

Peter O'Neill. Brothers. Original in oil on linen, 30" × 40".

A growing number of pediatric cancer patients use complementary therapies as part of their treatment regimen to attempt to improve outcomes or enhance quality of life.

Complementary Therapies and Childhood Cancer

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Background: The use of complementary and alternative therapies by children with cancer is common. Up to 84% of children have used complementary therapies along with conventional medical treatment for cancer.

Methods: We reviewed the PubMed and CINAHL databases for studies published between 1994 and 2004 on the use of complementary and alternative therapies by children with cancer and reports from any publication year through 2004 of clinical trials involving complementary and alternative therapies for children with cancer.

Results: Fourteen studies were retrieved reporting the results of survey or interview data collected from parents on children's use of complementary and alternative therapies during or after childhood cancer. Across studies, the use of such therapies ranged from 31% to 84%. Common reasons for using complementary and alternative therapies were to do everything possible for their child, to help with symptom management, and to boost the immune system. Many parents indicated they also hoped to treat or cure the cancer. In most cases, the child's treating physician had not been informed of the child's use of complementary and alternative therapies.

Conclusions: Use of complementary therapies by children with cancer is common, although methodological variations limit the ability to compare results across studies. Treating physicians often do not know the child is using complementary therapies in addition to medical treatments. The scientific evidence is limited regarding the effects and mechanisms of action of complementary or alternative therapies, but research is being conducted on these topics.

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Introduction

In the past decade, the results of several survey and interview studies have been published in which parents of a child diagnosed with cancer have been asked about their child's use of complementary or alternative therapies after the time of diagnosis. Results have indicated that 31% to 84% of children used some form of complementary therapy along with conventional medical therapy for cancer.¹⁻¹⁴ Some portion of the range of responses is likely due to varied survey methods and definitions used across studies. For example, the terms *unconventional*, *alternative*, and *complementary* have been defined differently across studies.

This paper summarizes data published from 1994 to 2004 regarding complementary therapy use by children during and after childhood cancer. This time period was selected for review because increased scientific, medical, and public interest in complementary and alternative medicine was reflected in the opening of the National Institutes of Health Office of Alternative Medicine in 1993. This office became the National Center for Complementary and Alternative Medicine in 1998. The National Cancer Institute's Office of Cancer Complementary and Alternative Medicine was also established in 1998. Surveys and interview studies are discussed in chronological order by publication date. For each study discussed, the terms complementary, alternative, and unconventional are reproduced here as they were used by the investigators of the study. In addition, results of clinical trials of complementary therapies carried out in samples of children diagnosed with cancer are presented in order to understand the evidence base relating to complementary therapies in pediatric oncology samples. Research reports through the year 2004 were complied from PubMed, the database provided by the National Library of Medicine, and from CINAHL (Cumulative Index of Nursing and Allied Health Literature). Research reports are summarized using the organizational framework for five domains of complementary and alternative therapies delineated by the National Institutes of Health National Center for Complementary and Alternative Medicine. These five domains include biologically based complementary therapies, manipulative and body-based therapies, mind-body interventions, alternative medical systems, and energy therapies. Specific search terms employed within each domain are presented in the section on clinical trials.

Data on the Use of Complementary and Alternative Medicine

Sawyer et al¹ administered questionnaires to parents of 48 Australian children 4 to 16 years of age who were diagnosed with cancer (excluding brain tumors). Parents were asked to describe "any dietary supplements or alternative therapies used by the children" since the time of

diagnosis. Parents indicated approximately one half (46%) of the children had used at least one such therapy since diagnosis. The most commonly used therapies included imagery, hypnotherapy, relaxation, diets, and multivitamins. Spiritualism, faith healing, meditation, megavitamins, chiropractic, and homeopathy were also used. Most parents (56%) viewed the therapies as harmless and thus did not disclose the use of complementary therapies to the child's treating physician.

Friedman et al² collected parental reports from a convenience sample on the use of alternative therapies, specifically, practices that were not prescribed by a physician or not considered a proven medical treatment. They interviewed 81 parents of pediatric cancer patients and 80 parents of a control group of children attending routine checkups or noncancer acute care in the southeastern United States. Interviewers provided the study definition of alternative therapy to parents and offered clarification in response to questions. Parents indicated that 65% of the children treated for cancer and 51% of the noncancer patients had used alternative therapy, most often prayer. Excluding prayer, the two groups of children appeared more similar, with 45% of the cancer group and 42% of the control group using alternative therapies. Among the parents of children with cancer, the most frequently cited reasons for using alternative therapies were faith in the healing powers of prayer (21%) and supplementation of conventional medicine (7%). Only 2 parents of children with cancer and 3 parents of children in the control group indicated that dissatisfaction with conventional medicine contributed to providing alternative therapy to their children. The parents who discussed the use of alternative therapies with their child's physician were most often parents of a child with cancer (53% vs 22% of parents in the control group), those with higher income (59%), and those who were white (47%).

Mottonen and Uhari³ prospectively studied the use of biologically based products such as micronutrients and unconventional drugs taken internally by children in Finland (n = 15, mean age 7.3, range 4.3 to 12.6 years) with acute lymphoblastic leukemia (ALL) in the remission stage, most of whom had reached the continuation phase of therapy. They then randomly selected healthy children (n = 26) matched for age, sex, and socioeconomic status. Daily diary data collected for 2 years indicated that children with ALL took micronutrients and vitamins much more often than did children in the control group. Forty percent of children with ALL compared to 7.7% of the control group had taken biologically based products, including preparations of multivitamins, trace elements, fluoride tablets, and other minerals. Four children with ALL took a mixture of trace elements, 3 took shark liver tablets, and 1 took oil of evening primrose.

Grootenhuis et al⁴ conducted semistructured interviews and administered questionnaires to children and parents to assess the use of "alternative treatment" by 84

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children 8 to 18 years of age with a cancer history. Among these 84 children, 43 were in first continuous remission and 41 had relapsed or had a second malignancy. Overall, nearly one third (31%) of children used one or more alternative therapy, with relapsed patients using these more often (46%) than patients who were in remission (16%). No other medical characteristic (eg, number of hospitalizations, time since diagnosis) predicted use vs nonuse of alternative therapy. Homeopathy and macrobiotic diet were among the most often used therapies (used by 15 children). Massage, applied kinesiology, and light therapy were in the next most commonly used group of therapies (used by 9 children). Psychic healing, imagery healing, and faith healing were in the third most commonly used group (used by 6 children), while diets claiming to prevent cancer were used by 2 children. One child in the remission group and 7 in the relapsed group used more than one kind of alternative therapy. The investigators concluded that the prospect for survival was the strongest predictor for using one or more alternative therapies.

Fernandez and colleagues⁵ conducted a retrospective cohort questionnaire survey of parents of 583 children who were diagnosed with cancer between 1989 and 1995 in British Columbia and who were referred to tertiary care. Definitions of alternative and complementary therapies were included in the introductory letter to parents. Alternative therapies were defined as "remedies that are used by individuals for cancer and other aspects of health that are characterized by a lack of scientific testing and lack of recognition of effectiveness by conventional medicine." Complementary therapies were defined as "those used in addition to conventional medicine to improve the well-being of the child and relieve symptoms." A total of 366 parents participated in the survey. Results indicated that 156 children (42.6%) had used complementary or alternative therapies, with herbal teas, plant extracts, relaxation/imagery strategies, vitamins, massage, diets, and therapeutic touch among the most frequently employed therapies. Most (68%) began using them while still on their initial medical treatment. Among children who relapsed or died, 60% used complementary or alternative therapies. Most parents believed the therapies were beneficial (49%) or very beneficial (20%) to their child's quality of life. No parent ascribed serious adverse effects to the complementary or alternative therapies, although 8 parents described mild adverse effects (eg, unpleasant taste, diarrhea, pain). Factors associated with the use of complementary or alternative therapies included their prior use, a positive attitude toward the therapies, information on them from family, friends, or alternative caregivers, high risk of death at diagnosis, and advanced education of at least 1 parent. Most parents indicated that they initiated the use of complementary and alternative therapies in order to do everything possible for their child (n = 126) or to "boost" the immune system (n = 117). Additional goals were to cure the cancer (n = 60), to give "softer" treatment

(n = 57), to slow the progression of the cancer (n = 52), to use a more holistic approach (n = 50), and to use psychologic forces (n = 45). Therapies were most often used in conjunction with conventional medical treatment; however, 8 parents of children with a poor-prognosis disease reported using alternative therapies in place of recommended conventional medical treatments. More than half of the parents (55%) did not believe the oncologist was aware of their child's use of complementary or alternative therapies. Reasons for not using them included lack of knowledge about complementary and alternative therapies and concerns about their potential interference with medical treatment.

Yeh et al⁶ conducted semistructured, individual, indepth interviews with parents of 63 pediatric oncology patients at least 2 months postdiagnosis in Taiwan about their child's use of "alternative therapy" such as non-Western therapies including traditional Chinese medicine, Eastern spiritual practices, and folk remedies in conjunction with Western conventional oncology medicine. Seventythree percent of the children had used at least one non-Western therapy. The most commonly reported remedies were packaged liquids or powders purported to be high in nutritional value and capable of limiting side effects, increasing immune function, and improving prognosis (48%). Spiritual practices such as worshipping in Buddhist temples or consulting a shaman were also frequently used (41%). Folk medicine and herbal remedies were used by 28% of children, and practitioners of traditional Chinese medicine had treated 19% of children. Reasons for use of non-Western therapies included, in order of frequency, reducing pain, shortening the therapeutic cycle, limiting side effects, increasing the child's internal strength, improving the child's ability to cope with unpleasant medical events, and curing the disease. Use of non-Western approaches was not predicted by education or the family's social status. Ten parents disclosed the use of non-Western therapies. Those who did not (77%) cited their concern that such disclosure might imperil relationships with their child's medical providers.

Kelly et al7 administered a questionnaire in a face-toface interview or by telephone interview to parents of 75 cancer patients 3 months to 26 years of age who were at least 3 months postdiagnosis and receiving conventional medical care for cancer or follow-up for conventional medical care at an urban academic hospital in the northeastern United States. Fourteen of the patients themselves, ranging in age from 10 to 26 years, were also interviewed. Results indicated that 84% of patients had used one or more "unconventional therapies," defined as "an agent or practice initiated since diagnosis that was not part of the standard care of the child with cancer." Most often these therapies were changes in diet, nutritional supplements, herbal remedies, and mind-body approaches, especially prayer. Use was not predicted by cancer diagnosis, race, ethnicity, socioeconomic status, or educa-

tion. The most common intended purpose for using unconventional therapies was to improve the general health of the child (29%). Relaxation was also frequently mentioned (14%), particularly for mind-body therapies and touch therapies. Additional intended goals for use included detoxification (13%), improvement in immune function (8%), tumor reduction (8%), improvement in appetite/digestion (7%), wound healing (5%), decrease of nausea (4%), prevention of recurrence (2%), and pain control (2%). Fifty-five of the patients were enrolled in clinical protocols for primary treatment, of whom 85% were concurrently using unconventional therapies including several ingested products with potential biologic activity that could potentially interact with chemotherapy. Of the various unconventional therapies used, half were reported to the treating physician.

Bold and Leis⁸ conducted a cross-sectional survey and telephone interviews of 44 parents of children 14 years of age or younger when diagnosed with cancer within a 2year period in Saskatchewan, Canada. The investigators defined unconventional therapies as "those therapies other than medical treatments that are considered standard ... that pediatric cancer patients received specifically for their cancer and/or associated symptoms of conditions, regardless of the type of provider (eg, alternative practitioner, health food store operator, health professional)." The interview asked for information on the use of "other treatments, therapies, and health practices" as a measure of unconventional therapy. Results showed that 16 families (36%) had used or were using some form of unconventional medicine to complement the child's care. One family reported substituting unconventional treatment for medical treatment, although they continued to have the child medically monitored. Twenty-one percent had considered using unconventional treatment but were not currently. Forty-three percent had not used or considered use of unconventional therapy, mostly because of progress in current regimen and confidence in the medical system. Herbal remedies had the highest usage (47%), with Essiac being the most common remedy. Reflexology, aromatherapy, color therapy, and massage therapy comprised the next most highly used group of therapies (19%). Relaxation and musical techniques and traditional/ethnomedicine (including acupuncture and aboriginal healing) both had usage rates of 13%. Shark cartilage (categorized as a pharmacologic/biological) was used by 9%. The most frequently mentioned expectations given by parents for using unconventional therapies were to fight or stop cancer, to boost the immune system, to shrink the tumor, to improve general health, to help with side effects of medical treatment, and to cope with emotional effects of having cancer. Parents who expressed some dissatisfaction with their child's medical experience, such as delays in diagnosis and treatment and concerns about adequate information, were more likely to provide unconventional therapy to the child. Unlike the majority of studies

in which parents indicate that most physicians are unaware of the child's use of unconventional therapies, in this sample 72% of the physicians knew about the use of unconventional therapy either because the parents initiated a discussion about it or because the therapy (eg, relaxation training or acupuncture) was provided by the physician or an allied health professional.

Neuhouser et al9 conducted a population-based, computer-assisted telephone interview system to administer a structured questionnaire to parents of pediatric cancer patients in the northwestern United States, resulting in completed interviews with the primary caregiving parent of 75 children with a first primary neoplasm. Parents were asked if during the past 12 months the child had seen providers (eg, acupuncturist, naturopathic doctor, homeopathic physician), used any supplements (eg, vitamin, herbal), or made any lifestyle changes aimed at coping with or controlling cancer. A patient was categorized as an "alternative medicine user" if the parent reported the child received care from an alternative provider or used at least one alternative supplement, lifestyle change, or therapy. Nearly three quarters (73%) of children in the sample used alternative medicine, with 35% having used herbal preparations, 28% having used high-dose dietary supplements such as vitamins C or E, and 21% having seen an acupuncturist, naturopathic doctor, or other provider. The most common reason for alternative therapy use was to treat the symptoms or side effects of the cancer itself or the medical treatments, followed by to prevent recurrence or spread of the cancer, to prevent or treat noncancer conditions such as cold or flu, and to maintain good health. Alternative therapies were used most by children whose parents were not fully satisfied with the child's physician. Sixty to 90% of parents reported improvements in their child's well-being due to use of alternative medicine; however, 2 parents attributed severe adverse side effects (eg, nausea, vomiting, skin irritation, or sleep disturbance) to the use of herbal preparations.

Kemper and Wornham¹⁰ reported on a complementary therapy consultation service for inpatients in a children's hospital in the northeastern United States during the first year of the consultation service. Most of the 70 consultations (n = 43) involved oncology patients. The most frequent goal for complementary therapy use was to help manage symptoms such as nausea, pain, anxiety, depression, insomnia, poor appetite, or agitation. The second most frequent goal was for assistance in building the child's system, enhancing immune function, increasing strength or resilience, and eliminating toxins. The most common modalities included herbs, dietary supplements, diet and nutrition, biofeedback, and massage. Families also used prayer or wanted to learn more about energy-healing techniques.

Fletcher and Clarke¹¹ interviewed 29 parents of children (mean age 5.4 years) who had been diagnosed with cancer in the past 5 years. Each parent underwent an

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open-ended, 1- to 4-hour telephone interview administered by a trained interviewer who was the mother of a child successfully treated for cancer. The purpose was to learn about the parent's opinions of the experience of having a child with cancer. Ten children (34%) had used treatments other than those prescribed by physicians, including chiropractic, herbals, Essiac, dietary and nutritional supplements, homeopathic, Reiki, and prayer. Reasons cited for use, in order of frequency, were improvement in the child's health, a perception of having nothing to lose, a boost to the immune system, an increase in relaxation/comfort, and removal of the cancer.

McCurdy and colleagues¹² administered a questionnaire listing definitions of complementary and alternative therapies to parents or legal guardians of pediatric oncology patients in the oncology clinic. Nearly one half (47%) of a sample of pediatric oncology patients (n = 195) in the southeastern United States had used one or more complementary or alternative therapies at some time since receiving a cancer diagnosis. The most commonly employed therapies were faith healing (41%), megavitamins/minerals (35%), massage (25%), other dietary supplements (22%), relaxation techniques (22%), and herbal medicines/teas (20%). Eighty-two percent of those using complementary or alternative therapies did so with the intended purpose of treating the underlying disease, with one fourth believing the complementary or alternative therapy would definitely help cure the condition. Children in very religious families were more likely to use complementary and alternative medicine. The investigators also inquired about the use of prayer and found that 87% of the respondents reported regularly praying for the patient. Reanalyzing the complementary and alternative medicine data to include prayer, the prevalence of complementary and alternative medicine use in their sample increased from nearly one half to 92%. Forty-one percent had not discussed complementary and alternative medicine use with the physician.

Gagnon and Recklitis¹³ administered an anonymous questionnaire survey during oncology clinic visits about the use of 27 complementary therapies to parents of pediatric patients at least 1 month postdiagnosis and currently receiving cancer treatment or having completed treatment within the past 2 years at a comprehensive cancer center in the northeastern United States. Complete data from 118 parents indicated that 46% of children had used a complementary therapy during the child's lifetime, and 33% of parents had initiated use of a complementary therapy for their child since the child's cancer diagnosis, including 14% reporting new use of biochemical complementary therapies taken internally (eg, herbal preparations, dietary supplements). The parents' decision to use complementary therapies for their child related in part to their own healthcare preferences. The majority of parents (86%) preferred an active role in medical decision-making. New use of external therapies (eg, acupressure, acupuncture, chiropractic, healing touch, magnets, massage, Reiki) postdiagnosis was associated with the parents having a greater desire for active participation in medical decision-making vs passive compliance with medical care. Additionally, parental desire for active participation was associated with the child's use of a greater number of complementary therapies.

Molassiotis and Cubbin¹⁴ reported on questionnaire data collected from 49 parents (for a response rate of 51%) of children from 5 to 17 years of age who were receiving or had received conventional medical treatment for cancer in an oncology unit in the United Kingdom. Children were 28 months postdiagnosis, on average. Thirty-three percent of children were using complementary therapies, most often more than one therapy. The most commonly used therapies were multivitamins (56%), aromatherapy massage (50%), and diets and dietary supplements (38%). Parents rated their perception of the helpfulness of each therapy on a scale of 0 to 10, and these three most commonly used therapies were all rated between 6 and 8, with aromatherapy massage perceived as the most helpful. The most frequently stated reasons for complementary therapy use by parents were to use every possible option in healthcare, to improve the child's general health, to help the child to relax, to decrease the child's anxiety, and to reduce side effects from treatment. Most parents (63%) administering complementary therapies did so daily.

Clinical Trials of Biologically Based Therapies

The following search terms were used to seek clinical trials of biologically based therapies using substances found in nature and used by cancer patients: shark cartilage, diet, herbal, laetrile, megavitamins, melatonin, mistletoe, phytotreatment, plant, or vitamin. Using these search terms, no randomized clinical trials were obtained, but two preliminary studies were located (Table 1).^{15,16} An informative tutorial paper by Kemper¹⁷ on herbs and supplements used to treat childhood cancers was also located that provides information to educate consumers and clinicians about potential risks and benefits of remedies used by many patients, while underscoring the need to test these therapies systematically in children.

Searching for clinical trials of manipulative and body-based methods produced two records for pilot studies of massage therapy (Table 2).^{18,19} This line of research is currently going forward in a National Institutes of Health-funded multisite randomized clinical trial to study the effects of massage therapy provided by professional massage therapists 3 times per week for 30 minutes as part of multicomponent therapy for children hospitalized during bone marrow transplantation.²⁰ The National Institutes of Health also has funded a feasibility study of massage ther-

apy for palliation of pain in children with advanced or progressive cancer.²¹

Mind-body interventions include a variety of techniques that aim to increase the mind's capacity to enhance bodily function and reduce symptoms. These techniques include meditation, prayer, medical uses of hypnosis, expressive therapies such as music, art, dance therapy, and yoga and other movement therapies. Several pediatric clinical trials of mind-body therapies were located, 22-29 mostly using hypnosis for symptom control (Table 3). With regard to clinical trials of expressive therapies, such as music, art, or dance, two pilot studies were located (Table 4). 30,31 Additional small pilot studies with pediatric samples 32-34 also suggest that music therapy merits further study in pediatric oncology populations. No trials were located testing meditation, prayer, yoga, or other movement therapies.

To search for alternative medicine systems, the search terms acupuncture, Ayurvedic, homeopath, and naturopath were entered into PubMed and CINAHL. No published clinical trials in pediatric oncology samples were located in which alternative medical systems were tested. With regard to energy therapies, searching with the terms energy, healing, magnetic, and Reiki, no pediatric oncology trials of energy therapies were located.

Conclusions

The above studies found that complementary therapies are commonly used among children diagnosed with cancer. Parents' intended purpose in choosing to provide their child with complementary therapies included doing everything that they could for their child to contribute to their health, help with symptom management, improve the immune system, and have a direct anticancer effect including hopes of curing the cancer. Whereas popular belief is that use of complementary and alternative therapies is a result of dissatisfaction with conventional medicine, only 3 of the 15 studies cited dissatisfaction with conventional medicine as one of the main reasons for use of complementary therapies. All In the reported studies,

Table 1. — Clinical Trials of Biologically Based Therapies

Study	Sample	Research Design, Methods, Outcome Measures	Reported Findings/Conclusions
Bell et al ¹⁵ (2001)	28 children with refractory acute myelogenous leukemia (AML). Mean age 7.5 yrs; range 8 months to 16.5 yrs.	Uncontrolled phase II trial, 10-day continuous IV infusion of homoharringtonine. Potential outcomes assessed by bone marrow aspiration were complete response (0-5% blasts or blasts plus abnormal promyelocytes of 0-10%), partial response (5-25% blasts or percent blasts plus abnormal promyelocytes of 10-30%), or no response (more than 25% blasts or percent blasts plus abnormal promyelocytes of more than 30%).	4 complete responses, 1 partial response (5/28 = 18% response rate). Investigators concluded homoharringtonine has activity against chemotherapy-resistant acute myelogenous leukemia in children, with tolerable toxicity.
Garami et al ¹⁶ (2004)	22 children ≤18 with malignant disease. Experimental group (n = 11) mean age 11 yrs, control group (n = 11) mean age 10.6 yrs.	Matched-pair open-label study, self-selected treatment vs control. One patient in each pair received fermented wheat germ extract orally twice daily in addition to standard anticancer treatment; control received standard anticancer treatment.	Number and frequency of febrile neutropenic events were significantly lower in group receiving medical nutriment (30 episodes) vs control (46 episodes).

Table 2. — Clinical Trials of Manipulative and Body-Based Therapies

Study	Sample	Research Design, Methods, Outcome Measures	Reported Findings/Conclusions
Field et al ¹⁸ (2001)	20 children with acute lymphoblastic leukemia.	Mean age 6.9 yrs.	Random assignment to daily 15-minute massage from parent for 30 days vs wait list. Assessed anxiety, mood in children and parents before and after first massage and on the last day of trial. Child's complete blood count assessed first and last days of study. Massage was associated with reduced negative mood in children and parents and increased white blood cell count in children.
Phipps ¹⁹ (2002)	21 children hospitalized for bone marrow transplant. Mean age 8.8 yrs; range <1 year to 20 yrs.	Uncontrolled cohort feasibility study of multi- component intervention teaching parents to give their child a 15-minute massage daily during the hospitalization.	Children and parents rated massage as a favorite component of the intervention.

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Table 3. — Clinical Trials of Mind-Body Interventions: Hypnosis

Study	Sample	Research Design, Methods, Outcome Measures	Reported Findings/Conclusions
Zeltzer and LeBaron ²² (1982)	33 pediatric oncology patients undergoing lumbar punctures and bone marrow aspirations (BMA). Mean age 10.1 (SD 3.17), range 6 to 17 yrs.	Random assignment to hypnosis or non-hypnotic intervention group.	Pain during lumbar punctures was reduced only by hypnosis. Anxiety was reduced by hypnosis and nonhypnotic techniques. Greater anxiety was reduced with hypnosis. Pain during bone marrow aspirations was reduced by hypnotic and nonhypnotic techniques. Pain was reduced with hypnosis. Anxiety was reduced only by hypnosis.
Kellerman et al ²³ (1983)	16 adolescent oncology patients undergoing bone marrow aspirations, lumbar punctures, and chemotherapeutic injections. Mean age 14 yrs (SD 1.6).	Multiple baseline, subjects as own control. Assessed distress, anxiety, self-esteem, health locus of control, illness impact before and after hypnosis training for stressful procedures.	Hypnosis was associated with reduced anxiety and reduced discomfort.
Zeltzer et al ²⁹ (1984)	19 children with cancer experiencing chemothera-py-related nausea or vomiting. Mean age 11.3 yrs (SD 3), range 6 to 17 yrs.	Random assignment to hypnosis or supportive counseling.	Hypnosis and supportive counseling were both associated with reduced nausea, vomiting, and distress. Symptomatic improvement was maintained.
Katz et al ²⁴ (1987)	36 children with acute lymphoblastic leukemia who had undergone at least three bone marrow aspirations (BMAs) and were scheduled for repeated BMAs. Mean age 8 yrs 3 months (SD 1.68).	Randomized to hypnosis or play.	Hypnosis and play were both associated with reduced self-report of pain and distress. No between-groups difference.
Wall and Womack ²⁵ (1989)	20 pediatric oncology out- patients undergoing bone marrow aspiration or lumbar puncture. Age 5 to 18 yrs.	Random assignment to hypnosis or cognitive distraction.	Hypnosis and cognitive distraction were associated with pain reduction. Neither was associated with anxiety reduction. Hypnotizability did not correlate with pain reduction.
Zeltzer et al ²⁸ (1991)	54 pediatric cancer patients reporting significant chemotherapy-related nausea and/or vomiting during baseline assessment. Mean age 11.67 yrs (SD 3.35), range 5 to 17 yrs.	Random assignment to hypnosis, nonhypnotic relaxation/distraction techniques, or attention placebo control.	Symptom level was maintained with relaxation/distraction, decreased with hypnosis, and increased with placebo control.
Liossi and Hatira ²⁶ (1999)	30 children with leukemia undergoing bone marrow aspirations. Age 5 to 15 yrs.	Random assignment to hypnosis, cognitive behavioral coping skills training, or no intervention control group.	Both active treatments were associated with less procedure-related pain and pain-related anxiety compared to control. Coping skills training was associated with more anxiety and more behavioral distress relative to hypnosis.
Liossi and Hatira ²⁷ (2003)	80 pediatric oncology patients undergoing lumbar punctures. Mean age 8.73 yrs (SD 2.86).	Random assignment to direct hypnosis with standard medical treatment, indirect hypnosis with standard medical treatment, attention control with standard medical treatment, or standard medical treatment alone.	Symptom level was maintained with relaxation/distraction, decreased with hypnosis, and increased with placebo control.

Table 4. — Clinical Trials of Mind-Body Therapies: Expressive Arts

Study	Sample	Research Design, Methods, Outcome Measures	Reported Findings/Conclusions
Favara-Scacco et al ³¹ (2001)	32 children with leukemia. Age range 2 to 14 yrs (17 additional children in the historical comparison).	Behavioral observation comparison of effects of art therapy compared with historical comparison group that did not receive art therapy (n = 17).	Art therapy provided before, during, and after lumbar punctures was associated with more collaborative behavior and fewer resistive behaviors compared to the historical comparison.
Barrera et al ³⁰ (2002)	65 pediatric oncology inpatients with varied diagnoses and stages of illness and treatment. Mean age 7 yrs (SD 4.8); range 6 months to 17 yrs.	Uncontrolled pilot study of one to three 15- to 45-minute therapy sessions with an accredited music therapist in hospital room. Outcome measure faces pain scale completed pre- and postintervention sessions by children ≥3 yrs of age or by parents of younger children.	Pain improved according to child and parent report.

where participants were largely recruited from patient care settings or postmedical treatment, nearly all studies reported complementary therapy use in conjunction with medical treatment for cancer. There were exceptions, however; 9 families substituted alternative therapies for conventional treatments, most often when there was a poor prognosis.^{5,8}

Methodologic variability and the lack of a single, agreed-upon measurement strategy across studies hamper the comparability of results obtained in separate studies and constitute a limitation when estimating prevalence of use of complementary and alternative therapies. The field would benefit in the future from agreement on standardized definitions of terminology and definitions of therapies. Efforts in this direction have been put forth. For example, the National Center for Complementary and Alternative Medicine at the National Institutes of Health has provided definitions for specific therapies and defines complementary medicine as therapies used together with conventional medicine, as opposed to alternative medicine, which is used in place of conventional medicine.³⁵ Additional evaluative components have been attached to the terms complementary and alternative by one leading group of investigators,³⁶ stating that complementary therapies can relieve symptoms and improve physical and emotional well-being when used in conjunction with mainstream care, while alternative therapies are unproven methods that might be harmful in some cases and are typically promoted for use instead of conventional cancer treatment. However, the evolution of terminology continues, and currently there is no consensus within the field.

An important recurring finding is that physicians are often not aware of children's use of complementary therapies. In several studies, fewer than half of patients and families using complementary therapies reported this use to their physician. The lowest disclosure rate was found in a study carried out in Taiwan, where non-Western therapies were often used in conjunction with Western medical treatment for children's cancer. Parents were reluctant to disclose the use of non-Western care to physicians providing Western care in order to avoid offending the physician and to preserve the relationship.⁶ It may be that cultural

influences on patient-physician communication are illustrated by the contrast between the reasons given by American adults for nondisclosure about their own use of complementary therapies compared with reasons given by Taiwanese adults. In the United States, parents considered that "it was not important for the doctor to know," "the doctor never asked," "it was none of the doctor's business," and "the doctor would not understand." ³⁷

Complementary therapy use needs to be addressed with each family. The importance of accurate estimation of use lies in safety (including toxicities associated with ingested products as well as their interactions with medical regimens used in cancer treatment) and in the interpersonal implications of communication in the patient-health-care provider relationship.^{38,39} In addition to protecting patients from harmful therapies, parents also deserve to be provided with unbiased, evidence-based information on potentially helpful complementary therapies that they may safely incorporate into their child's care.

Several relatively small clinical trials of varying quality have been conducted on selected complementary therapies in pediatric oncology samples. Evidence, in most cases preliminary, has emerged for the safe and effective use of hypnosis, relaxation, distraction, massage, and expressive arts therapies, and further investigation with larger randomized clinical trials is warranted for each of these promising therapies. Certain biological agents appear to hold promise to help children with cancer, and these should be studied as well. We know so little as yet, and there is tremendous need and opportunity for further study in order to help safeguard young patients' well-being by protecting them from potentially harmful interventions while identifying helpful therapies. Juxtaposing the results of a decade of surveys indicating the popularity of complementary therapies against the scientific evidence provided by clinical research highlights several knowledge gaps regarding the use of complementary therapies in conjunction with medical treatment for childhood cancer. More research is needed to evaluate the safety, cost effectiveness, efficacy, and comparative effectiveness of most complementary therapies.

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