

# Health Effects of Pesticide Exposure in Latin American and the Caribbean Populations: A Scoping Review

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**BACKGROUND:** Multiple epidemiological studies have shown that exposure to pesticides is associated with adverse health outcomes. However, the literature on pesticide-related health effects in the Latin American and the Caribbean (LAC) region, an area of intensive agricultural and residential pesticide use, is sparse. We conducted a scoping review to describe the current state of research on the health effects of pesticide exposure in LAC populations with the goal of identifying knowledge gaps and research capacity building needs.

**METHODS:** We searched PubMed and SciELO for epidemiological studies on pesticide exposure and human health in LAC populations published between January 2007 and December 2021. We identified 233 publications from 16 countries that met our inclusion criteria and grouped them by health outcome (genotoxicity, neurobehavioral outcomes, placental outcomes and teratogenicity, cancer, thyroid function, reproductive outcomes, birth outcomes and child growth, and others).

**RESULTS:** Most published studies were conducted in Brazil (37%,  $n = 88$ ) and Mexico (20%,  $n = 46$ ), were cross-sectional in design (72%,  $n = 167$ ), and focused on farmworkers (45%,  $n = 105$ ) or children (21%,  $n = 48$ ). The most frequently studied health effects included genotoxicity (24%,  $n = 62$ ) and neurobehavioral outcomes (21%,  $n = 54$ ), and organophosphate (OP) pesticides were the most frequently examined (26%,  $n = 81$ ). Forty-seven percent ( $n = 112$ ) of the studies relied only on indirect pesticide exposure assessment methods. Exposure to OP pesticides, carbamates, or to multiple pesticide classes was consistently associated with markers of genotoxicity and adverse neurobehavioral outcomes, particularly among children and farmworkers.

**DISCUSSION:** Our scoping review provides some evidence that exposure to pesticides may adversely impact the health of LAC populations, but methodological limitations and inconsistencies undermine the strength of the conclusions. It is critical to increase capacity building, integrate research initiatives, and conduct more rigorous epidemiological studies in the region to address these limitations, better inform public health surveillance systems, and maximize the impact of research on public policies. <https://doi.org/10.1289/EHP9934>

## Introduction

The Latin America and the Caribbean (LAC) region accounts for 14% of global agricultural production and 23% of the world's exports of agricultural and fisheries commodities.<sup>1</sup> The rapid increase of farming in the region in the last decades has been coupled with an extensive use of pesticides (defined as chemical compounds that may either kill, obstruct, or manage the growth

of any organism that damages a crop)<sup>2,3</sup> and a lack of pesticide use regulations or implementation thereof.<sup>4–6</sup> It is estimated that pesticide use in LAC countries accounts for 20% of worldwide consumption<sup>3</sup> and that more pesticides are used in Central and South America on a per capita basis (1.84 and 1.78 kg of pesticide per person per year, respectively<sup>3,7</sup>) than in other regions in the world.

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Intensive use of pesticides in the LAC region for agricultural and public health vector control purposes<sup>8</sup> has resulted in widespread chronic human exposure, particularly among those living in agricultural communities. Pathways of chronic exposure include pesticide drift from treated fields to nearby homes or schools,<sup>9–12</sup> take-home exposure,<sup>13</sup> and consumption of contaminated food and water.<sup>14–17</sup> Elevated occupational exposures in this region are also a concern as workers who apply pesticides or work in treated agricultural fields are exposed to mixtures of pesticides, such as insecticides [e.g., organophosphate (OP) and organochlorine (OC) pesticides],<sup>18,19</sup> herbicides (e.g., glyphosate, the most widely used pesticide in the world),<sup>20</sup> and fungicides (e.g., chlorothalonil, bisdithiocarbamates, and benzimidazoles).<sup>21</sup>

Although multiple studies around the world, including those conducted in LAC countries, have shown that pesticides have a negative impact on human health,<sup>22,23</sup> public health surveillance and monitoring systems on pesticide use and associated illness are nonexistent or extremely limited in the LAC region.<sup>5,24–28</sup> In addition, several pesticides banned in the United States, Europe, and Canada because they were deemed as a potential threat to human health have been or continue to be used in some LAC countries.<sup>28–30</sup> Climate change could also exacerbate the health risks of pesticide exposures among LAC populations owing to enhanced chemical toxicity, increased rates of chemical degradation, enhanced volatilization of pesticides to the atmosphere or surface deposition of airborne pesticides, or changes in the frequency and amount of pesticides used.<sup>31,32</sup>

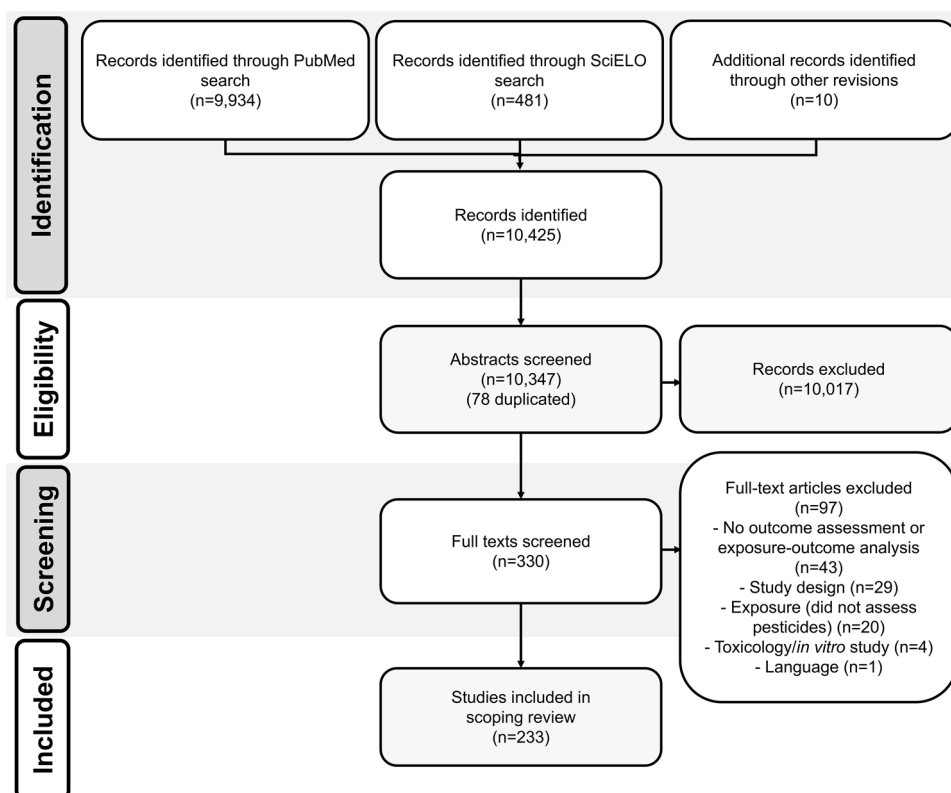
Promotion of high-quality epidemiological studies with standardized direct exposure assessment methods, the establishment of biomonitoring and environmental surveillance programs, and the development of evidence-based prevention policies and interventions have been suggested as means to protect the health of populations exposed to pesticides.<sup>33–35</sup> Still, there is little information on the current state of research on the health effects of pesticides in the LAC region. Previous systematic literature reviews and meta-analyses of studies conducted in LAC populations have focused on one specific class of pesticides or specific active ingredient (e.g., OP pesticides,<sup>36,37</sup> pyrethroids,<sup>38</sup> glyphosate<sup>39</sup>), one specific age group (e.g., children<sup>37,40–42</sup>), or one health outcome (e.g., genotoxicity,<sup>43</sup> neurobehavior,<sup>36,37,40</sup> or respiratory health<sup>41</sup>). To address existing gaps of knowledge and identify research capacity building needs in the region, we conducted a scoping review to describe the current state of research on the health effects of pesticide exposure in LAC populations.

## Methods

### Search Strategy

We undertook a scoping review of the literature to identify all primary published data encompassing health effects of occupational or environmental exposure to pesticides in LAC populations. Our methods were guided by the Preferred Reporting Items for Systematic reviews and Meta-Analyses—Extension for Scoping Reviews (PRISMA-ScR) statement.<sup>44</sup> We searched PubMed and the Scientific Electronic Library Online (SciELO) for all studies published between January 2007 and December 2021. For PubMed, we used the following search string: (pesticides [All Fields] AND “Latin America” [All Fields]) OR (pesticides [All Fields] AND Aruba [All Fields]) OR (pesticides [All Fields] AND Bahamas [All Fields]) OR (pesticides [All Fields] AND Barbados [All Fields]) OR (pesticides [All Fields] AND “Cayman Islands” [All Fields]) OR (pesticides [All Fields] AND Cuba [All Fields]) OR (pesticides [All Fields] AND Curacao [All Fields]) OR (pesticides [All Fields] AND Dominica [All Fields]) OR (pesticides [All Fields] AND “Dominican Republic” [All

Fields]) OR (pesticides [All Fields] AND Grenada [All Fields]) OR (pesticides [All Fields] AND Guadeloupe [All Fields]) OR (pesticides [All Fields] AND Haiti [All Fields]) OR (pesticides [All Fields] AND Jamaica [All Fields]) OR (pesticides [All Fields] AND Martinique [All Fields]) OR (pesticides [All Fields] AND “Puerto Rico” [All Fields]) OR (pesticides [All Fields] AND “Saint Barthélemy” [All Fields]) OR (pesticides [All Fields] AND “Saint Kitts and Nevis” [All Fields]) OR (pesticides [All Fields] AND “Saint Lucia” [All Fields]) OR (pesticides [All Fields] AND “Saint Maarten” [All Fields]) OR (pesticides [All Fields] AND “Saint Vincent and the Grenadines” [All Fields]) OR (pesticides [All Fields] AND “Trinidad and Tobago” [All Fields]) OR (pesticides [All Fields] AND “Turks and Caicos Islands” [All Fields]) OR (pesticides [All Fields] AND “Virgin Islands” [All Fields]) OR (pesticides [All Fields] AND Belize [All Fields]) OR (pesticides [All Fields] AND “Costa Rica” [All Fields]) OR (pesticides [All Fields] AND “El Salvador” [All Fields]) OR (pesticides [All Fields] AND Guatemala [All Fields]) OR (pesticides [All Fields] AND Honduras [All Fields]) OR (pesticides [All Fields] AND Mexico [All Fields]) OR (pesticides [All Fields] AND Nicaragua [All Fields]) OR (pesticides [All Fields] AND Panama [All Fields]) OR (pesticides [All Fields] AND Argentina [All Fields]) OR (pesticides [All Fields] AND Bolivia [All Fields]) OR (pesticides [All Fields] AND Brazil [All Fields]) OR (pesticides [All Fields] AND Chile [All Fields]) OR (pesticides [All Fields] AND Colombia [All Fields]) OR (pesticides [All Fields] AND Ecuador [All Fields]) OR (pesticides [All Fields] AND “French Guiana” [All Fields]) OR (pesticides [All Fields] AND Guyana [All Fields]) OR (pesticides [All Fields] AND Paraguay [All Fields]) OR (pesticides [All Fields] AND Peru [All Fields]) OR (pesticides [All Fields] AND Suriname [All Fields]) OR (pesticides [All Fields] AND Uruguay [All Fields]) OR (pesticides [All Fields] AND Venezuela [All Fields]) AND (“2007/01/0”[Date— Publication]: “2021/12/3”[Date— Publication])) (i.e., names of the 43 LAC countries and territories, as defined by the International Society of Environmental Epidemiology (ISEE) LAC Chapter).<sup>45</sup> For SciELO, we used the following search string: ((pesticides AND Latin America)) OR ((pesticides AND Aruba)) OR ((pesticides AND Bahamas)) OR ((pesticides AND Barbados)) OR ((pesticides AND Cayman islands)) OR ((pesticides AND Cuba)) OR ((pesticides AND Curacao)) OR ((pesticides AND Dominica)) OR ((pesticides AND Dominican Republic)) OR ((pesticides AND Grenada)) OR ((pesticides AND Guadeloupe)) OR ((pesticides AND Haiti)) OR ((pesticides AND Jamaica)) OR ((pesticides AND Martinique)) OR ((pesticides AND Puerto Rico)) OR ((pesticides AND Saint Barthelemy)) OR ((pesticides AND saint Kitts and Nevis)) OR ((pesticides AND Saint Lucia)) OR ((pesticides AND Saint Maarten)) OR ((pesticides AND Saint Vincent and the Grenadines)) OR ((pesticides AND Trinidad and Tobago)) OR ((pesticides AND Turks and Caicos islands)) OR ((pesticides AND Virgin Islands)) OR ((pesticides AND Belize)) OR ((pesticides AND Costa Rica)) OR ((pesticides AND El Salvador)) OR ((pesticides AND Guatemala)) OR ((pesticides AND Honduras)) OR ((pesticides AND Mexico)) OR ((pesticides AND Nicaragua)) OR ((pesticides AND Panama)) OR ((pesticides AND Argentina)) OR ((pesticides AND Bolivia)) OR ((pesticides AND Brazil)) OR ((pesticides AND Chile)) OR ((pesticides AND Colombia)) OR ((pesticides AND Ecuador)) OR ((pesticides AND French Guiana)) OR ((pesticides AND Guyana)) OR ((pesticides AND Paraguay)) OR ((pesticides AND Peru)) OR ((pesticides AND Suriname)) OR ((pesticides AND Uruguay)) OR ((pesticides AND Venezuela)) and filtered the results by date of publication. The initial search was conducted on 30 May 2017, with subsequent updates on 1 May



**Figure 1.** PRISMA-ScR flow diagram of study selection. Note: PRISMA-ScR, Preferred Reporting Items for Systematic reviews and Meta-Analyses—Extension for Scoping Reviews; SciELO, Scientific Electronic Library Online.

2019, 4 February 2021, and 27 April 2022 (for papers published until 31 December 2021). We also identified potentially relevant citations not retrieved by the initial literature searches by scanning the references of relevant studies throughout the course of title and abstract screening and data abstraction (Figure 1; see Supplemental Material for the list of studies retrieved from PubMed and SciELO).

### Study Selection

After removing duplicate records, titles and abstracts of literature search results were scanned for eligibility by two reviewers, with discrepancies resolved by a third reviewer. Studies were selected for full-text review when they met all of our inclusion criteria: *a*) original full paper that presented unique data from an analytical observational epidemiological study (i.e., cohort, cross-sectional, or case-control study); *b*) environmental or occupational exposure to pesticides; *c*) conducted in one of the 43 LAC countries and territories, as defined by the ISEE LAC Chapter<sup>45</sup>; and *d*) published in English, Spanish, or Portuguese. We excluded studies if they met one of the following criteria: *a*) did not report original results (i.e., reviews, meta-analysis, comments, letters, editorials, and case reports); *b*) were experimental, toxicological, or ecological studies; *c*) were based on animal or human tissues; or *d*) reported preliminary results (e.g., conference abstracts or papers that were later updated or revised in a peer-reviewed journal article). Full texts were assessed by two reviewers for final inclusion, with a third reviewer again resolving any discrepancies.

### Data Abstraction

We abstracted the following characteristics from the selected publications: bibliographic citation information (i.e., authors, year of publication, and country), characteristics of the study population

(i.e., sample size, study area), study design, type of pesticides assessed (e.g., pesticide class or pesticide active ingredient), exposure and health outcome assessment methods, and main study findings. We grouped the studies into eight categories based on the main health outcome assessed: *a*) genotoxicity, *b*) neurobehavioral outcomes, *c*) placental outcomes and teratogenicity, *d*) cancer, *e*) thyroid function, *f*) reproductive outcomes, *g*) birth outcomes and child growth, and *h*) other health outcomes.

Because of the expected methodological heterogeneity among the selected studies (e.g., variability in study design; exposure and outcome assessment methods), results were not intended to be combined through meta-analysis. Instead, we conducted a narrative synthesis to highlight the strengths and limitations of the current evidence base and to ultimately draw conclusions about the state of research on the health effects of pesticide exposure in LAC populations, including key challenges moving forward.

### Results

The PubMed and SciELO search retrieved 9,934 and 481 citations, respectively, and the review of references from relevant publications yielded 10 additional citations (Figure 1). After removing 78 duplicates, 10,023 publications that did not meet inclusion criteria based on titles/abstracts, and 91 that did not meet inclusion criteria based on full-text reviews, 233 publications were included in this review. Although publications reported on studies from 16 (37%) of the 43 LAC countries and territories, most studies were conducted in Brazil (37%,  $n = 88$ ) and Mexico (20%,  $n = 46$ ) (Table 1). Studies were primarily cross-sectional in design (72%,  $n = 167$ ), and the most frequently studied populations were farmworkers (45%,  $n = 105$ ) or children (21%,  $n = 48$ ). Between 2007 and 2021, the average number  $\pm$  standard deviation (SD) of publications was  $\sim 15.6 \pm 7.0$ /y, range: 5 in 2008 to 27 in 2020 (Figure S1). Nearly half



**Table 1.** Characteristics of Latin American and the Caribbean studies on pesticide exposure and health outcomes published between 2007 and 2021 ( $n = 233$ ).

Characteristic	<i>n</i> (%)
Study country <sup>a</sup>	
Argentina	21 (8.9)
Bolivia	6 (2.6)
Brazil	88 (37.4)
Chile	7 (3.0)
Colombia	9 (3.8)
Costa Rica	14 (6.0)
Dominican Republic	1 (0.4)
Ecuador	17 (7.2)
El Salvador	1 (0.4)
Guadeloupe	14 (6.0)
Jamaica	1 (0.4)
Mexico	46 (19.6)
Nicaragua	4 (1.7)
Paraguay	1 (0.4)
Peru	2 (0.8)
Venezuela	3 (1.3)
Study design	
Cohort	41 (17.5)
Cross sectional	167 (71.7)
Case-control	25 (10.7)
Study population	
Farmworkers	105 (45.1)
Other workers (e.g., vector control program workers)	9 (3.9)
General population	38 (16.3)
Mother-child pairs	27 (11.6)
Pregnant women only	6 (2.6)
Children only	48 (20.6)
Pesticide exposure assessment method <sup>b,c</sup>	
Indirect	
Questionnaire only	103 (43.1)
Other (e.g., job status ascertained via death certificate or surveillance system, residential proximity)	9 (3.8)
Direct	
Cholinesterase activity <sup>d</sup>	57 (23.8)
Pesticides or pesticide metabolites measured in biological matrix	70 (29.3)
Biological matrix used for pesticide exposure assessment <sup>e</sup>	
Blood	99 (73.9)
Breast milk	2 (1.5)
Hair	4 (3.0)
Urine	28 (20.9)
Toenail	1 (0.7)
Pesticides assessed <sup>f</sup>	
Insecticides in general (no class specified)	5 (1.6)
Organophosphates	81 (26.2)
Organophosphates and carbamates <sup>g</sup>	20 (6.5)
Organochlorines	46 (14.9)
Pyrethroids	20 (6.5)
Neonicotinoids	2 (0.6)
Herbicides	21 (6.8)
Fungicides	11 (3.6)
Larvicides	1 (0.3)
Rodenticides	1 (0.3)
Natural pesticides	1 (0.3)
Multiple pesticide classes (unspecified)	100 (32.3)
Main health outcomes <sup>h</sup>	
Genotoxicity	62 (24.0)
Neurobehavioral outcomes	54 (20.9)
Placental outcomes and teratogenicity	13 (5.1)
Cancer	14 (5.4)
Thyroid function	16 (6.2)
Reproductive outcomes	16 (6.2)
Birth outcomes and child growth	13 (5.1)
Other effects	70 (27.1)
Kidney function <sup>i</sup>	9 (3.5)
Respiratory and allergic outcomes <sup>i</sup>	7 (2.7)
Liver injury <sup>i</sup>	8 (3.1)
Hematological parameters and lipid profile <sup>i</sup>	17 (6.6)

**Table 1.** (Continued.)

Characteristic	<i>n</i> (%)
Acoustic damage <sup>i</sup>	8 (3.1)
Others <sup>i</sup>	26 (10.1)

<sup>a</sup> $n > 233$  because one published study (Maluf et al.<sup>245</sup>) was conducted in three countries (Argentina, Brazil, and Mexico).

<sup>b</sup>A total of 125 published studies employed direct exposure assessment methods, with some measuring both cholinesterase activity and pesticide metabolites concentrations. Of these, 81 (65.3%) used data from the direct exposure assessment in exposure-outcome analyses (e.g., some studies measured urinary biomarkers of exposure and ascertained occupational status via questionnaire but only reported exposure-outcome associations using occupational status).

<sup>c</sup> $n > 233$  because some published studies employed more than one exposure assessment method (e.g., measurement of cholinesterase activity in blood and urinary pesticide metabolites).

<sup>d</sup>A total of 57 published studies measured cholinesterase activity only; 4 studies measured cholinesterase activity in addition to other pesticide metabolites.

<sup>e</sup>Only for published studies with direct pesticide exposure assessment, but nine studies measured pesticides in more than one biological matrix.

<sup>f</sup> $n > 233$  because some published studies assessed multiple pesticide groups.

<sup>g</sup>Exposure assessed via acetylcholinesterase activity monitoring and authors did not differentiate if they were primarily examining organophosphates or carbamates.

<sup>h</sup> $n > 233$  because some published studies assessed outcomes from more than one group.

<sup>i</sup>Proportion of published studies that assessed this outcome out of all the studies included in the review ( $n = 233$ ); total studies that assessed other health effects  $> 70$  because some assessed multiple outcomes in this category (e.g., several published studies examined liver injury and hematological parameters).

(47%,  $n = 112$ ) of the published studies relied solely on indirect pesticide exposure assessment methods (e.g., questionnaire, job status ascertainment via death certificate or surveillance system) (Table 1 and Table S1). Blood was the biological matrix most frequently used to assess pesticide exposure (74%,  $n = 99$  of the 124 studies that used direct exposure assessment methods). Most published studies focused on OP pesticides (26%,  $n = 81$ ) or multiple classes of pesticides (32%,  $n = 100$ ). The most studied health effects included genotoxicity (24%,  $n = 62$ ) and neurobehavioral outcomes (21%,  $n = 54$ ) (Table 1 and Table S1).

### Genotoxicity

Sixty-two publications examined associations of pesticide exposure with cytogenetic or DNA damage (Table 2). Most publications were derived from cross-sectional studies that evaluated DNA damage from accessible tissues, such as blood or buccal cells, via comet assays, telomere attrition, or DNA methylation of candidate genes. Eleven of the 62 publications focused on children. Three of these 11 publications assessed exposure to OC pesticides by measurement of blood or hair OC pesticide concentrations,<sup>46–48</sup> whereas the remaining 8 examined exposure to a mixture of pesticides including OP pesticides, pyrethroids, herbicides, or “multiple pesticide classes” via questionnaire.<sup>30,49–55</sup> Of the 3 publications that measured blood or hair OC pesticide concentrations,<sup>46–48</sup> 2 were from cross-sectional studies of school-age Mexican children and reported associations with genotoxic damage—as indicated by DNA damage assessed via comet assay<sup>47</sup> or higher frequency of micronuclei and other nuclear abnormalities in buccal cells.<sup>48</sup> A third publication from a cross-sectional investigation of mother-child pairs in Mexico reported null associations with DNA and cytogenetic damage measured in maternal blood at delivery and cord blood.<sup>46</sup> Five publications examining exposures to more than one pesticide class in children from Mexico,<sup>49,51</sup> Argentina,<sup>50,54</sup> and Paraguay<sup>53</sup> reported associations of higher residential or parental occupational pesticide exposure with cytogenetic damage—assessed via buccal micronuclei and other nuclear abnormalities. Similarly, in a prospective study of school-age children living near a tobacco-producing region in Brazil, researchers found that malondialdehyde, protein carbonyl, and vitamin C levels were higher at the beginning of the pesticide application period than at the leaf harvest period.<sup>52</sup>

**Table 2.** Characteristics of Latin American and the Caribbean studies on pesticide exposure and genotoxicity published between 2007 and 2021 (*n* = 62).

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
<b>Studies on OCs</b>								
1. Alvarado-Hernández et al. <sup>46</sup>	2013/Mexico	50 mother-child (newborns) pairs living in a rural agricultural area	Cross-sectional	OCs	Maternal (collected at delivery) and cord blood HCH, HCB, aldrin, heptachlor epoxide, oxychlorane, chlordane, DDT, DDE, nonachlor, mirex, and endosulfan	Median (P25-P75) (ng/g lipid): Maternal: $\alpha$ -HCH = 367 (243–617); $\beta$ -HCH = 1,320 (1,009–2,094); $\gamma$ -HCH = 391 (252–638) HCB = 58 (46–76); aldrin = 412 (208–528); heptachlor epoxide = 3,762 (2,941–5,167); oxychlorane = 1,672 (977–2,232); t-chlordane = 1 (0.4–9); c-chlordane = 8 (1–16); <i>cis</i> -nonachlor = 2 (0.8–17); mirex = 18 (8–24); endosulfan 1 = 153 (97–221); endosulfan 2 = 90 (62–118); DDE = 472 (153–1,041); DDT = 204 (11–341) Cord blood: $\alpha$ -HCH = 1,251 (755–2,532); $\beta$ -HCH = 2,815 (2,017–4,337); $\gamma$ -HCH = 995 (695–1,193); HCB = 137 (107–175); aldrin = 906 (608–1,197); heptachlor epoxide = 8,707 (5,809–10,651); oxychlorane = 1,411 (466–2,237); t-chlordane = 3 (0.5–23); c-chlordane = 21 (0.2–35); <i>cis</i> -nonachlor = 31 (2–49); mirex = 27 (5.9–50); endosulfan 1 = 401 (53–557); endosulfan 2 = 265 (163–368); DDE = 192 (22–536); DDT = 421 (0.1–707) Mean $\pm$ SD (ng/g lipid): Range of total blood DDT concentrations in 11 communities: from 12.5 $\pm$ 5 to 21,500 $\pm$ 6,800	DNA damage: comet assay Cytogenetic damage: MN, CHBs, NPBs	Null associations of OC pesticides with markers of cytogenetic or DNA damage.
2. Jasso-Pineda et al. <sup>47</sup>	2015/Mexico	276 children (6–12 years of age) living in communities with industrial activities (e.g., agriculture)	Cross-sectional	OCs	Questionnaire (drinking water, occupational and parental exposure history) Serum DDT	Mean $\pm$ SD (ng/g lipid): Range of total blood DDT concentrations in 11 communities: from 12.5 $\pm$ 5 to 21,500 $\pm$ 6,800	DNA damage: comet assay	Children with high total DDT concentrations (defined as higher than the national geometric mean) had a higher DNA damage compared with those with low total DDT concentrations ( $p < 0.05$ ). Children exposed to PAHs (from biomass combustion) and DDT had the highest DNA damage compared with children in the other three exposure scenarios (high PAHs, high arsenic, and low lead exposure) ( $p < 0.05$ ). Higher frequency of PK, BN, KL, LN, and AT abnormalities among exposed children compared with unexposed ( $p < 0.05$ for each). Among all participants, those in the highest tertile of total OC concentrations had higher numbers of TAC compared with those in the lowest tertile ( $p < 0.05$ ).
3. Auguiano-Vega et al. <sup>48</sup>	2020/Mexico	63 children (6–13 years of age) exposed to pesticides near school/24 controls (6–13 years of age)	Cross-sectional	OCs	Questionnaire (parental occupational exposure history) Hair HCH, aldrin, dieldrin, endrin, chlordane, heptachlor, epoxyheptane, endosulfan, DDD, DDE, DDT	Total (mean) OCs ( $\mu$ g/g): Exposed: 28.2 (0.95) unexposed: 4.4 (0.18)	Cytogenetic damage: MN, CC Cytotoxicity: KR, PK, BN, KL, LN, AN, TAC	Children with high total DDT concentrations (defined as higher than the national geometric mean) had a higher DNA damage compared with those with low total DDT concentrations ( $p < 0.05$ ). Children exposed to PAHs (from biomass combustion) and DDT had the highest DNA damage compared with children in the other three exposure scenarios (high PAHs, high arsenic, and low lead exposure) ( $p < 0.05$ ). Higher frequency of PK, BN, KL, LN, and AT abnormalities among exposed children compared with unexposed ( $p < 0.05$ for each). Among all participants, those in the highest tertile of total OC concentrations had higher numbers of TAC compared with those in the lowest tertile ( $p < 0.05$ ).
<b>Studies on OPs or CBs</b>								
4. Franco et al. <sup>49</sup>	2016/Brazil	161 community health agents/88 controls	Cross-sectional	OPs	Questionnaire (occupational exposure history)	Not applicable	DNA damage: comet assay Transcriptome: <i>LRP1</i> , <i>IGF2R</i> , <i>IGL</i> , family, <i>IGL</i> , <i>CXCL5</i> , <i>CCL3</i> , <i>NSH</i> , <i>LGALS14</i> , <i>NBPFF</i> Oxidative stress: CAT, SOD, GSH/GSSG ratio, TBARS	Exposed individuals had higher DNA damage than controls ( $p = 0.003$ ). Higher DNA damage in <i>GSTM1</i> -positive individuals than <i>GSTM1</i> -null individuals ( $p = 0.05$ ). Sixteen genes with differential gene expression between exposed and controls. Compared with the controls, <i>LRP1</i> and <i>IGF2R</i> genes were underexpressed and gene <i>IGL</i> family and <i>IGL</i> were overexpressed in the exposed group.
5. Martinez et al. <sup>67</sup>	2016/Argentina	27 urban patients with SLE/17 rural patients with SLE/30 urban healthy controls/28 rural healthy controls	Cross-sectional	OPs and CBs	Questionnaire (residential exposure history) Blood AChE, BChE <sup>a</sup>	Not applicable	Oxidative stress: CAT, SOD, GSH/GSSG ratio, TBARS	Increase in TBARS (18.3%, $p = 0.01$ ) in rural SLE cases compared with urban SLE cases.
6. Silvério et al. <sup>57</sup>	2017/Brazil <sup>b</sup>	94 farmworkers exposed to pesticides including OPs/94 farmworkers exposed to pesticides not including OPs/50 controls	Cross-sectional	OPs	Questionnaire (occupational exposure history) Urinary DAPs <sup>a</sup> Blood AChE, BChE <sup>a</sup>	Mean $\pm$ SD ( $\mu$ g/L): Occupationally exposed to complex mixtures with OPs: DETP = 0.27 $\pm$ 0.25; DEDTP = 0.06 $\pm$ 0.04 Occupationally exposed to complex mixtures without OPs: DETP = 0.09 $\pm$ 0.005; DEDTP = 0.08 $\pm$ 0.02 Control group: DETP < LOQ; DEDTP < LOQ	Cytogenetic damage: MN, BN, NBUDs Cytotoxicity: CC, KR, PN, KL	Farmworkers exposed to pesticides including OPs had higher NBUDs, CC, and KL than those exposed to pesticides but not OPs ( $p < 0.05$ ). Both exposed groups had higher MN, BN, CC, KR, PN, and KL than controls ( $p < 0.05$ ).

Table 2. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
7. Simonello et al. <sup>46</sup>	2017/Argentina	50 urban patients with SLE/39 rural patients with SLE/54 urban healthy controls/53 rural healthy controls	Cross-sectional	OPs	Questionnaire (residential exposure history) Blood AChE, BChE <sup>a</sup>	Not applicable	DNA damage: comet assay Endo sites Oxidative stress: CAT, SOD, TBARS, GSH, GSSG	Endo sites and SOD ( $p < 0.05$ , $p < 0.03$ , $p = 0.01$ , respectively) were higher in rural patients with SLE than urban ones. Rural patients with SLE had increased risk of having oxidative DNA damage than urban patients with SLE (OR = 3.5; 95% CI: 1.4, 8.8).
8. Zepeda-Arce et al. <sup>38</sup>	2017/Mexico	60 sprayers with motor pump (high-exposure group)/126 solid pesticides sprayers (moderate-exposure group)/22 controls	Cross-sectional	OPs, pyrethroids, CBs	Questionnaire (occupational exposure history) Blood AChE, BChE <sup>a</sup>	Not applicable	DNA damage: comet assay Oxidative stress: MDA, SOD, CAT, GPx, GR	No differences in CAT, SOD, GPx, GR activities, DNA damage, and MDA levels between groups.
9. Benitez-Trinidad et al. <sup>39</sup>	2018/Mexico	127 urban pesticide sprayers/63 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood BChE <sup>a</sup>	Not applicable	DNA methylation: LINE-1	Decreased percentage of methylated cytosines in both moderate- and high-exposure groups compared with controls ( $p < 0.05$ ). Those occupationally exposed had decreased %5mC LINE-1 methylation (OR = 0.4; 95% CI: 0.2, 0.8).
10. Xodanihua-Gervacio et al. <sup>40</sup>	2018/Mexico	58 spraying brigade workers (high-exposure group)/120 non-sprayer workers (moderate-exposure group)/23 controls	Cross-sectional	OPs, pyrethroids	Questionnaire (occupational exposure history) Urinary DAPs <sup>a</sup>	Mean (range) of total DAPs (ng/mL): Ref = 33.5 (24.6–41.3); moderate-exposure group = 58.5 (24.5–353.3); high-exposure group = 122.5 (25.6–488.4)	Cytogenetic damage: MN, NBUDs, NPBs Oxidative stress: GPx, GR, SOD, CAT	No differences in MN frequency between exposed workers and controls. A marginal decrease in SOD and CAT activities was observed in the high-exposure group compared with the reference group.
11. Herrera-Moreno et al. <sup>41</sup>	2019/Mexico	60 spraying brigade workers (high-exposure group)/126 pesticide distributors or occasional farmworkers (moderate-exposure group)/102 controls	Cross-sectional	OPs	Questionnaire (occupational exposure history) Urinary DAPs <sup>a</sup>	Mean (range) of total DAPs (ng/mL): Ref = 33.5 (24.6–41.3); moderate-exposure group = 58.5 (24.5–353.3); high-exposure group = 122.5 (25.6–488.4)	DNA methylation: CDKN2B, CDKN2A	Lower DNA methylation of CDKN2B gene in both pesticide-exposed groups compared with controls ( $p < 0.001$ ); higher methylation of the CDKN2A promoter in the moderate-exposure group compared with controls ( $p < 0.001$ ). Association between pesticide exposure and methylation pattern in CDKN2B ( $\beta = 0.03$ ; $p < 0.01$ and $\beta = 0.04$ ; $p < 0.01$ for moderate and high-exposure groups, respectively) and CDKN2A ( $\beta = 1.5$ ; $p < 0.01$ for moderate-exposure group).
12. Paredes-Céspedes et al. <sup>48</sup>	2019/Mexico	164 urban mestizo sprayers/189 indigenous persons without occupational pesticide exposure/91 mestizo individuals without occupational pesticide exposure (reference group)	Cross-sectional	OPs	Questionnaire (past and present pesticide exposure) Urinary DAPs	Mean (range) of total DAPs (ng/μL): Ref = 34.10 (24.58–41.32); mestizo sprayers = 107.64 (24.45–488.40); indigenous group = 44.60 (15.68–147.70)	DNA methylation: %5mC of WRAP53 <sup>a</sup> gene	Increased %5mC in CpG sites 1 and 2 in mestizo sprayers compared with reference and indigenous groups ( $p < 0.05$ ). Lower %5mC among indigenous group for CpG site 3 compared with reference and mestizo sprayer groups ( $p < 0.05$ ). No correlations between total urinary DAP concentrations and %5mC in any group. Among the two mestizo groups, self-reported use of deltamethrin was associated with decreased odds of having %5mC levels above the GM (OR = 0.2; 95% CI: 0.5, 0.9), and self-reported use of temephos was associated with increased odds of having %5mC levels above the GM (OR = 2.8; 95% CI: 1.3, 5.7).
13. Butinof et al. <sup>62</sup>	2019/Argentina <sup>b</sup>	47 pesticide applicators/52 unexposed controls	Cross-sectional	OPs, CBs	Questionnaire (occupational exposure history) Blood BChE <sup>a</sup>	Not applicable	DNA damage: comet assay Cytogenetic damage: CAs, MN	Higher CA and MN frequencies and DNA damage in pesticide applicators compared with unexposed ( $p < 0.01$ for each).
14. Bernieri et al. <sup>63</sup>	2020/Brazil	12 male soybean growers/12 unexposed control males	Cross-sectional	OPs	Questionnaire (occupational history) Blood BChE (measured in samples collected during periods of high and low exposure in the same year) <sup>a</sup>	Not applicable	DNA damage (measured in samples collected during periods of high and low exposure in the same year): comet assay	DNA damage index higher in soybean growers during high exposure period compared with the low exposure period and with controls ( $p < 0.01$ for each). No correlation between exposure time and DNA damage.
15. Alausa et al. <sup>65</sup>	2019/Argentina	30 pesticide applicators/22 unexposed controls	Cross-sectional	OPs, carbamates	Questionnaire (occupational and environmental exposure history) Blood BChE <sup>a</sup>	Not applicable	DNA damage: comet assay Cytogenetic damage: CA, MN	Higher mean CA, MN, and DNA fragmentation values ( $p < 0.05$ ) in pesticide applicators than in unexposed controls.

Table 2. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
16. Valencia-Quintana et al. <sup>64</sup>	2021/Mexico	54 farmworkers/26 unexposed controls	Cross-sectional	OPs, carbamates	Questionnaire (occupational exposure history) Blood AChE, BChE <sup>a</sup>	Not applicable	DNA damage: comet assay Cytogenetic damage: MN Cytotoxicity: KR, KL, CC, PN	Farmworkers had higher frequency of MN, KR, KL, CC, PN, and all other measured parameters than controls ( $p < 0.01$ for each).
Studies on other pesticides or multiple pesticide classes								
17. Gómez-Arroyo et al. <sup>69</sup>	2013/Mexico	125 children (1–13 years of age) living around areas of intensive agriculture/125 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (residential exposure history)	Not applicable	Cytogenetic damage: MN, BN, NBUDs Cytotoxicity: KL, KR	Exposed children had higher frequency of MN (OR = 3.1; 95% CI: 2.7, 3.5), BN (OR = 4.3; 95% CI: 3.9, 4.6), KL (OR = 2.6; 95% CI: 2.6, 2.7), KR (OR = 17.8; 95% CI: 14.8, 20.8), and NBUDs (OR = 1.5; 95% CI: 1.5, 1.8) than controls.
18. Bernardi et al. <sup>50</sup>	2015/Argentina	50 children (4–14 years of age) living near pesticide application areas/25 controls	Cross-sectional	OPs, pyrethroids, glyphosate	Questionnaire (residential exposure history)	Not applicable	Cytogenetic damage: MN	Children living $\leq 500$ m from pulverized areas had higher frequency of MN ( $p < 0.05$ ) than children living $> 500$ m and controls ( $> 3,000$ m).
19. Barrón Cuenca et al. <sup>55</sup>	2015/Bolivia	41 children with chronic malnourishment/14 cases $\leq 3$ years of age	Cross-sectional	Multiple pesticide classes	Questionnaire (maternal occupational exposure history)	Not applicable	Cytogenetic damage: MN	Null associations between pesticide exposure and markers of cytogenetic damage.
20. Cusiñeda-Yslas et al. <sup>51</sup>	2016/Mexico	34 children of farmworkers (4–11 years of age)/38 child controls (7–14 years of age)/37 female farmworkers/35 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational and parental exposure history)	Not applicable	Cytogenetic damage: MN, BN, NBUDs, NA, LN Cytotoxicity: KR, KL, CC, PN	Frequencies of MN ( $p < 0.001$ ), LN ( $p < 0.001$ ), and CC ( $p < 0.001$ ) were higher, and PN ( $p = 0.004$ ) lower in children of farmworkers than in children of controls. Higher MN ( $p < 0.001$ ) and CC ( $p = 0.04$ ), and lower PN ( $p < 0.001$ ) frequencies in female farmworkers than controls.
21. Nascimento et al. <sup>52</sup>	2017/Brazil <sup>b</sup>	40 children (6–12 years of age) living near a tobacco-producing region	Prospective cohort	Multiple pesticide classes	Questionnaire (parental and seasonal exposure history)	Not applicable	Oxidative damage: MDA, PCO, vitamin C	MDA, PCO, and vitamin C ( $p < 0.05$ ) were higher at the beginning of application period than at leaf harvest period.
22. Ruiz-Guzmán et al. <sup>30</sup>	2017/Colombia	50 children (5–15 years of age) from agricultural villages/13 controls from nearby city	Cross-sectional	OPs, pyrethroids, atrazine, bipyrifol	Blood AChE, BChE <sup>a</sup> Questionnaire (parental and residential exposure history) Urinary ATZ and its metabolites ADI and ADDI	Mean $\pm$ SD ( $\mu\text{g/g creatinine}$ ): Pelayito: ATZ = $18.6 \pm 4.3$ ; ADI = $3.5 \pm 4.6$ ; ADDI = $16.8 \pm 10.0$ ; Aguas Negras: ADDI = $154.6 \pm 32.5$	Cytogenetic damage: MN, NBUDs, apoptotic cells	Null associations of urinary ATZ and its metabolites with MN, NBUDs, or apoptotic cells.
23. Quintana et al. <sup>54</sup>	2017/Argentina <sup>64,65</sup>	151 mother–newborn pairs living in a rural area/38 mother–newborn pairs from an urban area (controls)	Cross-sectional	OPs	Questionnaire (residential and seasonal exposure history) Cord blood AChE, BChE <sup>a</sup>	Not applicable	DNA damage: comet assay Oxidative stress: SOD, CAT	DNA damage index was higher in RG-SS than controls ( $p < 0.01$ ), but not significantly different between RG-SS and RG-NSS. SOD activity was lower in RG-SS compared with RG-NSS and controls ( $p = 0.01$ ).
24. Leite et al. <sup>53</sup>	2019/Paraguay	43 children (5–10 years of age) living in agricultural community surrounded by transgenic soy bean crops/41 children living in agricultural community using biological control of pests	Cross-sectional	Multiple pesticide classes	Questionnaire Blood AChE <sup>a</sup>	Not applicable	DNA damage: comet assay Cytogenetic damages: MN, BN, BE Cytotoxicity: KR, KL, CC, PN	Higher MN, BN, BE, KR, KL, PN, and CC in exposed group compared with control group ( $p < 0.01$ for each). Higher mean values of tail length and tail movement among exposed vs. unexposed group ( $p < 0.01$ for each).
Studies in adults								
25. Jøes et al. <sup>69</sup>	2007/Bolivia	48 farmworkers/33 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	DNA damage: comet assay Cytogenetic damage: CAs	Higher DNA damage and frequencies of CAs in farmworkers than in controls ( $p < 0.001$ ). Number of CAs increased with the intensity of pesticide exposure.
26. Kahdy et al. <sup>70</sup>	2007/Brazil	29 sanitation workers/30 controls	Cross-sectional	OPs, pyrethroids, rodenticides	Questionnaire (occupational exposure history)	Not applicable	Cytogenetic damages: MN, NPBs, APOP, NECR, NDI	Higher frequencies of MN, NB, and NECR in sanitation workers than in controls ( $p < 0.01$ ). No difference in APOP frequency between groups. NDI was lower in the sanitation workers than controls ( $p < 0.01$ ).
27. da Silva et al. <sup>86</sup>	2008/Brazil	108 vineyard farmworkers/65 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	DNA damage: comet assay Cytogenetic damage: MN, BNMN	Higher BNMN frequency, DI, and DF in farmworkers compared with controls ( $p \leq 0.001$ ). Higher MN frequency in <i>PON1 Gln/Gln</i> individuals in the exposed group, compared with <i>PON1 Arg/Arg</i> in the exposed group ( $p \leq 0.05$ ).

Table 2. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
28. Simoniello et al. <sup>91</sup>	2008/Argentina	27 pesticide applicator farmworkers/27 non-pesticide applicator farmworkers/30 controls	Cross-sectional	Multiple pesticide classes	Occupation (pesticide applicator farmworker, non-pesticide applicator farmworker, non-farmworker)	Not applicable	DNA damage: comet assay, damage index repair assay	Pesticide applicators and non-applicator farmworkers had higher DNA damage than unexposed controls ( $p < 0.01$ ).
29. Bortoli et al. <sup>92</sup>	2009/Brazil	29 farmworkers/37 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Cytogenetic damage: MN	Significantly higher mean MN frequency in farmworkers than in controls ( $p < 0.01$ ).
30. Martínez-Valenzuela et al. <sup>93</sup>	2009/Mexico	70 farmworkers/70 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Cytogenetic damage: SCE, MN, NA, CPK	Significantly higher mean SCE and MN frequencies in farmworkers than in controls ( $p < 0.01$ for each).
31. Remor et al. <sup>94</sup>	2009/Brazil <sup>b</sup>	37 farmworkers/20 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	DNA damage: comet assay	Higher DI ( $p \leq 0.001$ ) and DF ( $p \leq 0.005$ ) in farmworkers than in controls. MN frequencies were not different between groups.
32. Simoniello et al. <sup>95</sup>	2010/Argentina	45 farmworkers applicator/50 farmworkers non-applicator/50 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood BChE <sup>a</sup>	Not applicable	DNA damage: comet assay	Increased TBARS levels among farmworkers directly exposed ( $p < 0.001$ ) but not among those indirectly exposed. CAT reduction in both exposed groups respect to controls ( $p = 0.005$ and $p < 0.001$ , respectively). IDEC and IDER increased in both exposed groups ( $p < 0.001$ ).
33. Paz-y-Miño et al. <sup>105</sup>	2011/Ecuador	92 exposed from communities with aerial spraying/90 controls	Cross-sectional	GLY	Questionnaire (residence exposure history)	Not applicable	Cytogenetic damage: CAs, karyotype	Levels of cytogenetic damage and DNA alterations were similar between groups.
34. Payán-Rentería et al. <sup>96</sup>	2012/Mexico <sup>b</sup>	25 farmworkers and applicators/21 controls	Cross-sectional	OCs, OPs, herbicides	Medical examination Questionnaire (occupational exposure history)	Not applicable	DNA damage	Higher circulating DNA fragments ( $p < 0.001$ ) in farmworkers than in controls.
35. Benedetti et al. <sup>97</sup>	2013/Brazil	81 farmworkers/46 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood AChE <sup>a</sup> Blood BChE <sup>a</sup>	Not applicable	DNA damage: comet assay Cytogenetic damage: MN, BN, NBUDs Cytotoxicity: CC, KR, KL	Farmworkers had higher DNA damage ( $p < 0.01$ ), frequency of MN ( $p < 0.001$ ), NBUDs ( $p < 0.010$ ), BN ( $p < 0.01$ ), and cell death (CC, $p < 0.05$ ; KR, $p < 0.01$ , and KL, $p < 0.05$ ) compared with controls.
36. Khayat et al. <sup>71</sup>	2013/Brazil	41 farmworkers/32 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	DNA damage: comet assay Cytogenetic damage: MN	Higher MN ( $p < 0.0001$ ) and BN frequencies ( $p < 0.0001$ ), %DNA in the tail ( $p < 0.05$ ), TM ( $p < 0.05$ ), OTM ( $p < 0.05$ ) in farmworkers than controls, but not in TL ( $p < 0.05$ ).
37. Varona-Urbe et al. <sup>106</sup>	2014/Colombia	223 farmworkers	Cross-sectional	OCs, OPs, CBs, fungicides	Blood OPs: bromophos-ethyl, bromophos-methyl, chlorpyrifos, dimethoate, malathion, methamidophos, methyl parathion, pirimiphos, profenofos Blood CBs: aminocarb, bendiocarb, metolcarb, pirimicarb, propoxur Blood OCs: BHC, HCB, heptachlor, heptachloro epoxide, chlordane, endosulfan, DDT DDE, carbofuran, mirex Urinary	Median (P25–P75) (ng/mL): Bromophos-ethyl = 1 (1–62), bromophos-methyl = 1 (1–97), chlorpyrifos < LOD, dimethoate = 0 (0–14.3), malathion = 1 (1–39), methamidophos = 1 (1–60), methyl parathion = 1 (1–16), pirimiphos < LOD, profenofos = 1 (1–64), bendiocarb = 0 (0–14.3), pirimicarb < LOD, metolcarb < LOD, ETU = 0, $\alpha$ -BCH = 2.4 (2–6.7), $\beta$ -BCH = 0 (0–18.9), HCB = 1.8 (1.5–15.6), heptachlor = 25.5 (8.1–43.7), heptachloro epoxide = 0 (0–10.4), $\alpha$ -chlordane = 8.6 (0–15.3), $\gamma$ -chlordane = 0 (0–5.1), oxychlordane = 16.1 (13.6–22.4), $\alpha$ -endosulfan = 0 (0–5.3), $\beta$ -endosulfan = 50 (5–66), endosulfan sulfate = 11.7 (3.2–27.5), 2,4-DDT = 17.1 (14.5–27.5), 4,4-DDE = 24.6 (2.2–31), carbofuran < LOD, mirex = 0 (0–107)	Higher concentrations of $\alpha$ -BHC, $\beta$ -BHC, and HCB (as a mixture) ( $\beta = 1.21$ ; 95% CI: 0.33, 2.10) and of pirimiphos-methyl, malathion, bromophos-methyl, and bromophos-ethyl (as a mixture) ( $\beta = 11.97$ ; 95% CI: 2.34, 21.60) were associated with higher DNA damage and comet tail length, respectively.	



**Table 2.** (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
38. Adad et al. <sup>58</sup>	2015/Brazil <sup>b</sup>	80 men farmworkers from state association/20 men farmworker from a private company/100 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood BChE <sup>a</sup>	Not applicable	Cytogenetic damage: MN, BN Cytotoxicity: KR, KL	Higher frequencies of MN ( $p < 0.001$ ), KR (state group $p < 0.001$ ; private group $p < 0.01$ ), KL (both exposed groups $p < 0.001$ ), and BN cells (both exposed groups $p < 0.01$ ) in both exposed groups than in controls.
39. Wilhelm et al. <sup>72</sup>	2015/Brazil	37 floriculturists/37 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	DNA damage: comet assay Cytogenetic damage: MN, NBUDs, BN Cytotoxicity: KR	MN, NBUDs, BN, and KR frequencies were similar between exposed and controls. Higher DNA damage in the exposed compared with controls ( $p < 0.001$ for DI and DP).
40. Alves et al. <sup>73</sup>	2016/Brazil <sup>b</sup>	77 tobacco farmworkers/60 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Cytotoxicity: KR DNA damage: comet assay	MN frequency, DP, and DI were higher in farmworkers than controls ( $p < 0.01$ ). Higher SOD activity in exposed relative to unexposed group ( $p = 0.001$ ). Higher MN frequency in <i>PON1 Glu/Gln</i> individuals in the exposed group, compared with <i>PON1 Arg/-</i> individuals in the exposed group ( $p < 0.01$ ).
41. Kahl et al. <sup>74</sup>	2015/Brazil	62 tobacco farmworkers/62 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	aTL Oxidative stress: TBARS, TEAC Cytogenetic damage: CAs	Farmworkers had higher TEAC ( $p < 0.001$ ) and TBARS ( $p < 0.05$ ), but lower aTL ( $\beta = -14.4$ , SE = 3.2) than controls.
42. Bianco et al. <sup>89</sup>	2017/Argentina	76 farmworkers/53 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood AChE <sup>a</sup>	Not applicable	Cytogenetic damage: CAs	Farmworkers had higher CAs frequency ( $p < 0.001$ ) than controls.
43. Chaves et al. <sup>75</sup>	2017/Brazil	97 farmworkers/55 controls	Cross-sectional	CBs, OPs, pyrethroids	Questionnaire (occupational and lifestyle exposures history)	Not applicable	Cytogenetic damage: CAs, MN	Increased frequency of CAs ( $p < 0.05$ ) and MN ( $p < 0.05$ ) in farmworkers than in controls.
44. Hilgert Jacobsen-Pereira et al. <sup>60</sup>	2018/Brazil	50 farmworkers/46 controls from the same agricultural area/29 controls from urban area	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood AChE, BChE <sup>a</sup>	Not applicable	DNA damage: comet assay. Cytogenetic damage: MN, NBUDs, NPBs Oxidative stress: TBARS, CAT activity	Higher DI ( $p < 0.001$ ), MN ( $p < 0.005$ ), NBUD ( $p < 0.005$ ), and NPB ( $p < 0.001$ ) frequencies in farmworkers than controls. TBARS level was higher in exposed and in rural controls than urban controls. CAT activity was similar among groups.
45. Tomiazzi et al. <sup>76</sup>	2017/Brazil	30 nonfarmer smokers/30 nonsmoker farmworkers/30 smokers and farmworkers/30 controls	Cross-sectional	OPs, pyrethroids, glyphosate	Questionnaire (occupational exposure history)	Not applicable	Cytogenetic damage: MN, BNMN Cytotoxicity: KR, CC	MN frequency and the total cytogenetic abnormalities were higher in all exposed groups than in controls ( $p < 0.05$ ).
46. Vazquez-Boucard et al. <sup>77</sup>	2017/Mexico	107 consumers of well or tap water/40 consumers of bottled water (controls)	Case-control	OCs, OPs, neonics	Questionnaire (occupational exposure history) Regional water sampling	Not applicable	DNA damage: comet assay	Higher DNA damage in those who consumed well or tap water than in control group ( $p < 0.001$ ). Individuals who consumed well or tap water and worked in agriculture had higher DNA damage than controls ( $p < 0.001$ ).
47. Marcedino et al. <sup>90</sup>	2017/Brazil	18 farmworkers/18 unexposed controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	DNA damage: comet assay Cytogenetic damage: MN	Significantly higher DNA and cytogenetic damage in exposed group compared with unexposed group ( $p < 0.01$ for each).
48. Hutter et al. <sup>78</sup>	2018/Dominican Republic	38 exposed farmworkers/33 control farmworkers	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Cytogenetic damage: MN, BUD, BN Cytotoxicity: CC, KR, KL, PN	All cytogenetic damage and cytotoxicity biomarkers were more frequent among farmworkers: MN (OR = 4.0; 95% CI: 1.3, 7.4), total MN (OR = 2.5; 95% CI: 1.2, 5.2), BUD (OR = 1.9; 95% CI: 1.5, 2.5), BN (OR = 1.4; 95% CI: 1.2, 1.7), CC (OR = 1.3; 95% CI: 1.1, 1.6), KR (OR = 1.2; 95% CI: 1.0, 1.4), KL (OR = 1.3; 95% CI: 1.1, 1.5), PN (OR = 4.5; 95% CI: 2.5, 8.2).
49. Kahl et al. <sup>80</sup>	2018/Brazil	56 tobacco farmworkers/74 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	DNA damage: comet assay Telomere length Oxidative stress: TEAC, TBARS DNA methylation: global and p16 methylation	Farmworkers had higher DNA damage ( $p < 0.001$ ), lower percentage global DNA methylation, shorter telomeres ( $p < 0.001$ ), and p16 hypermethylation ( $p = 0.003$ ) compared with controls.

Table 2. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
50. Carelan et al. <sup>88</sup>	2018/Brazil <sup>88</sup>	84 farmworkers who used pesticides/68 farmworkers who did not use pesticides	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Cytogenetic damage: MN Oxidative stress: CAT, GPx, GSH, SOD, TBARS, carbonylated protein levels	Lower mean TBARS ( $p=0.02$ ), GPx ( $p<0.01$ ), GSH ( $p<0.01$ ), and SOD ( $p<0.01$ ) values in farmworkers who did not use pesticides than in those who did use pesticides. No differences in MN frequency between groups.
51. Kahl et al. <sup>89</sup>	2018/Brazil	40 tobacco farmworkers/40 unexposed controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Cytogenetic damage: MN, NPB, NBUDs Telomere length DNA methylation: global <i>MTHFR</i> and <i>TERT</i> genotypes	Higher frequencies of MN, NPB, NBUD, and binucleated cells in farmworkers than controls ( $p<0.001$ for each). Shorter telomere length ( $p=0.02$ ) and lower DNA global methylation levels ( $p<0.01$ ) in exposed group. Allele and genotype frequencies of <i>MTHFR</i> gene were different between exposed and unexposed groups ( $p<0.01$ ). No differences between groups for <i>TERT</i> polymorphism frequencies.
52. Claudio et al. <sup>79</sup>	2019/Brazil	21 male banana farmworkers/20 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Cytogenetic damage: MN Cytotoxicity: PN, KR, KL	Higher MN and KR frequencies in farmworkers than controls ( $p=0.05$ for both), but KL and PN were similar between groups.
53. de Oliveira et al. <sup>101</sup>	2019/Brazil	76 soybean farmworkers/72 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history). Blood BCE <sup>92</sup>	Not applicable	Cytogenetic damage: MN, BN, NBUDs Cytotoxicity: PN, KR, KL, CC Telomere length <i>XCCRI1 TrpL</i> and <i>PON1 ArgL</i> genes	Increased cytogenetic damage (MN and NBUDs $p<0.001$ ; BN $p<0.05$ ) and cell death (CC and KR $p<0.001$ ) in the exposed group compared with controls. Telomere length was similar in both groups. Higher frequencies of BN cells in farmworkers ( $p=0.03$ ), and NBUDs in controls ( $p=0.04$ ) belonging to those carrying <i>XCCRI1 TrpL</i> and <i>PON1 ArgL</i> genes.
54. Arévalo-Jaramillo et al. <sup>81</sup>	2019/Ecuador <sup>81</sup>	62 women living in 2 agricultural communities/53 unexposed women from control community	Cross-sectional	Multiple pesticide classes	Questionnaire	Not applicable	Cytogenetic damage: MN, NBUDs, notched cells, BN Cytotoxicity: PK, KL, KR, CC	Lower BN ( $p<0.01$ ) and higher KL ( $p=0.05$ ) and KR ( $p=0.05$ ) among those in the first agricultural community compared with controls. Higher NBUDs ( $p=0.05$ ) and notched cells ( $p<0.01$ ) among those in the second agricultural community compared with the controls. Mean MN not statistically different between controls and exposed groups. Increased frequency of KL, KR, and CC cells among individuals with genetic polymorphisms in <i>PON1</i> and <i>GSTP1</i> genes.
55. Barrón Cuenca et al. <sup>82</sup>	2019/Bolivia	297 men and women (17–70 years of age) from three agricultural communities	Cross-sectional	Fungicides, OPs, pyrethroids, herbicides	Questionnaire (occupational history) Urinary metabolites of: tebuconazole, chlorpyrifos, permethrin, cypermethrin, cyfluthrin, phenoxo herbicides, bifenthrin, thiafenozole, pyrimethanil	Mean (IQR) of pesticide metabolites (ng/mL) in total population: TEB-OH = 3.18 (0.2–1.4); TCPy = 17.6 (3.1–12.2); 3-BPA = 3.2 (1.0–3.4); DCCA = 3.0 (1.1–4.8); 2,4-D = 15.8 (0.2–0.8); MCPA = 0.05 (<LOD); CFCA = 0.4 (<LOD–0.3); 4F3BPA = 0.1 (<LOD); 5-OH-TBZ = 0.08 (<LOD); OH-PYR = 2.5 (<LOD)	DNA damage Cytogenetic damage: MN	Increased MN frequency among those with $\geq 8$ y active farming compared with those with <8 y active farming. Days of active spraying per month was not associated with genotoxic damage. Increased odds of DNA strand breaks among those with high exposure to 2,4-D (OR = 2.0; 95% CI: 1.1, 3.6 for tail movement and OR = 1.8; 95% CI: 1.0, 3.1 for %DNA in tail). Decreased odds of DNA strand breaks among those with high exposure to pyrethroids (OR = 0.5; 95% CI: 0.3, 0.9 for %DNA in tail and OR = 0.5; 95% CI: 0.3, 1.0 for tail movement). High exposure to certain mixtures of pesticides (containing mainly 2,4-D or cyfluthrin) was associated with increased DNA strand breaks, but not increased chromosomal aberrations ( $p<0.05$ ). Higher levels of DNA strand breaks among participants with certain <i>GSTM1</i> genotypes.
56. Cepeda et al. <sup>83</sup>	2020/Colombia	5 farmers/5 unexposed controls	Cross-sectional	Multiple pesticide classes	Questionnaire (pesticide exposure history)	Not applicable	Cytogenetic damage: CA, chromosomal instability	Increased total clonal and non-clonal CAs were observed in pesticide-exposed individuals compared with unexposed individuals ( $p<0.01$ ). Higher frequency of fragilities and chromatid/chromosomal breakage in exposed group compared with unexposed group ( $p<0.01$ for each).
57. Hunter et al. <sup>84</sup>	2021/Ecuador	34 male farmworkers engaged in conventional farming/37 male unexposed controls engaged in ecological farming	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Cytogenetic damage: MN, BUD, BN Cytotoxicity: CC, KR, KL, PK, basal cells	Compared with controls working on ecological farms, those working on conventional farms had higher frequency of MN, BUD, BN, KR, CC, and KL ( $p<0.01$ for each).

Table 2. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
58. Salazar-Flores et al. <sup>85</sup>	2020/Mexico	113 farmworkers/93 unexposed controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Oxidative stress: GSH, GSSG, GSH/GSSG ratio, carbonyl groups in proteins, nitrites–nitrites, lipoperoxides, membrane fluidity	Lower levels of GSH, GSSG, carbonyl groups in proteins, nitrites–nitrites, lipoperoxides, and membrane fluidity among farmworkers compared with unexposed controls ( $p < 0.01$ for each). No differences in most markers of oxidative stress between farmworkers and controls when farmworkers were grouped in four exposure categories.
59. Lovison Sasso et al. <sup>102</sup>	2021/Brazil <sup>b</sup>	50 male farmworkers/50 male controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood BChE <sup>a</sup>	Not applicable	Oxidative stress: GSH, CAT, GR, GPx, SOD, TBARS, carbonylated protein levels	Lower SOD, CAT, GSH, GR, and GPx activity, but higher TBARS and carbonylated protein levels, among exposed group compared with controls ( $p < 0.05$ for each).
60. de Souza Espindola Santos et al. <sup>87</sup>	2021/Brazil	52 farmworkers/68 non-farmworkers	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Oxidative stress: CAT, SOD, thiols, GST, GPx, GR, 8-ISO	No differences in biomarkers of oxidative stress between farmworkers and non-farmworkers.
61. Filippi et al. <sup>103</sup>	2021/Argentina <sup>b</sup>	47 pesticide applicators/53 unexposed controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood HCB, HCH, endosulfan, DDE, DDT, AChE, BChE <sup>a</sup>	Not applicable	DNA damage: comet assay Cytogenetic damage: SCE, CA, MN	Pesticide applicators had more DNA damage, as well as higher SCE, CA, MN frequencies, compared with controls ( $p < 0.01$ for each).
62. Mañas et al. <sup>104</sup>	2021/Argentina	41 adults living in area of intensive agricultural production (<1,000 m from sprayed fields)/24 unexposed adults (>1,000 m from sprayed fields)	Cross-sectional	Multiple pesticide classes	Residential proximity to agricultural fields	Not applicable	Cytogenetic damage: CAs, BNMN	Higher frequencies of CAs and BNMN in exposed group compared with unexposed group ( $p < 0.05$ for each). Among exposed group, higher CAs among those living $\leq 500$ m from fields compared with those living $> 500$ m ( $p < 0.05$ ).

None; %5mC, percentage 5mC; %DNA, percentage DNA; 2,4-D, 2,4-dichlorophenoxy acetic acid; 8-ISO, 8-isoprostane; 3-BPA, 3-phenoxybenzoic acid; 4FBPA, 4-fluoro-3-phenoxybenzoic acid; 5-OH-TBZ, 5-hydroxytribenzazole; AChE, acetylcholinesterase; ADI, atrazine desionyl; ADDI, atrazine desethyl-desionyl; APOF, apoptotic cells; AT, apoptosis; BChE, butyrylcholinesterase; BE, benzo[e]pyrene hexachloride; BN, binucleated cells; BNMN, binucleated cells with micronuclei; BUD, nuclear buds and broken eggs; CAs, chromosomal aberrations; CAT, catalase; CBs, carbamates; CC, condensed chromatin; CCL3, cyclin dependent kinase inhibitor 2B; CFCA, chloroform; CYP1A1, cytochrome P-450 1A1; CYP1B1, cytochrome P-450 1B1; CYP2D6, cytochrome P-450 2D6; CYP2E1, cytochrome P-450 2E1; CYP3A4, cytochrome P-450 3A4; CYP3A5, cytochrome P-450 3A5; CYP3A6, cytochrome P-450 3A6; CYP3A7, cytochrome P-450 3A7; CYP3A8, cytochrome P-450 3A8; CYP3A9, cytochrome P-450 3A9; CYP3A10, cytochrome P-450 3A10; CYP3A11, cytochrome P-450 3A11; CYP3A12, cytochrome P-450 3A12; CYP3A13, cytochrome P-450 3A13; CYP3A14, cytochrome P-450 3A14; CYP3A15, cytochrome P-450 3A15; CYP3A16, cytochrome P-450 3A16; CYP3A17, cytochrome P-450 3A17; CYP3A18, cytochrome P-450 3A18; CYP3A19, cytochrome P-450 3A19; CYP3A20, cytochrome P-450 3A20; CYP3A21, cytochrome P-450 3A21; CYP3A22, cytochrome P-450 3A22; CYP3A23, cytochrome P-450 3A23; CYP3A24, cytochrome P-450 3A24; CYP3A25, cytochrome P-450 3A25; CYP3A26, cytochrome P-450 3A26; CYP3A27, cytochrome P-450 3A27; CYP3A28, cytochrome P-450 3A28; CYP3A29, cytochrome P-450 3A29; CYP3A30, cytochrome P-450 3A30; CYP3A31, cytochrome P-450 3A31; CYP3A32, cytochrome P-450 3A32; CYP3A33, cytochrome P-450 3A33; CYP3A34, cytochrome P-450 3A34; CYP3A35, cytochrome P-450 3A35; CYP3A36, cytochrome P-450 3A36; CYP3A37, cytochrome P-450 3A37; CYP3A38, cytochrome P-450 3A38; CYP3A39, cytochrome P-450 3A39; CYP3A40, cytochrome P-450 3A40; CYP3A41, cytochrome P-450 3A41; CYP3A42, cytochrome P-450 3A42; CYP3A43, cytochrome P-450 3A43; 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CYP3A76, cytochrome P-450 3A76; CYP3A77, cytochrome P-450 3A77; CYP3A78, cytochrome P-450 3A78; CYP3A79, cytochrome P-450 3A79; CYP3A80, cytochrome P-450 3A80; CYP3A81, cytochrome P-450 3A81; CYP3A82, cytochrome P-450 3A82; CYP3A83, cytochrome P-450 3A83; CYP3A84, cytochrome P-450 3A84; CYP3A85, cytochrome P-450 3A85; CYP3A86, cytochrome P-450 3A86; CYP3A87, cytochrome P-450 3A87; CYP3A88, cytochrome P-450 3A88; CYP3A89, cytochrome P-450 3A89; CYP3A90, cytochrome P-450 3A90; CYP3A91, cytochrome P-450 3A91; CYP3A92, cytochrome P-450 3A92; CYP3A93, cytochrome P-450 3A93; CYP3A94, cytochrome P-450 3A94; CYP3A95, cytochrome P-450 3A95; CYP3A96, cytochrome P-450 3A96; CYP3A97, cytochrome P-450 3A97; CYP3A98, cytochrome P-450 3A98; CYP3A99, cytochrome P-450 3A99; CYP3A100, cytochrome P-450 3A100; CYP3A101, cytochrome P-450 3A101; CYP3A102, cytochrome P-450 3A102; CYP3A103, cytochrome P-450 3A103; CYP3A104, cytochrome P-450 3A104; CYP3A105, cytochrome P-450 3A105; CYP3A106, cytochrome P-450 3A106; CYP3A107, cytochrome P-450 3A107; CYP3A108, cytochrome P-450 3A108; CYP3A109, cytochrome P-450 3A109; CYP3A110, cytochrome P-450 3A110; CYP3A111, cytochrome P-450 3A111; CYP3A112, cytochrome P-450 3A112; CYP3A113, cytochrome P-450 3A113; CYP3A114, cytochrome P-450 3A114; CYP3A115, cytochrome P-450 3A115; CYP3A116, cytochrome P-450 3A116; CYP3A117, cytochrome P-450 3A117; CYP3A118, cytochrome P-450 3A118; CYP3A119, cytochrome P-450 3A119; CYP3A120, cytochrome P-450 3A120; CYP3A121, cytochrome P-450 3A121; CYP3A122, cytochrome P-450 3A122; CYP3A123, cytochrome P-450 3A123; CYP3A124, cytochrome P-450 3A124; CYP3A125, cytochrome P-450 3A125; CYP3A126, cytochrome P-450 3A126; CYP3A127, cytochrome P-450 3A127; CYP3A128, cytochrome P-450 3A128; CYP3A129, cytochrome P-450 3A129; CYP3A130, cytochrome P-450 3A130; CYP3A131, cytochrome P-450 3A131; CYP3A132, cytochrome P-450 3A132; CYP3A133, cytochrome P-450 3A133; CYP3A134, cytochrome P-450 3A134; CYP3A135, cytochrome P-450 3A135; CYP3A136, cytochrome P-450 3A136; CYP3A137, cytochrome P-450 3A137; CYP3A138, cytochrome P-450 3A138; CYP3A139, cytochrome P-450 3A139; CYP3A140, cytochrome P-450 3A140; CYP3A141, cytochrome P-450 3A141; CYP3A142, cytochrome P-450 3A142; CYP3A143, cytochrome P-450 3A143; CYP3A144, cytochrome P-450 3A144; CYP3A145, cytochrome P-450 3A145; CYP3A146, cytochrome P-450 3A146; CYP3A147, cytochrome P-450 3A147; CYP3A148, cytochrome P-450 3A148; CYP3A149, cytochrome P-450 3A149; CYP3A150, cytochrome P-450 3A150; CYP3A151, cytochrome P-450 3A151; CYP3A152, cytochrome P-450 3A152; CYP3A153, cytochrome P-450 3A153; CYP3A154, cytochrome P-450 3A154; CYP3A155, cytochrome P-450 3A155; CYP3A156, cytochrome P-450 3A156; CYP3A157, cytochrome P-450 3A157; CYP3A158, cytochrome P-450 3A158; CYP3A159, cytochrome P-450 3A159; CYP3A160, cytochrome P-450 3A160; CYP3A161, cytochrome P-450 3A161; CYP3A162, cytochrome P-450 3A162; CYP3A163, cytochrome P-450 3A163; CYP3A164, cytochrome P-450 3A164; CYP3A165, cytochrome P-450 3A165; CYP3A166, cytochrome P-450 3A166; CYP3A167, cytochrome P-450 3A167; CYP3A168, cytochrome P-450 3A168; CYP3A169, cytochrome P-450 3A169; CYP3A170, cytochrome P-450 3A170; CYP3A171, cytochrome P-450 3A171; CYP3A172, cytochrome P-450 3A172; CYP3A173, cytochrome P-450 3A173; CYP3A174, cytochrome P-450 3A174; CYP3A175, cytochrome P-450 3A175; CYP3A176, cytochrome P-450 3A1

Investigators did not use exposure biomarker concentrations in multivariate analyses.

<sup>b</sup>Also included in Table 9 (other health effects).

<sup>a</sup>Also included in Table 3 (other health effects).

<sup>d</sup>Also included in Table 8 (birth outcomes and child growth).

In contrast, 2 publications from small cross-sectional studies of children from Colombia<sup>30</sup> and Bolivia<sup>55</sup> reported null associations of maternal occupational pesticide exposure—assessed via questionnaire—and urinary atrazine concentrations with cytogenetic damage.

Thirteen publications from cross-sectional studies examined associations of exposure to OP or carbamate pesticides with cytogenetic or DNA damage in adults, primarily among those occupationally exposed (Table 2). One cross-sectional study assessed OP pesticide exposure via questionnaire only and reported higher DNA damage—quantified via comet assay—among workers compared with controls.<sup>56</sup> The other 12 studies assessed exposure to OP or carbamate pesticides using urinary dialkyl phosphate (DAP) metabolite concentrations or blood cholinesterase (ChE) measurements, but 11 of them evaluated exposure–outcome associations using predetermined categorical exposure variables based on occupation (e.g., high, moderate, and no exposure)<sup>57–65</sup> or residence (e.g., rural or urban).<sup>66</sup> Nine of these 11 publications reported associations with genotoxic outcomes, such as changes in DNA methylation patterns of candidate tumor suppressor genes, among moderate- or high-exposure groups.<sup>57,59,61–67</sup> Two publications reported no differences in markers of cytogenetic or DNA damage between exposed workers and controls.<sup>58,60</sup> The only cross-sectional study that used urinary DAP concentrations in its exposure–outcome analyses reported null associations with DNA methylation but observed group differences when OP pesticide exposure was assessed as a categorical variable.<sup>68</sup>

Thirty-eight publications examined associations of exposure to pesticides other than OCs, OPs, or carbamates or exposure to multiple pesticide classes with genotoxicity among adults (Table 2). Twenty-five publications estimated occupational pesticide exposure using questionnaire data only and all reported associations of exposure to pesticides with increased cytogenetic damage, including higher frequencies of chromosomal aberrations and micronuclei, DNA damage, oxidative stress, or telomere shortening.<sup>69–93</sup> In addition, 10 publications from cross-sectional studies of farmworkers/pesticide applicators and controls assessed pesticide exposure using blood ChE measurements but only evaluated exposure–outcome associations using categorical exposure variables.<sup>94–103</sup> All 10 publications reported that occupational pesticide exposure was associated with higher levels of DNA or cytogenetic damage, such as higher frequencies of chromosomal aberrations, nuclear buds, or cell death. Similarly, a publication from a cross-sectional study in Argentina reported increased cytogenetic damage among those living near agricultural fields (<500 m),<sup>104</sup> whereas a publication from a cross-sectional study in Ecuador reported null associations of residential use of the herbicide glyphosate with chromosomal aberrations frequency and karyogram alterations.<sup>105</sup> Last, a publication from a cross-sectional study of rice field workers in Colombia reported associations of two pesticide mixtures (one mixture of OC pesticides and one of carbamates)—assessed via measurement of pesticide metabolites in blood and urine—with DNA damage.<sup>106</sup>

Overall, studies published to date provide consistent evidence of an association between exposure to different pesticide classes such as OP pesticides and carbamates and genotoxic damage in children and adults living in LAC countries. Notably, most of the studies that have been published were cross-sectional in design, assessed pesticide exposure via questionnaire, and had small sample sizes.

### Neurobehavioral Outcomes

Fifty-four publications, primarily derived from cross-sectional studies, examined the potential neurobehavioral effects of pesticide exposure in children, adolescents, and adults (Table 3). Twelve

of these 53 publications reported on the association between exposure to OC pesticides and child neurodevelopment<sup>107–115</sup>; 6 publications focused on the same Mexican cohort,<sup>107–109</sup> 12–114 5 focused on the same Guadeloupean cohort,<sup>110,111,115–117</sup> and 1 was a cross-sectional study from Brazil. Three publications from the prospective cohort study in Mexico reported that higher prenatal dichlorodiphenyltrichloroethane (DDT) exposure—as indicated by measurement of its primary breakdown product dichlorodiphenyldichloroethylene (DDE) in serum—was associated with lower psychomotor development during the first year of life,<sup>107</sup> poorer verbal and memory skills and a poorer general cognitive index at 3.5–5 years of age,<sup>112</sup> and poorer spatial orientation at 5 years of age.<sup>113</sup> A fourth publication from the same cohort study reported that maternal intake of omega-3 and -6 fatty acids during pregnancy modified the association of prenatal DDT exposure with poorer motor and memory skills at 3.5–5 years of age,<sup>114</sup> whereas 2 other publications from this cohort reported null associations of prenatal DDT exposure with child neurodevelopment at 1 month<sup>109</sup> and at 12–30 months of age.<sup>108</sup> Four publications from the prospective Guadeloupean cohort study reported that higher cord blood concentrations of chlordecone—an OC pesticide that was extensively used in banana plantations in the French West Indies—were associated with impaired cognitive and motor function at 7 months of age,<sup>110</sup> lower fine motor scores at 18 months of age (among boys only),<sup>111,117</sup> and poorer visual contrast sensitivity at 7–8 years of age.<sup>115</sup> A fifth publication from the Guadeloupean cohort study reported null associations of prenatal and childhood chlordecone exposure with sex-typed play behavior at 7 years of age.<sup>116</sup> The one Brazilian cross-sectional study reported that higher concentrations of several OC pesticide metabolites were associated with poorer performance intelligence quotient, resistance to distraction, or processing speed at 6–16 years of age.<sup>118</sup> The only publication that examined the association of OC pesticide exposure—as indicated by measurement of  $\beta$ -hexachlorocyclohexane ( $\beta$ -HCH), DDT, DDE, and dieldrin in serum—with neurodegenerative disorders among adults was from a cross-sectional study conducted in Costa Rica and reported null associations.<sup>119</sup>

Eleven publications examined the association of OP or carbamate pesticides with neurobehavioral outcomes in children or adolescents (Table 3). Six publications from cross-sectional studies in Ecuador reported that children and adolescents who lived in floricultural communities—in which OP pesticides and carbamates are intensively used—or whose mothers worked as floriculturists during pregnancy had adverse neurobehavioral outcomes, including poorer motor or socioindividual skills at 3–61 months of age<sup>120,121</sup>; attention, executive function, and memory deficits at 4–9 years of age (in boys only)<sup>122</sup>; impaired motor coordination, visual performance, and visual memory at 6–8 years of age<sup>123</sup>; and more depression symptoms at 11–17 years of age (particularly among girls).<sup>124,125</sup> In line with these findings, a seventh publication reported that Ecuadorian children 4–9 years of age who were examined sooner after the end of an increased pesticide use period had lower attention/inhibitory control, visuospatial processing, and sensorimotor scores than children examined later.<sup>126</sup> A publication from a cross-sectional study of Chilean school-age children who lived in agricultural communities reported associations of OP pesticide exposure—as indicated by measurement of urinary DAP metabolites—with poorer processing speed.<sup>127</sup> A publication from a prospective cohort study in Mexico reported that prenatal exposure to the OP pesticide chlorpyrifos—assessed by measurement of 3,5,6-trichloro-2-pyridinol (TCPy) in maternal urine samples collected during the third trimester of pregnancy—was associated with increased attention problems in school-age boys and girls.<sup>128</sup> Conversely, two cross-sectional studies found null or protective



**Table 3.** Characteristics of Latin American and the Caribbean studies on pesticide exposure and neurobehavioral outcomes published between 2007 and 2021 (*n* = 54).

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
<b>Studies on OCs</b>								
1. Torres-Sánchez et al. <sup>107</sup>	2007/Mexico	244 mother-child (0–12 months of age) pairs from malaria-endemic zone	Prospective cohort	OCs	Maternal serum DDE before and during each trimester of pregnancy	Geometric mean $\pm$ geometric SD (GSD) (ng/mL): <i>p,p'</i> -DDE: first trimester = 6.4 $\pm$ 2.8; second trimester = 6.8 $\pm$ 2.9; third trimester = 7.8 $\pm$ 2.8	Neurodevelopment: mental and psychomotor development (BSID-II)	Higher DDE during first trimester of pregnancy was associated with lower PDI scores in first year of life ( $\beta$ per 2-fold increase in DDE = -0.5; 95% CI: -1.0, -0.1). Null associations between DDE and MDI scores.
2. Torres-Sánchez et al. <sup>108</sup>	2009/Mexico	270 mother-child (12–30 months of age) pairs	Prospective cohort	OCs	Maternal serum DDE during each trimester of pregnancy	Mean $\pm$ SD (ng/mL): <i>p,p'</i> -DDE: first trimester = 6.3 $\pm$ 3.1; second trimester = 6.5 $\pm$ 3.0; third trimester = 7.9 $\pm$ 2.8; <i>p,p'</i> -DDT: first trimester = 0.008 $\pm$ 2.7; second trimester = 0.006 $\pm$ 2.0; third trimester = 0.006 $\pm$ 2.3	Neurodevelopment: mental and psychomotor development (BSID-II)	Null associations of prenatal DDE with PDI and MDI scores.
3. Bahena-Medina et al. <sup>109</sup>	2011/Mexico	265 mother-child (1 month of age) pairs	Prospective cohort	OCs	Maternal serum DDE during each trimester of pregnancy	Geometric mean $\pm$ geometric SD (GSD) (ng/mL): First trimester: normal reflexes = 6.2 $\pm$ 3.1; one abnormal reflex = 7.1 $\pm$ 2.6; $\geq$ 2; abnormal reflexes = 5.4 $\pm$ 3.2; non-neurological soft signs = 6.0 $\pm$ 3.0; one neurological soft sign = 7.0 $\pm$ 2.9; $\geq$ 2 neurological soft signs = 5.2 $\pm$ 2.2 Second trimester: normal reflexes = 7.5 $\pm$ 2.8; one abnormal reflex = 7.3 $\pm$ 3.1; $\geq$ 2 abnormal reflexes = 4.2 $\pm$ 2.9; non-neurological soft signs = 6.4 $\pm$ 3.1; one neurological soft sign = 7.8 $\pm$ 2.9; $\geq$ 2 neurological soft signs = 5.4 $\pm$ 2.0 Third trimester: normal reflexes = 7.5 $\pm$ 2.7; one abnormal reflex = 8.1 $\pm$ 2.9; $\geq$ 2 abnormal reflexes = 5.1 $\pm$ 3.3; non-neurological soft signs = 7.7 $\pm$ 2.8; one neurological soft sign = 7.0 $\pm$ 3.1; $\geq$ 2 neurological soft signs = 4.3 $\pm$ 2.2	Neurodevelopment: neonatal reflexes (NBAS), neurological soft signs (Graham-Rosenblith scale), mental and psychomotor development (BSID)	Null associations between prenatal DDE exposure and neonatal neurodevelopment.
4. Dallaire et al. <sup>110</sup>	2012/Guadeloupe	153 mother-child (7 months of age) pairs living near banana plantations	Prospective cohort	OCs (chlordecone)	Questionnaire (infant dietary intake history) Cord blood chlordecone Breast milk chlordecone at 3 months	Mean $\pm$ SD chlordecone ( $\mu$ g/L): Cord blood = 0.53 $\pm$ 1.97; breast milk = 1.09 $\pm$ 1.15	Neurodevelopment: visual recognition, memory, and processing speed (FTII, TAC, Brunet-Lezine scale)	Those in the highest tertile of cord blood chlordecone concentrations (classified as concentrations $>$ median) scored lower on the novelty preference test ( $\beta$ = -0.2; 95% CI: -0.4, 0) than those in the second tertile of cord chlordecone concentrations (classified as concentrations $>$ LOD and $\leq$ median) ( $\beta$ = 0.1; 95% CI: -0.3, 0.1). Detectable concentrations of chlordecone in cord blood were associated with increased odds of low fine motor scores (OR = 1.3; 95% CI: 1.1, 1.5). Higher chlordecone concentrations in cord blood were associated with lower fine motor scores among boys ( $\beta$ = -0.32; <i>p</i> = 0.03).
5. Boucher et al. <sup>111</sup>	2013/Guadeloupe	141 mother-child (18 months of age) pairs living near banana plantations	Prospective cohort	OCs (chlordecone)	Questionnaire (infant dietary intake history) Cord blood chlordecone Breast milk chlordecone at 3 months	Mean $\pm$ SD chlordecone ( $\mu$ g/L): Cord blood = 0.41 $\pm$ 0.6; breast milk = 0.93 $\pm$ 0.90	Neurodevelopment: personal-social, communication, problem-solving, fine motor, and gross motor (ASQ-19)	Higher DDE during third trimester of pregnancy was associated with poorer verbal ( $\beta$ per 2-fold increase in DDE = -1.1; 95% CI: -2.2, -0.1), quantitative ( $\beta$ = -2.1; 95% CI: -3.2, -1.0), and memory ( $\beta$ = -1.3; 95% CI: -2.2, -0.3) skills and a poorer general cognitive index ( $\beta$ = -2.0; 95% CI: -3.6, -0.4) at 42–60 months of age.
6. Torres-Sánchez et al. <sup>112</sup>	2013/Mexico	203 mother-child (42–60 months of age) pairs	Prospective cohort	OCs	Maternal serum DDE during each trimester of pregnancy	Median (P10–P90) (ng/g lipid): DDE: first trimester = 1,255.40 (259.26–4,964.21); second trimester = 1,138.16 (154.39–2,857.14); third trimester = 812.75 (153.23–2,919.00); DDT: first trimester = 0.0123 (0.0123–31.48); second trimester = 0.0123 (0.123–2.54); third trimester = 0.0123 (0.123–4.21) Mean $\pm$ SD <i>p,p'</i> -DDE (ng/g lipid): First trimester: female = 1,624 $\pm$ 1,376; male = 1,997 $\pm$ 2,266; second trimester: female = 1,424 $\pm$ 1,494; male = 1,297 $\pm$ 1,194; third trimester: female = 1,434 $\pm$ 1,457; male = 1,121 $\pm$ 1,280	Neurodevelopment: verbal, perceptual performance, quantitative, memory, motor skills, and general cognitive index (MSCA)	Higher DDE during second trimester of pregnancy was associated with poorer spatial orientation ( $\beta$ per 2-fold increase in DDE = -0.2; 95% CI: -0.4, 0.04).
7. Osorio-Valencia et al. <sup>113</sup>	2015/Mexico	167 mother-child (60 months of age) pairs	Prospective cohort	OCs	Maternal serum DDE during each trimester of pregnancy		Neurodevelopment: lateralization and spatial orientation (MSCA)	

Table 3. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
8. Campos et al. <sup>118</sup>	2015/Brazil	46 children (6–16 years of age)	Cross-sectional	OCs	Child serum HCH, HCB, DDE, DDT, endosulfan, aldrin, endrin, dieldrin, methoxychlor, and mirex	Median (range) (ng/mL): α-HCH = 3.75 (< LOD–20,558.86); β-HCH = 7.09 (< LOD–33,088.2); γ-HCH = 2.03 (< LOD–5,160.83); p,p'-DDT = 3.98 (< LOD–5,300.06); p,p'-DDE = 0.50 (< LOD–2,145.75); p,p'-DDE = 6.63 (< LOD–33,556.54); p,p'-DDD = 1.06 (< LOD–803.79); aldrin = 3.17 (< LOD–2,090.23); endrin = 1.71 (< LOD–1,476.47); dieldrin = 0.89 (< LOD–4,161.32); endosulfan 1 = 0.57 (< LOD–2.49); endosulfan 2 = 0.29 (< LOD–2.53); mirex = 0.51 (< LOD–879.11); methoxychlor < LOD (< LOD–1.43)	Neurodevelopment: cognitive function (WISC-III)	Higher α-HCH was associated with poorer performance IQ (β per 1 ng/mL increase = –0.5; 95% CI: –0.9, 0), resistance to distraction (β = –0.3; 95% CI: –0.6, 0), and processing speed (β = –0.5; 95% CI = –0.9, –0.1). Higher γ-HCH was associated with poorer resistance to distraction (β = –1.7; 95% CI = –3.1, –0.4) and processing speed (β = –1.8; 95% CI = –3.6, 0). Higher p,p'-DDT was associated with poorer processing speed (β = –0.8; 95% CI = –1.4, –0.3).
9. Cordier et al. <sup>117</sup>	2015/Guadeloupe <sup>d</sup>	75 mother–child (18 months of age) pairs	Prospective cohort	OCs	Cord blood and breast milk chlordecone, cord blood DDE	Median (P25–P75) (μg/L) in entire study population (111 mother–child pairs): Cord blood chlordecone = 0.13 (< LOD–0.31); cord blood p,p'-DDE = 0.30 (0.09–1.05); breast milk chlordecone = 0.60 (< LOD–1.16)	Neurodevelopment: personal–social, communication, problem-solving, fine motor, and gross motor (ASQ-19)	Association between cord chlordecone and fine motor scores among boys (reported by Boucher et al. <sup>111</sup> ) was not mediated by TSH.
10. Ogaz-Gonzales et al. <sup>114</sup>	2018/Mexico	142 mother–child (42–60 months of age) pairs	Prospective cohort	OCs	Questionnaire (pesticide use history) Maternal serum DDE during first and third trimester of pregnancy	Mean (P10–P90) DDE (ng/mL): First trimester = 7.6 (< 1.8–23.1) Second trimester = 8.1 (1.3–23.5) Third trimester = 9.0 (1.7–29.2)	Neurodevelopment: verbal, perceptual performance, quantitative, memory, motor skills, and general cognitive index (MSCA)	Higher third-trimester maternal DDE was associated with lower motor development in children whose mothers had lower intake of DHA (an omega-3 fatty acid) (β per 2-fold increase in DDE = –1.3; 95% CI: –2.6, 0.1), but not in children whose mothers had a higher DHA intake. Higher maternal DDE was associated with poorer memory skills in children whose mothers had lower ARA (an omega-6 fatty acid) intake (β per 2-fold increase in DDE = –1.3; 95% CI: –2.3, –0.3) but not in children whose mothers had a higher ARA intake. Higher cord plasma chlordecone (continuous) was associated with lower scores (β = –0.1; 95% CI: –0.1, 0). Child chlordecone (continuous) was associated with lower scores among boys (β = –0.1; 95% CI: –0.2, 0).
11. Saint-Amour et al. <sup>115</sup>	2020/Guadeloupe	285 mother–child (7–8 years of age) pairs	Prospective cohort	OCs (chlordecone)	Cord blood and child (7 years of age) blood chlordecone	Median (range) chlordecone (μg/L): Cord blood = 0.80 (0.06–29.78); child blood = 0.17 (0.02–7.01)	Neurodevelopment: visual contrast sensitivity (FrACT)	Null associations of cord blood and child chlordecone with sex-typed play behavior.
12. Cordier et al. <sup>116</sup>	2020/Guadeloupe	116 mother–child (7 years of age) pairs	Prospective cohort	OCs (chlordecone)	Cord blood and child (7 years of age) blood chlordecone	Median (range) chlordecone (μg/L): Cord blood = 0.17 (< LOD–7.4); child blood = 0.04 (< LOD–1.0)	Neurodevelopment: sex-typed play behavior (feminine, masculine, or neutral play reported as a proportion of the complete playing time)	Null associations of cord blood and child chlordecone with sex-typed play behavior.
Studies in adults 13. Steenland et al. <sup>119</sup>	2014/Costa Rica	89 adults from historically (and now partially) agricultural area	Cross-sectional	OCs	Questionnaire (occupational exposure history) Serum HCH, DDE, DDT, and dieldrin	Mean ± SD (ng/mL): Past occupational pesticides exposure: p,p'-DDE = 0.7 ± 0.55; p,p'-DDT = 0.14 ± 0.08; dieldrin = 7.58 ± 19.63; β-HCH = 0.78 ± 0.30 No past occupational pesticides exposure: p,p'-DDE = 1.20 ± 1.46; p,p'-DDT = 0.12 ± 0.12; dieldrin = 3.40 ± 6.48; β-HCH = 0.73 ± 0.19	Neurodegeneration: spatial and temporal orientation, short-term memory, attention, calculation, language, praxis (MMSE); tremor-at-rest (UPDRS)	Null associations of serum OC (parent compounds or metabolites) with MMSE and tremor-at-rest.
Studies on OPs or CBs Studies in children 14. Handal et al. <sup>120</sup>	2007/Ecuador	142 children (24–61 months of age) from 2 communities with industrial flower farms and from a community with local agriculture and crops for food	Cross-sectional	CBs, OPs	Questionnaire (parental occupational and residential exposure history, child outdoor activities)	Not applicable	Neurodevelopment: communication, fine motor, gross motor, problem-solving, personal-social (ASQ); visual-motor skills (Beery-Buktenica VMI developmental test)	Maternal employment in the flower industry at time of child assessment was associated with improved communication (%change = 6.9; 95% CI: –0.3, 8.5) and problem-solving (%change = 8.4; 95% CI: 0.7, 9.4) skills. Pesticide use on domestic crops was also associated with better gross motor (%change = 8.1; 95% CI: 0.6, 9.2) and personal-social (%change = 7.0; 95% CI: –0.7, 9.0) scores, whereas pesticide use within the home was associated with lower communication scores (%change = –7.5; 95% CI: –8.8, –0.3). Children who played with irrigation water had lower fine motor (%change = –8.2; 95% CI: –9.3, –0.5) and problem-solving (%change = –7.3; 95% CI: –8.4, –0.4) scores.

Table 3. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
15. Handal et al. <sup>121</sup>	2007/Ecuador	154 children (3–61 months of age) from 2 communities with industrial flower farms/129 children from a community with local agriculture and crops for food	Cross-sectional	CBs, OPs	Questionnaire (parental occupational and residential exposure history)	Not applicable	Neurodevelopment: communication, fine motor, gross motor, problem solving, personal-social (ASQ)	Children 3–23 months of age from industrial flower farms communities had lower gross motor ( $\beta = -8.8$ , $p = 0.002$ ), fine motor ( $\beta = -5.0$ , $p = 0.06$ ), and sociototal ( $\beta = -5.8$ , $p = 0.02$ ) scores compared with children from a local agriculture community. Children 24–61 months of age from industrial flower farms communities had lower gross motor scores compared with children of similar ages from a local agriculture community ( $\beta = -3.8$ , $p = 0.06$ ).
16. Handal et al. <sup>120</sup>	2008/Ecuador	121 children (3–23 months of age) from 2 communities with industrial flower farms and from a community with local agriculture and crops for food	Cross-sectional	CBs, OPs	Questionnaire (maternal occupational exposure history during pregnancy)	Not applicable	Neurodevelopment: communication, fine motor, gross motor, problem solving, personal-social (ASQ), pre-tension and visual acuity (targeted development tests)	Children whose mothers worked as floriculturists during pregnancy had lower communication ( $\beta = 4.6$ ; 95% CI: $-9.6$ , $0.3$ ) and fine motor ( $\beta = -8.0$ ; 95% CI: $-13.0$ , $-3.1$ ) scores and had an increased risk of poor visual acuity (OR = 4.7; 95% CI: 1.1, 20) than children whose mothers did not.
17. Harari et al. <sup>123</sup>	2010/Ecuador	84 children (6–8 years of age) living in a floricultural area	Cross-sectional	OPs	Questionnaire (parental occupational and residential exposure history) Urinary DAPs <sup>a</sup> Blood AChE <sup>b</sup>	Not applicable	Neurodevelopment: simple motor speed (finger tapping task), motor coordination (Santa Ana Form Board), attention (CPT), short-term auditory memory (WISC and Stanford-Binet), visual performance (Raven's test and Stanford-Binet copying test), visual memory (Stanford-Binet copying recall test)	Children whose mothers were exposed to pesticides during pregnancy showed poorer motor speed ( $\beta = -7.1$ ; 95% CI: $-12.5$ , $-1.6$ ), motor coordination (OR = 5.3; 95% CI: 1.03, 27.6), visual performance (Raven's test: $\beta = 0.5$ ; 95% CI: 0.2, 1.0), and visual memory (OR = 6.6; 95% CI: 1.02, 42.9) compared with children of unexposed mothers. Children whose fathers were exposed to pesticides during pregnancy showed poorer visual memory (OR = 13.4; 95% CI: 1.8, 101.9) than children of unexposed fathers. Children with current exposure (i.e., at least one detectable urinary DAP metabolite) had longer reaction times compared with children with no exposure ( $\beta = 64.7$ ; 95% CI: $-12.4$ , 141.7).
18. Muñoz-Quesada et al. <sup>127</sup>	2011/Chile	25 children (6–11 years of age) from rural communities	Cross-sectional	OPs	Child urinary DAPs	Geometric mean (range) ( $\mu\text{g/L}$ ): DMP = 7.3 (2.5–63.6); DMTP = 7.0 (2.5–51.4); DEP = 17.3 (2.5–49.9)	Neurodevelopment: cognitive function (WISC-III)	Negative association between urinary DMTP and processing speed ( $r = -0.44$ , $p = 0.01$ ). Null associations of other DAP metabolites and WISC-III outcomes.
19. Martos-Mula et al. <sup>129</sup>	2013/Argentina	42 children (7–10 years of age) living in an agricultural area/29 children living in a nonagricultural area	Cross-sectional	OPs, CBs	Questionnaire Blood AChE, BChE	Not applicable	Neurodevelopment: associative memory (Digit and Symbol subtest), short-term memory (Digit Memory test), maze test (motor, visuospatial processing), cognitive function (WISC-III), gross motor and balance tests	Children living in an agricultural area had poorer motor function and visuospatial processing than children living in a nonagricultural area ( $p < 0.01$ ). Null associations between enzyme activities and neurodevelopmental outcomes.
20. Suarez-Lopez et al. <sup>122</sup>	2013/Ecuador	307 children (4–9 years of age) living in floricultural communities	Cross-sectional	OPs	Questionnaire (parental occupational and residential exposure history) Blood AChE	Not applicable	Neurodevelopment: attention and inhibitory control, language, memory and learning, sensorimotor, visuospatial processing (NEPSY-II)	Boys, but not girls, in the highest tertile of AChE activity had increased odds of poor neurodevelopment ( $< 9$ th percentile) than boys in the lowest tertile (total neurodevelopment OR = 5.1; 95% CI: 0.8, 31.5; attention/executive functioning OR = 4.6; 95% CI: 1.2, 17.4); memory/learning OR = 0.0; 95% CI: 1.2, 31.1).
21. Fortenberry et al. <sup>128</sup>	2014/Mexico	187 mother-child (6–11 years of age) pairs	Prospective cohort	OPs (chlorpyrifos)	Maternal urinary TCPy during third trimester of pregnancy	Geometric mean (P10–P90) TCPy (ng/mL): 1.76 (0.45–6.40)	Neurodevelopment: attention and hyperactivity (CRS-R, CPT, BASC-2)	Increased ADHD index for the highest TCPy tertile compared with the lowest tertile for boys ( $\beta = 5.6$ , 95% CI: $-0.2$ , 11.3). Increased attention problems for the middle TCPy tertile compared with the lowest tertile for girls ( $\beta = 5.8$ , 95% CI: $-0.8$ , 12.4).
22. Suarez-Lopez et al. <sup>126</sup>	2017/Ecuador	308 children (4–9 years of age) living in floricultural communities	Cross-sectional	OPs	Questionnaire (parental occupational and residential exposure history) Blood AChE	Not applicable	Neurodevelopment: attention and inhibitory control, language, memory and learning, sensorimotor, visuospatial processing (NEPSY-II)	Children examined sooner after Mother's Day had lower attention/inhibitory control (score difference per 10.8 d = 0.4; 95% CI: 0.10, 0.7), visuospatial processing (0.6; 95% CI: 0.3, 0.9), and sensorimotor (0.4; 95% CI: 0.1, 0.8) scores than children examined later. Further adjustment for AChE activity had overall a small effect on most associations but strengthened associations in the attention and inhibitory control domain by about 16%.
23. Suarez-Lopez et al. <sup>124</sup>	2019/Ecuador	529 adolescents (11–17 years of age) living in floricultural communities	Cross-sectional	OPs	Blood AChE	Not applicable	Mental health disorders: anxiety (MASC-2) and depression symptoms (CDI-2)	Lower AChE activity was associated with more depression symptoms ( $\beta$ per SD decrease in AChE activity = 1.1; 95% CI: 0.2, 2.2). Associations were stronger among girls ( $\beta = 1.6$ ; 95% CI: 0.1, 3.1) than boys ( $\beta = 0.7$ ; 95% CI: $-0.9$ , 2.3) and among younger ( $\beta = 1.6$ ; 95% CI: $-0.2$ , 3.4) than older children ( $\beta = 0.6$ ; 95% CI: $-0.8$ , 2.0). No associations were observed with anxiety scores.

Table 3. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
24. Suarez-Lopez et al. <sup>129</sup>	2021/Ecuador	300 adolescents (11–17 years of age) living in floricultural communities	Cross-sectional	OPs	Blood AChE	Not applicable	Mental health disorders: anxiety (MASC-2) and depression symptoms (CDI-2)	Lower AChE activity was associated with more depression symptoms ( $\beta$ per 10% decrease in AChE activity = 1.0; 95% CI: 0.1, 1.9) and increased odds of an elevated depression score (OR = 1.7; 95% CI: 1.0, 2.7). These associations were stronger among girls than boys. Adjustment for cortisol, testosterone and dehydroepiandrosterone reduced gender differences by 18%–62%.
25. Wesseling et al. <sup>136</sup>	2010/Costa Rica	78 male banana farmworkers with poisoning/130 non-poisoned workers from company payrolls	Cross-sectional	OPs, CBs	Questionnaire (occupational exposure history, history of OP pesticide poisoning) Blood AChE <sup>b</sup>	Not applicable	Mental health disorders: psychological distress and suicidal ideation (BSI)	Farmworkers with history of OP pesticide poisonings had increased odds of somatization (OR = 3.1; 95% CI: 1.6, 6.0), obsessive-compulsiveness (OR = 3.2; 95% CI: 1.6, 6.2), interpersonal sensitivity (OR = 2.9; 95% CI: 1.5, 5.8), depression (OR = 2.4; 95% CI: 1.3, 4.7), hostility (OR = 2.3; 95% CI: 1.1, 4.6), anxiety (OR = 2.3; 95% CI: 1.4, 4.4), phobia (OR = 1.9; 95% CI: 1.0, 3.6), and psychoticism (OR = 2.2; 95% CI: 1.1, 4.3). Individuals with history of OP pesticide poisonings had increased odds of having suicidal thoughts in the previous month (OR = 3.6; 95% CI: 1.5, 8.8), with increasing risk for those with more poisonings (PR = 5.0; 95% CI: 1.7, 14.5). Farmworkers with history of CB pesticide poisonings had increased odds of somatization (OR = 2.6; 95% CI: 1.1, 6.2).
26. Muñoz-Quezada et al. <sup>132</sup>	2016/Chile	93 farmworkers/84 controls	Cross-sectional	OPs	Questionnaire (occupational exposure history)	Not applicable	Neurobehavioral performance: cognitive function (WAIS-IV), visuospatial memory and visual perception (ROCF), visual memory and visuoconstruction skills (BVRT), neurological alterations with frontal involvement (MMSE), and motor performance	Farmworkers had lower WAIS-IV verbal comprehension ( $\beta$ = -3.2; 95% CI: -6.1, -0.2), processing speed ( $\beta$ = -4.4; 95% CI: -8.6, -0.3), and total IQ ( $\beta$ = -4.0; 95% CI: -6.8, -0.7) scores than controls. Farmworkers also had lower MMSE scores ( $\beta$ = -1.0; 95% CI: -1.7, -0.1) and poorer discrimination sensitivity ( $\beta$ = 1.0; 95% CI: 0.2, 1.2) and deep reflexes ( $\beta$ = 1.1; 95% CI: 0.0, 2.2) than controls.
27. Corral et al. <sup>131</sup>	2017/Chile	32 farmworkers/32 individuals living in agricultural communities/38 controls	Cross-sectional	OPs	Questionnaire (occupational exposure history)	Not applicable	Neurobehavioral performance: spatial and temporal orientation, short-term memory, attention, calculation, language, praxis (MMSE), memory and attention (WAIS-R DST), visuoconstruction skills and visual memory (ROCF), divided attention and resistance to interference (Stroop), attention (d2), executive function (FAB), and verbal fluency (Barcelona for Animals and Letter P)	Both farmworkers and people living in agricultural communities had increased odds of poorer (i.e., below cutoff value) executive function (OR = 44.9; 95% CI: 5.6, 359.7 and OR = 7.3; 95% CI: 1.7, 32.4, respectively), memory and attention (DST forward: OR = 4.9; 95% CI: 1.6, 14.9 and DST backward: OR = 7.4; 95% CI: 2.4, 22.4; DST forward: OR = 4.5; 95% CI: 1.4, 13.8 and DST backward: OR = 2.9; 95% CI: 1.02, 8.3, respectively), and verbal fluency (animals: OR = 5.7; 95% CI: 1.3, 25.6 and Letter P: OR = 16.7; 95% CI: 4.3, 64.6; animals: OR = 4.5; 95% CI: 1.04, 19.4 and Letter P: OR = 8.1; 95% CI: 2.1, 31.3, respectively) than the unexposed group.
28. Grillo Pizarro et al. <sup>135</sup>	2018/Chile	55 farmworkers/58 unexposed controls	Cross-sectional	OPs	Questionnaire (occupational and residential exposure history)	Not applicable	Periphereal polynuropathy	Farmworkers exposed to OP pesticides had increased odds of periphereal polynuropathy compared with controls (OR = 3.6; 95% CI: 1.2, 10.5)
29. Serrano-Medina et al. <sup>137</sup>	2019/Mexico	140 farmworkers/100 controls	Cross-sectional	OPs	Questionnaire (occupational exposure history) Blood AChE	Not applicable	Mental health disorders: neuropsychiatric disorders (MINI based on DSM-IV)	Farm work was associated with increased odds of suicide (OR = 5.3; 95% CI: 2.4, 11.9), whereas higher AChE activity levels were associated with decreased odds of suicide (OR = 0.5, $p < 0.01$ ).
30. Bualiti et al. <sup>138</sup>	2020/Brazil <sup>c</sup>	42 pesticide applicators/36 farmworkers who did not apply pesticides	Cross-sectional	OPs	Questionnaire (occupational exposure history) Blood AChE, BCHE <sup>b</sup>	Not applicable	CMD (SRQ-20)	Farmworkers who did not spray pesticides had a higher probability of feeling easily tired (PR = 3.2; 95% CI: 1.3, 7.7) and worthless (PR = 7.2; 95% CI: 1.7, 31.0) compared with pesticide applicators.



Table 3. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
31. Ramirez-Santana et al. <sup>134</sup>	2020/Chile	87 adults occupationally exposed (OE/81 environmentally exposed (EE)/100 unexposed controls (RG)	Cross-sectional	OPs, CBs	Questionnaire (occupational and residential exposure history) Blood AChE, BChE, APEH	Not applicable	Neurobehavioral performance at one (RG) or two (OE and EE) time points: general mental status (MMSE), memory (WMS III, Digit span forward, ROCF memory, 10/36 A-B and A-B recall), language (WAIS subtest vocabulary), constructive praxis (ROCF copy, WAIS subtest block design), executive function (Tower of London movements and time resolution tests, WCST perseverative errors, Barcelona test categorical evocation animals and words), attention (WAIS digit span backward, d2 test, Stroop word-color and inhibitory control tests, Trail Making Test A, WAIS symbols), Psychomotricity (Purdue pegboard test, MOART reaction time, MOART finger tapping test), Mood (BDI-II depression inventory, Hamilton anxiety scale)	Both exposure groups (OE and EE) had poorer executive function (Tower of London time, WCST perseverative errors), psychomotricity (MOART reaction time (right and left hand)), and mood (BDI-II depression inventory, Hamilton anxiety scale) than the RG. Seasonal exposure impaired performance in both exposure groups on all tests except those related to attention and mood. During the spray season, BChE activity was associated with decreased scores on tests of logical, auditory, and visual memory; inhibitory control of cognitive interference; constructional and planning abilities; executive function; and motor speed and coordination among those in the EE group. Weaker associations were observed for AChE levels and tests of logical memory, constructional abilities, and fine motor coordination in the EE group. In the OE group, levels of the three biomarkers were associated with worse performance on tests of inhibitory control of cognitive interference (2 tests with AChE, 2 tests with BChE, and 1 test for APEH); results were only significant for AChE.
32. Ramirez-Santana et al. <sup>133</sup>	2020/Chile	78 adults occupationally exposed (OE/78 environmentally exposed (EE)	Cross-sectional	OPs, CBs	Questionnaire (occupational and residential exposure history) Blood AChE, BChE	Not applicable	Changes in neurobehavioral performance from pre-spray to spraying season in OE and EE: General mental status (MMSE), memory (WMS III, Digit span forward, ROCF memory, 10/36 SRT A-B and A-B recall), language (WAIS subtest vocabulary), constructive praxis (ROCF copy, WAIS subtest block design), executive function (Tower of London movements and time resolution tests, WCST perseverative errors, Barcelona test categorical evocation animals and words), attention (WAIS digit span backward, d2 test, Stroop word-color and inhibitory control tests, Trail Making Test A, WAIS symbols), Psychomotricity (Purdue pegboard test, MOART reaction time, MOART finger tapping test), Mood (BDI-II depression inventory, Hamilton anxiety scale)	<p>AChE inhibition was associated with worse performance on tests of attention (Stroop word-color and inhibitory control test, Trail Making A test) in the EE group and worse performance on tests of memory (WMS) and attention (Trail Making A test) in the OE group.</p> <p>BChE inhibition was associated with worse performance on tests of general mental status (MMSE), memory (WMS III-I, WMS III-II, Digit span forward, 10/36 SRT-A, 10/36 SRT-B, 10/36 SRT-A recall, 10/36 SRT-B recall), language (WAIS), attention (Stroop word-color and inhibitory control tests), executive function (Tower of London movements, WCST perseverative errors, Barcelona tests animals) in the EE group and worse performance on a test of attention (Stroop word-color test) in the OE group.</p>

Table 3. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
Studies on other pesticides or multiple pesticide classes								
33. Eckerman et al. <sup>143</sup>	2007/Brazil	38 adolescents (10–18 years of age) from rural areas/28 adolescents from urban areas	Cross-sectional	Multiple pesticide classes	Questionnaire (exposure index based on 86 occupational history questions plus number of hours worked per day applying chemical plus number of years worked)	Not applicable	Neurobehavioral: BARS (CPT, MTS, DST, PRT, RTT, SAT, SDL, SDT, TAP)	Compared with adolescents from rural areas, adolescents from urban areas performed better on tests of response speed and coordination (TAP_NP), attention and working memory (DS-F), and complex function (SD_LAT), but worse on a cognition test (SDL) ( $p < 0.1$ ). Among the youngest age group (10–11 y), rural participants had poorer mean scores in tests of response time and coordination (TAP_P, TAP_NP, TAP_ALT), motivation (PRT), attention and working memory (DS-F; CPT_HLAT; SAT_LAT), reaction time (RT_ALL), complex function (SDT_LAT), and visual memory and delay (MTS_LAT) ( $p < 0.1$ for each) than urban participants.
34. Lu et al. <sup>139</sup>	2009/Costa Rica	18 children (4–10 years of age) of conventional coffee farmworkers/17 children of organic coffee farmworkers	Cross-sectional	OPs, herbicides, pyrethroids	Child urinary 2,4-D, TCPy, 3-PBA, and IMPY	Mean $\pm$ SD ( $\mu\text{g/L}$ ): La Amistad: 2, 4-D = $0.21 \pm 0.22$ ; 3-PBA = $0.75 \pm 1.61$ ; CIT = $0.27 \pm 0.41$ ; IMPY = $0.92 \pm 2.15$ ; TCPy = $0.31 \pm 0.91$ Las Melizitas: 2,4-D = $0.41 \pm 0.49$ ; 3-PBA = $0.4 \pm 0.22$ ; CIT = $0.14 \pm 0.26$ ; IMPY = $0.52 \pm 1.05$ ; TCPy = $1.45 \pm 2.29$ Median (P25–P75) ( $\mu\text{g/L}$ ): TCPy = $1.4 (0.7–3.1)$ ; ETU = $1.2 (0.7–3.0)$ ; 3-PBA = $0.8 (0.5–1.5)$	Neurodevelopment: cognition (BARS, figure-drawing task, long-term memory test)	Null associations between urinary pesticide metabolites and neurodevelopmental outcomes.
35. van Wendel et al. <sup>140</sup>	2016/Costa Rica	140 rural children (6–9 years of age) living near banana and plantain plantations	Cross-sectional	Mn-containing fungicides, OPs, pyrethroids	Questionnaire (parental occupational exposure history) Child urinary TCPy, ETU, and 3-PBA	Median (P25–P75) ( $\mu\text{g/L}$ ): TCPy = $1.4 (0.7–3.1)$ ; ETU = $1.2 (0.7–3.0)$ ; 3-PBA = $0.8 (0.5–1.5)$	Neurodevelopment: cognitive function (WISC-IV), behavioral problems (CPRS R), visual sensory function (LDD-15), visuospatial construction and visual memory (ROCF), verbal memory and learning abilities (CAVLT-2), visual-motor coordination (DTVP-2), fine motor function (WRAYMA), and attention (RTT)	Higher TCPy was associated with poorer working memory in boys ( $\beta$ per 10-fold increase in TCPy = $-7.5$ ; 95% CI: $-14.4, -0.7$ ) and poorer visual-motor coordination ( $\beta$ = $-1.4$ ; 95% CI: $-2.7, -0.1$ ); oppositional disorders (OR = 6.8; 95% CI: 1.8, 28.6) and decreased ability to discriminate colors (OR = 6.6; 95% CI: 1.6, 30.3) in boys and girls combined. Higher was associated with poorer verbal learning outcomes ( $\beta$ = $-7.0$ ; 95% CI: $-12.7, -1.3$ ). Higher 3-PBA was associated with poorer processing speed scores, particularly in girls ( $\beta$ = $-8.8$ ; 95% CI: $-16.1, -1.4$ ).
36. Watkins et al. <sup>142</sup>	2016/Mexico	187 mother–child (2–3 years of age) pairs	Prospective cohort	Pyrethroids	Maternal urinary 3-PBA during third trimester of pregnancy	Geometric mean $\pm$ GSD 3-PBA (ng/mL): $0.26 \pm 1.80$	Neurodevelopment: cognitive, language, personal-social, and gross motor development (BSID-II)	Children whose mothers had medium and high 3-PBA during pregnancy had lower MDI scores at 24 months than children whose mothers had low 3-PBA ( $\beta$ = $-3.5$ ; 95% CI: $-7.9, 0.8$ and $\beta$ = $-3.8$ ; 95% CI: $-8.4, 0.8$ , respectively). Null associations of prenatal 3-PBA with PDI scores at 24 or 36 months.
37. Mora et al. <sup>141</sup>	2018/Costa Rica	355 mother–child (1 year of age) pairs living near banana plantations aerially sprayed	Prospective cohort	Mn-containing fungicides	Maternal urinary ETU, blood Mn, and hair Mn during pregnancy	Mean $\pm$ SD ( $\mu\text{g/L}$ ): ETU = $4.4 \pm 7.1$ ; hair Mn ( $\mu\text{g/g}$ ) = $3.7 (5.4)$ ; blood Mn = $24.4 \pm 6.2$	Neurodevelopment: cognition, motor function, language, and social-emotional development (BSID-III)	Girls whose mothers had higher urinary ETU during pregnancy had lower social-emotional scores ( $\beta$ per 10-fold increase = $-7.4$ points; 95% CI: $-15.2, 0.4$ ), whereas those whose mothers had higher hair Mn during pregnancy had lower cognitive scores ( $\beta$ per 10-fold increase = $-3.0$ points; 95% CI: $-6.1, 0.1$ ). Among boys, higher hair Mn during pregnancy was associated with lower social-emotional scores ( $\beta$ per 10-fold increase = $-4.6$ points; 95% CI: $-8.5, -0.8$ ). Null associations for blood Mn, language, and motor outcomes.
38. Christian et al. <sup>145</sup>	2018/Jamaica	298 children (2–8 years of age) with ASD/298 controls without ASD	Case-control	Multiple pesticide classes	Questionnaire (maternal exposure history)	Not applicable	ASD (ADOS, ADI-R)	Maternal exposure to pesticides from 3 months before pregnancy to end of breastfeeding was associated with increased risk of ASD (OR = 1.7; 95% CI: 1.1, 2.6), with some evidence of effect modification by exposure to oil-based paints and paint solvents.
39. Friedman et al. <sup>144</sup>	2020/Ecuador	307 children (4–9 years of age) living in floricultural communities	Cross-sectional	Multiple pesticide classes	Proximity to floricultural crops	Not applicable	Neurodevelopment: attention and inhibitory control, language, memory and learning, sensorimotor, visuospatial processing (NEPSY-II)	For every 100 m closer in proximity to treated floricultural crops, participants had increased odds of low memory/learning (OR = 1.2; 95% CI: 1.1, 1.5) and language (OR = 1.1; 95% CI: 1.0, 1.2) scores. Compared with those living >500 m from crops, those living within 50 m of crops had lower language ( $\beta$ = $-1.3$ ; 95% CI: $-2.5, -0.1$ ), attention/inhibitory control ( $\beta$ = $-1.2$ ; 95% CI: $-2.5, -0.0$ ), and memory/learning ( $\beta$ = $-0.9$ ; 95% CI: $-2.0, 0.2$ ) scores.

Table 3. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
Studies in adults 40. Araújo et al. <sup>159</sup>	2007/Brazil <sup>159</sup>	102 farmworkers	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood AChE	Not applicable	Neurological symptoms (neurological examination and perception of neurological symptoms)	Null association between inhibition of AChE activity and intoxication symptoms.
41. Steenland et al. <sup>146</sup>	2013/Costa Rica <sup>146</sup>	400 adults >60 years of age from historically (and now partially) agricultural area	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Neurodegeneration: spatial and temporal orientation, short-term memory, attention, calculation, language, praxis (MMSE); PD risk (UPDRS)	Exposed subjects performed worse on the MMSE than the nonexposed ( $p=0.01$ ), had increased odds of abnormal scores on two UPDRS items (tremor-at-rest OR = 2.3; 95% CI: 1.3–5.2 and finger tapping OR = 2.9; 95% CI: 1.03, 8.4), and had an increased risk of PD (OR = 2.6; 95% CI: 0.9, 7.3).
42. Faria et al. <sup>152</sup>	2014/Brazil <sup>152</sup>	2,400 tobacco farmworkers	Cross-sectional	Fungicides, herbicides, neonicotinoids, OPs, pyrethroids	Questionnaire (occupational exposure history)	Not applicable	Mental health disorders: MPD (SRQ-20)	Increased risk of MPD among those who entered the treated area following application (PR = 1.7; 95% CI: 1.3, 2.2) and those who had contact through clothes wet from pesticides (PR = 1.4; 95% CI: 1.1, 1.7). Workers from farms in which OPs were used had an increased risk of MPD compared with those who were not exposed (PR = 1.5; 95% CI: 1.2, 1.9). Number of poisonings was positively associated with risk of MPD (PR for 1 episode = 1.6; 95% CI: 1.1, 2.2; PR for 2 episodes = 2.5; 95% CI: 1.8, 3.4).
43. Portilla-Portilla et al. <sup>155</sup>	2014/Colombia <sup>155</sup>	49 adults from a rural area	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational and environmental history of exposure to neurotoxic pesticides)	Not applicable	Neurological symptoms (self-reported)	Participants with pesticide exposure had increased odds of irritability (PR = 1.8; 95% CI: 1.1, 2.8), dizziness (PR = 2.3; 95% CI: 1.1, 4.9), phosphorus (PR = 2.6; 95% CI: 1.0, 6.6), epistaxis (PR = 2.9; 95% CI: 1.0, 8.3), and fasciculations (PR = 8.7; 95% CI: 1.1, 66.9). Ever feeling ill after a pesticide application was associated with common mental disorders (OR = 2.6; 95% CI: 1.6, 4.3) and self-reported depression (OR = 2.6; 95% CI: 1.6, 4.2). Age at onset of pesticide exposure $\leq 15$ y (OR = 1.7; 95% CI: 1.7, 2.8), exposure to pyrethroids (OR = 1.8; 95% CI: 1.0, 3.2) and aliphatic alcohol (OR = 2.0; 95% CI: 1.04, 3.8), and greater period of exposure to dimethoate (OR = 2.2; 95% CI: 1.0, 4.7) and sulfonyl urea (OR = 5.0; 95% CI: 1.1, 23.0) were associated with self-reported depression.
44. Campos et al. <sup>149</sup>	2016/Brazil <sup>149</sup>	869 adults from a rural population	Cross-sectional	Herbicides, natural pesticides, OPs, OCs, pyrethroids	Questionnaire (occupational exposure history)	Not applicable	Mental health disorders: MPD (SRQ-20) and depression (self-reported)	Null association of cumulative pesticide exposure load (calculated by multiplying years of application, frequency of application, and hours worked per day) with essential tremor. Workers who had applied pesticides for 16–16.9 y had increased odds of essential tremor compared with workers who had applied pesticides for $\leq 13$ y (OR = 4.9; 95% CI: 1.3, 18.0). Higher pesticide spraying intensity was associated with increased odds of poor postural balance among those exposed to pyrethroids (OR per 1-quantile increase in intensity = 3.83; 95% CI: 1.1, 13.6). Higher spraying intensity was also associated with worse neurocognitive performance ( $\beta$ per 1-quantile increase for all workers = $-0.4$ ; 95% CI: $-0.7$ , $-0.2$ and $\beta$ for workers exposed to pyrethroids only = $-1.3$ ; 95% CI: $-2.2$ , $-0.5$ ). Cumulative pesticide exposure was associated with worse neurocognitive performance ( $\beta$ per 1-quantile increase for all workers = $-0.4$ ; 95% CI: $-0.6$ , $-0.1$ and $\beta$ for workers exposed to pyrethroids only = $-1.4$ ; 95% CI: $-2.3$ , $-0.4$ ). Pesticide exposure was associated with increased odds of more severe depressive symptoms (OR = 5.5; 95% CI: 1.2, 25.9).
45. Azevedo and Meyer <sup>158</sup>	2017/Brazil <sup>158</sup>	51 endemic disease control agents with essential tremor/204 endemic disease control agents with no tremor (controls)	Case-control	Larvicides, OCs, OPs, pyrethroids	Questionnaire (occupational exposure history)	Not applicable	Neurodegeneration: essential tremor	Null association of hair and toenail Mn concentrations with brain activity during working memory task.
46. Hansen et al. <sup>147</sup>	2017/Bolivia <sup>147</sup>	120 male endemic disease control agents	Cross-sectional	Pyrethroids	Questionnaire (occupational exposure history)	Not applicable	Neurobehavioral performance: hand tremor, postural balance, vocabulary (BNT), audiovisual reaction (RTT), cognition (BARS), visual attention (CPT), complex cognitive function (SDT), attention and memory (DST, SDL), and visual memory (MTS)	
47. Conti et al. <sup>148</sup>	2018/Brazil <sup>148</sup>	220 male farmworkers	Cross-sectional	Glyphosate, fungicides, neonicotinoids	Questionnaire (occupational exposure history) Hair and toenail Mn	Not applicable	Mental health disorders: depression (BDI-II)	
48. Paizes et al. <sup>160</sup>	2019/Costa Rica <sup>160</sup>	48 farmworkers	Cross-sectional	Mn-containing fungicides		Mean $\pm$ SD ( $\mu\text{g/g}$ ) Mn: Hair = $0.40 \pm 3.53$ ; toenail = $0.24 \pm 3.54$	Cortical brain activity (fNIRS)	

**Table 3.** (Continued.)

Note: %change, percentage change; 2,4-D, 2,4-dichlorophenoxyacetate; 3-PBA, 3-phenoxybenzoic acid; AChE, acetylcholinesterase; ADHD, attention deficit hyperactivity disorder; ADI-R, Autism Diagnostic Interview-Revised; ADOS, Autism Diagnostic Observation Schedule; ADPAPEH, acyl peptide hydrolase; APP, acute pesticide poisoning; ASQ, Ages and Stages Questionnaire; BARS, BChE, butyrylcholinesterase; Behavioral Assessment and Research System; BASC-2, Behavior Assessment System-2; BMDP, BMDP Statistical Software; BNT, Boston Naming Test; BSI, Brief Symptom Inventory; BSID-II, Bayley Scales of Infant Development, 2nd edition; BVRT, Benton Visual Retention Test; CAVLT-2, Children's Auditory Verbal Learning Test, 2nd edition; CB, carbamate; CDI-2, Children's Depression Inventory, 2nd edition; CI, confidence interval; CITI, 5-chloro-1,2-dihydro-1-isopropyl-1H-1,3H-imidazole-4-carboxylate; CPT, Continuous Performance Test; CPT-FLAT, Continuous Performance Test for Hits; DAP, dialkylphosphate; DDE, dichlorodiphenylchloroethylene; DDT, dichlorodiphenyl ether; DEP, diethylphosphate; DHA, docosahexaenoic acid; DMP, dimethylphosphate; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders; DST, Digit Span Test; DTVP-2, Frostig Developmental Test of Visual Perception, 2nd edition; EE, environmentally exposed; ETU, ethyleneurea; FAB, Frontal Assessment Battery; NIRS, functional near-infrared spectroscopy; FRAXT, functional acute contrast test; FTII, Fagan Tests of Infant Intelligence; GSD, geometric standard deviation; HCH, hexachlorocyclohexane; IMPY, 2-isopropyl-4-methyl-6-hydroxypyrimidinol; IQ, intelligence quotient; LOD, limit of detection; LDD-15, Lambtony Apparatus D-15 Test; MASC-2, Multidimensional Anxiety Scale for Children, 2nd edition; MDI, Mental Development Index; MINI, Mini International Neuropsychiatric Interview; MMSE, Mini-Mental State Exam; MNI, manganese; MOART, multi-occupational apparatus for reaction time; MPD, minor psychiatric disorders; MSCA, McCarthy Scales of Children's Abilities; MTS, matching to sample; NEPSY-II, A Developmental Neuropsychological Assessment; NIBAS, Brazelton Neonatal Behavioral Assessment; OC, organochlorine; OP, organophosphate; OR, odds ratio; PD, Parkinson's disease; PDD, Pervasive Developmental Disorder; PDI, Peabody Developmental Inventory; PDI-R, Peabody Developmental Inventory-Revised; PDI-S, Peabody Developmental Inventory-Scale; PDI-T, Peabody Developmental Inventory-Triple; PDI-X, Peabody Developmental Inventory-X; PDI-Y, Peabody Developmental Inventory-Y; PDI-Z, Peabody Developmental Inventory-Z; PDI-1, Peabody Developmental Inventory-1; PDI-2, Peabody Developmental Inventory-2; PDI-3, Peabody Developmental Inventory-3; PDI-4, Peabody Developmental Inventory-4; PDI-5, Peabody Developmental Inventory-5; PDI-6, Peabody Developmental Inventory-6; PDI-7, Peabody Developmental Inventory-7; PDI-8, Peabody Developmental Inventory-8; PDI-9, Peabody Developmental Inventory-9; PDI-10, Peabody Developmental Inventory-10; PDI-11, Peabody Developmental Inventory-11; PDI-12, Peabody Developmental Inventory-12; 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PDI-171, Peabody Developmental Inventory-171; PDI-172, Peabody Developmental Inventory-172; PDI-173, Peabody Developmental Inventory-173; PDI-174, Peabody Developmental Inventory-174; PDI-175, Peabody Developmental Inventory-175; PDI-176, Peabody Developmental Inventory-176; PDI-177, Peabody Developmental Inventory-177; PDI-178, Peabody Developmental Inventory-178; PDI-179, Peabody Developmental Inventory-179; PDI-180, Peabody Developmental Inventory-180; PDI-181, Peabody Developmental Inventory-181; PDI-182, Peabody Developmental Inventory-182; PDI-183, Peabody Developmental Inventory-183; PDI-184, Peabody Developmental Inventory-184; PDI-185, Peabody Developmental Inventory-185; PDI-186, Peabody Developmental Inventory-186; PDI-187, Peabody Developmental Inventory-187; PDI-188, Peabody Developmental Inventory-188; PDI-189, Peabody Developmental Inventory-189; PDI-190, Peabody Developmental Inventory-190; PDI-191, Peabody Developmental Inventory-191; PDI-192, Peabody Developmental Inventory-192; PDI-193, Peabody Developmental Inventory-193; PDI-194, Peabody Developmental Inventory-194; PDI-195, Peabody Developmental Inventory-195; PDI-196, Peabody Developmental Inventory-196; PDI-197, Peabody Developmental Inventory-197; PDI-198, Peabody Developmental Inventory-198; PDI-19

<sup>b</sup>Investigators did not use exposure biomarker concentrations in multivariate analyses.



associations of OP pesticide exposure with neurodevelopmental outcomes among children.<sup>121,129</sup> In a publication from Ecuador, investigators reported that maternal employment in the flower industry or pesticide use on domestic crops at the time of child assessment was associated with improved communication, gross motor, and problem-solving skills at 24–61 months of age.<sup>130</sup> A publication from Argentina reported null associations of OP exposure—assessed via blood ChE levels—with motor function and visuospatial processing at 7–10 years of age, but it also reported worse neurodevelopmental outcomes among children living in an agricultural community compared with those living in a nonagricultural community.<sup>129</sup>

Eight publications examined the association of OP or carbamate pesticides with neurobehavioral outcomes and neurodegenerative disorders among adults (Table 3). Seven of the studies described in these publications were cross-sectional and found that workers exposed to pesticides (i.e., farmworkers and endemic disease control agents) and adults who lived in agricultural communities had impaired cognitive, executive function, memory and attention, and verbal fluency skills<sup>131–134</sup>; poorer discrimination sensitivity and deep reflexes<sup>132</sup>; increased odds of polyneuropathy<sup>135</sup>; or increased odds of psychological distress and suicidal ideation.<sup>136,137</sup> Conversely, a publication from a cross-sectional study in Brazil reported that farmworkers who did not handle/apply pesticides—but who used less personal protective equipment (PPE) and had less training on safe pesticide use practices—had more adverse health outcomes (e.g., feeling easily tired, feeling worthless) than pesticide applicators.<sup>138</sup>

Seven publications from two prospective cohort studies, four cross-sectional studies, and one case–control study examined the associations of exposure to multiple pesticide classes with child neurodevelopment (Table 3). Of these seven publications, four assessed exposure using direct assessment methods<sup>139–142</sup>; two examined exposure using predetermined categorical exposure variables based on residence<sup>143</sup> or proximity to treated agricultural fields<sup>144</sup>; and one examined maternal pesticide exposure history via questionnaire.<sup>145</sup> A publication from a prospective cohort study in Costa Rica found an association of prenatal exposure to manganese (Mn)-containing fungicides—assessed by measurement of urinary ethylenethiourea (ETU) as well as blood and hair Mn in maternal samples collected during pregnancy—with lower social-emotional and cognitive scores in children at 1 year of age.<sup>141</sup> A publication from a prospective cohort study in Mexico reported that prenatal exposure to pyrethroids—as indicated by measurement of 3-phenoxybenzoic acid (3-PBA) in maternal urine samples collected during the third trimester of pregnancy—was associated with lower mental development scores at 24 months of age, but not at 36 months of age.<sup>142</sup> Notably, a publication from a cross-sectional study of school-age children in Costa Rica reported that higher urinary 3-PBA concentrations were associated with poorer processing speed scores (particularly in girls), but also that urinary TCPy concentrations were associated with poorer working memory (among boys only), visual-motor coordination, and decreased ability to discriminate colors.<sup>140</sup> In contrast, a publication from a small cross-sectional study also conducted in Costa Rica<sup>139</sup> reported null associations of exposure to OP pesticides, pyrethroids, and herbicides—assessed via pesticide-specific metabolites (e.g., urinary 3-PBA and TCPy concentrations)—and neurodevelopmental outcomes among children 4–10 years of age. A publication from a study conducted in Jamaica reported that maternal exposure to pesticides from 3 months before pregnancy to the end of breastfeeding was associated with an increased risk of autism spectrum disorder.<sup>145</sup> Last, two publications from cross-sectional studies in Ecuador<sup>144</sup> and Brazil<sup>143</sup> reported that children and adolescents

who lived near agricultural fields in which OP pesticides and other pesticide classes were extensively used had poorer neurodevelopmental outcomes compared with those who lived farther from the fields (or in nonagricultural communities), including poorer cognitive skills, motor function, memory/learning, visuospatial processing, or attention/inhibitory control.

Fifteen publications evaluated the neurobehavioral effects of exposure to multiple pesticide classes, predominantly assessed via occupational exposure history, among adults (Table 3). Nine of these publications reported that workers exposed to pesticides (i.e., farmworkers and endemic disease control agents), farmworkers who had experienced an acute pesticide poisoning (APP), and adults who lived in agricultural or rural communities had cognitive impairment<sup>146,147</sup>; increased odds of minor psychiatric disorders such as depression, anxiety, and somatic disorders<sup>148–152</sup>; suicidal ideation<sup>153,154</sup>; or an array of neurological symptoms.<sup>151,155</sup> Three publications from cross-sectional and case–control studies conducted in Costa Rica<sup>119</sup> and Brazil<sup>156,157</sup> reported associations between exposure to multiple classes of pesticides—assessed via questionnaire—and increased odds of Parkinson's disease. Notably, publications from two studies of Brazilian workers reported null associations of pesticide exposure with essential tremor<sup>158</sup> and acute intoxication symptoms.<sup>159</sup> A publication from a small cross-sectional study of farmworkers in Costa Rica reported a null association between exposure to Mn-containing fungicides—assessed by measurement of toenail and hair Mn concentrations—and cortical brain activity during a working memory task.<sup>160</sup>

Overall, studies published to date provide consistent evidence of associations between prenatal and childhood exposure to pesticides such as OP pesticides and carbamates and impaired neurodevelopment in LAC children and adolescents. Some of the adverse neurodevelopmental outcomes that have been reported include poorer cognition, memory, and attention, as well as anxiety and depression. Publications from studies of farmworkers in LAC countries also provide consistent evidence of associations between exposure to multiple classes of pesticides—assessed mainly via questionnaire—and impaired neurobehavioral performance, psychological distress, suicidal ideation, and neurodegenerative disorders.

### Placental Outcomes and Teratogenicity

Thirteen publications from seven cross-sectional studies, five case–control studies, and one prospective cohort study reported on the potential placental and teratogenic effects of pesticide exposure (Table 4). Seven of these 13 publications reported on the association of exposure to OC pesticides or multiple pesticide classes with congenital malformations. A case–control study conducted in Mexico reported that children whose mothers had higher serum hexachlorobenzene (HCB),  $\beta$ -HCH, DDT, or DDE concentrations at delivery had increased odds of cryptorchidism.<sup>161</sup> Similarly, publications from studies conducted in Brazil<sup>162–164</sup> and Mexico<sup>165</sup> reported associations of parental occupational pesticide use or environmental pesticide exposure (e.g., being born in a floricultural community) before or during pregnancy—ascertained via questionnaire—with increased odds of congenital malformations, including male external genital malformations. In contrast, publications from case–control studies in Brazil<sup>166</sup> and Guadeloupe<sup>167</sup> found null associations between pesticide exposure and malformations in general.

Six publications, all from cross-sectional studies conducted either in Mexico or Argentina, reported on the associations between exposure to OP or carbamate pesticides and placental outcomes (Table 4). Each of these studies measured blood ChE or placental carboxylesterase activity levels but used predetermined exposure

**Table 4.** Characteristics of Latin American and the Caribbean studies on pesticide exposure and placental outcomes and teratogenicity published between 2007 and 2021 (*n* = 13).

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
Studies on OCs Studies in children 1. Bustamante Montes et al. <sup>161</sup>	2010/Mexico	641 cases with cryptorchidism/41 controls	Case-control	OCs	Maternal serum HCB, HCH, DDT, DDE after delivery	Median (range) (ng/kg): Controls: HCB = 0.13 (0.03–0.33); β-HCH = 0.26 (0.09–0.89); p,p'-DDE = 2.22 (0.89–4.61); o,p'-DDT = 0.01 (0.01–0.18); p,p'-DDT = 0.27 (1.22–5.39); Σ DDT = 1.22 (2.55) Cryptorchidism cases: HCB = 0.17 (0.03–0.64); β-HCH = 0.19 (0.03–0.54); p,p'-DDE = 2.60 (1.27–6.14); o,p'-DDT = 0.01 (0.02–0.32); p,p'-DDT = 0.46 (0.19–1.28); Σ DDT = 3.19 (1.62–7.62)	Cryptorchidism	Children whose mothers had higher OC pesticide concentrations at delivery had increased odds of cryptorchidism (HCB OR = 1.2; 95% CI: 1.1, 1.3; p,p'-DDE OR = 1.1; 95% CI: 1.1, 1.2; o,p'-DDT OR = 1.3; 95% CI: 1.1, 1.4; p,p'-DDT OR = 1.1; 95% CI: 1.1, 1.2; p,p'-DDE/o,p'-DDT OR = 1.4; 95% CI: 1.1, 1.8).
2. Rouget et al. <sup>167</sup>	2020/Guadeloupe	36 cases with congenital malformations/1,052 controls	Case-control	OCs	Maternal plasma (at delivery) and cord plasma chlordecone	Median (range) chlordecone (μg/L): Maternal plasma: 0.39 (<LOD–19.7); cord plasma: 0.20 (<LOD–29.8)	Congenital malformations	Null associations of maternal and cord plasma chlordecone concentrations with risk of overall malformations or underscended testes.
Studies on OPs or carbamates Studies in pregnant women 3. Acosta-Maldonado et al. <sup>171</sup>	2009/Mexico	9 pregnant women exposed to pesticides/76 nonexposed	Cross-sectional	OPs	Questionnaire (residential and partner exposure history) Blood AChE <sup>a</sup> Questionnaire (occupational and seasonal exposure histories) Blood AChE and BChE, placental CE <sup>a</sup>	Not applicable	Placental maturity	Pesticide exposure was associated with PMI of central area of placenta (β = 7.4, <i>p</i> = 0.01).
4. Vera et al. <sup>168</sup>	2012/Argentina	40 pregnant women living on agricultural farms	Cross-sectional	OPs	Questionnaire (residential and seasonal exposure history) Blood AChE and BChE, placental CE <sup>a</sup>	Not applicable	Nuclear and mitochondrial lipid composition of placenta	Total cholesterol and SM content of nucleus were higher in PP than RP ( <i>p</i> < 0.05), PE content of light mitochondria was lower in PP, whereas CL content was higher ( <i>p</i> < 0.05). The CL increased and the PE content decreased in the light mitochondrial fraction, whereas total cholesterol and SM increased in the nuclear fraction ( <i>p</i> < 0.05) in PP.
5. Bulgaroni et al. <sup>170</sup>	2013/Argentina	46 pregnant women from a rural area/36 pregnant women from urban area (controls)	Cross-sectional	OPs	Questionnaire (residential and seasonal exposure history) Blood AChE and BChE, placental CE <sup>a</sup>	Not applicable	Cytokines, arginase, and ornithine decarboxylase expression in placenta IL-13, TNF-α, and TGF-β Placental weight, p/w/hw ratio	IL-13 increased during SS in the rural group ( <i>p</i> < 0.001), whereas the expression frequency of TNF-α ( <i>p</i> < 0.05) and TGF-β ( <i>p</i> < 0.01) increased in the rural group in SS and NSS. The arginase activity ( <i>p</i> < 0.001), arginase II protein content ( <i>p</i> < 0.01), and ODC expression ( <i>p</i> < 0.001), increased in placentas collected during SS compared with those collected during NSS. No differences in placenta weight or p/w/hw ratio among groups.
6. Chiappella et al. <sup>172</sup>	2014/Argentina <sup>b</sup>	46 mother–newborn pairs from a rural area/24 mother–newborn pairs from an urban area (controls)	Cross-sectional	OPs	Questionnaire (residential and seasonal exposure history) Placental CE <sup>a</sup>	Not applicable	Placental weight, p/w/hw ratio Placental oxidative status (CAT, GPx, GSH, protein carbonyl, lipid peroxidation, anti-Nrf2 levels)	No differences in placental antioxidant/oxidant status, placental weight, or placental index between groups.
7. Rivero Osimani et al. <sup>169</sup>	2016/Argentina <sup>b</sup>	43 mother–newborn pairs from a rural area/20 mother–newborn pairs from an urban area (controls)	Cross-sectional	OPs	Questionnaire (residential and seasonal exposure history) Placental CE <sup>a</sup>	Not applicable	Placental weight Placental CT and SCT mitochondrial function (mitochondrial respiratory complex activity, CAT, Mn-SOD, GST, progesterone) and eNOS expression	No differences in placental parameters between newborns from RG-SS and controls SS ( <i>p</i> = 0.02). RG-SS had higher complex IV activity than RG-NSS ( <i>p</i> < 0.001) and CG ( <i>p</i> < 0.05). HNE levels in SCT mitochondria were lower in RG-SS than in CG ( <i>p</i> = 0.02). The antioxidant defense enzyme activity in CT and SCT mitochondria was similar among groups and seasons. Progesterone level was lower in RG-SS ( <i>p</i> < 0.05) than CG, and eNOS expression was lower in RG-NSS ( <i>p</i> = 0.001) and RG-SS ( <i>p</i> = 0.006) than CG.
8. Quintana et al. <sup>154</sup>	2017/Argentina <sup>b,c,d</sup>	151 mother–newborn pairs living in a rural area/38 mother–newborn pairs from an urban area (controls)	Cross-sectional	OPs	Questionnaire (residential and seasonal exposure history) Cord blood AChE, BChE <sup>a</sup>	Not applicable	Placental weight	Higher placental weight and p/w/hw for vaginal RG-SS and RG-NSS than in CG ( <i>p</i> = 0.01).

Table 4. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
Studies on other pesticides or multiple pesticide classes								
Studies in children								
9. Silva et al. <sup>166</sup>	2011/Brazil	42 cases with congenital malformations/84 controls	Case-control	Multiple pesticide classes	Questionnaire (parental, occupational and residential exposure history)	Not applicable	Congenital malformations	Null association of parental occupational exposure to pesticides and residential proximity to agricultural fields with congenital malformations.
10. Gaspari et al. <sup>164</sup>	2012/Brazil	2,710 male newborns from an intensive-use pesticide area	Cross-sectional	Herbicides, insecticides	Questionnaire (parental exposure history)	Not applicable	Cryptorchidism, hypospadias, and micropenis	Among the 56 cases of malformations detected (2.1%), 79% of the parents reported living in areas of high pesticide use for vector control; 80% of the mothers and 59% of the fathers were occupationally exposed to pesticides or other EDC before and during pregnancy, and 95% and 89% of the mothers reported residential exposure to pesticides or other EDCs before and during pregnancy, respectively.
11. Oliveira et al. <sup>162</sup>	2014/Brazil	219 cases with congenital malformations/862 live births controls	Case-control	Multiple pesticide classes	Questionnaire (residential exposure history at the periconceptional period) Exposure index from records (pesticides in formation systems and pesticide invoices) Questionnaire (parental exposure history)	Not applicable	Congenital malformations	Increased odds of congenital malformations in those children in the highest quartile of pesticide exposure in the 6 months prior to conception (OR = 2.0; 95% CI: 1.2, 3.6) and in the third and fourth quartiles of pesticide exposure after conception (OR = 1.7; 95% CI: 1.0, 2.8; OR = 1.9; 95% CI: 1.1, 3.2, respectively) compared with children in the lowest quartile.
12. Ueker et al. <sup>163</sup>	2016/Brazil	137 cases with congenital malformations (<5 years of age at enrollment)/274 controls	Case-control	Multiple pesticide classes	Questionnaire (parental exposure history)	Not applicable	Congenital malformations	Children whose fathers applied pesticides during the 12 months before conception and whose mothers had a low educational level had increased odds of congenital malformations (OR = 8.4; 95% CI: 2.2, 32.5). Null association between paternal pesticide use and congenital malformations among children whose mothers had a high educational level.
13. Castillo-Cadena et al. <sup>165</sup>	2017/Mexico	1,149 newborns from floricultural community/5,069 newborns from urban area (controls)	Prospective cohort	Multiple pesticide classes	Questionnaire (residential exposure history)	Not applicable	Congenital malformations	Congenital malformations were more prevalent among children born in a floricultural community (20%) than among those born in an urban area (6%) ( $p \leq 0.001$ ).

Note: AChE, acetylcholinesterase; BChE, butyrylcholinesterase; CAT, catalase; CE, carboxylesterase; CG, control group; CI, confidence interval; CL, cardioliplip + oxidized cardioliplip; CT, dichlorodiphenylchloroethylene; DDE, dichlorodiphenylchloroethylene; DDT, dichlorodiphenylchloroethylene; EDC, endocrine disrupting chemical; eNOS, endothelial nitric oxide synthase; GPX, glutathione peroxidase; GSH, glutathione; HCH, hexa-chlorocyclohexane; IL-13, interleukin-13; Mn, manganese; HNE, 4-hydroxynonenal; NfY2, nuclear factor erythroid 2-related; LOD, limit of detection; NSS, non-spraying season; OC, organochlorine; ODC, ornithine decarboxylase; OR, odds ratio; PE, phosphatidylethanolamine; PMI, placental maturity index; PP, pulverization period; pw/nw, placental weight/neonate weight ratio; RG, rural group; RP, recess period; SCT, syncytiotrophoblast; SM, sphingomyelin; SOD, superoxide dismutase; SS, spraying season; TGF- $\beta$ , transforming growth factor beta; TNF- $\alpha$ , tumor necrosis factor-alpha.

<sup>a</sup>Investigators did not use exposure biomarker concentrations in multivariate analyses.

<sup>b</sup>Also included in Table 8 (birth outcomes and child growth).

<sup>c</sup>Also included in Table 2 (genotoxicity).

<sup>d</sup>Also included in Table 9 (other health effects).

categories (e.g., rural vs. urban) in exposure–outcome analyses. Among the most prevalent outcomes associated with pesticide exposure were alterations in lipid composition and oxidative status of placental mitochondria,<sup>168,169</sup> as well as changes in the expression of placental cytokines and levels of placental enzymes (e.g., arginase, ornithine decarboxylase).<sup>170</sup> Publications from two cross-sectional studies conducted in Mexico and in Argentina reported that pesticide exposure was associated with a higher placental maturity index<sup>171</sup> and higher placental weight.<sup>54</sup> Conversely, three publications from Argentina reported largely null associations with placental morphological parameters (e.g., weight, placental weight to neonate weight ratio).<sup>169,170,172</sup>

To date, a small number of publications have reported on the association of pesticide exposure with placental or teratogenic outcomes in LAC populations and their findings are inconsistent. Some published studies found associations of exposure to OCs, OPs/carbamates, and multiple pesticide classes (retrospectively assessed via questionnaire in case–control studies) with outcomes such as alterations in lipid composition and oxidative stress of placental mitochondria and increased odds of congenital malformations. Other studies observed null associations with outcomes such as placental morphological parameters and risk of malformations.

## Cancer

Fourteen publications examined the association of pesticide exposure with cancer or cancer-related mortality in children or adults (Table 5). Thirteen publications reported findings from case–control studies; 12 of these studies used indirect exposure assessment methods (i.e., questionnaires or death certificates indicating occupation at the time of death) and 11 examined multiple pesticide classes. Two studies, 1 case–control and 1 prospective cohort, examined associations of serum OC pesticide concentrations with the risk of prostate cancer or prostate cancer recurrence.<sup>173,174</sup>

Five publications reported that children whose mothers were occupationally or environmentally exposed to pesticides before, during, or after pregnancy had increased odds of leukemia.<sup>175–179</sup> For instance, in a Brazilian case–control study, children whose mothers were exposed to pyrethroid insecticides during pregnancy had increased odds of acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) at 0–23 months of age.<sup>178</sup> Similarly, in a Costa Rican case–control study, boys, but not girls, whose mothers reported using insecticides inside their homes in the year before pregnancy, during pregnancy, and while breastfeeding had increased odds of childhood ALL.<sup>175</sup> Maternal report of pesticides sprayed on farms or companies near the home during pregnancy and while breastfeeding was also associated with childhood ALL in the Costa Rican study.<sup>175</sup> Another publication from this Costa Rican case–control study reported that children whose fathers were occupationally exposed to any pesticide during pregnancy, but particularly the second trimester, had increased odds of leukemia.<sup>176</sup>

Five publications examined the association of pesticide exposure with breast cancer,<sup>180,181</sup> cutaneous melanoma,<sup>182</sup> prostate cancer,<sup>174</sup> and prostate cancer recurrence<sup>173</sup> in adults. Two publications reported that women who reported using insecticides in their homes during adulthood (>18 years of age)<sup>180</sup> or who lived near agricultural fields<sup>181</sup> had increased odds of breast cancer. Another publication found that study participants who were ever exposed to pesticides had increased odds of cutaneous melanoma, with stronger associations among those with indoor residential pesticide exposure, particularly for those with a high frequency of use ( $\geq 4$  times per year) or long duration of exposure (>10 y).<sup>182</sup> In addition, two studies from Guadeloupe reported associations of serum concentrations of two OC pesticides,

DDE and chlordecone, with increased risk of prostate cancer<sup>174</sup> or its biochemical recurrence.<sup>173</sup>

Four publications assessed the association of occupational pesticide exposure with mortality by non-Hodgkin lymphoma<sup>183</sup> or esophageal,<sup>184</sup> brain,<sup>185</sup> or stomach<sup>186</sup> cancer in adults using death certificate data to ascertain occupation at the time of death. More specifically, a publication from a study conducted in Brazil reported mostly null associations between agricultural work and the risk of death by non-Hodgkin lymphoma.<sup>183</sup> Conversely, three publications reported that farmworkers had increased odds of dying from esophageal, brain, and stomach cancers than non-farmworkers; two of these publications also reported increased odds of dying from brain<sup>185</sup> and stomach<sup>186</sup> cancer among farmworkers who lived in the areas of greatest pesticide use.

The small number of studies published to date and included in this scoping review provide somewhat consistent evidence of associations between maternal pesticide exposure before or during pregnancy and increased risk of leukemia among LAC children. In addition, eight of nine publications of studies conducted in adults reported evidence of residential or occupational pesticide exposure with an increased risk of various types of cancer or death by cancer. Nevertheless, these findings must be interpreted with caution given that all studies assessed exposure to multiple pesticide classes via questionnaire and examined different types of cancer.

## Thyroid Function

Sixteen publications from 10 cross-sectional studies and 6 prospective cohort studies reported on the associations of pesticide exposure with thyroid function (Table 6). Four of these 16 publications examined the potential thyroid effects of OC pesticide exposure—assessed via measurement of OC pesticide metabolites in blood or breast milk—among children.<sup>117,187–189</sup> Briefly, a publication from a cross-sectional study of mother–newborn pairs in Bolivia reported null associations of cord blood DDT and DDE concentrations with neonatal thyroid-stimulating hormone (TSH) levels.<sup>188</sup> However, a publication from a cross-sectional study of Brazilian children (0–14 years of age) found that higher concentrations of 17 (of 19) OC pesticides, including DDE and DDT but not chlordecone, were associated with increased levels of total triiodothyronine (T3) or free thyroxine (T4), but not with TSH.<sup>187</sup> Two publications from a prospective cohort study in Guadeloupe reported associations of early-life chlordecone exposure—as indicated by measurement of chlordecone in cord blood and breast milk samples—with elevated TSH or decreased T3 and T4 at 3 months and at 7 years of age, with some evidence of effect modification by sex.<sup>117,189</sup>

Five publications reported on the association between exposure to OC pesticides and thyroid function in adults (Table 6). A publication from a cross-sectional study of individuals living near an abandoned pesticide factory in Brazil reported various associations of OC pesticide concentrations with thyroid hormone levels, which differed between men and women.<sup>190</sup> For example, among men, higher endosulfan 2 concentrations were associated with decreased T3 levels, whereas higher  $\beta$ -HCH and DDT concentrations were associated with decreased free T4 levels. Among women, higher  $\alpha$ -chlordane, DDT, endosulfan 2, and methoxychlor concentrations were associated with increased T3 levels, whereas higher HCB, heptachlor, and DDT concentrations were associated with increased T4 levels.<sup>190</sup> A publication from a cross-sectional study of farmworker families in Brazil also reported associations of several OC pesticide concentrations with increased TSH (i.e.,  $\gamma$ -chlordane), total T3 (i.e.,  $\gamma$ -chlordane,  $\beta$ -HCH, heptachlor epoxide B, *trans*-nonachlor, DDE, and endosulfan 2), or free T4 (i.e., dieldrin).<sup>191</sup> Two publications from



**Table 5.** Characteristics of Latin American and the Caribbean studies on pesticide exposure and cancer published between 2007 and 2021 (*n* = 14).

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
<b>Studies in children</b>								
1. Monge et al. <sup>176</sup>	2007/Costa Rica	344 childhood leukemia cases (<15 years of age)/ 579 controls	Case-control	Herbicides, fungicides, insecticides	Questionnaire (parental occupational exposure during the year before conception, pregnancy, and first year of life of the child)	Not applicable	Childhood leukemia (ALL, AML, other leukemias)	Children whose mothers were occupationally exposed to any pesticide during the year before conception (OR = 2.4; 95% CI: 1.0, 5.9), first trimester (OR = 22; 95% CI: 2.8, 171.5), second trimester (OR = 4.5; 95% CI: 1.4, 14.7) of pregnancy, or at any time (OR = 2.2; 95% CI: 1.0, 4.8) had increased odds of leukemia. Children whose fathers were occupationally exposed to any pesticide during the second trimester of pregnancy had increased odds of leukemia (OR = 1.5; 95% CI: 1.0, 2.3).
2. Hernández-Morales et al. <sup>177</sup>	2009/Mexico	47 childhood leukemia cases (<14 years of age)/ 47 controls	Case-control	Multiple pesticide classes	Questionnaire (parental occupational exposure and residential exposure during the 3 months before pregnancy, pregnancy, at birth, and at the time of diagnosis; residential proximity to agricultural fields)	Not applicable	Childhood leukemia (ALL, AML)	Children whose parents used pesticides inside their homes during the 3 months before pregnancy (OR = 2.1; 95% CI: 1.5, 2.9) or during pregnancy (OR = 1.5; 95% CI: 1.0, 2.3) had increased odds of leukemia. Children whose parents used pesticides in their gardens during the 3 months before pregnancy (OR = 1.8; 95% CI: 1.2, 2.6) or during pregnancy (OR = 1.6; 95% CI: 1.0, 2.6) also had increased odds of leukemia.
3. Ferreira et al. <sup>179</sup>	2012/Brazil	292 childhood leukemia cases (<13 years of age)/ 541 controls	Case-control	Herbicides, insecticides	Questionnaire (parental occupational and environmental exposure during the 3 months before pregnancy, pregnancy, and while breastfeeding)	Not applicable	Childhood leukemia (ALL, AML)	Children whose mothers were occupationally or environmentally exposed to chemicals (including pesticides) during pregnancy had increased odds of leukemia (OR = 1.4; 95% CI: 1.2, 1.6).
4. Ferreira et al. <sup>178</sup>	2013/Brazil	252 childhood leukemia cases (<24 months of age)/423 controls	Case-control	Multiple pesticide classes	Questionnaire (parental occupational and environmental exposure during the 3 months before pregnancy, pregnancy, and while breastfeeding)	Not applicable	Childhood leukemia (ALL, AML)	Children whose mothers were occupationally or environmentally exposed to pesticides during the 3 months before pregnancy had increased odds of ALL (OR = 2.4; 95% CI: 1.2, 4.8) and AML (OR = 3.8; 95% CI: 1.3, 10.8) at 0–11 months of age and increased odds of AML (OR = 2.5; 95% CI: 1.2, 5.1) at 12–23 months of age. Children whose mothers were occupationally or environmentally exposed to pesticides during pregnancy and while breastfeeding had increased odds of AML (e.g., OR for exposures during the third trimester = 3.7; 95% CI: 1.3, 10.4) at 0–11 months of age. Children whose mothers were occupationally or environmentally exposed to any pyrethroid pesticide during pregnancy had increased odds of ALL (OR = 1.8; 95% CI: 1.1, 2.9) and AML (OR = 3.4; 95% CI: 1.7, 16.8) at 0–23 months of age. Increased odds of ALL or AML were also observed among children whose mothers were exposed to individual pyrethroids during pregnancy.
5. Hyland et al. <sup>175</sup>	2018/Costa Rica	251 childhood leukemia cases (<15 years of age)/ 577 controls	Case-control	Multiple pesticide classes	Questionnaire (residential use and nearby pesticide applications in the year prior to pregnancy, during pregnancy, while breastfeeding, and during childhood)	Not applicable	Childhood leukemia (ALL)	Boys whose mothers reported using insecticides inside the home in the year before pregnancy (OR = 1.6; 95% CI: 1.1, 2.5), during pregnancy (OR = 1.8; 95% CI: 1.1, 2.7), and while breastfeeding (OR = 1.8; 95% CI: 1.1, 2.7) had increased odds of ALL. Children whose mothers reported a high average frequency of insecticide use inside their homes (>36 times/y) in the year before pregnancy, during pregnancy, and while breastfeeding had increased odds of ALL compared with children whose mothers reported a low frequency of insecticide use (<2.5 times/y) during these exposure periods (e.g., OR for exposure during pregnancy = 1.6; 95% CI: 1.1, 2.3). Maternal report of pesticides sprayed on farms or at companies near the home during pregnancy, while breastfeeding, and during any time period was also associated with childhood ALL (e.g., OR for exposure during pregnancy = 1.4; 95% CI: 1.0, 2.1).
<b>Studies in adults</b>								
6. Ortega-Iacone et al. <sup>180</sup>	2010/Brazil	110 breast cancer cases/101 controls	Case-control	Insecticides	Questionnaire (lifetime residential use of insecticides)	Not applicable	Breast cancer	Women who used insecticides in their homes during adulthood (>18 years of age) had increased odds of breast cancer (OR = 4.9; 95% CI: 1.8, 12.9).
7. Meyer et al. <sup>184</sup>	2011/Brazil	5,782 deaths by esophageal cancer/5,782 deaths by causes other than neoplasms and diseases of the digestive system	Case-control	Multiple pesticide classes	Death certificates (occupation at the time of death)	Not applicable	Esophageal cancer mortality	Agricultural workers had increased odds of dying from esophageal cancer compared with nonagricultural workers (OR = 1.4; 95% CI: 1.2, 1.6).

Table 5. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
8. Miranda-Filho et al. <sup>185</sup>	2012/Brazil	2,040 deaths in males by brain cancer/4,140 deaths in males by causes other than neoplasms and diseases of the central nervous system	Case-control	Multiple pesticide classes	Death certificates (occupation at the time of death) and pesticide sales per region of residence	Not applicable	Brain cancer mortality	Agricultural workers had increased odds of dying from brain cancer compared with nonagricultural workers (OR = 1.8; 95% CI: 1.2, 2.7). Slightly increased brain cancer mortality odds were also observed in agricultural workers who resided in municipalities in Rio de Janeiro state in the third (OR = 1.2; 95% CI: 1.0, 1.5) and fourth (OR = 1.2; 95% CI: 0.9, 1.5) quartiles of per capita use of pesticides. Agricultural workers had increased odds of dying from stomach cancer compared with nonagricultural workers (OR = 1.4; 95% CI: 1.3, 1.8). Among agricultural workers, those who resided in the areas with the highest levels of pesticide use had slightly increased odds of stomach cancer (e.g., OR for the highest quartile = 1.4; 95% CI: 0.9, 2.1). Those who were ever exposed to pesticides had increased odds of cutaneous melanoma compared with those who were never exposed (OR = 2.0; 95% CI: 1.0, 6.9). Indoor residential pesticide use was associated with increased odds of cutaneous melanoma; exposure for >10 y was associated with increased odds compared with exposure for ≤10 y (OR = 2.8; 95% CI: 1.6, 5.3) and high frequency of indoor pesticide use (≥4 times/y) associated with increased odds compared with low frequency of use (≤3 times/y) OR = 1.4; 95% CI: 1.1, 3.5). Null associations between residential outdoor pesticide exposure and cutaneous melanoma. History of occupational exposure to pesticides was also associated with increased odds of cutaneous melanoma (OR = 4.2; 95% CI: 1.9, 6.3).
9. Boccolini et al. <sup>186</sup>	2014/Brazil	1,176 stomach cancer deaths cases/11,557 controls who died by causes other than neoplasms and diseases of the digestive system	Case-control	Multiple pesticide classes	Death certificates (occupation at the time of death and pesticide expenditure per agricultural worker)	Not applicable	Stomach cancer mortality	Agricultural workers had increased odds of dying from brain cancer compared with nonagricultural workers (OR = 1.8; 95% CI: 1.2, 2.7). Slightly increased brain cancer mortality odds were also observed in agricultural workers who resided in municipalities in Rio de Janeiro state in the third (OR = 1.2; 95% CI: 1.0, 1.5) and fourth (OR = 1.2; 95% CI: 0.9, 1.5) quartiles of per capita use of pesticides. Agricultural workers had increased odds of dying from stomach cancer compared with nonagricultural workers (OR = 1.4; 95% CI: 1.3, 1.8). Among agricultural workers, those who resided in the areas with the highest levels of pesticide use had slightly increased odds of stomach cancer (e.g., OR for the highest quartile = 1.4; 95% CI: 0.9, 2.1). Those who were ever exposed to pesticides had increased odds of cutaneous melanoma compared with those who were never exposed (OR = 2.0; 95% CI: 1.0, 6.9). Indoor residential pesticide use was associated with increased odds of cutaneous melanoma; exposure for >10 y was associated with increased odds compared with exposure for ≤10 y (OR = 2.8; 95% CI: 1.6, 5.3) and high frequency of indoor pesticide use (≥4 times/y) associated with increased odds compared with low frequency of use (≤3 times/y) OR = 1.4; 95% CI: 1.1, 3.5). Null associations between residential outdoor pesticide exposure and cutaneous melanoma. History of occupational exposure to pesticides was also associated with increased odds of cutaneous melanoma (OR = 4.2; 95% CI: 1.9, 6.3).
10. Segatto et al. <sup>182</sup>	2015/Brazil	95 cutaneous melanoma cases/96 controls	Case-control	Multiple pesticide classes	Questionnaire (lifetime occupational and residential exposure)	Not applicable	Cutaneous melanoma	Agricultural workers had increased odds of dying from brain cancer compared with nonagricultural workers (OR = 1.8; 95% CI: 1.2, 2.7). Slightly increased brain cancer mortality odds were also observed in agricultural workers who resided in municipalities in Rio de Janeiro state in the third (OR = 1.2; 95% CI: 1.0, 1.5) and fourth (OR = 1.2; 95% CI: 0.9, 1.5) quartiles of per capita use of pesticides. Agricultural workers had increased odds of dying from stomach cancer compared with nonagricultural workers (OR = 1.4; 95% CI: 1.3, 1.8). Among agricultural workers, those who resided in the areas with the highest levels of pesticide use had slightly increased odds of stomach cancer (e.g., OR for the highest quartile = 1.4; 95% CI: 0.9, 2.1). Those who were ever exposed to pesticides had increased odds of cutaneous melanoma compared with those who were never exposed (OR = 2.0; 95% CI: 1.0, 6.9). Indoor residential pesticide use was associated with increased odds of cutaneous melanoma; exposure for >10 y was associated with increased odds compared with exposure for ≤10 y (OR = 2.8; 95% CI: 1.6, 5.3) and high frequency of indoor pesticide use (≥4 times/y) associated with increased odds compared with low frequency of use (≤3 times/y) OR = 1.4; 95% CI: 1.1, 3.5). Null associations between residential outdoor pesticide exposure and cutaneous melanoma. History of occupational exposure to pesticides was also associated with increased odds of cutaneous melanoma (OR = 4.2; 95% CI: 1.9, 6.3).
11. Emesville et al. <sup>174</sup>	2015/Guadeloupe	576 prostate cancer cases/655 controls	Case-control	OCs	Serum DDT, DDE, chlordane	Median (P25-P75) (μg/L): p,p'-DDT ≤ LOD (< LOD-0.07) for controls and < LOD (< LOD-0.06) for cases; p,p'-DDD ≤ LOD (< LOD-0.04) for controls and < LOD (< LOD-0.03) for cases; p,p'-DDE = 2.06 (0.98–4.37) for controls and 2.55 (1.11–5.74) for cases; Chlordane = 0.42 (0.17–0.83) for controls and 0.43 (0.18–0.94) for cases	Prostate cancer	Agricultural workers had increased odds of dying from brain cancer compared with nonagricultural workers (OR = 1.8; 95% CI: 1.2, 2.7). Slightly increased brain cancer mortality odds were also observed in agricultural workers who resided in municipalities in Rio de Janeiro state in the third (OR = 1.2; 95% CI: 1.0, 1.5) and fourth (OR = 1.2; 95% CI: 0.9, 1.5) quartiles of per capita use of pesticides. Agricultural workers had increased odds of dying from stomach cancer compared with nonagricultural workers (OR = 1.4; 95% CI: 1.3, 1.8). Among agricultural workers, those who resided in the areas with the highest levels of pesticide use had slightly increased odds of stomach cancer (e.g., OR for the highest quartile = 1.4; 95% CI: 0.9, 2.1). Those who were ever exposed to pesticides had increased odds of cutaneous melanoma compared with those who were never exposed (OR = 2.0; 95% CI: 1.0, 6.9). Indoor residential pesticide use was associated with increased odds of cutaneous melanoma; exposure for >10 y was associated with increased odds compared with exposure for ≤10 y (OR = 2.8; 95% CI: 1.6, 5.3) and high frequency of indoor pesticide use (≥4 times/y) associated with increased odds compared with low frequency of use (≤3 times/y) OR = 1.4; 95% CI: 1.1, 3.5). Null associations between residential outdoor pesticide exposure and cutaneous melanoma. History of occupational exposure to pesticides was also associated with increased odds of cutaneous melanoma (OR = 4.2; 95% CI: 1.9, 6.3).
12. Boccolini et al. <sup>183</sup>	2016/Brazil	1,317 non-Hodgkin lymphoma death cases/2,634 controls who died by causes other than neoplasms or hematological diseases	Case-control	Multiple pesticide classes	Death certificates (occupation at the time of death and pesticide expenditure per agricultural worker)	Not applicable	Non-Hodgkin lymphoma	Agricultural workers had increased odds of dying from brain cancer compared with nonagricultural workers (OR = 1.8; 95% CI: 1.2, 2.7). Slightly increased brain cancer mortality odds were also observed in agricultural workers who resided in municipalities in Rio de Janeiro state in the third (OR = 1.2; 95% CI: 1.0, 1.5) and fourth (OR = 1.2; 95% CI: 0.9, 1.5) quartiles of per capita use of pesticides. Agricultural workers had increased odds of dying from stomach cancer compared with nonagricultural workers (OR = 1.4; 95% CI: 1.3, 1.8). Among agricultural workers, those who resided in the areas with the highest levels of pesticide use had slightly increased odds of stomach cancer (e.g., OR for the highest quartile = 1.4; 95% CI: 0.9, 2.1). Those who were ever exposed to pesticides had increased odds of cutaneous melanoma compared with those who were never exposed (OR = 2.0; 95% CI: 1.0, 6.9). Indoor residential pesticide use was associated with increased odds of cutaneous melanoma; exposure for >10 y was associated with increased odds compared with exposure for ≤10 y (OR = 2.8; 95% CI: 1.6, 5.3) and high frequency of indoor pesticide use (≥4 times/y) associated with increased odds compared with low frequency of use (≤3 times/y) OR = 1.4; 95% CI: 1.1, 3.5). Null associations between residential outdoor pesticide exposure and cutaneous melanoma. History of occupational exposure to pesticides was also associated with increased odds of cutaneous melanoma (OR = 4.2; 95% CI: 1.9, 6.3).
13. Silva et al. <sup>181</sup>	2019/Brazil	85 breast cancer cases/266 controls	Case-control	Multiple pesticide classes	Questionnaire (environmental and occupational exposure history)	Not applicable	Breast cancer	Agricultural workers had increased odds of dying from brain cancer compared with nonagricultural workers (OR = 1.8; 95% CI: 1.2, 2.7). Slightly increased brain cancer mortality odds were also observed in agricultural workers who resided in municipalities in Rio de Janeiro state in the third (OR = 1.2; 95% CI: 1.0, 1.5) and fourth (OR = 1.2; 95% CI: 0.9, 1.5) quartiles of per capita use of pesticides. Agricultural workers had increased odds of dying from stomach cancer compared with nonagricultural workers (OR = 1.4; 95% CI: 1.3, 1.8). Among agricultural workers, those who resided in the areas with the highest levels of pesticide use had slightly increased odds of stomach cancer (e.g., OR for the highest quartile = 1.4; 95% CI: 0.9, 2.1). Those who were ever exposed to pesticides had increased odds of cutaneous melanoma compared with those who were never exposed (OR = 2.0; 95% CI: 1.0, 6.9). Indoor residential pesticide use was associated with increased odds of cutaneous melanoma; exposure for >10 y was associated with increased odds compared with exposure for ≤10 y (OR = 2.8; 95% CI: 1.6, 5.3) and high frequency of indoor pesticide use (≥4 times/y) associated with increased odds compared with low frequency of use (≤3 times/y) OR = 1.4; 95% CI: 1.1, 3.5). Null associations between residential outdoor pesticide exposure and cutaneous melanoma. History of occupational exposure to pesticides was also associated with increased odds of cutaneous melanoma (OR = 4.2; 95% CI: 1.9, 6.3).
14. Brureau et al. <sup>173</sup>	2020/Guadeloupe	340 incident prostate cancer patients who underwent radical prostatectomy	Prospective cohort	OCs	Serum chlordane, DDE	Median (P25-P75) (μg/L): Chlordane = 0.38 (0.16–0.69); p,p'-DDE = 2.33 (0.93–4.68)	Biochemical recurrence of prostate cancer (defined as two consecutive PSA measurements >0.2 ng/mL)	Agricultural workers had increased odds of dying from brain cancer compared with nonagricultural workers (OR = 1.8; 95% CI: 1.2, 2.7). Slightly increased brain cancer mortality odds were also observed in agricultural workers who resided in municipalities in Rio de Janeiro state in the third (OR = 1.2; 95% CI: 1.0, 1.5) and fourth (OR = 1.2; 95% CI: 0.9, 1.5) quartiles of per capita use of pesticides. Agricultural workers had increased odds of dying from stomach cancer compared with nonagricultural workers (OR = 1.4; 95% CI: 1.3, 1.8). Among agricultural workers, those who resided in the areas with the highest levels of pesticide use had slightly increased odds of stomach cancer (e.g., OR for the highest quartile = 1.4; 95% CI: 0.9, 2.1). Those who were ever exposed to pesticides had increased odds of cutaneous melanoma compared with those who were never exposed (OR = 2.0; 95% CI: 1.0, 6.9). Indoor residential pesticide use was associated with increased odds of cutaneous melanoma; exposure for >10 y was associated with increased odds compared with exposure for ≤10 y (OR = 2.8; 95% CI: 1.6, 5.3) and high frequency of indoor pesticide use (≥4 times/y) associated with increased odds compared with low frequency of use (≤3 times/y) OR = 1.4; 95% CI: 1.1, 3.5). Null associations between residential outdoor pesticide exposure and cutaneous melanoma. History of occupational exposure to pesticides was also associated with increased odds of cutaneous melanoma (OR = 4.2; 95% CI: 1.9, 6.3).

Note: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CI, confidence interval; DDE, dichlorodiphenyldichloroethylene; DDT, dichlorodiphenyltrichloroethane; HR, hazard ratio; LOD, limit of detection; OC, organochlorine; OR, odds ratio; P, percentile; PSA, prostate-specific antigen.

**Table 6.** Characteristics of Latin American and the Caribbean studies on pesticide exposure and thyroid function published between 2007 and 2021 ( $n = 16$ ).

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
<b>Studies on OCs</b>								
<b>Studies in children</b>								
1. Freire et al. <sup>187</sup>	2012/Brazil	193 children (0–14 years of age) from an old factory	Cross-sectional	OCs	Questionnaire (occupational and residential history of parents) Serum HCH, HCB, chlordane, <i>trans</i> -nonachlor, heptachlor, DDT, DDE, endosulfan, aldrin, endrin, dieldrin, methoxychlor, mirex	Median (P20–P80) (ng/mL): $\alpha$ -HCH = 7.8 (1.1–18.0); $\beta$ -HCH = 10.2 (2.0–27.0); $\gamma$ -HCH = 2.5 (0.5–6.7); HCB = 0.8 (0.2–2.0); $\alpha$ -chlordane = 0.6 (< LOD–1.6); $\gamma$ -chlordane = 0.5 (< LOD–0.9); <i>trans</i> -nonachlor = 0.9 (0.1–1.7); heptachlor = 1.1 (< LOD–2.3); $p,p'$ -DDE = 10.2 (2.0–35.7); $p,p'$ -DDT = 1.2 (< LOD–2.2); $p,p'$ -DDD = 6.9 (1.1–17.7); $p,p'$ -DDD = 1.2 (0.3–2.6); endosulfan 1 = 0.7 (< LOD–1.0); endosulfan 2 = 0.7 (< LOD–1.4); aldrin = 3.4 (0.7–19.3); endrin = 1.5 (0.3–3.6); dieldrin = 1.1 (0.3–2.9); methoxychlor = 0.7 (< LOD–0.5); mirex = 1.0 (< LOD–1.7)	Serum TSH, total T3, fT4	Higher concentrations of 17 of 19 OC pesticides were associated with increased total T3 levels [ $\beta$ (95% CI)] for highest quintile of exposure compared with lowest quintile of exposure: $\alpha$ -HCH = 14.9 (–2.6, 27.2); $\beta$ -HCH = 12.1 (–0.12, 24.4); $\gamma$ -HCH = 13.8 (1.5, 26.2); HCB = 14.8 (2.7, 26.9); $\alpha$ -chlordane = 21.4 (9.7, 33.1); $\gamma$ -chlordane = 16.0 (4.5, 27.4); <i>trans</i> -nonachlor = 19.6 (7.5, 31.6); $p,p'$ -DDE = 11.5 (–0.6, 23.6); $p,p'$ -DDT = 8.8 (–2.5, 20.1); $p,p'$ -DDD = –10.6 (–1.4, 22.6); endosulfan 1 = 17.3 (6.4, 28.2); endosulfan 2 = 15.1 (4.3, 25.9); aldrin = 13.1 (0.8, 25.3); endrin = 13.3 (1.2, 25.4); dieldrin = 20.3 (8.1, 32.6). For mirex, exposure was categorized into quartiles and the highest quartile of exposure was associated with increased total T3 levels compared with the lowest quartile ( $\beta$ = 10.3; 95% CI: –0.1, 20.7). Highest quartile of DDD ( $\beta$ = 0.1; 95% CI: 0, 0.2), endosulfan 1 ( $\beta$ = 0.1; 95% CI: 0, 0.1), and dieldrin ( $\beta$ = 0; 95% CI: –0.1, 0.11) were associated with increased fT4 levels. Mostly null associations between OC pesticides and TSH levels.
2. Arrebola et al. <sup>188</sup>	2016/Bolivia <sup>a</sup>	200 mother–newborn pairs from agricultural area	Cross-sectional	OCs	Questionnaire (residential exposure history) Cord blood DDT and DDE Cord blood and breast milk chlordecone, cord blood DDE	Median (P25–P75) (ng/g lipid): $p,p'$ -DDE = 196.8 (52.8–475.0); $p,p'$ -DDT = 39.5 (19.3–75.1) Median (P25–P75) ( $\mu$ g/L): Cord blood chlordecone = 0.13 (< LOD–0.31); cord blood $p,p'$ -DDE = 0.30 (0.09–1.05); breast milk chlordecone = 0.60 (< LOD–1.16)	Serum TSH	Null associations of cord blood DDT and DDE with neonatal TSH levels.
3. Cordier et al. <sup>117</sup>	2015/Guadeloupe <sup>b</sup>	111 mother–child (18 months of age) pairs	Prospective cohort	OCs	Cord and child blood chlordecone, cord blood DDE	Median (P25–P75) ( $\mu$ g/L): Cord blood chlordecone: boys = 0.25 (0.08–0.41), girls = 0.21 (0.07–0.37); child chlordecone: boys = 0.06 (< LOD–0.11), girls = 0.05 (< LOD–0.11); cord blood DDE: boys = 0.22 (0.09–0.64), girls = 0.31 (0.10–0.74)	Serum TSH, fT3, fT4	Cord chlordecone was associated with increased TSH, particularly among boys ( $p < 0.01$ ). Postnatal chlordecone was associated with decreased fT3 among boys and decreased fT4 among girls ( $p < 0.05$ ). Third quartile of cord blood chlordecone associated with elevated TSH levels in girls ( $\beta$ = 0.2; 95% CI: 0, 0.4), relative to first quartile. Null associations of cord blood chlordecone with fT3 and fT4. No report on associations of child chlordecone and cord blood DDE with thyroid hormones.
4. Ayhan et al. <sup>189</sup>	2021/Guadeloupe <sup>c,d</sup>	285 mother–child (7 years of age) pairs	Prospective cohort	OCs	Cord and child blood chlordecone, cord blood DDE	Median (P25–P75) (ng/mL): Women: $\alpha$ -HCH = 2.6 (1.0–6.0); $\beta$ -HCH = 7.0 (2.8–17.6); $\gamma$ -HCH = 1.0 (0.4–2.2); HCB = 0.4 (0.2–0.7); $\alpha$ -chlordane = 0.3 (< LOD–0.6); $\gamma$ -chlordane = 0.2 (< LOD–0.4); <i>trans</i> -nonachlor = 0.4 (0.2–0.8); heptachlor = 0.4 (< LOD–0.8); $p,p'$ -DDE = 9.6 (3.5–28.9); $p,p'$ -DDT = 0.4 (< LOD–1.1); $p,p'$ -DDD = 3.2 (1.0–7.6); $p,p'$ -DDD = 0.7 (0.2–1.4); endosulfan 1 = 0.2 (< LOD–0.4); endosulfan 2 = 0.2 (< LOD–0.7); aldrin = 2.4 (0.8–14.1); endrin = 0.6 (0.3–1.5); dieldrin = 0.6 (0.2–1.2); methoxychlor = 0.4 (< LOD–1.0); mirex < LOD (< LOD–0.3)	Serum TSH, total T3, fT4 TPOAb, TGAb	Among men, higher endosulfan 2 was associated with decreased total T3 levels ( $\beta$ = –2.3; 95% CI: –4.6, –0.01); higher $\beta$ -HCH was associated with decreased fT4 levels ( $\beta$ = –0.003; 95% CI: –0.006, –0.001) and slightly increased TSH levels ( $\beta$ = 0.003; 95% CI: 0.001, 0.007); higher $p,p'$ -DDT was associated with decreased fT4 ( $\beta$ = –0.003; 95% CI: –0.006, –0.001). Men with detected methoxychlor had an increased risk for presence of TPOAb (OR = 2.2; 95% CI: 1.3, 3.8). Among women, higher $\alpha$ -chlordane ( $\beta$ = 5.7; 95% CI: 1.1, 10.2); $p,p'$ -DDT ( $\beta$ = 0.4; 95% CI: 0.1, 0.7), endosulfan 2 ( $\beta$ = 3.5; 95% CI: 0.1, 7.0), and methoxychlor ( $\beta$ = 8.5; 95% CI: 1.7, 15.4) was associated with increased total T3 levels; higher HCB ( $\beta$ = 0.02; 95% CI: 0.001, 0.04); heptachlor ( $\beta$ = 0.02; 95% CI: 0.003, 0.03).
<b>Studies in adults</b>								
5. Freire et al. <sup>190</sup>	2013/Brazil	608 adolescents and adults (> 14 years of age) living near an abandoned pesticide factory	Cross-sectional	OCs	Questionnaire (residential exposure history) Serum HCH, HCB, chlordane, <i>trans</i> -nonachlor, heptachlor, DDT, DDE, endosulfan, aldrin, endrin, dieldrin, methoxychlor, mirex	Median (P25–P75) (ng/mL): Women: $\alpha$ -HCH = 2.6 (1.0–6.0); $\beta$ -HCH = 7.0 (2.8–17.6); $\gamma$ -HCH = 1.0 (0.4–2.2); HCB = 0.4 (0.2–0.7); $\alpha$ -chlordane = 0.3 (< LOD–0.6); $\gamma$ -chlordane = 0.2 (< LOD–0.4); <i>trans</i> -nonachlor = 0.4 (0.2–0.8); heptachlor = 0.4 (< LOD–0.8); $p,p'$ -DDE = 9.6 (3.5–28.9); $p,p'$ -DDT = 0.4 (< LOD–1.1); $p,p'$ -DDD = 3.2 (1.0–7.6); $p,p'$ -DDD = 0.7 (0.2–1.4); endosulfan 1 = 0.2 (< LOD–0.4); endosulfan 2 = 0.2 (< LOD–0.7); aldrin = 2.4 (0.8–14.1); endrin = 0.6 (0.3–1.5); dieldrin = 0.6 (0.2–1.2); methoxychlor = 0.4 (< LOD–1.0); mirex < LOD (< LOD–0.3) Men: $\alpha$ -HCH = 2.5 (1.0–0.7); $\beta$ -HCH = 6.0 (2.1–15.4); $\gamma$ -HCH = 1.0 (0.4–2.2); HCB = 0.3 (0.1–0.6);	Serum TSH, total T3, fT4 TPOAb, TGAb	Among men, higher endosulfan 2 was associated with decreased total T3 levels ( $\beta$ = –2.3; 95% CI: –4.6, –0.01); higher $\beta$ -HCH was associated with decreased fT4 levels ( $\beta$ = –0.003; 95% CI: –0.006, –0.001) and slightly increased TSH levels ( $\beta$ = 0.003; 95% CI: 0.001, 0.007); higher $p,p'$ -DDT was associated with decreased fT4 ( $\beta$ = –0.003; 95% CI: –0.006, –0.001). Men with detected methoxychlor had an increased risk for presence of TPOAb (OR = 2.2; 95% CI: 1.3, 3.8). Among women, higher $\alpha$ -chlordane ( $\beta$ = 5.7; 95% CI: 1.1, 10.2); $p,p'$ -DDT ( $\beta$ = 0.4; 95% CI: 0.1, 0.7), endosulfan 2 ( $\beta$ = 3.5; 95% CI: 0.1, 7.0), and methoxychlor ( $\beta$ = 8.5; 95% CI: 1.7, 15.4) was associated with increased total T3 levels; higher HCB ( $\beta$ = 0.02; 95% CI: 0.001, 0.04); heptachlor ( $\beta$ = 0.02; 95% CI: 0.003, 0.03).

Table 6. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
						$\alpha$ -chlordane = 0.2 (< LOD–0.6); $\gamma$ -chlordane = 0.2 (< LOD–0.4); <i>trans</i> -nonachlor = 0.3 (0.2–0.8); heptachlor = 0.3 (< LOD–0.9); $p,p'$ -DDE = 8.3 (2.9–21.9); $\alpha,p'$ -DDT = 0.3 (< LOD–0.9); $p,p'$ -DDT = 3.1 (1.0–7.0); $p,p'$ -DDD = 0.6 (0.2–1.3); endosulfan 1 = 0.2 (< LOD–0.5); endosulfan 2 = 0.2 (< LOD–0.7); aldrin = 1.9 (0.7–11.0); endrin = 0.6 (0.2–1.5); dieldrin = 0.6 (0.3–1.3); methoxychlor = 0.5 (< LOD–1.0); mirex < LOD (< LOD–0.3)		$\alpha,p'$ -DDT ( $\beta = 0.02$ ; 95% CI: 0.01, 0.04), and $p,p'$ -DDT ( $\beta = 0.003$ ; 95% CI: 0.001, 0.01) were associated with increased FT4 among women. Aldrin was associated with the presence of TPOAb (OR = 1.01; 95% CI: 1.0, 1.02).
6. Blanco-Muñoz et al. <sup>192</sup>	2016/Mexico	136 male floriculture workers	Prospective cohort	OCs	Questionnaire (occupational and residential exposure history)	Median (P25–P75) (ng/mL) Rainy season $p,p'$ -DDE = 4.9 (2.9–11.1); dry season $p,p'$ -DDE = 4.7 (2.2–11.1)	Serum TSH, total T3, total T4	Higher $p,p'$ -DDE was associated with increased total T3 ( $\beta = 0.01$ ; 95% CI: –0.01, 0.03) and total T4 ( $\beta = 0.01$ ; 95% CI: 0.0, 0.1) levels. Null association of $p,p'$ -DDE with TSH levels. Farmworkers had higher total T3 ( $\beta = 1.1$ ; 95% CI: 1.01, 1.1) than non-farmworkers. Higher $\gamma$ -chlordane was associated with increased TSH levels ( $\beta = 1.3$ ; 95% CI: 1.01, 1.5), whereas higher dieldrin was associated with increased FT4 ( $\beta = 0.9$ ; 95% CI: 0.9, 1.0). Higher $\gamma$ -chlordane ( $\beta = 1.1$ ; 95% CI: 1.0, 1.1), $\beta$ -HCH ( $\beta = 1.1$ ; 95% CI: 1.0, 1.1), heptachlor epoxide B ( $\beta = 1.1$ ; 95% CI: 1.0, 1.2), <i>trans</i> -nonachlor ( $\beta = 1.1$ ; 95% CI: 1.0, 1.2), $p,p'$ -DDE ( $\beta = 1.03$ ; 95% CI: 1.0, 1.1), and endosulfan 2 ( $\beta = 1.1$ ; 95% CI: 1.0, 1.3) were associated with increased total T3. AChE and BCHE inhibitions were not associated with thyroid hormones.
7. Piccoli et al. <sup>191</sup>	2016/Brazil	275 men and women from farmworker families	Cross-sectional	OCs, OPs	Questionnaire (residential and occupational exposure history) Serum HCH, HCB, chlordane, heptachlor, heptachlor epoxide B, <i>trans</i> -nonachlor, DDT, DDE, DDD, endosulfan, aldrin, endrin, dieldrin, methoxychlor, mirex, pentachloroisole Blood AChE, BCHE	Median (range) (ng/g): $\alpha$ -HCH < LOD (< LOD–21.8); $\beta$ -HCH < LOD (< LOD–77.9); $\gamma$ -HCH < LOD (< LOD–24.4); HCB < LOD (< LOD–31.9); pentachloroisole < LOD (< LOD–20.0); endrin (< LOD–179.7); dieldrin < LOD (< LOD–21.4); heptachlor epoxide B < LOD (< LOD–11.6); $\gamma$ -chlordane < LOD (< LOD–22.2); heptachlor < LOD (< LOD–39.9); $\alpha,p'$ -DDT < LOD (< LOD–53.4); $p,p'$ -DDT < LOD (< LOD–84.9); $\alpha,p'$ -DDE < LOD (< LOD–66.3); $p,p'$ -DDE < LOD (< LOD–112.3); $p,p'$ -DDD < LOD (< LOD–40.4); endosulfan 1 < LOD (< LOD–58.5)	Serum TSH, total T3, FT4	Women with > LOQ DDE concentrations had higher total T3 levels ( $\beta = 0.2$ ; 95% CI: 0.06, 0.3) than those with < LOQ. Mostly null associations of serum DDE with total and free T4 and TSH levels. Higher $p,p'$ -DDE (OR = 3.8; 95% CI: 1.6, 9.2), heptachlor (OR = 1.7; 95% CI: 1.0, 3.2), endosulfan 1 (OR = 6.2; 95% CI: 1.6, 24.8), and $\geq 3$ OCs in blood (OR = 1.8; 95% CI: 1.1, 3.3) were associated with increased odds of subclinical hypothyroidism. Null associations of chlordane concentrations and hypothyroidism.
8. Hernández-Mariano et al. <sup>193</sup>	2017/Mexico	430 pregnant women living in a floriculture area	Prospective cohort	OCs	Serum DDE during pregnancy	Mean $\pm$ SD (ng/g lipid) $p,p'$ -DDE = 111.75 $\pm$ 140.20	Serum TSH, total T3, FT3, total T4, FT4	Lower AChE activity was marginally associated with increased FT4 levels ( $\beta$ per SD decrease in AChE activity = 0.03; 90% CI: 0.00, 0.06), but not with TSH ( $\beta = -0.01$ ; 90% CI: –0.38, 0.36). In girls, lower AChE activity was associated with increased FT4 levels ( $\beta = 0.05$ ; 90% CI: 0.01, 0.10) and decreased TSH levels ( $\beta = -0.51$ , 90% CI: –1.00, –0.02). Null associations were observed in boys.
9. Londoño et al. <sup>194</sup>	2018/Colombia	819 farmworkers and their partners from plantain and coffee farms	Cross-sectional	OCs, OPs	Serum chlordane, DDT, DDE, endosulfan, HCB, aldrin, endrin, heptachlor, methoxychlor, chlordane	Median (range) (ng/mL): Heptachlor = 1.31 (0.11–9.48); $p,p'$ -DDE = 8.3 (NA)	Serum TSH, FT4 TPOAb	Higher $p,p'$ -DDE (OR = 3.8; 95% CI: 1.6, 9.2), heptachlor (OR = 1.7; 95% CI: 1.0, 3.2), endosulfan 1 (OR = 6.2; 95% CI: 1.6, 24.8), and $\geq 3$ OCs in blood (OR = 1.8; 95% CI: 1.1, 3.3) were associated with increased odds of subclinical hypothyroidism. Null associations of chlordane concentrations and hypothyroidism.
Studies on OPs or CBs Studies in children 10. Phillips et al. <sup>195</sup>	2021/Ecuador	80 adolescents (12–17 years of age) living in agricultural areas	Cross-sectional	OPs	Questionnaire Blood AChE	Not applicable	Serum TSH, FT4	Lower AChE activity was marginally associated with increased FT4 levels ( $\beta$ per SD decrease in AChE activity = 0.03; 90% CI: 0.00, 0.06), but not with TSH ( $\beta = -0.01$ ; 90% CI: –0.38, 0.36). In girls, lower AChE activity was associated with increased FT4 levels ( $\beta = 0.05$ ; 90% CI: 0.01, 0.10) and decreased TSH levels ( $\beta = -0.51$ , 90% CI: –1.00, –0.02). Null associations were observed in boys.
Studies in adults 11. Lacasaña et al. <sup>196</sup>	2010/Mexico	136 male floriculture workers	Prospective cohort	OPs	Questionnaire (occupational and residential exposure history) Urinary DAPs	Mean $\pm$ SD ( $\mu$ g/g creatinine): Rainy season: $\Sigma$ DMP = 1.5 $\pm$ 29.0; $\Sigma$ DEP = 0.3 $\pm$ 0.9; $\Sigma$ DAP = 2.0 $\pm$ 29.1; DDE = 6.2 $\pm$ 18.2 ng/mL Dry season: $\Sigma$ DMP = 0.3 $\pm$ 0.9; $\Sigma$ DEP = 0.1 $\pm$ 0.4; $\Sigma$ DAP = 0.5 $\pm$ 1.0; DDE = 4.7 $\pm$ 20.4 ng/mL	Serum TSH, total T3, total T4	Higher $\Sigma$ DMP ( $\beta = 0.2$ ; 95% CI: 0.1, 0.3), $\Sigma$ DEP ( $\beta = 0.3$ ; 95% CI: 0.1, 0.4), and $\Sigma$ DAP ( $\beta = 0.3$ ; 95% CI: 0.1, 0.4) were associated with increased TSH levels. Higher $\Sigma$ DMP ( $\beta = 0.2$ ; 95% CI: 0.1, 0.3) and $\Sigma$ DAP ( $\beta = 0.2$ ; 95% CI: 0.1, 0.3) were associated with increased total T4 levels. Null associations were observed for total T3.

Table 6. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
12. Lacasana et al. <sup>197</sup>	2010/Mexico	136 male floriculture workers	Prospective cohort	OPs	Questionnaire (occupational and residential exposure history) Urinary DAPs	Mean $\pm$ SD ( $\mu$ g/g creatinine): Rainy season: $\Sigma$ DMP = $1.5 \pm 29.0$ ; $\Sigma$ DEP = $0.3 \pm 0.9$ ; $\Sigma$ DAP = $2.0 \pm 29.1$ ; DDE = $6.2 \pm 18.2$ ng/mL Dry season: $\Sigma$ DMP = $0.3 \pm 0.9$ ; $\Sigma$ DEP = $0.1 \pm 0.4$ ; $\Sigma$ DAP = $0.5 \pm 1.0$ ; DDE = $4.7 \pm 20.4$ ng/mL	Serum TSH, total T3, total T4	Interaction between $PON1$ and $\Sigma$ OPs and $\Sigma$ DAP on TSH ( $\beta = 0.3$ ; 95% CI: 0.05, 0.6) and total T3 ( $\beta = 0.1$ ; 95% CI: 0.0, 0.2) levels, and between $PON1$ and $\Sigma$ OPs and $\Sigma$ DAP on TSH ( $\beta = 0.3$ ; 95% CI: 0.02, 0.5). No interaction between $PON1$ and $\Sigma$ OPs and $\Sigma$ DAP on total T3 and total T4 ( $p < 0.05$ ). Null associations of serum hormones with cholinesterase levels.
13. Miranda-Contreras et al. <sup>200</sup>	2013/Venezuela <sup>c</sup>	64 male farmworkers/35 controls	Cross-sectional	OPs, CBs	Questionnaire (occupational exposure history) Blood AChE, BChE	Not applicable	Serum TSH, FT4	Null associations of para-occupational exposure to OP pesticides and urinary DAPs with hypothyroidism. No interaction was observed between pesticides, para-occupational exposure and $PON1$ polymorphisms.
14. Torres-Sanchez et al. <sup>199</sup>	2019/Mexico	381 pregnant women living in a floricultural area	Cross-sectional	OPs	Questionnaire (para-occupational exposure history) Urinary DAPs in a subsample	Median total DAPs ( $\mu$ mol/g creatinine): Para-occupationally exposed = $1.16$ ; non-para-occupationally exposed = $0.83$ (data not shown in tables)	Serum TSH, FT4	Farmworkers had lower TSH ( $p < 0.10$ ) but higher total T3 and FT4 ( $p < 0.01$ for each) than controls.
15. Bernieri et al. <sup>198</sup>	2019/Brazil	46 rural farmworkers/27 controls	Cross-sectional	OPs, CBs	Questionnaire (occupational exposure history) Blood BChE <sup>d</sup>	Not applicable	Serum FT4, total T3, TSH	Use of dithiocarbamate fungicides in the past week ( $-34\%$ ; 95% CI: $-54$ , $-6$ ) and no use of full PPE during the last pesticide application ( $-34\%$ ; 95% CI: $-55$ , $-2$ ) was associated with decreased TSH levels. Use of cyhalothrin in the past week was associated with decreased FT4 ( $-11\%$ ; 95% CI: $-19$ , $-1$ ) and total T4 ( $-7\%$ ; 95% CI: $-20$ , $-9$ ), whereas use of paraquat in the past week was associated with decreased FT3 ( $-9\%$ ; 95% CI: $-16$ , $-1$ ). Lifetime use ( $>20$ y) of OP pesticides was associated with decreased FT4 ( $-11\%$ ; 95% CI: $-20$ , $-1$ ) and total T4 ( $-11\%$ ; 95% CI: $-19$ , $-3$ ). Lifetime use ( $1-20$ y) of mancozeb was associated with decreased total T4 ( $-9\%$ ; 95% CI: $-16$ , $-1$ ) and FT3 ( $-7\%$ ; 95% CI: $-12$ , $-2$ ).
Studies on other pesticides or multiple pesticide classes Studies in adults								
16. Santos et al. <sup>201</sup>	2019/Brazil <sup>e</sup>	122 individuals living in small farms	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational, residential, and seasonal exposure history)	Not applicable	Serum TSH, total T3, FT3, total T4, FT4	Use of dithiocarbamate fungicides in the past week ( $-34\%$ ; 95% CI: $-54$ , $-6$ ) and no use of full PPE during the last pesticide application ( $-34\%$ ; 95% CI: $-55$ , $-2$ ) was associated with decreased TSH levels. Use of cyhalothrin in the past week was associated with decreased FT4 ( $-11\%$ ; 95% CI: $-19$ , $-1$ ) and total T4 ( $-7\%$ ; 95% CI: $-20$ , $-9$ ), whereas use of paraquat in the past week was associated with decreased FT3 ( $-9\%$ ; 95% CI: $-16$ , $-1$ ). Lifetime use ( $>20$ y) of OP pesticides was associated with decreased FT4 ( $-11\%$ ; 95% CI: $-20$ , $-1$ ) and total T4 ( $-11\%$ ; 95% CI: $-19$ , $-3$ ). Lifetime use ( $1-20$ y) of mancozeb was associated with decreased total T4 ( $-9\%$ ; 95% CI: $-16$ , $-1$ ) and FT3 ( $-7\%$ ; 95% CI: $-12$ , $-2$ ).

Note: AChE, acetylcholinesterase; BChE, butyrylcholinesterase; CBs, carbamate pesticides; CI, confidence interval; CPO, chlorpyrifos; DAP, dialkylphosphate; DDE, dichlorodiphenyldichloroethane; DDT, dichlorodiphenyltrichloroethane; DEP, diethylphosphate; DETP, diethylthiophosphate; DM, dimethyl; DMDTP, dimethyldithiophosphate; DMP, dimethylphosphate; HCB, hexa-chlorobenzene; FT3, free triiodothyronine; FT4, free thyroxine; HCH, hexa-chlorocyclohexane; LOD, limit of detection; OC, organochlorine; OP, organophosphate; OR, odds ratio; P, percentile; PON1, paraoxonase-1; PPE, personal protective equipment; T3, triiodothyronine; T4, thyroxine; TGAb, thyroglobulin antibodies; TPOAb, thyroid peroxidase antibodies; TSH, thyroid-stimulating hormone.

<sup>a</sup>Also included in Table 8 (birth outcomes and child growth).

<sup>b</sup>Also included in Table 3 (neurobehavioral outcomes).

<sup>c</sup>Also included in Table 7 (reproductive outcomes).

<sup>d</sup>Also included in Table 9 (other health effects).

<sup>e</sup>Investigators did not use exposure biomarker concentrations in multivariate analyses.



different prospective cohort studies in Mexico reported associations of serum DDE concentrations with increased total T3 or T4 levels among male floriculture workers<sup>192</sup> and pregnant women living in a floriculture area.<sup>193</sup> In addition, a cross-sectional study of Colombian farmworkers and their partners found associations of serum DDE, heptachlor, endosulfan 1, and three or more OC pesticides with increased odds of subclinical hypothyroidism.<sup>194</sup>

Six publications examined associations of OP or carbamate pesticide exposure—assessed by measurement of urinary DAP metabolite concentrations or blood ChE activity—with thyroid function (Table 6), but only one focused on children.<sup>195</sup> The latter publication from a cross-sectional study of Ecuadorian adolescents living in agricultural areas reported that lower acetylcholinesterase (AChE) activity was associated with increased free T4 and decreased TSH levels among girls, but not boys.<sup>195</sup> Two publications from a prospective cohort study of adult floriculture workers in Mexico reported that higher DAP metabolite concentrations were associated with increased TSH and total T4 levels<sup>196</sup> and that these associations were modified by paraoxonase 1 (*PON1*<sub>192RR</sub>).<sup>197</sup> Similarly, a publication from a cross-sectional study in Brazil reported increased TSH, but also decreased T3 and T4 levels, among farmworkers compared with unexposed controls.<sup>198</sup> In contrast, two publications from cross-sectional studies in Mexico<sup>199</sup> and Venezuela<sup>200</sup> reported null associations of occupational or para-occupational exposure to OP pesticides with thyroid hormone levels. Last, a publication from a cross-sectional study in Brazil examined associations between exposure to multiple pesticide classes—ascertained via questionnaire—and thyroid function among adults and reported associations of recent use of dithiocarbamate fungicides with decreased TSH levels, recent use of  $\lambda$ -cyhalothrin (pyrethroid insecticide) with decreased free and total T4 levels, and recent use of paraquat (herbicide) with decreased free T3 levels.<sup>201</sup> Overall, published studies on the associations of pesticide exposure and thyroid function among LAC populations have reported mixed findings with notorious differences between pesticide active ingredients, age groups, and sexes.

### Reproductive Outcomes

Sixteen publications reported on the association of pesticide exposure with reproductive outcomes such as reproductive hormone profiles among adults (Table 7). Four of these 16 publications focused on OC pesticide exposure and used direct pesticide exposure assessment methods.<sup>189,202–204</sup> A publication from a prospective cohort study in Guadeloupe reported that higher cord blood chlordecone concentrations were associated with elevated androsterone and testosterone in 7-y-old boys and girls.<sup>189</sup> Notably, a publication from a prospective cohort study of male floriculture workers in Mexico reported that higher serum DDE concentrations were associated with decreased prolactin and testosterone, but also with increased inhibin B.<sup>202</sup> A publication from a cross-sectional study of individuals living near an abandoned pesticide factory in Brazil (mentioned above) reported that higher serum heptachlor and DDT concentrations were associated with decreased testosterone levels among men and that higher serum aldrin, HCB, DDT, endosulfan 2, and mirex concentrations were associated with increased estradiol levels, decreased luteinizing hormone (LH) levels, or decreased follicle-stimulating hormone (FSH) levels among peri-/postmenopausal women.<sup>203</sup> Furthermore, a publication from a case-control study in Brazil reported that infertile women had higher detectable serum DDE concentrations than fertile women.<sup>204</sup>

Seven publications examined associations of OP or carbamate pesticide exposure with reproductive outcomes, six ascertained exposure via urinary DAP metabolites or blood ChE levels,<sup>200,205–209</sup>

and one assigned exposure based on the season of sample collection (spray vs. nonspray)<sup>210</sup> (Table 7). A publication from a prospective cohort study in Mexico reported lower sperm volume and count among farmworkers who sprayed OP pesticides compared with non-farmworkers, but mostly null associations between urinary DAP metabolite concentrations and seminal parameters.<sup>209</sup> Three publications from cross-sectional studies conducted in Peru,<sup>208</sup> Mexico,<sup>207</sup> and Venezuela<sup>200</sup> reported increased seminal pH, lower percentage of live sperm, and lower seminal fructose levels among farmworkers compared with non-farmworkers. The study conducted in Venezuela also reported that lower butyrylcholinesterase (BChE) activity was associated with an increased damage to sperm chromatin among farmworkers.<sup>200</sup> A publication from a cross-sectional study of male floriculture workers in Mexico reported that higher urinary DAP metabolite concentrations were associated with decreased inhibin B, FSH, or LH levels, but also with increased testosterone levels.<sup>207</sup> Another publication based on the same study population reported that higher urinary DAP metabolite concentrations were associated with increased FSH and prolactin levels, but decreased testosterone and inhibin B levels.<sup>205</sup> Last, although one publication from a prospective cohort study of pregnant women in Argentina reported a weak association between higher AChE activity and increased progesterone levels,<sup>206</sup> a cross-sectional study of women in Argentina reported no difference in progesterone and estradiol levels measured in the spray and non-spray seasons.<sup>210</sup>

Five publications from four cross-sectional studies and one retrospective cohort study reported on the associations of exposure to pesticides other than OCs, OPs, or carbamates or exposure to multiple pesticide classes with reproductive outcomes (Table 7). All studies relied on questionnaires to assess environmental or occupational pesticide exposure,<sup>201,211–213</sup> but one of them also measured blood ChE activity.<sup>214</sup> Two publications from studies conducted in Brazil<sup>214</sup> and Venezuela<sup>213</sup> reported associations of pesticide exposure with reduced sperm quality—as indicated by parameters such as decreased sperm concentration and higher sperm DNA fragmentation index—among farmworkers/rural men compared with controls/urban men. The publication from the cross-sectional study conducted in Brazil also reported that men living in rural areas and who mixed or applied pesticides had increased testis volume, decreased LH levels, or increased testosterone:LH ratios compared with men living in rural areas and who did not mix or apply pesticides, but the publication reported null associations of blood ChE activity with reproductive hormones and semen quality.<sup>214</sup> A publication from another cross-sectional study in Brazil reported that recent use of fungicides in general,  $\lambda$ -cyhalothrin (pyrethroid insecticide), and phthalimide (fungicide) was associated with increased LH levels in men living in agricultural communities.<sup>201</sup> A cross-sectional study of reproductive-age women in Venezuela found that women who were occupationally exposed to pesticides had longer menstrual cycles than those who were not exposed.<sup>212</sup> Last, a publication from a retrospective cohort of fertile women aurally exposed to glyphosate in Colombia reported null associations with fecundability.<sup>211</sup>

Overall, publications from studies conducted to date provide some evidence of associations between exposure to pesticides, particularly OC pesticides, OP pesticides, and carbamates, with reproductive outcomes such as infertility, changes in sex hormone levels (e.g., testosterone and estradiol), and alterations in semen quality among adults in LAC countries. Although 10 of 16 studies employed direct exposure assessment methods, most were cross-sectional in design and had small sample sizes, limiting causal inference.

**Table 7. Characteristics of Latin American and the Caribbean studies on pesticide exposure and reproductive outcomes published between 2007 and 2021 (*n* = 16).**

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Fertility	Health effect and assessment method/instrument	Results
Studies on OCs	2013/Brazil	15 women seeking help for infertility treatment/21 women spontaneously pregnant	Case-control	OCs	Questionnaire (occupational and reproductive history). Serum HCH, DDT, DDE, DDD	Mean $\pm$ SD (ng/mL): Fertile women: HCB = $0.1 \pm 0.10$ ; $p,p'$ -DDE = $0.9 \pm 0.8$ ; $p,p'$ -DDT = $0.7 \pm 0.1$ Infertile women: HCB = $0.2 \pm 0.4$ ; $p,p'$ -DDE = $3.1 \pm 3.6$ ; $p,p'$ -DDT = $9.1 \pm 11.9$	Fertility	Serum FSH, LH, prolactin, testosterone, estradiol, inhibin B	Infertile women had higher detectable serum DDE concentrations than fertile women ( $p = 0.001$ ).  $p,p'$ -DDE concentrations were negatively associated with prolactin ( $\beta = -0.04$ ; 95% CI: $-0.07$ , $-0.01$ ) and testosterone ( $\beta = -0.04$ ; 95% CI: $-0.08$ , $0.001$ ), but positively associated with inhibin B ( $\beta = 0.11$ ; 95% CI: $0.02$ , $0.21$ ). Null associations of $p,p'$ -DDE with FSH, LH, or estradiol.  Higher heptachlor and $\alpha,p'$ -DDT were associated with decreased testosterone levels among men ( $\beta = -0.03$ ; 95% CI: $-0.04$ , $-0.01$ , and $\beta = -0.02$ ; 95% CI: $-0.05$ , $-0.01$ , respectively).  Among peri-/postmenopausal women, higher aldrin was associated with increased estradiol levels ( $\beta = 0.006$ ; 95% CI: $0.001$ , $0.01$ ), but decreased LH ( $\beta = -0.01$ ; 95% CI: $-0.02$ , $-0.003$ ) and FSH ( $\beta = -0.007$ ; 95% CI: $-0.01$ , $-0.0001$ ) levels. Higher $p,p'$ -DDD and endosulfan 1 were associated with decreased LH ( $\beta = -0.09$ ; 95% CI: $-0.17$ , $-0.02$ , and $\beta = -0.24$ ; 95% CI: $-0.46$ , $-0.03$ , respectively) and FSH ( $\beta = -0.09$ ; 95% CI: $-0.15$ , $-0.03$ ; $\beta = -0.23$ ; 95% CI: $-0.41$ , $-0.05$ , respectively) levels. Higher HCB ( $\beta = -0.13$ ; 95% CI: $-0.2$ , $-0.02$ ), $p,p'$ -DDT ( $\beta = -0.01$ ; 95% CI: $-0.02$ , $-0.003$ ), endosulfan 2 ( $\beta = -0.14$ ; 95% CI: $-0.25$ , $-0.03$ ), and mirex ( $\beta = -0.07$ ; 95% CI: $-0.12$ , $-0.02$ ) were also associated with decreased LH levels among this group of women.  Among premenopausal women, no associations were found.
						Median (range) (ng/g): Rainy season: $p,p'$ -DDE = $677.2$ ( $9.4$ – $12,696.5$ ) Dry season: $p,p'$ -DDE = $626.7$ ( $9.4$ – $13,688.1$ )			
2. Blanco-Muñoz et al. <sup>202</sup>	2012/Mexico	84 male floriculture workers	Prospective cohort	OCs	Questionnaire (occupational history) Serum DDE	Median (range) (ng/mL): Prenatopausal women: $\alpha$ -HCH = $2.8$ ( $1.0$ – $6.1$ ); $\beta$ -HCH = $6.3$ ( $2.5$ – $14.4$ ); $\gamma$ -HCH = $0.9$ ( $0.4$ – $2.3$ ); HCB = $0.4$ ( $0.1$ – $0.6$ ); $\alpha$ -chlordane = $0.3$ ( $< LOD$ – $0.6$ ); $\gamma$ -chlordane = $0.2$ ( $< LOD$ – $0.4$ ); <i>trans</i> -nonachlor = $0.4$ ( $0.2$ – $0.8$ ); heptachlor = $0.4$ ( $< LOD$ – $0.9$ ); $p,p'$ -DDE = $8.0$ ( $3.0$ – $21.8$ ); $\alpha,p'$ -DDT = $0.4$ ( $< LOD$ – $1.1$ ); $p,p'$ -DDT = $3.0$ ( $1.0$ – $7.3$ ); $p,p'$ -DDD = $0.6$ ( $0.2$ – $1.2$ ); endosulfan 1 = $0.2$ ( $< LOD$ – $0.4$ ); endosulfan 2 = $0.2$ ( $< LOD$ – $0.8$ ); aldrin = $2.1$ ( $0.8$ – $13.4$ ); endrin = $0.6$ ( $0.3$ – $1.6$ ); dieldrin = $0.6$ ( $0.2$ – $1.3$ ); methoxychlor = $0.4$ ( $< LOD$ – $1.0$ ); mirex = $< LOD$ ( $< LOD$ – $0.3$ ) Peri-/postme nopausal women: $\alpha$ -HCH = $2.4$ ( $1.1$ – $6.1$ ); $\beta$ -HCH = $11.7$ ( $4.8$ – $36.3$ ); $\gamma$ -HCH = $1.1$ ( $0.6$ – $2.0$ ); HCB = $0.4$ ( $0.2$ – $0.8$ ); $\alpha$ -chlordane = $0.3$ ( $0.1$ – $0.6$ ); $\gamma$ -chlordane = $0.2$ ( $< LOD$ – $0.4$ ); <i>trans</i> -nonachlor = $0.4$ ( $0.2$ – $0.8$ ); heptachlor = $0.3$ ( $< LOD$ – $0.7$ ); $p,p'$ -DDE = $20.6$ ( $6.2$ – $65.6$ ); $\alpha,p'$ -DDT = $0.4$ ( $< LOD$ – $1.2$ ); $p,p'$ -DDT = $4.7$ ( $1.2$ – $10.7$ ); $p,p'$ -DDD = $0.9$ ( $0.3$ – $1.8$ ); endosulfan 1 = $0.2$ ( $< LOD$ – $0.5$ ); endosulfan 2 = $0.3$ ( $< LOD$ – $0.6$ ); aldrin = $3.8$ ( $1.0$ – $20.1$ ); endrin = $0.5$ ( $0.2$ – $1.4$ ); dieldrin = $0.6$ ( $0.3$ – $1.2$ ); methoxychlor = $0.5$ ( $0.2$ – $1.0$ ); mirex = $< LOD$ ( $< LOD$ – $0.5$ )	Serum testosterone, estradiol, progesterone, prolactin, LH, FSH	Higher heptachlor and $\alpha,p'$ -DDT were associated with decreased testosterone levels among men ( $\beta = -0.03$ ; 95% CI: $-0.04$ , $-0.01$ , and $\beta = -0.02$ ; 95% CI: $-0.05$ , $-0.01$ , respectively). Among peri-/postmenopausal women, higher aldrin was associated with increased estradiol levels ( $\beta = 0.006$ ; 95% CI: $0.001$ , $0.01$ ), but decreased LH ( $\beta = -0.01$ ; 95% CI: $-0.02$ , $-0.003$ ) and FSH ( $\beta = -0.007$ ; 95% CI: $-0.01$ , $-0.0001$ ) levels. Higher $p,p'$ -DDD and endosulfan 1 were associated with decreased LH ( $\beta = -0.09$ ; 95% CI: $-0.17$ , $-0.02$ , and $\beta = -0.24$ ; 95% CI: $-0.46$ , $-0.03$ , respectively) and FSH ( $\beta = -0.09$ ; 95% CI: $-0.15$ , $-0.03$ ; $\beta = -0.23$ ; 95% CI: $-0.41$ , $-0.05$ , respectively) levels. Higher HCB ( $\beta = -0.13$ ; 95% CI: $-0.2$ , $-0.02$ ), $p,p'$ -DDT ( $\beta = -0.01$ ; 95% CI: $-0.02$ , $-0.003$ ), endosulfan 2 ( $\beta = -0.14$ ; 95% CI: $-0.25$ , $-0.03$ ), and mirex ( $\beta = -0.07$ ; 95% CI: $-0.12$ , $-0.02$ ) were also associated with decreased LH levels among this group of women.  Among premenopausal women, no associations were found.	
						Median (P25–P75) (ng/L): Cord blood chlordane: boys = $0.25$ ( $0.08$ – $0.41$ ), girls = $0.21$ ( $0.07$ – $0.37$ ); child chlordane: boys = $0.06$ ( $< LOD$ – $0.11$ ), girls = $0.05$ ( $< LOD$ – $0.11$ ); cord blood DDE: boys = $0.22$ ( $0.09$ – $0.64$ ), girls = $0.31$ ( $0.10$ – $0.74$ )			
4. Ayhan et al. <sup>189</sup>	2021/Guadeloupe <sup>a,b</sup>	285 mother-child (7 years of age) pairs	Prospective cohort	OCs	Cord and child blood chlordane, cord blood DDE	Men: $\alpha$ -HCH = $2.5$ ( $1.0$ – $0.7$ ); $\beta$ -HCH = $6.0$ ( $2.1$ – $15.4$ ); $\gamma$ -HCH = $1.0$ ( $0.4$ – $2.2$ ); HCB = $0.3$ ( $0.1$ – $0.6$ ); $\gamma$ -chlordane = $0.2$ ( $< LOD$ – $0.5$ ); $\gamma$ -chlordane = $0.2$ ( $< LOD$ – $0.4$ ); <i>trans</i> -nonachlor = $0.3$ ( $0.2$ – $0.8$ ); heptachlor = $0.3$ ( $< LOD$ – $0.9$ ); $p,p'$ -DDE = $8.3$ ( $2.9$ – $21.9$ ); $\alpha,p'$ -DDT = $0.3$ ( $< LOD$ – $0.9$ ); $p,p'$ -DDT = $3.1$ ( $0.9$ – $7.0$ ); $p,p'$ -DDD = $0.6$ ( $0.2$ – $1.3$ ); endosulfan 1 = $0.2$ ( $< LOD$ – $0.5$ ); endosulfan 2 = $0.2$ ( $< LOD$ – $0.7$ ); aldrin = $1.9$ ( $0.7$ – $11.0$ ); endrin = $0.6$ ( $0.2$ – $1.5$ ); dieldrin = $0.6$ ( $0.3$ – $1.3$ ); methoxychlor = $0.5$ ( $< LOD$ – $1.0$ ); mirex = $< LOD$ ( $< LOD$ – $0.3$ ) Median (P25–P75) (ug/L): Cord blood chlordane: boys = $0.25$ ( $0.08$ – $0.41$ ), girls = $0.21$ ( $0.07$ – $0.37$ ); child chlordane: boys = $0.06$ ( $< LOD$ – $0.11$ ), girls = $0.05$ ( $< LOD$ – $0.11$ ); cord blood DDE: boys = $0.22$ ( $0.09$ – $0.64$ ), girls = $0.31$ ( $0.10$ – $0.74$ )	Serum DHEA, TT, DHT, estradiol	Third quartile of cord blood chlordane was associated with elevated DHEA ( $\beta$ for boys = $0.5$ ; 95% CI: $0.1$ , $1.0$ ; $\beta$ for girls = $0.4$ ; 95% CI: $0.0$ , $0.7$ ), TT (OR for boys = $3.2$ ; 95% CI: $1.1$ , $9.6$ ; OR for girls = $3.3$ ; 95% CI: $1.3$ , $8.2$ ), and DHT (OR for boys = $3.7$ ; 95% CI: $1.3$ , $10.6$ ; OR for girls = $3.2$ ; 95% CI: $1.0$ , $10.2$ ) levels in boys and girls, relative to first quartile of cord blood chlordane.	
						Median (P25–P75) (ug/L): Cord blood chlordane: boys = $0.25$ ( $0.08$ – $0.41$ ), girls = $0.21$ ( $0.07$ – $0.37$ ); child chlordane: boys = $0.06$ ( $< LOD$ – $0.11$ ), girls = $0.05$ ( $< LOD$ – $0.11$ ); cord blood DDE: boys = $0.22$ ( $0.09$ – $0.64$ ), girls = $0.31$ ( $0.10$ – $0.74$ )			
Studies on OPs or CBs	2008/Mexico	19 sprayer farmworkers/16 non-sprayer farmworkers/7 non-farmworkers	Prospective cohort	OPs	Questionnaire (occupational, residential, and seasonal exposure histories). Urinary DAPs	Mean $\pm$ SD total DAPs (ppb): Non-occupationally exposed = $1,004.8 \pm 2,380.49$ Farmworkers but not OP sprayers = $1,054.6 \pm 1,916.2$ Sprayers exposed to OP = $1,283.7 \pm 2,304.9$	Semen quality		Sprayer farmworkers had lower sperm volume ( $\beta = -0.7$ , $p = 0.002$ ) and lower sperm count ( $\beta = -2.2$ , $p = 0.03$ ) than non-farmworkers. During low exposure period, non-sprayer farmworkers had lower rapid progressive motility ( $\beta = -17.2$ , $p = 0.04$ ). During medium exposure period sprayer farmworkers had lower sperm volume ( $\beta = -0.3$ , $p = 0.02$ ). During high exposure period, seminal parameters were similar among all groups. Sperm vitality was lower at higher levels of DMDTP ( $\beta = -146.3$ , $p = 0.006$ ). No other seminal parameters were associated with DAP levels.

Table 7. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
6. Yuera et al. <sup>208</sup>	2008/Peru	31 male farmworkers/31 controls	Cross-sectional	OPs	Questionnaire (occupational exposure history) Urinary DAPs	Geometric mean $\pm$ GSD ( $\mu\text{g/L}$ ): Nonexposed: DEP = 3.0 $\pm$ 2.1; DEDTP = 10.2 $\pm$ 54.5; DETP = 2.7 $\pm$ 1.0; DMP = 9.6 $\pm$ 19.5; DMDTP = 56.4 $\pm$ 6.7; DMTP = 9.7 $\pm$ 68.7 Exposed: DEP = 3.8 $\pm$ 8.2; DEDTP = 25.3 $\pm$ 78.6; DETP = 3.9 $\pm$ 7.2; DMP = 14.2 $\pm$ 42.4; DMDTP = 5.3 $\pm$ 4.5; DMTP = 22.9 $\pm$ 48.6	Semen quality Serum testosterone, estradiol, FSH, LH	Higher concentrations of ethylated OP metabolites were associated with lower seminal volume ( $p=0.02$ ), whereas higher concentrations of methylated OP metabolites were associated with higher seminal pH ( $p=0.02$ ). After controlling for ethylated OP metabolites, exposure to pesticides (yes/no) was associated with increased seminal pH ( $p=0.02$ ). After controlling for methylated OP metabolites, exposure to pesticides (yes/no) was associated with increased seminal pH ( $p=0.002$ ) and decreased seminal fructose levels ( $p=0.04$ ). Null associations of pesticide exposure and serum hormone levels. Higher DMP ( $\beta = -0.001$ ; 95% CI: $-0.002$ , $-0.0002$ ), DEP ( $\beta = -0.001$ ; 95% CI: $-0.002$ , $-0.002$ ), DETP ( $\beta = -0.004$ ; 95% CI: $-0.01$ , $-0.0001$ ) and total DAP ( $\beta = -0.001$ ; 95% CI: $-0.001$ , $-0.0002$ ) concentrations were associated with decreased inhibin B levels. Higher DEP concentrations were associated with decreased FSH ( $\beta = -0.002$ ; 95% CI: $-0.004$ , $-0.0005$ ). Higher DEP ( $\beta = -0.002$ ; 95% CI: $-0.0001$ , $0.004$ ) and total DAP ( $\beta = -0.0001$ ; 95% CI: $0.00005$ , $0.0003$ ) concentrations marginally associated with increased testosterone levels. Higher DETP marginally was associated with decreased LH levels ( $\beta = -0.001$ ; 95% CI: $-0.002$ , $0.0001$ ). Higher AChE activity was associated with increased progesterone levels ( $\beta = 57.8$ ; $p \leq 0.05$ ).
7. Blanco-Muñoz et al. <sup>207</sup>	2010/Mexico	104 male floriculture workers	Cross-sectional	OPs	Questionnaire (occupational exposure history) Urinary DAPs	Median (range) ( $\mu\text{g/g creatinine}$ ): Low exposure: DMP = 17.4 (5.4–196.8); DMTP = 11.0 (4.6–156.8); DMDTP = 7.8 (4.6–165.2); DEP = 16.2 (5.4–29.9); DETP = 8.3 (4.7–14.4); DEDTP = 8.6 (2.4–31.0); total DAPs = 77.8 (35.0–305.3) Medium exposure: DMP = 89.9 (12.3–9213.9); DMTP = 31.6 (6.0–377.2); DMDTP = 9.6 (3.0–88.1); DEP = 20.3 (4.3–113.6); DETP = 10.6 (3.5–40.2); DEDTP = 5.5 (3.0–51.5); total DAPs = 216.5 (59.3–9324.3) High exposure: DMP = 76.6 (6.9–986.3); DMTP = 29.0 (3.3–1359.0); DMDTP = 9.3 (3.2–437.0); DEP = 15.9 (3.1–153.9); DETP = 9.6 (2.7–625.5); DEDTP = 6.2 (2.7–34.9); total DAPs = 190.7 (34.3–2,770.8)	Serum FSH, LH, prolactin, testosterone, inhibin B, estradiol	Higher DMP ( $\beta = -0.001$ ; 95% CI: $-0.002$ , $-0.0002$ ), DEP ( $\beta = -0.001$ ; 95% CI: $-0.002$ , $-0.002$ ), DETP ( $\beta = -0.004$ ; 95% CI: $-0.01$ , $-0.0001$ ) and total DAP ( $\beta = -0.001$ ; 95% CI: $-0.001$ , $-0.0002$ ) concentrations were associated with decreased inhibin B levels. Higher DEP concentrations were associated with decreased FSH ( $\beta = -0.002$ ; 95% CI: $-0.004$ , $-0.0005$ ). Higher DEP ( $\beta = -0.002$ ; 95% CI: $-0.0001$ , $0.004$ ) and total DAP ( $\beta = -0.0001$ ; 95% CI: $0.00005$ , $0.0003$ ) concentrations marginally associated with increased testosterone levels. Higher DETP marginally was associated with decreased LH levels ( $\beta = -0.001$ ; 95% CI: $-0.002$ , $0.0001$ ). Higher AChE activity was associated with increased progesterone levels ( $\beta = 57.8$ ; $p \leq 0.05$ ).
8. Cocchi et al. <sup>26</sup>	2012/Argentina <sup>a</sup>	97 pregnant women living in a rural area with intensive use of pesticides	Prospective cohort	OPs	Questionnaire (residential exposure history) Blood AChE and BChE $\beta$ -glucuronidase	Not applicable	Serum progesterone (measured during spray and pre-spray season)	Farmworkers had higher seminal pH ( $p=0.004$ ) and lower percentage of live sperm ( $p<0.001$ ) than controls. Farmworkers with decreased BChE activity had higher DFI ( $r = -0.3$ , $p=0.027$ ). Null associations of serum hormones with cholinesterase levels.
9. Miranda-Contreras et al. <sup>209</sup>	2013/Venezuela <sup>b</sup>	64 male farmworkers/35 controls	Cross-sectional	OPs, CBs	Questionnaire (occupational exposure history) Blood AChE and BChE	Not applicable	Semen quality Sperm chromatin integrity (DFI) Serum testosterone, FSH, LH, PRL	Farmworkers had higher seminal pH ( $p=0.004$ ) and lower percentage of live sperm ( $p<0.001$ ) than controls. Farmworkers with decreased BChE activity had higher DFI ( $r = -0.3$ , $p=0.027$ ). Null associations of serum hormones with cholinesterase levels.
10. Aguilar-Garduño et al. <sup>206</sup>	2013/Mexico	136 male floricultural workers	Prospective cohort	OPs	Urinary DAPs	Median (GM) total DAPs ( $\mu\text{mol/g creatinine}$ ): Rural season = 1.62 (2.00); Dry season = 0.48 (0.48)	Serum FSH, LH, prolactin, testosterone, estradiol, inhibin B	Higher total DAP concentrations were associated with increased FSH and prolactin levels ( $p<0.01$ for each) and decreased testosterone ( $p<0.01$ ) and inhibin B levels ( $p=0.11$ ). Progesterone and estradiol levels did not differ between spray and non-spray seasons.
11. Silvia et al. <sup>210</sup>	2020/Argentina <sup>c</sup>	53 pregnant women living in areas with intensive pesticide application	Cross-sectional	OPs, CBs	Questionnaire (residential exposure history) Blood AChE, BChE <sup>d</sup>	Not applicable	Plasma estradiol, progesterone (measured during spray and non-spray season)	Progesterone and estradiol levels did not differ between spray and non-spray seasons.
Studies on other pesticides or multiple pesticide classes	12. Sunin et al. <sup>211</sup>	2,592 fertile women from regions with different levels of aerial glyphosate spraying	Retrospective cohort	Glyphosate	Questionnaire (residential and occupational exposure history) Ecological exposure index (different levels of exposure according to agricultural practices)	Not applicable	TTP	Reduced fecundability was not associated with aerial glyphosate spraying.
13. Rojas and Guevara <sup>212</sup>	2014/Venezuela	180 women of reproductive age	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Menstrual cycle and bleeding duration	Women who were occupationally exposed to pesticides had longer menstrual cycles than women who did not have contact with pesticides ( $p<0.01$ ). Null association between bleeding duration and pesticide exposure.
14. Miranda-Contreras et al. <sup>213</sup>	2015/Venezuela	64 male farmworkers/64 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Semen quality Sperm chromatin integrity (DFI)	Farmworkers had decreased sperm concentration ( $p=0.01$ ), vitality ( $p<0.001$ ), slow progressive motility ( $p=0.01$ ), lower sperm membrane integrity ( $p=0.001$ ), and high DFI ( $p<0.001$ ) compared with controls.

Table 7. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
15. Cremonese et al. <sup>214</sup>	2017/Brazil	99 rural young men/36 urban young men	Cross-sectional	Multiple pesticide classes	Questionnaire (residential, occupational, and reproductive exposure history) Blood AChE and BCHE	Not applicable	Semen quality Genital measurements (AGD, TV) Serum testosterone, LH, FSH, SHBG, prolactin	Rural men had decreased normal sperm morphology ( $\beta = 0.7$ ; 95% CI: 0.6, 0.9), increased sperm count ( $\beta = 1.6$ ; 95% CI: 1.01, 2.5), increased TV ( $\beta = 1.3$ ; 95% CI: 1.1, 1.5), decreased LH levels ( $\beta = 0.8$ ; 95% CI: 0.7, 1.0) and increased T:LH ratio ( $\beta = 1.3$ ; 95% CI: 1.1, 1.6) compared with urban men. Farmers who had $\geq 6$ y working had decreased T:LH ratio ( $\beta = 0.8$ ; 95% CI: 0.7, 1.0) and decreased TV ( $\beta = 0.8$ ; 95% CI: 0.8, 1.0) (Ref <6); who had > 1 y handling pesticides had decreased LH levels ( $\beta = 0.8$ ; 95% CI: 0.7, 1.0), increased T:LH ratio ( $\beta = 1.2$ ; 95% CI: 1.1, 1.4), lower normal morphology ( $\beta = 0.7$ ; 95% CI: 0.6, 0.9) and increased TV ( $\beta = 1.2$ ; 95% CI: 1.1, 1.4) (Ref $\leq 1$ ), and who had $\geq 5$ dy handling pesticides had increased LH levels ( $\beta = 1.2$ ; 95% CI: 1.0, 1.4) and lower normal morphology ( $\beta = 0.8$ ; 95% CI: 0.8, 1.0) (Ref <5). Those farmworkers who used pesticides in the high use season had increased prolactin levels ( $\beta = 1.4$ ; 95% CI: 1.2, 1.7), and those who did not use PPE had decreased testosterone levels ( $\beta = 0.9$ ; 95% CI: 0.8, 1.0) and TV ( $\beta = 0.8$ ; 95% CI: 0.8, 1.0). Maternal farming during pregnancy was associated with increased AGD ( $\beta = 1.1$ ; 95% CI: 1.01, 1.1) and TV ( $\beta = 1.2$ ; 95% CI: 1.02, 1.3). Cholinesterase activities were not associated with reproductive hormones or semen quality.
16. Santos et al. <sup>201</sup>	2019/Brazil <sup>b</sup>	122 farmworkers and their families	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational, residential, and seasonal exposure history)	Not applicable	Serum LH, testosterone, estradiol, LH, FSH	Recent use of fungicides in general (% change = 41%; 95% CI: 11, 80), $\gamma$ -cyhalothrin (59%; 95% CI: 13, 123), and phthalimide (95%; 95% CI: 37, 176) was associated with increased LH levels in men. Working in agriculture (1–30 y) was associated with increased testosterone levels in men (20%; 95% CI: 2, 40) (reference group never worked in agriculture).

Note: %change, percentage change; AChE, acetylcholinesterase; AGD, anogenital distance; BCHE, butyrylcholinesterase; CBS, carbamate pesticides; CE, carboxylesterases; CI, confidence interval; DAP, dialkylphosphate; DDD, dichlorodiphenyldichloroethane; DDE, dichlorodiphenyldichloroethylene; DDT, dichlorodiphenyltrichloroethane; DEDTP, diethylthiophosphate; DEP, diethylphosphate; DETP, diethylthiophosphate; DFL, fragmentation index; DHEA, dehydroepiandrosterone; DHT, dihydrotestosterone; DMDTP, dimethyldithiophosphate; DMP, dimethylphosphate; FSH, follicle-stimulating hormone; GSD, geometric standard deviation; HCB, hexa-chlorobenzene; IQR, interquartile range; LH, luteinizing hormone; LOD, limit of detection; OC, organochlorine; OF, organophosphate; P, percentile; PPE, personal protective equipment; PRL, Prolactin; Ref, reference group; SD, standard deviation; SHBG, sex hormone-binding globulin; T:LH, testosterone/luteinizing hormone ratio; T1, total testosterone; TTP, time to pregnancy; TV, testis volume.

<sup>a</sup>Also included in Table 9 (other health outcomes).

<sup>b</sup>Also included in Table 6 (thyroid function).

<sup>c</sup>Also included in Table 8 (birth size and child growth).

<sup>d</sup>Investigators did not use exposure biomarker concentrations in multivariate analyses.

**Table 8.** Characteristics of Latin American and the Caribbean studies on pesticide exposure and birth size and child growth published between 2007 and 2021 (*n* = 13).

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolic concentrations	Health effect and assessment method/instrument	Results
<b>Studies on OCs</b>								
1. Cipul-Uicab et al. <sup>215</sup>	2010/Mexico	788 mother-child (13–43 months of age, boys only) pairs from an area where DDT was recently used	Prospective cohort	OCs	Questionnaire (residential and seasonal exposure at prenatal period) Maternal serum DDT and DDE at delivery	Median (IQR) (μg/g) <i>p,p'</i> -DDE = 2.7 (4.3) <i>p,p'</i> -DDT = 0.3 (0.6)	Weight, height	Null associations of prenatal DDT exposure with height and BMI in boys up to 43 months of age.
2. Garced et al. <sup>216</sup>	2012/Mexico	223 mother-child (0–12 months of age) pairs	Prospective cohort	OCs	Maternal serum DDE in each trimester of pregnancy	Geometric mean ± GSD (ng/g) <i>p,p'</i> -DDE: first trimester = 1,105.1 ± 2.7; second trimester = 842.6 ± 2.9; third trimester = 710.6 ± 3.0 <i>p,p'</i> -DDT: first trimester = 0.03 ± 9.5; second trimester = 0.02 ± 6.6; third trimester = 0.03 ± 8.5 Median (P25–P75) (μg/L) Chlorcone = 0.39 (0.18–0.83); <i>p,p'</i> -DDE (for subgroup of 358 women) = 0.59 (0.22–1.26).	Weight, length, head circumference during the first year of life	Null associations between prenatal DDE exposure and child growth during the first year of life.
3. Kuchel et al. <sup>220</sup>	2014/Guadeloupe	818 mother-newborn pairs	Prospective cohort	OCs	Cord blood chlorcone and DDE	Chlorcone = 0.39 (0.18–0.83); <i>p,p'</i> -DDE (for subgroup of 358 women) = 0.59 (0.22–1.26).	Length of gestation, preterm birth	Higher cord blood chlorcone concentrations were associated with shorter length of gestation (β per 10-fold increase = −0.3 wk; 95% CI: −0.5, 0) and increased risk of preterm birth (HR = 1.6; 95% CI: 1.0, 2.3). Null associations of cord blood DDE with birth outcomes.
4. Costet et al. <sup>222</sup>	2015/Guadeloupe	222 mother-child (3–18 months of age) pairs	Prospective cohort	OCs	Questionnaire (dietary intake of food contaminated with chlorcone) Cord plasma and breast milk (3 months of age) chlorcone	Median (IQR) (μg/L): Cord plasma chlorcone = 0.11 (< LOD–0.33); breast milk chlorcone = 0.76 (0.40–1.70)	Body length, weight, BMI at 3, 8, and 18 months of age	Highest tertile of cord blood chlorcone was associated with higher BMI in boys at 3 months of age (β = 0.9; 95% CI: 0, 1.8) and in girls at 8 (β = 0.7; 95% CI: 0, 1.5) and 18 (β = 0.7; 95% CI: −0.1, 1.4) months of age.
5. Arebola et al. <sup>148</sup>	2016/Bolivia <sup>a</sup>	200 mother-newborn pairs from an agricultural area	Cross-sectional	OCs	Questionnaire (residential exposure history) Cord blood DDT and DDE	Median (P25–P75) (ng/g lipid) <i>p,p'</i> -DDE = 196.8 (52.8–475.0) <i>o,p'</i> -DDT = 39.5 (19.3–5.1)	Birth weight, head circumference, birth length, ponderal index, length of gestation	Higher cord blood <i>o,p'</i> -DDT was associated with lower birth weight (β = −0.01; 95% CI: −0.03, −0.001), whereas higher <i>p,p'</i> -DDE was associated with higher birth weight (β = 0.02; 95% CI: 0.003, 0.02). Higher cord blood <i>p,p'</i> -DDE was also associated with shorter gestation length (β = −0.004 [95% CI: −0.01, −0.001]). Higher <i>o,p'</i> -DDT was associated with smaller head circumference (β = −0.004; 95% CI: −0.01, 0).
6. Motta et al. <sup>217</sup>	2016/Brazil	40 mother-newborn pairs living in a rural area	Cross-sectional	OCs	Questionnaire (residential, occupational, and domestic exposure history) Maternal blood (at delivery) and cord blood DDT, DDE, HCH, HCB, chlordanes	Data not shown	Birth weight, head circumference, birth length	Null associations of maternal and newborn contamination indices (calculated using both metal and pesticide concentrations) with birth outcomes ( <i>p</i> > 0.05).
7. Hervé et al. <sup>221</sup>	2016/Guadeloupe	593 mother-newborn pairs	Prospective Cohort	OCs	Cord blood chlorcone and DDE	Median (P25–P75) (μg/L) Chlorcone = 0.20 (0.08–0.41); <i>p,p'</i> -DDE = 0.25 (0.09–0.63)	Birth weight	Among mothers in the highest quartile of GWG, newborns with low and medium cord blood chlorcone concentrations had greater mean reduction in birth weight, compared with those with low cord blood chlorcone (β = −184 g; 95% CI: −348, −20, and β = −153 g; 95% CI: −326, 20, respectively).
<b>Studies on OPs or CBs</b>								
8. Chiappella et al. <sup>172</sup>	2014/Argentina <sup>b</sup>	46 mother-newborn pairs from a rural area/24 mother-newborn pairs from an urban area (controls)	Cross-sectional	OPs	Questionnaire (residential and seasonal exposure history) Placental CE <sup>c</sup>	No applicable	Birth weight, birth length, head circumference, ponderal index, length of gestation	No differences in fetal growth measurements between exposure groups.
9. Rivero Osimani et al. <sup>169</sup>	2016/Argentina <sup>b</sup>	43 mother-newborn pairs from a rural area (RG)/20 mother-newborn pairs from an urban area (controls)	Cross-sectional	OPs	Questionnaire (residential and seasonal exposure history) Placental CE <sup>c</sup>	No applicable	Birth weight, birth length, head circumference, length of gestation	Mean birth weight was lower in RG-SS (difference of 9.6%; <i>p</i> = 0.02) and RG-NSS (difference of 7.8%; <i>p</i> = 0.06) compared with the control group. No differences in other birth outcomes between exposure groups.



Table 8. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
10. Quintana et al. <sup>54</sup>	2017/Argentina <sup>a,c,e</sup>	151 mother–newborn pairs living in a rural area/38 mother–newborn pairs from an urban area (controls)	Cross-sectional	OPs	Questionnaire (residential and seasonal exposure history) Cord blood AChE, BChE	Not applicable	Birth weight, birth length, head circumference, length of gestation	Mean birth weight was lower in cesarean RG-SS than cesarean control group (difference of 14%; $p = 0.04$ ). No differences in other birth outcomes between exposure groups. Null associations of cord blood AChE with birth outcomes.
11. Silva et al. <sup>210</sup>	2020/Argentina	53 mother–newborn pairs living in areas with intensive pesticide application	Cross-sectional	OPs, CBs	Questionnaire (residential exposure history) Blood AChE, BChE <sup>f</sup>	Not applicable	Birth weight, birth length, head circumference, preterm birth, intrauterine growth retardation	No differences in birth weight, length, head circumference, head circumference/weight ratio, and ponderal index between children born during SS and those born during NSS.
Studies on other pesticides or multiple pesticide classes								
12. Mora et al. <sup>218</sup>	2015/Costa Rica	380 mother–newborn pairs living near banana plantations	Prospective cohort	Mn-containing fungicides	Maternal blood and hair Mn in each trimester of pregnancy	Mean $\pm$ SD: Blood Mn ( $\mu\text{g/L}$ ) = $24.5 \pm 6.1$ ; hair Mn ( $\mu\text{g/g}$ ) = $3.5 \pm 5.3$	Birth weight, birth length, head circumference, chest circumference, ponderal index, length of gestation	Hair Mn during the second and third trimesters of gestation were associated with chest circumference ( $\beta$ per 10-fold increase = 0.6 cm; 95% CI: 0.2, 1.1), and $\beta = 0.6$ cm; 95% CI: –0.2, 1.3, respectively). Null associations between blood Mn and birth outcomes.
13. Cecchi et al. <sup>219</sup>	2021/Argentina	418 rural mother–newborn pairs living in proximity to intensive pesticide application/358 urban mother–child pairs	Prospective cohort	Multiple pesticides	Questionnaire (previous history of pesticide exposure and residential pesticide exposure)	Not applicable	Birth weight, birth length, head circumference	No differences in birth weight between groups. Birth length ( $p < 0.01$ ) and head circumference ( $p < 0.05$ ) z-scores were lower in exposed group than in unexposed group.

Note: AChE, acetylcholinesterase; BChE, butyrylcholinesterase; BMI, body mass index; CI, confidence interval; DDE, dichlorodiphenylchloroethylene; DDT, dichlorodiphenyltrichloroethane; GWG, gestational weight gain; HCB, hexa-chlorocyclohexane; HR, hazard ratio; NSS, non-spraying season; Mn, manganese; OC, organochlorine; OP, organophosphate; OR, odds ratio; RG, rural group; SS, spraying season.

<sup>a</sup>Also included in Table 6 (thyroid function).

<sup>b</sup>Also included in Table 4 (placental outcomes and teratogenicity).

<sup>c</sup>Investigators did not use exposure biomarker concentrations in multivariate analyses.

<sup>d</sup>Also included in Table 2 (genotoxicity).

<sup>e</sup>Also included in Table 9 (other health effects).

## Birth Outcomes and Child Growth

Thirteen publications reported on the association of pesticide exposure with birth outcomes and infant/child growth (Table 8). Of the 13 publications, 7 focused on OC pesticides,<sup>188,215–217</sup> 4 on OP pesticides or carbamates,<sup>54,169,172,210</sup> 1 on Mn-containing fungicides,<sup>218</sup> and 1 on multiple pesticide classes.<sup>219</sup> A publication from a small cross-sectional study in Brazil reported null associations of maternal and newborn contamination indices—estimated using metal and OC pesticide concentrations measured in maternal blood at delivery and cord blood—with birth outcomes.<sup>217</sup> In contrast, a publication from a cross-sectional study of mother–newborn pairs from Bolivia reported that higher cord blood DDT concentrations were associated with lower birth weight, whereas higher cord blood DDE concentrations were associated with higher birth weight and shorter gestation length.<sup>188</sup> Publications from two prospective cohort studies in Mexico reported null associations of prenatal DDT or DDE exposure with birth outcomes and child growth during the first year of life<sup>216</sup> and up to 43 months of age.<sup>215</sup> Three publications from a prospective cohort study in Guadeloupe reported that higher cord blood chlordecone concentrations were associated with shorter length of gestation and increased risk of preterm birth,<sup>220</sup> lower birth weight in children whose mothers gained a large amount of weight during pregnancy,<sup>221</sup> and higher body mass index (BMI) at 3–18 months of age.<sup>222</sup>

Four publications from cross-sectional studies in Argentina examined the association between prenatal OP pesticide exposure and fetal growth. Two of them reported a lower mean birth weight among mother–newborn pairs from a rural area compared with controls,<sup>54,169</sup> whereas the other two found no differences in growth parameters between exposure groups.<sup>172,223</sup> A publication from a prospective cohort study conducted in Argentina reported lower birth length and smaller head circumference in children living in proximity to pesticide applications compared with those living in an urban area.<sup>219</sup> Finally, a publication from a prospective cohort study of mother–newborn pairs living near banana plantations aerially sprayed with Mn-containing fungicides in Costa Rica found that maternal Mn concentrations in hair, but not blood, were positively associated with infant chest circumference.<sup>218</sup>

Overall, the small number of published studies that have examined the association of pesticide exposure with birth size and child growth in LAC populations have reported mixed findings. More specifically, about half of the studies found some evidence of adverse outcomes and the other half reported null associations.

## Other Health Problems

**Kidney function.** Nine publications reported on the association between pesticide exposure—ascertained only via questionnaire—and kidney function (Table 9). Notably, six of these nine publications reported null associations with estimated glomerular filtration rate (eGFR) levels or prevalence of chronic kidney disease (CKD).<sup>224–229</sup> In contrast, a publication from a cross-sectional study conducted in Nicaragua reported that accidental pesticide inhalation (ever), but not lifetime days of mixing/applying pesticide or lifetime days of working in fields with pesticide use, was associated with reduced eGFR.<sup>230</sup> A publication from a cross-sectional study in Mexico reported a reduction in eGFR levels among migrant and seasonal farmworkers (who did not apply or mix pesticides) from preharvest to late harvest, as well as lower GFR levels among farmworkers who worked in conventional fields compared with those who worked in organic fields.<sup>231</sup> Last, a publication from a prospective cohort study of school-age children from a tobacco-producing region in Brazil reported increased levels of

**Table 9.** Characteristics of Latin American and the Caribbean studies on pesticide exposure and other health effects published between 2007 and 2021 (*n* = 70).

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
Kidney function 1. Snoff et al. <sup>28</sup>	2010/Nicaragua	124 renal insufficiency cases/ 873 controls	Case-control	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Renal insufficiency (defined by eGFR)	Null association between pesticide exposure and odds of renal insufficiency.
2. Raines et al. <sup>29</sup>	2014/Nicaragua	78 cases of reduced eGFR/ 205 controls from area with high prevalence of CKD	Cross-sectional with case-control analysis	Multiple pesticide classes	Questionnaire (occupational and residential exposure history)	Not applicable	eGFR	Null associations of lifetime days mixing/applying pesticides and lifetime days working in fields with pesticide use with reduced eGFR. Accidental pesticide inhalation (ever) was associated with reduced eGFR (OR = 2.6; 95% CI: 1.0, 6.9).
3. Vela et al. <sup>25</sup>	2014/EI Salvador	223 subjects (> 15 years of age) from two farming communities	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	CKD (defined by eGFR or markers for renal damage: hematuria, proteinuria with hematuria, microalbuminuria)	Similar prevalence of CKD between farmworkers and non-farmworkers (descriptive analyses only).
4. Wesseling et al. <sup>26</sup>	2016/Nicaragua	86 male sugarcane cutters/56 male construction workers/52 male small-scale farmers	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Kidney dysfunction (defined by eGFR)	Null association between self-reported (ever) pesticide use and eGFR levels.
5. Nascimento et al. <sup>32</sup>	2017/Brazil <sup>10</sup>	40 children (6–12 years of age) living in a tobacco-producing region	Prospective cohort	Multiple pesticide classes	Questionnaire (parental exposure history) Blood BChE	Not applicable	Kidney function: microalbuminuria, NAG activity Serum vitamin C Hematological parameters: hemoglobin, Hb, WBC, RBC, platelets (all parameters measured at two different crop periods: in the beginning of the leaf harvest)	Microalbuminuria levels were higher at the beginning of the application period than during leaf harvest period ( <i>p</i> < 0.05). No difference in NAG activity between both periods. Neutrophils, monocytes ( <i>p</i> < 0.05), and basophils ( <i>p</i> < 0.01) were lower, and Hb and lymphocytes were higher during the pesticide application period ( <i>p</i> < 0.01).
6. Snopce et al. <sup>27</sup>	2019/Nicaragua	57 adults from rural communities	Nested case-control (nested within a prospective cohort)	Herbicides, pyrethroids, OPs, fungicides	Questionnaire (occupational exposure history) Urinary metabolites of fungicides (ETU, OH-PYR, 5-OH-TBZ), OPs (TCPy), pyrethroids (DCCA, 3-PBA); herbicide 2,4-D (measured once or twice)	Median (P25–P75) (μmol/mol creatinine): 2,4-D: men visit 1 = 1.0 (0.3–2.5); men visit 2 = 0.3 (0.1–0.7) women visit 1 = 0.1 (< LOD–1.1); 3-PBA: men visit 1 = 0.9 (0.6–1.7); men visit 2 = 0.7 (0.3–0.8) women visit 1 = 2.0 (0.5–2.2); women visit 2 = 1.0 (0.6–2.3) DCCA: men visit 1 = 0.9 (0.4–1.6); men visit 2 = 0.5 (0.3–0.9); women visit 1 = 1.4 (0.5–1.7); women visit 2 = 1.4 (0.5–2.9); men visit 1 = 0.7 (0.2–1.6); men visit 2 = 0.4 (0.2–0.7); women visit 1 = 0.4 (0.2–1.7); women visit 2 = 0.3 (0.2–2.6) TEB-OH: men visit 1 = 0.2 (0.1–0.3); men visit 2 = 0.1 (0.1–0.2); women visit 1 = 0.1 (0.1–0.2); women visit 2 = 0.1 (< LOD–0.3) TCP: men visit 1 = 0.5 (0.3–1.1); men visit 2 = 0.1 (< LOD–0.2); women visit 1 = 0.5 (0.2–0.7); women visit 2 = 0.0 (< LOD–0.2) Glyphosate: men visit 1 = 0 (< LOD–0.1); men visit 2 = 0 (< LOD–0.04); women visit 1 ≤ LOD; women visit 2 = 0 (< LOD–0.1) 4F3PBA, CPFA, MCPA, OH-PYM, 5-OH-TBZ: men visit 1 ≤ LOD; men visit 2 ≤ LOD; women visit 1 ≤ LOD; women visit 2 ≤ LOD Not applicable	Decline in kidney function (defined by eGFR; parameters estimated at two time points: baseline (before the harvest or visit 1) and 6 months later (at the end of the harvest or visit 2))	No differences in pesticide metabolic concentrations between those whose kidney function remained stable over the follow-up period and those whose kidney function declined.
7. Ruiz-Alejos et al. <sup>24</sup>	2021/Peru	1,1514 adults from urban and rural areas	Cross-sectional	Multiple pesticide classes	Questionnaire (environmental and occupational exposure history)	Not applicable	Impaired kidney function (defined by eGFR)	Null association between self-reported pesticide exposure and impaired kidney function.
8. López-Gálvez et al. <sup>231</sup>	2021/Mexico	101 migrant and seasonal farmworkers (who did not directly apply or mix pesticides)/50 nonagricultural office workers	Cross-sectional	Multiple pesticide classes	Questionnaire (residential and occupational exposure history) during preharvest and late harvest	Not applicable	eGFR	Farmworkers had lower eGFR levels than office workers. eGFR in farmworkers decreased from preharvest to late harvest ( <i>p</i> < 0.001). Farmworkers who worked in conventional fields had lower eGFR levels than those who worked in organic fields ( <i>p</i> = 0.002).
9. Prudente et al. <sup>229</sup>	2021/Brazil	208 farmworkers	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood BChE	Not applicable	eGFR	Null association between pesticide exposure and eGFR reduction.
Respiratory and allergic outcomes 10. Fieten et al. <sup>232</sup>	2009/Costa Rica	69 indigenous women exposed to pesticides while working in plantain fields/58 indigenous women unexposed	Cross-sectional	OPs and paraquat	Questionnaire (occupational and residential exposure history)	Not applicable	Respiratory symptoms (European Community Respiratory Health Survey), spirometry (FVC, FEV <sub>1</sub> )	Exposure to chlorpyrifos and terbufos was associated with increased risk of wheeze among nonsmokers (OR = 6.7; 95% CI: 1.6, 28.0 and OR = 5.9; 95% CI: 1.4, 25.6, respectively). Exposure to chlorpyrifos was also associated with shortness of breath among nonsmokers (OR = 2.6; 95% CI: 1.0, 7.3). Null associations of pesticide exposure with FVC and FEV <sub>1</sub> .

Table 9. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
11. Cupul-Uicab et al. <sup>237</sup>	2014/Mexico	747 mother-child (12–30 months of age; boys only) pairs from an area where DDT was recently used	Prospective cohort	OCs	Questionnaire (residential and seasonal exposure at pre-natal period) Maternal serum DDT and DDE at delivery	Median (IQR) (μg/g) $p,p'$ -DDT = 0.3 (0.7); $p,p'$ -DDE = 2.7 (4.5)	LRTIs (physician-diagnosed between birth and 30 months of age and reported by mothers)	Null associations of prenatal DDT exposure with LRTIs in boys up to 30 months of age.
12. Bunali et al. <sup>238</sup>	2018/Brazil	48 farmworkers and 34 relatives residing in a rural area	Cross-sectional	Multiple pesticide classes	Questionnaire (residential, occupational, and intoxication history) Blood AChE and BChE <sup>a</sup>	Not applicable	Respiratory symptoms (European Community Respiratory Health Survey), spirometry (FVC, FEV <sub>1</sub> , FEV <sub>1</sub> /FVC ratio, FEV <sub>1</sub> 25%–75%) (all parameters measured at two different crop season and off-season)	Crop season was associated with increased odds of waking up with a cough (OR = 5.5; 95% CI: 1.2–51.1), but not with other respiratory symptoms. Years of working with pesticides or rural work were associated with decreased FVC ( $\beta$ = −0.01; 95% CI: −0.3–0.11); FEV <sub>1</sub> ( $\beta$ = −0.003; 95% CI: −0.01–0.002), and FEV <sub>1</sub> 25%–75% ( $\beta$ = −0.05; 95% CI: −0.07–0.03) during the crop season, but also during the off-season ( $\beta$ FEV <sub>1</sub> = −0.02; 95% CI: −0.03–0.01; $\beta$ FEV <sub>1</sub> /FVC ratio = −0.001; 95% CI: −0.001–0.001; $\beta$ FEV <sub>1</sub> 25%–75% = −0.03; 95% CI: −0.04–0.02).
13. Diaz-Criollo et al. <sup>234</sup>	2019/Colombia	217 farmworkers	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational and domestic exposure history) Job-exposure matrix (proxy of chronic exposure) Urinary paraquat	Mean (range) paraquat (ng/mL): Carmende Vival = 9.61 (1–54.4); La Unión = 13.22 (1–57.1); Granada = 10.95 (1–52.2)	Self-reported respiratory symptoms (e.g., cough, wheezing), spirometry (FVC, FEV <sub>1</sub> , FEV <sub>1</sub> /FVC ratio)	Self-reported use of pesticide mixtures containing paraquat, profenofos, and methomyl was associated with increased prevalence of flu (PR = 2.3; 95% CI: 1.6–3.3), whereas use of pesticide mixtures containing paraquat and profenofos, and methamidophos was associated with thoracic pain (PR = 4.1; 95% CI: 1.7–9.9). Exposure to pesticide mixtures containing paraquat and profenofos (PR = 2.7; 95% CI: 1.1–7.0) or paraquat and glyphosate (PR = 3.4; 95% CI: 1.2–9.8) was associated with increased prevalence of allergic rhinitis. Self-reported use of pesticide mixtures containing paraquat and methamidophos was associated with an obstructive pattern in spirometry (PR = 4.4; 95% CI: 1.1–17.5). Chronic paraquat exposure was associated with self-reported asthma (PR = 1.1; 95% CI: 1.0–1.1).
14. Mora et al. <sup>236</sup>	2020/Costa Rica	355 mother-child (1 year of age) pairs living near banana plantations aerially sprayed	Prospective cohort	Fungicides, OPs, pyrethroids, herbicides	Questionnaire Urinary metabolites of fungicides (OH-PYR, 5-OH-TBZ), OPs (TCPY), pyrethroids (DCCA, 3-PBA), herbicide 2,4-D during each trimester of pregnancy	Median (range) (ng/mL) (pregnancy average): ETU = 3.4 (0.8–127.4); TCPY = 1.8 (0.4–63.0); 3-PBA = 0.8 (0.1–17.0); 2,4-D = 0.3 (0.1–79.8); DCCA = 1.3 (0.2–23.6); OH-PYR = 0.6 (<LOD–308.6); 5-OH-TBZ = 0.1 (<LOD–339.0)	LRTIs and wheeze (physician- or nurse-diagnosed in first year of life and reported by mothers at 11–19 months of age)	High (≥2/5) during the first half of pregnancy was associated with increased odds of LRTIs (OR = 2.5; 95% CI: 1.0–6.3), whereas high (≥2/5) during second half of pregnancy was associated with decreased odds of wheezing (OR = 0.5; 95% CI: 0.3–1.0). Null associations of other pesticide metabolites with LRTIs and wheeze.
15. Alhami et al. <sup>235</sup>	2021/Costa Rica	266 women living near banana plantations aerially sprayed	Prospective cohort	Fungicides, OPs, pyrethroids, herbicides	Questionnaire (residential pesticide use) Urinary metabolites of fungicides (ETU, OH-PYR, 5-OH-TBZ), OPs (TCPY), pyrethroids (DCCA, 3-PBA), herbicide 2,4-D	Min–max (μg/L): ETU = 0.1–57.7; TCPY = 0.1–16.4; 2,4-D = 0.01–39.4; OH-PYR = 0.02–21.0; 5-OH-TBZ = 0.01–300.0; 3-PBA = 0.1–41.4; DCCA = 0.1–30.3	Self-reported respiratory outcomes: wheeze, doctor-diagnosed asthma, asthma score Allergic outcomes: rhinitis, eczema, itchy rash	Current pesticide use in the home was associated with increased odds of diagnosed asthma (OR = 2.0; 95% CI: 1.1–3.9). Higher 5-OH-TBZ was associated with increased odds of a high asthma score (OR = 1.8; 95% CI: 1.1–3.3). Women who worked in agriculture had decreased odds of rhinitis (OR = 0.2; 95% CI: 0.0–0.9) but increased odds of eczema (OR = 2.5; 95% CI: 1.3–4.9) and itchy rash (OR = 3.2; 95% CI: 1.2–7.7). Living close to agricultural fields (OR = 4.0; 95% CI: 1.5–11.8), farmworkers in the household (OR = 5.9; 95% CI: 2.1–16.5), and aerial spraying close to the home (OR = 4.2; 95% CI: 1.5–11.9) were associated with increased odds of uncontrolled asthma.
16. Rocha et al. <sup>217</sup>	2021/Brazil	319 cases with uncontrolled asthma/319 controls (ages 6–7 and 13–14 years of age)	Case-control	Multiple pesticide classes	Questionnaire (residential pesticide exposure, exposure to pesticides from nearby agricultural spraying)	Not applicable	Uncontrolled asthma (ISAAC)	AST levels, AST/ALT ratio, and albumin levels increased by 17% ( $p \leq 0.05$ ), 21% ( $p \leq 0.05$ ), and 8% ( $p \leq 0.01$ ), respectively, during the spraying period compared with the prespraying period. No differences in ALT or glucose levels between study periods. Null associations between pesticide exposure and liver function markers.
Liver injury 17. Cecchi et al. <sup>236</sup>	2012/Argentina <sup>a</sup>	97 pregnant women living in a rural area with intensive use of pesticides	Prospective cohort	OPs	Questionnaire (residential exposure history) Blood AChE, BChE, $\beta$ -glucuronidase <sup>a</sup>	Not applicable	Liver enzymes: AST, ALT Other biochemical parameters: albumin, glucose (all parameters were measured during spraying and prespraying season)	AST levels, AST/ALT ratio, and albumin levels increased by 17% ( $p \leq 0.05$ ), 21% ( $p \leq 0.05$ ), and 8% ( $p \leq 0.01$ ), respectively, during the spraying period compared with the prespraying period. No differences in ALT or glucose levels between study periods. Null associations between pesticide exposure and liver function markers.
18. Bahia et al. <sup>240</sup>	2014/Brazil	354 general population living near OC factory (45 high/103 moderate/206 low exposure)	Cross-sectional	OCs	Questionnaire (residential, occupational, and dietary exposure history)	Not applicable	Liver enzymes: AST, ALT, GGT, alkaline phosphatase Other biochemical parameters: albumin	ALT ( $p = 0.02$ ), AST ( $p = 0.04$ ), and creatinine ( $p < 0.0001$ ) were higher in farmworkers than in controls, but only among females. No differences in GGT, urea, and hematological parameters between farmworkers and controls.
19. Lermen et al. <sup>238</sup>	2018/Brazil	73 orange grower farmworkers/50 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood BChE <sup>a</sup>	Not applicable	Liver enzymes: ALT, AST, GGT Hematological parameters: hemoglobin, WBC, RBC, platelets Other biochemical parameters: creatinine, urea Self-reported symptoms	ALT ( $p = 0.02$ ), AST ( $p = 0.04$ ), and creatinine ( $p < 0.0001$ ) were higher in farmworkers than in controls, but only among females. No differences in GGT, urea, and hematological parameters between farmworkers and controls.

Table 9. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
20. Ruiz-Ariza et al. <sup>243</sup>	2018/Mexico	55 applicators (high exposure)/119 occasional applicators (moderate exposure)/46 controls	Cross-sectional	OPs, carbamates, pyrethroids	Questionnaire (occupational exposure history) Urinary DAPs <sup>a</sup> Blood AChE, BCHE <sup>b</sup> Blood $\beta$ -glucuronidase	Geometric mean (95% CI) total DAPs (ng/mL): Ref = 33.4 (26.5, 42.2); moderate-exposure group = 58.5 (48.2, 71.0); high-exposure group = 122.5 (81.4, 184.4) Geometric mean: $\beta$ -glucuronidase (U/dL): Ref = 5.80; moderate-exposure group = 9.21; high-exposure group = 6.59	Liver enzymes: AST, ALT, GGT Hematological parameters: hematoctrit, Hb Lipid profile: cholesterol, triglycerides, LDL, VLDL, HDL Other biochemical parameters: glucose, albumin HDL levels ( $p < 0.05$ ) Lower alkaline phosphatase, total cholesterol, albumin, leucocytes, platelets, and monocytes among farmworkers who had used pesticides compared with those who had not ( $p < 0.01$ for each).	Higher $\beta$ -glucuronidase activity was associated with increased AST, ALT, and GGT levels ( $p < 0.05$ ). Higher $\beta$ -glucuronidase activity was also associated with increased glucose, total lipids, triglycerides, cholesterol, atherogenic index, VLDL, hematoctrit, and hemoglobin levels ( $p < 0.05$ ) and with lower HDL levels ( $p < 0.05$ ).
21. Candelan et al. <sup>48</sup>	2018/Brazil <sup>48</sup>	84 farmworkers who used pesticides/68 farmworkers who did not use pesticides	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Liver enzymes: AST, ALT, GGT, alkaline phosphatase Lipid profile: total cholesterol, HDL, LDL, triglycerides Other biochemical parameters: glucose, albumin, creatinine, total proteins, urea, uric acid Lipid profile: total cholesterol, HDL, LDL, triglycerides	Lower alkaline phosphatase, total cholesterol, albumin, leucocytes, platelets, and monocytes among farmworkers who had used pesticides compared with those who had not ( $p < 0.01$ for each).
22. Arévalo-Jaramillo et al. <sup>49</sup>	2019/Ecuador <sup>49</sup>	62 women living in 2 separate agricultural communities/53 controls (living in a commercial city)	Cross-sectional	Multiple pesticide classes	Questionnaire	Not applicable	Liver enzymes: AST, ALT, GGT Hematological parameters: hematoctrit, leukocytes, number and percentage of neutrophils, lymphocytes, eosinophils, monocytes, basophils, platelets Other biochemical parameters: glucose, total bilirubin, direct bilirubin, urea, creatinine, high sensitivity C-reactive protein, total proteins Immunological parameters: complement C3, complement C4, IgA, IgM, IgG Adhesion molecules: percentage of LFA-1, ICAM-1, and L-selectin surface protein expression in lymphocytes and monocytes	Higher percentage of ALT ( $p = 0.03$ ) and AST values ( $p < 0.01$ ) exceeding normal levels in women from the first agricultural community compared with controls. Higher percentage of GGT values exceeding normal levels ( $p = 0.06$ ) in women from the second agricultural community compared with controls. Higher hemoglobin and hematocrit levels, but lower platelet count and cholesterol levels, in exposed women than in controls ( $p < 0.01$ ). Farmworkers had lower AST and ALT levels, but higher glucose, urea, total protein, IgM, and C3 levels, than controls ( $p < 0.01$ ). Farmworkers had a higher number of neutrophils and a higher mean platelet volume but lower numbers of lymphocytes, monocytes, and platelets than controls ( $p < 0.05$ ). Farmworkers showed a decrease in monocyte and an increase in lymphocyte expression for both LFA-1 and ICAM-1 compared with controls. AChE activity was negatively correlated with glucose levels ( $r = -0.2$ ; $p = 0.02$ ), whereas BCHE activity was negatively correlated with IgG levels ( $r = -0.2$ ; $p = 0.02$ ). Null associations of AChE and BCHE activities with liver enzymes, LFA-1 and ICAM-1 surface protein expression in lymphocytes was positively associated with exposure time to pesticides in years ( $r = 0.4$ for both; $p < 0.001$ ), whereas LFA-1 and ICAM-1 surface protein expression in monocytes was inversely associated with exposure time to pesticides ( $r = -0.4$ and $-0.3$ , respectively; $p < 0.001$ ). Farmworkers had higher urea and creatinine levels, but lower ALT levels, than controls ( $p < 0.05$ ). Farmworkers had higher AST, urea and creatinine levels, as well as higher blood plasma antioxidant potential values ( $p < 0.05$ ), during the high pesticide exposure period compared with the low exposure period.
23. Cestonaro et al. <sup>241</sup>	2020/Brazil	62 famworkers/54 unexposed controls	Cross-sectional	OPs, CBs	Questionnaire (occupational exposure history) Blood AChE, BCHE	Not applicable	Liver enzymes: ALT, AST, GGT Hematological parameters: RBC, hematoctrit, leukocytes, number and percentage of neutrophils, lymphocytes, eosinophils, monocytes, basophils, platelets Other biochemical parameters: glucose, total bilirubin, direct bilirubin, urea, creatinine, high sensitivity C-reactive protein, total proteins Immunological parameters: complement C3, complement C4, IgA, IgM, IgG Adhesion molecules: percentage of LFA-1, ICAM-1, and L-selectin surface protein expression in lymphocytes and monocytes	Farmworkers had lower AST and ALT levels, but higher glucose, urea, total protein, IgM, and C3 levels, than controls ( $p < 0.01$ ). Farmworkers had a higher number of neutrophils and a higher mean platelet volume but lower numbers of lymphocytes, monocytes, and platelets than controls ( $p < 0.05$ ). Farmworkers showed a decrease in monocyte and an increase in lymphocyte expression for both LFA-1 and ICAM-1 compared with controls. AChE activity was negatively correlated with glucose levels ( $r = -0.2$ ; $p = 0.02$ ), whereas BCHE activity was negatively correlated with IgG levels ( $r = -0.2$ ; $p = 0.02$ ). Null associations of AChE and BCHE activities with liver enzymes, LFA-1 and ICAM-1 surface protein expression in lymphocytes was positively associated with exposure time to pesticides in years ( $r = 0.4$ for both; $p < 0.001$ ), whereas LFA-1 and ICAM-1 surface protein expression in monocytes was inversely associated with exposure time to pesticides ( $r = -0.4$ and $-0.3$ , respectively; $p < 0.001$ ). Farmworkers had higher urea and creatinine levels, but lower ALT levels, than controls ( $p < 0.05$ ). Farmworkers had higher AST, urea and creatinine levels, as well as higher blood plasma antioxidant potential values ( $p < 0.05$ ), during the high pesticide exposure period compared with the low exposure period.
24. Bemieri et al. <sup>239</sup>	2021/Brazil	50 soy bean farmworkers/63 controls from 2 different areas	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood BCHE <sup>b</sup>	Not applicable	Liver enzymes: AST, ALT, GGT Other biochemical parameters: urea, creatinine Antioxidant capacity (FRAP) (measured during the high and low pesticide exposure periods)	Farmworkers had higher urea and creatinine levels, but lower ALT levels, than controls ( $p < 0.05$ ). Farmworkers had higher AST, urea and creatinine levels, as well as higher blood plasma antioxidant potential values ( $p < 0.05$ ), during the high pesticide exposure period compared with the low exposure period.
Hematological parameters and lipid profiles 25. Remor et al. <sup>54</sup>	2009/Brazil <sup>48</sup>	37 famworkers/20 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood BCHE, ALA-D <sup>b</sup>	Not applicable	Hematological parameters: hematoctrit, Hb, WBC, RBC, platelets Lipid profile: total cholesterol, LDL, triglycerides, HDL Aplastic anemia (AA) and agranulocytosis by medical diagnosis	No differences in hematological parameters or lipid profiles between groups.
26. Mufaf et al. <sup>245</sup>	2009/Brazil, Argentina, Mexico	173 adults with aplastic anemia/692 healthy controls	Case-control	Multiple pesticide classes	Questionnaire (occupational or domestic exposure history to pesticides and other chemical products)	Not applicable	Exposure to pesticides was associated with increased odds of AA (OR = 2.2; 95% CI: 1.1, 4.7). High frequency of exposure ( $> 30$ times/yr) to OP pesticides (OR = 3.0; 95% CI: 0.9, 10.1) and pyrethroids (OR = 1.8; 95% CI: 1.0, 3.1) was also associated with increased odds of AA.	Exposure to pesticides was associated with increased odds of AA (OR = 2.2; 95% CI: 1.1, 4.7). High frequency of exposure ( $> 30$ times/yr) to OP pesticides (OR = 3.0; 95% CI: 0.9, 10.1) and pyrethroids (OR = 1.8; 95% CI: 1.0, 3.1) was also associated with increased odds of AA.

Table 9. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
27. Payán-Rentería et al. <sup>86</sup>	2012/Mexico <sup>a</sup>	25 farmworkers/21 controls	Cross-sectional	OCs, OPs, TRZ	Medical examination Questionnaire (occupational exposure history) Blood AChE <sup>b</sup>	Not applicable	Hematological parameters: hemoglobin, Hb, WBC, RBC, platelets Lipid profile: LDL, HDL, total cholesterol, triglycerides Other biochemical parameters: albumin and globulin levels, albumin/globulin relation, total bilirubin, direct bilirubin, and indirect bilirubin Self-reported fertility problems, birth defects, and cancer	Higher hemoglobin ( $p = 0.02$ ) and hematocrit ( $p = 0.04$ ) levels in farmworkers than in controls. No differences in other hematological or biochemistry outcomes between farmworkers and controls. Farmworkers reported more fertility problems, birth defects, and cancer in themselves or their family members than controls.
28. Adad et al. <sup>88</sup>	2015/Brazil <sup>c</sup>	80 male farmworkers from state association/20 male private company/100 matched controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood BChE <sup>b</sup>	Not applicable	Hematological parameters: hemoglobin, Hb, WBC, RBC, platelets Lipid profile: LDL, HDL, triglyceride	No differences in hematological parameters or lipid profiles between groups.
29. Alves et al. <sup>73</sup>	2016/Brazil <sup>c</sup>	77 tobacco farmworkers/60 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Hematological parameters: hemoglobin, Hb, WBC, RBC, platelets	Lower mean levels of band neutrophils ( $p < 0.05$ ) and monocytes ( $p < 0.05$ ) in exposed group compared with control group. All other hematological parameters were similar between groups.
30. Quinana et al. <sup>24</sup>	2017/Argentina <sup>a,de</sup>	151 mother–newborn pairs living in a rural area/38 mother–newborn pairs from an urban area	Cross-sectional	OPs	Questionnaire (residential and seasonal exposure history) Cord blood AChE, BChE <sup>b</sup>	Not applicable	Hematological parameters: hemoglobin, Hb, WBC, RBC, platelets, osmotic fragility	No differences in cord blood hematological parameters between groups.
31. Siller-López et al. <sup>251</sup>	2017/Colombia	205 coffee harvesters	Cross-sectional	OPs	Questionnaire (occupational exposure history) Blood BChE	Not applicable	Lipid profile: cholesterol and triglycerides Atherosclerotic cardiovascular disease (ASCVD) Hypertension	Association between BChE activity and hypercholesterolemia (total cholesterol $\geq 200$ mg/dL) ( $r = 0.3$ ; $p < 0.01$ ). Null associations of BChE activity with ASCVD and hypertension. Higher prevalence of hypertension was associated with Q allele carriers of <i>POV1</i> <sub>rs</sub> polymorphism in both dominant model (QR+RR) (OR = 1.9; 95% CI: 1.03, 3.4) and recessive model (QR+QQ) (OR = 2.9; 95% CI: 1.1, 7.4).
32. Cortés-Iza et al. <sup>248</sup>	2017/Colombia	92 farmworkers	Cross-sectional	OPs, CBs	Questionnaire (occupational exposure history) Blood AChE, BChE <sup>b</sup>	Not applicable	Hematological parameters: hemoglobin, Hb, WBC, RBC, platelets, MCV, MCH, MCHC, RDW	Leucocytes and monocytes below the reference range in farmworkers exposed to pesticides for 6–9 h, and farmworkers who handled pesticides for 1–10 y. MCH above the reference range and RDW below the reference range in farmworkers exposed to pesticides for $> 10$ y.
33. Piccoli et al. <sup>249</sup>	2019/Brazil	275 farmworkers and their families	Cross-sectional	OCs	Questionnaire (occupational exposure history) Serum HCH, HCB, chlordane, <i>trans</i> -nonachlor, heptachlor, DDT, DDE, endosulfan, aldrin, endrin, dieldrin, methoxychlor, mirex, and pentachloroanisole	Median (P25–P75) (ng/g lipid): $\alpha$ -HCH < LOD ( $< \text{LOD} - 10.1$ ); $\beta$ -HCH < LOD ( $< \text{LOD} - 29.5$ ); $\gamma$ -HCH = 3.7 ( $< \text{LOD} - 12.4$ ); HCB < LOD ( $< \text{LOD} - 11.5$ ); heptachlor < LOD; heptachlor epoxide A < LOD ( $< \text{LOD} - 21.1$ ); heptachlor epoxide B < LOD; $\alpha$ -chlordane = 0; $\gamma$ -chlordane < LOD; <i>trans</i> -nonachlor < LOD; $\alpha$ -p,p'-DDT < LOD; $p,p'$ -DDT < LOD; $\alpha$ -p,p'-DDE < LOD ( $< \text{LOD} - 40.6$ ); $p,p'$ -DDE < LOD; $\alpha$ -p,p'-DDD < LOD ( $< \text{LOD} - 30.3$ ); $p,p'$ -DDD < LOD; aldrin < LOD; endrin < LOD; dieldrin < LOD; endosulfan I < LOD; endosulfan 2 < LOD; methoxychlor < LOD; mirex < LOD; pentachloroanisole < LOD ( $< \text{LOD} - 0.71$ )	Hematological parameters: hemoglobin, Hb, WBC, RBC, platelets, MCV, MCH, MCHC, RDW	Detachable concentrations of $\gamma$ -HCH ( $\beta = 0.9$ ; 95% CI: 0.8, 0.9); heptachlor ( $\beta = 0.8$ ; 95% CI: 0.8, 0.9); $p,p'$ -DDT ( $\beta = 0.9$ ; 95% CI: 0.8, 1.0); $\alpha$ -p,p'-DDE ( $\beta = 0.8$ ; 95% CI: 0.7, 1.0); and $p,p'$ -DDE ( $\beta = 0.9$ ; 95% CI: 0.8, 1.0) were associated with decreased monocytes. Detachable concentrations of $\gamma$ -HCH ( $\beta = 0.8$ ; 95% CI: 0.7, 1.0), heptachlor ( $\beta = 0.8$ ; 95% CI: 0.6, 0.9), <i>trans</i> -nonachlor ( $\beta = 0.5$ ; 95% CI: 0.3, 0.9), $\alpha$ -p,p'-DDD ( $\beta = 0.7$ ; 95% CI: 0.4, 1.0), $p,p'$ -DDD ( $\beta = 0.7$ ; 95% CI: 0.6, 0.9), endrin ( $\beta = 0.7$ ; 95% CI: 0.6, 0.9), endosulfan I ( $\beta = 0.8$ ; 95% CI: 0.6, 0.9), and methoxychlor ( $\beta = 0.7$ ; 95% CI: 0.5, 1.0) were associated with decreased eosinophils. Detachable concentrations of $\gamma$ -chlordane were associated with decreased hemoglobin levels ( $\beta = -0.4$ ; 95% CI: $-0.8$ , 0).
34. Dabó et al. <sup>247</sup>	2019/Brazil	142 farmworkers	Cross-sectional	Multiple pesticides	Questionnaire (occupational exposure history)	Not applicable	Hematological parameters: RBC, hemoglobin, hematocrit, MCV, MCH, MCHC	Lower leukocytes and platelets ( $p < 0.01$ for each), but higher percentage band neutrophils ( $p < 0.01$ ) and percentage neutrophils ( $p < 0.0001$ ) during the pesticide application period compared with the harvest period (period without pesticide exposure).
35. Molina-Pinto et al. <sup>246</sup>	2020/Mexico	60 sprayers with motor pump (high exposure)/126 solid pesticides sprayers (moderate exposure)/22 controls	Cross-sectional	OPs	Questionnaire (occupational exposure history) Blood BChE Urinary DAPs <sup>b</sup>	Mean (range) total DAPs (ng/mL): Control group: 33.5 (24.6–41.3); moderate-exposure group: 58.5 (24.5–83.3); high-exposure group: 122.5 (25.6–488.4)	Lipid profile: cholesterol, LDL, VLDL, triglycerides, atherogenic index Other biochemical parameters: glucose, albumin, creatinine	Lower LDL, cholesterol, and albumin levels among highly exposed group compared with moderately exposed and control groups ( $p < 0.05$ ). Positive correlations of BChE activity with triglycerides, VLDL, and total lipids among normal-weight individuals. Positive correlations of BChE activity with glucose, cholesterol, atherogenic index, triglycerides, LDL, VLDL, and total lipids among overweight individuals.



Table 9. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
36. Jacobson-Pereira et al. <sup>246</sup>	2020/Brazil	43 farmworkers/30 unexposed controls	Cross-sectional	Multiple pesticides	Questionnaire (occupational exposure history)	Not applicable	Cellular immune profile: total leukocytes, neutrophils, monocytes, eosinophils, lymphocytes, cytokines	Higher classical monocytes ( $p < 0.001$ ), dendritic cells ( $p < 0.001$ ), total T cells ( $p = 0.04$ ), central memory CD8 T cells ( $p = 0.02$ ), effector inflammatory IL-6 ( $p = 0.040$ ) in farmworkers than in controls. Lower total B cells ( $p = 0.01$ ), regulatory B cells ( $p < 0.001$ ) and plasmablasts ( $p < 0.001$ ) in farmworkers than in controls.
Acoustic damage 37. Guida et al. <sup>252</sup>	2010/Brazil	48 male workers exposed to malathion and noise/76 male workers exposed to noise	Cross-sectional	OPs (malathion)	Questionnaire (occupational exposure history)	Not applicable	Hearing loss: DPOAE	Worse performance in workers exposed to noise and malathion at the frequencies of 3 kHz on the left ear ( $p = 0.01$ ), and 4 kHz on both ears (left ear $p = 0.01$ ; right ear $p = 0.02$ ) than in workers exposed only to noise.
38. Bazilio et al. <sup>253</sup>	2012/Brazil	33 farmworkers	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Meatotomy, audiometry, DPT, GIN (500 Hz and 1 and 2 kHz)	Higher pesticide exposure indices were associated with increased risk of worse performance in DPT for right ear (OR = 2.0; 95% CI: 1.1, 3.7) and left ear (OR = 1.9; 95% CI: 1.2, 3.1), and in GIN for right ear (OR = 2.0; 95% CI: 1.2, 3.4) and left ear (OR = 1.2; 95% CI: 0.9, 1.5). For right ear, farmworkers had lower level of response for TEOAE at 1 and 1.5 kHz ( $p < 0.001$ ), and for DPOAE at 6,000 ( $p = 0.004$ ) and 7,069 Hz ( $p < 0.001$ ) but higher at 750 ( $p < 0.01$ ) and 984 Hz ( $p < 0.05$ ). For left ear, farmworkers had lower level of response for TEOAE at 1 ( $p < 0.001$ ), 1 kHz, and total 7,069 Hz ( $p < 0.001$ ) but higher at 750 ( $p < 0.001$ ) and 984 Hz ( $p = 0.04$ ).
39. Alcuris et al. <sup>254</sup>	2013/Brazil	25 farmworkers exposed to malathion and noise with normal hearing/30 controls	Cross-sectional	OPs (malathion)	Questionnaire (occupational exposure history)	Not applicable	Hearing loss: TEOAE, DPOAE	Farmworkers had lower scores for physical outcomes and general health status and poorer mental health and emotional regulation than controls ( $p < 0.01$ for each).
40. de Sena et al. <sup>255</sup>	2013/Brazil	235 farmworkers/116 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (current or past occupational exposure history)	Not applicable	Hearing loss: airborne tonal thresholds Quality of life: SF-36 Self-reported health status Hearing loss: TEOAE and DPOAE	Students in the highest quartile of pesticide exposure had increased odds of failing TEOAE test (OR = 3.7; 95% CI: 1.4, 9.9) and showing alterations in cochlear function assessed by DPOAE (OR = 2.6; 95% CI: 1.2, 7.2) compared with students in the lowest quartile.
41. Garcia et al. <sup>256</sup>	2017/Brazil	205 students living in an agricultural area	Cross-sectional	Multiple pesticide classes	Questionnaire (residential and occupational exposure history)	Not applicable		Increased incidence of hearing threshold loss at high frequency and of downward sloping audiometric curve configuration and alteration of stapedial reflex in groups exposed to pesticides compared with controls ( $p < 0.05$ ).
42. Tomiazzi et al. <sup>257</sup>	2019/Brazil	30 smokers/30 subjects exposed to pesticides for at least 1 y/30 farmers exposed to pesticides who were smokers/37 controls not exposed to pesticides and who never smoked	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Meatotomy, pure-tone audiometry (250–8,000 kHz), vocal audiometry (SRT and SRP), immittance testing	Null association between AChE activity and hearing loss.
43. Mutiazzi et al. <sup>259</sup>	2019/Brazil	71 rural workers exposed to pesticides	Cross-sectional	OPs, CBs	Questionnaire (occupational exposure history) Blood AChE (measured in a subset of 50 workers)	Not applicable	Hearing loss: air conduction auditory thresholds	
44. de Souza Alcuris et al. <sup>258</sup>	2021/Brazil	38 male endemic disease control agents/18 male workers without occupational pesticide exposure	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Central auditory function: inspection of external acoustic meatus, pure-tone audiometry, acoustic immittance, BAEP, dichotic digits test, TEOAE	Increase in waves III and V absolute latencies, and I–III and I–V interpeak latencies in exposed workers compared with controls with auditory thresholds up to 25 dB HL at the frequencies from 2,000 to 4,000 Hz. Mean dichotic digits test performance was worse in exposed workers than in controls. No differences between groups in the TEOAE test.
Other outcomes 45. de Souza et al. <sup>276</sup>	2011/Brazil	298 rural agriculture or livestock workers from three rural counties	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational, para-occupational, and residential exposure history)	Not applicable	Chronic diseases: self-reported symptoms and illness	Pesticide exposure was associated with the report of several diseases with neurological (OR = 2.5; 95% CI: 1.8, 3.4) and oral diseases (OR = 1.5; 95% CI: 1.4, 1.6) being the most prevalent.
46. Suarez-Lopez et al. <sup>280</sup>	2013/Ecuador	138 children (4–9 years of age) living with flower plantation workers/133 living with no agricultural workers	Cross-sectional	OPs, CBs	Questionnaire (residential and parental exposure history) Blood AChE	Not applicable	Resting heart rate, blood pressure (SBP and DBP)	Decrease in AChE activity was associated with a decrease in SBP ( $\beta = -2.9$ ; 95% CI: $-5.2$ , $-0.5$ ) and in DBP ( $\beta = -2.9$ ; 95% CI: $-5.0$ , $-0.8$ ). Children living with flower workers had lower SBP ( $\beta = -1.7$ ; 95% CI: $-3.5$ , $0.1$ ). Null associations were found between exposures and heart rate.

Table 9. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
47. Saunders et al. <sup>318</sup>	2014/Guadeloupe	779 pregnant women	Prospective cohort	OCs	Maternal plasma chlordane at delivery	Data not shown	Gestational diabetes, gestational hypertension, preeclampsia	Higher chlordane concentrations were associated with decreased risk of gestational hypertension (OR per 10-fold increase in concentrations = 0.4; 95% CI: 0.2, 0.6). Null associations of chlordane exposure with risk of preeclampsia or gestational diabetes.
48. Butinof et al. <sup>267</sup>	2015/Argentina	880 farmworkers handling pesticides	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Health status by perception of symptoms as irritation (i.e., skin and eye irritation, nausea, vomiting, respiratory disorders), fatigue/tiredness, headache, nervousness or depression, medical consultation, and hospitalizations	Farmworkers who had worked for >10 y or had mixed/applied >10 pesticides had increased odds of irritation (OR = 1.7; 95% CI: 1.1, 2.6; OR = 1.6; 95% CI: 1.04, 2.4, respectively). Adequate use of PPE was associated with decreased odds of irritation (OR = 0.6; 95% CI: 0.4, 0.9). Use of endosulfan was associated with increased odds of hospitalization (OR = 2.7; 95% CI: 0.9, 8.1).
49. Cezar-Vaz et al. <sup>268</sup>	2016/Brazil	331 workers from two rural municipalities	Cross-sectional	Multiple pesticide classes	Questionnaire (residential and occupational exposure history)	Not applicable	Health status related to work: mental and nervous system, respiratory, gastric, circulatory, and dermatological outcomes	Rural workers who used pesticides had a 90% higher prevalence of dermatologic disorders than those who did not (PR = 1.9; 95% CI: 1.4, 2.6). No differences in prevalence of mental and nervous system, respiratory, gastric, and circulatory diseases between rural workers who used and did not use pesticides.
50. Muñoz-Quezada et al. <sup>277</sup>	2017/Chile	114 farmworkers/93 controls	Cross-sectional	OPs	Questionnaire (occupational and residential exposure history)	Not applicable	Health status: self-reported skin allergies, anemia, asthma, cancer, liver damage, depression, diabetes mellitus, epilepsy, hypertension, kidney failure, heart problems, anxiety, symptoms of recent OP pesticide poisoning, and hospitalization for pesticide poisoning	An increasing number of years of OP pesticide use was associated with increased odds of symptoms of recent OP pesticide poisoning (OR = 1.0; 95% CI: 1.0, 1.1), but not with other health problems.
51. Cupul-Uicab et al. <sup>283</sup>	2017/Mexico	448 urban newborn boys/299 rural newborn boys	Cohort	OCs	Questionnaire (residential exposure history) Maternal serum DDE and DDT at birth	Median (IQR) (μg/g): Urban residents: DDT = 0.2 (0.3); DDE = 2.2 (2.9) Rural residents: DDT = 0.7 (1.5); DDE = 4.3 (7.0)	Gastrointestinal infection: diarrhea	Among boys living in the urban area, those with the highest DDE (>9 μg/g serum lipid) had higher incidence rate of diarrhea than those in the lowest category (≤3 μg/g serum lipid) (IRR = 1.4; 95% CI: 1.1, 1.8). Among boys from a rural area, higher DDE and DDT were not associated with a higher incidence rate of diarrhea.
52. Silvério et al. <sup>27</sup>	2017/Brazil <sup>a</sup>	94 farmworkers exposed to pesticides including OPs/94 farmworkers exposed to pesticides not including OPs/50 controls	Cross-sectional	OPs	Questionnaire (occupational exposure history) Urinary DATP <sup>b</sup> Blood AChE, BChE <sup>b</sup>	Mean ± SD (μg/L): Occupationally exposed to complex mixtures with OPs: DETP = 0.3 ± 0.3; DEDTP = 0.1 ± 0.04; occupationally exposed to complex mixtures without OPs: DETP = 0.1 ± 0.005; DEDTP = 0.1 ± 0.02; control group: DETP < LOQ; DEDTP < LOQ Not applicable	Clinical changes in systems: cardiovascular, CNS, digestive, respiratory, auditory, urinary, and skin and mucous membranes.	High prevalence of changes in CNS, respiratory, and auditory systems in both exposed groups compared with controls ( <i>p</i> < 0.05).
53. Suarez-Lopez et al. <sup>261</sup>	2018/Ecuador	310 children (4–9 years of age) living near flower plantations	Cross-sectional	Multiple pesticide classes	Questionnaire (parental and residential exposure histories) Teriles of residential distance to the nearest plantation Blood AChE <sup>b</sup>	Not applicable	Blood pressure (SBP and DBP)	For every 1,000 m greater proximity to a plantation, SBP increased by 3 mmHg (95% CI: 0.5, 5.8), and SBP z-score increased by 0.3 SD (95% CI: 0.1, 0.5). For every 1,000 m <sup>2</sup> of flower plantation areas, SBP increased by 0.4 mmHg (95% CI: 0.03, 0.7) and SBP z-score increased by 0.03 (95% CI: 0.00, 0.06).
54. Mejía-Sánchez et al. <sup>265</sup>	2018/Mexico	169 floriculturists/96 controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Blood GST and GSTT1 activities	Higher total GST and GSTT1 enzymatic activity in exposed floriculturists than controls ( <i>p</i> < 0.001). Significant difference in total GST, but not GSTT1 activity, between those who applied pesticides in the past 0–10 d and those who applied pesticides in the past 11–20 d ( <i>p</i> = 0.05).
55. Michado et al. <sup>266</sup>	2018/Brazil	1,421 subjects living in rural areas	Cross-sectional	Multiple pesticide classes	Questionnaire (residential exposure history)	Not applicable	Sleep problems (MSQ score)	Having had a pesticide intoxication, but not living in a rural area, was associated with more sleep problems (β = 2.6; 95% CI: 1.1, 4.1).

Table 9. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
56. Barrón Cuenca et al. <sup>223</sup>	2019/Bolivia	297 men and women living in three agricultural communities	Cross-sectional	Fungicides, OPs, pyrethroids, herbicides	Questionnaire (occupational history) Urinary metabolites of tebuconazole, chlorpyrifos, pyrethroids, 2,4-D, MCPA, thiazendazole, pyrimethanil <sup>a</sup>	Mean (range) (ng/mL) TEB-OH = 3.2 (< LOD–458); TCP = 17.6 (0.8–439); 3-PBA = 40.3 (0.2–40.3); DCCA = 5.0 (0.1–150); 2,4-D = 15.8 (< LOD–1,705); MCP = 0.1 (< LOD–0.4); CFCA = 0.4 (< LOD–1.4); 4E3PBA = 0.2 (< LOD–3.9); 5-OH-TBZ = 0.1 (< LOD–4.1); OH-PYR = 2.4 (< LOD–395)	Self-reported symptoms of pesticide poisoning (headache, dizziness, fatigue), respiratory outcomes (dyspnea, cough), muscular outcomes (cramps, fasciculations), digestive outcomes (abdominal pain, nausea, vomiting, red skin, itchy skin, eyes burning, red eyes), reproductive outcomes (miscarriages, stillbirths, congenital malformations)	No differences in self-reported miscarriages, congenital malformations, and stillbirths between female farmers and nonfarmers. No report on differences in other symptoms between farmers and nonfarmers.
57. Suarez-Lopez et al. <sup>262</sup>	2019/Ecuador	310 children (4–9 years of age) living near flower plantations	Cross-sectional	OPs, CBs	Questionnaire (parental and residential exposure histories) Blood AChE <sup>b</sup>	Not applicable	Blood pressure (SBP and DBP), resting heart rate	Inverse relationship of time after the spray season with percentiles of SBP ( $\beta$ per 10.9 d after the harvest = -4.3; 95% CI: -6.9, -1.7) and DBP ( $\beta$ = -7.5; 95% CI: -9.6, -5.4). For every 10.9 d that a child was examined sooner after the harvest, the OR of elevated BP/hypertension doubled (OR = 2.0; 95% CI: 1.3, 3.1).
58. Burinot et al. <sup>62</sup>	2019/Argentina <sup>a</sup>	47 pesticide applicators/52 unexposed controls	Cross-sectional	OPs, CBs	Questionnaire (occupational exposure history) Blood AChE <sup>b</sup>	Not applicable	Health status by perception of general, neurological, cardiorespiratory, dermatological, gastrointestinal, ocular, and urinary symptoms	Higher presence of general, cardiorespiratory, and dermatological symptoms among pesticide applicators compared with controls ( $p < 0.01$ for each).
59. Buratti et al. <sup>138</sup>	2020/Brazil <sup>c</sup>	42 pesticide applicator/36 farmworkers who did not apply pesticides	Cross-sectional	OPs	Questionnaire (occupational exposure history) Blood AChE, BChE <sup>b</sup>	Not applicable	Self-reported symptoms of pesticide poisoning	Farmworkers who did not spray pesticides had a higher prevalence of headache (PR = 2.1; 95% CI: 1.1, 4.0), dyspnea (PR = 3.8; 95% CI: 1.5, 9.5), wheezing (PR = 16.7; 95% CI: 2.4, 108.8), cough (PR = 2.6; 95% CI: 1.1, 6.5), and poor digestion (PR = 7.85; 95% CI: 1.17, 52.89) compared with pesticide applicators.
60. Okuyama et al. <sup>274</sup>	2020/Brazil	3,826 patients with pesticide poisoning	Case-control	Multiple pesticide classes	Pesticide poisoning reported to surveillance system	Not applicable	Death by pesticide poisoning	Farmworkers had increased odds of death from pesticide poisoning (OR = 2.2; 95% CI: 1.2, 4.2) compared with those not working in the agricultural sector. Those poisoned by pesticides classified as having "extreme" toxicity had increased odds of death compared with those poisoned by pesticides categorized as having "high/moderate/low" toxicity (OR = 2.8; 95% CI: 1.8, 4.2).
61. Schneider Medeiros et al. <sup>273</sup>	2020/Brazil	150 patients with idiopathic PD	Prospective cohort	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Mortality risk from PD	Exposed patients with PD had increased risk of death compared with unexposed patients with PD (HR = 2.3; 95% CI: 1.2, 4.7). Occupational pesticide exposure was associated with elevated mortality rate (HR = 2.2; 95% CI: 1.1, 4.6). Evidence of dose-dependent relationship between occupational pesticide exposure and mortality rate; patients with $\geq 10$ y of occupational pesticide exposure had significantly elevated mortality rate compared with patients with <10 y of exposure (HR = 2.8; 95% CI: 1.2, 6.7).
62. de Carvalho et al. <sup>269</sup>	2020/Brazil	2,649 tobacco farmworkers	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Thoracic spine pain (NQMS)	Lifetime history of pesticide poisoning was associated with increased prevalence of thoracic spine pain in the previous year among females (PR = 1.8; 95% CI: 1.3, 2.5). Effect of pesticide poisoning on prevalence of thoracic spine pain was not reported among men.
63. Fiasa et al. <sup>270</sup>	2020/Brazil	2,649 tobacco farmworkers	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Neck pain (NQMS)	Pesticide poisoning in the past year was associated with increased prevalence of neck pain among males (PR = 3.9; 95% CI: 1.1, 14.1), but not females.
64. Campos et al. <sup>272</sup>	2020/Brazil	354 small tobacco farmers	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Green tobacco sickness (defined as urinary cotinine levels >50 ng/mL, contact with tobacco leaves in up to 48 h before sample collection and report of headache, dizziness, nausea, vomiting, weakness, or belly ache)	Farmers with current exposure to pesticides had increased odds of green tobacco sickness compared with those without current exposure to pesticides (OR = 3.6; 95% CI: 1.4, 9.3).

Table 9. (Continued.)

Study	Year of publication/country	Population and sample size	Study design	Pesticides assessed	Exposure assessment method	Pesticide or metabolite concentrations	Health effect and assessment method/instrument	Results
65. Luce et al. <sup>273</sup>	2020/Guadeloupe	11,112 farm owners and farmworkers who worked on banana plantations between 1973 and 1993	Retrospective cohort	Multiple pesticide classes	Agricultural census	Not applicable	All-cause mortality, all-cancer mortality, cancer-specific mortality	Lower all-cause mortality in male (SMR = 0.9; 95% CI: 0.9, 1.0), but not female (SMR = 1.0; 95% CI: 0.9, 1.0), farm owners and farmworkers compared with the general population. All-cancer mortality did not differ from that of the general population. Excess of deaths from stomach cancer (SMR = 2.6; 95% CI: 1.3, 4.5) and pancreatic (SMR = 2.3; 95% CI: 1.1, 4.4) cancer in female, but not male (SMR = 1.0; 95% CI: 0.7, 1.3 and SMR = 0.8; 95% CI: 0.5, 1.2, respectively) farm owners.
66. Lovison Sasso et al. <sup>102</sup>	2021/Brazil <sup>a</sup>	50 male exposed farmworkers/50 unexposed male controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational history) Blood BChE <sup>b</sup>	Not applicable	Inflammatory response (IL-6, TNF- $\alpha$ ), cholinergic (AChE, 8), and anti-inflammatory (IL-10) interleukins	The exposed group had higher IL-8 and IL-10 concentrations than the control group.
67. Huter et al. <sup>139</sup>	2021/Ecuador	34 male farmworkers engaged in conventional farming/37 male unexposed controls engaged in ecological farming from 5 different communities	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Self-reported conditions: headache, vision problems, dizziness, nausea, vomiting, excess salivation, strong fatigue, exhaustion, stomach pain, diarrhea, sleeplessness, burning eyes, skin irritation, runny nose, breathing difficulties, irregular heartbeat, watering eyes, skin rash, cough, twitches/trembling	Compared with controls working in ecological farms, participants exposed to pesticides in conventional farms had increased odds of dizziness (OR = 4.8; 95% CI: 1.6, 14.9), nausea/vomiting (OR = 7.5; 95% CI: 1.8, 31.8), strong fatigue (OR = 5.0; 95% CI: 1.7, 14.9), diarrhea (OR = 6.4; 95% CI: 1.1, 39.0), sleeplessness (OR = 3.4; 95% CI: 1.2, 9.9), burning eyes (OR = 4.1; 95% CI: 1.4, 12.3), skin irritation (OR = 3.6; 95% CI: 1.1, 11.7), and irregular heartbeat (OR = 5.8; 95% CI: 1.1, 30.7).
68. Filippi et al. <sup>103</sup>	2021/Argentina <sup>a</sup>	47 pesticide applicators/53 unexposed controls	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history) Blood HCB, HCH, endosulfan, DDE, DDT, AChE, BChE <sup>b</sup>	Not applicable	Perceived health symptoms (general, dermatological, neurological, ocular, cardiovascular, respiratory, urinary)	Higher prevalence of perceived general ( $p = 0.02$ ), dermatological ( $p < 0.01$ ), neurological ( $p = 0.04$ ), and cardiovascular ( $p = 0.03$ ) health symptoms among pesticide applicators compared with controls.
69. de Araújo et al. <sup>271</sup>	2021/Brazil	122 farmworkers and their family members	Cross-sectional	Multiple pesticide classes	Questionnaire (occupational exposure history)	Not applicable	Height, weight, waist circumference Overweight (BMI $\geq 25$ kg/m <sup>2</sup> ) Abdominal obesity (waist circumference $\geq 88$ cm in women and $\geq 102$ cm in men)	Long-term use of insecticides in general ( $>20$ y) (PR = 1.5; 95% CI: 1.0, 2.1), particularly OP pesticides (PR = 1.5; 95% CI: 1.0, 2.1), was associated with a higher prevalence of overweight but not of abdominal obesity.
70. Aylun et al. <sup>189</sup>	2021/Guadeloupe <sup>a,c</sup>	285 mother-child (7 years of age) pairs	Prospective cohort	OCs	Cord and child blood chlordane, cord blood DDE	Median (P25-P75) ( $\mu$ g/L): Cord blood chlordane: boys = 0.25 (0.08-0.41), girls = 0.21 (0.07-0.37); child chlordane: boys = 0.06 ( $<$ LOD-0.11), girls = 0.05 ( $<$ LOD-0.11); cord blood DDE: boys = 0.22 (0.09-0.64), girls = 0.31 (0.10-0.74)	Serum IGF-1, adiponectin, leptin	Null associations of cord blood chlordane with IGF-1, adiponectin, and leptin. No report on associations of child chlordane and cord blood DDE with these hormones.

Note: 2,4-D; 2,4-dichlorophenoxy acetic acid; 3-PBA, 3-phenoxybenzoic acid; 4F3BPA, 4-fluoro-3-phenoxybenzoic acid; 5-OH-TBZ, 5-hydroxythiabendazole; AChE, acetylcholinesterase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BAEP, brainstem auditory evoked potentials; BMI, body mass index; BChE, butyrylcholinesterase; BP, blood pressure; CB, carbamate; CFCA, chloro-3,3,3-trifluoro-1-propen-1-yl-2,2-dimethylcyclopropanecarboxylic acid; CI, confidence interval; CKD, chronic kidney disease; CNS, central nervous system; DAP, dialkyl phosphates; DBP, diastolic blood pressure; DCCA, 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid; DDE, dichlorodiphenylchloroethane; DDT, dichlorodiphenyltrichloroethane; DPOAE, Distortion Product Otoacoustic Emissions; DPT, Duration Pattern test; eGFR, estimated glomerular filtration rate; ETU, ethylenethiourea; FEF<sub>25-75%</sub>, forced expiratory flow between 25% and 75%; FEV<sub>1</sub>, forced expiratory volume in the first second; FRAP, ferric-reducing ability of plasma; FVC, forced vital capacity; GGT, gamma glutamyl transpeptidase; GIN, Gaps-in-Noise test; GST, glutathione S-transferases; GSTT1, glutathione S-transferases theta 1; Hb, hemoglobin; HCB, hexa-chlorobenzene; HDL, high-density lipoprotein; HL, hearing loss; HR, hazard ratio; HZ, Hertz; ICAM-1, Interleukin Adhesion Molecule 1; Ig, immunoglobulin; IGF-1, insulin growth factor-1; IL, interleukin; IQB, interquartile range; IQR, interquartile range; ISAAC, International Study of Asthma and Allergies in Childhood; LDL, low-density lipoproteins; LFA-1, Lymphocyte Function-Associated Antigen 1; LOD, limit of detection; LRTI, lower respiratory tract infection; max, maximum; MCH, mean corpuscular hemoglobin concentration; MCPA, 4-chloro-2-methylphenoxy acetic acid; MCY, mean corpuscular volume; mHA, meth-ylthiopyr; min, minimum; MSQ, Mini Sleep Questionnaire; NAG, N-acetyl- $\beta$ -D glucosaminidase; NQMS, Nordic Questionnaire for Musculoskeletal Symptoms; OC, organochlorine; OP, organophosphate; OR, odds ratio; OH-PYR, hydroxypyrimethamid; PD, Parkinson's disease; PON1, paraoxonase 1; PPE, personal protective equipment; PR, prevalence ratio; RDW, red cell distribution width; RBC, red blood cells; Ref, reference group; SBP, systolic blood pressure; SD, standard deviation; SF, short format; SMP, standardized mortality ratio; SPG, smoking + pesticide group; SRPI, speech recognition percentage index; SRT, speech reception threshold; TCPy, 3,5,6-trichloro-2-pyridinol; TEOAE, transient evoked otoacoustic emissions; TNF- $\alpha$ , tumor necrosis factor-alpha; TRZ, atrazine; VENG, vector electrocardiography; VLDL, very low-density lipoproteins; WBC, white blood cells.

<sup>a</sup>Also included in Table 2 (genotoxicity).

<sup>b</sup>Investigators did not use exposure biomarker concentrations in multivariate analyses.

<sup>c</sup>Also included in Table 7 (reproductive outcomes).

<sup>d</sup>Also included in Table 4 (placental outcomes and teratogenicity).

<sup>e</sup>Also included in Table 8 (birth outcomes and child growth).

<sup>f</sup>Also included in Table 3 (neurobehavioral outcomes).

<sup>g</sup>Also included in Table 6 (thyroid function).

microalbuminuria at the beginning of the pesticide application period compared with the leaf harvest period, suggesting that children environmentally exposed to xenobiotics in rural areas may suffer from early kidney dysfunction.<sup>52</sup>

**Respiratory and allergic outcomes.** Seven publications from three cross-sectional studies, two prospective cohort studies, and one case–control study reported on the associations of pesticide exposure with respiratory and allergic outcomes (Table 9). Publications from all three cross-sectional studies focused on occupational exposure to pesticides,<sup>232–234</sup> but only one examined exposure–outcome associations using direct methods of pesticide exposure assessment.<sup>234</sup> One of the publications reported increased odds of wheeze and shortness of breath among Costa Rican female farmworkers exposed to chlorpyrifos and terbufos compared with the control group (organic farmworkers/unexposed women) but found no differences in lung function between groups.<sup>232</sup> In contrast, a cross-sectional study of farmworkers and their relatives living in rural areas in Brazil observed associations between years of working with pesticides and pesticide handling frequency with decreased pulmonary function.<sup>233</sup> A publication from a study of Colombian farmworkers reported that those exposed to mixtures of pesticides containing paraquat—assessed via urinary biomarkers—and profenofos or glyphosate—assessed via questionnaire—had an increased prevalence of allergic rhinitis.<sup>234</sup> This publication also reported that farmworkers chronically exposed to paraquat had an increased prevalence of self-reported asthma.

Four studies examined the potential effects of pesticide exposure on respiratory and allergic outcomes among mothers and their children. For instance, a publication from a prospective cohort study in Costa Rica reported that self-reported current pesticide use near the home (yes/no) and higher urinary concentrations of 5-hydroxytiabendazole (5-OH-TBZ)—a metabolite of the fungicide thiabendazole—were associated with increased odds of asthma among mothers, whereas previous work in agriculture was associated with decreased odds of rhinitis but increased odds of eczema.<sup>235</sup> A publication from this same cohort study in Costa Rica reported an association between high urinary ETU concentrations during the first half of pregnancy and increased odds of lower respiratory tract infections (LRTIs) in the first year of life.<sup>236</sup> This publication also reported that high ETU concentrations during the second half of pregnancy were associated with decreased odds of wheezing in the first year of life. Notably, a publication from a prospective cohort study in Mexico reported null associations of prenatal DDT or DDE exposure with LRTIs months among boys assessed up to 30 months of age.<sup>237</sup> At last, a publication from a case–control study of school-age children in Brazil reported that factors such as living close to agricultural activity, and aerial pesticide spraying near the home were associated with increased odds of uncontrolled asthma at 6–7 and 13–14 years of age.<sup>235</sup>

**Liver injury.** Eight publications reported on the association of pesticide exposure with markers of liver injury (Table 9). Six of the eight publications were from studies that ascertained pesticide exposure only via questionnaire,<sup>81,88,206,238–240</sup> whereas two studies measured blood ChE<sup>241</sup> or blood  $\beta$ -glucuronidase activity.<sup>242</sup> A publication from a cross-sectional study in Mexico reported that a higher activity of  $\beta$ -glucuronidase—a sensitive biomarker of OP pesticide exposure<sup>243,244</sup>—was associated with increased aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyl transpeptidase (GGT) levels.<sup>242</sup> Notably, a publication from a cross-sectional study conducted in Brazil reported null associations of AChE and BChE activities with markers of liver injury, but it also reported that farmworkers had lower AST and ALT levels than controls.<sup>241</sup> In contrast, a

publication from a second study in Brazil reported higher AST levels in farmworkers than in controls during the high pesticide exposure period, but it also reported lower ALT levels in farmworkers during both the high and low pesticide exposure periods.<sup>239</sup> A publication from a prospective cohort study of rural pregnant women environmentally exposed to OP pesticides in Argentina reported higher AST, but not ALT, levels during the spraying period compared with the prespraying period.<sup>206</sup> Likewise, a publication from a cross-sectional study conducted in Brazil reported higher AST and ALT levels in Brazilian female, but not male, farmworkers occupationally exposed to multiple classes of pesticides than in controls.<sup>238</sup> A published cross-sectional study conducted in Ecuador also found that women living in one agricultural community, but not women living in another agricultural area, had a greater percentage of ALT and AST levels exceeding normal levels compared with controls.<sup>81</sup> A publication from a separate cross-sectional study in Brazil reported lower alkaline phosphatase levels in farmworkers who had worked with pesticides than in those who had not.<sup>88</sup> Last, a publication from a cross-sectional study of individuals living close to an uncontrolled contaminated site containing the residues and leftovers of a deactivated OC pesticide factory in Brazil reported null associations of pesticide exposure with markers of liver injury.<sup>240</sup>

**Hematological parameters and lipid profiles.** Fourteen publications reported on the associations of pesticide exposure with hematological parameters (Table 9). Twelve of the 14 publications relied on questionnaires to assess environmental or occupational pesticide exposure<sup>52,54,73,81,94,96,98,238,245–248</sup>; only 2 ascertained exposure via direct exposure assessment and used these measurements in their exposure–outcome analyses.<sup>242,249</sup> Four publications reported null associations with hematological parameters.<sup>54,94,98,238</sup> Conversely, 2 publications from cross-sectional studies conducted in Mexico<sup>96</sup> and Ecuador<sup>81</sup> reported higher hemoglobin and hematocrit levels in those occupationally or environmentally exposed to pesticides than in those unexposed. In addition, a publication from a different cross-sectional study in Mexico (mentioned above) found that higher  $\beta$ -glucuronidase activity was associated with higher hemoglobin and hematocrit levels.<sup>242</sup> A case–control study conducted in Brazil, Argentina, and Mexico found increased odds of aplastic anemia among adults exposed to pesticides.<sup>245</sup>

A publication from a cross-sectional study in Brazil reported decreased neutrophils and monocytes among tobacco farmworkers exposed to multiple pesticide classes, but not among controls.<sup>73</sup> Notably, a publication from a prospective cohort study of school-age children from a tobacco-producing region in Brazil (mentioned above) also reported lower numbers of neutrophils, monocytes, and basophils, but higher hemoglobin levels and lymphocytes, at the beginning of the pesticide application period compared with the leaf harvest period.<sup>52</sup> Similarly, a publication from a cross-sectional study of Brazilian farmworkers and their families reported that detectable serum concentrations of various OC pesticides [i.e., hexachlorocyclohexane (HCH), aldrin, heptachlor, *trans*-nonachlor, endosulfan, endrin, DDT, DDE, and methoxychlor] were associated with lower numbers of white blood cells, particularly monocytes and eosinophils.<sup>249</sup> This publication also reported that detectable serum concentrations of  $\gamma$ -chlordane were associated with lower hemoglobin levels. Last, cross-sectional studies conducted in Brazil<sup>246,247</sup> and Colombia<sup>248</sup> reported associations between farm work, length of pesticide exposure (i.e., >10 y), and exposure during the harvest period with alterations in various hematological parameters, including hemoglobin levels and number of leukocytes, platelets, and monocytes.



Eight publications reported on associations between pesticide exposure and lipid profiles in LAC populations (Table 9); three of them reported null associations.<sup>94,96,98</sup> Two publications from cross-sectional studies conducted in Ecuador<sup>81</sup> and Mexico<sup>250</sup> reported lower cholesterol or low-density lipoprotein levels among individuals with high pesticide exposure compared with those with moderate or no exposure. The study in Mexico also found associations of higher blood BChE activity with higher cholesterol, triglyceride, very low-density lipoprotein, or total lipid levels, but these associations varied by BMI.<sup>250</sup> A publication from another cross-sectional study in Mexico (mentioned above) found that higher  $\beta$ -glucuronidase activity was associated with higher cholesterol, triglyceride, and total lipid levels, but also with lower high-density lipoprotein levels.<sup>242</sup> A publication from a cross-sectional study of coffee harvesters in Colombia exposed to OP pesticides reported that higher blood BChE activity was associated with hypercholesterolemia (defined as total cholesterol  $\geq 200$  mg/dL).<sup>251</sup> Conversely, a cross-sectional study in Brazil reported higher total cholesterol levels among farmworkers who had not worked with pesticides.<sup>88</sup>

**Acoustic damage.** Eight publications from cross-sectional studies conducted in Brazil evaluated the association of exposure to either the OP pesticide malathion or several pesticide classes—assessed via questionnaire—with hearing problems (Table 9). Seven of the eight publications reported that elevated pesticide exposure was associated with acoustic damage, as indicated by poorer performance in tests such as the Distortion Product Otoacoustic Emissions (DPOAE) test, the Transient Stimulus Otoacoustic Emissions (TSOAE) test, the Duration Pattern test (DPT), and the Gaps-in-Noise test (GIN).<sup>252–258</sup> In contrast, a publication from a small cross-sectional study of rural workers in Brazil reported null associations between AChE activity and hearing loss.<sup>259</sup>

**Other outcomes.** Single publications reported on the associations of pesticide exposure with various health outcomes (Table 9). Overall, these publications—which were primarily from cross-sectional studies that ascertained exposure solely through questionnaires—reported associations of exposure to several classes of pesticides with a variety of outcomes, including changes in blood pressure,<sup>251,260–262</sup> diarrhea,<sup>263</sup> rheumatoid arthritis,<sup>264</sup> high blood glucose levels,<sup>242</sup> and glutathione *S*-transferase activity,<sup>265</sup> sleep disorders,<sup>266</sup> skin problems,<sup>62,84,103,267,268</sup> thoracic spine and neck pain,<sup>269,270</sup> changes in interleukin expression,<sup>102</sup> overweight/obesity,<sup>271</sup> green tobacco sickness,<sup>272</sup> and death<sup>273–275</sup>; however, results should be interpreted with caution given the limited weight of evidence. In addition, some publications reported that pesticide exposure was associated with poorer general health status or symptoms of APP (e.g., fatigue/tiredness, nervousness, headache, anxiety, and depression).<sup>57,62,84,103,138,159,223,267,268,276,277</sup>

Overall, publications from studies conducted to date provide somewhat consistent evidence of the associations between pesticide exposure with acoustic damage and changes in markers of liver injury (e.g., when comparing exposed with unexposed or when comparing exposed during the spraying and prespraying season). Conversely, published studies that have examined the associations of pesticide exposure with kidney function, respiratory/allergic outcomes, and hematological parameters and lipid profiles in LAC populations have reported mixed findings. All these reported associations need to be interpreted with caution given that most published studies were relatively small, cross-sectional in design, and assessed exposure to multiple classes of pesticides via questionnaire.

## Discussion

The results of our scoping review provide some evidence that exposure to pesticides may adversely impact the health of LAC populations. For instance, we observed that occupational and

residential exposure to OP pesticides or several pesticide classes was consistently associated with higher levels of increased chromosomal aberration frequency, nuclear buds, oxidative stress, or cell death. We also observed relatively consistent evidence of the adverse neurobehavioral effects of elevated OP pesticide and carbamate exposure levels, particularly among children and farmworkers. The latter finding is in line with those of previous systematic reviews on the neurobehavioral effects of OP pesticide exposure.<sup>23,36,37,40,278,279</sup> Published studies on teratogenicity and placental outcomes, cancer, thyroid function, reproductive outcomes, and birth outcomes and child growth were largely heterogeneous in terms of pesticide exposure and outcome assessment methods and their results were mixed. Findings on other health outcomes, including respiratory and allergic effects, were too sparse to discern the directionality of an effect, if any.

To our knowledge, only one literature review besides ours has focused on the health effects of pesticide exposure in different populations from a specific region of the world.<sup>280</sup> This systematic literature review of all research on environmental and human health issues associated with pesticide exposure in sub-Saharan Africa published between 2006 and 2021 reported some findings consistent with ours.<sup>280</sup> For example, the review of sub-Saharan Africa literature found that OC and OP pesticides were the pesticides classes most frequently studied in the region. In our scoping review, we found that OC and OP pesticides such as DDT, endosulfan, and chlordane—pesticides that have been banned by countries in the European Union and the United States<sup>281–283</sup>—were among the pesticides classes most frequently examined in the LAC region. Both reviews identified that published studies were primarily cross-sectional in design and relied largely on indirect pesticide exposure assessment methods (e.g., questionnaire, job status ascertainment). Notably, the most frequently examined health effects in sub-Saharan Africa studies were signs and symptoms of APP (self-reported and doctor-diagnosed), whereas genotoxicity and neurobehavioral outcomes were the most frequently assessed among LAC populations.

As more research on the health effects of pesticide exposure is conducted in LAC countries, we believe that it is critical to address three fundamental limitations to the current body of literature. First, there must be a more widespread investment in research capacities across the LAC region. In our scoping review, we identified studies from 16 of the 43 LAC countries and territories, and 2 countries—Brazil and Mexico—accounted for nearly 60% of the included studies. Central American countries (except for Costa Rica) and Caribbean territories were among those with the lowest research outputs, and evidence suggests that efforts to increase research capacities often focus on the countries with some existing capacity,<sup>284</sup> perpetuating health inequities in countries with the lowest levels of research and support. Second, future research must address limitations in study design and data collection to increase the rigor and robustness of epidemiological findings. Given the limited funding to develop infrastructure and conduct research in most LAC countries,<sup>285</sup> most studies included in this review were small cross-sectional studies—which are important in terms of hypothesis generation but have limited causal inference. In addition, nearly half of the studies included in this review relied on indirect exposure assessment methods (e.g., questionnaires or exposure classification based on self-report, job title, or area of residence), which may result in exposure misclassification that could bias epidemiological findings toward the null<sup>286–288</sup> and potentially account for conflicting study findings.<sup>289</sup> Self-reported pesticide exposure may be particularly prone to recall bias<sup>288,289</sup> and may be worsened under certain conditions, including studies of participants with low educational attainment or high residential mobility.<sup>290</sup> Furthermore, pesticide use in LAC countries varies by crop and season—which causes

significant exposure variation, both in terms of intensity and chemical composition<sup>291</sup>—and farmworkers or pesticide applicators are often not informed of the specific pesticide active ingredients used in their farms.<sup>233,277,292</sup> In our scoping review, most of the studies that assessed pesticide exposure via biomonitoring relied on analysis of a single sample and may have not accurately captured chronic exposure to pesticides with short biological half-lives and high inter- and intra-individual variability,<sup>293,294</sup> which are frequently used in LAC countries. This potential exposure misclassification due to single time point sampling may have biased study findings toward or away from the null, depending on the time in which the exposure was captured. Last, studies included in our review employed a wide range of health outcome assessment methods, which were often not validated nor considered gold standards, hindering comparisons of study findings across populations within and outside of the LAC region. Third, studies should employ more robust statistical analyses and more systematic reporting of methods and results to facilitate comparisons across study populations. We found that many studies lacked clear presentation of key information, such as the covariates used in multivariable analyses or the specific pesticide(s) being examined (e.g., some publications solely indicated they collected samples to be analyzed for AChE activity, and we inferred they were examining OPs and carbamates). In addition, multiple studies did not report effect estimates and simply reported the prevalence of the outcome among exposed and unexposed groups. Strengthening research capacity in the LAC region is needed to increase the rigor of epidemiological studies and generate robust evidence regarding associations between pesticide exposure and its health effects.

In addition to addressing the limitations raised above, several knowledge gaps remain regarding the health effects of pesticides in LAC populations. As an example, a limited number of studies included in our review have assessed exposure to current-use pesticides that are applied widely in the LAC region and the rest of the world, such as pyrethroids, glyphosate, neonicotinoids, and fungicides.<sup>20,295–297</sup> Similarly, few studies have examined the health effects of early-life exposure to pesticides—a critical period of brain<sup>298,299</sup> and lung<sup>300,301</sup> development—or the effects of pesticides on common chronic diseases, such as cardiometabolic disorders and neurodegenerative diseases.<sup>302,303</sup> Although farmworkers and those living in agricultural areas are simultaneously exposed to numerous pesticides,<sup>304</sup> only three studies have examined the health effects of exposure to pesticide mixtures using statistical methods that accounted for copollutant confounding.<sup>82,106,234</sup> More studies are needed to understand the true independent and aggregate effect of exposure to mixtures of pesticides,<sup>305,306</sup> which may require more widespread training of researchers in environmental mixtures methods. Finally, it is increasingly understood that the health effects of environmental chemicals may be due in part to interactions with nonchemical exposures, such as poverty, neighborhood violence, and malnutrition.<sup>307–310</sup> Socioeconomically disadvantaged populations in LAC countries, such as immigrants or indigenous people, have less access to legal protections and are frequent victims of unregulated work arrangements, leading to disproportionately high levels of pesticide exposure<sup>292</sup> and potentially more adverse health outcomes. Nevertheless, few of the studies included in our scoping review examined the joint effects of pesticides and unique psychosocial stressors experienced by populations in the region.

### Recommendations for Future Research

In LAC countries and territories, generating robust evidence on the health effects of pesticide exposure is essential to inform agricultural policies and public health surveillance programs aimed at post-registration control of pesticides and the development and implementation of pesticide safety guidelines. Given the resource

limitations and sociocultural context of agricultural populations across the LAC region, potential areas of prioritization for future work include the following:

- *Increasing funding for research and capacity building.* The Pan American Health Organization (PAHO), a regional office of the World Health Organization (WHO) for the Americas, has called for strengthening research in each member country to promote health equity and socioeconomic development.<sup>311</sup> Given the widespread use of pesticides across the LAC region, it is imperative to strengthen institutional capacities to produce research and generate robust evidence that could be used to inform national and regional health policies. For example, difficulties associated with pesticide biomonitoring may be amplified in studies conducted in LAC countries owing to limited laboratory capacity and availability of analytical techniques to measure biomarkers of exposure. In addition, insufficient funding and infrastructure limit the ability to carry out large-scale epidemiological studies, which may contribute to the widespread reliance on small cross-sectional studies.

To improve the quality and quantity of health research in the LAC region, capacity building must become a key component of global research funding, with a focus on countries where the infrastructure and capacity do not currently exist.<sup>285</sup> Although some models have proposed increased “North–South” collaborations, these projects often align with the priorities of the funders, rather than the countries’ needs, and few projects have resulted in sustainable long-term partnerships that are equitable to the investigators in the home countries where the research was conducted.<sup>312</sup> We recommend that any collaborations with institutions outside of the LAC region explicitly include local researchers in the design and implementation of the study,<sup>313</sup> focus on capacity development in the country, and critically examine power dynamics to ensure more equitable partnerships where the research is tailored to the needs of the local populations.<sup>314</sup>

- *Increasing collaboration within the LAC region.* Beyond collaborations outside of the LAC region, we recommend increasing research synergies and the development of more interdisciplinary research teams across LAC countries. For example, the creation of networks of researchers within the region could contribute to the homogenization of exposure and health outcomes assessments (e.g., specific test or scale employed, age of assessment) and the systematization of reporting methods and results in publications, improving the ability to compare and synthesize results across studies. Previous literature discussing the need for increased research synergies in the LAC region have specifically focused on supporting early career researchers through initiatives such as in the development of national and regional graduate programs that strengthen regional collaborations, enable sustainable research careers, and decrease the high mobility of doctoral students and early career researchers outside of the region.<sup>315</sup>

Although farming systems and ecological conditions vary across the LAC region,<sup>316</sup> increased homogenization of research within the region could potentially contribute to the homogenization of regulatory decisions, such as banning particular hazardous pesticides that are subject of international conventions and agreements, improving management and control of pesticides, restricting dispersive pesticide applications methods (e.g., light aircrafts, spray-booms), implementing pesticide-free buffer zones, and promoting sustainable agriculture and alternatives to pesticide use, which could result in more protective policies at both the national and regional levels.

- **Increasing rigor of epidemiological studies.** Studies that can incorporate biomonitoring should consider the use of biomarkers that reflect exposure to specific pesticides, including current-use pesticides (e.g., glyphosate, neonicotinoids, pyrethroids), and should assess exposure at multiple time points, if possible. In studies where biomonitoring is cost prohibitive or logistically infeasible, indirect exposure assessment may be improved by incorporating additional methods that are less prone to bias, including purchasing/inventory records, personal exposure monitoring (e.g., breathing zone air sampling, dermal wipes), environmental sampling data (e.g., ambient air monitoring, drinking water),<sup>9,11,12</sup> and development of surrogate exposure estimates based on nearby pesticide use assessed via Geographic Information Systems.<sup>33</sup> In addition, rather than dichotomously classifying participants as farmworkers vs. non-farmworkers, studies could employ more detailed occupational assessments and job-exposure matrices examining factors such as job titles and tasks, specific crops and active ingredients, and more complete occupational history that may decrease error due to exposure misclassification.<sup>288</sup> Studies should also use standardized and validated outcome assessment methods across population subgroups from different LAC countries and territories to improve researchers' ability to compare findings across studies inside and outside the region.

In addition to increasing the rigor when designing epidemiological studies, we recommend the inclusion of more robust statistical analyses and a shift away from the presentation of bivariate results alone. We also recommend the systematization of the presentation of key information in the methods and results of publications, including the specific pesticides being assessed, statistical methods used, and study results to facilitate comparisons across studies and better support causal inference.

### Strengths and Limitations of This Scoping Review

Given the methodological differences in study design, populations studied, and exposure and health outcome assessments employed across the studies included in this review, we were not able to summarize the evidence on health effects of pesticide exposure in LAC populations using a quantitative synthesis or meta-analysis. In addition, our search strategy was focused on the use of the word "pesticides" plus Latin America or "pesticides" plus each of the names of the 43 LAC countries and territories. This strategy may have led to missed information because some studies could have used more specific keywords such as the pesticide's nature (e.g., herbicides, fungicides, insecticides) or the names of pesticide active ingredients (e.g., mancozeb, chlordecone). Our literature search also focused solely on PubMed and SciELO, and it is possible that other common databases in the LAC region, such as Latindex and Latin American and Caribbean Health Sciences Literature (LILACS), could have yielded additional publications. Despite its limitations, we believe that this scoping review provides a useful overview of the status of the research regarding the health effects of pesticide exposure and gives insight into existing data gaps and research capacity building needs in the region.

### Conclusions

Our scoping review provides some evidence that exposure to pesticides may adversely impact the health of LAC populations. Nevertheless, methodological limitations such as reliance on cross-sectional study designs and indirect exposure assessment methods, as well as heterogeneity in the assessment of health

outcomes and presentation of study findings, undermine the strength of the conclusions. We recommend increasing capacity building, integrating research initiatives, and conducting more rigorous epidemiological studies that can address these limitations, better inform public health surveillance systems, and increase the impact of research on public policies.

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