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Children's Cancer and Environmental Exposures: Professional Attitudes and Practices

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Abstract

Background—Epidemiologic studies worldwide have provided substantial evidence of the contributions of environmental exposures to the development of childhood cancer, yet this knowledge has not been integrated into the routine practice of clinicians who care for children with this disease. To identify the basis of this deficit, we sought to assess the environmental history-taking behavior and perceptions of environmental health among pediatric hematologists and oncologists.

Procedure—A web-based survey was sent from June to October 2012 to 427 pediatric oncologists, fellows, and nurse practitioners from 20 U.S. institutions, with an overall response rate of 45%.

Results—Survey responses indicated that environmental exposures are of concern to clinicians. The vast majority of respondents (88%) reported receiving questions from families about the relationship between certain environmental exposures and the cancers they regularly treat. However, a lack of comfort with these topics appears to have limited their discussions with families about the role of environmental exposures in childhood cancer pathogenesis. Although 77% of respondents suspected that some of the cases they saw had an environmental origin, their methods of taking environmental histories varied widely. Over 90% of respondents believed that more knowledge of the associations between environmental exposures and childhood cancer would be helpful in addressing these issues with patients.

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Conflict of Interest Statement

None of the authors has a conflict of interest.

Conclusions—Though limited in size and representativeness of participating institutions, the results of this survey indicate a need for increased training for hematology/oncology clinicians about environmental health exposures related to cancer and prompt translation of emerging research findings in biomedical journals that clinicians read.

Keywords

Pediatric hematology/oncology; Epidemiology; Translational research; Medical education; Pediatric environmental health

Introduction

Mortality from childhood malignancies has declined significantly over the past 40 years, largely due to advances in pediatric cancer treatments. [1] Though childhood cancers remain one of the leading causes of death for children 1–14 years old in the U.S. [2], their origin is only partly understood. [3] However, a growing body of literature has implicated environmental hazards in the etiology of certain childhood cancers. The President’s Cancer Panel states in their 2008–2009 Annual Report that, “the true burden of environmentally induced cancer has been grossly underestimated.” [4]

Exposure to ionizing radiation from nuclear accidents, x-rays, or radiation therapy is associated with an increased risk of childhood leukemia [5–7] and solid tumors. [8–10] Exposures to solvents and ambient air pollutants, including benzene, may also contribute to an increased risk of childhood leukemia. [11–14] Evidence suggests a link between parental, prenatal, and childhood exposures to pesticides and childhood leukemia in both residential and occupational settings. [15–21] In utero exposure to household insecticides and indoor pesticides is linked to increased risk of childhood leukemia. [22] Finally, numerous studies from around the world have consistently identified associations between pesticide exposures and risk of lymphomas, brain tumors, and other solid tumors. [19, 23]

The U.S. Surgeon General and the State of California have reported prenatal and postnatal exposures to environmental tobacco smoke to have a suggestive association with childhood leukemia, lymphomas, and brain tumors. [24, 25] The International Agency for Research on Cancer (IARC) has classified tobacco smoke as carcinogenic to smokers’ children with sufficient evidence for hepatoblastoma and limited evidence for childhood leukemia. [26] Paternal smoking, in particular, before conception has also been linked to an increased risk of childhood acute lymphoblastic leukemia (ALL). [27]

Many of the above studies find odds ratios greater than 2 (including meta-analyses) for overall risk or specific exposure strata. The evidence from case-control studies (and meta-analyses based on them) is strengthened by additional studies finding polychlorinated biphenyls and polybrominated diphenyl ethers, fire retardant chemicals in house dust that are associated with elevated risk of childhood leukemia. These studies provide an objective measure of chemical exposure and eliminate recall bias. [28, 29] Due to the rarity of childhood cancer, the ability to form prospective studies is limited. Research collaborations such as the Childhood Leukemia International Consortium (CLIC) and the International Childhood Cancer Cohort Consortium (I4C) provide hope for the future, as pooled data and

biospecimens from large-scale studies will help identify more robust findings regarding childhood cancer causation. [30, 31]

Greaves has proposed that a delay in a child's exposure to common childhood infections may result in an improperly modulated immune system and a subsequent risk of aberrantly high levels of lymphoblastic cell proliferation following the barrage of infections when the child enters day care or preschool. [32] This delayed infection hypothesis has been supported by subsequent studies and meta-analyses showing that children exposed to common infections early in life via social contact (such as day care attendance), are at reduced risk of ALL. [33, 34]

Despite the growing insight into potentially modifiable risk factors for childhood cancer, there is little evidence that this knowledge is being translated to clinical practice. Surveys conducted among general pediatricians show that, while these physicians attach considerable importance to the impact of environmental exposures on children's health, they spend little time discussing this information with families. [35, 36] A literature review found consistent gaps in knowledge of environmental hazards and confidence in addressing these issues among pediatric healthcare providers in a variety of geographic regions. [36] Despite Institute of Medicine recommendations in 1988 that called for the integration of environmental health concepts into all levels of nursing and medical education, relatively little progress has been made. [37, 38] Few medical schools, pediatric residencies, or nurse practitioner training programs devote substantial training time to environmental contributors to disease. [39–41] Nevertheless, initiatives have begun in both the nursing and medical communities to bridge this gap. [42, 43]

We conducted a survey to learn whether practicing pediatric hematologists and oncologists encounter barriers to integrating environmental research findings into practice similar to those reported by general pediatricians. Specifically, we sought to assess their level of knowledge and attitudes related to potential environmental contributions to childhood cancers and their history-taking practices.

Materials and Methods

An online survey was sent from June to October 2012 to 20 clinical sites: 18 pediatric cancer treatment centers in California, plus the Dana-Farber Cancer Institute (Boston, MA) and the University of Utah Huntsman Cancer Institute (Salt Lake City, UT). Physicians who received the survey were identified through their participation as a clinical collaborator with the California Childhood Leukemia Study (CCLS) or their affiliations with one of the above institutions. [27] A single physician at each site was asked to distribute the online survey to all attending physicians, fellows, and nurse practitioners who were members of hematology/oncology or stem cell transplant services. All responses were collected anonymously with no respondent identifying information. Responses were collected using SurveyMonkey, Inc. of Palo Alto, CA. [44] A reminder email was sent to participants who had not completed the survey after approximately 4 weeks.

The survey consisted of 11 questions pertaining to demographic information, perceptions regarding the causes of childhood cancer, history-taking behaviors and training, patient experiences, and home practices; with multiple and open-ended responses allowed [see Supplemental Appendix I for the full-text survey]. A Likert scale of 1–5 (“strongly disagree” to “strongly agree”) was used to assess attitudes, and two questions allowed for open-ended responses. A pilot survey was conducted at Lucile Packard Children’s Hospital at Stanford University (n = 22), and slight modifications were made to the instrument based on these results. However, these pilot responses were not included in the final analyses. Descriptive analyses (frequencies, percentages, standard deviations) were performed overall and by respondents’ characteristics (type of position and years in practice), using SAS 9.2 (SAS Institute, Cary, NC). The survey was approved by the Institutional Review Boards at Stanford University, Dana-Farber Cancer Institute, and the University of Utah.

Results

The survey was distributed to 427 physicians and nurse practitioners, with 191 responding (overall response rate of 45%). The majority of respondents were attending physicians, most of whom had over 10 years of practice in pediatric hematology/oncology (Table I).

Participants were asked about their beliefs regarding the likely causes of leukemia in children. Their responses included genetics (92%), health status (e.g., stress, prenatal care and nutrition; 25%), environmental exposures (e.g., chemicals, contamination, second hand smoke, infections, and radiation; 78%), and none of the above (7%) (Table II). Open-ended responses varied, but commonly included: “all of the above,” previous exposures to chemotherapy agents, infertility treatments, and simply “bad luck.” A majority of respondents (61%) agreed that environmental exposures were important contributors to childhood cancer (mean Likert score 3.65).

When asked about their routine history-taking practices, the participants most frequently obtained information about parental occupations, household tobacco smoke, and radiation exposures (Figure 1). Nearly 25% reported not asking about any of the factors mentioned in the survey. Only 7% had reported ever receiving training in taking an environmental history.

Although half of the respondents reported rarely suspecting that a case was related to some factor in the patient’s environment, a large majority (88%) either “frequently” or “occasionally” received questions from parents or family members about potential workplace or environmental exposures contributing to their child’s disease. Forty four percent of respondents felt either “somewhat uncomfortable” or “not at all comfortable” discussing the disease implications of environmental exposures with patients and their families (Table II). An overwhelming majority (92%) stated they would find it helpful to have more information regarding the association between childhood cancers and environmental exposures in order to answer questions from parents, patients, or family members.

Respondents with 0–5 years in oncology practice were more likely to focus on genetics as a likely cause of childhood leukemia than practitioners with 5–10 and 10+ years of experience

(98%, 85%, and 91%, respectively; $p = 0.04$). Clinicians with 10+ years in practice were more likely to ask about exposure to pesticides, solvents, and paternal exposures to specific environmental hazards ($p = 0.01$) (Table III). Responses also varied across types of position (Table IV). Eighty-five percent of nurse practitioners agreed or strongly agreed that environmental exposures were important contributors to cancer induction, with only one nurse practitioner disagreeing with this statement (mean Likert score 4.0). By contrast, only 58% of fellows and 55% of attending physicians agreed or strongly agreed ($p = 0.03$). However, nurse practitioners were also more likely to be uncomfortable with discussing potential sources of exposure in relation to disease with patients and family, compared to other positions ($p < 0.001$). Attending physicians were significantly more likely to ask about pesticide use, solvents, and parental occupation than other provider types while taking a patient's history ($p = 0.01$, $p = 0.01$, and $p = 0.001$ respectively) (Table IV). Close to 25% of all respondents did not ask patients or their families about any of the queried factors associated with childhood cancers.

Sixty seven percent of all respondents engaged in at least one practice to protect themselves and their families from potentially hazardous environmental exposures (e.g., pesticides, cleaning products, organic foods, plastics, etc.). Fellows were significantly less likely to report participating in behaviors in their own home that might avoid exposures to chemicals associated with health risks than were nurse practitioners or attending physicians ($p < 0.001$) (Table IV). Those who attempted to avoid exposures at home were more likely to agree or strongly agree that environmental exposures are important contributors to the development of childhood leukemia (69%, SD: 8%, $p = 0.001$). Among those providers who attempted to avoid home exposures and also agreed or strongly agreed that environmental factors are important contributors to childhood cancers, only 53% were somewhat or very comfortable discussing these issues with their patients.

Discussion

This survey found that a majority of clinicians agreed that environmental exposures were important contributors to childhood cancers, but remained inconsistent in their history-taking for these events. Although most practitioners routinely received questions about the relationship between environmental exposures and disease, few were entirely comfortable addressing these issues. Over 90% of respondents believed they would benefit from more information on this topic.

Physician-patient communications

Previous surveys of the general public in the U.S. indicate widespread beliefs that the environment plays an important role in various health problems, and that parents would like more information from their pediatricians regarding environmental health topics. [45, 46] The findings of our survey support these previous results. Many respondents (48%) reported being frequently asked about environmental exposures to potential carcinogens by patients or their families. Greater familiarity with the emerging research on environmental contributions to childhood cancer would allow clinicians to be more responsive to these questions.

Providers with 5 or fewer years of experience were more likely to highlight genetics as a cause of childhood leukemia compared to providers with more experience, perhaps reflecting differences in curriculum and training that highlight more recent genetic studies. This group was also less likely to incorporate environmental health questions into their routine patient histories. Generational differences might account for this difference, as the more experienced clinicians were educated and trained during the height of the environmental movement, which could lead to greater awareness of environmental impacts on health. [47, 48]

Barriers to integration into practice

Our survey results indicate that clinical hematologists and oncologists engage in a variety of environmental history-taking practices. Many participants reported frequently asking about parental occupation, but not about any specific environmental hazards associated with that occupation. Anecdotal evidence and survey results suggest that clinicians have reservations about the appropriateness of asking the patients' families questions related to environmental exposures and other carcinogens. One factor contributing to this perception may be the notion that clinicians do not have a major role in assessing etiology, and that such questions could raise the parents' anxiety and guilt with little benefit to treatment outcomes. Though anticipation of negative parental reaction has been similarly cited by pediatricians as a common barrier to intervening with parents who smoke, the vast majority of smoking parents show strong support for addressing smoking at office visits. [49, 50]

Twenty-five percent of clinicians did not ask about any of the environmental factors mentioned in our survey, while 75% routinely asked at least some questions related to assessing environmental exposures. For both groups, a better grounding in the literature could ensure that responses to questions from patients and families regarding environmental hazards are addressed promptly and accurately. This assumption is supported by our result that providers uniformly believed that more information on environmental health research relevant to childhood cancer would be helpful.

Informing research agendas

Historically, alert clinicians have recognized environmental exposure trends in their patient populations, and brought them to the attention of public health authorities. This was seen in cases of mesothelioma and lung cancer in asbestos workers, and vaginal adenocarcinoma in women born to diethylstilbestrol-exposed mothers, among others. [51–53] Investigations of these cancer clusters led to the identification of previously unrecognized human carcinogens. By bringing an awareness of potential environmental etiologies to their oncology practice, clinicians can play an important role in raising issues in the research community and assisting investigators and public health officials in deciding potential areas of study.

Further illustration of this point can be seen in a recent case report, where the authors identified four cases of congenital fibrosarcoma linked to prenatal exposure to petroleum derivatives. [53] Through the use of a routine pediatric environmental health history questionnaire, the authors were able to compare case histories with toxicological databases

and identify exposures in each case to compounds associated with the development of fibrosarcoma in animals. [53] Although this case series does not establish a causal association, it may form the hypothesis for a full-scale study.

Health professionals use peer-reviewed journals, consultations with peers, and conference attendance as their primary sources of reliable information for clinical decision-making. [54, 55] We reviewed abstracts from the 2011 and 2012 American Society of Pediatric Hematology/Oncology (ASPHO) meetings to select those that examined causation or environmental risk factors (characterized broadly to include factors like diet and infectious agents). Of 569 abstracts, 8% dealt with questions of causation, and only 1% mentioned any environmental risk factors. During the same 2-year period, a PubMed search showed that 48 papers were published specifically on the topic of childhood cancers and environmental risk factors. However, these papers appeared primarily in nonclinical journals, such as *Environmental Health Perspectives*, *American Journal of Epidemiology*, and *Cancer Causes & Control*. It is likely that nonclinical journals do not have a widespread readership among busy clinicians. [56]

We reviewed federal funding to assess the proportion of resources devoted to studying environmental causes of childhood cancers. During 2010 and 2011, the National Institutes of Health (NIH) awarded 3–7% of its total funding for childhood leukemia research to studies evaluating environmental etiologies¹. The majority of funding for this research comes from the National Institute for Environmental Health Sciences (NIEHS). The National Cancer Institute (NCI) contributed around 1% of its funding for all childhood cancer toward environmental risk research. [57, 58] Despite an evolving understanding of environmental exposures associated with leukemia, funding for research that might inform activities aimed at prevention of childhood cancer remains limited.

Limitations

Though this is a relatively small survey, it is the first characterization of pediatric hematology-oncology practitioners' current perception of the importance of environmental exposures to their patient care responsibilities. Surveys, as a research tool, have disadvantages with respect to the data collected and representativeness of the sample. In our survey design, participants were restricted to specific responses, limiting the potential details collected. Two questions allowed for open-ended responses, which increased the depth of our investigation.

Our survey response rate of 45% may introduce bias in our results, as no information about the non-responders was collected. For example, if those who had a higher concern for environmental associations were more likely to respond to the survey, these perspectives would have been overestimated in our sample. Email surveys of general practitioners have reported response rates similar to ours [59], however a study found response rates among specialty-fellows to be lower than non-specialists. [60] In general, email surveys have

¹A broad definition of environment was used to include factors such as diet and infection, together with more traditional factors. Only projects that focused on cancer as the primary endpoint were considered. Projects exclusively focusing on adult populations were excluded, as well as those that investigated mechanisms that might be broadly implicated in cancer development.

significantly lower response rates than mailed questionnaires. [61, 62] We aimed to increase the response rate and ensure more representativeness of the sample by sending a reminder email to participants. The survey was distributed to clinicians at selected institutions and does not comprise a representative sample of all practitioners in this field. This may affect the generalizability of our results if clinicians at these institutions differ substantially in their attitudes and practices from their counterparts across the country.

Conclusion

This survey identifies an opportunity for improved training in and awareness of environmental health research among attending physicians, fellows, and nurse practitioners working in the field of pediatric hematology/oncology. To help bridge this gap, environmental health researchers and epidemiologists should publish their relevant findings in journals that are widely read by pediatric hematologists/oncologists and nurse practitioners.

Educational opportunities should also be made available at national meetings, as our survey revealed significant interest in increasing baseline knowledge of environmental factors contributing to cancer. Training in environmental history-taking, introduction of basic environmental history questions into the electronic medical record, and implementation of self-administered patient questionnaires during medical visits that address environmental exposures may aid in simplifying the collection of relevant information in the medical records of children with cancer. Moreover, the self-administered questionnaire may address the hesitancy of some clinicians to ask these questions during history taking. Ultimately, having gained a better understanding of current research findings, practitioners will utilize this information in ways appropriate to their particular practice setting.

Our results highlight the need for better integration of environmental health awareness in pediatric oncology practice and training. The translation of rigorous environmental health research findings to clinicians would potentially improve provider-patient communications, enhance data collection, and promote the role of alert clinicians in identifying sentinel events. With the convergence of research from CLIC and other groups, the body of evidence supporting environmental associations with childhood cancers is growing. Hazards, such as those mentioned in the Introduction, have already gained a significant body of supporting information. As the environment continues to change and more hazards are identified, there is an ever-present need for pediatric oncologists to keep pace with this emerging research.

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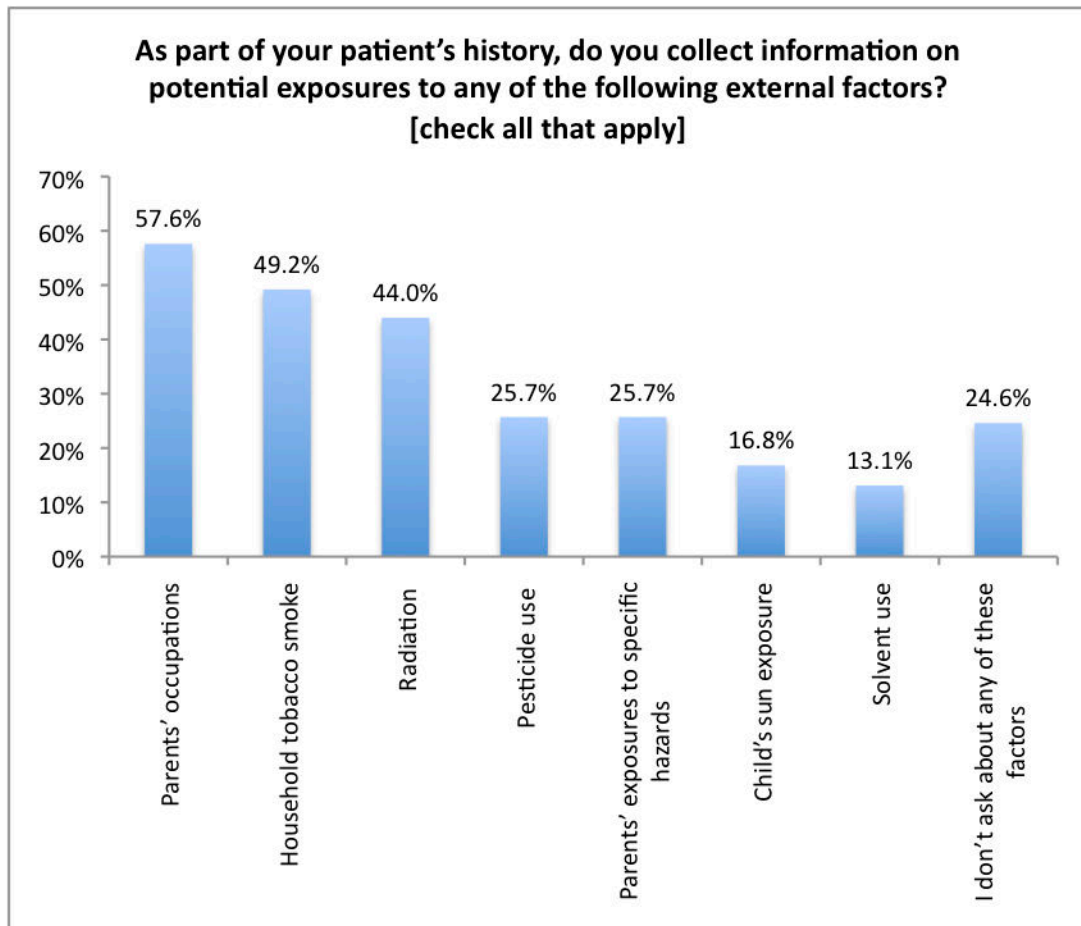


Figure 1.

As part of your patient's history, do you collect information on potential exposures to any of the following external factors?

Table I

Characteristics of respondents

Position	Number (%)
Attending physician	117 (61)
Fellow	40 (21)
Nurse practitioner	34 (18)
Years in Practice	
0-5	65 (34)
5-10	40 (21)
10+	86 (45)

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Table II

Percentage of respondents to selected survey questions

Which of the following do you think are likely causes of leukemia in children? ^a	
<i>Genetics</i>	92%
<i>Health status</i>	25%
<i>Environmental exposures</i>	78%
<i>None of the above</i>	7%
<i>Other</i>	13%
<hr/>	
In your opinion, are environmental exposures important contributors to childhood cancer? ^b	
<i>Strongly agree</i>	11%
<i>Agree</i>	50%
<i>Neutral</i>	25%
<i>Disagree</i>	13%
<i>Strongly disagree</i>	2%
<hr/>	
How often, if ever, have you had a case that you suspected was related to something in the patient's environment? ^b	
<i>Frequently</i>	1%
<i>Occasionally</i>	26%
<i>Rarely</i>	50%
<i>Never</i>	23%
<hr/>	
How often, if ever, have you received questions from parents or family members about potential workplace or environmental exposures as possible causes of disease? ^b	
<i>Frequently</i>	48%
<i>Occasionally</i>	40%
<i>Rarely</i>	11%
<i>Never</i>	1%
<hr/>	
What is your current level of comfort with discussing potential environmental sources of exposure in relation to disease with your patients and their family? ^b	
<i>Very comfortable</i>	7%
<i>Somewhat comfortable</i>	49%
<i>Somewhat uncomfortable</i>	35%
<i>Not at all comfortable</i>	9%

^a Multiple responses were allowed.^b Percentages may not add up to exactly one hundred due to rounding.

Table III

Responses to selected survey questions stratified by years in practice

Question	0–5 years % (SD) ^a	5–10 years % (SD)	10+ years % (SD)	P-Value
Which of the following do you think are likely causes of leukemia in children? ^b				
<input type="checkbox"/> Genetics	98 (3)	85 (11)	91 (2)	0.04
<input type="checkbox"/> Health status	29 (11)	18 (12)	24 (9)	0.40
<input type="checkbox"/> Environmental exposures	77 (10)	85 (11)	76 (9)	0.48
<input type="checkbox"/> Other	6 (6)	13 (10)	17 (8)	0.12
<input type="checkbox"/> None of the above	3 (4)	10 (9)	8 (6)	0.32
As part of your patient's history, information is collected on potential exposures to which of the following external factors? ^b				
<input type="checkbox"/> Household tobacco smoke	46 (12)	48 (15)	52 (11)	0.73
<input type="checkbox"/> Pesticide use	15 (9)	20 (12)	36 (10)	0.01
<input type="checkbox"/> Radiation	35 (12)	40 (15)	52 (11)	0.10
<input type="checkbox"/> Solvent use	8 (6)	5 (7)	21 (9)	0.01
<input type="checkbox"/> Child's sun exposure	14 (8)	15 (11)	20 (8)	0.59
<input type="checkbox"/> Parents' occupations	48 (12)	58 (15)	65 (10)	0.10
<input type="checkbox"/> Parents' exposures to specific hazards	17 (9)	18 (12)	36 (10)	0.01
<input type="checkbox"/> I don't ask about any of these factors	25 (11)	33 (14)	21 (9)	0.37

^aSD = standard deviation,^bMultiple responses were allowed

Note: We conducted stratified analyses for all questions by years in practice, and found no statistically significant differences other than those reported above.

Table IV

Responses to selected survey questions stratified by position

Question	Attending Physician % (SD) ^a	Fellow % (SD)	Nurse Practitioner % (SD)	P-Value
In your opinion, are environmental exposures important contributors to childhood cancer? ^b				
<input type="checkbox"/> Strongly Agree OR Agree	55 (9)	58 (15)	85 (12)	0.03
<input type="checkbox"/> Neutral	29 (8)	25 (13)	12 (11)	
<input type="checkbox"/> Strongly Disagree OR Disagree	16 (7)	18 (12)	3 (6)	
What is your current level of comfort with discussing potential environmental sources of exposure in relation to disease with your patients and their family? ^b				
<input type="checkbox"/> Very comfortable	11 (6)	0	3 (6)	< 0.001
<input type="checkbox"/> Somewhat comfortable	61 (9)	40 (15)	18 (13)	
<input type="checkbox"/> Somewhat uncomfortable	24 (8)	43 (15)	62 (16)	
<input type="checkbox"/> Not at all comfortable	4 (4)	18 (12)	18 (13)	
As part of your patient's history, information is collected on potential exposures to which of the following external factors? ^c				
<input type="checkbox"/> Household tobacco smoke	50 (9)	48 (15)	47 (4)	0.91
<input type="checkbox"/> Pesticide use	33 (9)	13 (10)	15 (12)	0.01
<input type="checkbox"/> Radiation	50 (9)	30 (14)	38 (16)	0.06
<input type="checkbox"/> Solvent use	19 (7)	5 (7)	3 (6)	0.01
<input type="checkbox"/> Child's sun exposure	15 (6)	13 (10)	29 (15)	0.09
<input type="checkbox"/> Parents' occupations	68 (8)	35 (15)	50 (17)	0.001
<input type="checkbox"/> Parents' exposures to specific hazards	31 (8)	13 (10)	24 (14)	0.07
<input type="checkbox"/> I don't ask about any of these factors	22 (8)	25 (13)	32 (16)	0.48
Do you and your family do anything at home to avoid exposures to potential environmental hazards (e.g. pesticides, cleaning products, organic foods, plastics, etc.)? (yes vs. no)				
<input type="checkbox"/> Yes	70 (8)	40 (15)	85 (12)	< 0.001

^aSD = standard deviation,^bPercentages may not add up to exactly one hundred due to rounding,^cMultiple responses were allowed.

Note: We conducted a stratified analysis for all questions by position, and found no statistically significant differences other than those reported above and in the text.