roberts, 2005

Implications for Practice and Research

Clinical implications for healthcare providers include recognition of the importance of clear communication of instructions and reinforcement of adherence-related behaviors in children and adolescents with ALL and their families. The multifaceted nature of adherence in this population may present challenges to healthcare providers, who must assess child and parental capacity for adherence, address knowledge deficits, and assist with common issues related to daily medication administration, such as pill-swallowing skills and reminder systems. A disease management plan that addresses the specific needs of individual children and adolescents and their families may be helpful in promoting adherence in this population.

Several gaps exist in the literature regarding adherence to oral chemotherapy in childhood ALL. Investigations are needed to determine the complexity of health behaviors required to be fully adherent with the prescribed maintenance chemotherapy regimen and the role of healthcare providers in fostering adherence in this population. In addition, the barriers and facilitators to adherence as perceived by children and adolescents with ALL and their parents or caregivers need to be identified. These data are critical to inform development of interventions aimed at improving adherence to oral chemotherapy, an area ripe for future research.

Conclusions

Adherence to oral chemotherapy in childhood ALL is a complex, multidimensional behavior that is predicated on the parent and child understanding and correctly carrying out complex instructions from the healthcare provider about a variety of medications, some with associated parameters regarding time of day when the medication is to be administered and/or administration without food or dairy products, and all of which may require frequent dose adjustments in response to blood counts, infections, clinical course, or changes in weight or body surface area. Therefore, adherence involves not only a willingness to stick to the prescribed regimen over a prolonged, defined period, but also the cognitive capacity and psychomotor skills to carry out the process (including the ability to identify and overcome potential barriers such as forgetfulness, change in routine, or lack of ability to swallow pills). Socioeconomic and cultural issues, such as financial and language barriers, and difficulty accessing medical care also may affect the patient and family's ability to adhere to the prescribed regimen.

Clear identification of the person responsible for ensuring that all prescribed doses of oral chemotherapy are administered at home on a daily basis may play an important role in fostering adherence in childhood ALL.

Table 4. Literature Support for Consequences

Consequence	Discipline and References
Increased self-esteem, pride, or accomplishment	**Medicine:** Cromer & Tarnowski, 1989; Nursing: Knight, 2005; **Psychology:** Putnam et al., 1994
Potential optimization of drug levels	**Medicine:** Davies & Lilleyman, 1995; Hale & Lilleyman, 1991; Traore et al., 2006; **Pharmacology:** Koren et al., 1990; Lennard et al., 1995; Relling et al., 1999
Potential improved outcome	**Medicine:** Hale & Lilleyman, 1991; **Pharmacology:** Koren et al., 1990; Relling et al., 1999

That may be particularly salient for adolescents, who often are assigned self-responsibility for their medications at a time when they are not ready to fully assume that responsibility (Tebbi, Richards, Cummings, Zevon, & Mallon, 1988; Tebbi, Zevon, Richards, & Cummings, 1989). Unlike treatment of other chronic childhood illnesses, treatment for ALL is time-limited and curative in intent; therefore, adherence is required for a finite, yet prolonged period, generally lasting two to three years. Methods aimed at achieving or improving adherence behaviors in children and adolescents with ALL, therefore, may require different approaches than those used for other chronic illnesses, such as diabetes or asthma, in which the patient must assume full responsibility for all aspects of self-care management during the late adolescent or young adult period to gain the skills and knowledge required to manage the condition throughout adulthood. In childhood ALL, it may not be necessary or desirable for the patient to achieve full independence for self-administering oral chemotherapy; in fact, working in partnership with an adult parent or caregiver and healthcare provider, the patient may optimize adherence to the oral chemotherapy regimen during therapy. Clearly defining the multiple components of the concept of adherence to oral chemotherapy in children and adolescents with ALL sets the stage for future research aimed at identification of specific barriers to adherence and development of interventional strategies to facilitate the process of adherence, despite the barriers encountered.

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1. What is a concept analysis? Is this a research article?
2. Why is it necessary to define and discuss all the different terms for adherence?
3. How did the author of this study define adherence?
4. This study was about adherence in children and adolescents with acute lymphoblastic leukemia. Would you define adherence differently in an adult population?
5. How can we help parents or caregivers of children and adolescents with acute lymphoblastic leukemia to adhere to oral therapy at home?
6. How important do you think motivation is to adherence?

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