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Associations of residential exposure to agricultural pesticides with asthma prevalence in adolescence: The PIAMA birth cohort

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ABSTRACT

Background: It has been suggested that children who are exposed to agricultural pesticides have an increased risk of asthma, but evidence for associations betweeen residential pesticide exposure and childhood asthma is inconsistent.
Objectives: To investigate the associations of residential pesticide exposure with the prevalence of asthma and related symptoms within a Dutch birth cohort study.
Methods: In this cross-sectional analysis, we included participants of the PIAMA birth cohort study with data on residential pesticide exposure and asthma from parent-completed questionnaires at age 14, collected in 2012 (N = 1473). We used spatial data on the presence of individual crops (cereals, open field vegetables, commercial crops, open field floriculture/bulbs, corn and potatoes) and pesticide application on these crops to estimate residential exposure to pesticides with known irritant properties for the respiratory system within distances of 100, 500, and 1000 m of the participants' homes. Logistic regression was used to estimate associations between exposure and outcomes, adjusting for potential confounders.
Results: No associations were found between living within 100, 500 and 1000 m of agricultural fields likely treated with pesticides and symptoms of asthma. For instance, for participants living within 100 m of fields with any crops likely treated with pesticides, the adjusted odds ratios (95% confidence interval) for the prevalence of asthma, shortness of breath and dry night cough at age 14 were 0.31 (0.07, 1.32), 0.61 (0.23, 1.57) and 1.26 (0.56, 2.80), respectively. No associations were found between estimated exposure to pesticides with known irritant properties for the respiratory system and asthma or related symptoms.
Conclusions: There was no association between living near agricultural fields likely treated with pesticides and asthma and related respiratory symptoms, among our study participants.

1. Introduction

Asthma is one of the most common chronic diseases among children (World Health Organization, 2017). Many factors have been associated with an increased risk of asthma including genetic and environmental factors.

Agricultural pesticides are frequently used to fight pests and to improve plant growth and increase agricultural production. When these pesticides are applied to agricultural fields, they can transfer through the air to nearby homes and may be harmful to health (Coronado et al., 2011; Lu et al., 2000; Deziel et al., 2017). Previous studies have suggested that children living close to agricultural treated fields may have an increased risk of asthma possibly due to the transfer of pesticides to their homes (Schwartz et al., 2015; Salameh et al., 2003).

Pesticides with respiratory irritant properties may lead to asthma through interaction with functional irritant receptors in the airways (Hernandez et al., 2011). These processes may promote neurogenic inflammation. In addition, cross talk between airway nerves and inflammatory cells can help to maintain chronic inflammation that eventually damages the bronchial epithelium (Hernandez et al., 2011).

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This has been hypothesized to increase the risk of developing asthma, exacerbate an existing asthmatic condition or trigger asthma attacks by increasing bronchial hyper-responsiveness. In addition, exposure to agricultural pesticides has been linked to increased levels of Th2 cytokines in children (Duramad et al., 2006). Th2 cytokines play an important role in the development of allergic diseases, including asthma and related respiratory symptoms (Holgate, 1999).

At present, epidemiological evidence for associations of residential pesticide exposure with childhood asthma is inconsistent (Gascon et al., 2014a; Gascon et al., 2014b; Karmaus et al., 2003; Karmaus et al., 2001; Liu et al., 2012; Mamane et al., 2015; Merchant et al., 2005; Perla et al., 2015; Reardon et al., 2009; Salam et al., 2004; Salameh et al., 2003; Sunyer et al., 2005; Sunyer et al., 2006; Tagiyeva et al., 2010; Weselak et al., 2007). As these studies were based on different designs, sample sizes, exposure and outcome definitions, it is not possible to conclude, which of these factors contributed most to the heterogeneity of the study findings. For example, in these studies, residential exposure to agricultural pesticides has been assessed in different ways, namely using (self-reported) distances from treated agricultural fields as a proxy (Salameh et al., 2003), biomonitoring (Coronado et al., 2011; Bouvier et al., 2005) as well as measurements of pesticides contaminants in house dust samples (Ward et al., 2006) and indoor air (Garron et al., 2009).

We tested our hypothesis of an association between residential exposure to pesticides and asthma and related respiratory symptoms among adolescents within our Dutch PIAMA birth cohort study. Our study is based on a very well defined cohort, and uses extensively documented methods of exposure (Bukalasa et al., 2017) and outcome (Pinart et al., 2014) assessment, which improves transparency of the findings and comparability with other studies.

2. Methodology

2.1. Study design and population

The PIAMA (Prevention and Incidence of Asthma and Mite Allergy) study is a prospective Dutch birth cohort study. The baseline study population consisted of 3963 participants from the northern, middle and western parts of the Netherlands, who were born in 1996 and 1997 (Wijga et al., 2014). The PIAMA study was designed to examine the influence of lifestyle and environmental factors on the development of asthma and allergies in children. Questionnaires were administered to parents during pregnancy, at the child's ages of 3 months and 1 year, and then annually until the age of 8 years. When the children were 11, 14 and 17 years old, questionnaires were completed by both parents and children.

The present study is a cross sectional analysis within the prospective PIAMA birth cohort study using data collected when the participants were about 14 years old. This study builds on our previous work on the assessment of pesticide exposure using proximity to agricultural fields with crops relevant for pesticide use and surface areas of these crops as a proxies for exposure among PIAMA participants (Bukalasa et al., 2017). We included all participants who were included in the exposure assessment study and who had information on at least one of the outcomes of interest, i.e. asthma and related respiratory symptoms at the age of 14. We restricted the current study population to participants with questionnaires completed in 2012, i.e. the year for which we had data on exposure, to assure that exposure preceded health outcomes ($N = 1473$, Fig. S1).

2.2. Health outcomes

We used data from standardized asthma outcomes questionnaires that were self-completed by the parents in the Dutch language when the children were 14 years old to define asthma and related symptoms at age 14. Asthma was defined as at least two positive answers to the following three questions: (1) has a doctor ever diagnosed asthma in your child, (2) has your child had wheezing or whistling in the chest in the last 12 months, (3) has your child been prescribed asthma medication during the last 12 months. This definition was developed by a panel of experts within the MeDALL consortium (Pinart et al., 2014). Additional outcomes of interest were shortness of breath during the past 12 months and dry night cough during the past 12 months.

2.3. Agricultural pesticides exposure assessment

The assessment of environmental pesticide exposure within the PIAMA birth cohort study has been described elsewhere (Bukalasa et al., 2017). In brief, we used areas of selected crops extracted from the Basic Registration of Crops (BRP, vector dataset with 1:10,000 underlying resolution) of 2012 (Dutch Ministry of Interior and Kingdom Relations, 2013) within 50, 100, 500 and 1000 m of the participants' home addresses at the time of the 14-year follow-up as proxies for environmental pesticide exposures. We used data for the same year for all participants. Since the 14-year questionnaires were completed by the parents between October 2011 and August 2013 we used data for 2012 (which is well within that period) to assess residential exposure to pesticides. In the present study, our assessment focused on 100, 500 and 1000 m buffers around the participants' homes to investigate exposure at short distances only (100 m buffer) and exposure at shorter and larger distances (500 and 1000 m buffers).

In addition, we assigned amounts of likely used pesticides (in gram of active ingredient per year) in the aforementioned buffers based on a 2012 farmer survey by Statistics Netherlands (CBS) in combination with the acreage of specific crops around the participants' homes as described previously (Bukalasa et al., 2017). We included in the present analysis pesticides with known irritant properties for the respiratory system identified through the pesticides properties database (PPD) and the pesticides manual (University of Hertfordshire, 2016).

For the assessment of associations with the presence of specific crops, we selected cereals, open field vegetables, commercial crops (sugar beet, cichorium, hemp (fiber), winter rapeseed, summer rapeseed, fodder beets (including topinambour), grass seeds (including clover seeds) and flax), open field floriculture/bulbs, corn and potatoes within 500 and 1000 m of the homes. We selected these crops as it is likely that they have been treated with pesticides and because they were present for at least 10% of the study participants in the the 1000 m buffer resulting in sufficient numbers of exposed children (Table 1). None of the crops met the 10% criterion with the 100 m buffer because we had only few participants living within a short distance of agricultural fields. Like for the specific crops, we restricted our analysis of associations with amounts of pesticides used to pesticides that were likely applied around at least 10% of the participants' homes. These included chlormequat, chlorothalonil, diquatdibromide, florasulam, iodosulfuron-methyl-sodium, mancozeb, mecoprop-P, mesosulfuron-

Table 1
Number and percentage of participants with relevant crops cultivated within 100, 500 and 1000 m of their home address at the time of the 14-year follow up ($N = 1473$).

	Radius of circular buffer		
	100 m	500 m	1000 m
	N (%)	N (%)	N (%)
Any crops	100 (6.8)	588 (39.9)	945 (64.2)
Cereals	29 (2.0)	236 (16.0)	459 (31.2)
Open field vegetables	5 (0.3)	51 (3.5)	145 (9.8)
Commercial crops	13 (0.9)	115 (7.8)	277 (18.8)
Open field floriculture/bulbs	4 (0.3)	81 (5.5)	222 (15.1)
Corn	41 (2.8)	412 (28.0)	790 (53.6)
Potatoes	30 (2.0)	188 (12.8)	336 (22.8)