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Authors

Whitehead, Todd P
Adhatamsoontra, Praphopphat
Wang, Yang
[et al.](#)

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Home Remodeling and Risk of Childhood Leukemia

Todd P. Whitehead^{*,a}, Praphopphat Adhatamsoontra^{*,a}, Yang Wang^a, Elisa Arcolin^b, Leonard Sender^c, Steve Selvin^a, and Catherine Metayer^a

^aSchool of Public Health, University of California, Berkeley, CA, USA

^bDepartment of Diagnostic, Clinical and Public Health Medicine, University of Modena and Reggio Emilia, Modena, Italy

^cSchool of Medicine, University of California, Irvine, CA, USA

Abstract

Purpose—We investigated the relationship between the risk of childhood leukemia and home remodeling, a surrogate for indoor chemical exposures.

Methods—We collected information on remodeling activities carried out between birth and diagnosis in homes of 609 acute lymphoblastic leukemia (ALL) cases, 89 acute myeloid leukemia (AML) cases, and 893 matched controls participating in the California Childhood Leukemia Study (1995 – 2008). We used multivariable logistic regression to estimate the risk of ALL and AML associated with six remodeling activities: construction, painting, recarpeting, reflooring, roofing, and weather proofing. Models were adjusted for age, sex, Hispanic ethnicity, race, household annual income, and residential mobility.

Results—Construction in the home between birth and diagnosis was associated with a significant increase in ALL risk (OR: 1.52, 95% CI: 1.14, 2.02) and a non-significant increase in AML risk (OR: 1.75, 95% CI: 0.98, 3.15). No other remodeling activities were associated with ALL or AML risk in the main analysis. When stratifying by Hispanic ethnicity, a positive relationship between ALL risk and painting was evident in Hispanic children (OR: 1.47, 95% CI: 1.04, 2.07).

Conclusions—Specific home remodeling activities appeared to be associated with increased risk of childhood ALL.

Keywords

Childhood acute lymphoblastic leukemia; Childhood acute myeloid leukemia; Construction materials; Environmental exposures

Correspondence to: Todd Whitehead, Ph.D., Assistant Researcher, Center for Integrated Research on Childhood Leukemia and the Environment, School of Public Health, University of California, Berkeley, 1995 University Ave., Suite 460, Berkeley, CA 94704, Phone: (510)643-2404; ToddPWhitehead@Berkeley.edu.

*Co-first authors

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INTRODUCTION

Leukemia is the most common childhood cancer (1), comprised primarily of acute lymphoblastic leukemia (ALL, 79%) and acute myeloid leukemia (AML, 18%) (2). Leukemia incidence peaks between ages two and four. Established risk factors including genetic conditions and ionizing radiation explain a small fraction of leukemia incidence (3, 4). Childhood exposures to chemicals may also contribute to disease development (5-7).

A variety of suspected carcinogens formerly used as constituents of building materials still remain in homes today (8) including, polychlorinated biphenyls (PCBs), used in joint sealants, glues, and plasticizers (9); polybrominated diphenyl ethers (PBDEs), used in insulation, roofing film, and wiring (10, 11); styrene (7) and lead (12), both used in paint; and asbestos, used in a insulation, shingles, and flooring (13). Moreover, building materials are reservoirs for chemical contamination; *e.g.*, drywall absorbs semivolatile pesticides applied indoors (14). Home remodeling can release these latent chemicals from building materials, *e.g.*, chipping, cutting, and sanding can generate lead dust (12) or disturb asbestos and PCBs (15). In addition to releasing latent chemicals, remodeling activities also introduce *new* residential chemical sources, *e.g.*, installation of carpets and carpet pads containing flame retardants (16) or application of paint containing volatile organic compounds. Construction activities also disturb settled dust (15), increasing the likelihood that residents will ingest or inhale contaminated dust. Settled dust is a source of exposure to indoor pollutants, as demonstrated by relationships observed between chemical levels in blood and dust for lead (17), PBDEs (18), and PCBs (19). Due to their tendency to make hand-to-mouth contact, young children are especially prone to ingesting contaminated dust (14).

As part of the California Childhood Leukemia Study (CCLS), we have previously demonstrated that several of the chemicals to which children may be exposed during remodeling activities, including PCBs (20), PBDEs (21), and indoor insecticides(5, 22), are putative risk factors for childhood leukemia. Another CCLS investigation indicated that indoor painting during early childhood was associated with increased risk of ALL (7), which was confirmed in pooled analyses(23). Moreover, a recent Chinese study reported an increased risk of childhood acute leukemia associated with home renovation after birth (24).

We hypothesize that remodeling releases chemicals into the home and that exposure to these chemicals increases the risk of childhood leukemia.

MATERIAL AND METHODS

Study population

The CCLS is a case-control study of incident childhood leukemia (all subtypes) diagnosed at nine pediatric oncology centers in 35 California counties from 1995-2008. Phase I of the study (1995-1999) included 17 counties in the San Francisco Bay Area, and Phase II (1999-2008) included 18 additional counties in the California Central Valley. Leukemia cases were identified within 72 hours of diagnosis and considered eligible for participation if they were: younger than 15, not previously diagnosed with cancer, and living in the study area with an English- or Spanish-speaking parent. Based on the California Cancer Registry,

the CCLS ascertained 76% of all cases diagnosed at participating and non-participating hospitals in the study area. Of the case families determined to be eligible, 86% consented to participate.

Controls had the same eligibility criteria as cases, including no previous history of cancer. For each case, four potential controls were randomly matched on age, sex, Hispanic ethnicity, and mother's race using birth certificates (California Office of Vital Records). Initially, two controls were enrolled per case, but, subsequently, 1:1 matching was employed. Out of all potential controls searched, 12% could not be located, 20% refused to be screened for eligibility, and 68% were successfully contacted and considered for eligibility (25). Among the eligible families, 86% agreed to participate in the study. The demographic characteristics of the participating controls were representative of the source population (26), with an income distribution similar to that of all California families with children under 18 years (27).

Children diagnosed with leukemia at less than one year of age were excluded ($N=46$, 4.6%, and their 42 corresponding controls) from the analysis because most cases of infant leukemia are believed to arise *in utero* (6). This analysis focuses on ALL and AML, excluding other leukemia subtypes ($N=9$). The sample for this analysis included 609 ALL cases, 89 AML cases, and 893 controls who provided a remodeling history.

The study was approved by the University of California, Berkeley Committee for Protection of Human Subjects, the California Health and Human Services Agency Committee for Protection of Human Subjects, and the institutional review boards of the participating hospitals. Written informed consent was obtained from participating parents.

Data collection

Interviews were conducted with the parent of the participating child, usually the biological mother. The median time between date of enrollment and the first interview was 4 months for cases and 14 months for controls. Residential histories were collected during an in-person interview administered by trained personnel. Respondents described remodeling activities that took place in each home occupied by the child between birth and diagnosis date (or at an equivalent reference date, for controls) including construction, painting, recarpeting, reflooring, roofing, and weather proofing. Demographic characteristics were collected, including child's sex, race, Hispanic ethnicity, and age at diagnosis/reference date, as well as household annual income (six levels) maternal education (four levels), and residential mobility (number of homes inhabited).

Missing data

Some participants were unable to provide a complete remodeling history for each residence the child inhabited between birth and diagnosis. As such, 301 respondents (19%) were missing data on construction, painting, recarpeting, reflooring, and weather proofing for at least one home and 526 (33%) were missing data on roofing. If a respondent indicated that a child was exposed to a remodeling activity in at least one home, the child was included in the analysis of that remodeling activity, even if the remodeling history was otherwise incomplete (*i.e.*, child treated as "exposed"). Alternatively, if the history of a particular

remodeling activity was incomplete and the respondent indicated that the child was not exposed to that remodeling activity in any of the homes that were discussed, then the participant was excluded from the analysis for that remodeling activity (*i.e.*, child's exposure status "unknown"). Because cases tended to have more missing data than controls, in sensitivity analyses we evaluated the potential for bias due to exposure misclassification in homes with missing data. In these analyses, if the remodeling history was incomplete and the respondent indicated that the child was not exposed to a remodeling activity in any of the homes, the child was classified as "unexposed."

In addition there was missing covariate data: 9 (1%) of the respondents did not report child's race, 2 (0.1%) did not report child's ethnicity, and 44 (3%) did not report household income. In multivariable models, missing data on child's race and ethnicity was replaced by the mother's race and ethnicity. Missing income data was replaced by the population average.

Statistical analysis

ALL and AML risks were analyzed separately because these subtypes are epidemiologically and clinically distinct (6). Although controls were initially matched to ALL and AML cases, the matching was not maintained in the main analysis due to missing data. The combined control group was used as a comparison for both ALL and AML cases, with adjustment made in statistical analyses for matching factors, *i.e.*, age at diagnosis/reference date, sex, Hispanic ethnicity, and race, and for potential confounders, income and residential mobility. In complementary analyses, we used a smaller number of matched cases and controls to conduct conditional logistic regression for ALL and AML, separately. We used logistic regression to estimate the risk of ALL and AML associated with construction, indoor painting, recarpeting, reflooring, roofing, and weather proofing using dichotomous exposure variables (odds ratio for any vs. none).

The increasing gap in ALL incidence between Hispanic and non-Hispanic children in California suggests the presence of distinct etiologic risk factors by ethnicity; as such we evaluated ALL risk associated with home remodeling while stratifying by Hispanic ethnicity (28). The routes by which children are exposed to indoor chemicals vary by age, so we also stratified our ALL risk analysis by age at diagnosis. Finally, because we found that income and residential mobility were potential confounders of the relationship between remodeling and ALL risk, we stratified by these factors as well. The relatively smaller number of AML cases were not sufficient to support stratified analyses.

RESULTS

Leukemia cases and controls were similarly distributed by sex, race, and ethnicity (Table 1). Children were most likely to be diagnosed with ALL between ages 2 to 6, whereas AML diagnoses were evenly distributed by age. Consequently, the age distribution varied between leukemia cases and the combined control group. Also, controls had greater household income, greater maternal education (data not shown), and less residential mobility than cases.

A total of 930 participants lived in a home that was remodeled between birth and diagnosis/reference date: 305 households did construction (33%), 707 painted indoors (76%), 302 recarpeted (32%), 317 refloored (34%), 123 did roofing (13%), and 137 weatherproofed (15%). Among controls, remodeling was more common for families with a girl than for families with a boy, and more common for Whites than non-Whites (Supplemental Table S1). In addition, older children and families with higher residential mobility were more likely than their younger, less mobile counterparts to have lived in a house which was remodeled. Families with higher income were more likely to undertake construction activities than low-income families (Supplemental Table S2).

In multivariable logistic regression, increased risks of childhood ALL were associated with any construction (OR: 1.52, 95% CI: 1.14, 2.02, Table 2 and Supplemental Table S3). Marginal associations were observed between ALL and indoor painting (OR for any vs. none: 1.20, 95% CI: 0.96, 1.51) and recarpeting (OR for any vs. none: 1.25, 95% CI: 0.94, 1.65). ALL risk associated with construction was similar for Hispanic and non-Hispanic children (Supplemental Table S4), while the association with painting was limited to Hispanics (OR any vs. none: 1.47, 95% CI: 1.04, 2.07, *p*-value for interaction: 0.21). The association between construction activities and ALL risk was also robust when stratifying by child's age, residential mobility, and income. That is, an odds ratio of at least 1.44 was observed in each strata (with the exception of children who lived in a single home from birth to diagnosis) and most of the odds ratios were statistically significant, despite the smaller sample sizes for stratified analyses.

In sensitivity analyses, the classification of children with some missing data as "unexposed" tended to marginally strengthen the observed relationships between remodeling activities and childhood ALL, resulting in statistically significant odds ratios for construction, painting, and recarpeting (Supplemental Table S5). Using a smaller set of matched cases and controls to conduct conditional logistic regression yielded a slightly attenuated relationship between construction activities and childhood ALL (OR: 1.40, 95% CI: 0.98, 1.99, Supplemental Table S6), which no longer reached statistical significance (*p*-value: 0.06).

We observed a non-statistically significant increased risk of childhood AML associated with any construction (OR: 1.75, 95% CI: 0.98, 3.15, Table 2). This relationship was not affected by the treatment of missing data (OR: 1.64, 95% CI: 0.97, 2.76, Supplemental Table S5), but was attenuated in the smaller set of matched AML cases and controls used for conditional logistic regression (OR: 1.30, 95% CI: 0.39, 4.34).

DISCUSSION

Our findings indicate that specific remodeling activities, including construction and possibly painting, increase risk of childhood leukemia, whereas other activities, *e.g.* weatherproofing, do not. In support of our observations, Chen *et al.* (24) recently reported an increased risk of childhood acute leukemia (all subtypes combined) associated with home renovation after birth in a small Chinese population (53 ALL, 9 AML, 4 other childhood leukemias, and 132 controls). Moreover, despite its marginal statistical significance, our finding that indoor painting is associated with increased risk of ALL replicates the results of a previous pooled

analysis (23) and a previous CCLS analysis (7), which employed a distinct set of interview questions to assess in-home use of “paints, stains, and lacquers”. Besides painting, studies relating home remodeling activities to childhood leukemia risk are scarce. In the CCLS, we previously assessed children’s exposure to chemicals that may be related to remodeling activities. For example, we demonstrated an association between PCB concentrations in house dust and ALL risk (20). Subsequently, we showed that while PCB concentrations in house dust decreased over time, the rate of decline was slower in homes where construction was done (29). This finding suggests that construction projects may have released PCBs indoors. Taken together, the association between construction and childhood leukemia in the current analysis and the previous CCLS findings suggest a plausible relationship between construction activities, PCB contamination in house dust, and increased childhood leukemia risk.

Population mixing has been associated with an increased risk of childhood leukemia, suggesting that exposure to an infectious agent can initiate the disease in a susceptible population (30). Is it therefore possible that, in our analysis, reported remodeling activities are merely acting as surrogates for coincident family relocations? Perhaps it was the child’s exposure to a new immunological milieu and not the subsequent home remodeling, which initiated leukemia. Despite the appealing logic of this explanation, we could not substantiate this hypothesis using our data – as shown in Supplemental Table S3, residential mobility was not associated with ALL or AML risk after accounting for the effect of construction activities.

Affluent families were more likely to undertake construction projects and control families had, on average, higher incomes than case families. As such, in multivariable models, we adjusted for income as a potential confounder of the relationship between ALL risk and remodeling activities. Odds ratios for childhood leukemia associated with construction in the home that were estimated from logistic regression models adjusted for income were larger than crude odds ratios. Regression analyses which stratified by income indicated that construction activities were associated with childhood ALL in low- and high-income households.

Our findings would be biased if case parents recalled home remodeling activities more readily than control parents, which is troublesome given that case parents were interviewed, on average, 10 months closer to the diagnosis/reference date than control parents. However, the strength and direction of the risk estimates differed by remodeling activity, which is evidence against a strong recall bias. Moreover, the relationship between construction activities and childhood ALL was not affected by the treatment of missing data.

Follow-up studies should seek to characterize home remodeling in greater detail, including the extent and intensity of the activities, whether the remodeling was done by the homeowners or by professionals, the number of times a specific remodeling activity was repeated within each home, the child’s time-activity pattern during remodeling activities, and the specific dates of remodeling activities. Future studies should also consider the pregnancy period as another critical window of exposure to remodeling activities that is potentially etiologically relevant.

CONCLUSIONS

Our study demonstrated that construction and possibly painting were associated with increased risk of childhood ALL. These findings complement previous CCLS investigations of the risk of childhood ALL associated with exposure to paints, stains, and lacquers (7) as well as CCLS investigations of the risk of childhood ALL associated with exposure to specific pollutants that may be released in the home during remodeling activities (20, 21). Until causal agents within building materials are implicated, it may be prudent for parents to reduce children's exposure to home remodeling.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

ALL	acute lymphoblastic leukemia
AML	acute myeloid leukemia
CCLS	California Childhood Leukemia Study
CI	confidence interval
PCBs	polychlorinated biphenyls
PBDEs	polybrominated diphenyl ethers
OR	odds ratio

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HIGHLIGHTS

- Collected data on remodeling activities done in homes of children with leukemia
- Construction activities associated with an increased risk of childhood leukemia
- Painting associated with an increased risk of leukemia in Hispanic children
- Findings support previously-observed link between paint exposure and leukemia risk

Table 1

Number (%) of Acute Lymphoblastic Leukemia (ALL) Cases, Acute Myeloid Leukemia (AML) Cases, and Controls participating in the California Childhood Leukemia Study, 1995-2008, by Important Covariables.

Characteristic	ALL Cases, N=609	AML Cases, N=89	Controls, N=893
Child's Sex			
Male	350 (57)	51 (57)	517 (58)
Female	259 (43)	38 (43)	376 (42)
Child's Race			
White	339 (56)	51 (59)	483 (54)
African American	15 (2)	3 (3)	21 (2)
Native American	10 (2)	0(0)	10 (1)
Asian	55 (9)	9 (10)	69 (8)
Mixed or Others	186 (31)	24 (28)	307 (34)
Child's Hispanic Ethnicity			
Hispanic	269 (44)	35 (39)	364 (41)
Non-Hispanic	338 (56)	54 (61)	529 (59)
Child's Age at Diagnosis ^{a,b}			
1-1.99 years	55 (9)	23 (26)	109 (12)
2-5.99 years	400 (66)	24 (27)	512 (57)
6-8.99 years	83 (14)	14 (16)	135 (15)
9 years	71 (12)	28 (31)	137 (15)
Household Annual Income ^{a,b}			
<\$15 K	80 (14)	17 (20)	69 (8)
\$15-29.99 K	104 (18)	18 (21)	107 (12)
\$30-44.99K	89 (15)	11 (13)	94 (11)
\$45-59.99K	74 (13)	5 (6)	104 (12)
\$60-74.99K	47 (8)	8 (9)	103 (12)
>\$75 K	197 (33)	27 (31)	393 (45)
Residential Mobility ^a			
1 home	284 (47)	41 (46)	481 (54)
2 homes	151 (25)	27 (30)	228 (26)
>2 homes	174 (29)	21 (24)	184 (21)

^aDistribution of participants by levels of the important covariable differed for ALL cases vs. controls, χ -squared test $P < 0.05$;

^bDistribution of participants by levels of the important covariable differed for AML cases vs. controls, χ -squared test $P < 0.05$

Risk for Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemia (AML) associated with six Remodeling Activities, for Children participating in the California Childhood Leukemia Study, 1995-2008.

Table 2

Remodeling Activity	ALL Cases, N	AML Cases, N	Controls, N	ALL OR <i>a</i> ; 95% CI	AML OR <i>a</i> ; 95% CI
Construction					
No	401	55	626	Referent	Referent
Yes	134	21	150	1.52; 1.14, 2.02	1.75; 0.98, 3.15
Painting					
No	299	45	476	Referent	Referent
Yes	282	44	381	1.20; 0.96, 1.51	1.17; 0.73, 1.88
Recarpeting					
No	400	60	622	Referent	Referent
Yes	130	15	157	1.25; 0.94, 1.65	0.81; 0.43, 1.53
Reflooring					
No	400	57	610	Referent	Referent
Yes	126	21	170	1.21; 0.92, 1.60	1.41; 0.79, 2.53
Roofing					
No	364	45	575	Referent	Referent
Yes	50	9	64	1.36; 0.91, 2.03	1.83; 0.84, 4.00
Weatherproofing					
No	458	68	674	Referent	Referent
Yes	48	7	82	0.90; 0.61, 1.33	0.66; 0.26, 1.66

OR=Odds ratio; CI=Confidence interval

^aOdds ratios adjusted for child's age at diagnosis/reference date, sex, race, and Hispanic ethnicity as well as household annual income and residential mobility