Environment International 134 (2020) 105210

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Pesticide exposures for residents living close to agricultural lands: A review

Clémentine Dereumeaux[a,*], Clémence Fillol[a], Philippe Quenel[b], Sébastien Denys[a]

[a] *Direction of Environmental Health, Santé Publique France, Saint Maurice Cedex, France*

[b] *Univ Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail) – UMR_S1085, F-35000 Rennes, France*

ARTICLE INFO

Handling Editor: Adrian Covaci

ABSTRACT

Background: Residents living close to agricultural lands might be exposed to pesticides through non-occupational pathways including spray drift and volatilization of pesticides beyond the treated area.

Objective: This review aimed to identify and analyze scientific literature measuring pesticide exposure in non-farmworker residents living close to agricultural lands, and to suggest practical implications and needs for future studies.

Methods: A review was performed using inclusion criteria to identify original articles of interest published between 2003 and 2018.

Results: From the 29 articles selected in this review, 2 belonged to the same study and were grouped, resulting in a total of 27 studies. Seven studies assessed exposure to pesticides using environmental samples, 13 collected biological samples and 7 analyzed both. Nine studies included a reference group of residents living far from agricultural lands while 11 assessed the influence of the spraying season or spray events on pesticide exposures. Studies included in this review provide evidence that residents living near to agricultural lands are exposed to higher levels of pesticides than residents living further away.

Discussion and conclusion: This review highlights that the following study design characteristics may be more appropriate than others to measure pesticide spray drift exposure in non-farmworker residents living close to agricultural lands: inclusion of a non-agricultural control group, collection of both biological and environmental samples with repeated sampling, measurements at different periods of the year, selection of numerous study sites related to one specific crop group, and measurements of pesticides which are specific to agricultural use. However, few studies to date incorporate all these characteristics. Additional studies are needed to comprehensively measure non-occupational pesticide exposures in this population in order to evaluate health risks, and to develop appropriate prevention strategies.

1. Introduction

Many non-farmworker residents live close to agricultural lands where pesticides are often used intensively. Due to the intrinsic toxicity of pesticides, it is important to evaluate the potential health consequences for this specific population, largely absent in studies to date (McDuffie, 2005). Some epidemiological studies suggest an association between proximity to agricultural lands and a wide range of associated adverse health outcomes including birth-related outcomes (e.g., preterm birth, fetal growth restriction, neural tube defects, hypospadias, gastroschisis and anotia) (Carmichael et al., 2016; Gemmill et al., 2013; Larsen et al., 2017; Meyer et al., 2006; Rappazzo et al., 2016; Rull et al., 2006b), childhood cancers (e.g., leukemia and lymphomas) (Carozza et al., 2009; Gómez-Barroso et al., 2016; Jones et al., 2014; Malagoli et al., 2016; Reynolds et al., 2005b; Rull et al., 2009), cognitive impairments (e.g., autism spectrum disorders, diminished intelligence quotient (IQ), verbal comprehension and attention, as well as hyperactivity and cognitive decline) (Coker et al., 2017; Corral et al., 2017; Gunier et al., 2017a; Gunier et al., 2017b; Paul et al., 2018; Roberts et al., 2007; Rowe et al., 2016; Shelton et al., 2014), respiratory outcomes (e.g., asthma) (Raanan et al., 2017), adult cancer (e.g., breast cancer and brain tumors) (Carles et al., 2017; El-Zaemey et al., 2013), Parkinson's disease (Brouwer et al., 2017; Costello et al., 2009; Manthripragada et al., 2010; Wang et al., 2011; Wang et al., 2014) and amyotrophic lateral sclerosis (Vinceti et al., 2017). However these associations are generally weak or inconclusive and contradictory results have been observed in other epidemiological studies (Brody et al., 2004; Bukalasa et al., 2018; Carmichael et al., 2013; Carmichael et al., 2014; Clementi et al., 2007; Cornelis et al., 2009; Reynolds et al., 2004; Reynolds et al., 2005a; Shaw et al., 2014; Shaw et al., 2018).

---

* Corresponding author.
E-mail address: clementine.dereumeaux@santepubliquefrance.fr (C. Dereumeaux).

https://doi.org/10.1016/j.envint.2019.105210
Received 13 May 2019; Received in revised form 16 September 2019; Accepted 21 September 2019

All the above-cited studies have limitations and weaknesses which could explain these inconsistent findings. These include not controlling for confounding factors like smoking, alcohol consumption, occupational exposure and other environmental exposure, the risk of ecological bias in spatially-based studies, and most importantly, the risk of misclassification in exposure characterization (Shirangi et al., 2011). With regard to the latter, several approaches have been used for exposure characterization, including self-administered questionnaires, interviews, biomonitoring measurements and geographic information system (GIS) models. However, self-reports of proximity to agricultural lands and pesticide exposure are potential sources for inaccuracy due to subjects' lack of knowledge about pesticide use, and the real distance of their homes from agricultural lands, as well as to recall bias (Rull et al., 2006a). Furthermore, biomonitoring data are generally limited to a specific and short exposure timeframe, for example during pregnancy (Buscail et al., 2015; Sagiv et al., 2018). Moreover, GIS models are generally based on the estimation of the agricultural surface area at a specific distance from residents' households. Participants are generally classified as living or not living near to agricultural lands, as opposed to being classified according to their pesticide exposure in terms of proximity to crops. In the best case scenario, they are classified as being exposed (or not) to a certain quantity of pesticide "probably used" within a specific distance from residence. These indirect indicators of exposure are subject to potential misclassification because of errors in the geocoding and/or in the assignment of proximity to crops. Other limitations include changes in land use (e.g., change of crop types), the lack of reliable information on the types and quantities of pesticides applied on treated areas, and the lack of identification of the correct buffer zone or distance that should be implemented between households and treated fields (Rull et al., 2006b). Therefore, a more refined measurement of pesticide exposure in terms of proximity to crops for non-farmworker residents is first needed in order to develop exposure models and indicators for large-scale epidemiological health studies investigating pesticide exposure pathways.

There is growing evidence that farmworkers and their families living close to agricultural lands are more exposed to agricultural pesticides – both in terms of concentration and type – than the general population (Curl et al., 2002; Curwin et al., 2007; Fenske et al., 2002; Hyland and Laribi 2017; Lu et al., 2000). Although exposure is mainly explained by occupational and take-home pathways (i.e., clothes), other modes exist, including inhalation of outdoor air, contamination of house dust, take-home from pets, ingestion of contaminated groundwater, recreation in fields, and eating produce directly from treated fields or from self-production (Deziel et al., 2015). These non-occupational exposure pathways are related to pesticide dispersal in the environment caused by spray drift and volatilization of pesticides beyond the treated area at the time of application or soon after (Felsot et al., 2010). In some cases, spray drift and volatilization can account for up to 90% of the application dose on crops(Bedos et al., 2002). However, little is known about the impact of these pathways in non-farmworker residents living close to agricultural lands.

An improved understanding of non-occupational pesticide exposure in this population is critical in order to evaluate health risks, and to develop appropriate prevention strategies. The objective of this review was to examine exposure measurement strategies and sampling methods used in a series of recent studies (2003–2018) which sought to characterize non-occupational pesticide exposure among residents, according to their residential proximity to agricultural lands, and to suggest practical implications and needs for future studies.

2. Methods

The review was based on the PRISMA guidance protocol (http://www.prisma-statement.org/). A comprehensive search of relevant studies was conducted using PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) and SCOPUS (http://www.scopus.com). Adapted from the PICO principle, the following algorithm was used: (Resident*[ALL FIELDS] OR residential proximity [ALL FIELDS]) AND (pesticides [TIAB] OR pesticide[TIAB] OR herbicides[TIAB] OR herbicide[TIAB] OR agrochemicals[TIAB] OR agrochemical[TIAB] OR insecticides [TIAB] OR insecticide[TIAB] OR fungicides[TIAB] OR fungicide[TIAB] OR agrochemicals[Mesh]) AND (Agriculture [ALL FIELDS] OR Agricultural [ALL FIELDS]) AND (Exposure [TIAB] OR expos*[TIAB]). The search was limited to peer-reviewed published articles in journals available in English or French between 1 January 2003 to 31 December 2018. The filters "Human" and "Humans" were applied.

The search yielded 235 articles from PubMed and 392 from Scopus for a total of 549 articles (78 duplicates) (Fig. 1). All articles were analyzed based on their title and abstract. Articles that did not report original results (reviews, case-reports, comments, letters, and editorials) (n = 124), methodology-based articles (analytical method or modeling validation) and articles highlighting study design without results (n = 31) were excluded. Animal studies (n = 7), studies assessing the risk of adverse health effects (n = 50), toxicological studies (n = 20), studies related to prevention, to knowledge, attitudes, practice" or to risk perception (n = 20) were also excluded.

The remaining 297 articles were critically analyzed using exclusion/inclusion criteria based on the study population (residents living close to agricultural lands) and exposure pathways (pathways related to agricultural pesticide applications). No limitations on geographic location were applied. Articles not related to pesticide exposure (n = 12) or agricultural-related exposure (n = 57) were excluded. A substantial number of articles referring to the general population (n = 40) and to the rural population (n = 30) were also excluded because they did not specifically focus on the target population. Articles related to farmworkers (n = 60) and farming families (n = 58) were also excluded because they estimated occupational exposure pathways to pesticides or take-home exposure pathways in agricultural workers that should not exist in non-farmworker residents. Studies estimating exposure to agricultural chemicals at the county scale or wider were excluded because this scale was not fine enough to estimate exposure in our target population. Studies characterizing exposure related to previous contamination of agricultural lands or biological insecticide use were also excluded. One model-based study (Wong et al., 2017) was excluded from the analysis because a hazard quotient model was used based on estimated exposures and therefore did not provide refined enough exposure measurements.

In summary therefore, 252 of the initial 549 articles were primarily excluded based on the critical analysis of their title and abstract. Another 245 were secondarily excluded after the analysis of exclusion/inclusion criteria based on the study population and exposure pathways. A further 23 were subsequently excluded after a full article review. Finally, 29 articles were identified as meeting all the review's inclusion criteria.

For each article, the following information was collected: the name of the first author and study, location, study design, population, time period, pesticides of interest, factors used to define 'exposed' status, exposure measurement strategy and main results. Exposure pathways, the methodology used to evaluate exposure and the distance considered to define exposure status, were all examined to help us identify the best tools to characterize exposure in the target population.

3. Results

Two studies had two related articles each and so we grouped the latter. Accordingly, 27 studies (29 articles) were included in this review. All these studies, including one meta-analysis (Deziel et al., 2017), aimed to measure pesticide exposure in residents living close to agricultural lands.

A large variety of pesticides, study designs, and methodologies were observed in the studies included. They are summarized in Tables 1–3 based on the methodology used: environmental monitoring,

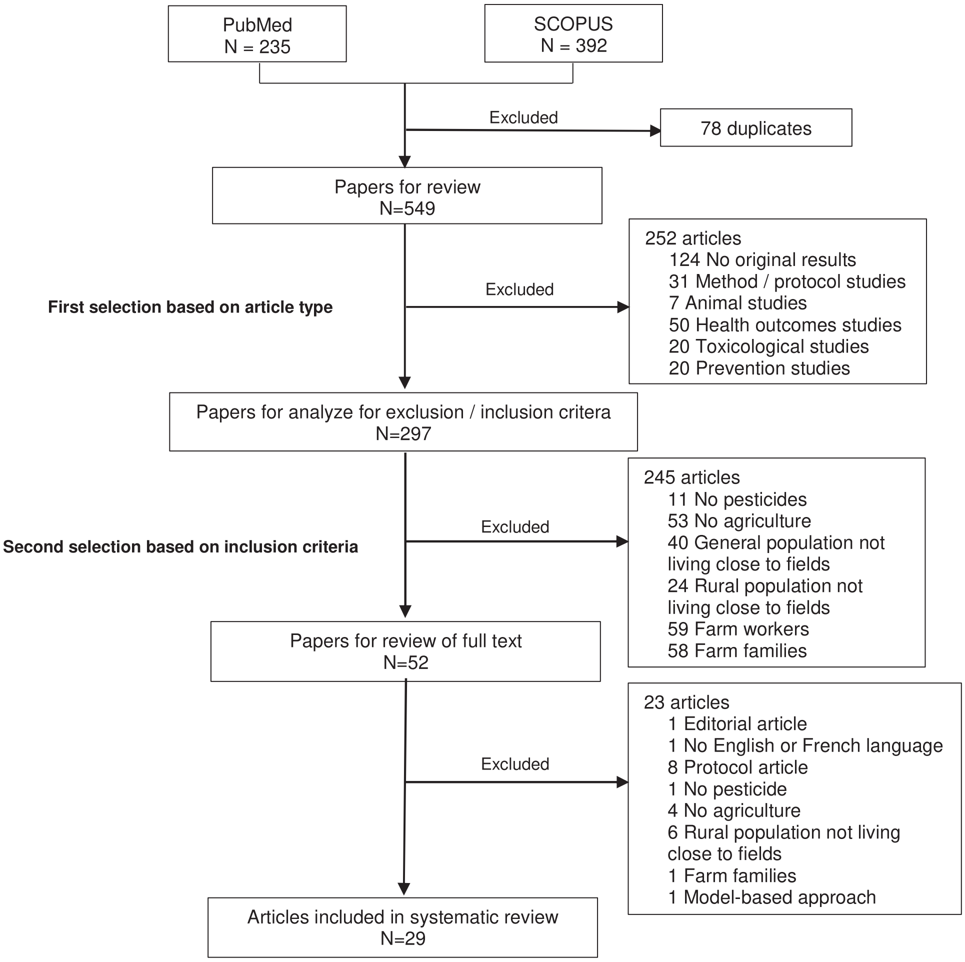

Fig. 1. Flow chart of identification and selection of original articles finally included in the review of pesticide exposures in residents living close to agricultural lands.

biomonitoring or both. Table 1 summarizes studies (n = 7) that analyzed environmental samples collected from the homes of study participants; Table 2 presents a summary of studies (n = 13) that analyzed biological samples collected from study participants, and Table 3 summarizes studies (n = 7) that analyzed both environmental and biological samples.

A large proportion of studies were conducted in North America (n = 10) – mainly in California and Washington state – and in South or Central America (n = 7), including Argentina and Costa Rica. The remainder assessed populations in various locations, including European countries (n = 5), Asia (n = 3), South Africa (n = 1) and Australia (n = 1).

Study populations were mainly children (12 studies) or pregnant women (4 studies), especially for biomonitoring studies which aimed to assess individual exposure to pesticides. The population of residents was either defined as people living in one specific area based on the *a priori* knowledge of agricultural activity and pesticide use (19 studies), or as people identified retrospectively as living close to agricultural lands (7 studies).

The majority of studies analyzed a combination of various pesticides. Organophosphorus (OP) compounds were the primary group of pesticides studied (n = 14), including chlorpyrifos, diazinon, phosmet, azinphos methyl, and malathion. Ten studies analyzed OP compounds only, whereas 4 other studies analyzed OP in combination with other insecticides, herbicides or fungicides such as pyrethroids, carbamates, captan, atrazine, glyphosate, iprodione. Five studies analyzed herbicides only. Two others focused on pyrethroid exposure, while 2 analyzed manganese-based pesticides only. Finally, 4 studies included a large combination of pesticides according to their application on fields or their toxicological effects.

3.1. Environmental monitoring studies

Table 1 presents a summary of the 7 studies which assessed pesticide exposure by analyzing results from environmental samples collected from study participants' homes and/or surroundings. Four studies were conducted in one or various specific areas identified *a priori* (Gibbs et al., 2017; Hogenkamp et al., 2004; Kawahara et al., 2005; Wofford et al., 2014), and 2 studies defined residents *a posteriori* based on the distance between households and crops (Gunier et al., 2011; Ward et al., 2006). Samples collected included dust from homes (Deziel et al., 2017; Gunier et al., 2011; Hogenkamp et al., 2004; Ward et al., 2006), as well as outdoor and indoor air samples (Gibbs et al., 2017; Kawahara et al., 2005; Wofford et al., 2014).

Two studies used a reference group within the population study (Gibbs et al., 2017; Ward et al., 2006) while 2 others also included a group of farmworkers (Gibbs et al., 2017; Hogenkamp et al., 2004). All these four studies showed that pesticide concentrations measured in households located close to agricultural lands were higher than those measured in control households. Households within 250 m of apple, peach, corn or wheat fields had higher outdoor concentrations and indoor surface deposition of chlorpyrifos than non-proximal households, although no differences were observed for indoor air measurements (Gibbs et al., 2017). Concentrations of herbicides in dust from homes with a higher density of corn and soybean fields located in a radius 750 m were four times higher than concentrations in homes with no crops nearby (Ward et al., 2006). A comparison between farmworker and non-farmworker resident households showed that in the former,

Table 1

Environmental measurements of pesticide exposures for residents living close to agricultural lands.

Study name, reference	Location, time period, population	Definition of resident groups living close to agricultural lands	Pesticides of interest	Exposure measurement	Results
Deziel et al. (2017)	Meta-analysis of studies conducted in North America	–	Chlorpyrifos, carbaryl, azinphos methyl, phosmet, ethyl parathion, diazinon, dimethyl organophosphates, atrazine, simazine, iprodione	House dust	7 studies reporting pesticide concentrations in house dust: meta-regression of the results showed a sharp, non-linear decrease in house dust pesticide concentrations with increasing distance from treated fields (between 3 and 1125 m. The magnitude of decrease varied according to pesticide type.
Gibbs et al. (2017)	USA Yakima Valley region of Washington 2011 13 households	Group 1: Proximal (< 250 m from crops) farmworker households Group 2: Proximal non-farmworker households Group 3: controls	Chlorpyrifos and azinphos methyl	Outdoor and indoor air Indoor surface deposition	Low or zero levels of Azinphos methyl were in outdoor air samples. The highest levels of chlorpyrifos in outdoor air were identified at non-farmworker and 1 farmworker households living within 100 m of crops. Proximal households had higher concentrations than non-proximal households (controls), and farmworker households had higher concentrations than proximal non-farmworker households. Indoor air concentrations were higher in farmworker households than non-farmworker households. No difference between proximal/non-proximal households was found. Proximal households had higher levels of chlorpyrifos on surfaces than non-proximal households. Outdoor air levels were higher than indoor air levels.
Gunier et al. (2011)	California 2001–2006 89 households	Estimation of agricultural pesticides used around the home (< 500 m, < 1250 m) during the 180, 365, 730 days before dust collection	Carbaryl, chlorpyrifos, chlorthal-dimethyl, diazinon, iprodione, phosmet, simazine	House dust	The highest concentrations were found for chlorpyrifos. Except from diazinon, pesticide concentrations were higher in residences closer to crops (500 m and 1250 m) than those not close to agricultural lands. Correlations were stronger when considering the density of crops within 1250 m during the previous 365 days than considering crops within a radius of 500 m only.
Hogenkamp et al. (2004)	Netherlands 27 households	Selection based of the location of the house near bulb fields (0–400 m)	chloridazon, chloropropham, metamitron (herbicides), flutolanil, procymidone, tolclofos-methyl, and vinclozolin (fungicides)	House dust	A significant difference was found in concentrations of chloropropham, which was 4 times higher in farmworkers' homes than in non-farmworker' homes. This difference was also statistically significant for other pesticides, except for vinclozolin and metamitron. Results showed a borderline statistically significant effect of the proximity to bulb crops on chloropropham in house dust.
Kawahara et al. (2005)	Japan 2003 55 households	Households located near paddy fields	Trichlorfon, dichlorvos, fenitrothion, chlorpyrifos, diazinon, malathion, fenthion	Indoor and outdoor air samples collected for 24 h following pesticide application in house and childcare facilities	Outdoor and indoor air concentrations of applied pesticides showed a significant inverse association with the distance from paddy fields: outdoor concentrations of fenitrothion and trichlorfon within 30 m were 5 times higher than those further away. A significant relationship existed between indoor and outdoor air concentrations. The indoor/outdoor ratio was higher when families opened house windows. Estimated exposure levels were below the level of the acceptable daily intake.

(*continued on next page*)

Table 1 (*continued*)

Study name, reference	Location, time period, population	Definition of resident groups living close to agricultural lands	Pesticides of interest	Exposure measurement	Results
Ward et al. (2006)	USA, Iowa 1998–2000 108 households	Group 1: households with no crops within 750 m Group 2: households located near corn and soybean fields (750 m)	Herbicides including 2,4-dichlorophenoxyacetic acid (2,4-D), dicamba, metolachlor, trifluralin, pendimethalin, atrazine, bentazon, acetochlor, fluazifo-p-buty, alachlor	House dust	2,4-D was the pesticide detected most often. Frequency of detection and concentration of herbicides in house dust increased with increasing corn and soybean planting acreage within 750 m of households. Concentrations of herbicides in dust in households situated close to a higher density of crops were 4 times higher than concentrations in households with no crops within 750 m. The distance to the closest crop field was associated with detection of herbicides in dust. Distance explained less variance than acreage
Wofford et al. (2014)	USA, California, 2006 Households located in Parlier city	Households located within 8 km of agricultural pesticide application fields	35 pesticides including diazinon, chlorpyrifos, dimethoate, endosulfan, malathion	Outdoor air monitoring	Residents were exposed to 19 compounds used as pesticides. The pesticides monitored accounted for 80% of the total kilograms of pesticides applied in Parlier city and the surrounding 8 km agricultural study area. The levels measured for diazinon exceeded thresholds for safe health

house dust concentrations of chloropropham were four times higher (Hogenkamp et al., 2004), and indoor air concentrations of chlorpyrifos were also higher (Gibbs et al., 2017).

The influence of the distance between households and agricultural lands was assessed in 6 studies (Deziel et al., 2017; Gibbs et al., 2017; Gunier et al., 2011; Hogenkamp et al., 2004; Kawahara et al., 2005; Ward et al., 2006). All found that the greater the distance, the lower the levels in pesticide concentrations in dust, outdoor and indoor air. Outdoor air concentrations of trichlorfon within 50 m of paddy fields were five times higher than those measured further away (Kawahara et al., 2005), and high levels of chlorpyrifos in outdoor air were identified at households located within 100 m of crops (Gibbs et al., 2017). Chlorpyrifos, chlorthal-dimethyl, iprodione, phosmet, and simazine dust concentrations were higher in residences located between 500 m and 1250 m from treated lands (Gunier et al., 2011). Similarly, the decrease in concentrations of chloropropham in house dust was borderline statistically significant with increased distance from agricultural fields (Hogenkamp et al., 2004). The meta-analysis performed in 2017 confirmed the sharp decrease in house dust pesticide concentrations with increased distance from treated fields (between 3 m and 1125 m) (Deziel et al., 2017)

The influence of the spraying season or spray events was not evaluated in any of the 7 environmental monitoring studies.

3.2. Biomonitoring studies

Table 2 presents a summary of the 13 studies that assessed pesticide exposures for residents living close to agricultural lands using biomonitoring. Four studies were conducted in one specific area identified *a priori* (Dalvie and London 2006; Doğanlar et al., 2018; Martínez-Perafán et al., 2018; Semchuk et al., 2003; Semchuk et al., 2007), 6 studies in various areas identified *a priori* (Babina et al., 2012; Cecchi et al., 2012; Galea et al., 2015; Mercadante et al., 2013; Quintana et al., 2017; Suarez-Lopez et al., 2018), and 3 studies defined residents *a posteriori* based on the distance between households and crops (Bradman et al., 2011; Chevrier et al., 2014; Wu et al., 2013).

Four studies used a reference group within the population study (Babina et al., 2012; Doğanlar et al., 2018; Martínez-Perafán et al., 2018; Quintana et al., 2017) and 2 included a group of farmworkers as a control (Dalvie and London 2006; Mercadante et al., 2013). The influence of residential proximity to agricultural fields or crops acreage around households was assessed in 5 studies (Bradman et al., 2011; Chevrier et al., 2014; Semchuk et al., 2003; Semchuk et al., 2007; Suarez-Lopez et al., 2018; Wu et al., 2013). The influence of the spraying season or spray events was assessed in 7 studies (Cecchi et al., 2012; Dalvie and London 2006; Doğanlar et al., 2018; Galea et al., 2015; Mercadante et al., 2013; Quintana et al., 2017; Suarez-Lopez et al., 2018). Only one study simultaneously evaluated the influence of both factors (Suarez-Lopez et al., 2018).

Six studies collected urine samples and 6 collected blood samples, including umbilical cord blood. In combination with urine or blood samples, one study also collected hair samples and one collected saliva. Biological collection methods were diverse depending on the study population and the final outcome. First or second morning void urine samples were preferred for adults and children aged 3 years (Babina et al., 2012; Chevrier et al., 2014; Galea et al., 2015; Mercadante et al., 2013), whereas spot urine samples were collected for children aged 2 or under (Bradman et al., 2011; Wu et al., 2013). Seven studies collected repeated biological samples to cover both the spraying and non-spraying seasons (Dalvie and London 2006; Doğanlar et al., 2018; Galea et al., 2015; Mercadante et al., 2013; Suarez-Lopez et al., 2018), and other temporal changes during childhood (Bradman et al., 2011). In these studies, 2–20 repeated samples were collected for each participant.

Pesticides and their metabolites were the primary biomarkers analyzed to evaluate exposure (8 studies). Six studies measured

Table 2
Biological measurements of pesticide exposures for residents living nearby agricultural lands.

Study name, reference	Location, Time period, population	Definition of resident groups living close to agricultural lands	Pesticides of interest	Exposure measurement	Results
Babina et al. (2012)	Australia 2003–2006 Children aged 2.5–6 years (n = 340)	Group 1: urban group Group 2: peri-urban group Group 3: rural group for children living close to pastures, orchards and vineyards	OP, Pyrethroids, chlorpyrifos, fenitrothion	Urine: single first-morning void (FMV) Metabolites of pesticides (DAP, 3,5,6-trichloro-2-pyridinol (TCPys), 3-methyl-4 nitrophenol)	69% of children from group 3 lived within 50 m of agricultural activity. The most commonly detected metabolites were TCPy, 3 PBA, DAP and 3-methyl-4 nitrophenol, with detection rates generally higher in the rural group. Higher concentrations of 3-methyl-4 nitrophenol and DAP were observed in the rural group than in the urban group. No significant difference was observed between concentrations of pyrethroids and TCPy.
CHAMACOS (Bradman et al., 2011)	California, USA 1999–2003 Children aged 6, 12, 24 months (n = 416, 404, 381)	Study staff recorded the distance between households and agricultural lands	OP	Urine: random spot samples Metabolites of DAP: dimethyl alkylphosphates (DMAP), diethyl alkylphosphates (DEAP)	Most children had at least one DAP detected at 6, 12 or 24 months. Urinary concentrations of DAP at 12 months were higher among children living or staying in a childcare facility within 60 m of agricultural land. Samples collected during spring/summer had higher concentrations than those collected during fall/winter but results were inconsistent across ages and between DMAP and DEAP metabolites.
Cecchi et al. (2012)	Argentina, Rio Negro 2007–2008 Pregnant women (n = 97)	Recruitment in towns near farms	OPs: azinphosmethyl, phosmet, chlorpyrifos, dimethoate, carbaryl, dithiocarbamates, ziram, captan, mancozeb	Blood: collection before and during the spraying season, during 1st and 2nd trimesters of pregnancy Plasma and erythrocyte cholinesterase, aspartate amine transferase (AST), alanine aminotransferase (ALT)	Significant decrease in cholinesterase during the spraying season in comparison to the pre-spraying season, when considering the 1st and 2nd trimester of pregnancy. Significant increase in the AST/ALD ratio between pre-spraying and spraying seasons when considering the 2nd trimester of pregnancy. It is difficult to assign differences observed as seasonal exposure changes or as modifications related to pregnancy.
Quintana et al. (2017)	Argentina, Rio Negro 2009–2015 Pregnant women (n = 151)	Group 1: living in towns near farms Group 2: control with no history of pesticide exposure	OP	Umbilical cord blood Acetylcholinesterase, butyrylcholinesterase, catalase (CAT), SOD, DNA damages (comet assay), methemoglobin.	No difference in umbilical cord blood in hemogram parameters, levels of methemoglobin, cholinesterase activity or CAT. The SOD activity decreased significantly in the exposed group between the spraying season and the non-spraying season. DNA damage was greater in the exposed group during the spraying season than in the control group.
Pelagie (Chevrier et al., 2014)	France, Brittany 2002–2006 Pregnant women (n = 570)	Proximity of corn crops within a 375 m radius of residences using GIS model-based satellite images	Herbicides	Urine: FMV Metabolites of pesticides	Herbicides were quantified in 5.3% to 39.7% of urine samples. Results showed an association between the proximity of residences to corn crops (< 375 m) and urinary concentrations of metolachlor. Multivariate analysis showed an increased risk of higher urinary concentrations of dealkylated triazine metabolite with greater residential proximity to crops.

(*continued on next page*)

Table 2 (*continued*)

Study name, reference	Location, Time period, population	Definition of resident groups living close to agricultural lands	Pesticides of interest	Exposure measurement	Results
Dalvie and London (2006)	South Africa, Cape Province 1996–1997 Adults (n = 320)	Group 1: controls Group 2: farmworkers Group 3: residents living in an area with intensive agricultural production	OP	Blood: 3 samples collected over 11 months Cholinesterase	Unexpected significant increase of cholinesterase during the spraying season among participants exposed both occupationally and environmentally to aerial pesticide applications. The effect of temperature may explain this result.
Doğanlar et al. (2018)	Turkey, Ipsala 2015–2016 Adults (n = 63)	Group 1: residents living in an intense monoculture rice production zone Group 2: controls	144 pesticide active ingredients	Blood: 3 samples collected covering 2 spraying seasons and 1 non-spraying season Multi-residues of pesticides and oxidative stress markers (SOD, CAT, DNA damage, heat shock proteins, etc.)	A higher concentration of pesticide residues among agricultural area residents than among controls. Concentrations were, respectively, 4.3 and 10 times higher in the 2 spraying seasons than in the non-spraying season. Residents also had excess generation of oxidative stress by reactive oxygen species (ROS), and a higher level of DNA damage.
Galea et al. (2015)	United kingdom 2011–2012 Adults and children (n = 296)	Residents living within 100 m of agricultural lands	captan, cypermethrin, chlormequat, chlorpyrifos	Urine: FMV collected during and after the spraying season + collection of an extra sample 1 or 2 days after a spraying event Metabolites of pesticides	Chlormequat was the pesticide most frequently detected in urine. Chlorpyrifos was detected more frequently after a spray event (93%). Captan and cypermethrin were rarely detected. Results showed an increase in chlomequat levels in residents following a spray event within 100 m of their home when compared with the non-spraying season. However, no difference was observed between levels measured just after a spray event and those measured during the spraying season. No significant increase was observed for chlorpyrifos.
Martínez-Perafán et al. (2018)	Argentina Adolescents (n = 62)	Group 1: residents living < 100 m from horticultural crops Group 2: residents living > 100 m from crops	glyphosate, chlorpyrifos, 2,4-D, paraquat	Blood Biomarkers of biological effects including butyrylcholinesterase (BuChE), micronuclei (MN), nuclear buds (NBUS), nucleoplasmic bridges binucleated, condensed chromatin (CC), karyorrhexis, pykonis, karyolysis (KYL)	Mean values of all parameters in both groups corresponded to values for healthy adolescents. Adolescents living close to horticultural fields had lower BuChE activity. Biomarkers of genetic damages (MN, NBUS) were negative in both groups. A higher frequency of cells with CC and KYL were observed in the control group than in adolescents living close to horticultural crops.
Mercadante et al. (2013)	Italy 2010 Adults (n = 43)	Group 1: farmworkers Group 2: non-farmworker residents living in a small village in the province of Cremona Group 3: controls	desethylterbuthylazine (DET) terbuthylatrazine (TBA)	Urine and hair: collection before and during spraying season Metabolites of pesticides	TBA and DET were never detected in urine samples of residents or controls. Only TBA was detected in residents' hair, with the detection rate higher during spraying season than before the spraying season. TBA levels in hair were higher in residents than in controls. Before the spraying season, no difference between TBA levels in farmworkers and residents was observed, but during the spraying season, levels among the former were higher.
PECOS study (Semchuk et al. 2003; Semchuk et al. 2007)	Canada, Saskatchewan 1996 Adults (n = 332)	Residents living in a predominantly grain-farming area	bromoxynil, 2,4-D, dicamba, fenoxaprop, 2-methyl-4-chlorophenoxyacetic acid (MCPA), ethalfluralin, triallate, trifluralin	Blood Metabolites of pesticide and anti-nuclear antibody (ANA)	Bromoxynyl was the most frequently detected pesticide (20%). The detection rate of bromoxynyl increased with the area of land farmed. Other factors were related to occupational exposure.

(*continued on next page*)

Table 2 (*continued*)

Study name, reference	Location, Time period, population	Definition of resident groups living close to agricultural lands	Pesticides of interest	Exposure measurement	Results
					A high prevalence of ANA was found in the study population but no factors were statistically significant predictors of ANA detection. However, for men, ANA presence was inversely associated with the detection of bromoxynil in blood plasma.
ESPINA study, (Suarez-Lopez et al. 2018)	Ecuador, Pedro Moncayo 2008 Children (n = 308)	Children living in towns with strong floriculture industry	Methiocarb, carbofuran, aldicarb, diazinon, dimethoate, acephate, chlorpyrifos	Blood: collection of samples on 20 different days including days after Mother's Day harvest (peak exposure) Acetylcholinesterase (AChE) and hemoglobin	No significant AChE activity was observed before or after the Mother's Day harvest. However, a significant positive association was observed between AChE activity and distance between households and the nearest flower plantation after the Mother's Day harvest. For children living within 500 m of flower plantations with the largest planted areas, a positive association was observed between AChE activity and the period post-Mother's Day harvest.
Wu et al. (2013)	China, Jiangsu province 2010–2011 Children (1 year old) (n = 481)	481 Infants aged 12 months	Pyrethroids: 3-phenoxybenzoic (3-PBA), cis-3-(2,2dichlorovinyl)-2,2-dimethylcyclopropane-carboxylic acid (cis-DCCA), trans-3-(2,2dichlorovinyl)-2,2-dimethylcyclopropane-carboxylic acid (trans-DCCA)	Urine: spot samples Metabolites of pesticides	3-PBA, cis-DCCA and trans-DCCA were the most frequently detected metabolites. Urinary concentrations of pyrethroids metabolites were higher among infants living in households immediately beside crops

Table 3
Combination of environmental and biological measurements of pesticide exposures for residents living nearby agricultural lands.

Study name, reference	Location, time period, population	Definition of resident groups living close to agricultural lands	Pesticides of interest	Exposure measurement	Results
CHAMACOS (Gunier et al. 2013; Gunier et al. 2014)	USA, California 1999–2000 378 households Children (n = 207)	Estimation of Mn fungicide use near the residence (within 1, 3, 5 km radii)	Manganese	Teeth House dust	Mn house dust concentrations were associated with agricultural Mn Pesticide use within 3 km during the month prior to dust sample collection. Agricultural applications of widely used Mn-containing fungicides during pregnancy showed an association with higher Mn levels in teeth.
Coronado et al. (2011)	USA, Washington state 2005–2006 Adults and children (n = 200)	Group 1: farmworker families Group 2: Non-farmworker families	OP, azinphos methyl and phosmet	Collection at 3 points during the agricultural season (thinning, harvest, non-spraying season) Biomonitoring: 3 independent void samples: blood, urine, and saliva Environment: dust at home and vehicles	Urinary levels of DMTP and house dust levels of azinphos-methyl and phosmet were higher in farmworkers than in non-farmworkers. Participants (farmworkers and non-farmworkers) who lived closer to farmland (< 61 m) had higher urinary levels of DMTP but this association was not observed for house dust concentrations.
Infants' Environmental Health Study Mora et al. (2014)	Costa Rica, Matina County 2010–2011 Pregnant women (n = 449)	Residents living close to banana plantations (< 5 km)	Manganese (Mn)	Biomonitoring: repeated blood and hair samples Environment: drinking water	Hair Mn concentrations were higher among women who worked in agriculture, those who lived with one or more agricultural workers, those who lived < 50 m from banana plantations, those who drank water from a well and those who reported aerial spraying near their home before sample collection.

(*continued on next page*)

Table 3 (*continued*)

Study name, reference	Location, time period, population	Definition of resident groups living close to agricultural lands	Pesticides of interest	Exposure measurement	Results
					All these factors were associated with lower Mn concentrations in blood.
Muñoz-Quezada et al. (2012)	Chile, Talca 2010–2011 Children (6–12 years) (n = 190)	Group 1: rural towns near farms Group 2: urban city	OP, chlorpyrifos, phosmet	Collection during 2 seasons: summer and fall. Biomonitoring: spot urine samples Environment: soil, drinking water, fruit, and vegetable samples	Chlorpyrifos and diazinon were more frequently detected in local fruit and vegetable samples than in markets. No OP pesticides were detected in soil or drinking water. DEAP was the metabolite most frequently detected in urine samples. Children who ate local fruit or vegetables had 2.8 times higher levels of DEAP metabolites in urine. Higher DEAP urinary levels were marginally associated with proximity to farms (< 500 m).
Rohitrattana et al. (2014)	Thailand 2011–2012 Children (6–8 years) (n = 53)	Group 1: children living nearby rice crops Group 2: controls	Pyrethroids	Biomonitoring: urine FMV collected during the wet and dry seasons Environment: hand wipes	3-PBA was the pyrethroid metabolite detected most frequently in urine samples. Pyrethroids were not detected for the most part in hand wipes. 3-PBA concentrations in residents and controls were not significantly different. Median 3-PBA concentrations in both groups were higher during the dry season than the wet season. Proximity to a rice farm was very weakly associated with increased pyrethroid exposure.
van Wendel de Joode et al. (2012)	Costa Rica 2007 Children (n = 140	Group 1: children living close to banana plantations (< 50 m) Group 2: children living 2 km from plantations Group 3: children living in areas with low use of pesticides	Chlorpyrifos	Biomonitoring: urine samples (FMV) and repeated samples Environmental samples in groups 1 and 2 only: hand and foot wipes, mattress dust, house dust, soil, and water Outdoor air (active and passive)	Children in groups 1 and 2 had significantly higher urinary TCPy concentrations than children in group 3 Chlorpyrifos was detected in almost all foot and hand wash samples collected in groups 1 and 2. Chlorpyrifos levels in children's hand and foot wipe samples were higher in group 1 than in group 2 but the difference was not statistically significant. Few house dust and soil samples had concentrations above the limit of detection.
Weppner et al. (2006)	USA, Washington state Children (2–12 years) (n = 8)	Families living 15–200 m from the nearest treated fields	Methamidophos	Samples collected 2 months prior to spraying event, 1 day prior, the day of the event and the day following the event. Biomonitoring: Urine (24 h urine void) and hand wipes. Environment: Outdoor air measurements and deposition plates.	In comparison with the day before the spraying event, the median outdoor air concentration was 10 times higher on the day of the spraying event and 4 times higher than the day after the spraying event. Metamidophos residues on playground equipment after spraying were higher than before. The median pesticide levels in hand wipe analyses on the spraying day were higher than pre-spray levels. Median urine levels between the spraying day and the day following spraying were higher than levels in urine collected before spraying. Urine levels were correlated with hand wipe measurements.

cholinesterase activity, transaminase activity, DNA damage, oxidative stress markers (superoxide dismutase, catalase, glutathione-S-transferase, and glutathione peroxidase), repair parameters (heat shock proteins) and hemoglobin parameters to evaluate biological effects potentially related to pesticide exposure. These biomarkers of biological effects were all measured in blood or saliva. Only one study analyzed biomarkers of exposures and biological effects in combination (Doğanlar et al., 2018).

Apart from one study (Dalvie and London 2006), all those that included a non-agricultural reference group, showed that agricultural residents presented at least one indicator of being more exposed to pesticides in comparison with controls, such as higher concentrations of dialkylphosphates (DAP) or 3-methyl-4-nitrophenol (metabolite of fenitrothion) in urine (Babina et al., 2012), higher concentrations of terbuthylazine (TBA) in hair (Mercadante et al., 2013), higher concentrations for multi-residue pesticides in blood (Doğanlar et al., 2018), higher levels of oxidative stress markers and DNA damage (Doğanlar et al., 2018; Quintana et al., 2017) and decreased activity of cholinesterase (Martínez-Perafán et al., 2018).

In all studies related to the influence of agricultural activities near households, higher concentrations of pesticide metabolites were associated with residential proximity to agricultural lands or with crop acreage around the residence. The 3 studies that defined residents of agricultural lands *a posteriori*, showed that children aged 12 months old had the highest urinary concentrations of pyrethroids and DAP metabolites when they were living in homes adjacent to (Wu et al., 2013) or 60 m from an agricultural field (Bradman et al., 2011), and that pregnant women had the highest urinary concentrations of metolachlor when living within 375 m of corn crops (Chevrier et al., 2014). A significant positive association was also observed between the acetylcholinesterase activity and the distance to the nearest flower plantation (Suarez-Lopez et al., 2018).

Comparisons between the spraying and non-spraying seasons showed significant higher levels of indicators of pesticide exposure during the former season in almost all studies that included biological collection at different periods (Cecchi et al., 2012; Doğanlar et al., 2018; Galea et al., 2015; Mercadante et al., 2013; Quintana et al., 2017; Suarez-Lopez et al., 2018). Some studies showed significant changes in cholinesterase and superoxide dismutase (SOD) activities in the spraying season in comparison with the non-spraying season (Cecchi et al., 2012; Quintana et al., 2017; Suarez-Lopez et al., 2018). One study showed that the detection rate of terbuthylatrazine in hair was higher during spraying season than before it (Mercadante et al., 2013). Another found a significant increase in urinary chlomequat levels just after a spray event within 100 m of residents' homes (Galea et al., 2015). Yet another study showed that pesticide residue concentrations in blood were up to 10 times higher in the spraying season than in the non-spraying season (Doğanlar et al., 2018).

The study which included a farmworker group, as a control, showed that before the spraying season there was no difference between pesticide levels in hair among workers and residents, but during the spraying season levels among workers were higher (Mercadante et al., 2013).

3.3. Environmental and biomonitoring studies

Table 3 presents a summary of the 7 studies that assessed pesticide exposure in residents living close to agricultural lands by analyzing both environmental and biological samples. Five studies were conducted in one or various areas identified *a priori* (Coronado et al., 2011; Mora et al., 2014; Rohitrattana et al., 2014; van Wendel de Joode et al., 2012; Weppner et al., 2006), and 2 others defined residents *a posteriori* based on the distance between households and crops (Gunier et al., 2013; Gunier et al., 2014; Muñoz-Quezada et al., 2012).

Three studies used a reference group within the population study (Muñoz-Quezada et al., 2012; Rohitrattana et al., 2014; van Wendel de Joode et al., 2012) whereas one included a group of farmworkers (Coronado et al., 2011). All these studies evaluated the influence of residential proximity to agricultural lands.

The number of biological and environmental samples taken ranged from a minimum of one of each (Gunier et al., 2013; Gunier et al., 2014; Rohitrattana et al., 2014) up to a combined total of 8 (van Wendel de Joode et al., 2012). Apart from one study (Gunier et al., 2013; Gunier et al., 2014), all collected repeated biological samples to evaluate within-subject variability or to study the influence of the spraying season or spraying events on pesticide exposure.

Results from different environmental and biological samples generally showed poor correlations: one study showed that participants (farmworkers and non-farmworkers) who lived very close to agricultural lands (< 60 m) had significantly higher urinary levels of dimethyl-thiophosphate (DMTP) than other participants, but this association was not observed in house dust concentrations (Coronado et al., 2011). Similarly, chlorpyrifos urinary levels were significantly higher in children living close to banana plantations than in children living in places with low use of pesticides. However, the association was not significant for hand and foot wipe measurements nor for house dust (van Wendel de Joode et al., 2012). Another study showed that manganese (Mn) concentrations in hair were higher among women who lived within 50 m of banana plantations, women who drank water from a well and women who reported aerial spraying near their home before sample collection. However, these factors were associated with lower Mn concentrations in blood (Mora et al., 2014). Hair measurements had better within-subject correlation than blood concentrations in that study, which could be explained by the longer half-life of pesticides in hair (Barr and Needham 2002). Other studies showed only marginal associations between biomonitoring levels and proximity to agricultural lands when considering diethyl alkylphosphate (DEAP) or pyrethroid urinary levels (Muñoz-Quezada et al., 2012; Rohitrattana et al., 2014), or the influence of the spraying and non-spraying seasons (Rohitrattana et al., 2014).

Only one study that collected outdoor air and used hand wipes as well as urine samples at 4 different periods (2 months before the spraying season, one day before pesticide application, the day of application and the day after application) found the same increase just before the spray event for each environmental and biological sample (Weppner et al., 2006). In that study, urine samples collected were 24 h urine voids which could partly explain the good correlation with environmental samples.

3.4. Results synthesis

Most studies selected in the present review included exposure measurements in a non-agricultural reference group or measurements before and after spraying events in order to estimate pesticide exposure related to spray-drift pathways in residents living close to treated agricultural lands (Babina et al., 2012; Cecchi et al., 2012; Doğanlar et al., 2018; Galea et al., 2015; Gibbs et al., 2017; Martínez-Perafán et al., 2018; Mercadante et al., 2013; Muñoz-Quezada et al., 2012; Quintana et al., 2017; Rohitrattana et al., 2014; Suarez-Lopez et al., 2018; van Wendel de Joode et al., 2012; Ward et al., 2006). Many of the studies showed that these residents are exposed to higher pesticide levels than reference groups. They are also more exposed to pesticides during the spraying season. However, study designs and methodologies for measuring pesticide exposures differed between studies and results were sometimes inconsistent for pesticide type and for environmental and biological samples.

Buffer zones considered between households and the nearest treated fields differed considerably between studies. For instance, authors measuring diazinon concentrations in air used buffer zones ranging from 30 m (Kawahara et al., 2005) to 8 km (Wofford et al., 2014). Although the meta-analysis performed in 2017 confirmed the overall decrease of pesticide concentrations in house dust with increased distance from treated fields – the distances considered ranging from 3 m to 1125 m, the magnitude of the decrease was not linear and varied according to pesticide type (Deziel et al., 2017). Moreover, the model used in that meta-analysis to predict house dust pesticide concentrations at varying distances up to 1125 m from agricultural lands did not show a distance threshold. Overall, results from studies suggest that using proximity only may not be a suitable indicator of pesticide exposure in residents living close to treated agricultural lands. Studies that included additional information, such as the amount of pesticides applied or acreage treated, were more likely to find an association (Semchuk et al., 2003). One study demonstrated that using proximity only explained less variance in the association with pesticide exposure than using acreage and proximity in combination (Ward et al., 2006). This could be partly explained by the fact that acreage is more likely related to the amount of pesticides applied in fields than proximity.

In studies included in our review, measurements of pesticide exposures included levels of pesticide metabolites in biological samples (urine, blood or hair), levels of pesticide residues in household samples (dust or indoor air) and levels of markers of biological effects potentially related to pesticide exposures. Results from the studies confirm that residents living closer to pesticide-treated agricultural lands tend to have higher levels of pesticide residues/metabolites in their households and/or biological samples, higher levels of oxidative stress markers, greater DNA damage and decreased activity of cholinesterase than residents living farther away. Results from 4 studies showed that house dust could be an appropriate medium to characterize residential accumulation of pesticides as a result of nearby agricultural use (Deziel et al., 2017; Gunier et al., 2011; Hogenkamp et al., 2004; Ward et al., 2006). Results from 2 studies also showed the capability of hair to accurately reflect long-term exposure to pesticides with lower within-subject variability and a better detection rate than in urine and blood samples (Mercadante et al., 2013; Mora et al., 2014). Another interesting sampling method, used in various studies, included the repeated collection of biological samples to estimate the temporal variation in exposure (Dalvie and London 2006; Doğanlar et al., 2018; Galea et al., 2015; Mercadante et al., 2013; Suarez-Lopez et al., 2018). However, for a given pesticide, results were often different between studies and/or between environmental or biological media. For instance, chlorpyrifos concentrations in outdoor air and house dust were higher close to treated fields (Gibbs et al., 2017; Gunier et al., 2011) whereas concentrations in urine samples or in hand- and foot-wipe samples did not show a significant increase (Galea et al., 2015; van Wendel de Joode et al., 2012). These differences in results could partly be explained by physico-chemical properties of pesticides which may influence concentrations in different media, for example manganese measurements in house dust or hair, which are less susceptible to within-individual variability than measurements in urine or blood (Gunier et al., 2013; Gunier et al., 2014; Mora et al., 2014). However, concentrations of a given pesticide in a given medium can also provide different results, for example the pyrethroid concentrations in urine measured in studies conducted in Australia and China (Babina et al., 2012; Wu et al., 2013). Study sites could partly explain these differences as meteorological conditions, topography, type of crops, pesticide application methods, and even lifestyle and housing characteristics differ between these two countries.

Some of the studies included analyzed biological markers of oxidative stress, DNA damage, repair parameters and cholinesterase activity (Cecchi et al., 2012; Dalvie and London 2006; Doğanlar et al., 2018; Martínez-Perafán et al., 2018; Quintana et al., 2017). However, the results of these studies were generally difficult to interpret.

4. Discussion

There are many challenges to accurately measuring non-occupational pesticide exposure in residents living close to agricultural land. Our review of a series of recent studies characterizing exposure in this population underlines the strengths and weaknesses of the different strategies and sampling methods used, and highlights requirements for future studies in order to accurately measure pesticide spray-drift exposure in this population.

4.1. *Study design for future studies*

4.1.1. *Comparison with a reference group or a reference period*

As the general population is exposed to numerous agricultural and non-agricultural pesticides via multiple pathways including diet, domestic use, and occupation, studies estimating exposure related to agricultural spray-drift in residents living close to agricultural lands should use a non-agricultural reference group for greater accuracy. Indeed, most studies in this review included either such a group or a non-spraying reference period (before or after the spraying season). If such studies show that residents living nearby crops are exposed to higher levels of pesticides than the non-agricultural reference group, this is most probably related to agricultural spray-drift exposure rather than other pathways like diet or domestic use. Similarly, if such studies show that the former population are more exposed during the spraying season than before or after the spraying season, this is also most probably related to agricultural spray-drift exposure.

4.1.2. *A multicentric setting*

Pesticide spray-drift exposure and, as a consequence, the characterization of exposed resident groups and their control groups, are influenced by numerous key parameters, such as the physico-chemical properties of pesticides, crop type, pesticide application method and environmental conditions – including meteorology, topography, and soil nature – which influence dissipation pathways (Bedos et al., 2002; Damalas and Eleftherohorinos 2011). Therefore, as demonstrated in some studies included in the present review, using distance as the unique parameter to characterize the target population and control groups is not an optimal choice. Additional parameters, such as those listed above, but also the amount of pesticides applied and acreage of treated fields, should improve accuracy. However, it could be difficult to simultaneously measure all these parameters in future studies because for some, data collection is difficult in large-scale studies, and the direction and the magnitude of correlations are quite unpredictable. This suggests the need to at least investigate associations between exposure to pesticides used for a specific crop, as correlations between amounts of pesticides and treated acreage depend on specific crop groups (Bukalasa et al., 2017). In addition, a multi-centric approach, where the number of study sites covering different environmental conditions (meteorology, topography, soil nature) is increased, would help reduce the impact of ecological bias and confounding factors, because it is not very likely that these factors – for example, the nature of the soil or the topography – impact exposure levels across the entire range of sites in the study (Kunzli and Tager 1997).

4.2. *Measurement of pesticide exposure*

4.2.1. *Analysis of the best pesticide-media pairings*

In a context of multi-pathway exposure, the identification of relevant pesticides used specifically in treated fields is essential to accurately evaluate exposure of residents specifically related to agricultural spray-drift. Accordingly, the physicochemical properties of pesticides and application methods should be considered as these can influence pesticide residue dispersion from treated areas and their concentrations in environmental and biological media. These properties should help identify the most appropriate pesticide-media pairings for exposure measurements. However, other external factors like the risk of sample contamination in the field or in laboratories and the analytical method used, may also influence results. Measuring this influence is difficult (LaKind et al., 2017). Our analysis shows that it could be useful to pair biomonitoring with environmental sampling in future studies as they are complementary approaches. Biological and environmental media are influenced differently by external factors and they reflect different exposure windows, with dust and hair samples representing a cumulative time window representing weeks or months, while air and urine often represent exposure in the hours to days prior to sample collection (Barr et al., 2006; Mercadante et al., 2018). Repeated biological and environmental sampling over time should also help limit the influence of some external factors and reduce the impact of peak exposure on background concentrations (depending of the study aims). Such a combined sampling design is particularly appropriate for the measurement of pesticides in air or urine which are rapidly eliminated from the human body or from the environment and which experience large intra-day variability (Attfield et al., 2014; Morgan et al., 2016). Future research with repeated combined biological and environmental measurements may increase investigators' capability to show associations and trends in pesticide exposure of residents living close to agricultural land.

4.2.2. Markers of biological effects

Markers of biological effects are good early warning indicators of disease caused by chronic low-level exposure to a mix of pesticides and have been used as biomarkers for pesticide genotoxicity in numerous studies (Ali et al., 2008; Bhalli et al., 2006; Bolognesi and Holland 2016; Lebailly et al., 2015; Ramirez-Santana et al., 2018; Singh et al., 2011). However, it can be difficult to interpret these measurements appropriately. For instance, certain cholinesterase-inhibiting compounds can inhibit red cell acetylcholinesterase more than butyrylcholinesterase in plasma (Karasova et al., 2017). Moreover, the interpretation of results needs to clearly determine an individual's baseline levels, using repeated measurements (Rohlman et al., 2019), or his/her "paraoxonase status" referring to PON1 function as a modulation factor of cholinesterase inhibition (Dardiotis et al., 2019). Furthermore, the method used for blood sample collection and analysis must be checked because cholinesterase activity is very dependent on the temperature at the moment of collection, and the variability in measurement assays could provide different results (Karasova et al., 2017). In the absence of a standardized approach and normal baseline range for the general population, it is extremely difficult to interpret the measurements of markers of biological effects in order to predict exposure and related medical issues.

4.3. Controlling the factors influencing pesticide exposure

As mentioned above, it is essential to collect data about external factors that can influence pesticide exposure measurements: meteorology, topography, crop type, application method and quality of measurements.

However, it is also essential to collect data about lifestyle (e.g. time spent outdoors, smoking and alcohol habits), food intake (including organic food and self-production), and professional and housing characteristics (e.g. presence of a garden, ventilation system, use of pesticides at home), as these can influence exposure to agricultural and domestic pesticides. This data collection in combination with pesticide exposure measurements is necessary to evaluate the contribution of agricultural spray-drift exposure to total pesticide exposure. Accordingly, future studies should include recall diaries, questionnaires and interviews to collect data about potential other sources of pesticide exposure.

5. Conclusion

To the best of our knowledge, this is the first review focusing on non-occupational pesticide exposure in non-farmworker residents living close to agricultural land. While accurate measurements of pesticide exposure are difficult for several reasons, such as the existence of multiple exposure pathways, studies included in this review provide evidence that this population is exposed to higher levels of pesticides than residents not living in proximity to agricultural lands. Exposure levels were influenced not only by the distance between households and the nearest treated field but also by the crop acreage around the residence and the time of the year (i.e., during or before, and after the spraying season).

This review highlights that some study design characteristics are more likely than others to accurately measure pesticide spray-drift exposure in residents: inclusion of a non-agricultural control group, collection of both biological and environmental samples with repeated sampling, measurements at different times of the year, selection of numerous study sites related to one specific crop group, and measurements of pesticides specific to agricultural use. However, such studies are still scarce.

Reliable measurements of pesticide exposure are needed to develop and validate exposure models and indicators for large-scale related epidemiological studies. Additional studies are therefore needed to comprehensively measure non-occupational pesticide exposure in residents living close to treated agricultural lands in order to evaluate health risks, and to develop appropriate prevention strategies.

Acknowledgments

The author(s) received no financial support for the research, authorship, and/or publication of this article. The authors certify that they have non affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

References

Ali, T., Bhalli, J.A., Rana, S.M., Khan, Q.M., 2008. Cytogenetic damage in female pakistani agricultural workers exposed to pesticides. Environ. Mol. Mutagen. 49, 374–380.

Attfield, K.R., Hughes, M.D., Spengler, J.D., Lu, C., 2014. Within- and between-child variation in repeated urinary pesticide metabolite measurements over a 1-year period. Environ. Health Perspect. 122, 201–206.

Babina, K., Dollard, M., Pilotto, L., Edwards, J.W., 2012. Environmental exposure to organophosphorus and pyrethroid pesticides in south australian preschool children: a cross sectional study. Environ. Int. 48, 109–120.

Barr, D.B., Needham, L.L., 2002. Analytical methods for biological monitoring of exposure to pesticides: a review. J. Chromatogr., B: Anal. Technol. Biomed. Life Sci. 778, 5–29.

Barr, D.B., Thomas, K., Curwin, B., Landsittel, D., Raymer, J., Lu, C., et al., 2006. Biomonitoring of exposure in farmworker studies. Environ. Health Perspect. 114, 936–942.

Bedos, C., Cellier, P., Calvet, R., Barriuso, E., Gabrielle, B. 2002. Mass transfer of pesticides into the atmosphere by volatilization from soils and plants: overview.

Bhalli, J.A., Khan, Q.M., Nasim, A., 2006. DNA damage in pakistani pesticide-manufacturing workers assayed using the comet assay. Environ. Mol. Mutagen. 47, 587–593.

Bolognesi, C., Holland, N., 2016. The use of the lymphocyte cytokinesis-block micronucleus assay for monitoring pesticide-exposed populations. Mutat. Res. 770, 183–203.

Bradman, A., Castorina, R., Barr, D.B., Chevrier, J., Harnly, M.E., Eisen, E.A., et al., 2011. Determinants of organophosphorus pesticide urinary metabolite levels in young children living in an agricultural community. Int. J. Environ. Res. Public Health 8, 1061–1083.

Brody, J.G., Aschengrau, A., McKelvey, W., Rudel, R.A., Swartz, C.H., Kennedy, T., 2004. Breast cancer risk and historical exposure to pesticides from wide-area apllications assessed with gis. Environ. Health Perspect. 112, 889–897.

Brouwer, M., Huss, A., van der Mark, M., Nijssen, P.C.G., Mulleners, W.M., Sas, A.M.G., et al., 2017. Environmental exposure to pesticides and the risk of parkinson's disease in the netherlands. Environ. Int. 107, 100–110.

Bukalasa, J.S., Brunekreef, B., Brouwer, M., Vermeulen, R., de Jongste, J.C., van Rossem, L., et al., 2017. Proximity to agricultural fields as proxy for environmental exposure to pesticides among children: the piama birth cohort. Sci. Total Environ. 595, 515–520.

Bukalasa, J.S., Brunekreef, B., Brouwer, M., Koppelman, G.H., Wijga, A.H., Huss, A., et al., 2018. Associations of residential exposure to agricultural pesticides with asthma prevalence in adolescence: the piama birth cohort. Environ. Int. 121, 435–442.

Buscail, C., Chevrier, C., Serrano, T., Pelé, F., Monfort, C., Cordier, S., et al., 2015.

Prenatal pesticide exposure and otitis media during early childhood in the pelagie mother-child cohort. Occup. Environ. Med. 72, 837–844.

Carles, C., Bouvier, G., Esquirol, Y., Piel, C., Migault, L., Pouchieu, C., et al., 2017. Residential proximity to agricultural land and risk of brain tumor in the general population. Environ. Res. 159, 321–330.

Carmichael, S.L., Yang, W., Roberts, E.M., Kegley, S.E., Wolff, C., Guo, L., et al., 2013. Hypospadias and residential proximity to pesticide applications. Pediatrics 132, e1216–e1226.

Carmichael, S.L., Yang, W., Roberts, E., Kegley, S.E., Padula, A.M., English, P.B., et al., 2014. Residential agricultural pesticide exposures and risk of selected congenital heart defects among offspring in the san joaquin valley of california. Environ. Res. 135, 133–138.

Carmichael, S.L., Yang, W., Ma, C., Roberts, E., Kegley, S., English, P., et al., 2016. Joint effects of genetic variants and residential proximity to pesticide applications on hypospadias risk. Birth Defects Res. A 106, 653–658.

Carozza, S.E., Li, B., Wang, Q., Horel, S., Cooper, S., 2009. Agricultural pesticides and risk of childhood cancers. Int. J. Hyg. Environ. Health 212, 186–195.

Cecchi, A., Rovedatti, M.G., Sabino, G., Magnarelli, G.G., 2012. Environmental exposure to organophosphate pesticides: assessment of endocrine disruption and hepatotoxicity in pregnant women. Ecotoxicol. Environ. Saf. 80, 280–287.

Chevrier, C., Serrano, T., Lecerf, R., Limon, G., Petit, C., Monfort, C., et al., 2014. Environmental determinants of the urinary concentrations of herbicides during pregnancy: the pelagie mother-child cohort (france). Environ. Int. 63, 11–18.

Clementi, M., Causin, R., Marzocchi, C., Mantovani, A., Tenconi, R., 2007. A study of the impact of agricultural pesticide use on the prevalence of birth defects in northeast italy. Reprod. Toxicol. 24, 1–8.

Coker, E., Gunier, R., Bradman, A., Harley, K., Kogut, K., Molitor, J., et al., 2017. Association between pesticide profiles used on agricultural fields near maternal residences during pregnancy and iq at age 7 years. Int. J. Environ. Res. Public Health 14.

Cornelis, C., Schoeters, G., Kellen, E., Buntinx, F., Zeegers, M., 2009. Development of a gis-based indicator for environmental pesticide exposure and its application to a belgian case-control study on bladder cancer. Int. J. Hyg. Environ. Health 212, 172–185.

Coronado, G.D., Holte, S., Vigoren, E., Griffith, W.C., Barr, D.B., Faustman, E., et al., 2011. Organophosphate pesticide exposure and residential proximity to nearby fields: evidence for the drift pathway. J. Occup. Environ. Med. 53, 884–891.

Corral, S.A., de Angel, V., Salas, N., Zuniga-Venegas, L., Gaspar, P.A., Pancetti, F., 2017. Cognitive impairment in agricultural workers and nearby residents exposed to pesticides in the coquimbo region of chile. Neurotoxicol. Teratol. 62, 13–19.

Costello, S., Cockburn, M., Bronstein, J., Zhang, X., Ritz, B., 2009. Parkinson's disease and residential exposure to maneb and paraquat from agricultural applications in the central valley of california. Am. J. Epidemiol. 169, 919–926.

Curl, C.L., Fenske, R.A., Kissel, J.C., Shirai, J.H., Moate, T.F., Griffith, W., et al., 2002. Evaluation of take-home organophosphorus pesticide exposure among agricultural workers and their children. Environ. Health Perspect. 110, A787–A792.

Curwin, B.D., Hein, M.J., Sanderson, W.T., Striley, C., Heederik, D., Kromhout, H., et al., 2007. Urinary pesticide concentrations among children, mothers and fathers living in farm and non-farm households in iowa. Ann. Occup. Hyg. 51, 53–65.

Dalvie, M.A., London, L., 2006. The impact of aerial application of organophosphates on the cholinesterase levels of rural residents in the vaalharts district, northern cape province, south africa. Environ. Res. 102, 326–332.

Damalas, C.A., Eleftherohorinos, I.G., 2011. Pesticide exposure, safety issues, and risk assessment indicators. Int. J. Environ. Res. Public Health 8, 1402–1419.

Dardiotis, E., Aloizou, A.M., Siokas, V., Tsouris, Z., Rikos, D., Marogianni, C., et al., 2019. Paraoxonase-1 genetic polymorphisms in organophosphate metabolism. Toxicology 411, 24–31.

Deziel, N.C., Friesen, M.C., Hoppin, J.A., Hines, C.J., Thomas, K., Freeman, L.E., 2015. A review of nonoccupational pathways for pesticide exposure in women living in agricultural areas. Environ. Health Perspect. 123, 515–524.

Deziel, N.C., Freeman, L.E., Graubard, B.I., Jones, R.R., Hoppin, J.A., Thomas, K., et al., 2017. Relative contributions of agricultural drift, para-occupational, and residential use exposure pathways to house dust pesticide concentrations: meta-regression of published data. Environ. Health Perspect. 125, 296–305.

Doğanlar, Z.B., Doğanlar, O., Tozkir, H., Gökalp, F.D., Doğan, A., Yamaç, F., et al., 2018. Nonoccupational exposure of agricultural area residents to pesticides: pesticide accumulation and evaluation of genotoxicity. Arch. Environ. Contam. Toxicol. 75, 530–544.

El-Zaemey, S., Heyworth, J., Fritschi, L., 2013. Noticing pesticide spray drift from agricultural pesticide application areas and breast cancer: a case-control study. Aust. N. Z. J. Public Health 37, 547–555.

Felsot, A.S., Unsworth, J.B., Linders, J.B., Roberts, G., Rautman, D., Harris, C., et al., 2010. Agrochemical spray drift; assessment and mitigation–a review. J. Environ. Sci. Health B 45, 889–911.

Fenske, R.A., Lu, C., Barr, D., Needham, L., 2002. Children's exposure to chlorpyrifos and parathion in an agricultural community in central washington state. Environ. Health Perspect. 110, 549–553.

Galea, K.S., MacCalman, L., Jones, K., Cocker, J., Teedon, P., Cherrie, J.W., et al., 2015. Urinary biomarker concentrations of captan, chlormequat, chlorpyrifos and cypermethrin in UK adults and children living near agricultural land. J. Expo. Sci. Environ. Epidemiol. 25, 623–631.

Gemmill, A., Gunier, R.B., Bradman, A., Eskenazi, B., Harley, K.G., 2013. Residential proximity to methyl bromide use and birth outcomes in an agricultural population in california. Environ. Health Perspect. 121, 737–743.

Gibbs, J.L., Yost, M.G., Negrete, M., Fenske, R.A., 2017. Passive sampling for indoor and outdoor exposures to chlorpyrifos, azinphos-methyl, and oxygen analogs in a rural agricultural community. Environ. Health Perspect. 125, 333–341.

Gómez-Barroso, Diana, García-Pérez, Javier, López-Abente, Gonzalo, Tamayo-Uria, Ibon, Morales-Piga, Antonio, Pardo Romaguera, Elena, Ramis, Rebeca, 2016. Agricultural crop exposure and risk of childhood cancer: new findings from a case–control study in Spain. Int. J. Health Geogr. 15 (1). https://doi.org/10.1186/s12942-016-0047-7.

Gunier, R.B., Ward, M.H., Airola, M., Bell, E.M., Colt, J., Nishioka, M., et al., 2011. Determinants of agricultural pesticide concentrations in carpet dust. Environ. Health Perspect. 119, 970–976.

Gunier, R.B., Bradman, A., Jerrett, M., Smith, D.R., Harley, K.G., Austin, C., et al., 2013. Determinants of manganese in prenatal dentin of shed teeth from chamacos children living in an agricultural community. Environ. Sci. Technol. 47, 11249–11257.

Gunier, R.B., Jerrett, M., Smith, D.R., Jursa, T., Yousefi, P., Camacho, J., et al., 2014. Determinants of manganese levels in house dust samples from the chamacos cohort. Sci. Total Environ. 497–498, 360–368.

Gunier, R.B., Bradman, A., Castorina, R., Holland, N.T., Avery, D., Harley, K.G., et al., 2017a. Residential proximity to agricultural fumigant use and iq, attention and hyperactivity in 7-year old children. Environ. Res. 158, 358–365.

Gunier, R.B., Bradman, A., Harley, K.G., Kogut, K., Eskenazi, B., 2017b. Prenatal residential proximity to agricultural pesticide use and iq in 7-year-old children. Environ. Health Perspect. 125.

Hogenkamp, A., Vaal, M., Heederik, D., 2004. Pesticide exposure in dwellings near bulb growing fields in the netherlands: an explorative study. Ann. Agric. Environ. Med. 11, 149–153.

Hyland, C., Laribi, O., 2017. Review of take-home pesticide exposure pathway in children living in agricultural areas. Environ. Res. 156, 559–570.

Jones, R.R., Yu, C.L., Nuckols, J.R., Cerhan, J.R., Airola, M., Ross, J.A., et al., 2014. Farm residence and lymphohematopoietic cancers in the iowa women[u+05f3]s health study. Environ. Res. 133, 353–361.

Karasova, J.Z., Maderycova, Z., Tumova, M., Jun, D., Rehacek, V., Kuca, K., et al., 2017. Activity of cholinesterases in a young and healthy middle-european population: relevance for toxicology, pharmacology and clinical praxis. Toxicol. Lett. 277, 24–31.

Kawahara, J., Horikoshi, R., Yamaguchi, T., Kumagai, K., Yanagisawa, Y., 2005. Air pollution and young children's inhalation exposure to organophosphorus pesticide in an agricultural community in japan. Environ. Int. 31, 1123–1132.

Kunzli, N., Tager, I.B., 1997. The semi-individual study in air pollution epidemiology: a valid design as compared to ecologic studies. Environ. Health Perspect. 105, 1078–1083.

LaKind, J.S., Burns, C.J., Naiman, D.Q., O'Mahony, C., Vilone, G., Burns, A.J., et al., 2017. Critical and systematic evaluation of data for estimating human exposures to 2,4-dichlorophenoxyacetic acid (2,4-d)–quality and generalizability. J. Toxicol. Environ. Health Part B Crit. Rev. 20, 423–446.

Larsen, A.E., Gaines, S.D., Deschenes, O., 2017. Agricultural pesticide use and adverse birth outcomes in the san joaquin valley of california. Nat. Commun. 8, 302.

Lebailly, P., Mirey, G., Herin, F., Lecluse, Y., Salles, B., Boutet-Robinet, E., 2015. DNA damage in b and t lymphocytes of farmers during one pesticide spraying season. Int. Arch. Occup. Environ. Health 88, 963–972.

Lu, C., Fenske, R.A., Simcox, N.J., Kalman, D., 2000. Pesticide exposure of children in an agricultural community: evidence of household proximity to farmland and take home exposure pathways. Environ. Res. 84, 290–302.

Malagoli, C., Costanzini, S., Heck, J.E., Malavolti, M., De Girolamo, G., Oleari, P., et al., 2016. Passive exposure to agricultural pesticides and risk of childhood leukemia in an italian community. Int. J. Hyg. Environ. Health 219, 742–748.

Manthripragada, A.D., Costello, S., Cockburn, M.G., Bronstein, J.M., Ritz, B., 2010. Paraoxonase 1, agricultural organophosphate exposure, and parkinson disease. Epidemiology (Cambridge, Mass) 21, 87–94.

Martínez-Perafán, F., Santoli, M.F., López-Nigro, M., Carballo, M.A., 2018. Assessment of the health status and risk of genotoxic and cytotoxic damage in argentinian adolescents living near horticultural crops. Environ. Sci. Pollut. Res. 25, 5950–5959.

McDuffie, H.H., 2005. Host factors and genetic susceptibility: a paradigm of the conundrum of pesticide exposure and cancer associations. Rev. Environ. Health 20, 77–101.

Mercadante, R., Polledri, E., Bertazzi, P.A., Fustinoni, S., 2013. Biomonitoring short- and long-term exposure to the herbicide terbuthylazine in agriculture workers and in the general population using urine and hair specimens. Environ. Int. 60, 42–47.

Mercadante, R., Polledri, E., Moretto, A., Fustinoni, S., 2018. Long-term occupational and environmental exposure to penconazole and tebuconazole by hair biomonitoring. Toxicol. Lett.

Meyer, K.J., Reif, J.S., Rao Veeramachaneni, D.N., Luben, T.J., Mosley, B.S., Nuckols, J.R., 2006. Agricultural pesticide use and hypospadias in eastern arkansas. Environ. Health Perspect. 114, 1589–1595.

Mora, A.M., Van Wendel De Joode, B., Mergler, D., Córdoba, L., Cano, C., Quesada, R., et al., 2014. Blood and hair manganese concentrations in pregnant women from the infants' environmental health study (isa) in costa rica. Environ. Sci. Technol. 48, 3467–3476.

Morgan, M.K., Sobus, J.R., Barr, D.B., Croghan, C.W., Chen, F.L., Walker, R., et al., 2016. Temporal variability of pyrethroid metabolite levels in bedtime, morning, and 24-h urine samples for 50 adults in north carolina. Environ. Res. 144, 81–91.

Muñoz-Quezada, M.T., Iglesias, V., Lucero, B., Steenland, K., Barr, D.B., Levy, K., et al., 2012. Predictors of exposure to organophosphate pesticides in schoolchildren in the province of talca, chile. Environ. Int. 47, 28–36.

Paul, K.C., Ling, C., Lee, A., To, T.M., Cockburn, M., Haan, M., et al., 2018. Cognitive decline, mortality, and organophosphorus exposure in aging mexican americans. Environ. Res. 160, 132–139.

Quintana, M.M., Vera, B., Magnarelli, G., Guiñazú, N., Rovedatti, M.G., 2017. Neonatal, placental, and umbilical cord blood parameters in pregnant women residing in areas with intensive pesticide application. Environ. Sci. Pollut. Res. 24, 20736–20746.

Raanan, R., Gunier, R.B., Balmes, J.R., Beltran, A.J., Harley, K.G., Bradman, A., et al., 2017. Elemental sulfur use and associations with pediatric lung function and respiratory symptoms in an agricultural community (california, USA). Environ. Health Perspect. 125.

Ramirez-Santana, M., Farias-Gomez, C., Zuniga-Venegas, L., Sandoval, R., Roeleveld, N., Van der Velden, K., et al., 2018. Biomonitoring of blood cholinesterases and acylpeptide hydrolase activities in rural inhabitants exposed to pesticides in the coquimbo region of chile. PLoS One 13, e0196084.

Rappazzo, K.M., Warren, J.L., Meyer, R.E., Herring, A.H., Sanders, A.P., Brownstein, N.C., et al., 2016. Maternal residential exposure to agricultural pesticides and birth defects in a 2003 to 2005 north carolina birth cohort. Birth Defects Res. A 106, 240–249.

Reynolds, P., Hurley, S.E., Goldberg, D.E., Yerabati, S., Gunier, R.B., Hertz, A., et al., 2004. Residential proximity to agricultural pesticide use and incidence of breast cancer in the california teachers study cohort. Environ. Res. 96, 206–218.

Reynolds, P., Hurley, S.E., Gunier, R.B., Yerabati, S., Quach, T., Hertz, A., 2005a. Residential proximity to agricultural pesticide use and incidence of breast cancer in california, 1988–1997. Environ. Health Perspect. 113, 993–1000.

Reynolds, P., Von Behren, J., Gunier, R., Goldberg, D.E., Hertz, A., 2005b. Agricultural pesticides and lymphoproliferative childhood cancer in california. Scandinavian J. Work Environ. Health 31 (Suppl 1), 46–54 discussion 45-47.

Roberts, E.M., English, P.B., Grether, J.K., Windham, G.C., Somberg, L., Wolff, C., 2007. Maternal residence near agricultural pesticide applications and autism spectrum disorders among children in the california central valley. Environ. Health Perspect. 115, 1482–1489.

Rohitrattana, J., Siriwong, W., Robson, M., Panuwet, P., Barr, D.B., Fiedler, N., 2014. Pyrethroid insecticide exposure in school-aged children living in rice and aquacultural farming regions of thailand. Risk Manage. Healthcare Policy 7, 211–217.

Rohlman, D.S., Ismail, A., Bonner, M.R., Abdel Rasoul, G., Hendy, O., Ortega Dickey, L., et al., 2019. Occupational pesticide exposure and symptoms of attention deficit hyperactivity disorder in adolescent pesticide applicators in egypt. Neurotoxicology 74, 1–6.

Rowe, C., Gunier, R., Bradman, A., Harley, K.G., Kogut, K., Parra, K., et al., 2016. Residential proximity to organophosphate and carbamate pesticide use during pregnancy, poverty during childhood, and cognitive functioning in 10-year-old children. Environ. Res. 150, 128–137.

Rull, R.P., Ritz, B., Shaw, G.M., 2006a. Validation of self-reported proximity to agricultural crops in a case-control study of neural tube defects. J Expo. Sci. Environ. Epidemiol. 16, 147–155.

Rull, R.P., Ritz, B., Shaw, G.M., 2006b. Neural tube defects and maternal residential proximity to agricultural pesticide applications. Am. J. Epidemiol. 163, 743–753.

Rull, R.P., Gunier, R., Von Behren, J., Hertz, A., Crouse, V., Buffler, P.A., et al., 2009. Residential proximity to agricultural pesticide applications and childhood acute lymphoblastic leukemia. Environ. Res. 109, 891–899.

Sagiv, S.K., Harris, M.H., Gunier, R.B., Kogut, K.R., Harley, K.G., Deardorff, J., et al., 2018. Prenatal organophosphate pesticide exposure and traits related to autism spectrum disorders in a population living in proximity to agriculture. Environ. Health Perspect. 126.

Semchuk, K.M., McDuffie, H.H., Senthilselvan, A., Dosman, J.A., Cessna, A.J., Irvine, D.G., 2003. Factors associated with detection of bromoxynil in a sample of rural residents. J. Toxicol. Environ. Health Part A 66, 103–132.

Semchuk, K.M., Rosenberg, A.M., McDuffie, H.H., Cessna, A.J., Pahwa, P., Irvine, D.G., 2007. Antinuclear antibodies and bromoxynil exposure in a rural sample. J. Toxicol. Environ. Health A 70, 638–657.

Shaw, G.M., Yang, W., Roberts, E., Kegley, S.E., Padula, A., English, P.B., et al., 2014. Early pregnancy agricultural pesticide exposures and risk of gastroschisis among offspring in the san joaquin valley of california. Birth Defects Res. A 100, 686–694.

Shaw, G.M., Yang, W., Roberts, E.M., Kegley, S.E., Stevenson, D.K., Carmichael, S.L., et al., 2018. Residential agricultural pesticide exposures and risks of spontaneous preterm birth. Epidemiology (Cambridge, Mass) 29, 8–21.

Shelton, J.F., Geraghty, E.M., Tancredi, D.J., Delwiche, L.D., Schmidt, R.J., Ritz, B., et al., 2014. Neurodevelopmental disorders and prenatal residential proximity to agricultural pesticides: the charge study. Environ. Health Perspect. 122, 1103–1109.

Shirangi, A., Nieuwenhuijsen, M., Vienneau, D., Holman, C.D., 2011. Living near agricultural pesticide applications and the risk of adverse reproductive outcomes: a review of the literature. Paediatr. Perinat. Epidemiol. 25, 172–191.

Singh, S., Kumar, V., Thakur, S., Banerjee, B.D., Chandna, S., Rautela, R.S., et al., 2011. DNA damage and cholinesterase activity in occupational workers exposed to pesticides. Environ. Toxicol. Pharmacol. 31, 278–285.

Suarez-Lopez, J.R., Butcher, C.R., Gahagan, S., Checkoway, H., Alexander, B.H., Al-Delaimy, W.K., 2018. Acetylcholinesterase activity and time after a peak pesticide-use period among ecuadorian children. Int. Arch. Occup. Environ. Health 91, 175–184.

van Wendel de Joode, B., Barraza, D., Ruepert, C., Mora, A.M., Cordoba, L., Oberg, M., et al., 2012. Indigenous children living nearby plantations with chlorpyrifos-treated bags have elevated 3,5,6-trichloro-2-pyridinol (tcpy) urinary concentrations. Environ. Res. 117, 17–26.

Vinceti, M., Filippini, T., Violi, F., Rothman, K.J., Costanzini, S., Malagoli, C., et al., 2017. Pesticide exposure assessed through agricultural crop proximity and risk of amyotrophic lateral sclerosis. Environ. Health Global. Access Sci. Sour. 16.

Wang, A., Costello, S., Cockburn, M., Zhang, X., Bronstein, J., Ritz, B., 2011. Parkinson's disease risk from ambient exposure to pesticides. Eur. J. Epidemiol. 26, 547–555.

Wang, A., Cockburn, M., Ly, T.T., Bronstein, J.M., Ritz, B., 2014. The association between ambient exposure to organophosphates and parkinson's disease risk. Occup. Environ. Med. 71, 275–281.

Ward, M.H., Lubin, J., Giglierano, J., Colt, J.S., Wolter, C., Bekiroglu, N., et al., 2006. Proximity to crops and residential exposure to agricultural herbicides in iowa. Environ. Health Perspect. 114, 893–897.

Weppner, S., Elgethun, K., Lu, C., Hebert, V., Yost, M.G., Fenske, R.A., 2006. The washington aerial spray drift study: children's exposure to methamidophos in an agricultural community following fixed-wing aircraft applications. J. Expo. Sci. Environ. Epidemiol. 16, 387–396.

Wofford, P., Segawa, R., Schreider, J., Federighi, V., Neal, R., Brattesani, M., 2014. Community air monitoring for pesticides. Part 3: Using health-based screening levels to evaluate results collected for a year. Environ. Monit. Assess. 186, 1355–1370.

Wong, H.L., Garthwaite, D.G., Ramwell, C.T., Brown, C.D., 2017. How does exposure to pesticides vary in space and time for residents living near to treated orchards? Environ. Sci. Pollut. Res. Int. 24, 26444–26461.

Wu, C., Feng, C., Qi, X., Wang, G., Zheng, M., Chang, X., et al., 2013. Urinary metabolite levels of pyrethroid insecticides in infants living in an agricultural area of the province of jiangsu in china. Chemosphere 90, 2705–2713.