



Original Contribution

Reported Residential Pesticide Use and Breast Cancer Risk on Long Island, New York

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Pesticides, common environmental exposures, have been examined in relation to breast cancer primarily in occupational studies or exposure biomarker studies. No known studies have focused on self-reported residential pesticide use. The authors investigated the association between reported lifetime residential pesticide use and breast cancer risk among women living on Long Island, New York. They conducted a population-based case-control study of 1,508 women newly diagnosed with breast cancer between August 1996 and July 1997 and 1,556 randomly selected, age-frequency-matched controls. Comprehensive residential pesticide use and other risk factors were assessed by using an in-person, interviewer-administered questionnaire. Unconditional logistic regression was used to calculate odds ratios and 95% confidence intervals. Breast cancer risk was associated with ever lifetime residential pesticide use (odds ratio = 1.39, 95% confidence interval: 1.15, 1.68). However, there was no evidence of increasing risk with increasing lifetime applications. Lawn and garden pesticide use was associated with breast cancer risk, but there was no dose response. Little or no association was found for nuisance-pest pesticides, insect repellants, or products to control lice or fleas and ticks on pets. This study is the first known to suggest that self-reported use of residential pesticides may increase breast cancer risk. Further investigation in other populations is necessary to confirm these findings.

breast neoplasms; case-control studies; environmental exposure; gardening; housing; pesticides

Abbreviations: CI, confidence interval; LIBCSP, Long Island Breast Cancer Study Project; OR, odds ratio.

The search for environmental factors associated with breast cancer is of great public interest. Pesticides are common environmental exposures that have been implicated in cancer etiology (1–3). Studies of breast cancer have primarily examined pesticide exposures among occupationally exposed individuals and among women in the general population (i.e., those not occupationally exposed) using biologic markers of exposure as well as indirect exposures such

as residential proximity to pesticide exposure sources. However, to our knowledge, no investigation of lifetime, self-reported residential pesticide use has been published.

Numerous pesticides have shown carcinogenicity of varying levels (4–6). They have also been found to be genotoxic, tumor promoters, immunotoxic, and estrogenic (1). Organochlorine pesticides, which include dichlorodiphenyl-trichloroethane (DDT), have been shown to have both

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estrogenic and carcinogenic properties (1, 7). This biologic plausibility and the fact that long-term exposure to organochlorine pesticides can be inferred from blood or adipose tissue levels account for why they are the most studied pesticide group in relation to breast cancer (1). However, epidemiologic studies have not provided convincing support for an adverse association with biomarkers of organochlorine pesticides (4–8). Many other pesticides commonly used in and around the home may have the potential to influence breast cancer risk but have not yet been studied. The use of biomarkers for many of these pesticides is limited since they may be short term or not available.

Therefore, a population-based, case-control study of the environment and breast cancer was conducted that assessed not only blood levels of organochlorine pesticides (9) but also a wide range of residential pesticide exposures through the use of an in-person, interviewer-administered questionnaire. The organochlorine pesticide biomarker investigation in the Long Island Breast Cancer Study Project (LIBCSP) population did not reveal an association with breast cancer risk (10). The analyses presented here investigate the relation between self-reported lifetime residential pesticide use and breast cancer risk among women living on Long Island, New York.

MATERIALS AND METHODS

Study population

Details of LIBCSP have been described previously (9). In brief, women who were residents of either Nassau or Suffolk Counties in New York State, newly diagnosed with invasive or in situ breast cancer between August 1, 1996, and July 31, 1997, were eligible as cases. Women residents of the same two counties during the same time period who had not been diagnosed with breast cancer were randomly selected as controls. Controls were frequency matched by 5-year age group to the expected age distribution of the cases. Controls were selected through random digit dialing if they were less than 65 years of age (screener response rate for random digit dialing = 77.9 percent) and were selected from Centers for Medicare and Medicaid Services (formerly the Health Care Financing Administration) rosters if 65 years of age or older. At the reference date (date of diagnosis for cases and date of identification for controls), women less than 65 years of age were required to have a residential telephone, and women 65 years of age or older were required to be Medicare participants.

Of 2,030 identified, eligible cases, 193 (9.5 percent) were not contacted because of physician refusal. Of those remaining, 1,508 cases (82.1 percent) were interviewed. Of 2,481 eligible controls, 1,556 (62.8 percent) completed the interview. For women less than 65 years of age, response rates were 89 percent for cases and 76 percent for controls. Among women 65 years of age or older, response rates were 72 percent for cases and 43 percent for controls. The most common reasons for both case and control nonparticipation were refusal and illness. The institutional review boards of all participating institutions approved the study protocol, and all participants provided informed consent.

Data collection

Trained interviewers administered a structured questionnaire that collected information on reproductive and medical history, occupational and residential history, and lifestyle and demographic characteristics. Detailed information on pesticide use, a primary focus of the study, was also obtained (<http://epi.grants.cancer.gov/documents/LIBCSP/projects/ques/sectc.pdf>). Participants were queried about pesticide use in and around their homes as well as their use of insect repellants, lice control products on themselves and others, and flea and tick control products on their pets. Usage patterns for seven lawn and garden pest categories and eight nuisance-pest categories were ascertained. For a particular pest category, participants identified all persons who applied the products, the various types of products applied, and the average yearly frequency of application and the number of years the products had been used. The number of lifetime applications for each individual category was derived by multiplying yearly application frequency by years of use.

Overall pesticide use (the sum of lifetime applications of all 15 categories), the two combined groups (lawn and garden and nuisance pest), and each of the 15 individual categories were considered in the analyses. Lifetime applications were categorized based on the control distribution. Women in the lowest quintile of overall pesticide use constituted the reference group in analyses of overall pesticide use. For the combined group analyses, women reporting no pesticide use for all individual pest categories within a combined group were the reference group. In this paper, individual category results are presented dichotomized as ever/never use because trends in breast cancer risk within each category were not observed. The use of two different combined group reference categories created reasonably sized groups of women who were unexposed regarding approximately half of the individual pest categories, which reduced exposure misclassification and provided more interpretable odds ratios because they were calculated by using the same reference group for a large number of categories. When odds ratios for individual pest categories were calculated based on all women who had not used pesticides for the category as the reference group, odds ratios were attenuated toward the null.

Patterns of pesticide use were examined in two ways: by applicator (self only/professional only/other or multiple applicators) and by product type (spray only/powder only/liquid only/other product or multiple types). Patterns of use could not be examined for two individual lawn and garden categories (other types of pesticides used outdoors and chemicals used on indoor plants) because of the infrequency of such pesticide use.

The analyses presented are based on 1,505 cases and 1,553 controls because three cases and three controls did not provide any pesticide information. To calculate total lifetime pesticide applications for women who reported pesticide use for an individual pest category but for whom data on use patterns were missing, the median value for the specific pattern variable was used (e.g., median years of weed killer use was used for women without reported duration of use); exclusion of these women did not materially change

estimates of association with lifetime applications. For all other analyses, women for whom data were missing were excluded.

Statistical analysis

Unconditional logistic regression was used to calculate odds ratios and 95 percent confidence intervals. Lifetime applications were entered into models as indicator variables for each quintile above the lowest. Characteristics assessed as possible confounders included race, marital status, religion, household income, age at menarche, parity, age at first birth, lactation, menopausal status, oral contraceptive use, hormone replacement therapy use, first-degree family history of breast cancer, history of benign breast disease, body mass index (weight in kilograms divided by height in meters squared) at the reference age and at age 20 years, alcohol use, smoking status, and physical activity. None of these factors were included in the final model because none resulted in at least a 10 percent change in the beta coefficient for the pesticide variables (11, 12). In addition to controlling all models for age, adjustment for education (defined as highest educational level attained: \leq high school graduate/some college/college graduate/postcollege) was included to control for possible confounding by socioeconomic status. Note that adjustment for education did not result in any substantial changes in the estimates of effect. Finally, models assessing one combined group (e.g., lawn and garden) were adjusted for the use of the other combined group (e.g., nuisance pests).

RESULTS

An increased breast cancer risk was associated with lifetime pesticide application for all pest groups combined (age- and education-adjusted odds ratio (OR) = 1.39, 95 percent confidence interval (CI): 1.15, 1.68 for quintiles 2–5 vs. quintile 1; table 1). However, there was no indication of increasing risk with increasing quintile of lifetime applications. Compared with never use of any lawn and garden pesticides, use of pesticides for these types of pests was associated with an elevated breast cancer risk (table 1). Adjustment for lifetime applications of nuisance-pest pesticides did not substantially change risk estimates. Although the age-adjusted odds ratio for ever use of combined nuisance-pest pesticides was elevated when compared with that for women who never used any pesticides for nuisance pests (age-adjusted OR = 1.20, 95 percent CI: 0.88, 1.63), further adjustment for use of lawn and garden pesticides reduced the odds ratio toward the null. No dose-response associations were observed for either combined group, and additional adjustment for education did not affect any odds ratios.

Individual lawn and garden categories

Ever use of pesticides for nearly all of the individual lawn and garden categories was associated with increased breast cancer risk (table 2). In general, within each category, no dose response was observed (data not shown). Little variation in breast cancer risk was observed for individual cate-

gories of lawn and garden pesticide application when classified according to the person who applied them (table 3). Women who exclusively self-applied lawn and garden pesticides were at a moderately increased risk of breast cancer (e.g., lawn insecticides OR = 1.56, 95 percent CI: 1.01, 2.43; chemicals for insects or diseases of outdoor plants OR = 1.58, 95 percent CI: 1.12, 2.22). However, these risk estimates were in the same range as those for pesticide use without consideration of applicator and were not generally different from those observed for women who had either professionals exclusively apply these pesticides (e.g., lawn insecticides OR = 1.41, 95 percent CI: 1.31, 1.77) or others perform the application (e.g., lawn insecticides OR = 1.32, 95 percent CI: 1.05, 1.67).

Overall, examination of breast cancer risk associated with use of different product types in the individual lawn and garden categories did not reveal any specific types as being associated with risk different from that observed without categorization by product type (table 3). For lawn insecticide application, exclusive use of the liquid form was associated with higher risk (OR = 1.77, 95 percent CI: 1.12, 2.77) than other product types. Women who used a combination of product types or some other product type for outdoor plant pest problems were at higher risk than women who used spray only (OR = 1.83, 95 percent CI: 1.27, 2.64).

Individual nuisance-pest categories

Lifetime applications of the individual categories of nuisance-pest pesticides did not appear to be related to breast cancer risk (table 2). Similarly, breast cancer risk was not elevated for nuisance-pest pesticide application when categorized by the person who performed the application or when classified by product types; the vast majority of the odds ratio estimates were at or near the null value (data not shown).

Subgroup analyses

We examined whether the relation of residential pesticide use and breast cancer varied within different subgroups of participants (data not shown). When the population was stratified by menopausal status (pre- vs. post-) or by length of residency (≥ 15 or < 15 years in the current home) or was restricted to participants less than age 65 years, the associations between pesticide use and breast cancer risk in the subgroups were not considerably different from those for the entire sample. The relation was also examined according to stage of disease, that is, invasive cases only (84.4 percent) and in situ cases only. Associations for the invasive cases were nearly identical to those observed for all cases combined. Among in situ cases, the findings for breast cancer risk and use of pesticides for nuisance pests were similar to those found for invasive cases. However, the associations for all pest groups combined and the lawn and garden pest group were stronger for some, but not all, of the quantiles of use (OR = 1.91, 95 percent CI: 1.17, 3.13; OR = 1.97, 95 percent CI: 1.21, 3.21; OR = 2.03, 95 percent CI: 1.25, 3.30; OR = 1.23, 95 percent CI: 0.72, 2.08 for quartiles 1–4, respectively, vs. never use of lawn and garden pesticides).

TABLE 1. Adjusted odds ratios and 95% confidence intervals for breast cancer, according to lifetime applications of pesticides, among 3,058 women in Nassau and Suffolk Counties, New York, 1996–1997

	Lifetime applications (no.)			Cases (no.)	Controls (no.)	Adjusted for age, education, and other combined pest group*	
	Minimum	Median	Maximum			OR	95% CI†
All pest groups combined							
Quintile 1 (reference)	0	6	16	230	310	1.00	Reference
Quintiles 2–5				1,275	1,243	1.39	1.15, 1.68
Quintile 2	17	32	50	298	315	1.30	1.03, 1.64
Quintile 3	51	77	111	313	307	1.39	1.10, 1.76
Quintile 4	112	159	242	347	311	1.49	1.19, 1.88
Quintile 5	243	482	20,834	317	310	1.37	1.08, 1.72
Lawn and garden combined group‡							
Never used lawn and garden pesticides				240	305	1.00	Reference
Ever used lawn and garden pesticides				1,254	1,231	1.34	1.11, 1.63
Quartile 1	1	6	15	282	303	1.25	0.98, 1.59
Quartile 2	16	28	44	341	313	1.44	1.14, 1.82
Quartile 3	45	70	108	301	307	1.30	1.02, 1.64
Quartile 4	109	180	20,820	330	308	1.38	1.09, 1.75
Nuisance-pest combined group§							
Never used nuisance-pest pesticides				100	117	1.00	Reference
Ever used nuisance-pest pesticides				1,404	1,436	1.07	0.80, 1.42
Quartile 1	1	4	8	290	364	0.88	0.64, 1.20
Quartile 2	9	16	29	338	358	1.07	0.78, 1.46
Quartile 3	30	53	96	393	357	1.20	0.88, 1.65
Quartile 4	97	223	9,608	383	357	1.16	0.85, 1.58

* Odds ratios (ORs) for the category of all pest groups combined were adjusted for age and educational status only (\leq high school graduate/some college/college graduate/postcollege).

† CI, confidence interval.

‡ Data for 11 cases and 17 controls were missing.

§ Data for one case were missing.

It is important to note that these latter measures were less stable because of the reduced sample size.

Insect repellants, lice control products, and flea and tick products used on pets

Breast cancer risk was not associated with frequent or long-term use of insect repellants (OR = 0.89, 95 percent CI: 0.60, 1.31 for ≥ 20 years vs. never use) or with use of lice control products (OR = 0.86, 95 percent CI: 0.71, 1.04 for use ≥ 2 times vs. never use). Likewise, no increased risk of breast cancer was associated with the use of flea and tick products on pets, when examined by frequency of application (OR = 1.08, 95 percent CI: 0.87, 1.33 for use ≥ 30 times

vs. never use), type of product used, or person who applied the product (data not shown).

DISCUSSION

Overall, women who reported the highest (quintiles 2–5 combined) pesticide use in and around their homes had more than a 30 percent increased risk of breast cancer relative to women who reported the lowest use. Lifetime applications and patterns of use of pesticides for nuisance pests were consistently observed to have little or no association with breast cancer risk when examined as either a combined group or by individual categories. On the other hand, use of the combined lawn and garden pesticides as well as the majority

TABLE 2. Adjusted odds ratios and 95% confidence intervals for breast cancer, according to lifetime applications of pesticides for individual categories of pests,* among 3,058 women in Nassau and Suffolk Counties, New York, 1996–1997

Ever used pesticides for individual categories of pests	Cases (no.)	Controls (no.)	Adjusted for age, education, † and other combined pest group	
			OR‡	95% CI§
Never used any lawn and garden pesticides	240	305	1.00	Reference
Weeds	1,109	1,083	1.43	1.17, 1.75
Lawn insects	799	766	1.48	1.20, 1.82
Insects or diseases of trees	539	514	1.46	1.17, 1.81
Pests in vegetable or fruit gardens	298	259	1.58	1.24, 2.01
Insects or diseases of outdoor plants	261	232	1.54	1.20, 1.98
Any other type of outdoor pest	70	48	1.13	0.86, 1.49
Insects or diseases of indoor plants	121	112	1.48	1.08, 2.02
Never used any nuisance-pest pesticides	100	117	1.00	Reference
Ants, carpenter ants, or cockroaches	1,160	1,171	1.06	0.79, 1.42
Bees or wasps	599	610	1.05	0.77, 1.43
Flies or mosquitoes	328	310	1.12	0.81, 1.55
Moths, silverfish, or caterpillars	388	352	1.19	0.87, 1.64
Mice, rats, gophers, or moles	246	268	1.02	0.73, 1.42
Fleas or ticks, except on pets	377	394	1.06	0.91, 1.23
Termites	731	712	1.10	0.81, 1.48
Any other type of pest in the home	50	52	1.06	0.65, 1.71

* For all individual categories, some data were missing.

† Educational status: ≤high school graduate/some college/college graduate/postcollege.

‡ Each odds ratio (OR) was derived from a separate model. To create a common combined-pest-category reference group, a set of three mutually exclusive indicator variables was used: never used combined-pest-category pesticides (reference), used pesticides for individual categories of pests, used combined-pest-category pesticides but not for individual categories of pests.

§ CI, confidence interval.

of the individual pest categories in this group consistently showed an elevation in breast cancer risk. Finally, use of insect repellants, lice control products, or pet flea and tick control products was not related to breast cancer risk.

Interpretation of these findings in the context of other studies is limited because, to our knowledge, there are no published studies of self-reported residential pesticide use and breast cancer. A recent review of the numerous studies that have examined biologic markers of various organochlorine pesticides concluded that there was little support for a positive association between dichlorodiphenyldichloro-

ethene or dichlorodiphenyltrichloroethane and breast cancer risk (13). Our own investigation of organochlorine levels among the LIBCSP population did not find increased breast cancer risk (10). The absence of an association for treatment of the home for termites in this analysis and in an earlier Long Island study that examined reported termiticide use (14) agrees with the lack of a breast cancer association with chlordane in the LIBCSP population (10). The observed null findings for lice control products is supported by the observed lack of association in the majority of epidemiologic studies that examined beta-hexachlorocyclohexane, a contaminant of lindane (gamma-hexachlorocyclohexane), and breast cancer risk (15–17).

Studies of agricultural workers, an occupational group with a high probability of pesticide exposure, have not shown an increased breast cancer risk among women (18–30). Many of the studies suffered from small sample size or lacked confounder information. Furthermore, occupation is a nonspecific indicator of pesticide exposure, possibly biasing results toward the null. In a recent study, breast cancer in farmers' wives was associated with their husbands' use of 2,4,5-trichlorophenoxypropionic acid, 2,4,5-trichlorophenoxyacetic acid, and captan (31), pesticides that could have been used on Long Island. Thus, these findings support our observation of increased breast cancer risk and use of pesticides for weeds and fruit tree pests.

Other classes of popular pesticides have replaced organochlorines over the years in a continuing search for less toxic, but effective agents. Organophosphates were formerly among the most widely used household pesticides, accounting for about 22 percent of nonagricultural usage in 2001, so that many women in our study would almost certainly have been exposed in the past. However, because of health concerns, two major organophosphate pesticides, chlorpyrifos (widely used in lawns and against termites—the active ingredient in Dursban (Dow Agrosciences, LLC, Indianapolis, Indiana)) and diazinon, were restricted or banned for residential use after 2001 by the Environmental Protection Agency. Dichlorvos, formerly used in home foggers and aerosols and to control insects in passenger aircraft, is now classified by the Environmental Protection Agency as a "Restricted Use Pesticide" and may be purchased legally by certified applicators only. It is still used in no-pest strips, pet collars, and kennels. Dichlorvos has an Environmental Protection Agency carcinogenicity classification of B2 (probable human carcinogen (32)) and a rating of 2B (possibly carcinogenic to humans) from the International Agency for Research on Cancer. Organophosphates are mostly nonestrogenic, but mixtures of several organophosphates were found to affect birth weight and fetal viability. Chlorpyrifos was regarded as nonestrogenic until recently, when two studies showed possible evidence of weak estrogenicity (33, 34).

Carbamates, another class of widely used insecticides, include the Sevin (Aventis CropScience, Inc., Strasbourg, France) brand of carbaryl. Since Dursban was banned, it has become one of the most popular brands of carbaryl insecticides for home garden use. Carbaryl currently has a carcinogenicity rating of group III (unclassifiable as to human carcinogenicity) from the International Agency for Research on Cancer, although one study has reported an increased risk

TABLE 3. Adjusted odds ratios and 95% confidence intervals for breast cancer, according to lifetime applications of pesticides, person who applied the pesticides, and type of lawn and garden pesticide product in individual categories,* among 3,058 women in Nassau and Suffolk Counties, New York, 1996–1997

Use of pesticides for individual lawn and garden pest problems	Person who applied the pesticides	Cases (no.)	Controls (no.)	Adjusted†		Type of product applied	Cases (no.)	Controls (no.)	Adjusted†	
				OR‡	95% CI‡				OR	95% CI
Never used any lawn and garden pesticides		240	305	1.00	Reference		240	305	1.00	Reference
Weeds	Self only	101	110	1.21	0.88, 1.68	Spray only	292	300	1.30	1.02, 1.65
	Professional only	363	348	1.36	1.08, 1.71	Powder only	290	298	1.30	1.02, 1.65
	Other§	640	623	1.36	1.10, 1.67	Liquid only	77	73	1.40	0.97, 2.03
						Other¶	437	408	1.43	1.14, 1.79
Lawn insects	Self only	51	44	1.56	1.01, 2.43	Spray only	197	205	1.32	1.01, 1.72
	Professional only	402	373	1.41	1.13, 1.77	Powder only	193	195	1.38	1.06, 1.81
	Other	336	340	1.32	1.05, 1.67	Liquid only	53	40	1.77	1.12, 2.77
						Other	340	313	1.49	1.18, 1.88
Insects or diseases of trees	Self only	15	30	0.67	0.35, 1.29	Spray only	426	418	1.40	1.12, 1.75
	Professional only	372	343	1.45	1.15, 1.83	Powder only	0	0		
	Other	148	140	1.42	1.06, 1.9	Liquid only	25	25	1.41	0.78, 2.53
						Other	83	68	1.69	1.17, 2.44
Pests in vegetable or fruit gardens	Self only	87	85	1.41	0.99, 1.99	Spray only	115	94	1.64	1.18, 2.27
	Professional only	14	8	2.29	0.94, 5.58	Powder only	107	97	1.50	1.08, 2.09
	Other	195	166	1.56	1.18, 2.04	Liquid only	7	9	1.13	0.41, 3.11
						Other	68	59	1.60	1.08, 2.38
Insects or diseases of outdoor plants	Self only	101	86	1.58	1.12, 2.22	Spray only	127	107	1.58	1.16, 2.17
	Professional only	49	37	1.79	1.12, 2.84	Powder only	31	47	0.91	0.56, 1.49
	Other	106	107	1.29	0.93, 1.78	Liquid only	8	12	0.93	0.37, 2.33
						Other	91	66	1.83	1.27, 2.64

* For all individual categories, some data were missing.

† All models were adjusted for age, education, and combined-nuisance-pest pesticide use.

‡ OR, odds ratio; CI, confidence interval.

§ Any combination of applicators or some person other than self or professional only.

¶ Any combination of product types or some type other than spray, powder, or liquid only.

of non-Hodgkin's lymphoma in farmers who used this pesticide (35). Estrogenicity of carbamates has not been extensively investigated, although there is one report of inhibition of 17 β -estradiol and progesterone activity in human breast and endometrial cancer cells (36).

Synthetic pyrethroids, common residential insecticides, have been found to possess estrogenic and antiprogestagenic properties in human breast cell assays (37, 38). These insecticides could have been included among categories of pesticides used for lawn and garden purposes for which an association with breast cancer was observed, such as problems on fruit trees, in vegetable gardens, and on outdoor as well as indoor plants. However, these insecticides could also have been used for nuisance-pest categories—such as ants, cockroaches, wasps, flies, mosquitoes, moths, silverfish, caterpillars, fleas, ticks, and termites—not associated with in-

creased risks. Another insecticide, rotenone, possibly used by participants on fruit trees, vegetable gardens, and indoor plants, has been shown to cause mammary tumors in rats (39) but has also been shown to have anticancer action in human breast cell culture (40).

In LIBCSP, information was not collected on the time frame of pesticide use. This is a possible limitation because it has been proposed that exposures occurring between menarche and first birth may be the most influential in initiating breast cancer (41). However, we were not able to examine the effect of exposures occurring during a particular period of a woman's reproductive life cycle. Additionally, several of the individual pest categories included pests for which different pesticides would be used, and the same pesticide could have been used for several of the individual categories. For example, chlorpyrifos and diazinon could have been

used for lawn insects as well as to treat ants and cockroaches. Because we did not ascertain the specific chemicals applied for any of the pest problems, we were not able to assign any observed increased risk to the use of a specific pesticide.

Many women reported a combination of pesticide applicators as well as multiple types of products but did not rank the frequency of use of a particular applicator or product type. Thus, distributing lifetime applications according to multiple reported persons or product types was not possible. Assigning an equal distribution (e.g., if both self and professional were reported, half of the lifetime applications would be attributed to self and half to the professional) assumed information beyond what we collected and was most likely unrepresentative. Therefore, to avoid introducing additional exposure misclassification, we categorized women as combination users or exclusive users of an applicator or type. Future investigations of patterns of pesticide use should consider asking women to rank their use of multiple applicators or product types.

The "lifetime applications" variable represents exposure opportunity rather than an actual exposure dose. The detailed information required to calculate a received dose of pesticides was not, nor could it be, ascertained by a questionnaire alone. The categorized lifetime application variable used as the measure of pesticide exposure in these analyses allowed women to be ranked according to their reported use and allowed for exploration of trends. The variable also enabled both reported frequency and number of years of use to be combined into a single exposure variable.

Finding no dose-dependent relation between exposure and breast cancer risk may be due to the imprecision of the exposure measure. It is possible that ever use of pesticides for individual categories was recalled accurately, but the details of use were not. Thus, the ranking of women according to their lifetime applications may have been incorrect, thereby masking any underlying association. Furthermore, the combination of frequency and duration may not be the optimal approach to assess residential pesticide exposure for some of the pesticide categories. For example, the vast majority of women had only one lifetime application of termite control pesticides; thus, frequency and duration have little meaning.

The reliability of self-reported lifetime residential exposure among the participants must be considered. The design of the questionnaire required women to integrate a considerable amount of information over their lifetime, resulting in potentially imprecise reporting of their pesticide exposures. The time interval between exposure and recall, the amount of detail required, age, how memorable the exposure was, and the social desirability of reporting the exposure may all influence the reproducibility of residential pesticide use recall (42). The hypothesis of an adverse association between pesticides and breast cancer was widely publicized, so it is likely that this heightened awareness influenced cases' reporting. This issue could have resulted in recall bias such that the observed associations are biased away from the null. However, data from our study indicate that cases and controls were equally likely to believe that environmental factors were associated with breast cancer etiology. Examination of self-reported beliefs about the cause of breast cancer revealed no case-control differences in the reporting of at least

one environmental factor (69 percent vs. 68 percent, respectively), suggesting that recall was not biased differentially.

The study's design lends many strengths to this investigation, including 1) a population-based design, which allows for generalizability of the results to the population of Long Island, New York, as well as similar populations; 2) a large sample size, which increases the power to detect associations; and 3) a comprehensive, in-person, interviewer-administered questionnaire, which provides well-measured confounding variables. Another strength of this study is long-term Long Island residency; nearly 60 percent of both cases and controls were residents of their current home for at least 15 years. For these long-term residents, pest problems they have encountered are likely to be stable over time (e.g., ant problems in the spring, wasp problems in the summer) so that a woman may have performed the same pesticide application routine for many years, making recall easier. When analyses were restricted to these women, the results were essentially the same, which could indicate that reporting of exposures was not differentially affected by length of residency, or it may reflect that the exposure assessment was not sensitive enough to capture any differences that may have existed.

Not all eligible women participated, and response rates varied by age (9). If the pesticide exposure of women who participated is different from that of those women who did not but does not differ by case-control status, then non-differential misclassification would occur, biasing the estimates of association between pesticide use and breast cancer toward the null. On the other hand, if the response difference between the cases and controls is somehow related to pesticide use, then differential misclassification would occur, and the estimate of the association could be biased in either direction. The results do not appear to be biased because of age-related nonresponse, since results of analyses restricted to participants less than 65 years of age were not materially different.

A great deal of detail about residential and personal pesticide use was ascertained, which allowed investigation of not only overall pesticide use but also patterns of use for specific pesticide groups. However, information on use of actual chemical products was not ascertained because it was found during pilot testing that women could not recall them. This limitation prevents identification of specific pesticides that require further investigation in relation to breast cancer risk.

To our knowledge, our study is the first to suggest that self-reported residential pesticide use may be associated with elevated breast cancer risk. However, the weak association, the absence of a dose response, the lack of support from studies of biologic measures of exposures, and the possibility of chance findings due to multiple comparisons all indicate the uncertain nature of the observed association. Further investigation in other populations is necessary before any definitive conclusions can be reached.

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