

Environmental and Health Impacts of Pesticides and Fertilizers and Ways of Minimizing Them

Envisioning A Chemical-Safe World

Chapter 4 of 12

# Environmental and health effects of pesticide use



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## About

In December 2017, Resolution 4 of the 3rd Session of the United Nations Environment Assembly (UNEA 3) requested “the Executive Director to present a report on the environmental and health impacts of pesticides and fertilizers and ways of minimizing them, given the lack of data in that regard, in collaboration with the World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO) and other relevant organizations by the fifth session of the United Nations Environment Assembly”. In response to this request, UNEP published a *Synthesis Report on the Environmental and Health Impacts of Pesticides and Fertilizers and Ways to Minimize Them*<sup>1</sup> in February 2022 (United Nations Environment Programme [UNEP] 2022).

The overall goal of the synthesis report is to provide the information base to enable other advocacy actions to be taken by stakeholders to minimize the adverse impacts of pesticides and fertilizers. Specific objectives of the synthesis report are to:

- ❖ Update understanding of current pesticide and fertilizer use practices;
- ❖ Present major environmental and health effects of pesticides and fertilizers, during their life cycle, and identify key knowledge gaps;
- ❖ Review current management practices, legislation and policies aimed at reducing risks in the context of the global chemicals, environmental and health agenda;
- ❖ Identify opportunities to minimize environmental and health impacts, including proven and innovative approaches.

This chapter on “Environmental and health effects of pesticide use” is the 4th in a series of 12 chapters that make up a comprehensive compilation of scientific information. The chapters were developed to both inform and further elaborate on the information provided in the synthesis report. Please note that the disclaimers and copyright from the synthesis report apply

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1 The Synthesis report is available at <https://www.unep.org/resources/report/environmental-and-health-impacts-pesticides-and-fertilizers-and-ways-minimizing>.





# Environmental and health effects of pesticide use

*Key findings for Chapters 4.3 (environmental effects) and 4.4 (health effects) are found at the beginning of each of those sections.*

*The annexes referred to in this chapter are provided as supporting information on the web page of the main report.<sup>1</sup>*

## 4.1 Overview

Pesticides are by definition biologically active compounds. They are among the few types of chemicals that are purposely administered in the environment rather than being a by-product of other processes. Their use can pose a risk to humans and other non-target organisms.

This report is not intended to provide a comprehensive review of all the environmental and health risks posed by different groups pesticides. The use of pesticides will virtually always pose certain risks. The likelihood and importance of these risks may depend on, for example, the dose, the use situation, the exposed organisms or ecosystems, and the timing of exposure. Nevertheless, pesticides are widely used because their risks have been judged to be acceptable, although often on the condition that specific risk mitigation measures are applied.

In this chapter the environmental and health effects of pesticides are reviewed. The focus of the chapter is on pesticides' observed effects following their actual use. Pesticide toxicity, or potential environmental and health risks, are not extensively covered. These topics are reviewed in detail elsewhere (Krieger 2010; Brock *et al.* 2010; National Research Council 2013; Roberts and Reigart 2013).

Furthermore, extensive regulatory hazard and risk assessments of individual pesticides have been published by international entities such as the Joint Meeting on Pesticide Residues (JMPR) (FAO 2020) and the International Agency for Research on Cancer (IARC) (2020a), as well as by major national or regional regulatory authorities such as the European Food Safety Authority (EFSA) (2020a), the United States Environmental Protection Agency (US EPA) (2020a) and the Australian Pesticides and Veterinary Medicines Authority (APVMA) (2000), among others.

<sup>2</sup> <https://www.unep.org/resources/report/environmental-and-health-impacts-pesticides-and-fertilizers-and-ways-minimizing>

Chapter 4.2 briefly introduces the hazard and risk assessment of pesticides. Chapter 4.3 discusses the adverse environmental effects of pesticide use. Chapter 4.4 reviews its adverse health effects. Major knowledge gaps with regard to the environmental and health effects of pesticide use are presented at the end of these chapters.

## 4.2 Pesticide hazards and risks

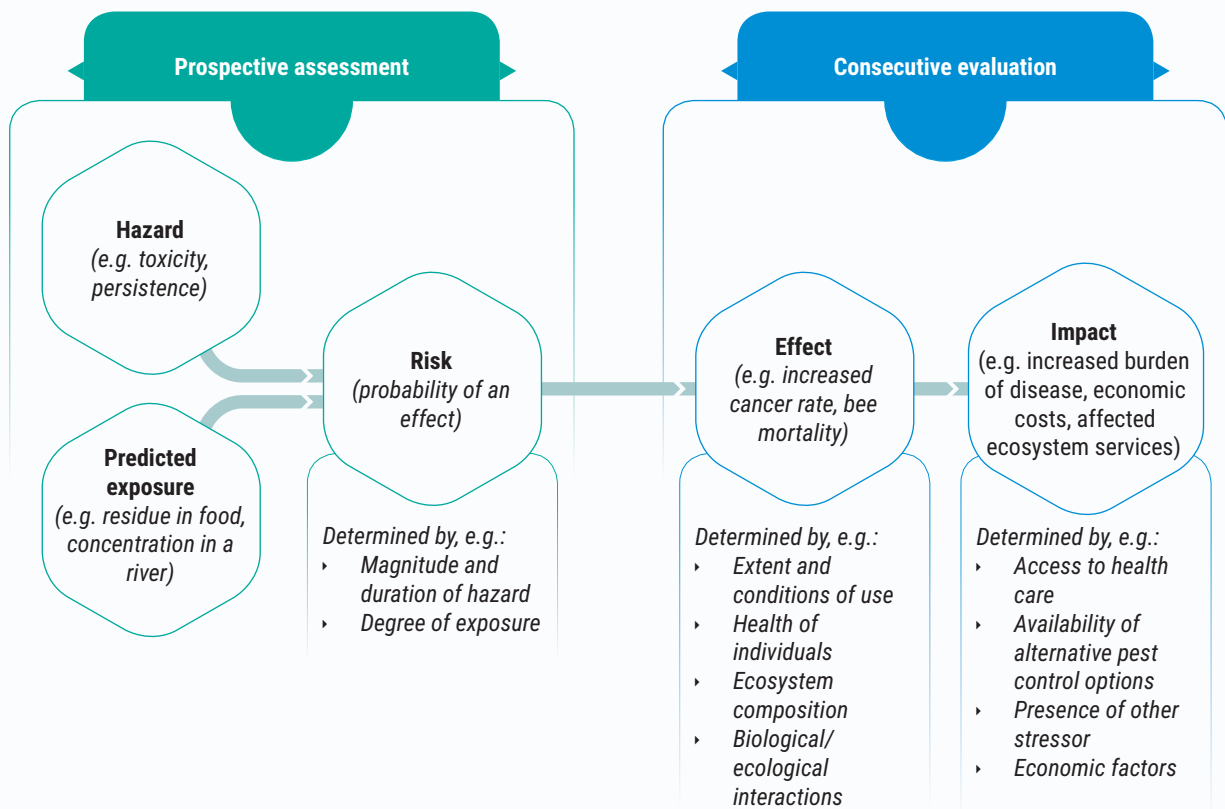
In many countries and regions, the risks of a pesticide to the environment and health are evaluated before it is authorized for use. This is done during the pesticide registration process. Only if a pesticide is judged not to pose unacceptable risks to the environment, or to human or animal health, under the conditions prevailing in a country/region will it be authorized.

In a risk assessment the hazard of a pesticide (e.g., its toxicity, persistence or bioaccumulative

potential) is assessed against a predicted exposure that may occur if the product is used (e.g., determined by the application rate, chemical properties, use of personal protective equipment, environmental conditions) (Box 4.2-1).

In some countries, risks are also weighed against a product's expected benefits. The principle of risk assessment is the same for environmental and human health risks, but the methods used are different. These are prospective assessments,

**Figure 4.2-1** Pesticide risk assessments are often prospective, in the sense that they are carried out before a pesticide is put on the market. Monitoring or studies of (adverse) effects of pesticide use are consecutive evaluations made after a pesticide is in use. As sufficient data are available, information about pesticide effects contributes to an evaluation of their impact on human health, the environment or society.



in the sense that they are carried out before a pesticide is authorized or re-authorized for use (Figure 4.2-1).

Only after a pesticide is marketed can the actual effects of the product be assessed under local conditions of use. This assessment may take place through regular monitoring, specific scientific studies, or feedback about incidents. As sufficient reliable information becomes available about the postulated (adverse) effects of the pesticide, its impact is evaluated (e.g., farmers' revenues, or gains/costs for society) (Box 4.2-1). These are referred to as consecutive evaluations (Figure 4.2-1).

For a new active ingredient or new pesticide formulation, prospective assessments provide the main information on risks because the pesticide has not yet been used. In the last few decades pesticide risk assessment methods for the environment and human and animal health have required more data. These methods have also become more precise, more locally specific, and often more complex. In addition, for compounds belonging to already assessed classes, the accumulated evidence related to the class serves as prior knowledge. A large number of environmental and health aspects are evaluated during the pesticide registration process (Box 4.2-2). Although there are limitations

to the risk assessment process, pesticides are without doubt among the chemicals that are most thoroughly evaluated before being placed on the market.

Nevertheless, despite increasingly comprehensive prospective risk assessments, either unexpected or greater than expected environmental or health effects may be observed following the introduction of a pesticide (Boyd 2018; Storck, Karpouzas and Martin-Laurent 2017; Vijver *et al.* 2017). This is because not all the potential effects of pesticides are being evaluated in the commonly used risk assessments under current testing and assessment requirements, nor can all environmental conditions or situations of use be modelled in advance. Moreover, certain effects simply cannot be known at the time of the prospective assessment. The identification of effects that become known post-authorization of a pesticide is not necessarily limited to historical cases, but continues to occur up until the present (Table 4.2-1).

Post-registration monitoring and studies that complement prospective risk assessments are therefore important tools, especially given that data on environmental settings and human populations can only become available after the market authorization of a compound. Many pesticide registration authorities will

**Box 4.2-1 Common hazard and risk assessment terminology applied in this report.**

<b>Hazard</b>	Inherent property of a substance, agent or situation having the potential to cause undesirable consequences (e.g. properties that can cause adverse effects or damage to health, the environment or property). (Food and Agriculture Organization of the United Nations and World Health Organization [FAO and WHO] 2014).
<b>Risk</b>	Probability and severity of an adverse health or environmental effect occurring as a function of a hazard and the likelihood and the extent of exposure to a pesticide or fertilizer. (based on FAO and WHO 2014)
<b>Effect</b>	Change in the state or dynamics of an organism, system, or (sub)population caused by the exposure to an agent. (World Health Organization [WHO] 2004)
<b>Adverse effect</b>	Change in the morphology, physiology, growth, development, reproduction, or life span of an organism, system, or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other influences. (WHO 2004)
<b>Exposure</b>	Concentration or amount of a particular agent that reaches a target organism, system, or (sub)population in a specific frequency for a defined duration. (WHO 2004)
<b>Impact</b>	A durable change in the condition of people or their environment brought about by the (adverse) effect(s) of a pesticide or fertilizer. (based on Hearn & Buffardi 2016)

**Table 4.2-1 Some examples of environmental or health effects of pesticides which had not been identified during prospective risk assessments, but became known after their use was authorized.**

Pesticide	Effects identified post-registration	Period when the effects observed	Selected reference (also see Chapters 4.3 and 4.4)
DDT	Population declines in birds of prey due to eggshell thinning	1950s-early 1970s	Peakall (1993)
Highly acutely toxic pesticides	High rate of fatalities from self-poisoning	1960s-present	Karunaratne <i>et al.</i> (2019)
Various pesticides	Population declines of amphibians	2000s-present	European Food Safety Authority (EFSA) (2018a)
Organophosphate pesticides	Prenatal exposure resulting in high risk of cognitive/behavioural deficits and neurodevelopmental disorders in children	2000s-present	Hertz-Picciotto <i>et al.</i> (2018)
Neonicotinoids	Possible declines of wild bee populations	2000s-present	Hladik, Main and Goulson (2018)

amend or cancel registrations of a product if consecutive evaluations show that use of a pesticide under local conditions results in unacceptable risks. Pesticide registrations are often subject to a periodic review process for re-authorization, which presents an opportunity to review, and take action on, the outcomes of post-registration monitoring and studies.

In this chapter the (adverse) environmental and health impacts of pesticides are reviewed, as reported through observational studies, large-scale field experiments and monitoring. These are environmental and health effects observed following actual use of and exposure to such substances. However, a major limitation of an assessment of actual effects is that they depend

**Box 4.2-2 Many risk assessments are generally conducted, as part of the pesticide registration process, to assess whether a pesticide may pose unacceptable risks to human or animal health or the environment.**

Human health		Animal health and the environment	
Type of risk	Questions being assessed	Type of risk	Questions being assessed
<b>Dietary</b>	Will residues of the pesticide in agricultural commodities or drinking water pose unacceptable risks to consumers?	<b>Surface waters</b>	Will the use of the pesticide lead to concentrations in e.g. rivers, lakes, estuaries that pose unacceptable risks to fish, crustaceans, algae and other aquatic organisms?
<b>Occupational</b>	Does the handling and application of the pesticide pose unacceptable risks to the user?	<b>Soils</b>	Will the use of the pesticide lead to concentrations in soils that pose unacceptable risks to earthworms, springtails and other soil organisms, or adversely affect soil microbial processes such as nitrogen cycling?
<b>Residential</b>	Will the use of the pesticide pose unacceptable risks to persons living in or close to the treated areas?	<b>Beneficial arthropods</b>	Will the use of the pesticide lead to unacceptable effects on pollinators, natural enemies of pests or other beneficial arthropods?
<b>Bystander</b>	Will the use of the pesticide pose unacceptable risks to persons?	<b>Terrestrial vertebrates</b>	Will the use of the pesticide pose unacceptable risks to birds, mammals, reptiles or other terrestrial vertebrates?
		<b>Plants</b>	Will the use of the pesticide lead to unacceptable affect to non-target vascular plants?

very much on local capacity for monitoring, which is weak in most parts of the world. As a result, reported effects are almost always incomplete.

The assessment of actual effects is also limited by the difficulty of causal inference (i.e., linking the adverse effects to an individual or class of pesticides). Furthermore, many chronic ecosystem/population effects or health effects only materialize after many years of use of a substance. Reports of the effects of more recently introduced pesticides will therefore be limited.

Finally, the population studies that provide valuable information on the proposed associations between pesticide exposure and environmental or health effects exhibit variable precision and validity.

Quantitative information on the impact of (adverse) effect(s) of pesticides – for example, on the global burden of disease, biodiversity and ecosystem health, and economic costs and benefits – are reviewed in Chapter 6.

## 4.3 Adverse environmental effects of pesticide use

### 4.3.1 Overview

Pesticides are applied in the environment on purpose. They will therefore, almost by definition, pose risks to non-target organisms. Depending on pesticide use patterns, the toxicity of the pesticide, the conditions of exposure of non-target organisms, and the type of agro-ecosystem exposed, environmental risks will range from very high to virtually absent.

The focus of this chapter is on observed or likely environmental effects of pesticides under current conditions of use. The review in the chapter is therefore essentially a consecutive evaluation of pesticide impact after pesticide products have been authorized (or registered) for use, as outlined in Figure 4.2-1.

The chapter is based on recent existing global or regional reviews, whenever these were available. If no recent reviews were available for a given topic, large-scale national studies were identified which could contribute to an understanding of pesticides' environmental impact. Literature reviews were initially conducted for relevant scientific publications published in the period 2010-2020, although older studies were sometimes included if they were particularly relevant.

Different lines of evidence regarding the environmental effects of pesticides were subsequently evaluated in this report (Table 4.3.1-1):

**Table 4.3.1-1 Principal lines of evidence investigated for this report to identify the environmental effects of pesticide use.**

Type of evidence	Pesticides in the environment	Pesticide effects			Pesticide risks
Type of study	Monitoring of environmental concentrations	Monitoring and field studies of effects on sustainability	Monitoring of environmental effects	Field studies of environmental effects	Measured environmental concentrations
Type of outcomes	Magnitude of residues Geographical distribution Time trends	Presence/absence of effects Time trends	Presence/absence of effects Time trends	Presence/absence of effects Dose-response data	Risks under actual pesticide use conditions (consecutive assessment)

Pesticides end up in different compartments of the environment, both after their intended and authorized use and following misuse or accidents. Residues of pesticides and their metabolites are therefore found in air, surface waters, groundwater, soil and biota. Regular monitoring of pesticide residues in the environment is mainly limited to high income countries. There are substantial information gaps in large parts of Africa, Asia and Latin America. Ad hoc studies of pesticide residues in the environment, as well as their behaviour and fate, are conducted more widely, although data from low and lower-middle income countries remain scarce (Stehle and Schulz 2015). [Chapter 4.3.2].

Wherever they have been measured in surface waters, pesticides have been found to be ubiquitous. In many cases the measured concentrations have exceeded national surface water standards and posed risks to aquatic organisms (European Union 2013). In most cases where time trends were reported, pesticide concentrations did not show downward trends over time. This holds true for both legacy organochlorine pesticides (OCPs) and current use pesticides (CUPs) (Stone, Gilliom and Ryberg 2014; Nesser *et al.* 2016; Wolfram *et al.* 2018; Bruce-Vanderpuije *et al.* 2019). [Chapter 4.3.2]

Atmospheric pesticide concentrations are less well documented than concentrations in other environmental compartments. A decrease in atmospheric concentrations of many OCPs has been observed globally. Nevertheless, OCPs are still detected in air almost everywhere in the world, often decades after their use has been ended (Shunthirasingham *et al.* 2010; UNEP 2017a; Rauert *et al.* 2018). Data on CUPs are more limited, and trends in their atmospheric concentrations have not been systematically reviewed. [Chapter 4.3.2]

Pesticide residues appear to be omnipresent in agricultural soils, but are also detected in non-treated soils of organic production systems (Silva *et al.* 2019; Pelosi *et al.* (2021)). OCP residues have been found in soils across the world, with concentrations often not showing significant declines over time (Camenzuli, Scheringer and Hungerbühler 2016). Most reports of soil

concentrations of current use pesticides were from Europe and China, where the large majority of agricultural soils contained pesticide residues. Certain herbicides and fungicides, as well as neonicotinoid insecticides, were most often encountered (Annex 4.3-3). [Chapter 4.3.2]

Data on pesticide concentrations in groundwater and drinking water are generally scarce for many parts of the world and for many pesticides. Legacy and current use pesticides, and (especially) their transformation products, have frequently been detected at concentrations above their legal limits in groundwater and drinking water (Postigo and Barceló 2015; Pirsabe *et al.* 2017; Pietrzak *et al.* 2019). Globally, herbicides are most often detected in groundwater (Close and Skinner 2012; McManus *et al.* 2014; Lopez *et al.* 2015; Karki *et al.* 2020). [Chapter 4.3.2] While it is difficult to establish trends over time, pesticides may remain present in groundwater for decades after their authorization has been discontinued (Lopez *et al.* 2015).

Pesticide use may have a direct or indirect impact on the sustainability of agricultural production or the effectiveness of disease vector control. As a result, rather than increasing production or reducing disease vector populations, pesticide use may have a negative mid- and long-term impact on agriculture and public health.

The development of resistance against pesticides in arthropods, diseases, weeds and rodents may lead to failure to control them and to subsequent increases in crop losses or disease prevalence. It also often results in an increase in pesticide use, with associated adverse environmental and health effects (FAO 2012). [Chapter 4.3.3]

Despite efforts to manage resistance, and some clear successes in slowing down its development (e.g., in Bt transgenic crops), the overall trend during the last decades has been a continuous increase in field-evolved pesticide resistance in arthropods, weeds and diseases (Gould, Brown and Kuzma 2018; Gould *et al.* 2018).

Acute mortality of honeybees due to pesticide applications has been reported regularly in the past. However, it appears to be declining

in countries with effective regulation or enforcement of mitigation measures. Incidents of insecticide-associated honeybee mortality may occur more often in other countries, but monitoring data to validate this are lacking (Kovács-Hostyánszki *et al.* 2016). [Chapter 4.3.3]

It remains unclear to what extent sublethal effects of pesticide exposure, which are recorded for individual insects, affect colonies and populations of managed bees and wild pollinators in the field, especially over the longer term. There are indications, however, that wild bees may be more affected than managed honeybee colonies (Kovács-Hostyánszki *et al.* 2016; Woodcock *et al.* 2016; Wood and Goulson 2017).

The use of insecticides, as well as other groups of pesticides, often adversely affects the abundance of natural enemies of pests (Cloyd 2012; Roubos, Rodriguez-Saona and Isaacs 2014). This may have an impact on natural pest control and can lead to pest resurgence or secondary pest development (Dutcher 2007; Wu *et al.* 2020).

Despite changes in pesticide chemistry, and an increased focus on integrated pest management, both pest resurgence and secondary pest development due to pesticide applications persist (Roubos, Rodriguez-Saona and Isaacs 2014; Hill, MacFadyen and Nash 2017). However, it is unclear whether resurgence and secondary pest development are less frequent today than they were in the past. [Chapter 4.3.3]

Pesticide applications in the field have led to variable effects on soil microbial communities and activity. There is only limited evidence that the observed effects have led to significant and long-lasting decreases in soil functions (Imfeld and Vuilleumier 2012; FAO and Intergovernmental Technical Panel on Soils [ITPS] 2017). [Chapter 4.3.4]

No review was available of post-registration monitoring of earthworm populations following real pesticide applications at recommended rates. However, several studies from Europe suggest that especially chronic risks to earthworms may be higher than previously estimated. Pesticide effects

on soil arthropods are less well studied than on earthworms (Pelosi *et al.* 2014).

Despite the importance of soil quality for agricultural production, relatively little monitoring and few large scale field studies have been conducted to assess the impact of current use pesticides on soil organisms and processes.

Pesticides may have a direct (lethal or sublethal) toxic effects on birds, or can act indirectly through food depletion or habitat alteration (EFSA 2009; Amaral *et al.* 2012a; Mineau 2013a; EFSA 2018a; Stanton, Morrissey and Clark 2018). [Chapter 4.3.4]

Although certain current use pesticides can have toxic effects on birds at recommended application rates, there does not appear to be much evidence of significant population reductions arising from direct effects of pesticides (Jahn *et al.* 2014; Tassin de Montaigu and Goulson 2020), with the possible exception of the use of anticoagulant rodenticides and deliberate wildlife poisoning with pesticides (López-Perea and Mateo 2018; Nakayama *et al.* 2019).

There are indications, however, that currently used pesticides may be one of the drivers of observed bird declines and, in some cases, may be the leading cause, likely through indirect effects (Jahn *et al.* 2014; Coates *et al.* 2017; Brain and Anderson 2019; Spiller and Dettmers 2019). Whether or not pesticides are the principal factor in bird population reductions is likely to depend on the type of pesticide applied, the species concerned, and pesticide application parameters such as dose and frequency of treatments (Bouvier *et al.* 2011; Mineau and Whiteside 2013; Emmerson *et al.* 2016; Stanton, Morrissey and Clark 2018; Miao and Khanna 2020).

Pesticides are likely to affect amphibian survival and health at environmentally relevant concentrations (Egea-Serrano *et al.* 2012; Baker, Bancroft and Garcia 2013). However, important data gaps still exist, particularly with regard to studies on non-anuran amphibians. Furthermore, it is still very difficult to link adverse effects in amphibians to individual pesticides, partly due to the virtual absence of in-depth field monitoring

studies and the presence of other stressors (Bishop *et al.* 2012; North *et al.* 2015; Orton and Tyler 2015).

Reptiles are not yet well studied with regard to the acute and chronic effects caused by pesticides or the different (qualitative and quantitative) ways in which reptiles are exposed to them (Köhler and Triebkorn 2013; EFSA 2018a). The limited information available indicates that adverse (sub)lethal effects may occur at realistic field exposure levels following the application of certain pesticides that are currently authorized for use (Wagner *et al.* 2015; Mingo, Lötters and Wagner 2016; Mingo, Lötters and Wagner 2017). In the absence of validated and robust risk assessment methods, pesticide registration procedures may not fully capture specific risks to this group of non-target vertebrates [Chapter 4.3.4].

Field monitoring of the effects of real pesticide use on aquatic organisms is not frequently conducted, nor are field studies evaluating the effects of pesticides on aquatic ecosystem structure and functioning despite an increase in the number of these studies conducted in recent years (Schäfer 2019; Zubrod *et al.* 2019; Rosic *et al.* 2020; Schepker *et al.* 2020). Nevertheless, available studies generally indicate high pesticide risks to aquatic organisms under current agricultural practices, especially in freshwater systems (Beketov *et al.* 2013; Sánchez-Bayo and Wyckhuys 2019; Schäfer 2019; Ito *et al.* 2020). [Chapter 4.3.5]

In major global biodiversity status reports, pesticides are often listed as a key driver of biodiversity loss in agricultural and natural ecosystems (FAO 2019; IPBES 2019; FAO *et al.* 2020; Sud 2020). However, the number of studies that are able to directly link pesticide use with adverse effects on biodiversity parameters, such as species richness, are relatively rare. Moreover, virtually all studies have been conducted in North America and Europe. There is an almost complete absence of data from other parts of the world (Annex 4.3-6). [Chapter 4.3.6]

Nevertheless, where large-scale studies have been conducted, pesticide use has frequently been

associated with adverse effects on biodiversity (Brittain *et al.* 2010; Beketov *et al.* 2013; Emmerson *et al.* 2016; Chiron *et al.* 2014; Forister *et al.* 2016; Sattler *et al.* 2020).

Substantial knowledge gaps have been identified with regard to the effects of pesticide use on the environment. They include the need to conduct more systematic reviews and meta-analyses of existing scientific data, particularly on topics of specific interest in regulatory decision-making (Group of Chief Scientific Advisors 2018). [Chapter 4.3.7]

Despite significant improvements in prospective regulatory risk assessment, unexpected environmental impacts are frequently identified (Boyd 2018; Group of Chief Scientific Advisors 2018; Brühl and Zaller 2019; Schäfer *et al.* 2019; Topping, Aldrich and Berny 2020). Some principal directions for improving pesticide environmental risk assessment have been proposed. [Chapter 4.3.7]

Due to the limitations in the current prospective risk assessment procedures discussed, and the lack of systematic post-registration monitoring, significant gaps in knowledge about adverse effects of current pesticide use on the environment persist. Strengthening post-registration environmental monitoring of pesticide concentrations and effects should therefore have the highest priority (Milner and Boyd 2017; Vijver *et al.* 2017; Group of Chief Scientific Advisors 2018; Rico *et al.* 2020; Topping, Aldrich and Berny 2020).

This chapter does not provide an in-depth review of approaches, methods and procedures for the prospective environmental risk assessment of pesticides. However, possible difficulties of (and gaps in) environmental risk assessment have been indicated where they might explain the observed environmental effects and consecutive risks of actual pesticide use. In order to better situate possible gaps in current risk assessment, the general principles of prospective environmental risk assessment, as conducted by major regulators, are summarized in Box 4.3-1.



**Box 4.3-1 Principles of environmental risk assessment of pesticides.**

Regulatory (prospective and retrospective) environmental risk assessment of pesticides is conducted based on similar principles for different non-target organisms and in different parts of the world. It tends to be built upon the following elements, as illustrated in the figure below (adapted from Babut *et al.* 2013; Boivin and Poulson 2017; United States Environmental Protection Agency [US EPA] 2020).

**1. Problem formulation**

The problem formulation outlines the objectives of the risk assessment and defines the pesticide use pattern(s), (agro-)ecosystem characteristics, protection goals (what needs to be protected from the pesticide, where, and how strictly), assessment endpoints, and a conceptual model that describes the main expected relationships between the pesticide and the assessment endpoint(s). Generally, an environmental risk assessment is conducted for an individual pesticide and its relevant metabolites.

**2. Effects characterization**

The effects characterization describes the types of effects a pesticide may produce in an organism and how those effects depend on the pesticide exposure levels. It is generally based on toxicity studies conducted in the laboratory (bioassays), in micro- and mesocosms, or in the field. Effect models of biological, toxicological and ecological processes have received increasing attention in recent years. The outcomes of the effects characterization are one or more assessment endpoints, generally a predicted no effect concentrations (PNEC) or a similar endpoint.

Since laboratory toxicity tests tend to be conducted with single species, while the protection goal is often an ecological community, extrapolations are made from one to more species and from the laboratory to the field. This can be done through modelling, using species sensitivity distribution, and/or applying an uncertainty factor (also referred to as a safety or assessment factor).

If an uncertainty factor is integrated into the effects characterization phase, the assessment endpoint is referred to as, for example, a regulatory acceptable concentration (RAC) or level of concern (LoC). However, the safety factor may also be integrated into the risk characterization phase.

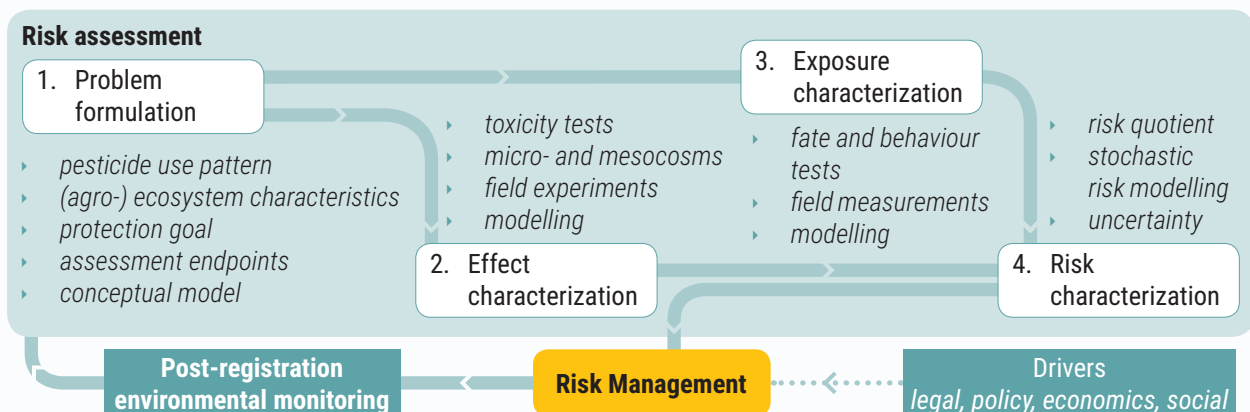
**3. Exposure characterization**

The exposure characterization estimates the potential exposure of environmental components (e.g. surface waters, soil) where non-target organisms are present. This characterization includes information about the estimated quantity, frequency and duration of the exposure of an organism to a pesticide.

Laboratory and field-derived data of pesticide fate and behaviour in the environment are at the basis of exposure characterization. Modelling tends to be used to generate exposure assessment endpoints, such as a predicted environmental concentration (PEC) or an estimated environmental concentration (EEC). A PEC is calculated on the basis of the intended use of the pesticide (e.g. application rate, frequency and timing, type of crop or other target), pesticide properties (e.g. solubility, vapour pressure, degradation rates), and environmental conditions or scenarios (e.g. wind speed, slope, weather).

**4. Risk characterization**

In the risk characterization phase, exposure and ecological effects endpoints are integrated into a risk estimation or risk quotient. If uncertainty factors have not been taken into account in the effects characterization phase, they can be incorporated into the risk estimation. Either way, the risk of the pesticide is generally considered acceptable if the predicted level of exposure is lower than the regulatory acceptable concentration or the level of concern. The integrated risk characterization therefore includes the assumptions, uncertainties, and strengths and limitations of the different risk assessment phases.



On the basis of the results of the risk assessment, risk management decisions about the pesticide are taken, e.g. authorization of the pesticide with or without risk mitigation measures, restricted use registration, or denial of authorization. Risk management decisions are based not only on the scientific risk assessment, but also on legal, policy, economic and social considerations, which are generally country-specific.

In many countries a tiered approach to risk assessment is followed. As a first tier, the results of standard toxicity tests with a limited number of species are compared to a reasonable worst-case PEC. If the first-tier assessment does not indicate an unacceptable risk, further assessments are generally not required. If, on the other hand, a risk is identified in the first tier, more realistic toxicity data and/or exposure estimates are needed. Higher tiers better reflect processes and characteristics of natural ecosystems and are tailored based on the outcomes of the lower tiers.

Regulatory pesticide risk assessments have become increasingly complex, with the aim of addressing risks for a wider range of non-target organisms, being more ecologically realistic, and reducing uncertainty. A large number of guidance documents and models have been published covering key environmental compartments and non-target organisms:

#### Selected regulatory environmental risk assessment guidance

Protection goal	Region	Guidance	Reference
General	Australia	<i>Risk Assessment Manual – Environment</i>	Australian Pesticides and Veterinary Medicines Authority (APVMA) 2019
	Brazil	<i>Manual para requerimento de avaliação ambiental: agrotóxico e afins</i>	Instituto Brasileiro do Meio Ambiente e dos Recursos Naturais Renováveis (IBAMA) 2009
	China	<i>Environmental Risk assessment Handbook for Pesticide Registration in China</i>	Peeters <i>et al.</i> 2014
	United States	<i>Generic Ecological Assessment Endpoints (GAEs) for Ecological Risk Assessment</i>	US EPA 2016
	United States	<i>Ecological risk assessment for pesticides: Technical overview</i>	US EPA 2020
Pollinators	EU	<i>Guidance on the risk assessment of plant protection products on bees (Apis mellifera, Bombus spp. and solitary bees)</i>	European Food Safety Authority (EFSA) 2013a)
	North America	<i>Guidance for Assessing Pesticide Risks to Bees</i>	US EPA, Heath Canada Pest Management Agency, and California Department of Pesticide Regulation 2014
Aquatic organisms	EU	<i>Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters</i>	EFSA 2013b
Terrestrial vertebrates	EU	<i>Guidance document on risk assessment for birds and mammals</i>	EFSA 2009

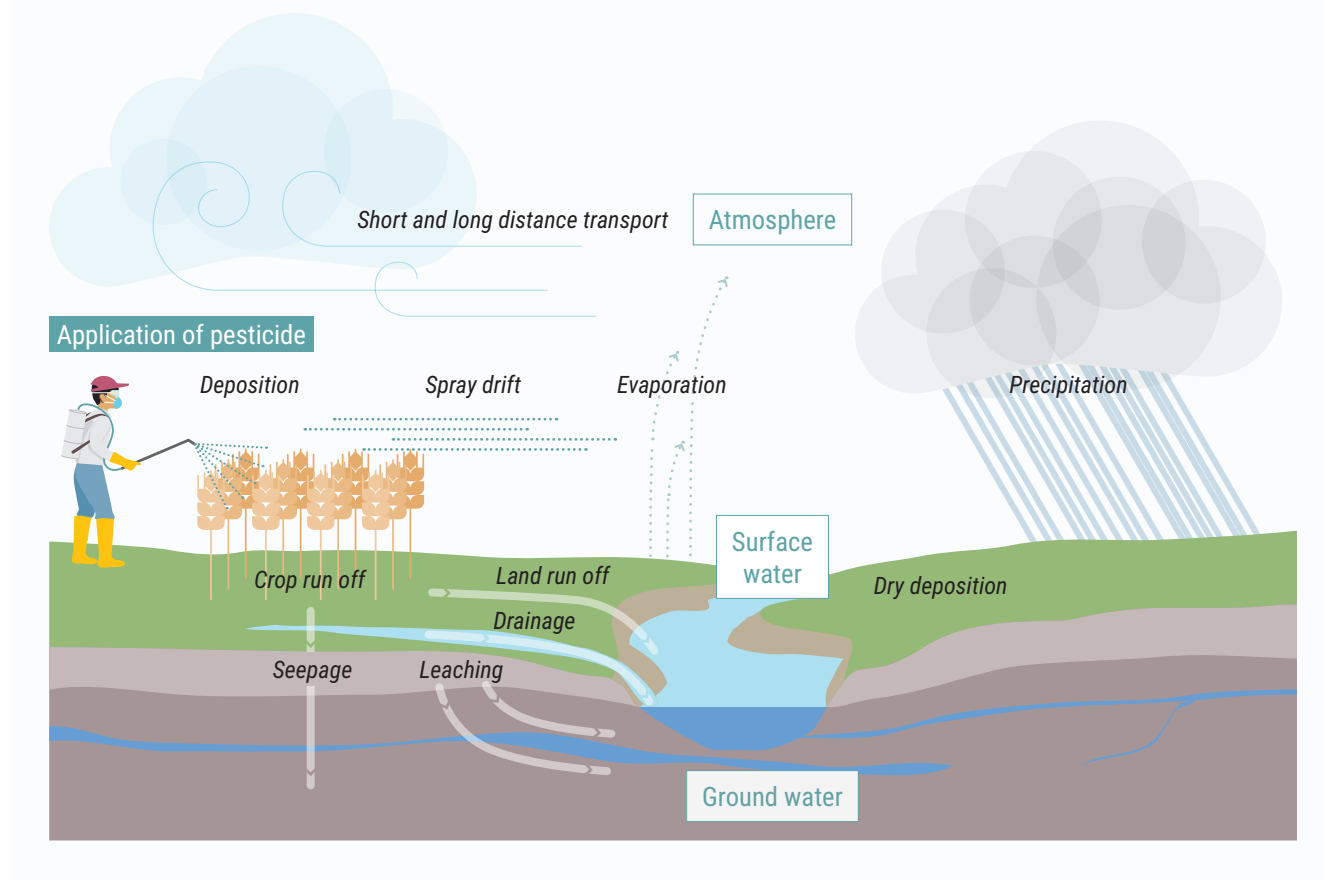
### 4.3.2 Pesticide concentrations in the environment

Pesticides will end up in different compartments of the environment after their intended and authorized use, or following misuse or accidents. Residues of pesticides and their metabolites are found in air, surface waters, groundwater, soil and biota (Figure 4.3.2-1). The degree of

contamination of the environment by pesticides provides an important indication of their risks to the environment and health. Therefore, increasingly, pesticide residues are monitored in the environment on a more or less regular basis.

In this chapter global and regional reviews concerning pesticide concentrations in the environment are evaluated and their potential

► Figure 4.3.2-1 Pesticides can contaminate surface water and groundwater through many different routes.



risks described. Reviews published since 2010 were compiled. Recent large-scale national studies not included in such global or regional reviews were also identified, especially if they included time trends.

Key questions addressed are: What geographical differences exist in observed pesticide residues in the environment? What time trends can be identified, and have pesticide concentrations been increasing or decreasing over time? Are certain (groups of) pesticides found more frequently in the environment than others? And what are the environmental risks of these concentrations (often assessed through exceedances of regulatory acceptable concentrations)? Data gaps are also identified. A distinction is made between persistent organic pollutant (POP) pesticides, which are internationally regulated under the Stockholm Convention on Persistent Organic Pollutants and are generally not used anymore (i.e., legacy pesticides), and other pesticides generally in current use (current use pesticides).

### Pesticides in surface waters

Surface waters, such as rivers, lakes, streams and ponds, can be exposed to pesticides in many ways. These include direct application to water bodies, drift of droplets during spraying, drainage of irrigation water, surface run-off during rain events, leaching through the soil, and deposition of evaporated pesticides (Figure 4.3.2-1 above). Pesticides can also contaminate water accidentally, e.g., after spills or as a result of inappropriate handling such as washing pesticide application equipment close to waterways. Finally, surface water may be exposed through illegal use of pesticides (e.g., in fishing).

Monitoring of pesticide concentrations in surface water bodies has been conducted in certain regions of the world for several decades through systematic and ad hoc monitoring or event-triggered sampling. For example, the United States Geological Survey's National Water Quality Assessment (United States Geological Survey 2020) has monitored pollutants such as pesticides

in streams, rivers and groundwater since 1991. The Swedish National Environmental Monitoring Programme of Pesticides in Surface Waters has conducted analyses in surface waters of almost all pesticides registered in Sweden for more than 15 years (Boye et al. 2019). In the Netherlands, although water quality monitoring had been conducted for many years, a harmonized national monitoring network for pesticides in surface waters was only established in 2014 to evaluate implementation of the national plant protection policy (de Weert *et al.* 2014). The European Environment Agency hosts the Waterbase – Water Quality database, which contains Europe-wide data on pesticide concentrations in rivers and lakes (European Environment Agency [EEA] 2019).

In many other parts of the world, especially Africa, Asia and Latin America, very limited if any surface water monitoring is carried out. Stehle and Schulz (2015) estimated that for about 90 per cent of high-intensity agricultural areas in the world, no scientific investigations of insecticide surface water exposure exist (Figure 4.3.2-2).

Monitoring of pesticide concentrations in surface water is constrained by the fact that pesticides tend to be applied only once or a few times per growing season. They often dissipate rapidly from the water column because of adsorption to sediment and organic matter in the water, degradation, and water flow (the latter in rivers and streams). This leads to discrete and often short-term exposure of water bodies, between which there may be long periods without exposure (Stehle, Knäbel and Schulz 2013). Nevertheless, pesticides may be highly toxic to aquatic life, so that even short-term exposure peaks can lead to significant adverse effects. It has been estimated that water monitoring based on fixed intervals, even if technically well conducted, would still miss 99 per cent or more insecticide exposure events that could cause adverse effects (Stehle, Knäbel and Schulz 2013). Monitoring programmes are thus likely to (greatly) underestimate concentrations of pesticides in surface waters. The fact that no pesticides were measured in a sample does not necessarily mean they were not present in the (recent) past or will not be found in the (near) future.

## Global reviews

Only three recent global reviews of pesticides in surface water were identified (Annex 4.3-1)<sup>3</sup>.

No global reviews of POP pesticides in surface water were available. The Global Monitoring Programme of the Stockholm Convention does not assess POP pesticides in surface water bodies.

Stehle and Schulz (2015) and Stehle, Bub and Schulz (2018) conducted the largest global review of insecticide surface water concentrations so far, covering 838 peer-reviewed studies, at >2,500 sites in 73 countries. They reported that there is a complete lack of scientific monitoring data for ~90 per cent of global cropland (Figure 4.3.2-2).

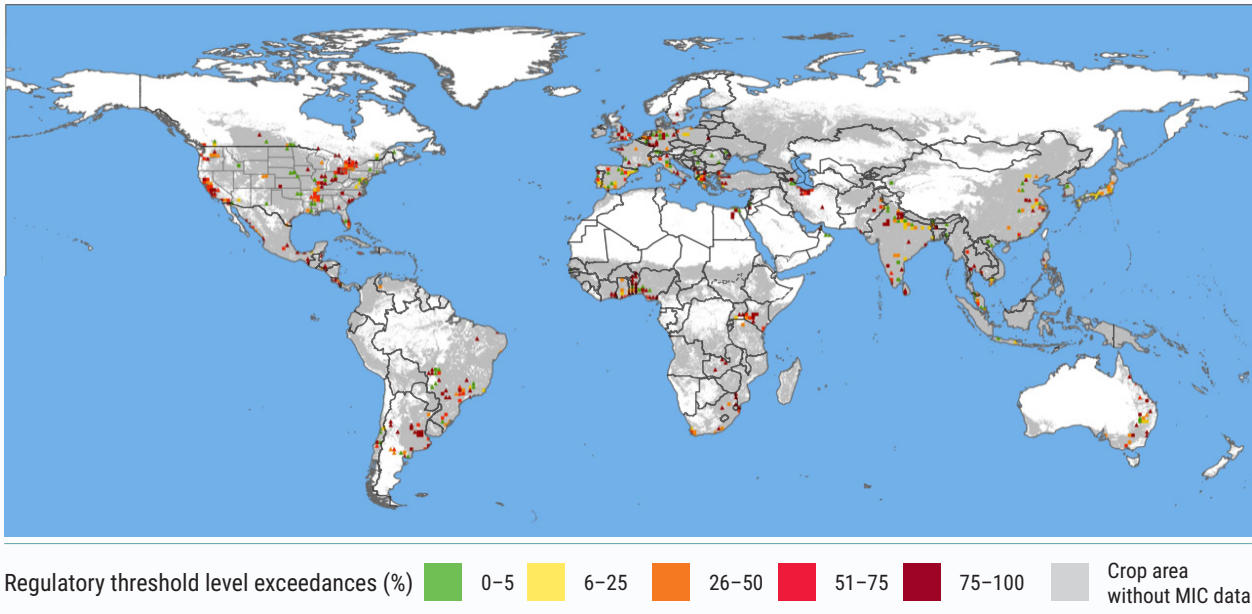
In 97 per cent of samples no insecticides were measured. However, of the remaining 11,300 samples, 52.4 per cent (5,915 cases; 68.5 per cent of sites) exceeded the legally accepted regulatory threshold levels for either surface water or sediments. Median concentrations of neonicotinoids, although limited in number, exceeded those of organochlorines and organophosphates by a factor of about 3 and those of pyrethroids by a factor 10. While most of the available insecticide monitoring data were from North America, Asia and Europe, the highest insecticide concentrations were detected in Africa, Asia and South America.

Recent global reviews were also available for neonicotinoids (Morrissey *et al.* 2015; Sánchez-Bayo, Goka and Hayasaka 2016) and for pyrethroids (Tang *et al.* 2018). Insecticides from these groups were widely found in surface water across all global regions. Average concentrations of neonicotinoids exceeded ecological thresholds in 74 per cent of cases. Sanchez-Bayo, Goka and Hayasaka (2016) found that neonicotinoid concentrations in surface water had increased during the previous 15 years.

In a global review of occurrences of pesticides in surface water published between 2012 and

3 Annex 4.3-1 is found at: <https://www.unep.org/resources/report/environmental-and-health-impacts-pesticides-and-fertilizers-and-ways-minimizing>

► **Figure 4.3.2-2 Global crop area and the distribution of regulatory threshold level exceedance rates for reported measured insecticide concentrations (MIC) aggregated in 1° grid cells.** Stehle and Schulz (2015).



2019, de Souza *et al.* (2020) found that the most frequently reported pesticides were the herbicides atrazine and its metabolites, as well as metolachlor, the insecticide chlorpyrifos, and the fungicides carbendazim and tebuconazole.

### Regional and national reviews

The presence of organochlorine pesticides (OCPs) in surface water has been reviewed for Caribbean and Pacific marine environments (Menzies *et al.* 2013) and freshwater systems in Africa (Taiwo 2019) and South Asia (Ali *et al.* 2014) (Annex 4.3-1). OCPs were encountered in almost all samples taken, even from locations far from human habitation and when the use of such pesticides had been prohibited for many years. Concentrations in freshwater bodies in Africa and Asia very often exceeded quality standards for surface water applied in Europe (European Union 2013).

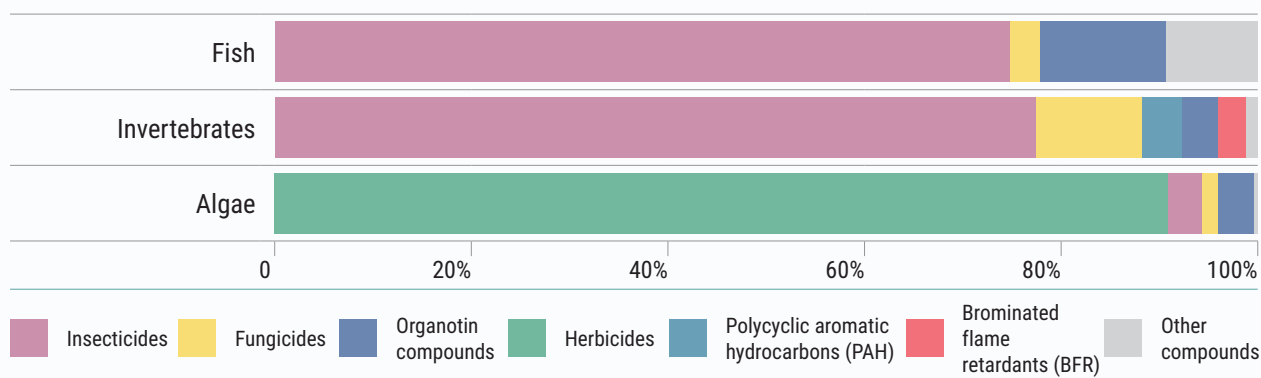
The ubiquitous presence of OCPs in aquatic environments observed in these regional reviews was confirmed by recent national studies and reviews in surface water and sediments in Africa, for example Egypt (Dahshan *et al.* 2016), Ethiopia (Dirbaba *et al.* 2018), Ghana (Bruce-Vanderpuije *et al.* 2019), South Africa (Ansara-Ross *et al.* 2012),

Sudan (Nesser *et al.* 2016) and Tanzania (Elibariki and Maguta 2017), and in Asia, for example China (Grung *et al.* 2015; Li, Li and Liu 2015) and India (Yadav *et al.* 2015).

Clear trends over time have generally not been established, with a reduction in OCP detections implied for the Nile in Sudan (Nesser *et al.* 2016) and significant increases in concentrations found in Ghana (Bruce-Vanderpuije *et al.* 2019). The studies reviewed did not provide indications that concentrations of POP pesticides in surface water showed downward trends in Africa and Asia.

Malaj *et al.* (2014) reviewed the presence and risks of organic chemicals at more than 4,000 sampling locations in freshwater ecosystems in Europe. The chemical risk per river basin was calculated by comparing reported pesticide concentrations with an acute and a chronic risk threshold for each organism group evaluated (fish, invertebrates and algae). Of all the monitoring sites, 14 per cent were likely to be acutely affected by organic chemicals, and 42 per cent to be affected chronically, for at least one organism group. Of the 223 chemicals monitored, pesticides were among the major contributors to chemical risk. They were responsible for 81 per cent, 87 per cent, and 96 per cent of observed exceedances of acute

► **Figure 4.3.2-3 Proportion of sampling sites in European freshwater ecosystems showing exceedance of acute regulatory thresholds by different chemical groups.** Malaj *et al.* (2014).



regulatory thresholds related to fish, invertebrates and algae, respectively (Figure 4.3.2-3).

More recently, Mohaupt *et al.* (2020) evaluated data from the European Environment Agency's Waterbase – Water Quality database on the presence of 180 pesticides in surface water reported by 34 European countries between 2007 and 2017. They found that 5-15 per cent of samples exceeded the environmental quality standards for herbicides and 3-8 per cent exceeded those for insecticides; exceedances of fungicides were less prevalent.

K'oroje *et al.* (2020) reviewed the literature regarding the occurrence of pesticides in Africa. They found that both POPs and current use pesticides are frequently reported in surface water on the continent at concentrations in the same order of magnitude as those found in Brazil, China and India.

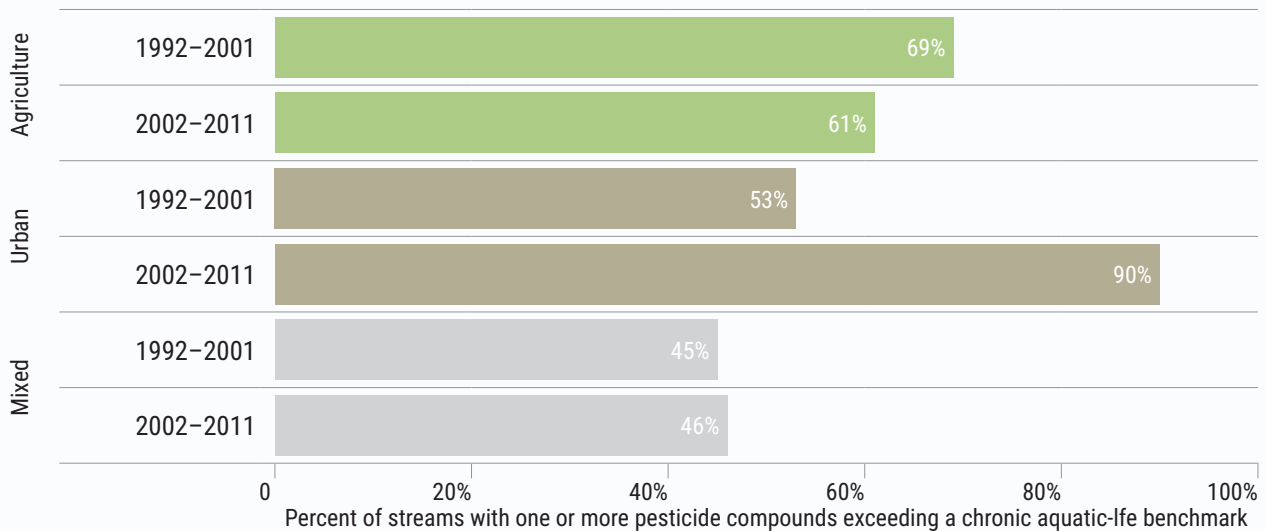
Residues of current use pesticides in surface water were also recently assessed in national studies such as those in Brazil (Albuquerque *et al.* 2016), China (Chen *et al.* 2019), Hungary (Székács, Mörtl and Darvas 2015), Italy (Meffe and de Bustamente 2014), Japan (Derbalah *et al.* 2019), Romania (Schreiner *et al.* 2021), Switzerland (Knauer 2016) and the United States (Stone, Gilliom and Ryberg 2014; Hladik and Kolpin 2016; Wolfram *et al.* 2018), among other countries (Annex 4.3-1). While many studies on OCPs were conducted in Africa and Asia, current use pesticide concentrations were

monitored more frequently in Europe and the United States.

Current use pesticides were frequently found in surface water at concentrations which could result in adverse effects on aquatic organisms. For example, Albuquerque *et al.* (2016) reviewed all published studies on pesticide concentrations in Brazilian freshwater systems and identified a potential risk to aquatic life for 59 per cent of the pesticides on which they had data. Chen *et al.* (2019), when monitoring neonicotinoids in river water in Eastern China, concluded that 27 per cent exceeded thresholds for acute and 84 per cent of chronic ecological risks. Meffe and de Bustamente (2014) found that 54 per cent of maximum pesticide concentrations measured in Italian surface water were above environmental quality standards. Wolfram *et al.* (2018) concluded, when reviewing 259 studies that covered 644 sampling sites in surface water in the United States, that 49 per cent of measured pesticide concentrations exceeded regulatory threshold levels. The only recent study which found that most pesticide concentrations in surface water did not appear to pose high risks was in Switzerland (Knauer 2016), where it was concluded that 95 per cent of measured concentrations were below national regulatory acceptable concentration.

Trends over time in water concentrations of current use pesticides were assessed in the United States. Both Stone, Gilliom and Ryberg (2014) and Wolfram *et al.* (2018) concluded that risks

► **Figure 4.3.2-4** The proportion of streams in the United States with one or more pesticides that exceeded a chronic aquatic life benchmark was very similar in the periods 1991-2001 and 2002-2011 for agricultural and mixed land use streams, but much greater in the period 2002-2011 for urban streams. Wolfram *et al.* (2018).



for aquatic organisms had not declined during the previous five decades (Figure 4.3.2-4). In the Netherlands, on the other hand, the number of exceedances of national water quality criteria fell between 2013 and 2018 by 15 per cent for chronic exposure and 30 per cent for acute exposure (Netherlands Environmental Assessment Agency 2019).

### Pesticides in air

Contamination of air by pesticides may occur through spray drift, volatilization from soils, plants and surface waters, and wind erosion of soil particles containing adsorbed pesticides (FOCUS 2008). Taking into account all these processes, the fraction of pesticides emitted to ambient air may be more than 30 per cent of the applied dose (Coscollà and Yusà 2016).

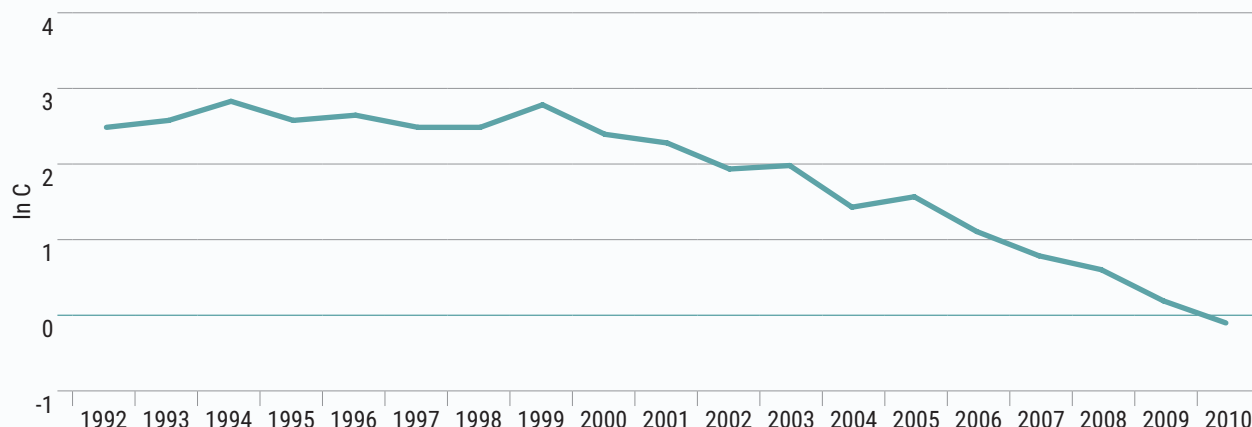
When pesticides reach higher levels in the atmosphere, they can be transported over short or long distances and deposited on land or water. This is particularly important in the case of pesticides not rapidly degraded in air. A well-known example is organochlorine pesticides used in tropical regions which have been found in the polar regions.

### Atmospheric concentrations

Atmospheric contamination by pesticides is less well documented than that of other environmental compartments. There are relatively few systematic monitoring programmes for pesticides in ambient air. Since 2005 the Global Atmospheric Passive Sampling (GAPS) programme has deployed passive air samplers at over 50 locations on seven continents (Shunthirasingham *et al.* 2010). GAPS provides global atmospheric data on POPs, emerging POPs and some current use pesticides, both to domestic monitoring initiatives and to international programmes such as the Global Monitoring Plan (GMP) of the Stockholm Convention (UNEP 2017a). Historically, more attention has been paid to persistent organochlorine pesticides, but there is increasing interest in the occurrence and fate of current use pesticides in ambient air.

Many OCPs have been measured in notable concentrations in ambient air, not only near emission regions but also in distant areas. OCPs can move through the atmosphere by volatilization in relatively warmer source regions, transport in air, and subsequent deposit in colder regions. Polar regions and high mountainous areas

► **Figure 4.3.2-5 Time trends for  $\gamma$ -HCH (lindane) measured in air at the Canadian Great Lakes site, Point Petre. Atmospheric decline rates of  $\gamma$ -HCH have accelerated in the Arctic and the Great Lakes region following North American restriction of the pesticide lindane. UNEP (2017a).**



then act as sinks (Kirchner *et al.* 2016; Wang *et al.* 2019).

The latest GMP monitoring report presents findings concerning aerial OCP concentrations at the global scale, based on information for the period 2000-2015 (UNEP 2017a). Time trends were mainly available for Asia, Europe and North America, and to a more limited extent for Africa, but were almost absent for Latin America. The GMP only covers studies of OCP concentrations conducted by institutions that are part of its network; other studies and publications are not reviewed by the programme (Annex 4.3-2).<sup>4</sup>

A clear decrease in ambient air concentrations of many OCPs has been observed in Asia, Europe, North America and the Caribbean, which seems to have followed their regulation in the 1980s and early 1990s (Shunthirasingham *et al.* 2010; UNEP 2017a; Rauert *et al.* 2018). For example, a reduction of lindane concentrations in the Great Lakes region of North America followed restrictions on the use of this pesticide (Figure 4.3.2-5). Similarly, reductions in emissions of  $\alpha$ -HCH, DDT and toxaphene appear to have resulted in reductions in atmospheric concentrations in the Arctic (Li and MacDonald 2005). However, reductions in atmospheric

concentrations of many other OCPs are less visible in polar and mountainous regions (Vorkamp and Rigét 2014; Kirchner *et al.* 2016; Wang *et al.* 2019).

By 2000, when the Stockholm Convention was adopted, the majority of primary sources of OCPs had been controlled. The relatively low levels currently measured in air do not show significant changes and appear to be driven by secondary sources (UNEP 2017a). Limited data available from Africa, however, do not show discernible downward trends in OCP air concentrations as yet.

OCPs such as hexachlorocyclohexane (HCH), endosulfan and DDT tend to be more prevalent in air in tropical regions (Shunthirasingham *et al.* 2010). For example, levels of DDT and its metabolites were a factor of 10-100 higher in tropical than in temperate countries (Mochungong and Zhu 2015). This was considered to be due to the continued use of DDT for vector control in Africa and Asia, as well as its higher dissipation in warmer climates.

Although concentrations of OCPs in the atmosphere are declining, they are still measured in air almost everywhere in the world, often decades after their use has been ended. This underlines the long time needed for these persistent compounds to disappear from the environment.

<sup>4</sup> Annex 4.3-2 is found at: <https://www.unep.org/resources/report/environmental-and-health-impacts-pesticides-and-fertilizers-and-ways-minimizing>



Coscollà and Yusà (2016) reviewed 34 studies on concentrations of pesticides in ambient air published between 2001 and 2014 (Annex 4.3-2). The more frequently monitored and/or detected CUPs worldwide were the fungicides chlorothalonil and folpet, as well as the insecticides chlorpyrifos, dimethoate, malathion and phosmet.

Shunthirasingham *et al.* (2010) observed declining concentrations of chlorothalonil in Europe; Vorkamp *et al.* (2014) found increasing concentrations of chlorpyrifos and trifluralin in the Arctic; and Guida *et al.* (2018) measured increasing concentrations of chlorpyrifos in Brazil. However, trends in atmospheric concentrations of CUPs have not been systematically reviewed.

Coscollà and Yusà (2016) concluded that inhalation exposure of CUPs from atmospheric concentrations in the general population does not represent a significant risk, except in some cases for chlorpyrifos. The combined risk resulting from exposure to organophosphate, pyrethroid and

carbamate pesticides was also considered to be acceptable.

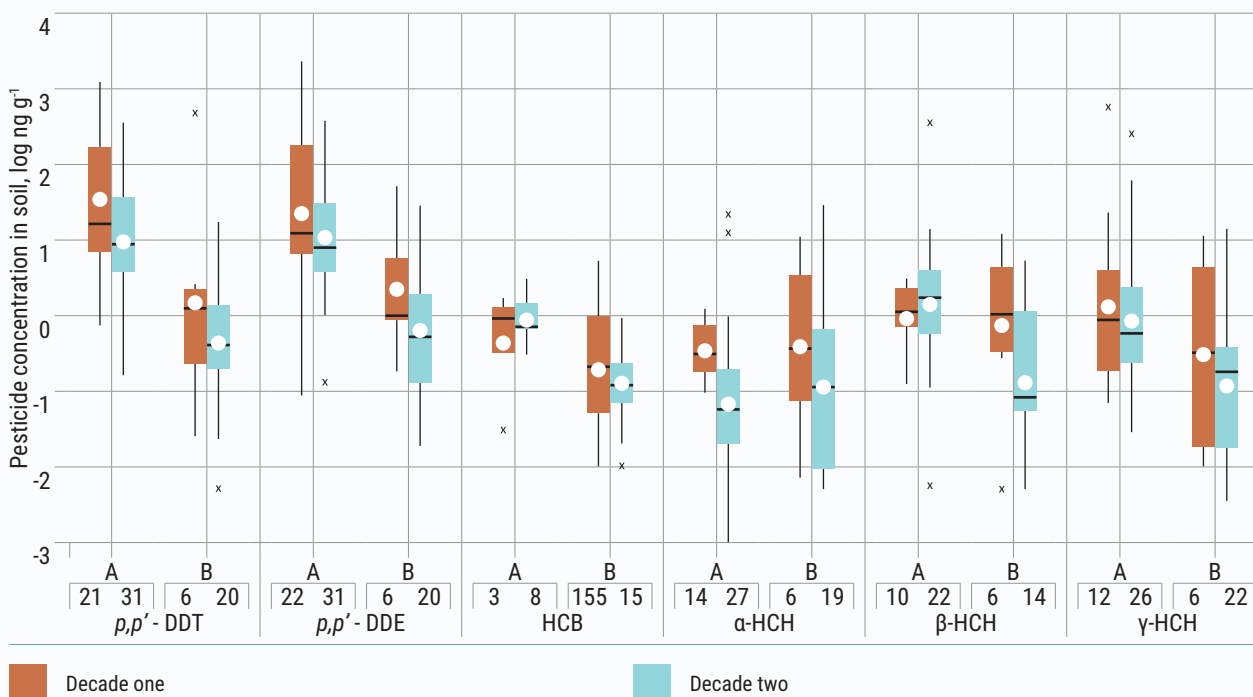
### Pesticides in soil

After the target crop, agricultural soils are generally the first recipient of pesticides following their application (Hvězdová *et al.* 2018). Outdoor pesticide spray applications will almost inevitably contaminate soils through direct deposition, spray drift and wash-off from leaves. Moreover, pesticide use against soil-borne pests and diseases, as well as the use of systemic pesticides, may directly target the soil (e.g., through granular applications and seed treatments).

Further sources of soil contamination are spills and leakage from (obsolete) pesticide storage facilities, as well as spills or discharges from pesticide manufacturing and formulation plants.

The focus of this section will be on pesticide residues in soils after intended uses of

► **Figure 4.3.2-6 Global mean soil concentrations of most organochlorine pesticides in agricultural soils (A) and background soils (B) did not significantly decrease over time (decade one (1993-2002) to decade two (2003- 2012)).** Camenzuli, Scheringer and Hungerbühler (2016).



Note: Each box plot indicates the median value (–), the mean value (o), the quartile values (box) and the 10th to the 90th percentile values (vertical lines). Distribution outliers are marked by x. The number of data points in each box plot is given at the bottom.

pesticide products. A summary of the reviewed assessments is provided in Annex 4.3-3.<sup>5</sup>

### Global reviews

The most recent global review of OCPs in soils was carried out by Camenzuli, Scheringer and Hungerbühler (2016). They reviewed all scientific publications on concentrations of DDT, DDE, HCB and HCH isomers in agricultural and background (unsprayed) soils, published between 1993 and 2012, and attempted to assess whether such concentrations had decreased over time. Statistically significant decreases were only observed for p,p'-DDT in agricultural soils and HCH isomers in background soils; concentrations of other OCPs in soil did not significantly decline during that period (Figure 4.3.2-6). This contrasts with the results of a global environmental fate and transport model, based on estimated emission data, which did suggest a decrease over time. The authors of the review therefore concluded that new emissions of DDT and HCH cannot be excluded.

Wang *et al.* (2019) recently reviewed OCP concentrations in soils in the polar regions (the Arctic, the Antarctic and the Tibetan Plateau). While currently measured concentrations were relatively low, DDTs, HCHs and HCB were found in soil in all these regions. They concluded that soils in cold regions can be considered sinks of POPs.

Few recent global reviews of current use pesticide concentrations in soils are available. Hvězdová *et al.* (2018) commented that “although agricultural soil is a primary sink and key reservoir of pesticides, large soil surveys of agricultural soils for current use pesticides are surprisingly rare”.

Komárek *et al.* (2010) reviewed worldwide data on pesticide residues in vineyard soils. They highlighted that copper, originating from the intensive application of copper-based fungicides, belongs to the most important contaminants of vineyard soils, and that soil residues exceed EU environmental standards in most evaluated cases.

Wood and Goulson (2017) compiled available information on neonicotinoid insecticides, which are under close scrutiny because of various suspected adverse environmental effects. They found that neonicotinoids can be present in soils several years after the last application date, although they do not continue to accumulate indefinitely, plateauing after two to six years of repeated application.

### Regional and national reviews

The large majority of regional and national studies on pesticides in soils concern OCPs even if, in many countries, these pesticides are not used anymore. Their persistence in soil makes them pesticides of interest for monitoring.

OCP residues in soil were detected in almost all countries where they had recently been measured, although concentrations were variable (Annex 4.3-3). In most cases soil concentrations were below national environmental standards (Sun *et al.* 2018 for China; Fosu-Mensah *et al.* 2016 for Ghana; Łozowicka *et al.* 2016 for Poland and Kazakhstan). High levels of OCPs in soil which exceeded health, environmental or trade standards were encountered in India (Mishra, Sharma and Kumar 2012), the French West Indies (Levillain *et al.* 2012) and Tanzania (Elibariki and Maguta 2017).

Contrary to the global trend described by Camenzuli, Scheringer and Hungerbühler (2016) (see above), Sun *et al.* (2018) did observe a decline in concentrations of OCPs in soil in China over time. Few other studies have assessed time trends of OCPs in soil.

The sources of OCPs in soil are not always clear. In many cases they persist from historical uses; in others legal or illegal recent uses of pesticides such as DDT and lindane have been identified (Mishra, Sharma and Kumar 2012; Fosu-Mensah *et al.* 2016). DDT residues in soils may also originate from the use of dicofol, which degrades into DDT in the environment.

Irrespective of the variability of OCP residues in soil, these residues are ubiquitous around the world, even when the OCPs are not (or are hardly)

5 Annex 4.3-3 is found at: <https://www.unep.org/resources/report/environmental-and-health-impacts-pesticides-and-fertilizers-and-ways-minimizing>

used anymore, underlining the “environmental legacy” of persistent pesticides.

Regional and national studies of current use pesticides in soils appear to be mainly from Europe and China (Annex 4.3-3).

Silva *et al.* (2019) sampled agricultural topsoils across 11 EU countries in six major cropping systems. They detected pesticide residues in 83 per cent of tested soils (58 per cent of samples contained multiple residues) and concluded that pesticide residues in agricultural soil are the rule rather than the exception. Glyphosate and its metabolite AMPA, and the broad-spectrum fungicides boscalid, epoxiconazole and tebuconazole, were found most frequently and at the highest concentrations. DDTs (DDT isomers) were also frequently found despite a decades-long ban on use of this pesticide in the EU. The authors concluded that pesticide concentrations in soil were generally below the respective toxic endpoints for standard in-soil organisms.

The pervasive presence of current use pesticides in soil is confirmed elsewhere. In the Czech Republic, Hvězdová *et al.* (2018) detected pesticide residues exceeding national acceptable soil limits in 81 per cent of samples across the country. Most of these residues were triazine herbicides and conazole fungicides. Humann-Guilleminot *et al.* (2019) conducted a country-wide survey of neonicotinoid residues in soil in Switzerland. They found that all soil in conventional fields contained neonicotinoid residues, as did 93 per cent of organic soils which were supposed to be free of pesticides, highlighting the importance of diffuse soil contamination from surrounding uses. Pelosi *et al.* (2021), in a recent study in France, found at least one current use pesticide in all the 180 soils sampled both in treated cereal fields and non-treated habitats such as hedgerows, grasslands and organic cereal fields. In 83 per cent of samples, five or more CUPs were detected. In addition, Pan *et al.* (2018) detected organophosphate pesticides in 93 per cent of soils sampled along the Yangtze River Delta.

### Pesticides in groundwater and drinking water

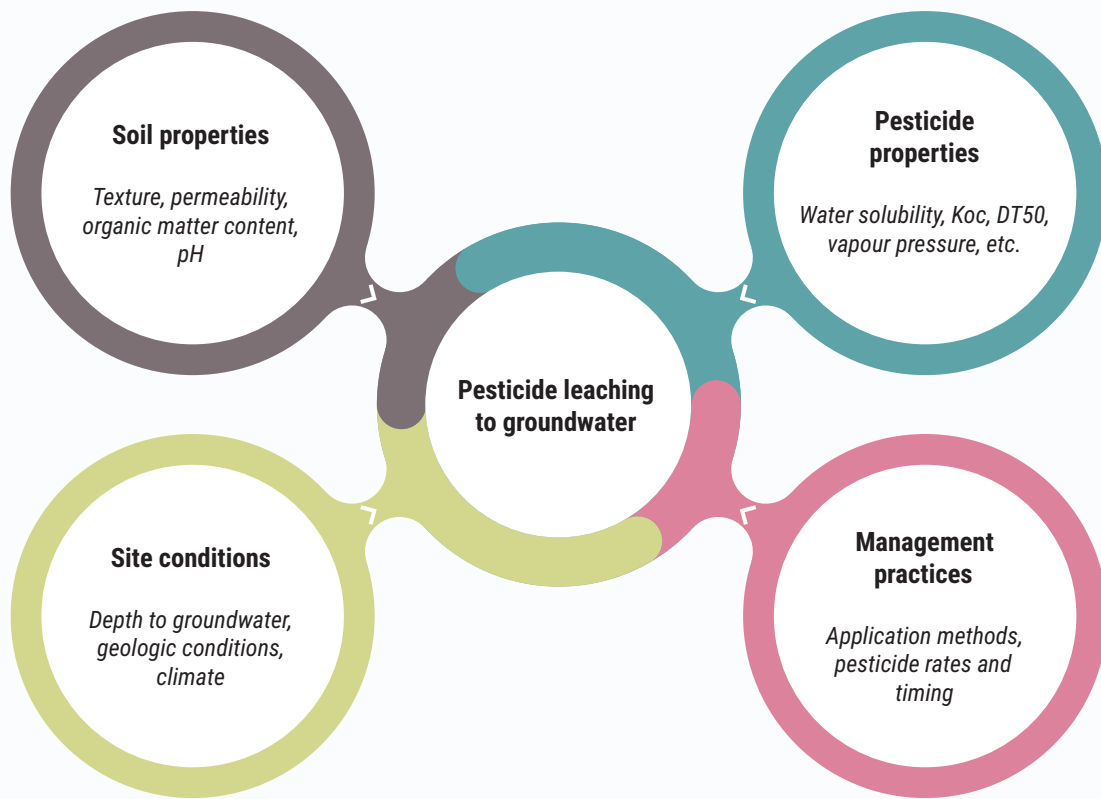
Pesticides applied to agricultural fields may be vertically displaced downwards from the topsoil through the soil profile and the unsaturated zone to groundwater, a process called leaching (Figure 4.3.2-1). Since groundwater is an important source of drinking water, both environmental and human health effects may be caused by groundwater pesticide pollution. The extent to which pesticides leach to groundwater depends on a large number of factors related to soil and pesticide properties, site conditions and management practices (Figure 4.3.2-7).

Pesticide properties also play an important role. The higher the water solubility of a pesticide, the greater its potential to dissolve in water infiltrating the soil. Pesticides for which there is only a short time to detect a 50 per cent decrease in pesticide concentration (detection time 50 per cent; DT50) may be degraded before reaching groundwater levels. Similarly, pesticides with a high soil adsorption coefficient (Koc) are expected to be retained in topsoil layers. It should be noted, however, that pesticides with low water solubility and high Koc (and DT50) values have greater potential for particle-bound transport, i.e., adsorption to particles in infiltrating water (Goss and Wauchope 1990).

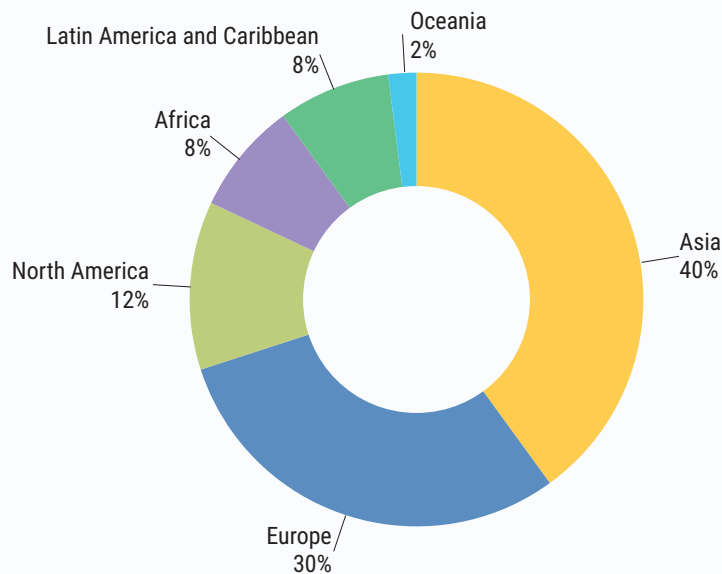
Besides soil and pesticide properties, site characteristics (e.g., depth to groundwater, weather and climate) and management practices (e.g., application dosage) affect pesticide leaching to groundwater. Ultimately, the combination of factors shown in Figure 4.3.2-8 will determine whether, and to what extent, pesticides will leach to groundwater under field conditions.

The difficult accessibility of groundwater ecosystems hampers monitoring of pesticides, which is often restricted by the availability of superficial sampling spots. In addition, although some countries have extensive national monitoring programmes, efforts in other parts of the world are meagre or non-existent (Pirsaheb *et al.* 2017).

► **Figure 4.3.2-7 Factors influencing pesticide leaching to groundwater.** Adapted from Pérez-Lucas et al. (2018).



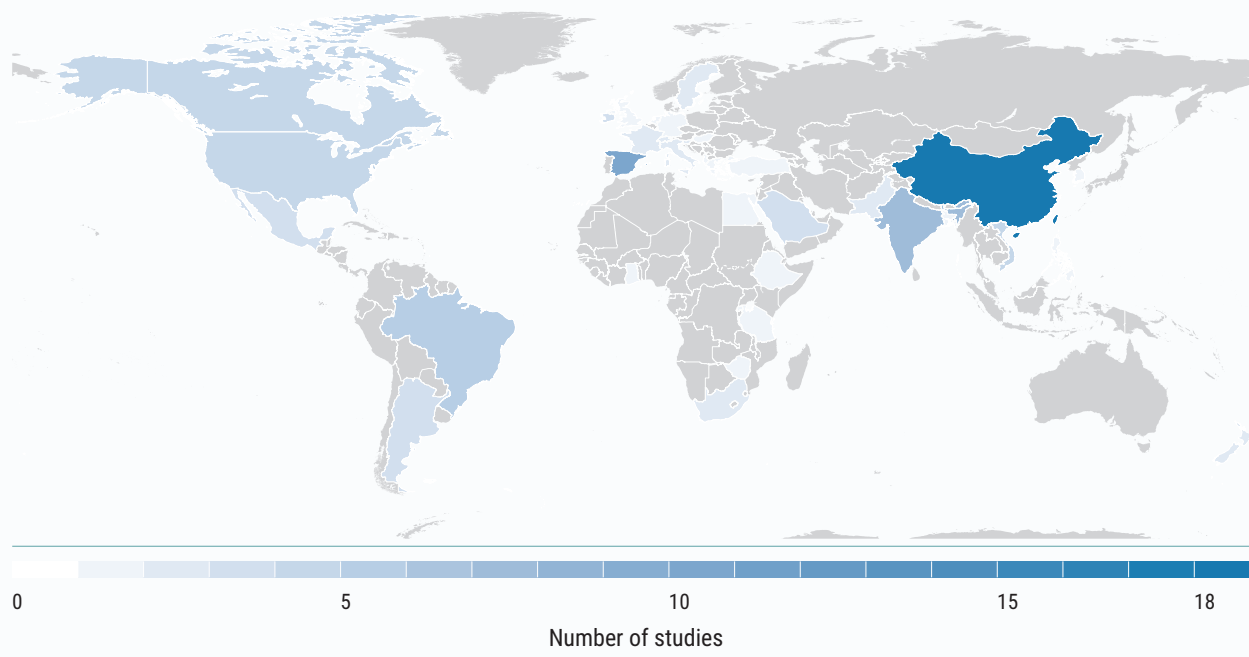
► **Figure 4.3.2-8 Relative availability of local and national groundwater monitoring/review studies per continent (total = 103 publications between 2010 and 2020).**



Based on studies of pesticides in groundwater and drinking water published since 2010 (listed in Annex 4.3-4), the geographical distribution per country and continent

of country-wide and local studies combined are shown in Figures 4.3.2-8 and 4.3.2-9. The main outcomes of the country-wide

► **Figure 4.3.2-9 Geographical distribution of available local and national groundwater monitoring/review studies (total = 103 publications between 2010 and 2020).**



monitoring or review studies are presented in Annex 4.3-4.<sup>6</sup>

The focus of this section is on pesticides in groundwater, as a source of drinking water. However, it should be emphasized that in some parts of the world, especially in Africa, East and Southeast Asia, surface water is (also) an important source of drinking water. Pesticides are commonly detected in surface water (Chapter 4.3.2) and the analysis of risk from pesticides through drinking water should not be limited to groundwater only.

The largest number of studies are available for Asia, followed by Europe and North America, while relatively few studies are available for the other continents (Figure 4.3.2-8). Within continents studies are not evenly distributed, with a few countries making up the bulk of available studies and many countries poorly or even not represented (Figure 4.3.2-9). For example, China and India account for 61 per cent of Asian studies, and in South America all available studies

are from Brazil and Argentina. For seven African countries a single study was found. There were two studies for South Africa. In Europe studies were available for 15 countries, with Spain having the highest number.

#### Global reviews

Only three recent global reviews of pesticides in groundwater were identified (Annex 4.3-4).

Pirsaheb *et al.* (2017) was the only available global review of the occurrence of OCPs in groundwater. Consistent with Figure 4.3.2-9, the authors noted that most studies had been conducted in Asian countries. OCP diversity and concentrations were generally lower than those of organophosphorus pesticides (OPPs) and concentrations in groundwater were lower than in surface waters. At the same time, many OCP concentrations above legal national limits were identified, especially in Asian countries.

Pesticides from the first and second EU Watch Lists were reviewed by Pietrzak *et al.* (2019). Neonicotinoids, especially imidacloprid, acetamiprid and thiamethoxam, were the most commonly monitored compounds. They were

<sup>6</sup> Annex 4.3-4 is found at: <https://www.unep.org/resources/report/environmental-and-health-impacts-pesticides-and-fertilizers-and-ways-minimizing>

found on almost every continent more than once at concentrations above EU legal drinking water limits. Only one study was available for pesticides from the Watch Lists other than neonicotinoids, which indicated an exceedance of the EU limit of 0.1 microgram/litre ( $\mu\text{g/L}$ ) (8  $\mu\text{g}$  oxadiazon/L in Italy).

A review by Postigo and Barceló (2015) concluded that pesticide transformation products (TPs) are not commonly included in monitoring studies. It noted that TPs from pesticides that are no longer locally registered, such as atrazine and terbuthylazine, were frequently detected. This was attributed to their long residence time in groundwater and/or the slow release of their precursors from the soil. Occasionally, pesticide TPs appear to be more ubiquitous and abundant than their parent molecules and to exceed EU limits.

#### Regional and national reviews

The regional review for Africa by K'oreje *et al.* (2020) confirms the low data availability for the continent (Figures 4.3.2-8 and 4.3.2-9). Although use of most organochlorine compounds (e.g., aldrin, DDT, dieldrin, endosulfan, endrin, heptachlor and lindane) has been discontinued in many African countries at different times since 1976, their recent high detections indicate their environmental persistence, their continuous

introduction into the environment, or weak enforcement of the ban. Moreover, in some countries (e.g., Kenya, South Africa) restricted use of DDT for malaria mosquito control is still allowed (K'oreje *et al.* 2020).

Several national reviews for India reveal high concentrations of HCHs and endosulfan isomers, as well as DDT metabolites, in groundwater (Yadav *et al.* 2015; Malyan *et al.* 2019; Sackaria and Elango 2019). Almost all reviewed studies indicate high groundwater concentrations (often to always  $> 0.1 \mu\text{g/L}$ ) throughout the country, especially during or shortly after the monsoon season. Since pesticide use in India is expected to increase, groundwater pollution in that country is also likely to increase in the future (Malyan *et al.* 2019).

In other parts of the world where OCPs have been banned, they frequently continue to be detected at low but often stable or only slowly decreasing levels (Annex 4.3-4). In the United States, Toccalino *et al.* (2014) reported increasing benchmark exceedances for dieldrin despite its having been banned for over 25 years, as well as increasing and frequent detections of pesticide TPs. Cattan *et al.* (2019) found that groundwater concentrations of the OCP chlordane decreased or remained stable between 2009 and 2015, but that its metabolite showed an increasing, although rather erratic, evolution overall (Figure 4.3.2-10).

► **Figure 4.3.2-10 Temporal trend in (A) chlordane (CLD) and (B) its metabolite chlordane-5b-hydro (5bCLD) between 2009 and 2015 in Chalvet (Martinique).** Cattan *et al.* (2019).



Besides slow release from soil, in which OCPs are very stable, high OCP groundwater levels have been attributed to dumping, illegal use and inappropriate storage (Eqani *et al.* 2012; Hasan, Shahriar and Jim 2019).

Three regional reviews of current use pesticides were identified. As in the case of POPs, the regional review for Africa by K'oreje *et al.* (2020) indicated that information for current use pesticides is scarce. The need for more information from the continent is underlined by the fact that groundwater concentrations of pesticides (other than OCPs) in Africa occur in the same order of magnitude as in Western countries (K'oreje *et al.* 2020). A regional review for French overseas departments (Guadeloupe, Martinique, Réunion, Mayotte and French Guiana) indicated that several pesticide concentrations exceeded the EU groundwater quality standard (Vulliet *et al.* 2014). Leusch *et al.* (2018) measured pesticide concentrations in drinking water in six countries in Europe, Africa and Oceania (France, Germany, the Netherlands, Spain, South Africa and Australia). None of the pesticides were detected in Germany, South Africa or Australia; individual pesticides were detected in other countries, but at concentrations below the EU drinking water standard of 0.1 µg/L.

In line with Leusch *et al.* (2018), a national study in Lebanon (Kouzayha *et al.* 2013) indicated pesticide concentrations in drinking water in the low nanogram (ng)/L range (maximum 20 ng/L). Routine monitoring data in the Netherlands collated by Sjerps *et al.* (2019), however, indicated that 15 of 24 recently authorized pesticides were detected, including neonicotinoids. In one-third of the abstraction areas pesticide and/or metabolite concentrations exceeded water quality standards according to the EU Water Framework Directive (EU 2000). In addition, while Leusch *et al.* (2018) did not detect any of these pesticides at the sites evaluated in South Africa, Odendaal *et al.* (2015) encountered atrazine and terbuthylazine in drinking water at concentrations > 0.1 µg/L in seven South African cities although WHO drinking water limits were not exceeded. Another local study in three catchments of South Africa (Machete and Shadung 2019) also detected several pesticides in drinking water. While most of these pesticides were detected at low concentrations, they included

(potentially) endocrine disrupting chemicals such as atrazine, alachlor and simazine.

Jurado *et al.* (2012) reported that Spanish groundwater was considerably less contaminated than other water bodies (e.g., rivers), although a wide array of compounds exceeded the EU limit of 0.1 µg/L. Two recent country-wide studies in China (Sun *et al.* 2020; Wang *et al.* 2020) also indicated higher herbicide concentrations in surface water than in groundwater. Concentrations in surface water derived tap water were higher than those detected in groundwater. However, there does not appear to be a clear consistent trend of higher concentrations in surface water than in groundwater. For example, Karki *et al.* (2020) found higher concentrations of the herbicides atrazine and bentazon in Swedish groundwater than in surface waters. Ultimately, the factors in Figure 4.3.2-7, in addition to treatment of received water in the case of drinking water, will determine pesticide concentrations in different water resources. Depending on these factors, pesticide detections range from undetected (i.e., < LOQ) to values that are clearly higher than the EU limit (Annex 4.3-4).

Overall, herbicides have generally been reported as the pesticide type with the most frequent detections, highest concentrations, and most frequent exceedances of regulatory limits (Close and Skinner 2012; McManus *et al.* 2014; Lopez *et al.* 2015). Close and Skinner (2012) indicated in their review for New Zealand that 17 of the 22 pesticides detected were herbicides. In France, Lopez *et al.* (2015) reported that detected pesticides in their country-wide monitoring campaigns were dominated by herbicides (68 per cent of sites), followed by fungicides (7.5 per cent) and insecticides (1.4 per cent). That might at least partly be due to the fact that herbicides appear to be included more frequently in monitoring studies (Annex 4.3-4). The 103 pesticides monitored in the study by Lopez *et al.* (2015) included 48 herbicides, 29 fungicides and 26 insecticides. The influence of research efforts may also be reflected in the detection of other pesticides. Jurado, Walther and Diaz-Cruz (2019) reported that imidacloprid was the only neonicotinoid detected in Spanish groundwater, but that other neonicotinoids were

the subject of only one or two studies. In their global review, Pietrzak *et al.* (2019) also indicated that neonicotinoids other than imidacloprid have hardly been studied in groundwater.

Temporal evaluations of groundwater pesticide concentrations have indicated stable (Close and Skinner 2012), decreasing (Köck-Schulmeyer *et al.* 2014) and increasing (Di Lorenzo *et al.* 2018) trends. Toccalino *et al.* (2014) reported a decrease in atrazine concentrations in the United States, but an increase in their TPs. Persistent pesticides such as atrazine, and especially their TPs, have consistently been detected in groundwater decades after their registration was discontinued due to their long residence time in the subsurface and/or the slow release of their precursors from the soil (Lopez *et al.* 2015 and references therein; Postigo and Barceló 2015; Karki *et al.* 2020). Differences in study designs (e.g., sampling and chemical analysis methods), locations and sampling dates make it difficult to establish national, let alone global, trends in groundwater pollution. Manamsa *et al.* (2016) concluded that the large monitoring dataset available for England and Wales (data for 2,650 sites from 2003 onwards) did not provide sufficient data for any compound for a single site to determine a trend.

#### Exceedances of drinking water standards

Annex 4.3-4 includes several studies that evaluated pesticide concentrations in drinking water at regional (Leusch *et al.* 2018; K'oreje *et al.* 2020) or national (Kouzayha *et al.* 2013; Odendaal *et al.* 2015; Karki *et al.* 2020; Sun *et al.* 2020, Wang *et al.* 2020) scales, covering studies conducted around the world (Australia, France, Germany, Lebanon, South Africa, Spain, Sweden, the Netherlands). Pesticide concentrations in many of these studies were reported in the low nanograms per litre (ng/L) range, with no human health risks expected at these exposure levels (Kouzayha *et al.* 2013; Leusch *et al.* 2018; Karki *et al.* 2020).

In their review of African studies, K'oreje *et al.* (2020) noted that in many African countries groundwater is generally used as drinking water without any treatment. They indicated that pesticides have been detected in groundwater in Ethiopia, Ghana, Kenya, Nigeria, South Africa and Zambia at concentrations

between 0.1 ng/L and 18.4 micrograms per litre ( $\mu\text{g/L}$ ). Pesticides were also detected in treated drinking water in Algeria, Ethiopia, Nigeria and South Africa, with concentrations ranging from 0.02 ng/L to 34  $\mu\text{g/L}$  (K'oreje *et al.* 2020).

Odendaal *et al.* (2015) conducted a national survey over four seasons of potential compounds of emerging concern, including pesticides, in the drinking water of major South African cities. The herbicides atrazine and terbuthylazine were most frequently detected, although concentrations were at least one order of magnitude lower than the guideline values set by the United States Environmental Protection Agency (US EPA) and the WHO. For example, maximum atrazine concentrations were between 150 and 200 ng/L, whereas the proposed WHO guideline value is 100  $\mu\text{g/L}$  and the maximum contaminant level stipulated by US EPA is 3  $\mu\text{g/L}$  (Odendaal *et al.* 2015). The European Drinking Water Directive, however, establishes a drinking water standard of 0.1  $\mu\text{g/L}$  for each individual pesticide and its toxicologically relevant metabolites, with the exception of aldrin, dieldrin, heptachlor and heptachlor epoxide (for which a quality standard of 0.03  $\mu\text{g/L}$  applies) (European Union 1998; European Union 2020a). Thus the maximum atrazine concentrations encountered by Odendaal *et al.* (2015) exceed the EU quality standards, but not those of US EPA and WHO.

Wang *et al.* (2020) discuss a similar situation in China: while maximum atrazine drinking water concentrations were well below the country's national quality standard and those set by Health Canada, US EPA and WHO, they exceeded the European standard of 0.1  $\mu\text{g/L}$ . The same conclusion was reached by Sun *et al.* (2020) in their country-wide study on drinking water concentrations of the herbicides 2,4-D and MCPA in China. This wide difference between the EU standard and others (e.g., those of US EPA and WHO) is related to the different approaches followed in setting these standards. The EU drinking water standard, which was set in the 1980s, followed the precautionary principle and corresponded to the contemporary detection limit for pesticides. On the other hand, the US EPA and WHO standards are health-based and calculated based on toxicity data.



### 4.3.3 Sustainability of agricultural production and vector control

Various adverse environmental effects of pesticide use may have a direct or indirect impact on the sustainability of agricultural production or of disease vector control. Rather than increasing production or reducing disease vector populations, pesticide use can have the opposite effect, with mid- and long-term effects on agriculture and public health. Such adverse effects include:

- development of resistance of pest organisms or disease vectors against pesticides;
- impact on bees and other pollinators and possible reduction of crop pollination;
- impact on natural enemies of pests, and possible pest resurgence or appearance of secondary pests;
- effects on soil organisms and possible reduction of soil fertility.

These unintended effects of pesticides on resistance development, pollinators and natural enemies are discussed in more detail below. Effects of pesticides on soil organisms are reviewed in Chapter 4.3.4.

#### Resistance

The development of resistance against pesticides in arthropods, diseases, weeds and rodents is an important agronomic, economic, ecological and public health problem throughout the world. Resistance development occurs when the genetic makeup of a pest population changes in response to selection by pesticides. This, in turn, may lead to repeated failure of a pesticide to achieve the expected level of control when used according to the label recommendation for that pest species.

As a response to the development of resistance, farmers often increase the dose and/or frequency of pesticide applications, which in turn may lead to greater resistance in the pest populations, encouraging greater pesticide use. Consequently, agricultural production becomes more expensive or even economically unviable; adverse health

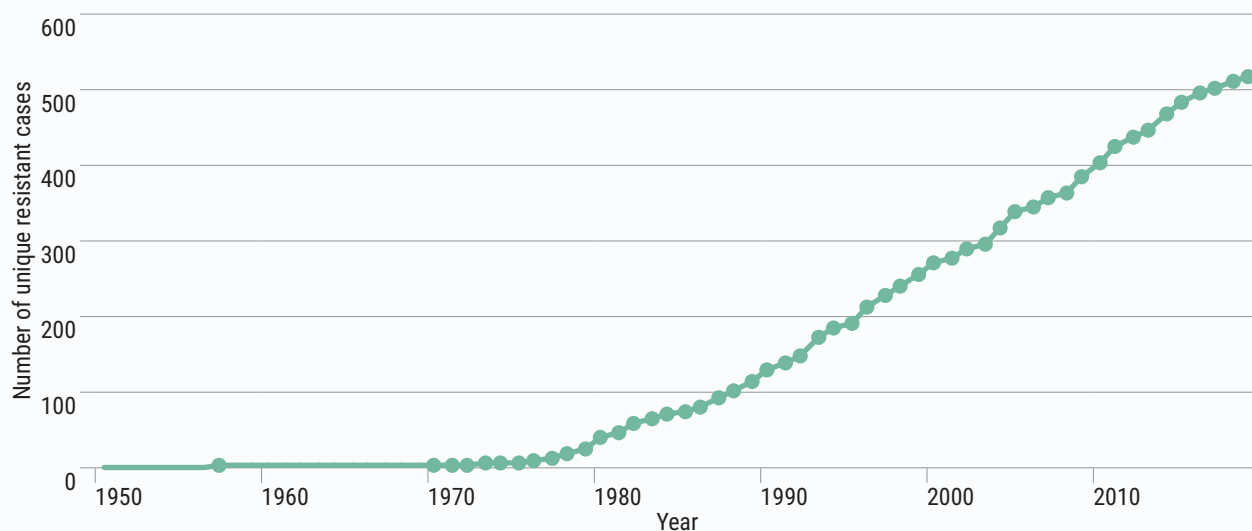
effects increase; pesticide residues in crops exceed acceptable standards; and environmental impact expands. In terms of public health (e.g., combatting malaria), resistance development may lead to a breakdown in vector control and an increase in the prevalence of a disease. Alternatively, to break resistance farmers and public health entities will need to change the type of pesticide used to one with a different mode of action or move completely away from chemical pesticides, replacing them with biological control. This may require a change in crop production or vector control methods and may increase costs (FAO 2012).

#### Herbicide resistance

By mid-2019 there were 502 unique cases of herbicide resistant weeds globally, comprising 258 different weed species (Heap 2019). Weeds have evolved resistance to 23 of the 26 known herbicide modes of action and to 167 different herbicides. Herbicide resistant weeds have been reported in 93 crops from 70 countries. The number of cases of herbicide resistance has been growing steadily since the early 1970s (Figure 4.3.3-1). Globally, during the last 30 years on average 13 new cases have been reported every year, irrespective of the introduction of new herbicides or herbicide resistance management programmes.

Herbicide resistance leads to very serious agronomic, economic and environmental challenges. A well-known case is the failure of ryegrass control as a result of herbicide resistance in Australia. For more than 20 years Australia was known for having the most serious cases of herbicide resistance in the world. Certain herbicides considered essential for farmers' cropping systems can no longer be used due to resistance, and in major cropping areas all ryegrass has become resistant to selective herbicides (Pannell *et al.* 2016). Alternative herbicides have had only a limited effective life, as ryegrass has been able to rapidly develop resistance to these chemicals as well. Alternative weed management options have had to be developed, such as new methods to capture and destroy weed seeds at harvest time, although at greatly increased costs (Stokstad 2013; Pannell *et al.* 2016).

► **Figure 4.3.3-1 Global increase of unique cases of herbicide resistance. A unique case is a weed species combined with a herbicide mode of action.** Heap (2019).



Similar problems in managing herbicide resistant weeds exist in all countries where chemical herbicides are used on a large scale. While farmers have often relied on applying new herbicides with new modes of action, no such new types of herbicide have been commercially developed in decades and there do not seem to be any “silver bullets” on the way (Pannell et al. 2016).

### Insecticide resistance

The first case of insecticide resistance occurred more than 100 years ago, when in 1913 the San Jose scale was found to resist sprays of sulphur in fruit trees in the United States (Whalon 2008). Since the 1960s the use of organic insecticides has taken off and arthropod resistance has been increasing steadily, with no sign of tapering off (Figure 4.3.3-2).

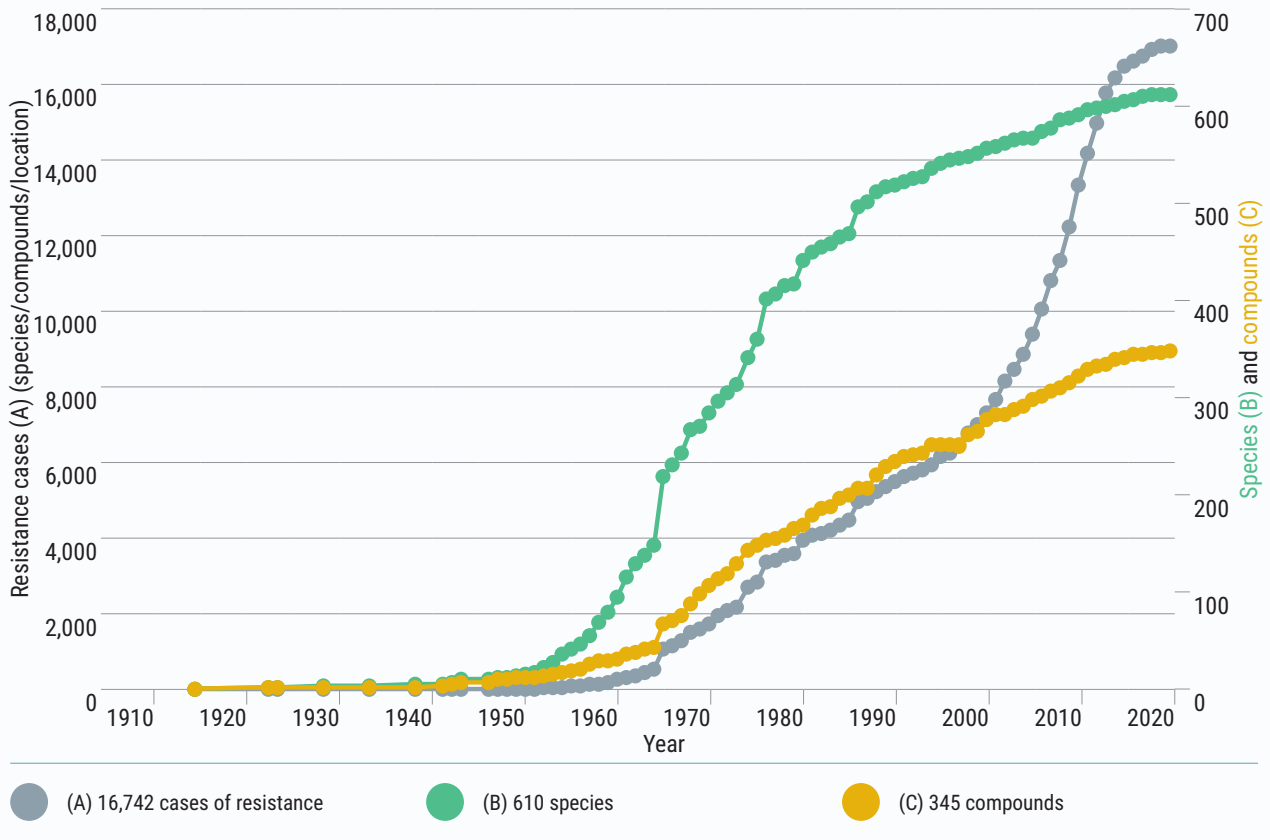
By late 2019 almost 17,000 cases of arthropod resistance to 345 different pesticides had been reported globally, representing more than 600 species of insects and mites. Of these, almost 14,000 cases of resistance against 587 species were field-evolved, i.e., the result of pesticide use under actual field conditions rather than in the laboratory (Mota-Sanchez and Wise 2019; Mota-Sanchez, R., personal communication).

The speed of development of arthropod resistance mainly depends on the species and is less

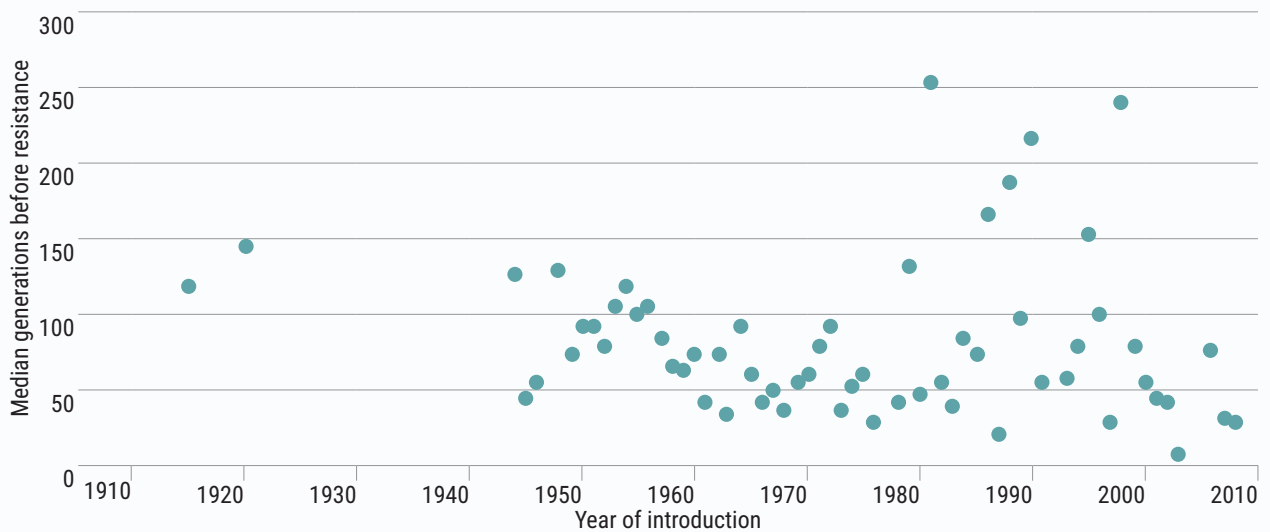
influenced by the pesticide’s mode of action (Brevik et al. 2018). However, more resistant species do not develop resistance faster than less resistant ones. On average, in 20 studied species of insects and mites, the median duration between the introduction of an insecticide and the first report of resistance was 66 generations or about 14 years. Importantly, the year of first introduction of a pesticide does not seem to influence the speed with which arthropods become resistant (Brevik et al. 2018) (Figure 4.3.3-3). This suggests that insecticide and acaricide resistance management programmes, which have been developed and implemented over several decades, do not appear to have significantly reduced the speed of insecticide resistance development.

Insecticide resistance is of particular concern for the control of disease vectors such as mosquitos or sandflies. In a recent evaluation, WHO (2020a) reported that pyrethroid resistance had been confirmed in major malaria vectors in 77 per cent of countries that conducted monitoring. In 37 countries at least one malaria vector species was resistant to three or four different classes of insecticides used in indoor residual spraying (Figure 4.3.3-4). Pyrethroid resistance in malaria mosquitos increased significantly between 2010 and 2016. Since pyrethroid insecticides are the only class of insecticides available to treat bed nets in many

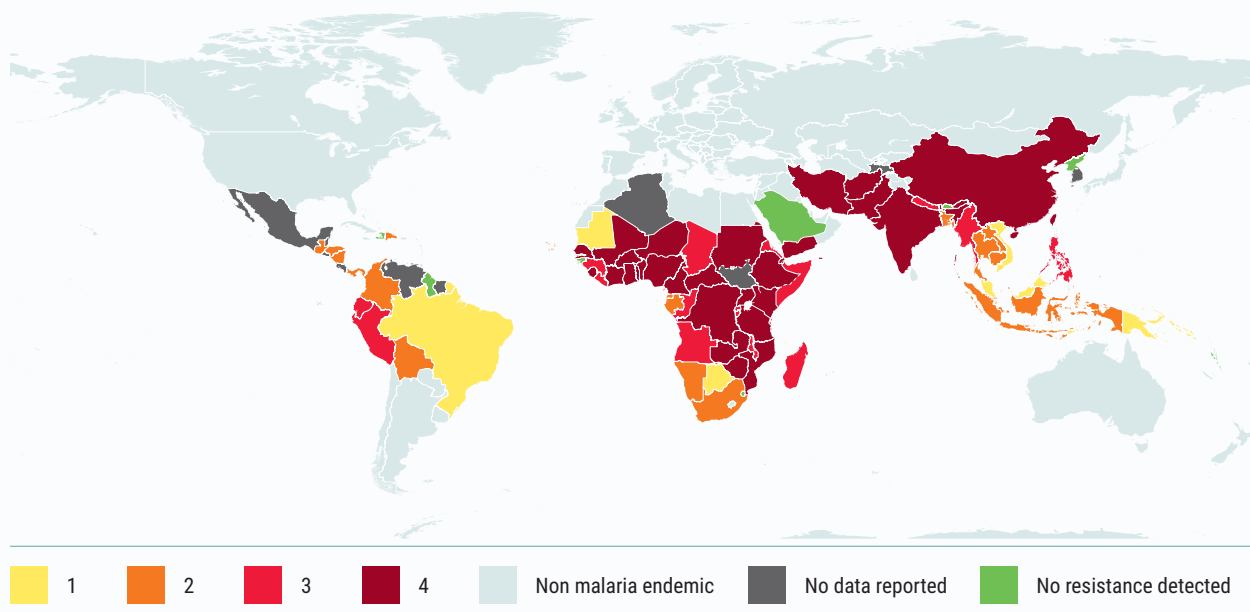
► **Figure 4.3.3-2** The evolution of pesticide resistance in arthropods shows a steady increase in the number of species, pesticide compounds and cases from 1914 to 2019. Mota-Sanchez and Wise (2019), Mota-Sanchez pers. comm.



► **Figure 4.3.3-3** Arthropods were becoming resistant to a pesticide as rapidly in 2010 as in the 1960s, indicating that there had not been a change in the “durability” of a pesticide over time. No significant relation was observed between the number of generations it takes for an arthropod to become resistant and the year of introduction of a pesticide. Brevik *et al.* (2018).



► **Figure 4.3.3-4 Number of classes to which resistance was confirmed in at least one malaria vector in at least one monitoring site, 2010–2019.** WHO (2020).



countries, widespread pyrethroid resistance, particularly in Africa, is a serious problem for effective malaria vector control (Ranson and Lissenden 2016).

Vector resistance to insecticides is not limited to malaria mosquitos. It is also found in other vectors of human disease. Dhiman and Yadav (2016) reviewed resistance in phlebotomine sandflies, which are vectors of visceral leishmaniasis (kala-azar). They found widespread resistance against DDT and local resistance against pyrethroids in areas of the Indian subcontinent where the disease is prevalent. A recent survey in North America also showed pyrethroid resistance to be widespread in Florida (United States) in *Aedes aegypti*, the mosquito vector of the Zika virus (Estep *et al.* 2018). Guedes *et al.* (2020) found a high prevalence of insecticide resistance of the same species in Latin America and the Caribbean.

#### Fungicide resistance

Fungicides have been used in agriculture for well over a century, but the earliest documented cases of fungicide resistance date from the 1960s. Overall, instances of confirmed resistance to fungicides remained rare until the 1970s, when novel classes of antifungal pesticides

were introduced and became widely used (Lucas, Hawkins and Fraaije 2015). Since then there has been an ever-increasing incidence of reported resistance cases in a wide range of plant pathogenic fungi (Table 4.3.3-1).

#### Genetically modified crops

Resistance development in genetically modified crops has focused on herbicide tolerant and insect resistant crops. In the former, weed resistance develops against herbicides applied to a crop; in the latter, insects become resistant to a pesticide incorporated in a crop.

The most successful insect resistant transgenic crops produce insecticidal proteins from the bacteria *Bacillus thuringiensis* (Bt). Increasingly, more than one toxin is built into the crop ("Bt crop pyramids") to increase efficacy and delay resistance. Tabashnik and Carrière (2017; 2019) recently reviewed 44 studies, from 12 countries on six continents, on the development of field-evolved insect pest resistance to transgenic crops. In 19 cases no decrease in susceptibility to Bt toxins was observed, in six cases there were early warning signs of the development of resistance, and in 19 cases practical resistance had evolved. The efficacy of the Bt crop in controlling insects

**Table 4.3.3-1 Time line of fungicide resistance in crop diseases for some major fungicide classes.** Lucas, Hawkins and Fraaije (2015).

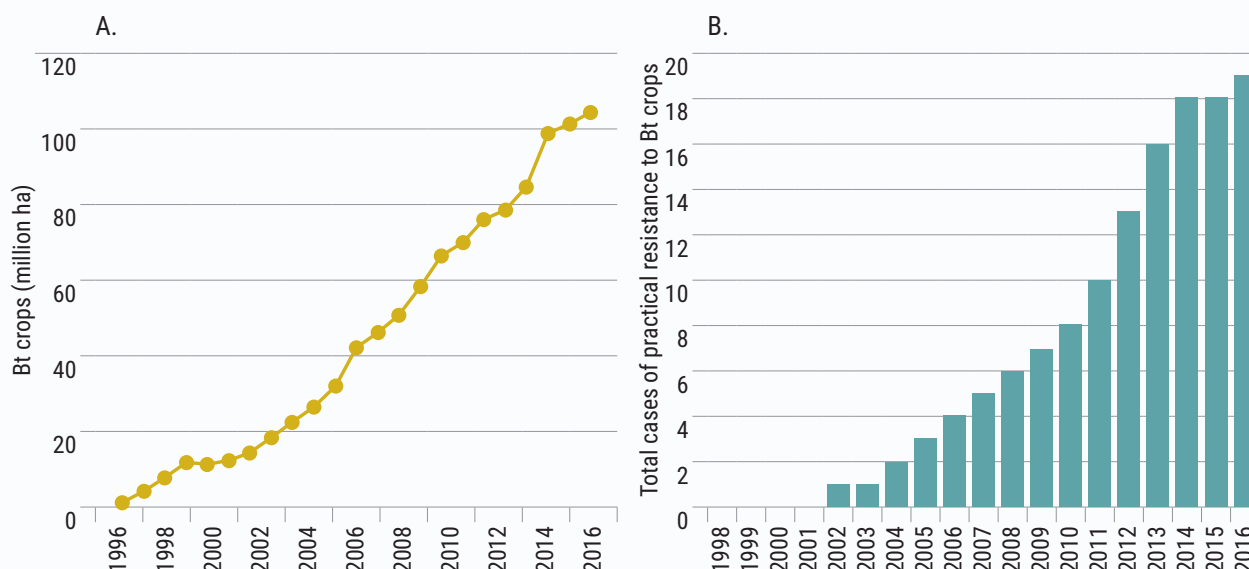
Period of introduction	Fungicide class	Approximate time to resistance (years)	Disease example
1960	Aromatic hydrocarbons	20	Citrus storage rots ( <i>Penicillium</i> spp.)
1964	Organomercury compounds	40	Cereal leaf spot ( <i>Pyrenophora</i> spp.)
1969	Dodine (guanidine) compounds	10	Apple scab ( <i>Venturia inaequalis</i> )
1970	Benzimidazoles	2	Many pathogens
1971	2-Aminopyrimidines	2	Powdery mildews
1980	Phenylamines	2	Potato late blight, grape downy mildew
1982	Demethylation inhibitors	7	Cereal powdery mildew and other diseases
1998	Quinone outside inhibitors	2	Cereal powdery mildew
2007	Succinate dehydrogenase inhibitors	4–5	<i>Alternaria alternata</i> (in nuts), potato early blight ( <i>Alternaria solani</i> )

was therefore reduced in 43 per cent of reports. In some cases (e.g., the Western corn rootworm in maize in the United States and the pink bollworm in cotton in India) effective alternative Bt transgenic crops were no longer available, while for the fall armyworm, which is spreading rapidly across the world, only half of Bt maize crop varieties in Brazil were still effective (Tabashnik and Carrière 2017). Although there has been an initial delay in the development of resistance following the introduction of Bt crops, there has

been a surge in new cases since the early 2000s (Figure 4.3.3-5).

Strict resistance management in Bt crops has been implemented, and is even mandatory, in some countries. The most widely applied approach is the high-dose refuge strategy, which combines high doses of the Bt toxins in the crop with growing a non-Bt crop on a certain fraction of the area (the “refuge”). This approach has been successful in delaying resistance

**Figure 4.3.3-5 Global trend in pest resistance to Bt crops: (A) hectares planted with Bt crops (B) cumulative cases of field-evolved practical resistance to Bt crops.** Tabashnik and Carrière (2017).



development. Many cases of pest resistance breaking down appear to have occurred where either refuge areas or toxin concentrations were insufficient (Huang, Andow and Buschman 2011; Tabashnik and Carrière 2017; Tabashnik and Carrière 2019). However, a recent review of resistance development of the fall armyworm (*Spodoptera frugiperda*) in Bt corn in the Americas suggests that current resistance management has been insufficient to avoid widespread development of resistance in this global pest (Huang 2020).

In contrast to the relatively regulated use of insect resistance, herbicide resistance has greatly increased with the adoption of herbicide resistant crops. The continuous use of glyphosate on glyphosate-tolerant crops in the United States quickly led to selection for weeds with evolved resistance to glyphosate (National Academies of Science, Engineering and Medicine 2016). More than 40 weed species are now reported to be resistant against glyphosate; many of them evolved in fields where herbicide resistant crops were grown (Heap 2019). To respond to this problem, companies have re-engineered crops to be tolerant to other herbicides, such as 2,4-D and dicamba, which have different modes of action to glyphosate. These herbicides were first commercialized in 1945 and 1967, respectively. It has been argued that there is a lack of knowledge about how to use these herbicides while avoiding the emergence of resistance (Gould, Brown and Kuzma 2018). The expected heavy use of 2,4-D and dicamba in herbicide resistant crops is likely to result in the development of further widespread weed resistance.

Only a few disease-resistant transgenic plant varieties have been commercially released (International Service for the Acquisition of Agri-Biotech Applications 2019). Limited experience therefore exists with diseases breaking the resistance of transgenic crops, and maintaining the durability of such disease resistance is likely to be a challenge (Nelson *et al.* 2018).

### The impact of resistance development

Pesticide resistance in arthropods has repeatedly led to severe pest management problems,

large increases in insecticide use, and even the total collapse of certain cultures. Examples from the past of pesticide resistance inhibiting crop growing include cotton production in Mexico (tobacco budworm) and Sudan (tobacco whitefly), rice in Southeast Asia (various pests) and vegetables in Asia and Africa (diamondback moth).

Glyphosate resistant weeds cost corn, cotton and soybean growers in the United States more than USD 1 billion per year (Frisvold, Bagavathiannan and Norsworthy 2017). Direct economic losses due to all types of resistance development have been estimated at USD 10 billion in that country alone (Gould, Brown and Kuzma 2018). It has also been calculated that pyrethroid resistance in mosquito vectors of malaria would imply about 26 million additional clinical cases of malaria per year in Sub-Saharan Africa (Gould, Brown and Kuzma 2018).

Nevertheless, the direct and indirect costs of resistance development, as well as its prevention, are rarely estimated in a systematic way when new pesticides are introduced or authorized.

### The effects of pesticides on pollinators

Pollination is an ecosystem function that is fundamental to plant reproduction, agricultural production, and the maintenance of terrestrial biodiversity. Most of the world's wild flowering plants (about 88 per cent) are pollinated by insects and other animals. It is estimated that about one-third of the global food volume produced benefits from animal pollination (Eardley *et al.* 2016). The global annual market value of additional crop production directly linked to pollination services is estimated to be USD 235-577 billion (Gallai *et al.* 2016).

Pollinators can be found in different groups of animals, but are dominated by insects. Although pollinators are mainly bees, they also include some species of flies, wasps, butterflies, moths, beetles, weevils, thrips, ants, midges, bats, birds, primates, marsupials, rodents and reptiles. Nearly all bee species are pollinators, while a smaller (and variable) proportion of species within the other taxa are pollinators (Eardley *et al.* 2016).

By far most of the information about the adverse effects of pesticides on pollinators – resulting from controlled laboratory and (semi-) field experiments, as well as from monitoring – address honeybees. Increasingly, data are also being generated on other managed bees and on wild bees. Adverse pesticide effects on the other pollinators (e.g., flies, butterflies or bats) are not much studied, but information may be available from more general monitoring of such groups. The chapter below focuses on bees.

### Susceptibility of bees to pesticides

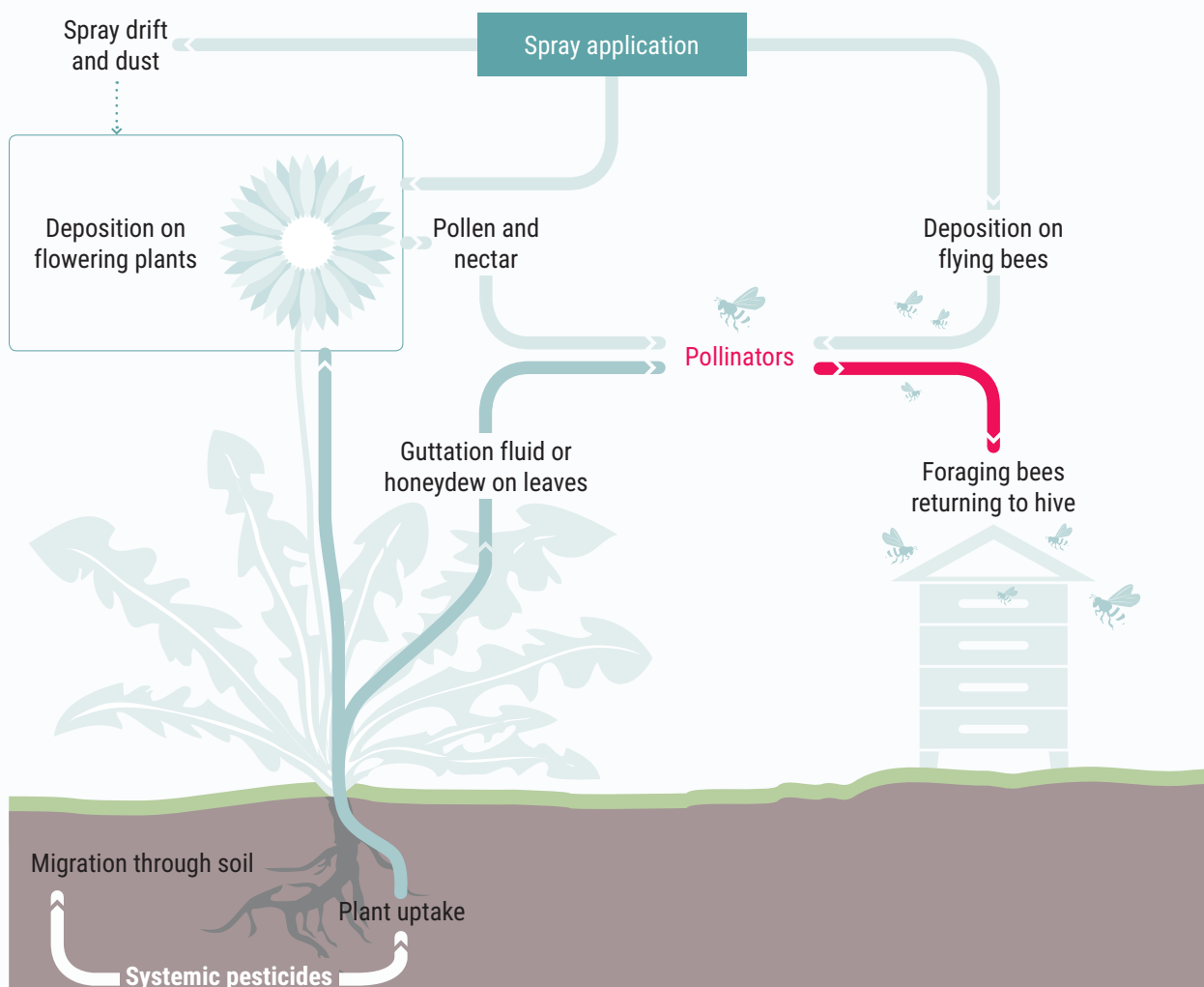
Pesticides vary widely in their toxicity to bees. Some cause high acute mortality at very low doses, while others can be applied to crops without much adverse effect. Most insecticides

are moderately or highly toxic to bees. However, other groups of pesticides (e.g., fungicides and herbicides) may also exert negative effects on bee health.

Bees can be exposed to pesticides in various ways, including overspraying, ingestion of contaminated pollen, nectar or honeydew, and contact with residues on foliage or flowers (Figure 4.3.3-6).

The direct adverse effects of pesticides on bees can be lethal (e.g., acute mortality immediately after applying a pesticides) or sublethal (e.g., reduced reproduction, increased susceptibility to pathogens, effects on learning or foraging by bees). Indirect effects of pesticides can occur if, for example, the use of herbicides

► **Figure 4.3.3-6 Main routes of exposure of honeybees to pesticides; similar routes of exposure are likely for other bees.** Kovács-Hostyánszki *et al.* (2016).



eliminates weeds in a crop which is important for bee foraging (Kovács-Hostyánszki *et al.* 2016).

### Adverse effects of pesticide use on bees

The most recent comprehensive assessment of the adverse effects of pesticides on pollinators in general, and bees in particular, was conducted under the auspices of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services (IPBES) (Potts, Imperatriz-Fonseca and Ngo 2016). The conclusions of the IPBES assessment report are summarized below, complemented by more recent information when available.

Pesticides, notably insecticides, have shown a broad range of lethal and sublethal effects on bees in controlled experimental conditions (Kovács-Hostyánszki *et al.* 2016). The extent to which such adverse effects result in impairment of honeybee and bumblebee vitality or wild bee populations has been the object of much research, more recently for neonicotinoid insecticides in particular.

There is no doubt that the operational use of certain insecticides has caused acute bee mortality. Most data on acute pesticide effects under field conditions come from incident monitoring schemes in a number of European countries, Canada, the United States, Australia and Japan. They are almost entirely limited to the mortality of honeybees. Few incident reports exist for bumblebees or wild bees. The number of pesticide-induced incidents in Germany, the Netherlands and the United Kingdom, where such schemes are long-running, dropped by more than 75 per cent between the 1980s and the mid-2000s (Kovács-Hostyánszki *et al.* 2016). Reporting from Canada on the period 2007-2012 suggests that moderate and major bee poisoning incidents are also relatively rare (Cutler, Scott-Dupree and Drexler 2014). An exception is cases of dust drift during the drilling of seeds coated with neonicotinoid insecticides, which caused bee kills in Europe and North America in the late 2000s (Nuyttens *et al.* 2013).

The majority of incidents reported in Europe appear to have occurred when farmers did not

use insecticides according to the instructions on the label (e.g., mistakenly applying the product on flowering crops, or while flowering weeds were present in the field). Better information, regulation and enforcement in these countries would probably have reduced the number of bee kill incidents. That suggests that in countries that do not have incident monitoring systems, or where there are no effective regulations or enforcement of mitigation measures, incidents of insecticide-associated honeybee mortality are likely to occur more regularly (Kovács-Hostyánszki *et al.* 2016). However, data to support this are lacking.

The IPBES assessment report evaluated nine published reviews of sublethal effects of pesticides on bees, three of which addressed pesticides in general and six the effects of neonicotinoid insecticides (the most recent reviews in the latter group were Godfray *et al.* 2015 and Pisa *et al.* 2015). Although the nine reviews overlapped in terms of the research included, their conclusions varied. There was agreement on the significant evidence for the adverse sublethal effects of neonicotinoids under controlled conditions. However, there were divergent views on the effects of pesticides under real-use field conditions, focusing on what constitute field-realistic doses of these insecticides that would lead to adverse effects on bees.

Kovács-Hostyánszki *et al.* (2016) therefore concluded in the IPBES assessment that how sublethal effects of pesticide exposure recorded for individual insects affect colonies and populations of managed bees and wild pollinators, especially over the longer term, was currently unresolved. The few available field studies assessing the effects of field realistic exposure provide conflicting evidence of effects, based on the species studied and pesticide used.

After the IPBES assessment report was published in 2016, Wood and Goulson (2017) reviewed evidence for environmental risks of neonicotinoids published between 2013 and 2016 (partly overlapping with the IPBES review). Their conclusions largely correspond to those of the IPBES assessment. However, the authors stated that new studies have provided stronger



indications of adverse effects of field-realistic doses of neonicotinoids on foraging behaviour, reproductive output and colony growth of bumblebees, as well as effects on reproduction of solitary bees.

More recently, the results of a number of field studies on the effects of neonicotinoids on bees were published (Table 4.3.3-2). These studies do not seem to fundamentally

change the conclusions of Kovács-Hostyánszki *et al.* (2016) and Wood and Goulson (2017). Honeybee colony viability has been shown to be affected in some cases, but not in others. Field studies have shown varying effects of neonicotinoids on population parameters of wild bees. It remains ambiguous under which circumstances neonicotinoid insecticides adversely affect honeybee or wild bee populations in the field.

**Table 4.3.3-2 Large-scale field studies on the effects on bees of seed treatments with neonicotinoids, not included in the review by Wood and Goulson (2017).**

Country	Insecticide	Bee species	Crop	Observed effects	Reference
Germany	clothianidin + beta-cyfluthrin	Mason bee ( <i>Osmia bicornis</i> )	Oilseed rape	No detrimental effects on the development or reproduction of mason bees was observed.	Peters, Gao and Zumkier (2016)
Hungary, Germany, United Kingdom	clothianidin, thiamethoxam	Honeybee ( <i>Apis mellifera</i> ) Bumble bee ( <i>Bombus terrestris</i> ) Mason bee ( <i>Osmia bicornis</i> )	Oilseed rape	Honeybees: Both negative (Hungary and the United Kingdom) and positive (Germany) effects on colony viability were observed. In Hungary negative effects on honeybees (associated with clothianidin) persisted over winter and resulted in smaller colonies in the following spring (24 per cent declines). Bumble bees and mason bees: Reproduction was negatively correlated with neonicotinoid residues.	Woodcock <i>et al.</i> (2017)
France, Germany	thiamethoxam	Mason bee ( <i>Osmia bicornis</i> )	Oilseed rape	Field and tunnel experiments. There were no significant effects from exposure to oilseed rape grown from thiamethoxam-treated seed from nest establishment through cell production to emergence under tunnel or field conditions. Oilseed rape contributed only 4 to 31 per cent of pollen provisions in the present study.	Ruddle <i>et al.</i> (2018)
Sweden	clothianidin	Honeybee ( <i>Apis mellifera</i> )	Oilseed rape	Large fluctuations between and within years were found in honeybee colony development, (attempted) swarming/supersedure, colony mortality, microbial composition and Varroa infestation. However, no negative effects of placement at the clothianidin-treated fields on these parameters were identified.	Osterman <i>et al.</i> (2019)
United States	acetamiprid, clothianidin, dinotefuran, imidacloprid, thiacloprid, thiamethoxam	Wild bees in field margins	Maize, soybean	Bee abundance was not affected by neonicotinoid insecticide concentrations in field margin soils. Neonicotinoid concentrations in margin soils were negatively associated with native bee richness.	Main <i>et al.</i> (2020)

The European Food Safety Authority (EFSA 2018b; EFSA 2018c; EFSA 2018d) conducted extensive regulatory reviews of the risks to honeybees, bumblebees and wild bees of seed and soil treatments with the neonicotinoid insecticides clothianidin, imidacloprid and thiamethoxam. They took into account laboratory studies, semi-field and field experiments, as well as monitoring results. EFSA concluded, for all three insecticides, that high risks exist to most or all groups of bees, and that low risks could not be excluded. Low risks were generally only concluded to exist for honeybees in certain specific crops. These risk assessments were an important reason the EU subsequently prohibited all uses of these insecticides except in greenhouses.

Weeds provide important, often exclusive, foraging resources for pollinators in agricultural landscapes. Their removal by physical means (e.g., tillage, mechanical weeding) or chemical herbicides can cause declines of native pollinators in agroecosystems (Kovács-Hostyánszki *et al.* 2016).

### Pollinator declines and pesticides

There is no clear evidence that pesticides, particularly the neonicotinoid insecticides, have directly contributed to longer-term colony losses in the EU or the United States. Some studies have highlighted fungicides as affecting honeybee health adversely, but their role in colony loss has not yet been demonstrated. Colony loss appears to be a multifactorial issue, with different drivers varying in space and time (Kovács-Hostyánszki *et al.* 2016).

Few studies provide clear links between pesticide use and pollinator declines. Woodcock *et al.* (2016) conducted a correlational study in the United Kingdom which showed a positive association between use of neonicotinoid seed treatments in oilseed rape and reduced persistence of wild bee populations. This negative correlation was not observed for the application of foliar insecticides.

The IPBES assessment concluded that changes in land use or climate, intensive agricultural management and pesticide use, invasive alien species and pathogens can all affect pollinator health, abundance, diversity and pollination.

Moreover, these multiple direct drivers have the potential to combine, synergistically or additively, leading to an overall increase in pressure on pollinators and pollination. It is rarely possible to rule out a single cause, such as pesticides, for changes in pollinator populations. A complex interplay of factors is likely to affect pollinator biodiversity and pollination, but the exact combination of factors will vary in space, time and across pollinator species (Kovács-Hostyánszki *et al.* 2016).

### Natural enemies of pests

Natural enemies of crop pests or disease vectors include arthropod predators and parasitoids, as well as vertebrate predators such as insectivorous birds and reptiles. Pathogens (e.g., bacteria, fungi) can also attack pest populations. Natural enemies will often keep pest populations below levels that cause crop losses.

The greatest amount of information is available on the effects of pesticides on arthropod natural enemies. A pesticide treatment may control the pest population, but can also kill, repel, irritate or otherwise deter the natural enemies of that pest (Croft 1990; Cloyd 2012; Roubos, Rodriguez-Saona and Isaacs 2014). If the residual activity of the insecticide then expires, the same pest population will be able to increase more rapidly and to a higher abundance than when natural enemies were present. This is called target pest resurgence (Dutcher 2007).

A crop may contain other potentially injurious organisms which are normally harmless because they are kept in check by natural enemies. Secondary pest development can occur when a pesticide treatment causes the destruction of natural enemies of such organisms, which was regulated below an economic injury level by the natural enemies. The secondary pest will then be elevated to primary pest status (Dutcher 2007).

Resurgence and secondary pest development may not always be caused solely by the removal of natural enemies. Pesticide treatments can cause changes in a pests' behaviour, dispersal, development and fecundity, leading to an increase in pest populations (Dutcher 2007; Wu *et al.* 2020).

Resurgence and secondary pest development have various adverse consequences, including an increase in crop damage and potential yield losses; greater disease vector populations, resulting in possible rise of disease transmission and prevalence; disruption of biological control programmes; higher costs of pest management for additional or more expensive alternative chemical control or for alternative biological control; and an increase in pest abundance that carries over to the next growing season (Dutcher 2007).

### Toxicity of pesticides to natural enemies

Until the mid-1960s observations of the effects of pesticides on natural enemies of crop pests tended to be incidental and generally part of pesticide efficacy trials. Studies on natural enemy responses to pesticides became more specific and were greatly expanded in the 1970s and 1980s, coinciding with the development of integrated pest management (IPM) as the recommended pest management approach in many countries (Croft 1990). Research on both the lethal and sub-lethal effects of pesticides on beneficial arthropods, as well as on the influence pesticides may have on pest and natural enemy interactions and population dynamics, have been conducted ever since. Regulatory testing of pesticides on natural enemies has also become part of the pesticide registration process, although this is limited mainly to Europe (Alix *et al.* 2012).

Given the importance of natural enemies for pest control and their susceptibility to many types of pesticides, the toxicity and selectivity of these products has been evaluated for a long time. In the mid-1980s Oregon State University (United States) established the SELCTV Database which, at the time, contained more than 12,000 records of pesticide effects on natural enemies (Croft and Theiling 1990). A decade earlier the Working Group on Pesticides and Beneficial Arthropods of the International Organization for Biological and Integrated Control (IOBC) started a joint testing programme in Europe on pesticides and beneficial arthropods (Franz *et al.* 1980). That work resulted in an on-line database on the selectivity of pesticides which includes both regulatory and academic information (Jansen 2013; International Organization for Biological

and Integrated Control – West Palearctic Regional Section [IOBC] 2019). The IOBC database demonstrates that insecticides and acaricides are the most hazardous to arthropod natural enemies, but other groups of pesticides are not without risk. While some of the newer groups of insecticides are more target-specific and less hazardous for many arthropod natural enemies (e.g., diacylhydrazines, sulfloximines), this is not the case for all (e.g., neonicotinoids, diamides).

### Biocontrol affected by pesticides

Pesticides have been widely studied and shown to have negative effects on natural enemy populations in many circumstances (Rusch *et al.* 2010). Many individual cases of pesticide-induced declines in biocontrol continue to be reported, as illustrated by the examples below.

Geiger *et al.* (2010) conducted a study in eight European countries on 270 cereal farms. They investigated the effects of 13 components of agricultural intensification on biodiversity, as well as on the potential for biological pest control of aphids. The use of insecticides adversely affected the potential for biocontrol of aphids in a consistent manner. Agro-environmental schemes using smaller amounts of pesticides had positive effects on biocontrol, but (somewhat surprisingly) this was not the case for organic farms.

Krauss, Gallenberger and Steffan-Dewenter (2011) compared aphid and predator densities in conventional versus organic triticale fields. They found that the abundance of cereal aphids was five times lower in organic fields, while their predator abundances were three times higher and predator-prey ratios were 20 times higher in organic fields, indicating a significantly higher potential for biological pest control in organic fields. Preventative insecticide application in conventional fields had only short-term effects on aphid densities, but long-term negative effects on biological pest control.

Ricci *et al.* (2019) conducted a large-scale study in three consecutive years in 80 fields of perennial and annual crops located in four French regions. They found that pesticide use intensity at local field level had clear negative effects on the

predation rates of pest insects. They suggested that the predation activity of a wide range of natural enemies (feeding on pests on the soil surface and on crop plants) was reduced when pesticide pressure was high.

Dainese *et al.* (2019) carried out a global synthesis of studies which measured richness and abundance of pollinators, pest natural enemies, and associated ecosystem services. They found clear evidence that the species richness of these organisms, as well as their abundance, positively influenced the delivery of ecosystem services such as pollination and pest control. They also found a positive correlation between natural enemy richness and crop production in areas not sprayed with insecticides. This link was not observed in sprayed areas, indicating that insecticide use undermines the full potential of natural pest control.

### Resurgence and secondary pest development due to pesticides

In a first review on the topic, Ripper (1956) found that pesticide-induced resurgences in the field had been recorded in temperate, sub-tropical and tropical climates for over 50 species of phytophagous arthropod pests almost immediately after the introduction of broad-spectrum synthetic pesticides.

Examples of target pest resurgence and secondary pest development which have caused major agronomic and economic problems include: early season applications of pyrethroid and organophosphate insecticides, leading to resurgence of bollworm in the United States (Dutcher 2007); application of insecticides to rice, leading to outbreaks of brown plant hopper in Asia (Wu *et al.* 2020); and applications of non-selective insecticides such as pyrethroids, which greatly increased populations of diamondback moth, a major pest of cabbages and other brassica crops

**Table 4.3.3-3 Examples of pest resurgence or secondary pest development induced by the use of pesticides.**

Crop	Resurgent or secondary pest	Description	Reference
Cotton (United States)	Cotton bollworm ( <i>Helicoverpa armigera</i> )	Early season applications with pyrethroids led to a resurgence of bollworm.	Dutcher (2007)
Cotton (United States)	Aphids, mites, armyworms	Early season application against <i>Lygus</i> plant bugs resulted in a 25 per cent increase in late season pesticide costs to control secondary pests.	Gross and Rosenheim (2011)
Cabbage and other brassicas (Africa, Asia)	Diamondback moth ( <i>Plutella xylostella</i> )	Early application of non-selective insecticides is an important initiating factor in subsequent diamondback moth outbreaks because it reduces, among others, parasitoid populations.	Grzywacz <i>et al.</i> (2010)
Apple (North America, Europe)	Two-spotted spider mite ( <i>Tetranychus urticae</i> )	Use of insecticides and fungicides in apple orchards kills predatory mites, leading to a resurgence of spider mites.	Hardman <i>et al.</i> (2006)
Cereals (West Africa)	Grasshoppers (Acrididae)	Control with broad-spectrum insecticides of early season grasshoppers augmented populations of late hatching grasshopper species.	van der Valk, Niassy and Bèye (1999)
Various arable crops in rotation (Australia)	Slugs ( <i>Milax gagates</i> , <i>Deroceras reticulatum</i> )	Application of organophosphate insecticides against mites and aphids resulted in an increase of slug populations and associated yield reduction in canola.	Hill, MacFadyen and Nash (2017)
Rice (Asia)	Brown planthopper ( <i>Nilaparvata lugens</i> )	Insecticide applications, especially in early season, killed generalist predators, resulting in an increase of planthopper populations.	Settle <i>et al.</i> (1996) Wu <i>et al.</i> (2020)

in the tropics and subtropics (Grzywacz *et al.* 2010) (Table 4.3.3-3)

#### 4.3.4 The terrestrial environment

##### Soil organisms

Soil organisms provide essential contributions to many soil functions, such as nutrient cycling, soil formation, regulation of pests and diseases, and food, fibre and water supply, among others (Adhikari and Hartemink 2016; Food and Agriculture Organization of the United Nations and Intergovernmental Technical Panel on Soils [FAO and ITPS] 2017). Examples of major functions performed by soil organisms are shown in Box 4.3.4-1.

The Intergovernmental Technical Panel on Soils (ITPS) conducted a global review of the impact of plant protection products on soil functions and soil ecosystems (FAO and ITPS 2017).

Other pesticides, such as biocides or domestic use products, were not considered. In its assessment the ITPS assumed that plant production products are applied on crops at locally relevant application rates. Point-source contamination through spills or leakage was not assessed. The conclusions of this review are provided below, along with the results of additional reviews and studies.

##### Soil microorganisms

Soil microorganisms, such as bacteria and fungi, can be important sources of plant disease that damage crops and reduce yields. However, they also play an essential role in organic matter decomposition and nutrient cycling, suppression of pathogens and pests, plant growth promotion and maintenance of soil structure (Box 4.3.4-1).

The ITPS (FAO and ITPS 2017) concluded that the use of plant protection products consistently resulted in measurable and statistically significant

**Box 4.3.4-1 Selected examples of major functions performed by soil organisms.** A more complete list is provided in FAO and ITPS (2017).

Function	Significance	Main soil organisms involved
<b>Carbon and nutrient cycling</b>		
Nitrogen fixation	Conversion of atmospheric nitrogen to a form available to plants	Bacteria
Nitrification	Conversion of immobile ammonium to mobile nitrate; production of nitrogen oxides	Bacteria
Decomposition of organic materials	Decomposition and degradation of plant residues	Bacteria, fungi, termites
Soil organic matter formation	Creation of stable forms of organic matter (humus)	Bacteria, fungi
Pesticide decomposition	Limits transfer of pesticides from farms to the broader environment	Bacteria, fungi
<b>Creation and maintenance of soil structure</b>		
Physical structure development	Creation of soil aggregates and porosity	Earthworms, potworms, soil arthropods
<b>Transfer of nutrients and energy through the food web</b>		
Nutrient release	Predation of bacteria, fungi, nematodes and consumption of readily decomposable organic matter	Protists, nematodes, mites, springtails, potworms, isopods
Food source for birds and other animals		Earthworms, insects, ants, termites, spiders
<b>Pest control</b>		
Pest control	Control of soil pests such as root-rot fungi, nematodes, grubs	Fungi, bacteria, actinomycetes

effects on soil microorganisms. These effects have led to both significant decreases and increases in attributes of soil microorganisms such as biomass, enzyme activity, respiration and species composition.

In a major review of published studies, Puglisi (2012) found that most often no significant difference was observed in microbial activity, abundance or biomass following the application of a pesticide (in a range of 25-55 per cent of cases, depending on the type of pesticide). In about one-third of cases, fungicides and herbicides resulted in a reduction of soil microbial activity or biomass; insecticides showed less adverse effects. The remaining studies demonstrated an increase in microbial activity or biomass caused by pesticides.

The structure of terrestrial microbial communities (e.g., species richness), on the other hand, was significantly affected in 80-95 per cent of cases, in the case of fungicides, herbicides or insecticides (Puglisi 2012). However, changes in structure do not necessarily imply a reduction in biodiversity or an adverse effect on soil functions owing to the very large number of microbial species present and the functional redundancy present in soil ecosystems (FAO and ITPS 2017).

There is only limited evidence that the observed effects of pesticides on soil microorganisms have led to significant and long-lasting decreases in soil functions. However, our understanding of the links between observed effects of pesticides on soil microorganisms on the one hand, and resulting changes in soil processes and functions on the other, is still inadequate (Imfeld and Vuilleumier 2012; FAO and ITPS 2017).

### Earthworms and potworms

Earthworms and potworms (Oligochaeta, Annelida) are important soil fauna because they represent a large fraction of soil living biomass in many temperate and tropical ecosystems and play an important role in soil functioning. They actively participate in soil aeration, water infiltration and mixture of soil horizons, and influence organic matter decomposition and soil structure (Box 4.3.4-1). They are also an important source

of food for many organisms like birds or moles (Pelosi *et al.* 2014). Earthworms have become a standard test and monitoring organism globally for the study of the environmental impact of pesticides and other contaminants.

There is considerable evidence for significant harmful effects of pesticides on earthworms (FAO and ITPS 2017). Based on their review, Pelosi *et al.* (2014) concluded that earthworms are impacted by pesticides at all organizational levels: they disrupt enzymatic activities, increase individual mortality, decrease fecundity and growth, change individual behaviour such as feeding rate, and decrease the overall community biomass and density, among others.

Soil fumigants generally have the greatest effects on earthworms, followed by fungicides, insecticides and herbicides in that order (FAO and ITPS 2017). Based on laboratory studies, Pelosi *et al.* (2014) concluded that the most harmful pesticides appeared to belong to the neonicotinoids, strobilurins, sulfonylureas, triazols, carbamates and organophosphates. The negative effects of copper-based fungicides on earthworms are also well established.

Vašíčková *et al.* (2019) evaluated the risks posed by residues of CUPs measured in 75 arable soils in the Czech Republic. They applied the EU risk assessment methodology for earthworms, potworms, springtails and soil mites as far as toxicity data were available. Their assessment shows that pesticide residues posed a risk to soil organisms at 35 per cent of the sites. Pelosi *et al.* (2021) also measured CUP residues in cereal fields, hedgerows and grasslands in France which were treated, untreated, or under organic farming practices (Annex 4.3.3). A high risk of chronic toxicity to earthworms was found in 46 per cent of samples, both in treated cereals and non-treated habitats considered to be refuges.

Römbke, Schmelz and Pélosi (2017) reviewed the effects of synthetic pesticides on enchytraeids (potworms) in agroecosystems. They found that very few pesticides have been studied intensively in both the laboratory and field, mainly the fungicide carbendazim. Most available data refer to organochlorine and organophosphate pesticides

which are rarely used while very few data are available on CUPs.

The effects of agricultural management practices in China and Europe on various soil quality parameters, including earthworm abundance, was recently evaluated by Bai *et al.* (2018). Most of the studies reviewed were long-term experiments. Their comparisons of no tillage and organic production systems with conventional production are of relevance to pesticide use. No-tillage refers to land cultivation with little or no soil surface disturbance, although herbicides are often used for weed control. No-tillage practices enhanced earthworm populations by a factor 1.7 unless herbicides or insecticides were applied. In organic agriculture few if any synthetic pesticides are used, although copper-based fungicides may be applied. Earthworm abundance almost doubled under organic agriculture when compared to conventional practices. Both comparisons illustrate the long-term adverse effects of pesticides on earthworms under realistic pesticide application scenarios.

No review was available of post-registration monitoring of earthworm populations following real pesticide applications at recommended rates. Pelosi *et al.* (2014) noted that studies based on realistic conditions in terms of soil, pesticide dose and experimental duration were lacking. The extent to which CUPs affect earthworm populations is therefore not well established, but the few studies from Europe cited above suggest that the risks may be higher than previously estimated.

### Soil arthropods

Many arthropods inhabit soils, including springtails (or collembolans), mites and ants, and perform important functions (Box 4.3.4-1). Soil (micro) arthropods affect soil organic matter directly by fragmenting detritus, and indirectly by influencing microbial activity. Furthermore, soil arthropods can impact soil and plant health directly by feeding on pest organisms or serving as alternate prey for larger predatory arthropods (Neher and Barbercheck 2019).

Pesticide effects on soil arthropods are less well studied than on earthworms (FAO and ITPS 2017).

A number of comparisons have been made of the sensitivity of soil arthropods to pesticides when compared to earthworms (Daam *et al.* 2011; Huguier *et al.* 2015; Kohlschmid and Ruf 2016). Partially different data sets were used, consisting mainly of laboratory toxicity studies. Certain variations were observed depending on pesticide, species and test conditions.

For insecticides and herbicides, no systematic differences in sensitivity between earthworms and soil arthropods were reported. Earthworms were generally found to be more sensitive than soil arthropods to fungicides. In comparison with other soil invertebrates (either earthworms or other arthropods), soil mites showed lower to similar sensitivities to chemicals (Huguier *et al.* 2015). Arachnids and isopods were more sensitive to insecticides, and nematodes to fungicides, as compared to earthworms.

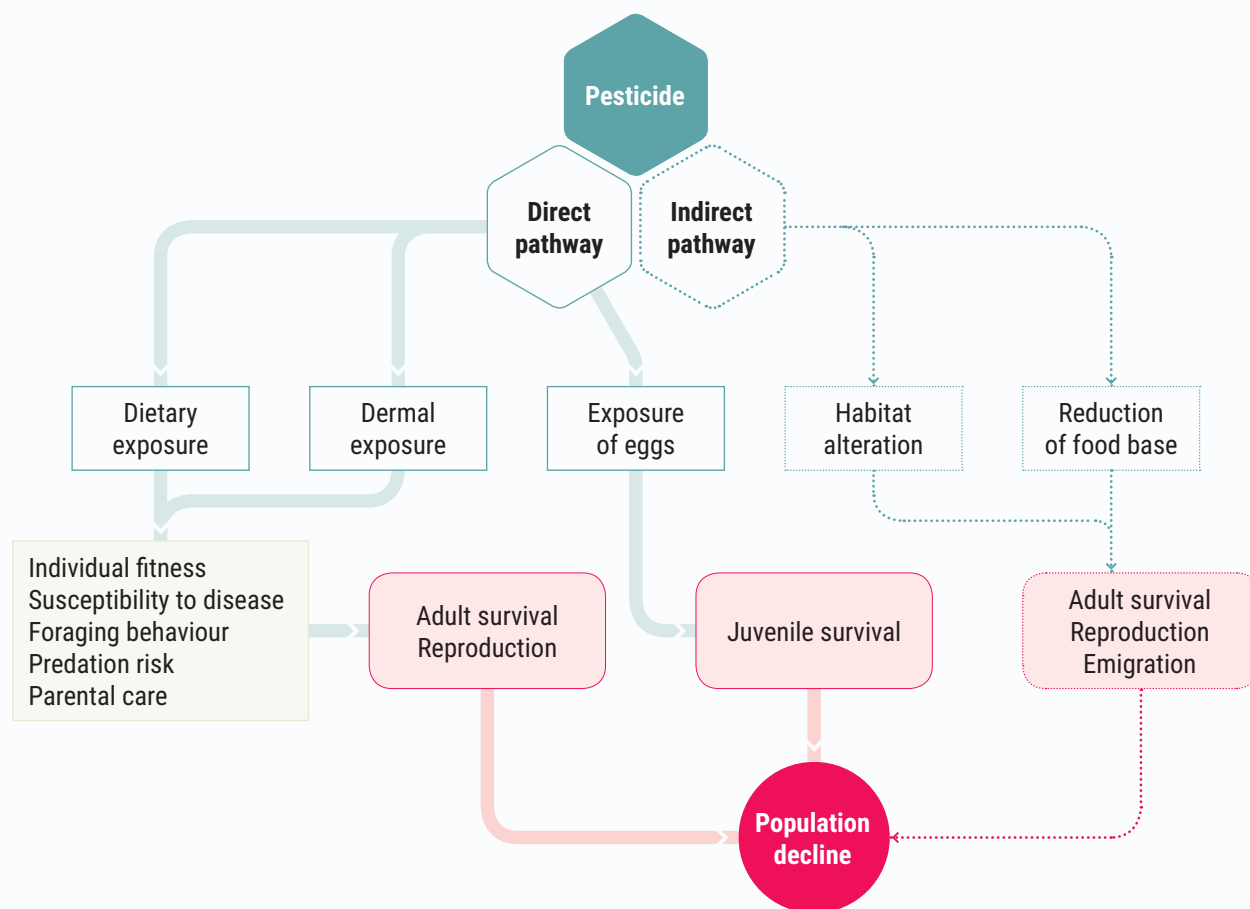
Since Jänsch *et al.* (2006), no review of semi-field and field studies of the effects of pesticides on soil arthropods seems to have been published. No global or regional evaluations were found of the monitoring of pesticide effects on soil arthropods.

### Terrestrial vertebrates

Terrestrial vertebrates, such as birds, mammals, amphibians and reptiles, can be exposed to pesticides through different routes (Figure 4.3.4-1). Contact exposure occurs if animals are exposed to spray drift, or come into contact with pesticides on soil and other surfaces or in water (e.g., for the aquatic phase of amphibians). Pesticides can also be absorbed by the eggs of amphibians and reptiles in water or soil. Dietary exposure arises through consumption of contaminated food items (such as seeds, vegetation, invertebrate and vertebrate prey) or pesticide granules and soil, or through preening and grooming. Such exposure may cause mortality or sublethal adverse effects (e.g., on reproduction, immunity systems and behaviour) and ultimately result in population declines (EFSA 2009; Amaral *et al.* 2012a; Mineau 2013a; EFSA 2018a; Stanton, Morrissey and Clark 2018).

Pesticide use can also indirectly affect terrestrial vertebrate populations by reducing their food base

► **Figure 4.3.4-1 Pathways through which pesticide application can ultimately lead to population declines in terrestrial vertebrates.** Based on Amaral *et al.* (2012a); Stanton, Morrissey and Clark (2018).



(e.g., if insecticides kill insect prey), or altering their habitat (e.g., if vegetative shelter is affected by herbicide use).

Most research into the effects of pesticides on terrestrial vertebrates published since the mid-1980s has focused on domestic and laboratory mammals and to a lesser extent on birds and amphibians. Köhler and Triebkorn (2013) indicated that less than 5 per cent of studies on terrestrial vertebrates concerned wild mammal species and reptiles. Based on the literature reviews conducted for this report, current knowledge about pesticide effects on terrestrial vertebrates appears to be skewed to a limited group of animals.

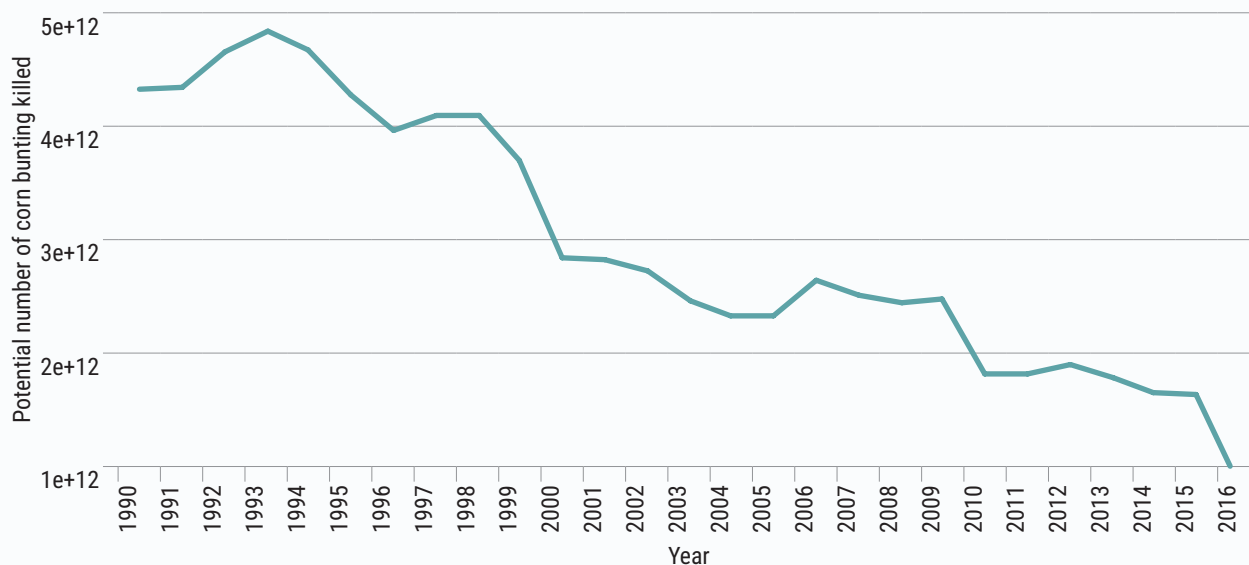
Historically, several distinct “periods” of pesticide effects on birds and other vertebrates can be recognized. Both acute lethal toxicity and effects on reproduction (e.g., eggshell thinning) were at

the basis of these effects slowly (Nygård *et al.* 2019; Sonne *et al.* 2020). Between the 1950s and 1970s populations of raptors, fish-eating birds, seals and other vertebrates were severely affected, and sometimes completely collapsed, due to persistent organochlorine pesticides such as aldrin, dieldrin, chlordane, DDT and its metabolites, among others (Peakall 1993; Mineau 2013a; Matthiessen, Wheeler and Weltje 2018; Sonne *et al.* 2020). In many cases populations recovered after organochlorine pesticides were banned, albeit sometimes very slowly (Nygård *et al.* 2019; Sonne *et al.* 2020).

Subsequently, with the introduction of acutely toxic organophosphates and carbamates, direct mortality of, in particular, bird populations became problematic. With the stricter regulation of these groups of pesticides in certain regions of the world, effects on bird populations also appeared to



► **Figure 4.3.4-2 Potential kill of corn bunting due to the application of the 294 pesticides included in an analysis in Great Britain fell by about 80 per cent between 1990 and 2016.** Tassin de Montaigu and Goulson (2020).



decline (Mineau and Whiteside 2006; Mineau and Whiteside 2013; Jahn *et al.* 2014).

The focus of the chapter below is on recent reviews, as well as on large-scale field studies looking at the effects of current use pesticides on populations of wild birds, amphibians and reptiles. No recent global or regional reviews were available concerning the effects of pesticides on wild mammal populations.

### Birds

Recent reviews of pesticide effects on populations of birds, as well reports of large-scale monitoring of such effects are summarized in Annex 4.3-5.<sup>7</sup>

During the last two decades there does not appear to be much evidence of significant population effects arising from direct effects of pesticides on farmland birds (Jahn *et al.* 2014). Time trends between 1991 and 2003 show a decreasing risk of pesticide lethality to birds in several major crops in the United States (Mineau and Whiteside 2006). Similarly, Tassin de Montaigu and Goulson (2020),

using acute toxicity data for the corn bunting as a model, estimated that the total toxic load for birds of pesticides applied in the United Kingdom fell by about 80 per cent between 1990 and 2016 (Figure 4.3.4-2). In both studies the decrease in risks was largely due to a reduction in the use of acutely toxic organophosphate and carbamate insecticides and their replacement by pesticides with lower vertebrate toxicity. The situation may be different in countries that have not yet removed pesticides with high bird toxicity from the market.

This does not mean that current use pesticides do not cause acute mortality in birds. In Canada pesticides were estimated to be the sixth source of bird mortality (out of 28 sources identified), resulting in 0.9-4.3 million deaths per year (Calvert *et al.* 2013; Mineau 2013b). Parsons, Mineau and Renfrew (2010), when reviewing the effects of rice cultivation on aquatic birds, reported direct mortality of many avian species as a result of pesticide applications, though mostly with “older” organochlorines, organophosphates and carbamates. There are also indications that certain neonicotinoid insecticides can cause acute mortality in granivorous birds following consumption of treated seeds at field-realistic doses (Gibbons, Morrissey and Mineau 2015; Wood and Goulson 2017).

<sup>7</sup> Annex 4.3-5 is found at: <https://www.unep.org/resources/report/environmental-and-health-impacts-pesticides-and-fertilizers-and-ways-minimizing>

#### Box 4.3.4-2 Effects of anticoagulant rodenticides on vertebrate wildlife.



Photo: © Martha de Jong-Lantink, Little owl - Steenuil (*Athene noctua*) CC BY-NC-ND 2.0

Rodents can be vectors of human or animal disease, damage crops, consume or foul stored food, and damage power supplies and electrical infrastructure. Rodenticides have been used for nearly a century to control rodent populations. They are also the most frequently used method to eradicate rodents from islands and fenced areas for the purpose of preserving or reintroducing native biodiversity (Lohr and Davis 2018; van den Brink *et al.* 2018a).

Most currently used rodenticides are anticoagulants, which prevent blood from clotting. First generation anticoagulants (e.g. warfarin, chlorophacinone) need to be consumed several times by rodents to cause mortality. Second generation anticoagulant rodenticides (e.g. brodifacoum, bromadiolone, difenacoum) have higher acute toxicities and are lethal after a single feed. They are also considerably more persistent in the animal's body, increasing the risk of bioaccumulation (Lohr and Davis 2018; Nakayama *et al.* 2019).

Recently, van den Brink *et al.* (2018b) brought together the available information on the environmental risks associated with rodent control with anticoagulant rodenticides (ARs). Primary exposure to ARs, mainly through ingestion of baits containing the rodenticide, has been widely reported for a range of non-target birds and mammals and, to a lesser extent, reptiles and insects. Primary exposure is thought to be more likely to cause acute mortality than secondary exposure. Effects of primary exposure to rodenticides on non-target populations have generally been found to be transient and populations recovered relatively rapidly. Exceptions, however, are situations in which baiting is permanent (e.g. in some urban settings or around farm buildings) or in areas where immigration is limited such as on islands (Shore and Coeurdassier 2018).

Secondary exposure to, and poisoning of, predators is caused by consumption of prey containing AR residues. i.e. of other animals that have been exposed due to bait ingestion (López-Perea and Mateo 2018). Secondary exposure of predators, particularly raptors, has been found to be widespread. Both López-Perea and Mateo (2018) and Nakayama *et al.* (2019) conducted global reviews of field monitoring studies and reported that AR residues were present on average in about 60 per cent of sampled predatory birds and mammals. Similar detection rates, ranging from 45 per cent to 90 per cent, were found in reptiles (Lettoof *et al.* 2020). In isolated environments such as islands, AR residues were detected in more than 80 per cent of sampled animals (Pitt *et al.* 2015). These data suggest that ARs are consistently and widely present in food webs of the ecosystems in which they are applied.

Many reports exist from around the world about mortality of non-target wildlife following AR exposure. Most commonly involved are bromadiolone and brodifacoum, both second generation ARs which are bioaccumulative and highly toxic. Sublethal effects of ARs are less well researched, but several studies have shown evidence of adverse effects of AR treatments on the breeding success of predators (López-Perea and Mateo 2018). Clear gaps exist, however, in knowledge about the long-term effects of exposure to ARs in populations of non-target organisms (Quinn 2019). Furthermore, despite the evidence of wide distribution of ARs in the environment as well as human consumption of wildlife, there is a distinct lack of information about the presence of AR residues in humans that is unrelated to pharmacological use (López-Perea and Mateo 2018).

Given the known risks of ARs to wildlife, their use has been regulated more or less strictly in many countries. Mitigation measures include restrictions on who can purchase and use these rodenticides, restrictions on where they can be used, requirements for protected bait stations, and removal of dead rodents and left-over baits. Such risk reduction measures are essential to limit primary and secondary exposure of non-target organisms to the rodenticides (Buckle and Prescott 2018). However, it has become clear that ARs travel beyond the point of application, through various means of primary and secondary exposure, and that these processes are largely outside of the control of the applicator. It has therefore been argued that mitigation measures based on the assumption that professional applicators will apply rodenticides more safely are likely to be limited in their effectiveness. A combination of measures will need to be developed and imposed for specific rodenticide use situations (Buckle and Prescott 2018; Quinn 2019).

Another group of current use pesticides causing bird mortality are second generation anticoagulant rodenticides, which are often implicated in wildlife poisoning, particularly of raptors. While there is much evidence that this group of rodenticides may kill large numbers of predatory birds, the extent to which they can cause long-term population declines is not established (Box 4.3.4-2).

With the acute risks of pesticides declining with the progressive introduction of pesticides with lower vertebrate toxicity, attention has shifted to sublethal effects, e.g., on bird physiological condition and behaviour (Eng *et al.* 2019), as well as indirect effects, e.g., through a reduction of food or shelter (Jahn *et al.* 2014).

Various recent studies and reviews have linked population declines of birds with the application of current use pesticides. A number of authors consider pesticides to be one of several factors that drive reductions in bird populations, e.g., Spiller and Dettmers (2019) for aerial insectivore birds in North America, Brain and Anderson (2019) for birds in North America, and Coates *et al.* (2017) for ring-necked pheasants in California (Annex 4.3-5).

Direct associations between pesticide use and bird population declines, or community composition have been found in several studies in both North America and Europe. Bouvier *et al.* (2011) observed that birds were significantly more abundant in French organic apple orchards than in IPM orchards, which in turn contained more birds than conventional orchards. They linked this abundance to levels of insecticide use. Chiron *et al.* (2014) found that herbicide use in cereal fields on France resulted in a shift in bird community composition from herbivore specialist to generalists. Mineau and Whiteside (2013) analysed surveys of grassland birds in the United States between 1980 and 2003 and found that the best predictors of species declines was lethal risk from insecticide use. Large-scale monitoring of breeding birds in cereal fields in eight European countries by Emmerson *et al.* (2016) indicated that applications of fungicides and insecticides were significantly associated with a lower total abundance of all breeding birds surveyed. In addition, a recent systematic review of

drivers of farmland bird declines in North America found that pesticides were the predominant factor (42 per cent of all studies) negatively affecting bird populations (Stanton, Morrissey and Clark 2018) (Annex 4.3-5).

In recent years the use of neonicotinoid insecticides has received increasing attention. In their review of environmental effects of neonicotinoids, Gibbons, Morrissey and Mineau (2014) included only one field population study, which reported an effect of imidacloprid on three insectivore bird species in forests in the United States. However, more recently several studies have indicated adverse effects of neonicotinoid use on bird populations. Hallmann *et al.* (2014) found that higher concentrations of imidacloprid in surface water in the Netherlands were consistently associated with lower or negative population growth rates of passerine insectivorous birds. Ertl *et al.* (2018) assessed bobwhite quail population data from Texas (United States) for the period 1978-2012 and found that of the six predictor variables tested, the strongest negative association was between bobwhite abundance and neonicotinoid use. Li, Miao and Khanna (2020) estimated that the use of neonicotinoids in the United States resulted in annual decreases of 4 per cent and 3 per cent in population abundance of grassland birds and insectivorous birds, respectively, between 2008 and 2014 (Annex 4.3-5).

### Amphibians

Amphibians are the most endangered group of vertebrate animals, with 41 per cent of currently existing species estimated to be threatened (International Union for Conservation of Nature 2020). Many causes for this decline have been cited, including habitat loss, emerging infectious diseases, invasive species, climate change and chemical pollution (Araújo *et al.* 2014; Whitfield, Lips and Donnelly 2016). The use of pesticides also figures explicitly as one of the drivers for observed declines in amphibian abundance and diversity (Hayes *et al.* 2010; Bishop *et al.* 2012; Brühl *et al.* 2013). Amphibians are particularly numerous in tropical and subtropical regions (Whitfield, Lips and Donnelly 2016). Some amphibians and reptiles inhabit agricultural

landscapes, either as residents or migrating through, and can thus be exposed to agricultural pesticides. Amphibians may also breed in water bodies adjacent to agricultural fields.

The state of the science on pesticide risk assessment for amphibians and reptiles was recently reviewed by the European Food Safety Authority (EFSA 2018a). Based on a limited comparison of the acute and chronic sensitivity of amphibians with the standard fish test species, they suggested that the sensitivity of amphibians may be covered by fish in some, but not all, cases. However, an additional extrapolation factor may be warranted when using fish toxicity data in amphibian risk assessments. EFSA (2018a) further concluded that recent evidence from both field and laboratory studies indicates that the use of plant protection products poses a risk to the reproduction and survival of amphibian field populations. In particular, studies on terrestrial stages of amphibians have shown that the use of currently registered pesticides at authorized rates can cause mortality in frogs and toads. They noted that existing risk assessment procedures for pesticides likely do not protect amphibians to a sufficient degree and further research is needed, especially taking into account the current endangered status of many of these animals (EFSA 2018a).

Most studies on the effects of pesticides on amphibians are experimental and have been conducted in the laboratory. Unlike studies on birds and aquatic fauna, for example, few studies have explored the effects of pesticides on amphibians under field conditions (Annex 4.3-5). Abnormalities and effects on biomarkers have most often been reported, but unequivocal links to pesticide field exposures have been difficult to make as other stressors might have caused similar effects (Agostini *et al.* 2020). Therefore, the strongest indications of impact of pesticides on amphibian population health currently come from reviews which have linked laboratory studies of pesticide effects to realistic concentrations of such compounds in the field (Annex 4.3-5).

Egea-Serrano *et al.* (2012) and Baker, Bancroft and Garcia (2013) conducted meta-analyses of laboratory studies of the effects of pesticides

on survival and physiological parameters of amphibians at concentrations expected to be encountered in the environment after spray events. Both concluded that pesticides adversely affected amphibian survival at environmentally realistic pesticide exposure levels. When European common frogs were oversprayed with various pesticides at recommended application rates, high acute mortality was observed even though these products were registered in one or more EU countries (Brühl *et al.* 2013).

Baker, Bancroft and Garcia (2013) identified carbamate, organophosphate and neonicotinoid insecticides, as well as triazine and phosphonoglycine herbicides, as negatively affecting amphibian survival. Organophosphate insecticides and phosphonoglycine herbicides also reduced amphibian growth. On the other hand, developmental time and frequencies of abnormalities were not found to be significantly affected by pesticides (Egea-Serrano *et al.* 2012).

Some of these effects were confirmed in a recently published field study from Argentina, in which Agostini *et al.* (2020) monitored the effects of five pesticides, applied according to farmer practices, on amphibian populations in 91 ponds adjacent to agricultural fields. They observed almost complete mortality of amphibians in the ponds after use of the insecticides cypermethrin, chlorpyrifos and endosulfan, as well as effects on amphibian mobility from the herbicides glyphosate and 2,4-D.

Schiesari and Corrêa (2016) evaluated the consequences of Brazilian sugarcane production for freshwater biodiversity including amphibians. To this end, they conducted field surveys across a gradient in land-use intensity ranging from seasonal Atlantic Forest and the Cerrado to pastures to sugarcane plantations in Southeast Brazil. They observed a reduction in amphibian diversity on sugarcane plantations. This was associated with habitat loss, intensification, and use of agrochemicals. Schiesari and Corrêa (2016) asserted that tadpole dieoffs in ponds adjacent to sugarcane fields could plausibly be explained by pesticide applications. This was confirmed in laboratory toxicity tests evaluating realistic exposure levels of the main pesticides used in the sugarcane fields (Moutinho *et al.* 2020).

Of particular concern have been the effects of endocrine disrupting chemicals (EDCs) on amphibians, which exert adverse effects through perturbations of hormonal systems (Box 4.3.4-3). In a review of the effects of EDCs on amphibian reproduction and development, Orton and Tyler (2015) concluded that many pesticides have the ability to alter hormone systems and affect reproductive development and function in frogs at relatively high concentrations. The herbicide atrazine was also found to exert such adverse effects at concentrations measured in some aquatic environments. They noted that there is now a substantial and growing body of evidence from field studies indicating that agriculture, herbicides and/or pesticides in general are associated with increased intersex in anurans. Caution was expressed, however, that the lack of analysis of the associated concentrations of these chemicals in anuran breeding habitats and/or body tissues makes assigning cause-effects relationships to individual pesticides difficult.

Pesticides may also affect amphibians in conjunction with other stressors. Emerging infectious diseases, such as chytrid fungi and ranaviruses, have been identified as important drivers of amphibian population declines (Bishop *et al.* 2012; North *et al.* 2015). Pesticides have been shown in the laboratory to increase the susceptibility of amphibians to diseases and indirectly to increase infection rates, leading to a reduction in survival or increased mortality due to predation (North *et al.* 2015, Bienentreu and Lesbarrères 2020; Campbell, Pawlik and Harrison 2020). This relationship appears to be reciprocal and the presence of a ranavirus has been shown to exacerbate the lethality of pesticides (Campbell, Pawlik and Harrison 2020).

Fewer studies have looked at the relationship between exposure to specific pesticides and pathogen infections in amphibians. North *et al.* (2015) found that Ranavirus prevalence in common frogs increased with the use of herbicides and slug pellets in British gardens. Another study conducted across the United States (Battaglin *et al.* 2016) showed a positive correlation between the prevalence of the fungus *Batrachochytrium dendrobatidis* in amphibian hosts and total fungicide concentrations in the environment.

## Reptiles

About one-third of currently existing chameleons, crocodiles and alligators, marine turtles and sea snakes are considered to be threatened with extinction (IUCN 2020). Several factors contribute to local and regional declines in reptile populations, including habitat loss, unsustainable removal (e.g., for skins and traditional medicines), climate change, invasive species (e.g., exotic predators or competitors for resources), diseases and parasites, as well as pollutants including pesticides (Todd *et al.* 2010).

Reptiles exhibit various ecological and life history characteristics that make them particularly vulnerable to pesticides. With the exception of a few lizard and turtle species, they are carnivorous and many occupy high trophic positions within food webs. As a result, they are at risk of high pesticide exposures from biomagnification through the food chain. Many reptiles are also long-lived and have small habitats, making them susceptible to long-term pesticide exposure (Todd *et al.* 2010). According to Köhler and Triebkorn (2013), however, less than 1 per cent of published pesticide effect studies concerned reptiles, making them one of the least studied groups of non-target organisms. This lack of data holds true for laboratory toxicity studies, but even more so for evaluations of causal relationships between pesticide use and reptile population declines (Wagner *et al.* 2015).

While studies regarding the ecotoxicological effects of pesticides on reptiles are scarce, lethal as well as sub-lethal effects have been observed. These include hormonal changes and enzymatic responses, oxidative stress, neurotoxic implications and immunosuppression, fertility, development and locomotor performance impairments, and hermaphroditism (Mingo, Lötters and Wagner 2017).

No recent comprehensive review has been published on pesticide toxicity to reptiles or pesticide effects on reptile populations in the field. In their review of the state of the science on pesticide risk assessment for amphibians and reptiles, EFSA (2018a) concluded that there is sufficient evidence from both field and laboratory

#### Box 4.3.4-3 Endocrine disruption and wildlife.

An endocrine disrupting chemical (EDC) has been defined as “an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub) populations” (UNEP and WHO 2012). The endocrine system is a complex network of glands that release hormones into the blood stream. They control growth, development, reproduction, metabolism and immune responses, among other functions. EDCs can mimic or antagonize natural hormones and thus interact with hormone receptors, which can disrupt the body’s normal functions. Some of the observed health effects associated with EDCs include cancers as well as reproductive, developmental, immunological and neurological disorders (UNEP and WHO 2012; UNEP 2017b).

Much research has been conducted into the mechanisms of endocrine disruption, identification of EDCs, and linkages between EDCs and the presence of adverse effects in human and animal populations. However, despite substantial advances in scientific understanding of EDCs, important uncertainties and knowledge gaps still exist. Even after several decades of research on EDCs, there is no consensus among scientists, regulators, the chemical industry and civil society groups about the outcomes and implications of such research (Encarnaç o *et al.* 2019; European Parliamentary Research Service 2019; La Merrill *et al.* 2020).

The latest global reviews of the effects of EDCs on human health and the environment were published almost a decade ago by UNEP and WHO (UNEP and WHO 2012; Bergman *et al.* 2013) and by the European Environment Agency (EEA 2012). Both reviews express serious concerns about the possible effects of EDCs on human health and wildlife: Many chemicals are known or suspected to be capable of interfering with hormone receptors, hormone synthesis or hormone conversion; human and wildlife populations are exposed to EDCs globally; and chemically induced endocrine disruption likely affects human and wildlife endocrine health the world over (UNEP and WHO 2012; EEA 2012).

Identifying which chemicals are likely to affect endocrine systems has been the subject of substantial research and screening. This is partly due to the scientific complexity of endocrine disruption. Consequently, different scientific and regulatory bodies apply different approaches and criteria (Slama *et al.* 2016; UNEP 2017b; European Chemical Agency and European Food Safety Authority 2018; La Merrill *et al.* 2020). UNEP (2017b) listed 28 initiatives to identify EDCs which could aid in overcoming this problem.

#### Pesticides as EDCs

There is currently no agreed global list of pesticides identified as EDCs or potential EDCs. Lists, established by regulatory bodies, tend to be variable. The International Panel on Chemical Pollution (IPCP) lists six pesticides (metam-sodium, zineb, ziram, thiram, tebuconazole and pentachlorophenol [PCP]) that were identified as EDCs following a publicly accessible, thorough scientific assessment using the World Health Organization and International Programme on Chemical Safety (WHO and IPCS) 2002 definition of EDCs and with multi-stakeholder involvement (UNEP 2017b). In 2016 the European Commission identified between 15 and 50 pesticide active ingredients as potential EDCs, out of a total of about 600 authorized compounds, depending on which criteria were followed (European Parliamentary Research Service 2019). Other regulators have identified a larger number of chemicals or chemical groups as potential EDCs or included them in current screening programmes (UNEP 2017b). It is very likely that with further screening and increased scientific understanding, more pesticides will be identified that with high likelihood can disrupt the endocrine system and affect wildlife populations (UNEP and WHO 2012).

Newer pesticides are less well understood in terms of their endocrine disrupting potential (Warner *et al.* 2020). There is ample evidence of mechanisms by which current use pesticides can disrupt endocrine systems in animals such as mammals (Pelch *et al.* 2011; Warner *et al.* 2020), fish (Martyniuk, Mehinto and Denslow 2020) or amphibians (Orton and Tyler 2015; Trudeau *et al.* 2020). However, there is less evidence of such pesticides causing adverse effects on wildlife due to endocrine disruption in the field or at environmentally realistic concentrations. This is partly due to the complexity of measuring such effects under realistic field conditions.

Endocrine disrupting effects of current use pesticides tend to be highly debated, in part due to the large economic value attributed to the use of some of them. For instance, reviews of the endocrine disrupting effects of atrazine on, in particular, amphibians have resulted in contrasting conclusions. Rohr and McCoy (2010), Hayes *et al.* (2010), Hayes *et al.* (2011) and Orton and Tyler (2015) concluded that atrazine does cause endocrine disruption in certain amphibians at environmentally realistic concentrations, but others have opposed that view (Matthiessen, Wheeler and Weltje 2018, Hanson *et al.* 2019). Gendron (2013) noted that these contrasting conclusions to a large extent positioned pesticide industry against certain research groups.

However, it is generally accepted that organochlorine and organotin pesticides have endocrine disrupting properties and that they have caused adverse effects on the growth and reproduction of wildlife populations (e.g., raptors, seals, fish, molluscs). The evidence that such pesticides cause wildlife population declines is reinforced by the recovery of some of these populations following bans or restrictions on their use (UNEP and WHO 2012; EEA 2012; Matthiessen, Wheeler and Weltje 2018; Encarnaç o *et al.* 2019; Plaza, Mart n-L pez and Lambertucci 2019; Martyniuk, Mehinto and Denslow 2020).

**Box 4.3.4-4** Effects observed on reptiles as a result of insecticides applied for locust control in Africa and Australia are highly dependent on the type of insecticide and the way it is applied.



© Wildlife Wanderer, Western Sahara Fringe-toed Lizard (*Acanthodactylus aureus*), Western Sahara

Country (type of study)	Insecticide	Reptile	Observed effects	Reference
Mauritania (laboratory)	<i>Metarhizium anisopliae</i> var. <i>acridum</i>  fipronil	<i>Acanthodactylus</i> spp. (lacertid lizard)	<i>M. anisopliae</i> var. <i>acridum</i> was considered to pose a low risk under field conditions. Acute risk of exposure to fipronil was considered high.	Peveling and Demba 2003
Madagascar (field)	fipronil (as full cover treatment) deltamethrin triflumuron	<i>Chalarodon madagascariensis</i> <i>Mabuya elegans</i> (lizards)	Significant declines in abundance of the two lizard species were observed in fipronil treated zones but not after deltamethrin or triflumuron treatments. Fipronil induced food shortages were considered the principal cause of the decline in lizards.	Peveling <i>et al.</i> 2003
Australia (laboratory)	fenitrothion	<i>Pogona vitticeps</i>	Oral doses expected to occur after locust control did not cause mortality and only minor poisoning symptoms. Except for a reduction in plasma cholinesterase, no sublethal effects were observed.	Bain <i>et al.</i> 2004
Australia (field)	fipronil (as barrier treatment) <i>Metarhizium acridum</i>	22 species	Neither reptile abundance nor community composition were significantly affected in the short term by the treatments.	Maute <i>et al.</i> 2015
Niger (field)	chlorpyrifos fenitrothion	<i>Acanthodactylus</i> spp. (lacertid lizard)	Significant reductions were found in the abundance of lizards in the case of both insecticides until about 30 days after treatment. Moribund and dead lizards were observed between nine and 21 days after treatment.	Abdou 2015

studies indicating that the use of plant protection products poses a risk to reproduction and survival of reptile populations. Selected studies published during the last decade are listed in Annex 4.3-5.

Wagner *et al.* (2015) and Mingo, Lötters and Wagner (2016) assessed the risk of pesticide exposure to reptiles in Europe, based on the occurrence of reptiles in agricultural areas where pesticides are used, reptile physiology, and their life

history. They concluded that about one-third of all European reptile species are at high risk of current exposure to pesticides, especially in Southern Europe. Many of these species are considered threatened and/or are protected in the region.

The few recent field studies concerning pesticide effects on reptile health or abundance in Europe and Oceania do not show short-term effects on population sizes (Annex 4.3-5). However, physiological and endocrinological effects have been observed following the application of herbicides, in some cases also resulting in adverse effects on the fitness of the organisms (Amaral *et al.* 2012a; Amaral *et al.* 2012b; Bicho *et al.* 2013; Mingo, Lötters and Wagner 2017).

The effects of insecticides on reptiles have received particular attention in locust control, which is often carried out in arid and semi-arid ecosystems where reptiles are an important part of vertebrate fauna (Box 4.3.4-4). While biological control with the entomopathogen *Metarhizium acridum* did not cause unintended effects under field conditions, treatments with organophosphate insecticides did. Furthermore, locust control with fipronil, when applied as full cover sprays, resulted in indirect effects on lizard populations through insect food shortage. However, when it was applied as a (partial) barrier treatment, such effects were not observed.

### Deliberate wildlife poisoning

The use of poisons to kill wildlife has a long history the world over. Highly toxic synthetic pesticides have become the preferred tool for deliberate wildlife poisoning, as they are silent, cheap, easy to obtain and use, and effective (Ogada 2014). Most information about wildlife poisoning is available from Africa, Europe and to a lesser extent Asia and the Americas (Plaza, Martínez-López and Lambertucci 2019).

In parts of Europe the deliberate use of pesticides to kill wildlife is a common practice, mostly associated with human-wildlife conflicts with predators, presumed pest species, feral dogs and birds of prey that compete with hunters and poachers (Guitart *et al.* 2010). Common reasons for wildlife poisoning in Africa are control of

damage-causing animals, harvesting fish and bushmeat for human consumption, and harvesting animals for traditional medicine. Pesticides are also increasingly used in poaching elephants for ivory, rhinos for horn and carnivores for fur, as well as in killing wildlife sentinels (e.g., vultures because their aerial circling alerts authorities to poachers' activities) (Ogada 2014; Ogada, Botha and Shaw 2016; Aziz *et al.* 2017).

Deliberate poisoning incidents with pesticides across Africa have been on the increase since the 1990s, resulting in an unsustainable number and diversity of African wildlife being killed. There is substantial evidence of corresponding population declines in lions, raptors, large mammals, vultures and hyenas (Ogada 2014; Richards *et al.* 2018). In Europe wildlife poisoning may have considerable implications for endangered species (Guitart *et al.* 2010; Grilo *et al.* 2021).

Of particular concern are vulture and condor species, of which about 70 per cent are threatened by human activities. Plaza, Martínez-López and Lambertucci (2019) concluded that the most important threat currently affecting vultures and condors worldwide is probably exposure to pesticides, both accidentally and through deliberate abuse. Ogada *et al.* (2016) came to a similar conclusion in regard to African vulture populations. When reviewing vulture mortality cases in 26 African countries, they found that poisoning, mainly by pesticides, was the cause of death in 60 per cent of cases. Vultures were deliberately poisoned or were unintentional victims when they consumed carcasses baited with highly toxic pesticides to kill carnivores such as lions, hyenas and jackals. It has been argued that if poisoning with pesticides is not stopped, this threatened avian group could become extinct very soon (Plaza, Martínez-López and Lambertucci 2019).

The pesticides most widely used to poison wildlife are organophosphates and carbamates with high acute toxicity, such as aldicarb, carbofuran, methomyl, monocrotophos, diazinon, parathion and fenthion. In recent years the pesticide most commonly used to deliberately kill wildlife has been carbofuran (Guitart 2010; Ogada 2014; Plaza, Martínez-López and Lambertucci 2019)



It should be emphasized that using pesticides to poison wildlife is illegal in most countries. The wildlife laws in 38 of 46 African countries specifically mention that it is illegal to use poison, poison bait, or poisoned weapons for the purpose of hunting wildlife (Ogada 2014). However, in many countries, especially low and middle income countries (LMICs), there is inadequate enforcement of such legislation and highly toxic pesticides are easily available even if their use is legally restricted. Proposed measures to mitigate this abuse of pesticides include banning the pesticides most used for wildlife poisoning (preferably by groups of neighbouring countries in order to minimize smuggling), stricter regulation, control of distribution and enforcement, higher penalties, and targeted educational programmes (Ogada 2014; Plaza, Martínez-López and Lambertucci 2019).

### Terrestrial arthropods

Pesticides can have an adverse impact on populations of terrestrial arthropods such as insects, mites and spiders. Pesticide exposure may result in lethal and sublethal effects in arthropods, but can also indirectly modify their food base or their environment. Insecticides and acaricides are most often implicated due to their modes of action, but fungicides and herbicides can also perturb terrestrial arthropod populations.

The effects of pesticides on various specific groups of terrestrial arthropods are discussed elsewhere in this report: pollinators in Chapter 4.3.3; natural enemies of pests in Chapter 4.3.3; and soil arthropods in Chapter 4.3.4. This section covers the effects of pesticides on the population abundance or biomass of arthropods in general, as observed in the field. Pesticides' impact on arthropod biodiversity (i.e., changes in number of taxa, functional groups, genetic composition, or other diversity parameters) are reviewed in Chapter 4.3.6. While changes in the abundance or biomass of specific arthropod taxa may correlate with changes in their taxonomic diversity, this is not necessarily always the case.

Reports of significant declines in arthropod populations in different parts of the world have recently received much attention. Most of them focus on insects (Leather 2018; Sánchez-Bayo and Wyckhuys 2019; Cardoso *et al.* 2020; Montgomery *et al.* 2020; Wagner 2020). It is not always clear whether the insect declines discussed refer to population abundance, biomass or species diversity. Sometimes these terms are used interchangeably.

The most recent worldwide meta-analysis of trends in insect abundance and biomass was conducted by van Klink *et al.* (2020), who evaluated 166 long-term insect surveys across 1,676 sites

**Table 4.3.4-1 Recent studies in the United Kingdom associating pesticide use with trends in terrestrial arthropod population abundance or biomass.**

Scope (study period)	Study method	Pesticide	Arthropods	Findings	Reference
Sussex (1970-2004)	Monitoring of ~100 cereal fields/year	Insecticides, fungicides, herbicides	26 taxonomic groups	Abundance of Coleoptera and Araneae declined with increasing total pesticide use. Trends in abundance of other groups of arthropods were more associated with weather parameters.	Ewald <i>et al.</i> (2015)
National (1985-2012)	Population abundance indices from the Butterfly Monitoring Scheme	Neonicotinoid insecticides	17 butterfly species	Area of farmland treated the previous year with neonicotinoids was negatively associated with butterfly abundance indices Abundance Indices for 15 of 17 species show negative associations with neonicotinoid usage.	Gilburn <i>et al.</i> (2015)

in 41 countries. They found strong evidence for a decline in terrestrial insect abundance (estimated to be almost 11 per cent per decade), particularly in North America and Europe. Insect abundance trends were negatively associated with urbanization and positively with degree of crop cover. No evaluation of the effects of agricultural intensification or pesticide use was made.

Wagner (2020), in his review of studies on insect declines, did find that these declines have been linked to agricultural intensification and to insecticide use. However, the number of studies that explicitly assess the effects of current insecticide use on the abundance or biomass of arthropods – other than pollinators or natural enemies of pests – is very small. A few studies in the United Kingdom have associated the use of pesticides with decreasing abundances of beetles, butterflies and spiders (Table 4.3.4-1).

Table 4.3.4-1 Recent studies in the United Kingdom associating pesticide use with trends in terrestrial arthropod population abundance or biomass.

It may seem clear that widespread pesticide, particularly insecticide, use would result in a decline in the abundance or biomass of terrestrial arthropod populations beyond the boundary of treated fields. However, very little field evidence appears to be available to confirm or disprove such a hypothesis. On the other hand, more evidence has been published indicating a decline in the diversity (e.g., number of species) of terrestrial arthropods which was associated with the use of pesticides (Chapter 4.3.6).

### 4.3.5 The aquatic environment

As discussed in Chapter 4.3.2, pesticides applied in agricultural fields may reach edge-of-field water bodies via spray drift and run-off, among other entry routes. Subsequently, pollution of these water bodies may result in toxic effects on aquatic biota and ecosystem functioning (Schäfer, van den Brink and Liess 2011).

Current pesticide toxicity assessments largely rely on laboratory bioassays and semi-field experiments in model ecosystems (i.e., microcosms and mesocosms)

(Schäfer 2019). Field studies evaluating the effects of pesticides on aquatic ecosystem structure and functioning are not frequently conducted. The high labour intensity, costs, spatial-temporal variation and difficulty of establishing causal dose-effect relationships are the most common reasons indicated for this low research effort using field testing and monitoring (Schäfer 2019; Zubrod *et al.* 2019; Rosic *et al.* 2020; Schepker *et al.* 2020).

#### Risk as a function of aquatic pesticide concentrations

Given the difficulty of conducting field studies and monitoring real-time pesticide use, an often applied method for evaluating the risks of pesticides to aquatic organisms is to compare field-measured pesticide concentrations with environmental or regulatory threshold values. These threshold values are usually set by using toxicity data derived in the above mentioned laboratory bioassays and/or semi-field studies.

Global and regional assessments of pesticide concentrations in freshwater ecosystems have been reviewed in Chapter 4.3.2. Such monitoring is heavily biased towards North America and Europe, with relatively little information available from other parts of the world. Whenever data have been available, however, measured pesticide concentrations have often exceeded environmental or regulatory threshold values. This implies that actual applications of pesticide products, which generally have been approved for use, frequently have a significant likelihood of causing adverse effects on aquatic organisms.

#### Field effects of pesticides in general

Schäfer (2019) reviewed studies concerning the effects of pesticides (mainly insecticides and fungicides) on field communities of freshwater macroinvertebrates. Of the 13 reviewed field studies from different world regions conducted during the last 15 years, nine found a clear or likely relationship between pesticide toxicity or concentrations on the one hand and biotic responses (e.g., community composition or different community indices) on the other (Table 4.3.5-1). These field studies indicate widespread effects from agricultural

**Table 4.3.5-1 Studies, covering at least five agricultural water bodies, which involved pesticide residue sampling and macroinvertebrate community sampling. Effects from urban and industrial land use were excluded. Studies reanalysing the same data are not considered independently.** Adapted from Schäfer (2019).

Region	Number and types of sites	Type of biological response	Relationship between pesticide exposure and biological response
Western France and southern Finland	29 streams	Species at risk of pesticides (SPEAR) index	Clear ( $R^2 = 0.64$ )
Central Germany	19 streams	SPEAR index	Clear ( $R^2 = 0.59$ )
Denmark	14 streams	SPEAR index	Clear (multiple time points, $R^2$ between 0.4 and 0.68)
Central Argentina	22 streams	SPEAR index	Clear (multiple time points, $R^2$ between 0.35 and 0.42)
South-eastern Australia	24 streams	SPEAR index	Clear ( $R^2 = 0.68$ )
Midwestern United States	98 streams	Multimetric index	Likely ( $R^2 = 0.22$ )
Central Argentina	6 channels	Species richness and total abundance	Likely ( $r = 0.59$ and $0.61$ )
Netherlands	14 ponds and ditches	Community composition	Clear (5.4 per cent of community variance explained)
Portugal	6 ditches	Community composition	Clear (23.7 per cent of community variance explained)
Northern Germany	9 streams	SPEAR index	Ambiguous (group-based comparison)
Eastern Argentina	8 streams	Community composition	Ambiguous (group-based comparison)
Southern Brazil and Paraguay	18 and 17 streams	27 indices including SPEAR	Ambiguous to none (most metrics exhibit no correlation including SPEAR)
Western Germany	23 streams	8 indices including SPEAR	Ambiguous (correlation with SPEAR and per cent EPT (ephemeroptera, plecoptera and trichoptera) between 0.26 and 0.4)

pesticide use despite the existence of pesticide regulation. Further field studies are required in order to understand the mechanisms underlying pesticide toxicity; provide the data to develop and critically evaluate effect models; and provide information about adaptation processes in aquatic communities and drivers of community composition in the face of global environmental change (Schäfer 2019).

Further effects of pesticides on the biological diversity of communities of aquatic organisms have been observed in the global review by Sánchez-Bayo and Wyckhuys (2019) and studies by Beketov *et al.* (2013) in Germany, France and Australia and Ito *et al.* (2020) in Japan (Chapter 4.3.6). Pesticides were one of several

drivers of aquatic biodiversity losses, albeit an important one.

Macroinvertebrates play an important role in the decomposition process such as leaf litter breakdown. Subsequently, a loss in aquatic macroinvertebrate abundance and diversity may exert impacts on ecosystem functioning. Schäfer *et al.* (2012) compiled data from eight field studies in Europe, Siberia and Australia to derive thresholds for the effects of pesticides on macroinvertebrate communities and leaf breakdown. Dose-response models for the relationship of pesticide toxicity and the abundance of sensitive macroinvertebrate taxa showed significant differences with reference sites at 1/1,000 to 1/10,000 of the median

acute effect concentration ( $EC_{50}$ ) for *Daphnia magna*. The invertebrate leaf breakdown rate was positively related to the abundance of pesticide-sensitive macroinvertebrate species in the communities (Schäfer *et al.* 2012).

In line with these findings, Peters, Bundschuh and Schäfer (2013) reported that more than one-third of the reviewed studies indicated reductions in ecosystem functions at pesticide concentrations that are assumed to be protective by regulatory standards. In addition to direct toxic effects on macroinvertebrates, negative effects on ecosystem functioning (e.g., decomposition and nutrient recycling) have been reported as a result of pesticide-induced toxicity to microorganisms at environmentally realistic concentrations (Staley, Harwood and Rohr 2015).

### Field effects of insecticides

In line with the previous chapter, the effects of insecticides on both water-dwelling (Brander *et al.* 2016) and benthic (Li, H. *et al.* 2017) invertebrates have been reported on a global scale at environmental realistic concentrations. Huang, Cui and Duan (2020) also demonstrated that measured environmental concentrations of the organophosphate insecticide chlorpyrifos were often above allowable environmental limits. These studies recommended the development of accurate sediment quality criteria and more effective ecological risk assessment methods. In the EU, the effects assessment of pesticides with regard to sediment-dwelling organisms in edge-of-field surface water has received increasing attention in recent years (EFSA 2015). In addition, a case study with chlorpyrifos has shown the potential of using post-registration monitoring data in environmental pesticide risk assessments (Rico *et al.* 2020).

Neonicotinoid insecticides have received increasing attention in surface water pesticide risk assessment, as the standard test species *Daphnia magna* is highly tolerant to this insecticide group (Sánchez-Bayo and Tennekes 2020). Apart from laboratory and mesocosm studies, however, limited research has been directed towards the role neonicotinoids may have in

structuring aquatic invertebrate communities in field settings (Schepker *et al.* 2020).

Two large-scale wetland field studies in Nebraska (United States) (Schepker *et al.* 2020) and Saskatchewan (Canada) (Cavallaro *et al.* 2019) revealed that neonicotinoid concentrations were significant factors in shaping invertebrate field communities. Schepker *et al.* (2020) further reported that the significant negative effects on aquatic invertebrate biomass observed across all wetlands studied occurred at neonicotinoid concentrations below benchmark concentrations proposed by government regulations.

Another issue that has been raised in regard to the risks of neonicotinoids to aquatic life is that their toxicity increases with exposure time, as much as with the dose, and has therefore been described as time-cumulative toxicity. Regulatory assessments for this class of compounds should not be based solely on exposure doses, but also need to consider the time factor (Sánchez-Bayo and Tennekes 2020).

Although OCPs were taken off the market decades ago in most parts of the world, they remain present in low concentrations due to their high persistence. Martyniuk, Mehinto and Denslow (2020) compiled the available data on molecular and apical endpoints and concluded that prolonged exposure to these low environmental OCP levels (in low to mid ng/L range) are likely to disrupt sex hormone production in male fish, including a reduction of testosterone. At the same time, there is an increase in vitellogenin, suggesting agonism of the oestrogen receptor. These changes lead to impaired sperm cell maturation and release and reduced fecundity (Martyniuk, Mehinto and Denslow 2020).

### Field effects of fungicides

In comparison to insecticides, exposure to and the effects of fungicides and herbicides in aquatic ecosystems have received considerably less attention (Maltby, Brock and Van Den Brink 2009; Rico, Brock and Daam 2019; Zubrod *et al.* 2019; Rosic *et al.* 2020). Zubrod *et al.* (2019) compiled laboratory bioassay, model ecosystem and field

studies, but only reported field studies for five different fungicides. The study also showed that environmentally realistic concentrations of fungicides are likely to exert moderate to high risks to aquatic life (Figure 4.3.5-1). The authors indicated that the reasons for these identified high risks are presumably manifold, such as underestimation of field concentrations by exposure modelling, application of safety factors that are too low, and use of higher-tier risk assessment methods that can strongly increase regulatory acceptable concentrations (RACs). The non-inclusion of the most sensitive organisms (lowest effect concentrations are often for fungi and fungal-like organisms) in regulatory testing might have further contributed to this situation (Zubrod *et al.* 2019).

Rico, Brock and Daam (2019) compared lower-tier (bioassays) and higher-tier (model ecosystems)

RACs for fungicides. They concluded that the current RACs for individual fungicides, with a few exceptions (e.g., tebuconazole), show a sufficient level of protection for structural and functional fungal endpoints, but that more data are needed to extend this comparison to other fungicides with different modes of action. Consistent with Zubrod *et al.* (2019), Rico, Brock and Daam (2019) also concluded that further research is needed on the impact of realistic exposure regimes of (mixtures of) fungicidal compounds on the decomposer food chain.

For insecticides (arthropods) and herbicides (primary producers), a most sensitive taxonomic group of test species can generally be distinguished. For fungicides, this appears not to be the case as it depends on the chemical group or mode of action of the fungicide of concern (e.g., see Maltby Brock and Van Den Brink 2009).

▶ **Figure 4.3.5-1 Risk quotients for algae (squares), fish (circles) and invertebrates (triangles) as ratios of maximum detected global field concentrations and acute standard toxicity data. Open symbols indicate that toxicity was provided as “greater than” values. Risk quotients > 0.01 (dashed line) and > 0.1 (solid line) indicate moderate and high risks, respectively.** Zubrod *et al.* (2019).



In the study by Zubrod *et al.* (2019), however, risks were relatively similar across algae, fish, and invertebrates although high risks tended to occur more frequently in the case of invertebrates than in that of algae or fish (Figure 4.3.5-1). A comparison across continents showed most frequent risks for Europe (11 substances), followed by North America (six), Asia (four to five), Africa (three) and South America (two). This situation might not reflect only intensity of use, but also monitoring efforts (Zubrod *et al.* 2019).

### Field effects of herbicides

As in the case of fungicides, the potential side-effects of environmentally realistic herbicide concentrations in agricultural edge-of-field surface water on primary producers and on ecosystem functioning have been poorly studied. Rosic *et al.* (2020) reviewed the potential risks related to realistic field concentrations of the herbicides bromoxynil, diquat and paraquat to Australian freshwater life. They concluded that at concentrations resulting from current agricultural practices, diquat exerted toxic effects on snails and bromoxynil on microalgae. The clearest and most consistent evidence of adverse effects was found for paraquat. At realistic field concentrations paraquat severely inhibited healthy bacterial growth (*E. coli*), distorted tropical freshwater plankton communities, and increased fish mortality (common carp) three times more than the weed (water hyacinth) it was employed to control (Rosic *et al.* 2020).

Model ecosystem studies in general, including those designed to evaluate the toxicity of herbicides, have traditionally been designed to evaluate a concentration series enabling the setting of a no observed effect concentration (NOEC), which is ultimately to be compared with a predicted environmental concentration in a prospective pesticide risk assessment (van den Brink and Daam 2014). However, those studies have little relevance to the purpose of this report. Model ecosystem studies evaluating realistic pesticide application scenarios (or concentrations) are conducted in prospective risk assessments, but their results are often confidential and/or confined to regulatory reports. An evaluation of such reports, in combination with reported

pesticide field concentrations, would therefore be an interesting way forward to elucidate actual field risks of pesticides.

Some model ecosystem studies evaluating the effects of environmentally realistic herbicide concentrations on primary producers have been published in the open literature. Mohr *et al.* (2007, 2008), for example, demonstrated that adverse effects on algae and macrophytes are likely to occur at concentrations well below those detected after the registered use of the herbicide metazachlor. Model ecosystem studies designed to evaluate pesticide mixture exposure resulting from crop-based permissible applications of pesticides are also a promising way forward to elucidate (mixture) effects of a pesticide in actual potato (Arts *et al.* 2006), strawberry (Arts *et al.* 2017) or bulb (van Wijngaarden *et al.* 2004) cultures. Mixture applications of triazine herbicides, for example, are known to potentially result in synergistic effects in the field (Cedergreen 2014).

### Pesticide effects on marine ecosystems

Mariculture activities and river inputs can lead to pollution of coastal seawater with micropollutants such as antibiotics and pesticides, with a seaward decreasing trend of pesticide concentrations mainly due to pesticide dilution, dispersion and degradation (Grant *et al.* 2018; Xie *et al.* 2019). On the other hand, these decreasing pesticide concentrations may not suffice to prevent side effects on (especially filter-feeding) marine organisms that may bioaccumulate pesticides even when present in very low concentrations in environmental matrices (Ojemaye *et al.* 2020 and references therein).

Pesticides used on land may therefore pose risks to marine organisms and especially to organisms in coastal areas (Xie *et al.* 2019; Ojemaye *et al.* 2020; Parsons *et al.* 2020), the more so since their sensitivity to pesticides has been demonstrated to be comparable to that of freshwater organisms (Maltby *et al.* 2005; Klok *et al.* 2012; EFSA 2013b; European Commission 2018).

No recent global reviews of the effects of pesticides on marine ecosystems were available,

however a few outlined below indicate that marine organisms may be exposed to pesticide concentrations that pose a risk to population health.

Ojemaye *et al.* (2020) detected five herbicides in seawater, sediment, seaweed and selected marine organisms, such as limpets (*Cymbula granatina*), mussels (*Mytilus galloprovincialis*), and sea urchins (*Parechinus angulosus*), which were present in the near shore environment of Camps Bay (Cape Town, South Africa). In addition to environmental risks, these herbicides were indicated to pose adverse health effects should an average sized human (70 kg) consume any of the marine species analysed in the study on a daily basis over a lifetime (Ojemaye *et al.* 2020). Deltamethrin, an anti-sea lice pesticide used in the salmonid aquaculture industry, was also found to pose a significant risk to European lobster in the Norwegian marine environment (Parsons *et al.* 2020).

Marine monitoring studies may be especially important in coastal areas with high biodiversity value such as the Great Barrier Reef. The annual report on inshore pesticide monitoring of the Great Barrier Reef Marine Park Authority indicated that the current water quality guideline values (levels to protect 99 per cent of marine species) were not exceeded at any site for any pesticide in 2016-2017 (Grant *et al.* 2018). The herbicides diuron, atrazine and hexazinone were the pesticides most frequently detected and in the highest concentrations, which was related to pesticide usage by the sugarcane industry in adjacent catchments. Despite overall low pesticide concentrations, Grant *et al.* (2018) argue that the cumulative effects of long-term exposure to the mixture of chemicals on the resilience of the reef ecosystem need to be evaluated, especially considering the multiple local, regional and global stressors already acting on this ecosystem such as cyclonic activity and the effects of global climate change (increasing sea temperatures, ocean acidification).

Recently Spilsbury *et al.* (2020) have indicated that an ecotoxicological risk exists resulting from pesticide mixtures in 38.5 per cent of samples

taken from Australian rivers discharging to the Great Barrier Reef. Analysis of land use patterns in the catchment areas showed an association between the sugarcane industry and elevated risk levels, which were driven by the presence of diuron (Spilsbury *et al.* 2020).

However, the chronic effects on corals and seagrass of low-level pesticide exposure, especially combined with other local and global pressures, remain poorly understood on the Great Barrier Reef (Grant *et al.* 2018). Furthermore, Brodie and Landos (2019) have indicated that potential effects on important local species of the reef's marine environment have only been studied through laboratory single species toxicity testing. Thus there is a need to include biological monitoring of field communities (e.g., through the use of biomarkers) along with exposure assessments in future coastal and marine monitoring campaigns (Varea, Piovano and Ferreira 2020).

#### 4.3.6 Pesticides and biodiversity

Biological diversity – or biodiversity – has been defined by the Convention on Biological Diversity (CBD) as *the variability among living organisms from all sources including, inter alia, terrestrial, marine and other aquatic ecosystems and the ecological complexes of which they are part; this includes diversity within species, between species and of ecosystems* (Convention on Biological Diversity [CBD] 1992, Chapter 3.2.4).

At its simplest, biodiversity is the number of species present in a given geographical unit: that is, species richness. More complex indices of species richness may include relative abundances, biomasses or productivities of coexisting species. However, biodiversity can also be evaluated at a smaller scale than a species, e.g., genetic diversity within the species; or at a larger scale, such as the variety of community types or ecosystems present in a region (Begon, Harper and Townsend 1996). The CBD recognizes three main components of biodiversity which are important for its conservation and sustainable use: genomes and genes; species and communities; and ecosystems and habitats (CBD 2019).

## Effects of pesticides on biodiversity

Many adverse effects of pesticides on non-target organisms and communities discussed in Chapter 4.3 above may have an impact on biodiversity. In this section studies will be discussed in which the use of pesticides has been explicitly linked to adverse effects on biodiversity.

No systematic global review of the effects of pesticides on biodiversity is currently available, however there are several global reviews and large-scale studies and partial reviews of effects on biodiversity. These are summarized in Annex 4.3-6. Included are reviews comparing organic with conventional agriculture, as the absence or strong limitation of pesticide use is an important characteristic of organic production.

The use of pesticides in agriculture, public health and elsewhere has consistently been mentioned in international reviews and reports as one of the drivers of biodiversity loss (Table 4.3.6-1). However, these reviews are generally not very specific as to the exact role of pesticides in the decline of biodiversity. With the exception of the IPBES assessment report on pollinators (Potts, Imperatriz-Fonseca and Ngo 2016), these status reports do not systematically review the effects of pesticides on biodiversity.

Relatively few studies have assessed the effects of pesticide use on parameters that describe or quantify biodiversity. More common are studies that assess the effects of agricultural intensification on biodiversity, although these studies may include consideration of factors such as fertilizer use, habitat destruction, increase in large-scale monocultures, reduction in crop rotation, besides pesticide use. The number of studies that attempt to disaggregate the importance of pesticides among other drivers of biodiversity loss is limited. In other cases, the effects of pesticides on abundance of individual taxa are assessed and subsequently cited as impact on biodiversity.

## Arthropod biodiversity

The majority of available assessments concern the effects of pesticides on biodiversity of insects

and other arthropods. This is not surprising given the fact that insecticides and certain fungicides, in particular, are well known to adversely affect both terrestrial and aquatic arthropods (Chapters 4.3.3, 4.3.4 and 4.3.5).

Sánchez-Bayo and Wyckhuys (2019) reviewed a large number of studies of insect declines across the globe, in both terrestrial and aquatic environments, and attempted to assess the underlying drivers. They found that 41 per cent of insect species are in decline and one-third of species are threatened with extinction. Among aquatic insects, habitat and dietary generalists, as well as pollutant-tolerant species, are replacing the large insect biodiversity losses experienced in water within agricultural and urban settings.

The main drivers of these species declines have been habitat loss and conversion to intensive agriculture and urbanization along with pollution, mainly by synthetic pesticides and fertilizers. When individual factors were assessed, the use of pesticides was associated with insect declines in 13 per cent of cases, the second most important factor identified, after intensive agriculture (in which pesticides may also be an integral factor). Although intensive agriculture and pesticides are the main factors associated with insect declines (Figure 4.3.6-1B), habitat loss appears to be the largest driver of decline, followed by pollution (including by pesticides) (Figure 4.3.6-1A).

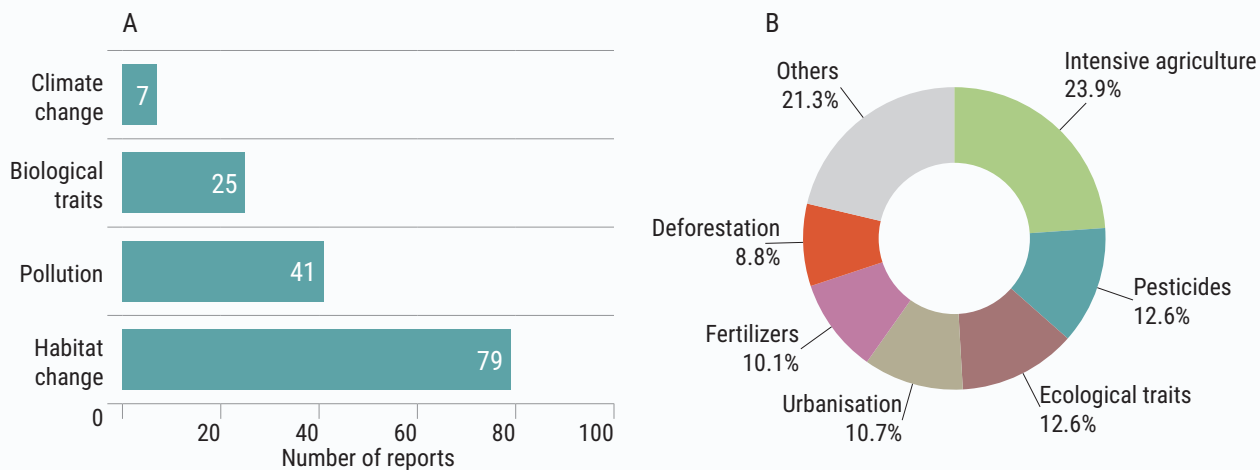
The impact of pesticides on insect biodiversity is further substantiated by global comparisons between organic and conventional agriculture, which showed that organic production was associated with significantly higher diversity of wild bee populations (Kennedy *et al.* 2013) or insects in general (Tuck *et al.* 2013). Other large-scale studies in the United States and Europe have confirmed that the use of pesticides, particularly insecticides, is associated with declines of wild bee diversity (Brittain *et al.* 2010; Park *et al.* 2015; Mallinger, Watts and Gratton 2015), as well as diversity of bumblebees and butterflies (Brittain *et al.* 2010; Forister *et al.* 2016). Sattler *et al.* (2020) have found that pesticide use has strong negative effects on



Table 4.3.6-1 Global biodiversity reviews and status reports citing pesticide use as one of the drivers of biodiversity loss

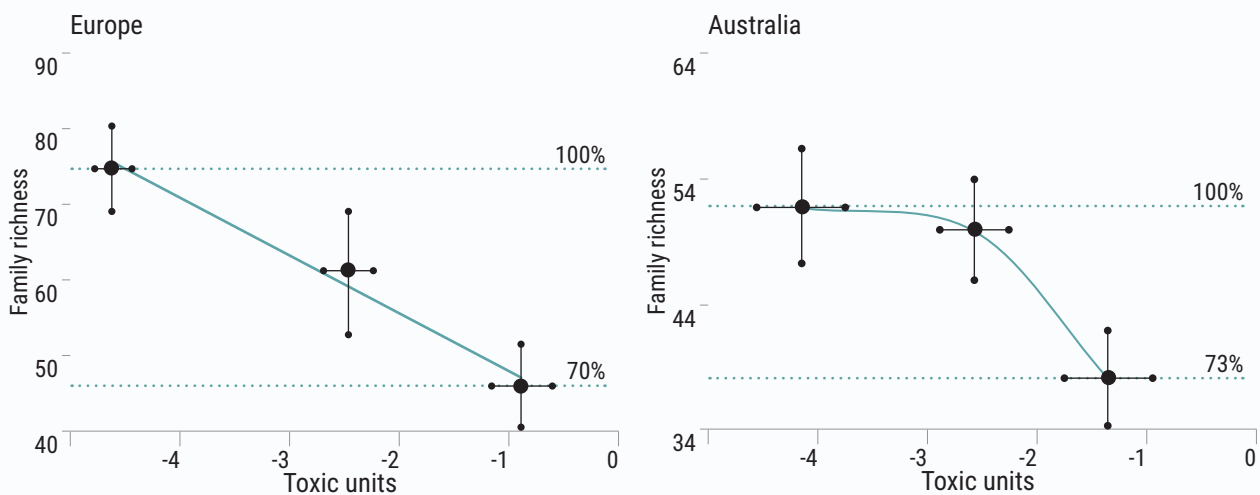
Publication year	International organizations	Title	Mentions of pesticide use affecting biodiversity
2020	Food and Agriculture Organization of the United Nations (FAO), Intergovernmental Technical Panel on Soils (ITPS), Global Soil Biodiversity Initiative, Secretariat of the Convention of Biological Diversity and European Commission	State of Knowledge of Soil Biodiversity – Status, Challenges and Potentialities (FAO, ITPS, Secretariat of the Convention on Biological Diversity and European Commission 2020)	Agricultural intensification, and associated greater use of external inputs such as pesticides, has resulted in decreased soil biodiversity.
2020	Organisation for Economic Co-operation and Development (OECD)	Managing the Biodiversity Impacts of Fertiliser and Pesticide Use: Overview and Insights from Trends and Policies across Selected OECD Countries (Sud 2020)	Various studies have shown that excessive use of pesticides has led to biodiversity loss and ecosystem degradation. (The report cites a number of studies.)
2019	FAO	The State of the World's Biodiversity for Food and Agriculture (FAO 2019)	There is abundant evidence that intensification of crop, livestock and aquaculture systems through excessive use of synthetic inputs adversely affects biodiversity for food and agriculture and particularly associated biodiversity. Examples are provided of effects of pesticides on pollinators, soil organisms, biological control agents and aquatic organisms.
2019	Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services (IPBES)	The Global Assessment Report on Biodiversity and Ecosystem Services (IPBES 2019)	Pesticides are mentioned as among the drivers of changes in biodiversity (Sections 2.1 and 2.3).
2016	IPBES	Assessment Report of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services on Pollinators, Pollination and Food Production (Potts, Imperatriz-Fonseca and Ngo 2016)	Changes in land use or climate, intensive agricultural management and pesticide use, invasive alien species and pathogens affect pollinator health, abundance, diversity and pollination directly.
2015	FAO and ITPS	Status of the World's Soil Resources (FAO and ITPS 2015)	The large-scale use of pesticides may have direct or indirect effects on soil biodiversity. However, studies on the effect that pesticides have on soil biodiversity have shown contradictory results.
2014-2020	Convention on Biological Diversity	Global Biodiversity Outlook (GBO), most recently the GBO 5 (2020) (Secretariat of the Convention on Biological Diversity 2020)	The use of fertilizers and pesticides has stabilized globally, though at high levels. Despite such progress, biodiversity continues to decline in landscapes used to produce food and timber; and food and agricultural production remains among the main drivers of global biodiversity loss... Pollution, including from excess nutrients, pesticides, plastics and other waste, continues to be a major driver of biodiversity loss.
2005	Millennium Ecosystem Assessment	Ecosystems and Human Well-being: Biodiversity Synthesis (Millennium Ecosystem Assessment 2005)	There have been worldwide declines in pollinator diversity... The causes of these declines are multiple, but habitat destruction and the use of pesticide are especially important.

► **Figure 4.3.6-1** The main drivers (A) and factors (B) associated with insect declines. Pesticides are identified as the second most important factor associated with declines of insect species' abundance and biodiversity. Shown is (A) the number and (B) the percentage of studies in which specific drivers and factors of decline were determined. Based on Sánchez-Bayo and Wyckhuys (2019).



► **Figure 4.3.6-2** Concentration-response dependence between the mean pesticide concentration and mean overall aquatic macroinvertebrate family richness measured in sampling sites in Europe and Australia. The dashed horizontal lines indicate maximum and minimum mean richness and are marked with the percentages compared to maximum richness. The error bars indicate 95 per cent confidence intervals.

Beketov *et al.* (2013).



taxonomic and functional diversity of terrestrial rice field arthropods.

For the aquatic environment, Beketov *et al.* (2013) evaluated the field effects of pesticides on the regional taxa richness of stream macroinvertebrates in Europe (Germany and France) and Australia (southern Victoria). By capturing episodic run-off events, it could be determined that pesticides caused statistically

significant effects on both species and family richness in both regions, with losses in family richness up to 42 per cent of recorded taxonomic pools (Figure 4.3.6-2). Furthermore, the effects in Europe were detected at concentrations that current legislation considers environmentally protective (Beketov *et al.* 2013).

Ito *et al.* (2020) evaluated the impacts of pesticides and other environmental stressors (including

eutrophication, decreased macrophyte coverage, physical habitat destruction and invasive alien species) on the taxonomic richness of freshwater animals in 21 irrigation ponds in Japan. Similarly to the conclusions of Sánchez-Bayo and Wyckhuys (2019), Ito *et al.* (2020) found that the taxonomic richness of freshwater animals in Japanese irrigation ponds has been affected by multiple stressors including pesticides.

In other cases, however, pesticide effects are less clear-cut, e.g., for soil fauna biodiversity (de Graaff *et al.* 2019). Indeed, studies evaluating the effects pesticides may have on soil biodiversity have shown contradictory results. Effects appear to be dependent on a variety of factors including chemical composition, the pesticide application rate, the buffering capacity of the soil, the soil organisms considered and the time scale of the study. There have been no comprehensive studies to quantify the effects of pesticides on soil organisms at multiple trophic levels across regions (FAO and ITPS 2015).

More generally, various authors have indicated that whether effects of pesticides on biodiversity are observed in the field may depend on many parameters and complex interactions. For instance, Mallinger, Werts and Gratton (2015) and Park *et al.* (2015) observed that pesticide use in apple orchards affected the species richness of certain groups of wild bees but not of others.

### Vertebrate biodiversity

Few large-scale studies and reviews of pesticide effects on vertebrate biodiversity are available, and most have focused on birds. In their global meta-analysis, Tuck *et al.* (2013) found 20 per cent greater bird species richness in organic agriculture compared to conventional production systems.

A large study was conducted on 270 cereal farms across eight European countries, in which the effects of 13 components of agricultural intensification on biodiversity were investigated across three trophic levels (diversity of wild plants, carabid beetles and breeding bird species) (Geiger *et al.* 2010; Emmerson *et al.* 2016). The use of pesticides, especially insecticides and fungicides, was reported to have consistent negative effects

on species diversity at all three trophic levels. Bird species diversity, in particular, declined with increasing frequency of fungicide applications. It was noted that while finding negative effects of pesticides on biodiversity may be unsurprising, these effects were found consistently at a pan-European scale and despite decades of policy to reduce pesticide risks.

In France, Chiron *et al.* (2014) observed that, as herbicide dose increased, there was a shift in functional groups from specialist species to more generalist ones but no effect on species richness. Losses of endangered mammal, bird, amphibian and reptile species of in Canada were found to be strongly associated with the proportion of the region treated with agricultural pesticides (Gibbs, MacKey and Currie 2009). Species losses were more strongly related to herbicide use than to the use of other pesticides.

### 4.3.7 Knowledge gaps on environmental effects of pesticides

#### Availability of systematic reviews

Many scientific studies have been and are being conducted on the occurrence of pesticides in the environment, as well as on their potential impact on non-target organisms and ecosystems. Nevertheless, very few systematic reviews have been conducted of the available data, or of what their implications may be for pesticide risks and their mitigation options.

To make full use of existing research, the scientific literature should be monitored and analysed on a regular basis through systematic reviews and/or meta-analyses, particularly for topics of specific interest with regard to regulatory decision-making (Group of Chief Scientific Advisors 2018). Such topics include, but are not limited to, pesticide concentrations in the environment and their potential risks; the accuracy of fate models (and their scenarios) in predicting pesticide field concentrations; the field effects of pesticides (mixtures) on populations and communities of non-target organisms; the impact of pesticides on the sustainability of agricultural production and disease vector control; and mechanistic studies

evaluating the underlying pathways from pesticide exposure until adverse effects in organisms.

It is important that the results of such reviews and meta-analyses be interpreted with consideration given to the risks of the current authorized use of the pesticides involved, and that results be made available to risk managers and decision-makers in other parts of the world. A specific platform may need to be established for the elaboration and publication of such reviews, similar, for example, to the Cochrane Reviews of research in health care and health policy (Cochrane Library 2020). As these systematic reviews would go beyond the environmental effects of individual pesticides (i.e., include pesticide mixtures), and thus current regulatory approaches to pesticide registration, dedicated efforts by research or regulatory bodies would likely be required.

### Environmental risk assessment

Substantial advances have been made in strengthening the environmental risk assessment procedures used as a basis for the registration of pesticides in many parts of the world. Toxicity data for a broader range of non-target organisms have been generated; adverse outcome pathways are increasingly being elucidated; more realistic exposure and ecological effect models have been developed; the protection of ecosystem services and biodiversity are better taken into account; and the validation of risk assessment approaches has improved.

Nevertheless, despite these significant improvements in prospective regulatory risk assessment, unexpected environmental impacts are frequently identified, typically many years after a pesticide has been placed on the market. Such impacts may be due to incorrect or unintended use of the pesticide; inadequate risk assessment models or approaches; or unforeseen adverse effects (Boyd 2018; Group of Chief Scientific Advisors 2018; Brühl and Zaller 2019; Schäfer *et al.* 2019; Topping, Aldrich and Berny 2020).

Many recommendations have been made on how best to strengthen environmental risk assessment,

either through the generation of additional pesticide toxicity or fate data, the development of new or better risk assessment models, or even the introduction of new risk assessment paradigms.

Some of the principal directions for improving pesticide risk assessment include the following:

- **Pesticide mixtures and other stressors:** Many organisms will be exposed to multiple pesticides, as well as to other stressors, which may result in larger effects on their long-term survival than separate exposure to each substance individually. There is a need to further develop methodologies that quantify the risks of exposure to multiple pesticides simultaneously or sequentially, as well as to other (chemical and non-chemical) stressors (Babut *et al.* 2013; Brühl and Zaller 2019; Topping, Aldrich and Berny 2020; Martin *et al.* 2021).
- **Neglected organisms and ecosystems:** Currently pesticide risk assessment focuses on a limited set of organism groups and ecosystems and is heavily biased towards temperate climatic conditions. Dedicated risk assessment procedures for (sub-)tropical and hot (semi-) arid ecosystems, microbial and fungal communities, amphibians and reptiles, and groundwater organisms are urgently needed (Sánchez-Bayo and Hyne 2011; EFSA 2018a; Ittner, Junghans and Werner 2018; Daam *et al.* 2019; Castaño-Sánchez, Hose and Reboleira 2020).
- **Indirect and delayed effects:** Pesticide ecotoxicological testing and risk assessment primarily aims at identifying direct lethal and sublethal effects on non-target organisms. However, indirect effects of pesticides, e.g., across trophic levels or by reducing plant cover, can also affect non-target populations and communities and require attention in risk assessment (Schäfer *et al.* 2019). In addition, pesticide effects may emerge, persist or even increase after the pesticide has dissipated from the ecosystem due to delayed (latent) effects or fitness costs associated with the adaptation

to pesticide exposure (Sánchez-Bayo and Tennekes 2020; Siddique *et al.* 2020). Such delayed effects are not yet well covered in risk assessment.

- **Agricultural sustainability:** While pesticides are known to affect the sustainability of agricultural production systems, prospective risk assessments on this topic tend to be limited to assessing the toxic effects of pesticides on a few non-target arthropods. Effects on ecosystem services such as natural pest control, pollination and nutrient cycling tend to become apparent only in post-registration studies and monitoring. There is a need to more systematically integrate the potential effects of pesticides on agro-ecosystem functioning and long-term agricultural sustainability up front in the prospective decision-making process.
- **Assessment at landscape scale:** At present, pesticide risks are evaluated based on a single product-single crop assessment. However, pesticides are applied at the landscape scale, where effects on non-target organisms are ultimately influenced by sequential pesticide applications in multiple fields and crops, migration and recovery of non-target populations across the landscape, and interactions among species, among others. Risk assessment approaches need to be developed which take into account “landscape dosing” with pesticides and the spatial dynamics of non-target organisms (Boyd 2018; Schäfer *et al.* 2019; Topping, Aldrich and Berny 2020).

### Monitoring

As discussed in the previous chapters, systematic monitoring of pesticide concentrations in environmental compartments such as air, surface waters, groundwater and soil is only conducted in some parts of the world; large data gaps exist in many others. Systematic monitoring of adverse effects on non-target organisms or communities is virtually absent in low and middle income countries and is rare even in high income economies.

The reasons for lack of environmental monitoring include its relatively high costs; the absence or inadequacy of pesticide residue analysis laboratories in many countries; the absence of relevant biomarkers of biological exposure; the complexity of field effects monitoring; and the difficulty of disaggregating the effects of individual pesticides from other (chemical and non-chemical) stressors on non-target organisms, communities and ecosystem functioning. Moreover, post-registration monitoring of environmental pesticide concentrations and effects is not legally required in many countries.

Due to limitations in the current prospective risk assessment procedures discussed above, and the lack of systematic post-registration monitoring, significant gaps in knowledge about adverse effects of current pesticide use on the environment persist. Recently, explicit calls for broader and more intensive post-registration monitoring or vigilance of pesticide use, concentrations and effects have therefore been made (Milner and Boyd 2017; Vijver *et al.* 2017; Group of Chief Scientific Advisors 2018; Rico *et al.* 2020; Topping, Aldrich and Berny 2020).

Post-registration environmental vigilance should ideally be based upon a combination of monitoring, modelling and experimental activities (Group of Chief Scientific Advisors 2018) and exploit existing large ecological and chemical datasets as well as currently scattered monitoring efforts (Vijver *et al.* 2017). It has been suggested that responsibility for such monitoring could be placed on pesticide manufacturers and users by applying previously registered designs for how data should be collected. New methods of precision farming also provide opportunities to facilitate data flows (Milner and Boyd 2017).

Data and knowledge obtained in this way could be used to assess or reassess risks as part of the national or regional pesticide registration system. In this way a “reality check” feedback loop would be established for the impact of pesticides on the environment which in turn can inform appropriate mitigation measures (Group of Chief Scientific Advisors 2018).

## 4.4 Adverse human health effects of pesticides

### 4.4.1 Overview

Almost all humans will be exposed in some way to pesticides, either when working with these products (e.g., farmers, gardeners, agricultural workers, professional pest control operators, workers in pesticide manufacturing, or those employed in pesticide sales, storage and disposal), through their diet (food, drinking water), via the environment (e.g., pesticides in air, dust and soil, or on treated surfaces in dwellings), or through products containing pesticides (e.g., impregnated mosquito nets or clothing, house paints).

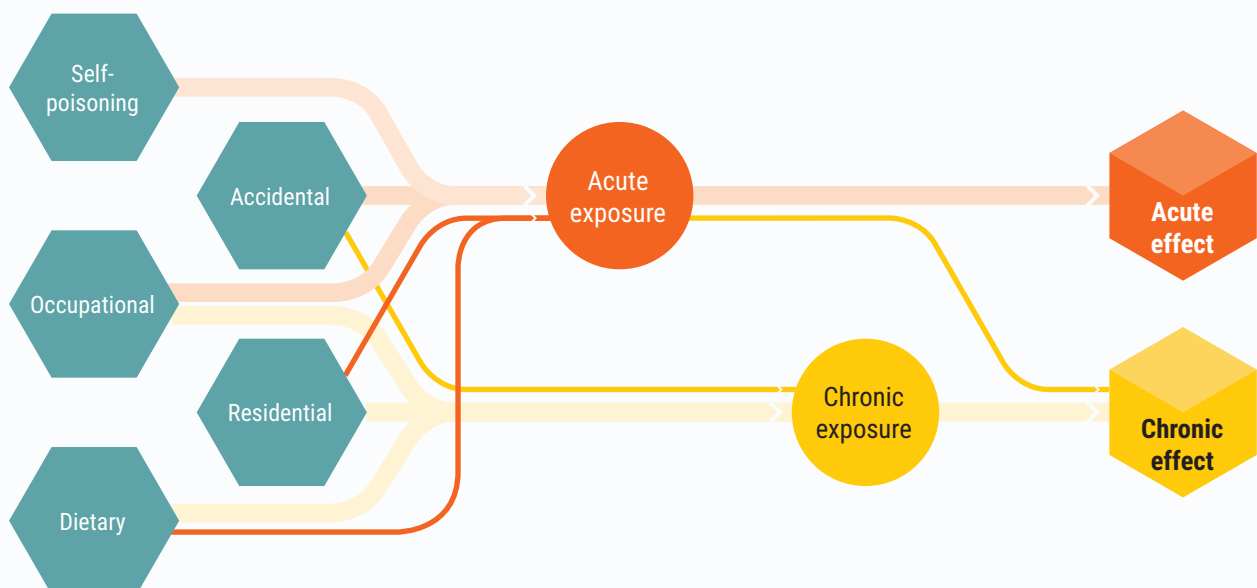
Exposure to pesticides can be acute or chronic (Figure 4.4-1). Examples of acute exposure are accidents, occupational exposure and self-poisoning, which tend to involve relatively high levels of exposure to pesticides. Chronic exposure occurs, for example, through diet, working for longer periods with pesticides, and exposure to pesticides in the local environment.

Human health effects can also be acute or chronic. Acute pesticide poisoning occurs rapidly

(within one to two days, sometimes within minutes or hours), after often high levels of acute exposure. Chronic health effects can develop over a longer period, sometimes many years. Chronic health effects may result from acute as well chronic exposure (Figure 4.4-1).

Most often, cases of acute unintentional pesticide poisoning tend to be occupational (e.g., poisoning of pesticide applicators or agricultural workers) or accidental (often in household settings). It has been estimated that in the 1980s, in developing countries alone, there were about 1 million serious unintentional poisoning cases per year, resulting in 20,000 deaths and an additional 25 million minor poisonings (WHO 1990; Jeyaratnam 1990). The only subsequent global estimate, based on a recent review of the scientific literature, suggests that about 385 million cases of unintentional acute pesticide poisoning occur every year, all severities combined, and that there are approximately 11,000 fatalities (Boedeker *et al.* 2020). This large increase in estimated acute pesticide poisoning may be partly due to growing pesticide use in many regions of the world. The Boedeker *et al.*

► **Figure 4.4-1 Human health effects of pesticides can show up in the short term (acute) or after a long period (chronic) and may be the result of activities leading to both acute and chronic exposure. Shown are the most common routes of poisoning (less likely options are indicated by thinner arrows).**



(2020) review applied a methodology which is likely to include a much larger number of minor pesticide poisoning cases than the estimates for the 1980s. [Chapter 4.4.2]

A limited number of pesticides appear to be responsible for most cases of acute pesticide poisoning. In cases representing all severities, these pesticides include widely available groups such as pyrethroids, disinfectants, anti-coagulant rodenticides and glyphosate based-herbicides. Moderate and severe intoxications are caused mostly by organophosphates, aluminium phosphide fumigants and bipyridylium herbicides (UNEP 2020). [Chapter 4.4.2]

Chronic exposure to pesticides has been associated with a wide range of adverse health effects (American Academy of Pediatrics 2012; Bergman *et al.* 2013; Mostafalou and Abdollahi 2013; Blair *et al.* 2015; Hertz-Picciotto *et al.* 2018). A large number of epidemiological studies published during the last decade have examined such associations. However, based on epidemiological studies alone it is difficult to demonstrate that a specific pesticide is causing an adverse health effect. This is due to the large number of pesticide active ingredients, the variety of study designs used, the long period of time that often occurs between exposure to a pesticide and the development of a disease, the frequently inadequate characterization and quantification of exposure to specific (groups of) pesticides, and the variable presence of confounding and bias (Blair *et al.* 2015; European Food Safety Panel on Plant Protection Products and their Residues [EFSA PPR Panel] 2017). [Chapter 4.4.3]

Despite these limitations, however, there is increasing evidence of significant positive associations between (mainly) occupational or residential exposure to specific (groups of) pesticides, or pesticides in general, and various adverse health outcomes, including both adult and childhood cancers as well as neurological, immunological and reproductive endpoints (Ntzani *et al.* 2013; Ntzani *et al.* 2020; Ohlander *et al.* 2020). [Chapter 4.4.3]

Most intentional pesticide poisoning consists of self-poisoning in suicide attempts. Suicides

with pesticides have been evaluated on a regular basis since the 1980s (Karunaratne *et al.* 2019). In the period 2006-2015 it was estimated that 1-2 million self-poisoning incidents related to pesticides occurred globally, resulting in about 168,000 deaths (Mew *et al.* 2017). Suicides by intentional pesticide ingestion occur primarily in rural areas of low and middle income countries in Africa, Asia and Central America (WHO 2014).

Pesticide suicides peaked in the 1990s and then started to decline (Karunaratne *et al.* 2019). Their number has fallen faster than that of overall suicides. The main drivers of this change are likely to be economic growth in some parts of the world and associated population shifts from rural to urban areas; further mechanization of agriculture; and stricter regulation of the most toxic pesticides (Mew *et al.* 2017; Gunnell *et al.* 2017; Karunaratne *et al.* 2019). [Chapter 4.4.4]

Many factors influence occupational pesticide exposure, related to the demography of the populations involved, pesticide application practices, the organization of the work environment, and workplace behaviours. A partial review of such factors shows a large variety of outcomes, indicating that whether a specific factor reduces or increases pesticide exposure and subsequent effects greatly depends on local conditions of use. [Chapter 4.4.5]

Demographic factors such as age, education and experience using pesticides have not been found to consistently increase or decrease pesticide health effects. Higher pesticide application rates and frequencies, or use of more toxic products, increase health effects, as do workplace behaviours that are in conflict with label instructions, good application practices or good occupational hygiene. Training in judicious pesticide use generally reduces pesticide exposure. If such training is conducted in isolation, however, its impact with regard to reducing health effects has been questioned (Table 4.4-1).

Long-sleeved shirts and trousers are worn by a majority of pesticide users across the world as basic protection against exposure. More specific personal protective equipment (PPE), such as gloves, masks, eye protection and chemical

**Table 4.4-1 Principal lines of evidence investigated for this report in order to identify human health effects of pesticide use.**

<i>Type of evidence</i>	Pesticide poisoning			Pesticide residues	Pesticide chronic effects	Risks factors
	Poison centre data	Published studies of poisoning	Suicide statistics	Monitoring of food and drinking water	Epidemiological studies	Various types of studies
<i>Type of study</i>	Mainly acute poisoning	Mainly acute poisoning	suicides	MRL exceedence, dietary risks	chronic effects	factors influencing pesticide exposure and effects
<i>Type of outcomes</i>	accidental, occupational, residential, self-poisoning	accidental, occupational, residential, self-poisoning	self-poisoning	dietary	occupational, dietary, residential	occupational residential

resistant footwear, is used by less than half of pesticide users globally. PPE is worn more regularly in high income than in low income countries. PPE may not be available or affordable for farmers in low income countries (Sapbamrer and Thammachai 2020). Moreover, many types of PPE are not suited to the hot and humid conditions in many of these countries (Garrigou *et al.* 2020; Sapbamrer and Thammachai 2020).

While not wearing appropriate PPE generally increases the incidence of poisoning, using this equipment does not always reduce it (Kim *et al.* 2013; Garrigou *et al.* 2020). Pesticide handling practices have a considerable influence on exposure. Furthermore, PPE does not provide complete protection against exposure. While proper use of PPE should always be promoted, in large parts of the world inadequate or partial use of PPE (together with the incomplete protection it provides) means PPE should be considered a last line of defence after other measures have been taken (Alli 2008; United States National Institute for Safety and Health 2015; European Agency for Safety and Health and Work 2018).

Residents living close to agricultural fields may be exposed to pesticides through different pathways. The most important are spray drift, volatilization of pesticides beyond the treated area, take-home exposure (e.g., when agricultural workers or

farmers have pesticide residues on their clothing or shoes), pesticide use in/around a residence, and dietary ingestion (Deziel *et al.* 2015).

Residents living closer to pesticide-treated agricultural lands have been found to have higher levels of pesticide residues/metabolites in their households and/or biological samples, higher levels of oxidative stress markers, greater DNA damage, and decreased activity of cholinesterase compared with people who live farther away. In addition, the amount of pesticides applied, the acreage treated, and the time of year compared with the spray season have been positively correlated with human exposure (Dereumeaux *et al.* 2020). Associations between proximity to agricultural fields and various adverse health outcomes have been observed, although studies have not always been conclusive (Dereumeaux *et al.* 2020; Health Council of the Netherlands 2020).

Residential exposure to pesticides is likely to be widespread, especially in areas where there is intensive agriculture. Risk mitigation measures (e.g., drift-reducing technologies, buffer zones and improved work hygiene) have been recommended or required in many countries.

Pesticide residues may remain in/on food or feed following pesticide applications to the crop or post-harvest treatments of the commodity,



or because of contamination from environmental sources. Many countries set maximum residue limits (MRLs), which are legally permitted levels of pesticide residues on food and feed commodities. Pesticide residues in food are monitored on a regular basis mainly in high and upper-middle income countries; in lower income economies, generally only irregular ad hoc residue assessments are conducted if at all (Table 4.4-11). [Chapter 4.4.6]

Pesticide residue monitoring programmes in high and upper-middle income countries show that exceedances of MRLs typically range from <1 to 10 per cent of samples taken in a given year (Table 4.4-12). No reviews were available for pesticide residues in commodities in lower income economies. However, there are indications that residues in food in these countries are higher, based on ad hoc local studies as well as monitoring of food imported into high income countries (FAO/WHO Joint Meeting on Pesticide Residues, personal communication).

Exceedance of MRLs indicates that good agricultural practices have not been respected, but does not mean that dietary risks are therefore unacceptable (Box 4.4-3). Most dietary risk assessments conducted in high and upper-middle income countries indicate that consumer health risks from pesticide residues in food are low. Scarcely any dietary risk assessments, on the other hand, are available from low and lower-middle income countries (Table 4.4-13).

Antimicrobial resistance (AMR) refers to microorganisms – bacteria, fungi, viruses and protozoans – that have acquired resistance to antimicrobial substances. An increasing number of human pathogens have become resistant to one or more antibiotics, severely reducing the options for treating the diseases they cause (WHO 2015). Pesticides may select or co-select for AMR (Wellcome 2018; FAO and WHO 2019; Taylor and Reeder 2020). [Chapter 4.4.7]

Antibiotics are used in crop protection, especially to control bacterial diseases (FAO 2015). Certain of these antibiotics (e.g., streptomycin, gentamycin, oxolinic acid) are considered very important in

human medicine (Berger *et al.* 2017; Wellcome 2018; WHO 2019; FAO and WHO 2019). However, they are used for crop protection much less than for veterinary purposes (FAO 2015; Taylor and Reeder 2020).

Furthermore, a rapid emergence is currently being seen of multi-drug resistant fungi for which the main treatment is antifungal medicines from the azole group (Fisher *et al.* 2018). The same group of chemicals is also among the fungicides most used in crop protection. There is increasing evidence that use of azole fungicides in agriculture is at least partly responsible for resistance development in human fungal diseases (Berger *et al.* 2017; Fisher *et al.* 2018; Wellcome 2018).

Copper fungicides, another widely used type of agricultural fungicides, although not used in human medicine, have been shown to co-select for AMR (Wellcome 2018; FAO and WHO 2019). The use of chemical disinfectants, of which a surge has been seen during the COVID-19 pandemic, may also select for AMR in antimicrobial human drugs, although evidence is still limited (FAO and WHO 2019).

Overall, the use of pesticides which have been shown (or have the potential) to select for AMR in human diseases, and possible subsequent failure of medical treatments, is receiving increasing attention.

Much knowledge has been amassed during the last few decades about the human health effects of pesticides. However, there is scope for further improvement in the scientific data that underpin human health risk assessments of pesticides and the methods by which such data are analysed (Science Advice for Policy by European Academies [SAPEA] 2018). [Chapter 4.4.8]

Knowledge gaps have been identified in the toxicological studies that generate data for risk assessments, the epidemiology of health effects of pesticides, in estimates of human exposure to pesticides and in post-marketing surveillance of approved pesticides (Milner and Boyd 2017; European Food Safety Authority Scientific Committee 2019; Liu *et al.* 2019).

Different lines of evidence regarding the effects of pesticide use on human health are evaluated in this report (Table 4.4-1). The focus of this chapter is on observed health effects of pesticides under real conditions of use. The chapter does not cover all possible human health risks of pesticide use, nor is it a detailed discussion of health risk assessment methodology. The dietary risk assessments discussed below are only included when they are based on pesticide residue levels following actual use.

#### 4.4.2 Acute unintentional pesticide poisoning

Acute unintentional pesticide poisoning tends to occur soon after exposure to relatively high levels of a pesticide. The main activities leading to acute health effects of pesticides are work-related (e.g., applying pesticides, harvesting and packing treated crops, manufacturing pesticides), accidental exposure, or self-poisoning. In some cases, bystanders and residents living close to areas treated with pesticides may be acutely poisoned (e.g., through pesticide drift), as may be consumers of food contaminated with high levels of a pesticide. However, the latter cases are less common and would often be classified as accidents.

Pesticide poisoning can have different levels of severity, ranging from minor (with only mild, transient symptoms) to severe (with life-threatening symptoms) or even death (Table 4.4-2). While mild

pesticide poisoning symptoms are often transient, this is not always the case. (e.g., Kamel *et al.* 2007; Baldi *et al.* 2011). Epidemiological studies on such effects are relatively scarce.

#### Historical estimates of pesticide poisoning

The earliest published global estimates of acute unintentional pesticide poisoning date to the early 1970s, when the WHO Expert Committee on the Safe Use of Pesticides, using a model based on poisoning statistics from 19 countries, arrived at a first estimate of about 500,000 accidental/occupational poisoning cases per year (Copplestone 1977). Subsequently, Levine (1986) updated these estimates using data until the mid-1980s from a larger number of countries; these estimates of annual acute unintentional poisoning ranged from 800,000 to 1.5 million cases, double to triple those made a decade earlier.

WHO (1990) and Jeyaratnam (1990), using the data from Levine (1986) and additional poisoning statistics mainly from Asia, subsequently estimated that there were 1 million serious unintentional poisoning cases per year, of which 70 per cent were occupational and the rest accidental. Furthermore, 25 million minor poisonings per year were estimated to occur in developing countries only.

Litchfield (2005) discussed the shortcomings of the previous estimates, suggesting that they

**Table 4.4-2 Poisoning severity score, as applied by the World Health Organization (WHO) and many national poison centres.** Persson *et al.* (1998); Roberts and Reigart (2013); WHO (2020b).

Severity grade		Examples of symptoms or signs of pesticide poisoning	
None	0	No symptoms or signs related to poisoning	
Minor	1	Mild, transient and spontaneously resolving symptoms	Irritation (respiratory, skin, eye), vertigo, headache, nausea, mild muscular pains
Moderate	2	Pronounced or prolonged symptoms	Pronounced or prolonged vomiting or diarrhoea, prolonged coughing, burns in the gastro-intestinal tract, confusion, agitation, unconsciousness, pronounced cholinergic/anticholinergic symptoms, infrequent, generalized or local seizures
Severe	3	Severe or life-threatening symptoms	Permanent eye damage, manifest respiratory insufficiency, pulmonary oedema, pulmonary fibrosis, frequent and generalized seizures, deep coma
Fatal	4	Death	

overestimated pesticide poisoning, but did not provide a comprehensive alternative. Others have argued that a large percentage of unintentional poisoning cases are not reported, suggesting that official data underestimate the real situation (see the chapter on poison centre statistics below).

Thereafter, no global estimates of unintentional pesticide poisoning were made until the effort by Boedeker *et al.* (2020) (see below). As a result, even recent reviews and discussions of acute pesticide poisoning (APP) (Jørs, Neupane and London 2018; Tyrell *et al.* 2019) cite estimates dating back 30 years which were made on the basis of even older poisoning statistics.

### Poison centre statistics

Poison centres are an important source of information about pesticide poisoning. In addition to providing advice on, and assistance with, the prevention, diagnosis and management of poisoning, they often maintain databases on cases of poisoning. Nevertheless, in early 2021 only 47 per cent of WHO member states had one or more poison centres, with a lack of coverage especially in low income countries (WHO 2020c) (Figure 4.4-2).

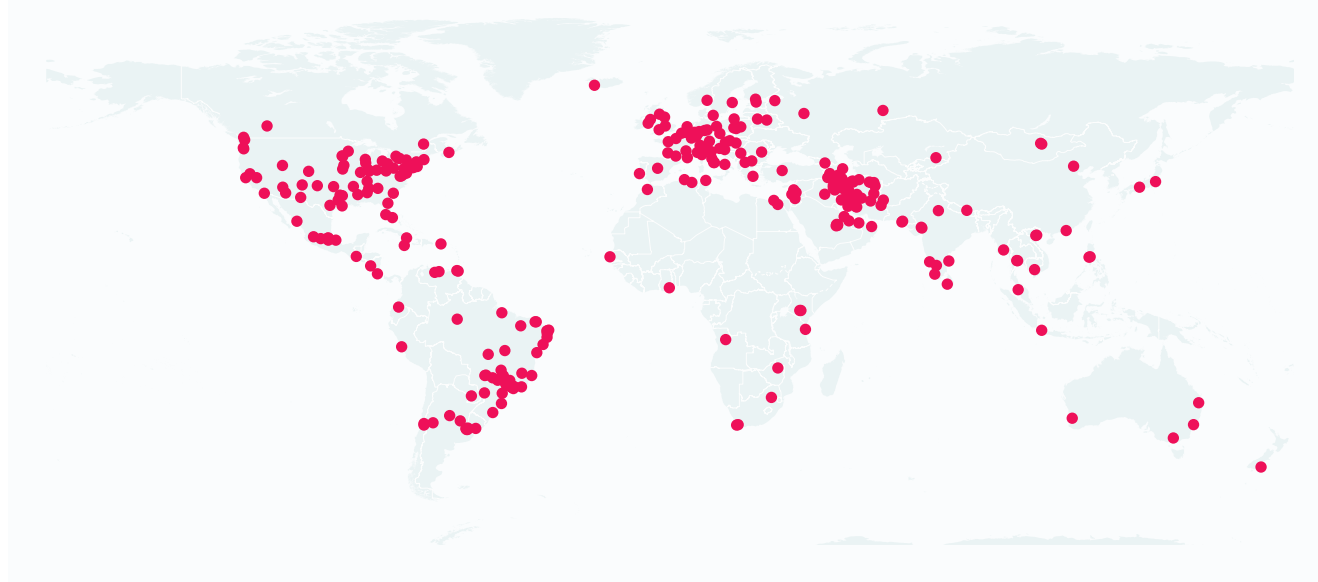
No recent global or regional reviews of pesticide poisoning statistics compiled by poison centres

have been published. However, a number of poison centres, or associations of poison centres, regularly publish their own data. In some countries specific pesticide poisoning monitoring programmes exist or have existed, such as the SENSOR (Sentinel Event Notification System for Occupational Risks)-Pesticides programme of the National Institute for Occupational Safety and Health (NIOSH) in the United States (Calvert *et al.* 2016) and the Pesticides Surveillance Study of the United Kingdom's National Poisons Information Service (NPIS) (Perry *et al.* 2014).

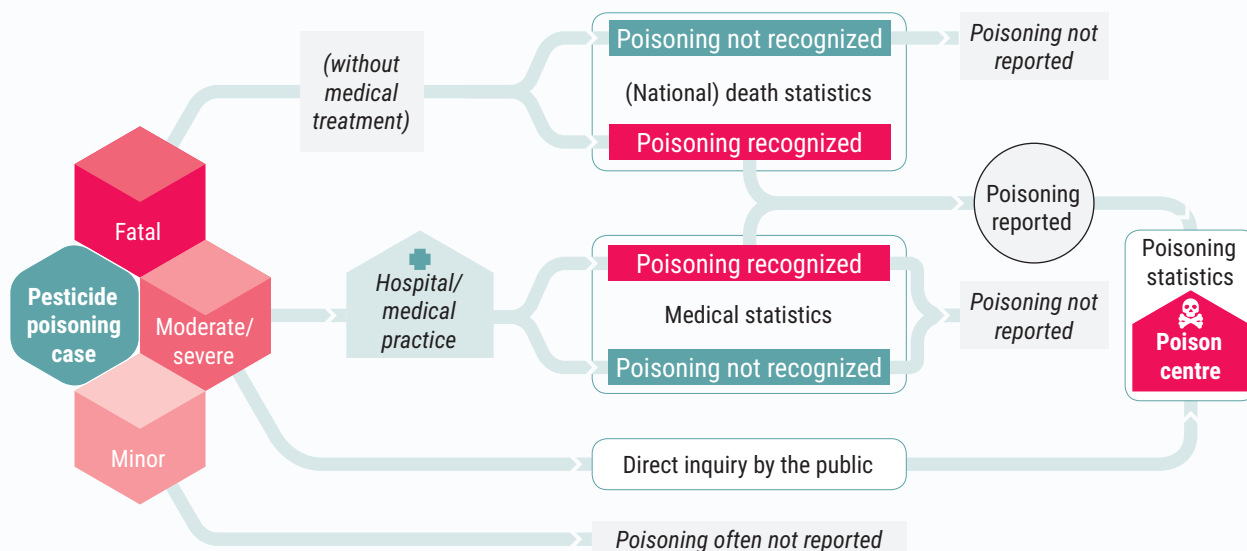
Poison centres use a variety of sources to compile statistics on pesticide poisoning (Figure 4.4-3). They include direct enquiries to a centre about possible poisoning cases (by health professionals or the public), cases recorded by medical facilities and subsequently reported to the centre (such notifications are mandatory in some countries), poisoning surveys carried out by the centre or other specialized institutions and researchers, and poisoning cases reported in the press.

Statistics reported by poison centres can therefore be quite variable or incomplete. If pesticide poisoning is relatively mild, cases will not usually be reported to medical practitioners at all. On the other hand, if severe pesticide poisoning leads to death before a medical facility is visited, a death certificate may not include pesticide poisoning as

► **Figure 4.4-2 Poison centres are primarily concentrated in high and middle income countries. They are much rarer in some low income parts of the world.** WHO (2020c).



► **Figure 4.4-3 Simplified representation of how pesticide poisoning information may, or may not, reach a poison centre database. Poison centres may use other sources to complete their poisoning statistics, such as surveillance reports, dedicated monitoring studies or media releases.** UNEP (2020).



the cause. Many countries and rural regions where pesticide poisoning occur do not have an adequate civil registration and vital statistics systems with which to record all deaths.

Even if a patient visits a doctor or hospital, the symptoms of pesticide poisoning may be non-specific and medical staff may therefore confuse them with symptoms of other health problems. Making diagnoses from non-specific signs of illness is often difficult, and patients will usually get better following acute poisoning, so that further investigations may not be carried out in busy health care systems. Moreover, decentralized medical facilities may not fully register cases of pesticide poisoning in a central database, for example because pesticide poisoning is not a notifiable event that requires mandatory registration

Pesticide poisoning statistics from poison centres have therefore been considered to be imprecise and variable over time, and generally to underestimate the real number of poisoning cases that occur (Calvert *et al.* 2016). Jeyaratnam (1990) suggested that, at least in developing countries, for every poisoning case reported to a hospital 25 milder cases were not reported. More recent studies suggest that 1-20 per cent (median value 6 per cent) of acute pesticide poisoning cases

are reported in national poisoning statistics (Table 4.4-3). This is only slightly higher than the estimates by Jeyaratnam (1990) up to three decades earlier, indicating that under-reporting of pesticide poisoning remains an important problem.

There can be many reasons why people acutely affected by pesticides do not seek medical care or report to public health facilities. For example, they may not feel ill enough to justify the expense, or they may have become habituated to poisoning symptoms as “normal” farming practice; medical facilities may be too far away, especially in rural areas; or farm workers may not be covered by health insurance or may be afraid to lose their jobs if they report pesticide exposure (Roberts and Reigart 2013; Lekei, Ngowi and London 2016). Under-reporting at the level of medical facilities may be due to incorrect or incomplete diagnosis (see above), inadequate disease registration systems, or lack of communication within the public health system. While high income countries may have better poisoning registration systems than countries with fewer resources, under-reporting appears to occur to some degree everywhere (Table 4.4-3) (Lekei, Ngowi and London 2016; Prado *et al.* 2017).

WHO has developed tools to facilitate the collection of internationally harmonized data

**Table 4.4-3 Levels of under-reporting of acute pesticide poisoning (APP) cases, as quantified in different parts of the world.**

Country	People who experience APP seeking medical care (per cent)	Cases of medical care for APP reported in poisoning statistics (per cent)	Overall degree of reporting of APP in poisoning statistics (per cent)	Source
South Africa		5-20		London and Bailie (2001)
Costa Rica, El Salvador, Guatemala, Nicaragua, Panama			8 (range 1-20)	Henao and Arbelaez (2002)
Honduras	--	80	--	
Nicaragua		4.5		Corriols <i>et al.</i> (2008)
Tanzania (occupational poisoning only)	21	21	4.5	Lekei, Ngowi and London (2016)
United States (farm workers only)			12	Prado <i>et al.</i> (2017)
Morocco		15		Rhalem <i>et al.</i> (2012); Rhalem, N., personal communication (2019)
Federal District of Brazil (fatal poisoning only)			9	Magalhães and Caldas (2018)
United Kingdom		50 (estimate)		National Poisons Information Service (United Kingdom) (2019)

on poisoning, including a common vocabulary for describing poisoning cases and a poisoning severity score (a standardized scale for grading the severity of acute poisoning) (Persson *et al.* 1998; WHO 2020b) (Table 4.4-2). Thundiyil *et al.* (2008) collaborated with WHO staff to further develop an international classification tool for acute pesticide poisoning. The European Union (EU) has also started to harmonize rules pertaining to data collection and reporting of pesticide poisoning cases (Settimi *et al.* 2016).

The UNEP, in collaboration with WHO, recently compiled poison centre reports and conducted a call-in of pesticide poisoning data from the WHO informal network of poison centres (UNEP 2020). Data from 17 countries referring to the period 2009-2019 were assessed, the large majority of which concerned upper-middle and high income economies.

Average annual pesticide poisoning incidences were highly variable, ranging from 0.22 to 24 cases per 100,000 inhabitants (median value 4.9) (Table 4.4-4). There was no significant correlation between country income group and poisoning incidence. However, the fraction of total poisoning cases in a country attributable to pesticides increased with the percentage rural population in that country, suggesting a link with pesticide use in agriculture (Figure 4.4-4).

In about half of countries the majority of reported pesticide poisoning cases were unintentional (either accidental or occupational) (Table 4.4-5). There was not a clear regional predominance in regard to the different circumstances of exposure.

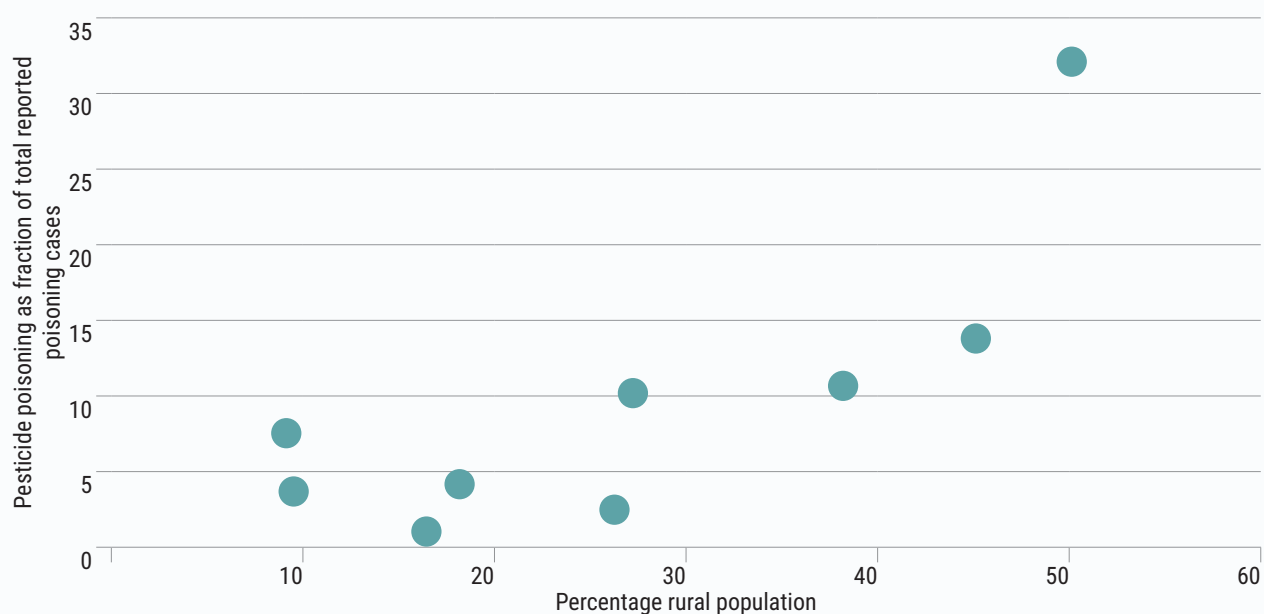
Cases of fatality due to pesticide poisoning reported to the poison centres examined in this exercise were positively correlated with the

**Table 4.4-4 Average number of reported pesticide poisoning cases in countries with national coverage; averages calculated over the last three years reported (where available).** UNEP (2020).

Country	Period	Average annual number of reported pesticide poisoning cases	Pesticide poisoning as a fraction of total poisoning (per cent)	Average annual pesticide poisoning incidence (per 100,000 inhabitants)
Algeria	2018	461	10.2	1.1 <sup>1</sup>
Brazil	2012-2014	12,132	-- <sup>3</sup>	6.2 <sup>2</sup>
Chile	2016-2018	560	--	3.0 <sup>1</sup>
Guatemala	2012-2013, 2018	36	32	0.22 <sup>1</sup>
Jamaica	2013-2015	56	13.8	2.0 <sup>1</sup>
Jordan	2016-2018	115	7.6	1.2 <sup>1</sup>
Morocco	2016-2019	1,499	10.7	4.9 <sup>1</sup>
Netherlands	2015-2017	1,326	3.8	8.0 <sup>1</sup>
Peru	2015-2017	2,244	--	12 <sup>2</sup>
Republic of Korea	2012-2014	6,052	--	9.0 <sup>2</sup>
Switzerland	2016-2018	812	2.5	9.6 <sup>1</sup>
United Kingdom	2018-2019	1,030	~ 0.3-1	1.5-3.3 <sup>1</sup>
United States	2015-2017	77,968	4.1	24 <sup>1</sup>

<sup>1</sup>calculated based on total annual population (FAOSTAT 2020); <sup>2</sup>national report; <sup>3</sup>-- = not available;

**Figure 4.4-4 Pesticide poisoning as a fraction of total reported poisoning cases is positively correlated with the percentage rural population in the respective countries.** UNEP (2020).



fractions of pesticide poisoning cases that were suicides, suggesting that most deaths resulted from self-poisoning. In countries where pesticide poisoning was mainly unintentional, moderate and severe poisoning cases made up 1-44 per cent (median 16 per cent) of all reported poisonings, implying that the large majority of unintentional pesticide poisonings were mild (UNEP 2020).

No consistent trends in reported pesticide poisoning over time were found in the poison centre data evaluated in this exercise. Some countries (e.g., Brazil and Jordan) showed increases in reported cases during the last decade, while Chile, the Republic of Korea and the United States showed clear declines. Reports on pesticide poisoning remained relatively stable for the period 2009-2019 in Jamaica, Morocco, Switzerland and the United Kingdom.

Comparisons between countries are inevitably subject to a number of caveats. The extent of coverage of poison centres varies from country to country. It may also vary over time in countries

with fewer resources. In addition, changes in the population's engagement with agriculture over time, or changes in agricultural practices such as types of crops grown, cannot be taken into account although these trends may differ between countries. As an example of differences between countries, many pesticide poisonings in the United Kingdom were caused by exposure to pre-diluted amateur pesticide formulations for household use (Perry *et al.* 2014); on the other hand, in low and middle income countries (e.g., Sri Lanka) the majority of pesticide poisonings were due to exposures to more toxic high-concentration agricultural formulations (Dawson *et al.* 2010).

The pesticide groups most reported to have caused poisoning are pyrethroid, organophosphorous and carbamate insecticides, anticoagulant rodenticides (especially coumarins), glyphosate and disinfectants. The groups that led to the most severe cases of poisoning were organophosphorus insecticides, the fumigant aluminium phosphide, and bipyridylum herbicides (paraquat and diquat) (UNEP 2020).

**Table 4.4-5 Fraction of pesticide poisoning according to circumstances of exposure and severity of pesticide poisoning cases, calculated as average percentage of moderate, severe and fatal cases (values are average percentages over the last three years reported).** UNEP (2020).

Country	Period	Circumstances of exposure			Severity of poisoning
		Unintentional	Intentional	Other/ unknown	Moderate, severe and fatal poisoning cases
<i>per cent of total reported pesticide poisoning cases in the country</i>					
Algeria	2018	70	28	2	<i>n.a.</i> <sup>1</sup>
Brazil	2012-2014	38	55	7	<i>n.a.</i>
Chile	2016-2018	87	13		17
Guatemala	2012-2013, 2018	60	30	10	<i>n.a.</i>
India	1999-2012	34	65	1	<i>n.a.</i>
Jordan	2016-2018	97	3		18
Morocco	2016-2018	60	39	1	37
Peru	2017	83	17		44
Philippines	2016-2018	49	50	1	<i>n.a.</i>
Poland	2004-2014	49	51		41
Switzerland	2016-2018	93	5	2	15
Uganda	2010-2014	37	63		<i>n.a.</i>
United Kingdom	2018-2019	92	8		1
United States	2015-2017	94	3	3	7

<sup>1</sup> *n.a.* = data not available

While poison centre statistics provide valuable information about the circumstances of pesticide poisoning, it is currently impossible to draw clear conclusions about differences in poisoning incidences among regions or country income groups. Poison centre data are also insufficient to extrapolate to larger geographical entities (UNEP 2020).

### Acute pesticide poisoning studies

Acute unintentional pesticide poisoning has also been evaluated through dedicated studies and surveys looking at signs, symptoms and effects following exposure to pesticides. These are often cross-sectional studies that investigate a population (e.g., a group of farmers) at a specific point in time. Symptoms and health effects are examined by medical specialists, but they may also be self-reported (e.g., through a questionnaire).

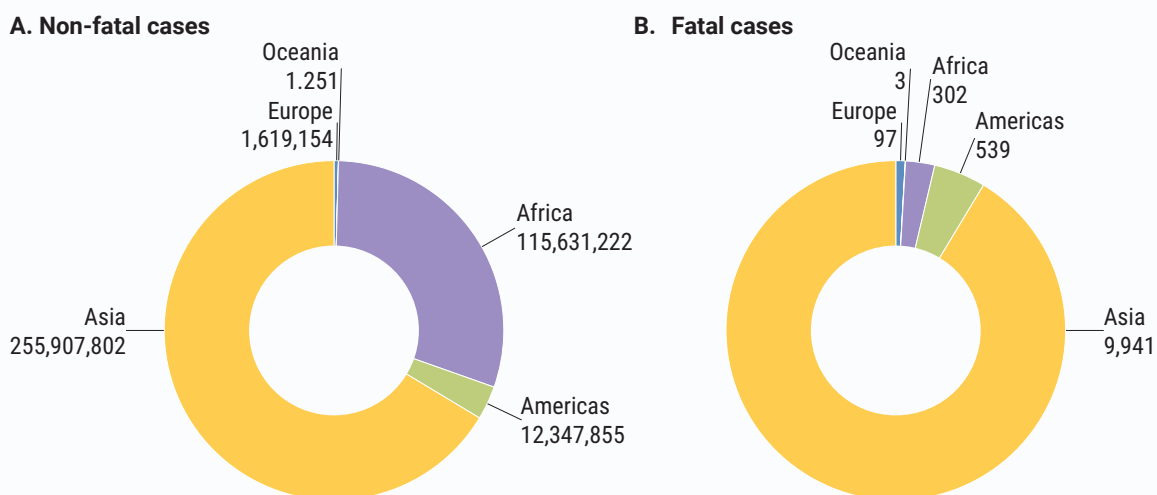
Since the 1980s such studies have shown a high incidence of acute pesticide poisoning in many parts of the world, including Central America (Henao and Arbelaz 2002; Wesseling, Corriols and Bravo 2005), Africa (London 2003; Lekei, Ngowi and London 2014; Lekei *et al.* 2020) and Asia (Ko *et al.* 2012). However, no detailed reviews of the outcomes of such studies have been available.

A major global systematic review of acute unintentional pesticides poisoning was conducted by Boedeker *et al.* (2020). A total 141 of countries were covered, including 58 using pesticide poisoning data from scientific articles published between 2006 and 2018 and an additional 83 using data from WHO's Cause of Death Query online (CoDQL), part of the WHO Mortality Database. Most of the scientific studies consulted focused on occupational poisoning of farmers and agricultural workers. Self-poisoning was excluded from the analysis (but see Chapter 4.4.4). All degrees of pesticide poisoning were combined in the assessment, ranging from mild symptoms to severe toxic effects.

This analysis found that the global incidence of unintentional acute pesticide poisoning was 43 per cent of the farming/occupational community (i.e., 43 cases of pesticide poisoning occur annually for every 100 persons working in agriculture). National incidences in the farming community were highly variable, ranging from <1 per cent in the United States to 84 per cent in Burkina Faso. Generally, poisoning incidences were higher in Africa and South and Southeast Asia than in the Americas, Europe and Oceania (Figure 4.4-5).

In 57 per cent of the reviewed studies poisoning was self-reported, while in 39 per cent

► **Figure 4.4-5 Regional distribution of the estimates of non-fatal and fatal cases of pesticide poisoning, all severities combined, estimated by Boedeker *et al.* (2020).**





researchers or medical staff identified the cases. As self-reporting by non-specialized persons could have overestimated pesticide poisoning cases, the relatively high fraction of self-reported studies may have biased poisoning estimates. However, only an 11 per cent increase was found in the summary average across studies reporting poisoning incidence from self-reporting when compared with the summary average from studies using scientist-reported cases, suggesting the bias was modest.

On the basis of this data set, Boedeker *et al.* (2020) estimated that globally about 385 million cases of unintentional acute pesticide poisoning occur annually, all poisoning severities combined. They also estimated that about 10,900 fatal cases per year result from unintentional acute pesticide poisoning.

Another recent report evaluated studies from 11 countries in Eastern Europe, Central Asia and Africa, all of which included self-reported cases of acute pesticide poisoning among smallholder farmers and farm workers (Pesticide Action Network UK [PAN UK] 2020). Similarly to the review by Boedeker *et al.*, high annual incidences of acute pesticide poisoning in farming communities were observed, ranging from 10 per cent in Moldova to 82 per cent in Belarus. Extrapolating from these results, the authors suggest that over 200 million farmers could be poisoned by pesticides every year.

The estimates of unintentional pesticide poisoning by Boedeker *et al.* (2020) and PAN UK (2020) are an order of magnitude higher than previous estimates. This may be because pesticide use has greatly increased since the 1990s, especially in Asia and Latin America. Another reason could be that the 1990 estimates were based primarily on national poisoning statistics (which tend to under-report incidences of poisoning in the field) while the recent estimates are mainly based on dedicated pesticide poisoning surveys. The significance of the latter explanation is underlined by the relatively low national pesticide poisoning incidences reported more recently by poison centres (Table 4.4-4) even when the fraction of the rural/farming population in these countries is taken into account.

Boedeker *et al.* (2020) do not distinguish among different poisoning severities in their estimates; the 385 million cases include mild effects as well as moderate and severe cases. It is not clear what fraction of these cases would require access to health services and/or medical treatment. The chapter on poison centre statistics, however, indicates that approximately 6 per cent of pesticide poisoning cases were reported to poison centres and 16 per cent of the reported cases were moderate or severe. Combining these figures would result in an estimate of a minimum of 3.7 million cases of moderate or severe non-fatal cases of unintentional pesticide poisoning annually, about four times more than previous estimates.

On the other hand, the estimate by Boedeker *et al.* (2020) that there are about 11,000 unintentional fatal poisonings is lower than previous ones, suggesting such cases are currently less common because treatment of severe poisoning is more effective or because the most hazardous pesticides are being withdrawn globally from agricultural use.

Overall, recent reviews of poisoning studies and surveys suggest that unintentional acute pesticide poisoning remains widespread. Moreover, it appears to have increased significantly compared to the often cited estimates from the 1990s, especially in farming communities in low and middle income countries.

However, data from different sources are variable and incomplete. There is a clear need to conduct more pesticide exposure and poisoning surveys following standardized protocols. Furthermore, the value of pesticide poisoning statistics from poison centres would increase considerably if information were gathered about reporting rates.

It should be noted that unintentional acute poisonings are only part of the acute impact of pesticides on health, and that incidences, case fatality and trends over time are different for self-poisoning (Chapter 4.4.4).

With respect to pesticides, the science of **epidemiology** investigates whether pesticides are associated with the distribution (frequency, pattern) of a disease<sup>1</sup> or health problem in humans, with the ultimate aim to control such problems.

All pesticide epidemiological studies are **observational**, in the sense that the investigator does not intervene, i.e. does not determine the degree of exposure of study persons to the pesticide. **Experimental** epidemiological studies with pesticides are not conducted as it is not considered ethical to willingly expose persons to a pesticide and study its health effects. However, there is a growing body of indirect evidence assessing the efficacy of various policies and practices on pesticide exposure and thus on the burden of pesticide-related diseases.

Different types of observational epidemiological studies can be recognized:

**Ecological (or correlational) study:** Comparison of aggregate disease estimates in different groups of people in different localities (or the same group of people at different times) with respect to the potential aggregate exposure estimates to a pesticide in this group.

*Example result:* The percentage of persons with dermatitis at the time of the study is higher in a region with high pesticide use compared to a region with low use.

This type of study can only identify correlations, using the location under study as the unit of analysis, but cannot determine causality; it is often exploratory in nature and may start more in-depth investigations.

**Cross-sectional (or prevalence) study:** The prevalence of a disease and possible pesticide exposure factors are investigated in a selected group of people at a specific point in time and at the individual participant level. This is often done through surveys.

*Example result:* Persons in the selected group of people who applied a pesticide three times or more during the last growing season, suffered more from headaches than those who had not applied pesticides.

This type of study can identify correlations, but can generally not determine causality. It is also exploratory in nature and can help to identify risk factors suitable for further scrutiny.

**Case-control study:** Persons having a disease (cases) are compared with persons without such an effect (controls) for the occurrence or degree of past exposure to a pesticide. The investigators measure disease occurrence at one point in time and try to identify exposure to the pesticide in the past. The main difficulty with case-control studies is to quantify exposure to the pesticide, which occurred retrospectively. This type of study is in particular useful for uncommon diseases.

*Example result:* Persons having a type of cancer were significantly more exposed to a pesticide during the previous 10 years than persons not having that type of cancer.

With appropriate controls and a good estimation of past exposure to the pesticide, case-control studies can be an important piece of evidence for validating postulated associations and moving towards establishing causality.

**Cohort (or follow-up) study:** A group of persons free of a disease (a cohort) is classified into subgroups according to exposure to a pesticide. The whole cohort is then followed (often up to many years) to see if a disease develops, and whether this development differs between the groups having different levels of exposure to the pesticide.

*Example result:* Those persons who, in the course of the study, were more exposed to a pesticide developed significantly more neurological deficiencies at a later age than persons who were less exposed during the study period.

Since the time sequence from exposure to disease can be determined, cohort studies provide the best information about the causation of disease. It is worth noting that the study design per se does not preclude the general study quality. Also, even when the exposure is captured prospectively, it may still be difficult to determine and quantify it.

Causal inference is the scientific process of determining whether observed associations between pesticide exposure and a disease are likely to be causal. The process of judging causation can be difficult and contentious, and pesticide epidemiology is no exception. Epidemiologists systematically evaluate various considerations for causation, either quantitatively or empirically; The “Bradford Hill criteria” is an example of a set of such considerations used empirically. They include questions such as: “does the cause precede the effect?”, “have similar results been shown in other studies?”, “is increased exposure associated with increased effect?”, “is a toxicological mechanism known that can result in the effect?”, and others. Based on causal inference methodology, epidemiologists can make a judgement about the likelihood that the pesticide may have caused the disease.

1 The term “disease” is used here for all types of health effects that may be caused by pesticides

### 4.4.3 Chronic pesticide poisoning

#### Epidemiology of pesticide exposure

Chronic exposure to pesticides has been associated with a wide variety of adverse health effects. They include different types of cancer, reduced nervous system functions, disturbed neurodevelopment of children, diabetes, decreased male and female fertility, birth defects and Parkinson's disease, among others (American Academy of Pediatrics 2012; Bergman *et al.* 2013; Mostafalou and Abdollahi 2013; Blair *et al.* 2015; Hertz-Picciotto *et al.* 2018).

One of the most recent WHO *Global Assessment of the Burden of Disease from Environmental Risks* report indicates positive associations between pesticides and chronic disease, such as certain cancers and Parkinson's disease (Prüss-Üstün *et al.* 2016). However, evidence for causal relationships was often considered limited.

Studying the presence and magnitude of associations between exposure to pesticides and health outcomes in humans is a challenging field of epidemiology. Its complexity lies in specific characteristics of pesticide epidemiology, such as the large number of active substances in the market; the number of different pesticides which

may be used by an individual farmer; and the different patterns of pesticide use, the variety of study designs and the inherent limitations of each design; the long period that often passes between exposure to a pesticide and the development of disease; the frequent lack of quantitative (and qualitative) data on exposure to individual pesticides; and the other chemicals that might be associated with a condition being studied (Blair *et al.* 2015; EFSA PPR Panel 2017).

Ohlander *et al.* (2020) conducted a global review of methods used to assess exposure to pesticides in occupational epidemiology studies. The large majority of exposure assessment methods were indirect, based in particular on self-reported exposures. Direct methods such as biomonitoring of blood or urine were used in only 21 per cent of studies. This situation did not change during the 25 years covered by the study, indicating that imprecise exposure estimations continue to hamper the determination of clear associations between pesticides and health outcomes.

It is also generally considered that while epidemiological studies may point to an association between pesticide exposure and a health outcome, it is very difficult to prove that a pesticide has caused an adverse health effect based on epidemiological studies alone.

**Table 4.4-6** Examples of large cohort studies addressing the health effects of pesticide exposure. IARC (2020).

Country	Study	Number and type of participants	Year of recruitment
United State (Iowa and North Carolina)	Agricultural Health Study (AHS)	52,394 licensed private pesticide applicators (mostly farmers) 32,345 of their spouses 4,916 commercial pesticide applicators	1993-1997
United States (Wisconsin)	Marshfield Epidemiologic Study Area (MESA) – Farm Resident Cohort	5,432 farm residents	1998
United States (California)	Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) Study	Pregnant women, and subsequently >800 children born from these women	1999
France	AGRIculture and CANcer (Agrican) cohort study	187,471 persons within the agricultural population	2005-2007
Australia	Pesticide-exposed workers cohort	14,092 persons, of which 4,775 agricultural workers	1960s- 1980s
Norway	Norway Farmer Cohort	8,482 farmers	1990-1992

More evidence is often needed to infer such causality (Box 4.4-1).

With the aim of obtaining better data on the long-term effects of exposure to pesticides, a number of dedicated longitudinal studies have been carried out. In cohort studies populations at risk (e.g., farmers, agricultural workers, rural families) are followed over a long period to determine the occurrence of disease (Box 4.4-1). However, achieving valid and precise exposure estimates remains difficult even in large cohort studies (EFSA PPR Panel 2017). A particular challenge is that while disease outcomes are ascertained after long follow-up periods, exposure estimates (or measurement of biomarkers) will inevitably be based on a limited time frame even in the case of very large, well-resourced studies.

Thus, trends or changes in the lifetime pesticide exposure patterns of the study participants are not captured and, unlike 'traditional' health-related behaviours (e.g., smoking) which may remain relatively stable for large periods of time, these patterns are not adequately studied for pesticides.

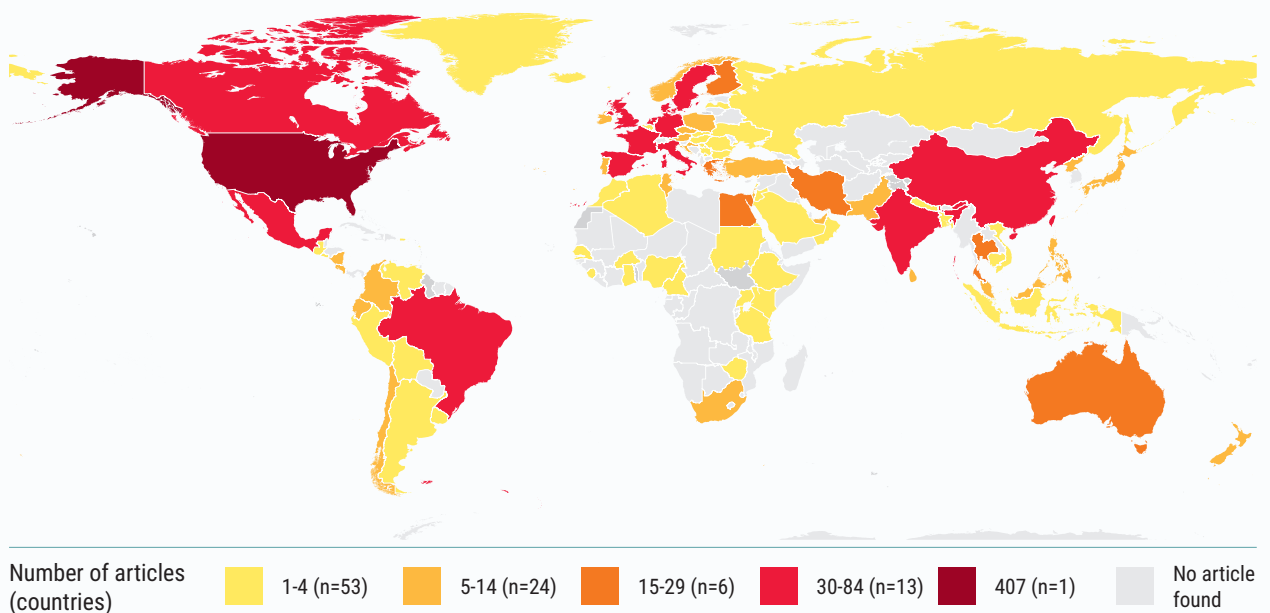
To coordinate activities and combine forces, in 2010 the United States National Cancer Institute (NCI) and the International Agency for Research on Cancer (IARC) established AGRICOH, a consortium of agricultural cohort studies (International Agency for Research on Cancer [IARC] 2020). As of June 2020, 28 cohorts from five continents were participating in AGRICOH. Some examples are shown in Table 4.4-6.

### Reviews of chronic pesticide effects

Numerous epidemiological studies have been conducted with the aim of assessing associations between exposure to pesticides and health outcomes such as the development of specific diseases. However, the majority of studies on occupational exposure to pesticides (83 per cent) originate in high and upper-middle income countries. Very few (1.1 per cent) are from low income countries (Figure 4.4-6) (Ohlander *et al.* 2020).

Three comprehensive reviews of the multiple chronic adverse effects of pesticides have been

► **Figure 4.4-6 The large majority of studies on occupational exposure to pesticides have been conducted in high and upper-middle income countries.**



Note: Shown is the number of articles on occupational exposure to pesticides and various health outcomes published between 1993 to 2017 per country serving as study location, retained in the review by Ohlander *et al.* 2020. Numbers in brackets represent the number of different study locations (countries).

**Table 4.4-7 Characteristics of the three major reviews of chronic adverse health effects of pesticides.**

Parameter	Inserm (2013)	Ntzani <i>et al.</i> (2013)	Ntzani <i>et al.</i> (2020)
Publication period	Up to June 2012	1 January 2006-30 September 2012	1 January 2006-30 June 2019
Number of publications included	Not summarized	602	1,166 (including the studies covered by Ntzani <i>et al.</i> 2013)
Number of health outcomes assessed	18	24 disease categories	29 disease categories
Method of quality control of publications described	No	Yes	Yes
Meta-analyses performed	No	Yes	Yes

published in the last 10 years (Table 4.4-7). In France, the National Institute for Health and Medical Research carried out an extensive review of the relationship between pesticide exposure and 16 different health outcomes and a formal meta-analysis was not carried out (Institut national de la santé et de la recherche [Inserm] 2013) (Table 4.4-7). At the request of the European Food Safety Authority (EFSA), Ntzani *et al.* (2013) conducted a systematic review as well as multiple meta-analyses of epidemiological studies published until 2012 examining the association between pesticide exposure and health outcomes in 24 major disease categories.

Since these two evaluations, a large number of epidemiological studies and reviews on this topic have been published due, in particular, to increased interest in the health effects of pesticides but also to the fact that a number of large cohort studies initiated years ago have begun to yield results. An update of the review done for EFSA (Ntzani *et al.* 2013) was therefore commissioned for this report, including all epidemiological studies published between January 2012 and June 2019 (Ntzani *et al.* 2020). It produced a database containing a total of 19,178 possible associations between pesticides and health outcomes (see Box 4.4-2 for more details). The conclusions of these three reviews regarding these possible associations between exposure and disease or other health outcomes are summarized in Table 4.4-8.

Based on the review and meta-analyses by Ntzani *et al.* (2020), positive associations between pesticides and certain health outcomes were reported (Table 4.4-8). Specifically:

- non-Hodgkin lymphoma and exposure to pesticides in general and insecticides in general;
- Parkinson's disease and exposure to pesticides in general, herbicides in general, insecticides in general, fungicides in general, organochlorine insecticides in general, and certain individual organophosphate insecticides;
- Parkinsonism and exposure to pesticides in general;
- diabetes and exposure to pesticides in general, organochlorine pesticides in general, and certain individual organochlorines;
- asthma and exposure to pesticides in general;
- spontaneous pregnancy loss and exposure to pesticides in general;
- childhood leukemia and maternal exposure during pregnancy to pesticides in general, herbicides or insecticides;
- childhood leukemia and paternal exposure or childhood exposure to pesticides in general.

Based on the epidemiological evidence, chronic adverse health effects are considered likely as a result of exposure to pesticides in general or to certain groups of pesticides. In only a few cases were associations between specific pesticides and a health outcomes characterized and quantified. This difficulty is inherent in regard to identifying specific exposures in epidemiological studies. However, such limitations do not necessarily preclude taking risk reduction measures before risk characterization becomes more precise.

**Box 4.4-3 Systematic review and meta-analyses of epidemiological studies examining the association between pesticide exposure and health outcomes.**

At the request of the European Food Safety Authority, Ntzani *et al.* (2013) conducted a systematic literature review of epidemiological studies examining the association between pesticide exposure and any health outcome published after 2006. In 2019, UNEP solicited the Department of Hygiene and Epidemiology of the University of Ioannina School of Medicine, in Greece, to update their review. The results of that work are available as a technical support document to the current report (Ntzani *et al.* 2020).

**Method**

The updated systematic review included observational (cohort, cross-sectional and case-control) studies assessing the association between pesticide exposure and health-related outcomes in adult, adolescents, or children published between January 2012 and June 2019.

Literature searches were conducted using PubMed, EMBASE, TOXNET OpenSigle and ProQuest Digital Dissertations and Theses; publications were identified without language or geographical restrictions.

Only studies with sufficient quantitative information to estimate effect sizes were included in the assessment. Studies assessing the effects of acute or accidental pesticide exposure, or of pesticide poisoning, were excluded.

Relevant information was extracted from eligible studies and recorded in a spreadsheet database.

Meta-regression analyses (MA), using random effect models, were carried out for specific disease entities, by pesticide group and window of exposure where available. Effects sizes were expressed as Relative Risks (RR) and corresponding 95% confidence intervals for binary study outcomes, or Summary Mean Differences and corresponding standard deviations for continuous outcomes.

**Results**

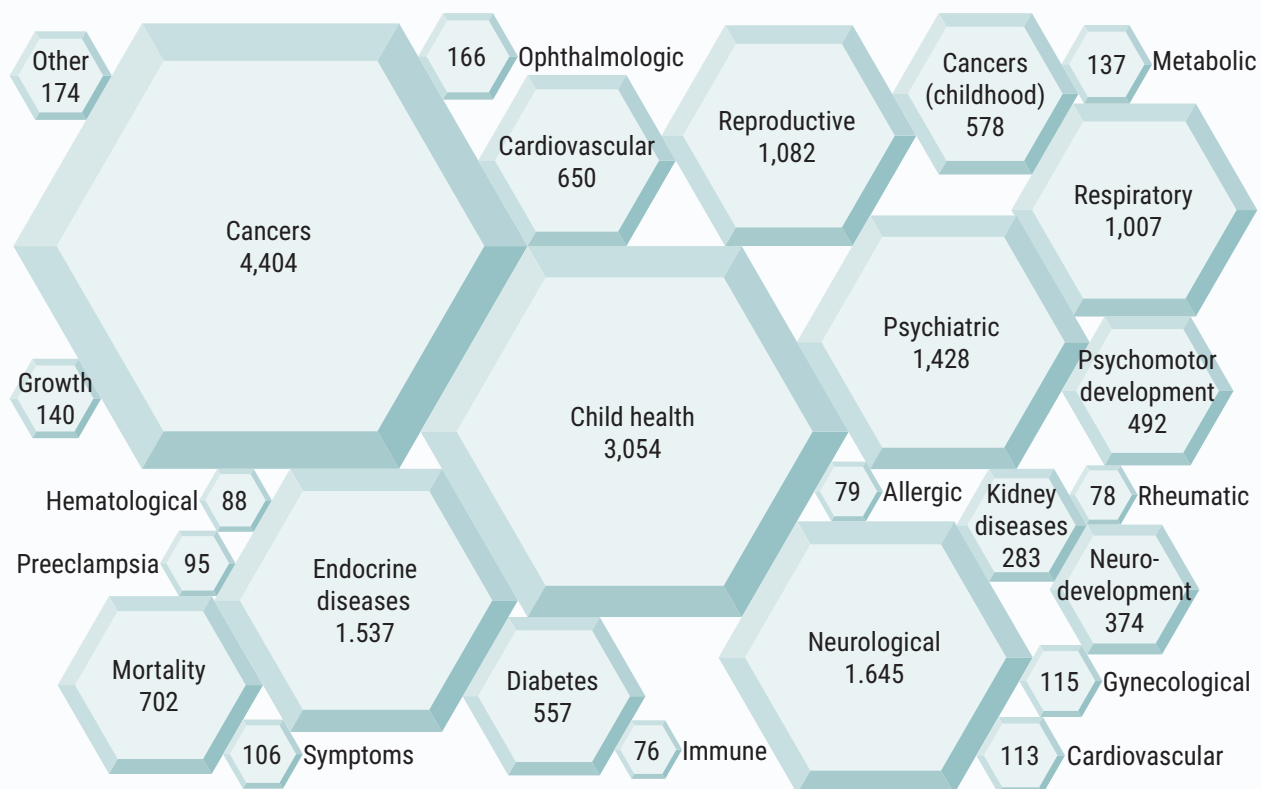
Based on the criteria used, and covering the entire period 2006 – 2019, 1,166 publications were considered eligible.

The largest number of publications was from the Americas (45%) followed by Europe (29%), Asia (17%) and Africa (4%). Sample size ranged from studies as small as including 37 participants to large cohorts with 1,832,969 participants. Cross sectional studies (34%), cohort studies (29%) and case control studies (36%) were present in comparable frequencies.

More than 19,000 postulated associations (i.e. links between an individual pesticide (group) and a specific health outcome) have been included in the database.

Most frequently studied health outcomes were cancers, child diseases, neurological diseases, neuropsychiatric disorders and endocrine system diseases (see bubble plot).

Results of assessments where a meta-analysis was possible are listed in Table 4.4-9. Health outcomes reviewed but for which meta-analyses was not feasible are provided in Annex 4.1-1.<sup>1</sup>



Relative importance of health outcomes studied in pesticide epidemiological studies published between 2006 and 2019. N = total number of studied associations

<sup>1</sup> Annex 4.4-1 is found at: <https://www.unep.org/resources/report/environmental-and-health-impacts-pesticides-and-fertilizers-and-ways-minimizing>

**Table 4.4-8 Associations between pesticide exposure and diseases or other health outcomes, as concluded in two recent comprehensive reviews.** Only associations for which a meta-analysis was performed by Ntzani *et al.* (2020) are listed. Associations studied without a meta-analysis are listed in Annex 4.4-1.

Health outcome	Pesticide or pesticide class	Inserm (2013) (systematic review)	Ntzani <i>et al.</i> (2020); Karalexi <i>et al.</i> (submitted) (systematic review and meta-analyses <sup>1</sup> )	
		Positive association	Positive association	Number of studies
<b>Effects on adults</b>				
Non-Hodgkin lymphoma	Pesticides <sup>2</sup>		Yes	11
	Insecticides		Yes	4
	Organochlorines		No	4
	Dieldrin		No	3
	DDT	Yes	No	6
	DDE		No	9
	Oxychlordane		Yes	4
	Trans-nonachlor		No	4
	HCB		No	7
	Organophosphates	Yes	No	3
	Chlorpyrifos		No	4
	Malathion	Yes	No	3
	Diazinon		No	3
	Terbufos		No	3
	Carbaryl		No	4
	Carbofuran		No	3
	Permethrin		No	3
	Herbicides/phenoxy herbicides		No	6
	Glyphosate		No	3
	MCPA		No	3
Follicular lymphoma/ follicular B-cell carcinoma	DDE		No	4
Diffuse large B-cell lymphoma/diffuse large cell lymphoma	DDE		No	5
	HCB		No	3
Prostate cancer	Pesticides	Yes	No	8
	Captan		No	3
	Chlordane		No	3
	Oxychlordane		No	4
	DDE		No	5
	DDT		No	4
	Dieldrin		No	3
	HCB		No	3
	Trans-nonachlor		No	3
	Organochlorine insecticides		No	3
Breast cancer	Pesticides		Yes	8
	DDT		No	5
	DDE		No	7
	HCB		No	3

Health outcome	Pesticide or pesticide class	Inserm (2013) (systematic review)	Ntzani <i>et al.</i> (2020); Karalexi <i>et al.</i> (submitted) (systematic review and meta-analyses <sup>1</sup> )	
		Positive association	Positive association	Number of studies
Bladder cancer	Pesticides		No	6
Lung cancer	Pesticides		No	3
Testicular cancer	DDE		No	5
Parkinson's disease	Pesticides	Yes	Yes	29
	Herbicides (broad definition)	Yes	Yes	9
	Paraquat		No	9
	Insecticides (broad definition)	Yes	Yes	10
	Organochlorine insecticides	Yes	Yes	4
	Rotenone		Yes	3
	2,4-D		No	4
	Benomyl		No	3
	Chlorpyrifos		No	4
	DDT		No	5
	Diazinon		Yes	5
	Dimethoate		No	3
	Malathion		Yes	4
	Mancozeb		No	3
	Maneb		No	5
	Parathion		No	6
	Ziram		No	3
	Fungicides (broad definition)		Yes	6
	Carbamate		Yes	4
	Organophosphorus		Yes	7
Parkinsonism	Pesticides		Yes	5
Diabetes (general)	Pesticides		Yes	6
	Organochlorine insecticides		No	3
	DDE		Yes	11
	DDT		No	7
	Dieldrin		No	4
	HCB		Yes	4
	Mirex		No	3
	Fungicides		No	3
	Herbicides		No	3
	Insecticides		No	3
Diabetes type 2	Organochlorine pesticides		Yes	3
	DDT		Yes	4
	DDE		Yes	11
	HCB		Yes	6
	Oxychlorane		Yes	5
	Trans-nonachlor		Yes	6
Gestational diabetes	DDE		No	3



Health outcome	Pesticide or pesticide class	Inserm (2013) (systematic review)	Ntzani <i>et al.</i> (2020); Karalexi <i>et al.</i> (submitted) (systematic review and meta-analyses <sup>1</sup> )	
		Positive association	Positive association	Number of studies
Asthma (in adults)	Pesticides		Yes	6
Depression	Pesticides		No	6
Spontaneous abortion	Pesticides		Yes	5
<b>Effects on child development</b>				
Childhood acute leukemia (overall)	Pesticides (maternal exposure, any time)		No	3
	Pesticides (maternal exposure, during pregnancy)		Yes	11
	Herbicides (maternal exposure, during pregnancy)		Yes	3
	Insecticides (maternal exposure, during pregnancy)		Yes	3
	Pesticides (paternal exposure, any time)		Yes	4
	Pesticides (paternal exposure, during preconception)		No	3
	Pesticides (parental exposure, any time)		Yes	6
	Pesticides (childhood exposure)		Yes	5
Childhood acute lymphoblastic leukemia	Insecticides (maternal exposure, any time)		No	3
	Pesticides (maternal exposure, during pregnancy)		Yes	3
	Herbicides (maternal exposure, during pregnancy)		No	3
	Insecticides (maternal exposure, during pregnancy)		No	4
	Pesticides (childhood exposure)		No	3
Childhood leukemia	Pesticides (exposure during pregnancy or childhood)	Yes		

<sup>1</sup> Meta-analyses were only conducted if at least three relevant studies were available.

<sup>2</sup> Pesticides means pesticides in general, without distinction of specific classes or active ingredients.

#### 4.4.4 Self-poisoning

Self-poisoning involves exposure to both the active ingredient and co-formulants, such as solvents and surfactants, which may have their own toxicity, especially when ingested in large quantities, and be more toxic than the active ingredient itself.

Unlike unintentional acute pesticide poisoning, intentional self-poisoning with pesticides (often with the intent to attempt suicide) has been evaluated in detail since the early 1990s. Recent systematic reviews were conducted for the period 1990-2007 (Gunnel *et al.* 2007) and for 2006-2015 (Mew *et al.* 2017; Karunarathne *et al.*

2019). The number of suicides due to pesticides in the early 2000s was estimated at 372,000 cases per year, or 31 per cent of global suicides (Gunnel *et al.* 2007). In the mid-2010s pesticide suicides were estimated at 168,000 per year, or about 20 per cent of all suicides globally (Mew *et al.* 2017) (Table 4.4-9). The authors estimated that the annual total number of pesticide self-poisonings ranged from 1 to 2 million. More recently, Karunarathne *et al.* (2019) calculated that there had been more than 14 million deaths due to self-poisoning with pesticides between 1960, when synthetic organic pesticides started to become available on a large scale, and 2018. More than 95 per cent of these deaths occurred

**Table 4.4-14 Global estimates of self-poisoning and suicides (deaths) by pesticides.**

Study period	Estimated number of pesticide deaths from suicides per year	Estimated number of pesticide self-poisonings per year	Source
1980s	200,000	2 million	WHO (1990)
1990-2007	372,000		Gunnell <i>et al.</i> (2007)
2006-2015	168,000	1-2 million	Mew <i>et al.</i> (2017)
2015-2018	134,000		Karunaratne <i>et al.</i> (2019)
	<b>Estimated total cumulative number of suicides</b>		
1960-2018	14.2-14.9 million		Karunaratne <i>et al.</i> (2019)

in low and middle income countries (WHO and FAO 2019a).

Suicide by intentional pesticide ingestion primarily occurs in rural areas of low and middle income countries in Africa, Central America, Southeast Asia and the Western Pacific (WHO 2014). The introduction of hazardous pesticides into rural communities during the Green Revolution resulted in a large increase in pesticide suicide deaths. Self-poisoning is often carried out spontaneously, with little planning and little time to change one's mind (Eddleston and Phillips 2004). The easy availability of these pesticides has greatly increased the lethality of self-poisoning, changing their outcomes from non-fatal to fatal (Karunaratne *et al.* 2019). The number of suicides has not been found to be correlated with the volume of pesticides sold. It is rather the pattern of pesticide use and products' toxicity that influence the likelihood they will be used for self-poisoning (Gunnell *et al.* 2007).

Pesticide suicides peaked in the 1990s and their incidence started to decline around 2000 (Karunaratne *et al.* 2019). The almost 65 per cent reduction in pesticide suicides between 1990 and 2018 occurred in the context of a 9 per cent decrease in the WHO estimate of the overall number of suicides between 2000 and 2012 (WHO 2014). The main drivers of this change are likely to be marked economic growth in parts of the world (e.g., China, where about half the world's pesticide suicides previously occurred), population shifts from rural to urban areas, further mechanization of agriculture, and the introduction of regulations to ban or reduce access to the most

toxic pesticides (Mew *et al.* 2017; Karunaratne *et al.* 2019). Bans on Highly Hazardous Pesticides (HHPs) in Sri Lanka, the Republic of Korea, Bangladesh and other countries have been associated with marked falls in both pesticide suicides and all suicides (Gunnell *et al.* 2017).

It has been reported from various countries that banning the most toxic pesticides has not been associated with adverse effects on agricultural yield (Manuweera *et al.* 2008; Cha *et al.* 2016; Chowdhury *et al.* 2018; Bonvoisin *et al.* 2020). Two estimates of the health care costs of treating pesticide self-poisoning cases in Sri Lanka have been published, showing that treatment costs for patients with severe pesticide poisoning greatly exceed all other costs for poisoned patients (Ahrensberg *et al.* 2019). Recently, Lee *et al.* (2020), using an economic modelling study across 14 countries, concluded that national bans of Highly Hazardous Pesticides (HHPs) are a potentially cost-effective and affordable intervention for reducing suicide deaths in countries with a high burden of suicides attributable to pesticides.

For many years pesticide self-poisoning was ignored as a public health and agricultural problem because it was considered a form of misuse. A number of parties to international treaties have argued against including pesticide self-poisoning in relevant provisions because self-poisoning was considered a form of misuse. It has therefore been excluded from international treaties such as the Rotterdam Convention. However, it has been argued that pesticide self-poisoning should be considered an occupational condition, akin to

alcoholism in bar staff, due to their availability and occupational use in small-scale farming communities where resources to store and use then safely are lacking (Eddleston 2018).

Despite the downward trend in pesticide suicide deaths during the last ten to 20 years, self-poisoning with these products is still the cause of one in five of the world's suicides (WHO and FAO 2019a). WHO and FAO have published guidance on approaches that regulators can take to prevent pesticide suicides (WHO and FAO 2019a).

#### 4.4.5 Factors affecting occupational and residential pesticide exposure

##### Occupational risk factors

Occupational pesticide exposure and the risk of subsequent adverse health effects may be influenced by a variety of factors related to the demography of the populations involved, pesticide application practices, the organization of the work environment, and workplace behaviours. These factors include experience with pesticide

**Table 4.4-10 Factors found to increase or reduce occupational pesticide exposure and/or health effects: outcomes from selected reviews and medium- or large-scale studies.**

Factor	Study number **						
	1	2	3	4	5	6	7
<b>Demographic factors</b>							
Younger age			↑*	↔			
Higher level of education			↔	↔			
Longer experience, confidence in practices			↓	↔			
More lifetime days of pesticide application					↑		↔
Large farm size					↑		
<b>Pesticide application and work environment</b>							
Control of all decisions on the farm			↓				
Pesticide safety training	●	↓					↓
Higher dose, frequency, toxicity of the pesticide	↑					↑	↑
Previous pesticide incident			↑				
Use of personal protective equipment	↓	↔	↔	↔	↓	↓	
Use of backpack sprayers				↑	↔		
Leaking or contaminated spray equipment			↑				
<b>Workplace behaviours</b>							
Use of pesticide in conflict with label		↑			↑		
Hand washing after work	↓						
Showering, changing clothes after work	●				↔		
Pesticide drift, application against the wind		↑			↑		
Early re-entry into sprayed fields		↑				↑	

\* ↓: found to reduce exposure/health effects; ↑: found to increase exposure/health effects; ↔: not found to have an effect on exposure/health; ●: insufficient evidence to draw conclusion

\*\* Studies:

1. Quandt *et al.* (2006): Review of 80 studies published since 1990; farmworker pesticide exposure, mainly in North America
2. Calvert *et al.* (2008): Analysis of pesticide poisoning cases in the United States from 1998 to 2005; factors linked to moderate or severe poisoning
3. Tomenson and Matthews (2009): Study of smallholder farmers in 24 countries worldwide; knowledge, attitude and practice (KAP) surveys linked to self-reported moderate or severe health effects
4. Pasiani *et al.* (2012): Study of smallholder farmers in mid-western Brazil; KAP study linked self-reported health effects and cholinesterase inhibition
5. Kim *et al.* (2013): Study of male farmers across the Republic of Korea, linking practices to self-reported moderate or severe health effects
6. Jørs (2016): Review of 20 studies published between 1995 and 2014, linking specific risk factors (focus on personal protection and the degree of pesticide exposure) with self-reported acute pesticide poisoning and/or cholinesterase inhibition
7. Fuhrman *et al.* (2019): Study of predictors of pesticide exposure of smallholder farmers in Costa Rica using a pesticide exposure algorithm

application, pesticide safety training, work hygiene, the type and maintenance of spray equipment, and use of personal protective equipment (PPE) (Table 4.4-10).

Many factors have been proposed to have direct, indirect or modifying effects on the extent to which farmers and farmworkers are exposed to pesticides; taking these factors into account often forms the basis for pesticide risk reduction measures (Quandt *et al.* 2006). However, when Quandt *et al.* (2006) conducted a first comprehensive review of workplace, household and personal predictors of pesticide exposure of farm workers, primarily in North America, they observed that research connecting the characteristics of workers' environments and behaviours with actual measurements of pesticide exposure was meagre. A more recent partial review of factors affecting acute pesticide poisoning in low and middle income countries (Jørs 2016) also yielded few quantitative data. No current comprehensive review quantifying the importance of risk factors for pesticide exposure and poisoning appears to be available.

Table 4.4-10 summarizes the outcomes of the above-mentioned reviews, as well as selected medium and large scale studies. It is striking that there are a large variety of outcomes, with certain risk factors reducing or increasing risk in some studies but not in others. This seems to indicate that whether a certain factor impacts pesticide exposure or health effects greatly depends on local conditions of use.

Demographic factors such as age, education, and experience with using pesticides have not been found to consistently increase or decrease pesticide exposure or effects. Factors linked with pesticide application and workplace organization have been evaluated more often. Using pesticides in higher doses or frequencies, or with higher toxicity, was found to increase health effects. Training in judicious pesticide use mostly appears to reduce pesticide exposure, although broader reviews of the impact of training on occupational health and safety have concluded that the longer-term impact of training – if conducted in isolation – is rather limited (Chapter 2.7.21).

Workplace behaviours in conflict with label instructions, good application practices or minimum occupational hygiene, on the other hand, were consistently found to increase pesticide exposure or effects.

Overall, studies quantifying the effects of workplace behaviours, demographic factors or pesticide application practices on occupational exposure or health effects remain infrequent.

### Personal protective equipment

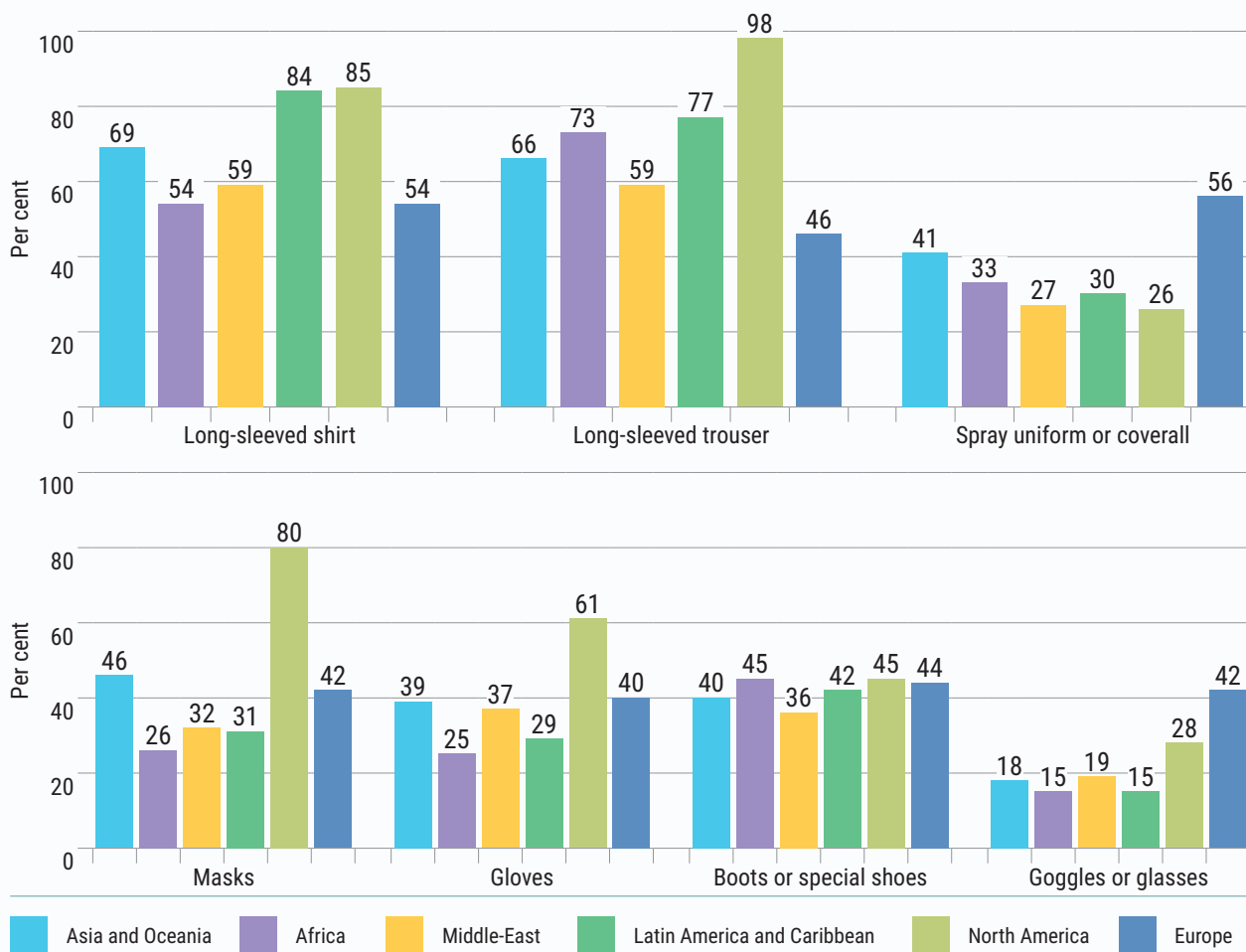
The use of personal protective equipment (PPE) is central to discussions of pesticide risk reduction for people who handle and apply pesticides or work in pesticide-treated fields or spaces. In many countries the authorization of moderate and high risk pesticides is conditional on the use of specific types of PPE. This equipment includes skin protection (aprons, coveralls, boots, gloves, hats/helmets), eye protection (face shields, goggles) and respiratory protective equipment (masks, respirators).

When studies on pesticide application under working conditions are reviewed, use of PPE either reduces exposure or does not seem to have a quantifiable effect; exposure reductions appear to be less than under controlled conditions. While not wearing PPE generally increases the incidence of poisoning, using it does not always reduce it (Kim *et al.* 2013; Garrigou *et al.* 2020). Calvert *et al.* (2008) noted that half of those poisoned by pesticides did wear.

Under controlled circumstances, proper use of adequate PPE significantly reduces occupational exposure to pesticides. Such exposure reduction factors have been incorporated into regulatory pesticide exposure models. For example, the European Food Safety Authority (EFSA 2014) considered that dermal pesticide exposure of pesticide applicators would be reduced by 90 per cent when chemical resistant gloves and coveralls or a single layer of work clothing are worn.

Based on a recent review of the scientific literature, Garrigou *et al.* (2020) found that both single-layer clothing and coveralls reduce occupational

► Figure 4.4-7 Use of PPE items in different regions of the world.



Shown are the average percentages of study populations using a PPE item, from the global review by Sapbamrer and Thammachai (2020).

exposure to a pesticide. However, a considerable fraction still passes through the fabric, even of chemical-resistant coveralls. The amount varies depending on the type of fabric, the area of the body, and the kind of pesticide under study. Most available research on the effectiveness of such equipment where PPE wearing practices are uncontrolled have shown that protective coveralls are not as effective as expected (Garrigou et al. 2020) (Table 4.4-10).

A global review of factors affecting the use of PPE by Sapbamrer and Thammachai (2020) looked at 121 scientific articles published between 1999 and 2019. It was found that, on average, about 70 per cent of pesticide handlers (farmers and farm workers) wore long-sleeved shirts and long trousers, but less than 30 per cent (also) wore dedicated coveralls or spray uniforms. On average, less than half of pesticide handlers used specific

PPE such as gloves, masks, boots and goggles. There was large variability among world regions, with PPE worn more regularly in high income than low income countries (Figure 4.4-7). However, even in OECD member countries, where conditions for wearing such equipment might seem most favourable, Garrigou et al. (2020) found that rates of PPE use were much lower than recommended.

Various reasons have been given to explain why farmers, pesticide applicators and farm workers are not, or are only partially, using PPE. The right PPE may not be available or affordable in some regions, an argument often made concerning subsistence farmers and workers in lower income countries. Non-provision or non-requirement by employers has been found to limit PPE use by farm workers. Literacy, higher education, the perceived benefits of PPE and dedicated training may increase its use, although the results

of studies linking education and training to PPE use are mixed (Garrigou *et al.* 2020; Sapbamrer and Thammachai 2020). PPE use has also been linked to farm size, with more (appropriate) PPE being worn on larger farms, possibly due to greater financial means.

Non-use of PPE can also be explained by characteristics of the equipment itself. Many items are uncomfortable, restrict the user's movements and can be very hot to wear, especially in warm and humid conditions. Under certain circumstances this can result in heat stress, potentially leading to loss of coordination and dangerous acute health effects (Garrigou *et al.* 2020; Sapbamrer and Thammachai 2020).

Garrigou *et al.* (2020) noted a dilemma in regard to PPE-dependent risk prevention: the more an item of PPE protects the wearer from pesticides, the more likely it is to be uncomfortable or even impossible to wear. In addition, the more effective it is, the more likely it is to be costly. They conclude that “the possibility of having PPE that is comfortable, suitable to practical conditions, affordable, and protects from contamination by any and all handled products has yet to be demonstrated”. It should be emphasized that this conclusion applies to high income OECD countries; it is likely to be even more true of PPE use in low income countries (Pesticide Action Network Asia Pacific 2010). This dilemma is especially relevant to the discussion of the use of Highly Hazardous Pesticides (HHPs) (Chapter 3.2.3), which require effective use of appropriate PPE.

Inadequate use of PPE in large parts of the world, together with the incomplete protection this equipment provides, means it should be considered a last line of defence after other measures have been taken (i.e., the “hierarchy of control” principle; see Chapter 6.2.5). The hierarchy of control is a fundamental principle of occupational health and safety around the world (Alli 2008; United States National Institute for Safety and Health 2015; European Agency for Safety and Health and Work 2018).

## Residential exposure to pesticides

People who live close to agricultural fields may be exposed to pesticides through various pathways, the most important of which are spray drift, volatilization of pesticides beyond the treated area, take-home exposure (e.g., through pesticide residues on the clothing of workers or farmers), pesticide use in/around the residence, and dietary ingestion (Deziel *et al.* 2015).

Those who live further from fields are mainly exposed through residential pesticide use (e.g., disease vector control, nuisance pest control, domestic and garden uses) and by dietary ingestion (Chapter 4.4.6).

Considerable concern has been (and continues to be) expressed about the exposure of people living close to agricultural fields, especially in areas with high intensity of pesticide use or where pesticide application methods entail potentially high drift (e.g., aerial applications, orchard spraying) (Dansereau *et al.* 2006; Lee *et al.* 2011; Human Rights Watch 2018; Health Council of the Netherlands 2020).

Dereumeaux *et al.* (2020) reviewed the scientific literature that quantifies pesticide exposure of non-farmworker residents living close to agricultural fields, who are expected to be exposed mainly through spray drift and pesticide volatilization. Most studies had been conducted in North, Central and South America. The study results confirm that those living closer to pesticide-treated agricultural land tend to have higher levels of pesticide residues/metabolites in their households and/or biological samples, higher levels of oxidative stress markers, greater DNA damage, and decreased activity of cholinesterase than those who live farther away. Moreover, the amount of pesticides applied, the acreage treated, and the time of year compared to the spray season were positively correlated with levels of human exposure.

Dereumeaux *et al.* (2020) and the Health Council of the Netherlands (2020) have pointed out that while associations between proximity to agricultural fields and various adverse health outcomes have been observed, but that the studies are not always

conclusive. This is partly due to the difficulty of characterizing and quantifying residents' exposure to pesticides. Stronger epidemiological evidence exists, however, for certain health effects due to occupational exposure (Chapter 4.4.3).

Deziel *et al.* (2015), in a review of evidence in the published literature for the contribution of non-occupational pathways of pesticide exposure in women living in North American agricultural areas, calculated that, on average, pesticide concentrations in house dust 250 metres from treated fields were still 36 per cent of the levels found in houses about 20 metres from fields. Lee *et al.* (2011) found that in the United States 73 per cent of non-occupational exposure to pesticide drift occurred more than 400 metres from the application site. However, on the basis of current observational studies assessing residential exposure and human health effects, it does not seem possible to define a safe distance between a residence and field that could ensure protection of human health (Teyssere *et al.* 2020).

There is also increasing evidence that the "take-home" (or "para-occupational") exposure pathway may contribute considerably to residential exposure to pesticides. Pesticide residues can be transferred from the workplace to the household environment on agricultural workers' clothing, skin, vehicles and shoes. A recent review provided evidence that these workers' families are exposed to pesticides at higher levels than those of non-agricultural workers (López-Gálvez *et al.* 2019). Levels may depend on several factors, including seasonality, parental occupation, cohabitation with a farmworker, behaviour at work/home, age and gender.

Good work practices, including the availability of laundry facilities, storing work boots at work instead of at home, frequent washing of hands before leaving the workplace, and receipt of pesticide training, have all been associated with lower residential pesticide contamination, suggesting that community based interventions that disrupt the take-home pathway can be effective in reducing pesticide exposure (Fenske *et al.* 2013; López-Gálvez *et al.* 2019). However many of the ways to lower such transfer may

not be available to subsistence farmers in low income countries.

While increasing evidence exists concerning residential exposure to pesticides, less is known about the adverse health effects that could result from such exposure. Teyssere *et al.* (2020) found that 71 per cent of the epidemiological studies included in their global assessment reported a significant association between at least one health outcome and residential exposure to pesticides. However, they did not evaluate the quality of these studies.

Recently the Health Council of the Netherlands (2020) reviewed the (mainly chronic) health risks posed to people living in the vicinity of agricultural land by the use of plant protection products. They conclude that the international epidemiological literature indicates the use of chemical agents for plant protection can be associated with impaired human health, although little is known about the exact level of risk involved or precisely which products are responsible.

The Health Council recognized that further research is not expected to provide clarity in the near future, nor can the approval procedure for these products ever fully eliminate risks. For these reasons it recommended application of the precautionary principle by redoubling efforts to reduce agricultural dependence on chemical plant protection products (Health Council of the Netherlands 2020).

On the basis of the above reviews it can be concluded that residential exposure to pesticides is likely to be widespread, especially in areas where there is intensive agriculture or residents live in close proximity to treated fields. Although risk mitigation measures such as drift reduction technologies, buffer zones and improved work hygiene have been recommended or required in many countries, this residential exposure remains extensive. The resulting health risks are less clear, but several epidemiological studies have found associations between residential exposure to pesticides and adverse health outcomes, indicating that health concerns about this exposure pathway are warranted.

#### 4.4.6 Pesticide residues in food

##### Residue monitoring

Pesticide residues may remain in/on a final food product following pesticide applications to the crop or post-harvest treatments of the commodity, or because of contamination from environmental sources (e.g., legacy pesticides remaining at low levels in the soil). Such residues may pose a dietary risk to the consumer. Many governments therefore set maximum residue limits (MRLs) for pesticides that are permitted on food commodities. At the international level, the Codex Alimentarius Commission (the Codex) establishes globally harmonized MRLs to protect the health of consumers as well as to ensure fair practices in the food trade.

To assess whether MRLs are respected, pesticide residues should be monitored on a regular basis in raw agricultural commodities and in processed food items. Different types of pesticide residue monitoring are conducted:

- monitoring programmes that attempt to provide a representative assessment of the situation of pesticide residues in food products

consumed in a country (these often follow random sampling methods);

- risk-based monitoring programmes focusing on pesticides or commodities originating from sources where relatively high residue levels have been found in the past or are expected (this is sometimes also referred to as “enforcement monitoring”);
- research projects, which tend to be ad hoc residue sampling programmes conducted to answer specific scientific questions (such sampling can be random, stratified or otherwise directed).

Residue monitoring may be carried out in both domestic and imported food products.

Residue monitoring programmes exist in certain countries, but most of them are high or upper-middle income economies (Table 4.4-11). Regular monitoring of pesticide residues in low and lower-middle income countries is rare, and most information on pesticide residues in food is collected through ad hoc research studies. A recent global survey indicated that only 58 per cent of responding countries had systems

► **Figure 4.4-8 On average, 58 per cent of countries have systems in place for monitoring pesticide residues in food and feed, but large differences exist among world regions (total number of responding countries = 50).** WHO and FAO (2019a).

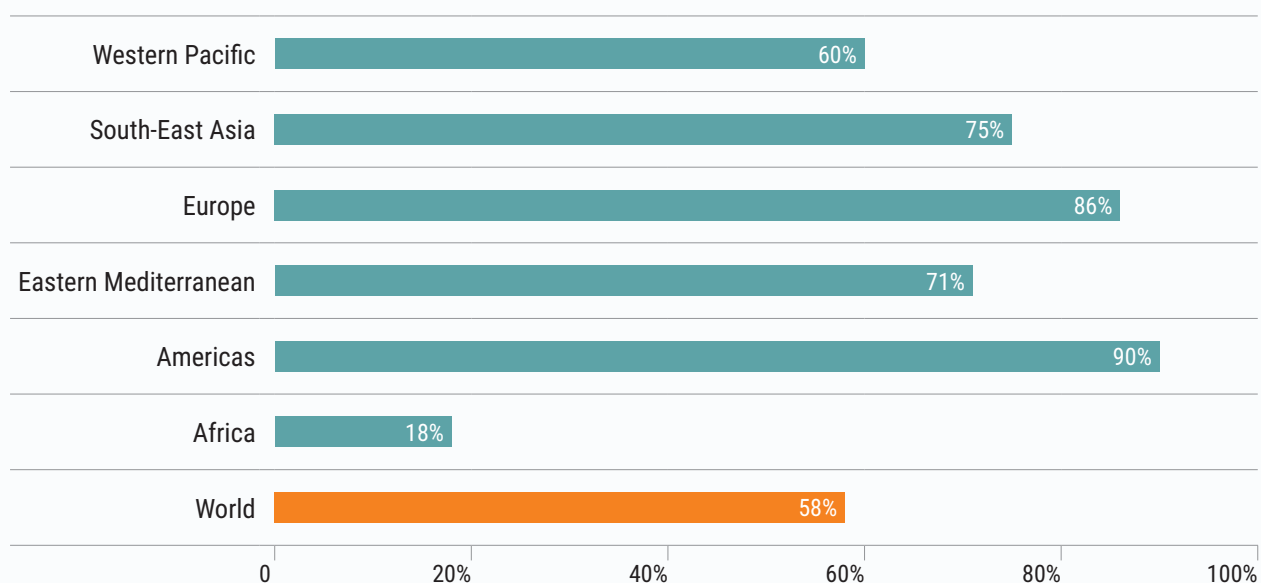




Table 4.4-11 Examples of national pesticide residue monitoring programmes.

Country	Programme and executing agency	Type of monitoring	Source
Australia	National Residue Survey (NRS), Department of Agriculture, Australia (DoA)	Risk based	DoA (2019)
Brazil	Programa de Análise de Resíduos de Agrotóxicos em Alimentos (PARA), Agencia Nacional de Vigilância Sanitária (ANVISA)		ANVISA (2019)
	Plano de Nacional de Controle de Resíduos e Contaminantes (PNCRC), Ministério da Agricultura, Pecuária e Abastecimento (MAPA)		PNCRC (2018; n.d.)
Canada	National Chemical Residue Monitoring Program (NCRMP), Canadian Food Inspection Agency (CFIA)	Random and risk based	CFIA (n.d.)
EU Member States, Norway and Iceland	EU-coordinated control programme (EUCP), European Food Safety Authority (EFSA)	Random	EFSA (2020b)
	National pesticide residue control programmes	Mainly risk based	
India	Monitoring of Pesticide Residues at National Level (MPRNL) scheme, Department of Agriculture, Cooperation and Farmers Welfare and Indian Council of Agriculture Research (ICAR)	Random	ICAR (n.d.)
New Zealand	Food Residues Survey Programme (FRSP) (plant products), National Chemical Residues Programme (NCRP) (animal products), New Zealand Food Safety (NZFS)	Random	NZFS (2020; n.d.)
United States	Pesticide Residue Monitoring Program, United States Food and Drug Administration (US FDA)	Risk based sampling, focused sampling and total diet studies	US FDA (2019)
	Pesticide Data Program (PDP), United States Department of Agriculture (USDA) (The PDP has also operated an on-line database with residue monitoring data since 1994.)	Representative, random	USDA (2019)

in place to monitor pesticide residues in food and feed, with a prominent lack of such surveillance in Africa (Figure 4.4-8) (WHO and FAO 2019b).

The outcomes of pesticide residue monitoring programmes or studies tend to be interpreted in two ways: the fraction of sample commodities that exceeds applicable MRLs, and/or the dietary risk of consuming food and drinking water containing measured levels of pesticide residues.

Exceedance of an MRL is an indication that a pesticide has not been applied in accordance with Good Agricultural Practices. However, because MRLs are not toxicological reference values exceedance of the MRL does not necessarily mean the consumer is exposed to an unacceptable dietary risk (Box 4.4-3). To know whether consumers run a health risk,

a dietary risk assessment needs to be conducted. Such an assessment is generally based on the consumption of all food sources that may contain residues of the pesticide in question.

#### Pesticide residue concentrations in food

There have been no global reviews of pesticide residues in food commodities and their potential risks to consumers. Regular monitoring programmes (as listed in Table 4.4-11) tend to publish detailed annual reports of their results, sometimes including dietary risk assessments. On the other hand, data from ad hoc residue monitoring studies, as conducted in many lower income countries, have never been systematically compiled and analysed (FAO/WHO Joint Meeting on Pesticide Residues, personal communication).

Box 4.4-3 Maximum Residue Limits (MRLs).

A **Maximum Residue Limit (MRL)** is the maximum concentration of a residue that is legally permitted or recognized as acceptable in or on a food or agricultural commodity or animal feedstuff (FAO/WHO 2014). MRLs can be defined nationally or globally, the latter by the Codex Alimentarius Commission (Chapter 3.2.3). Codex MRLs are primarily intended to facilitate international trade, while protecting the health of consumers.

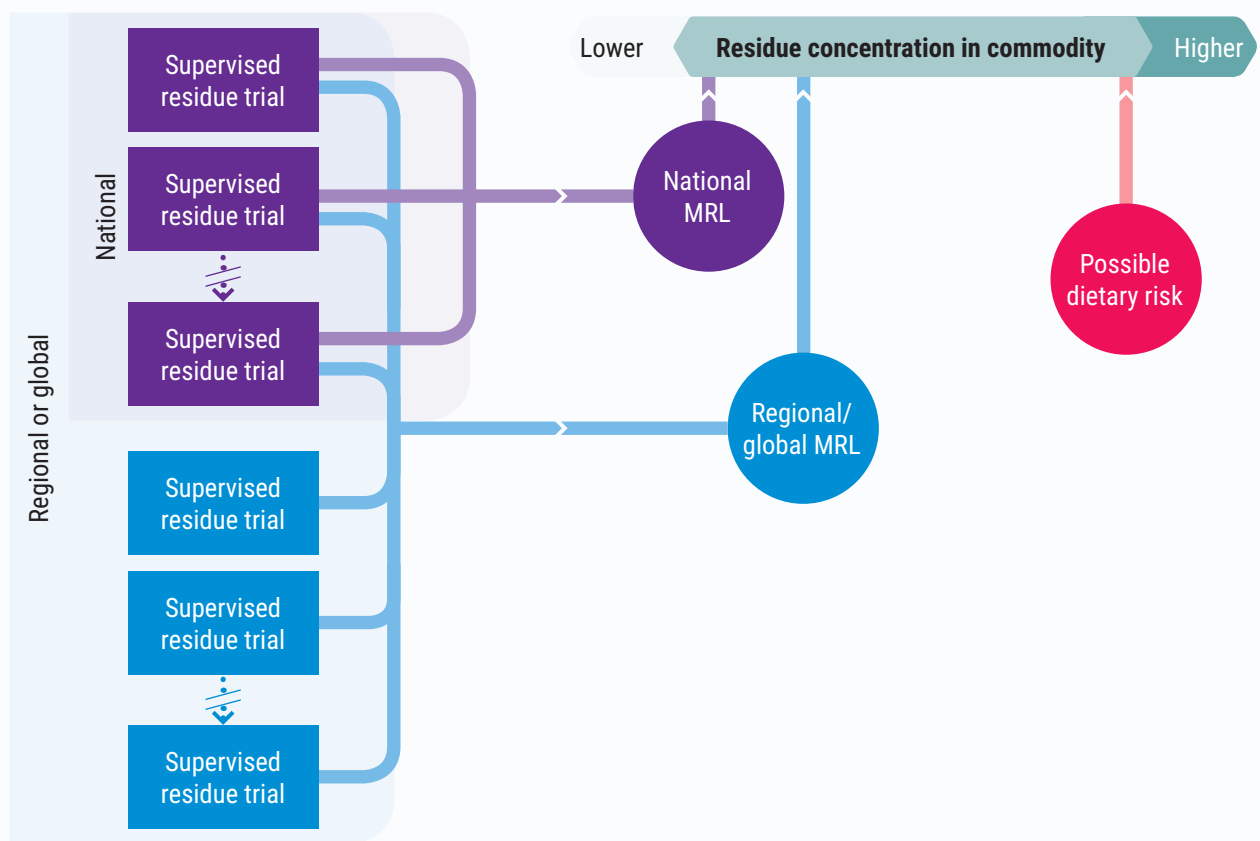
An MRL is derived on the basis of a toxicological assessment of the pesticide and its residue, and a review of residue data from supervised trials. They are always set for a specific pesticide active ingredient combined with a specific commodity (e.g. MRL of deltamethrin on tomatoes).

An MRL is estimated from residue levels measured in a series of supervised trials in which a specific pesticide is applied according to Good Agricultural Practice (GAP), i.e. the directions for the authorized use on the pesticide label. The use conditions leading to the highest residues (the critical GAP) are generally used to estimate the MRL for a given pesticide-commodity combination.

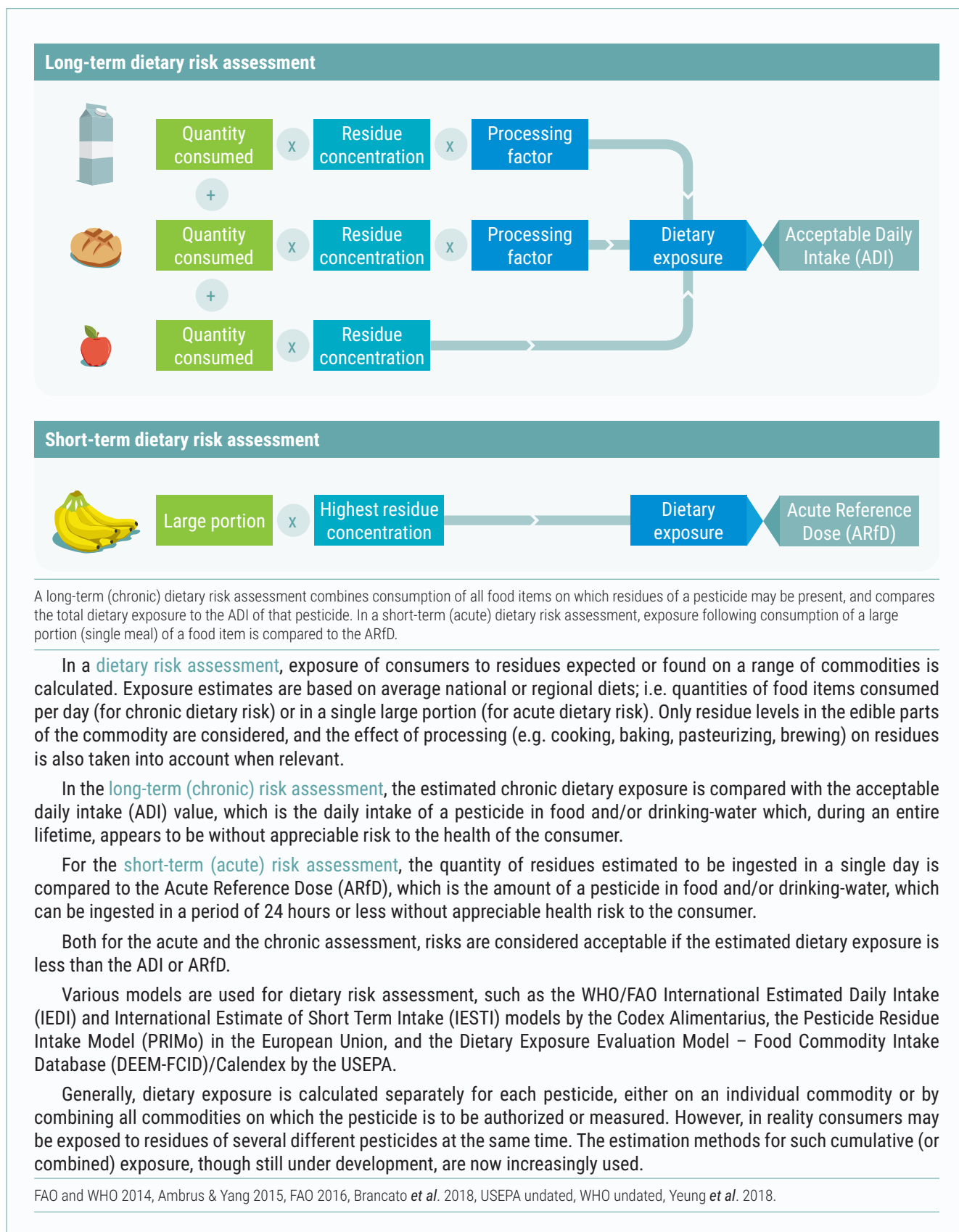
If a new MRL is established, a dietary risk assessment is also conducted (see below) to assess whether the residue levels used to estimate the MRL result in acceptable risks to the consumer. This is done for individual commodities and for all commodities combined for which the pesticide authorized. If the dietary risk is acceptable, the MRL can be adopted.

An MRL is not a toxicological reference value. It is a food standard reflecting the critical GAP in the country or region: it indicates the maximum residue that can be encountered on a commodity given the agronomic conditions in the country, and which does not pose an unacceptable dietary risk. MRLs can thus be different among countries because GAPs are different. For instance, a global (Codex) MRL may be higher than a national MRL because Codex includes pesticide residue studies from all over the world in their estimate, which may include situations where pesticide applications rates are higher due to climatic conditions; the critical GAP and thus the MRL may then be higher too. However, the higher MRL can only be adopted if the dietary risk is acceptable.

Exceedance of MRLs therefore signals that the GAP, i.e. recommended best pesticide application practices, have not been followed. It does not automatically mean that consumers run an increased dietary risk (although this may occur if exceedance of the MRL is large).



National or regional/global MRLs may be – but are not always – different, because they may be based on different residue trials with different GAPs. However, MRLs will always be below residue concentrations that can be expected to result in dietary risks.



Residue monitoring programmes in Europe, North America, Australia, New Zealand and India generally show that exceedances of MRLs are relatively limited, typically ranging from <1 to 10 per cent of samples taken in a given year.

In Table 4.4-12 only Brazil has a considerably higher exceedance rate for plant based food commodities. It should be noted that comparisons of residue monitoring programmes between countries is not straightforward, as countries may

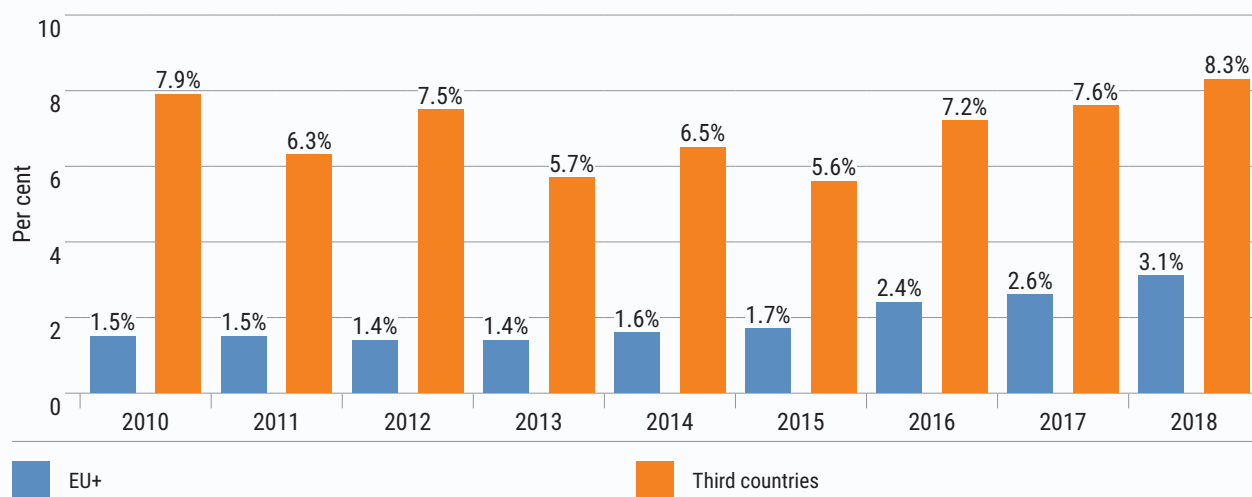
**Table 4.4-12 Recent levels of exceedance of pesticide maximum residue limits (MRLs) in countries with regular pesticide residue monitoring programmes in food commodities.**

Country	Year	Food commodities	Number of samples (origin)	Free of pesticide residues <sup>1</sup>	MRL exceedance <sup>1, 2</sup>	Source
Australia	2018-2019	Animal based	9,952	--	0.2 per cent	DoA (2019)
		Plant based	5,241		0.8 per cent	
Brazil	2017-2018	Selected plant based	4,616 (domestic)	49 per cent	23 per cent	ANVISA (2019)
	2018	Animal based	12,495	--	0.4 per cent	PNCRC (2018)
Canada	2018-2019	Selected plant based	3,348	60 per cent	0.7 per cent	CFIA (2019)
EU Member States, Norway and Iceland	2018	Selected animal and plant based	57,286 (domestic)	58 per cent	3.1 per cent	EFSA (2020b)
			24,495 (imported)		8.3 per cent	
India	2017-2018	Animal and plant based	23,660	81.9 per cent	2.2 per cent	Ministry of Agriculture and Farmers Welfare (2019)
New Zealand	2017-2019	Fruits and vegetables	591	--	6.2 per cent	NZFS (2020)
United States	2017	Animal and plant based	1,799 (domestic)	52.5 per cent	4.8 per cent	US FDA (2019)
			4,270 (imported)	50.0 per cent	10.4 per cent	
	2018	Mainly plant based	6,981 (domestic) 3,385 (imported)	47.8 per cent	6.0 per cent 9.0 per cent	USDA (2019)

1 MRL exceedance is expressed as percentage of total number of commodity samples.

2 Generally including samples with pesticide residues for which no MRL or tolerance has been established for that crop.

**Figure 4.4-9 Pesticide MRL exceedances of food commodities imported into the EU+ (EU Member States, Norway and Iceland) between 2010 and 2018 ranged between 5.5 and 8.5 per cent of samples (orange bars). Lower MRL exceedances are found for food originating from within the EU+, but these have been steadily increasing from 1.5 in 2010 to 3.1 per cent in 2018 (blue bars).** Based on EFSA (2013-2019).



differ in regard to the balance between random or “targeted” selection of samples for monitoring in their programmes.

In both the EU and the United States, MRL exceedance rates for imported food commodities are about twice the rates for domestically produced food. This suggests that agricultural practices in the exporting countries are not always able to meet national MRLs, e.g., due to higher pesticide application rates and frequencies or because pre-harvest intervals are not adequately respected.

MRL exceedance rates in the countries listed in Table 4.4-12 generally do not fluctuate much over time. MRL violations in regard to domestically produced food in the highly regulated EU have been steadily increasing during the last five years while still remaining fairly low (Figure 4.4-9). It is not clear why this has been the case.

Since very few regular pesticide residue monitoring programmes exist in low and middle income countries, information on violations of MRLs in these countries is limited.

In a global review on bananas, Gomes *et al.* (2020) found only a few published studies reporting the presence of pesticides on this fruit. In the available studies, however, depending on the standard-setting body (Brazil, the Codex, the EU), between 32 and 79 per cent of samples did not meet MRLs (either the MRL was exceeded or the pesticide found in the bananas did not have an established MRL).

No recent global reviews of pesticide residues in other commodities or cropping systems were available. However, ad hoc residue monitoring in low and middle income countries seems to indicate that the degree of exceedance of MRLs, across many commodities, may be significantly higher than the 1-10 per cent found in the high income countries mentioned above. Examples include studies in Ghana (Osei-Fosu *et al.* 2014), Thailand (Sapbamrer and Hongsoibong 2014), Pakistan (Faheem *et al.* 2015), Burkina Faso (Lehmann *et al.* 2017) and Bolivia (Skovgaard *et al.* 2017). Many of these studies compare residue levels with Codex MRLs, which were established

based on global critical GAPs. The relatively high exceedance levels observed suggest that farmers in low and middle income countries are often not able to meet the GAPs defined internationally by the Codex. Higher application rates and frequencies, inadequate adherence to pre-harvest intervals, and use of pesticides that do not have an MRL (including diversion of pesticides registered for use on non-food crops to use on foods) may all contribute to increased MRL exceedances. It is also possible that farmers who do not grow for export markets are not aware of (or are less likely to comply with) the GAPs and MRLs that may have been established for a pesticide.

### Dietary risk assessment

Dietary risk assessments are conducted to evaluate exposure to pesticide residues through food intake and the resulting risks to human health (Box 4.4-4). They generally have two different purposes (EFSA 2018e):

- Pre-registration (prospective) assessments are conducted to assess the risks to consumers resulting from pesticide residues expected on food, e.g., if a new active ingredient (or a new use of an already authorized active ingredient on a different crop) needs to be authorized.
- Post-registration assessments are conducted to assess the risk of actual exposure of consumers resulting from pesticide residues measured in pesticide monitoring programmes.

The risks of pesticide residues in food are mostly evaluated on a compound by compound basis. If potential exposure of consumers is below the relevant health based reference value (ADI or ARfD, see Box 4.4-4), the use of that pesticide is considered acceptable. However, consumers are frequently exposed to more than one pesticide residue in food at the same time. Assessing the risks of multiple pesticides in food is referred to as “cumulative risk assessment” (Boobis *et al.* 2008) or more commonly as “combined risk assessment” (European Food Safety Authority Scientific Committee 2019). Cumulative dietary risk assessments are considered most relevant for groups of pesticides with similar modes of action, or cumulative assessment groups (CAGs) (Boobis

*et al.* 2008,). Unlike the dietary risk assessment of individual pesticides, there is currently no internationally agreed protocol for the evaluation of combined dietary risks. However, several methods have been developed in the last decade and are increasingly applied at the national or regional levels (Meek *et al.* 2011; Jensen *et al.* 2015; Chang *et al.* 2018; EFSA 2020c; EFSA 2020d).

No global review of pesticide dietary risk assessments is currently available. Recent national or regional dietary risk assessments covering important groups of pesticides and food commodities have been compiled in Table 4.4-13. Apart from assessments in Brazil and Tunisia, all the others are from high income countries. In virtually all cases (countries, consumer age groups, and food commodities) actual acute and

**Table 4.4-13 Recent regional or national dietary risk assessments of pesticide residues in food: assessments are of the risks of exposure to single pesticides and of combined exposure to multiple pesticides.**

Country	Residue assessment period	Food commodities
<b>Single pesticide<sup>1</sup></b>		
Eight countries: Australia, Brazil, Canada, Czech Republic, France, Italy, Netherlands, United States	2008-2017	Both plant and animal based
For a limited number of pesticides, in certain countries, exposure of children exceeded 20 per cent of the ARfD (carbofuran, cypermethrin, cyfluthrin, fenpropathrin, prothioconazole).	Crépet <i>et al.</i> (2021)	
Tunisia (adults 19-65)	2009-2010	42 core food groups covering 97 per cent of the Tunisian diet
The authors conclude that there is low dietary exposure to pesticide residues of the Tunisian adult population.	Bouktif Zarrouk <i>et al.</i> (2020)	
New Zealand	2017-2019	Fruits and vegetables
	NZFS (2020)	
EU	2018	Selected plant and animal based commodities
182 a.i.'s (for chronic risk)	Deterministic (PRIMO)	Acute risk: For 143 pesticides there was no exposure concern. The remaining 33 pesticides exceeded the acute health based guidance value in 327 samples (1.4 per cent). EFSA considers it unlikely that this limited number of exceedances of the ARfD would pose concerns for consumer health.
Chronic risk: EFSA concluded that according to current scientific knowledge, chronic dietary exposure at the assessed levels for the food commodities analysed is unlikely to pose concerns for consumer health.	EFSA (2020b)	
Germany	2009-2014	Mainly plant based

chronic dietary risks of pesticides in food were considered very small. The only exception is dietary exposure of children in Israel, where the large majority of this population was exposed to residue levels above the acceptable daily intakes of up to 10 different pesticides.

Dietary risk assessments have been published in low and middle income countries, but only

for a small number of specific pesticides or commodities. There are few, if any, national assessments which include a broader range of pesticides and/or commodities. It is therefore difficult to evaluate whether the higher degree of MRL exceedance observed in these countries (see above) leads more often to unacceptable dietary risks.

Pesticides <sup>2</sup>	Method	Outcome (as reported by the study authors)	Reference
38 a.i.'s assessed	Probabilistic model of acute dietary exposure of adults and children	None of the exposure values for the 38 pesticides exceeded the ARfD.	
170 a.i.'s assessed, of which 21 were detected	Total diet study	The ADI was not exceeded for any pesticide except the bromide ion (methyl bromide, which has been banned).	
All MRL non-compliant a.i.'s from residue monitoring	Not defined	None of the survey samples exceeding the relevant MRLs resulted in any food safety concerns to consumers of all ages.	
176 a.i.'s (for acute risk)			
700 a.i.'s	Probabilistic model (MCRA)	693 pesticides were unlikely to pose chronic or acute dietary risks.	

Country	Residue assessment period	Food commodities
Short-term dietary exposure to chlorpyrifos, dimethoate/omethoate may present a public health concern.		
Dietary risks of copper, dimethylvinphos, halfenprox and tricyclazole remained inconclusive.	Sieke <i>et al.</i> (2018)	
Israel (children only)	2006-2010	Fruits, vegetables, tubers
90 per cent of the children had uptakes in excess of the ADI for between two and eleven compounds; 5.6 per cent of children had one exceedance and 4.8 per cent had none.		
Freeman <i>et al.</i> (2016)		
Cumulative <sup>2</sup>		
EU	2014-2016	Both plant and animal based
EU	2014-2016	Both plant and animal based
Brazil	2005-2015	Plant based
Brazil	2005-2015	Plant based
The same conclusion was made for cumulative chronic exposure to TR and DT in the case of individuals 10 years or older (up to 1 and 6.7 per cent of the respective ADIs).		
Oliveira Jardim <i>et al.</i> (2018b)		
Denmark	2013-2014	Plant based
United States	2011-2014	Fruits and vegetables
Denmark	2004-2011	Fruits, vegetables, cereals

1 Types of dietary risk assessment: Single pesticide = Risk estimation for all relevant food commodities combined, containing one specific pesticide; Cumulative = Risk estimation for all relevant food commodities combined, and combined exposure to multiple pesticides



Pesticides <sup>2</sup>	Method	Outcome (as reported by the study authors)	Reference
26 a.i.'s most often found in the food items	Deterministic (similar to WHO Global Environment Monitoring System [GEMS])	Surveyed children had higher potential exposures than the general population for >33 per cent of the compounds.	
Pesticides that have certain acute effects on the nervous system: >119 a.i.'s belonging to the same CAG	Two probabilistic models	For all populations studied (toddlers, children, adults) it is concluded with varying degrees of certainty that cumulative exposure to pesticides that have the studied acute effects on the nervous system does not exceed the threshold for regulatory consideration.	EFSA (2020c)
Pesticides that have certain chronic effects on the thyroid: 133 a.i.'s belonging to the same CAG	Two probabilistic models	For all populations studied (toddlers, children, adults) it is concluded with varying degrees of certainty that cumulative exposure to pesticides that have the studied chronic effects on the thyroid does not exceed the threshold for regulatory consideration.	EFSA (2020d)
Organophosphorus (OP), carbamate(CA) and pyrethroid (PY) insecticides	Relative potency factors, probabilistic model (MCRA)	The cumulative acute exposure did not exceed the ARfD for OP, CA and PY insecticides at the 99.9 percentile of the intake distribution. It does not therefore represent a health concern for the population under consideration (10 years or older).	Oliveira Jardim <i>et al.</i> (2018a)
Triazole (TR) and dithiocarbamate (DT) fungicides	Relative potency factors, probabilistic model (MCRA)	The cumulative acute exposure of TR accounted for up to 0.5 per cent of the ARfD at the 99.9 percentile of the intake distribution and therefore did not represent a health concern for the relevant population (women of child-bearing-age).	
198 a.i.'s	Hazard Index (HI)	HI = 0.44 for children and 0.16 for adults, indicating that adverse health effects from chronic pesticide exposure through food are very unlikely.	Larsson <i>et al.</i> (2018)
Seven neonicotinoid insecticides	Relative potency factor (RPF) approach	The estimated average daily intakes were several orders of magnitude lower than the current chronic reference dose (cRfD). Chronic dietary risks of neonicotinoids through fruit and vegetable consumption are therefore unlikely.	Chang <i>et al.</i> (2018)
~ 330 a.i.'s and metabolites	HI	HI = 0.44 for children and 0.18 for adults, indicating that food consumption did not pose chronic dietary risks for adults or children, including for high consumption of fruits.	Jensen <i>et al.</i> (2015)

2 a.i. = active ingredient; CAG = cumulative assessment group (i.e. pesticides with a common toxicological mode of action); ADI = acceptable daily intake; ARfD = acute reference dose; cRfD = chronic reference dose; HI = Hazard Index; MCRA = Monte Carlo simulation for risk assessment

#### 4.4.7 Pesticides and antimicrobial resistance

##### Introduction

Antimicrobial resistance (AMR) refers to microorganisms – bacteria, fungi, viruses and protozoans – that have acquired resistance to antimicrobial substances (FAO 2015; WHO 2015; WHO 2020e). When microbes become resistant to medicines, the options for treating the diseases they cause are reduced. This resistance to antimicrobial medicines is occurring in all parts of the world for a broad range of microorganisms. The direct consequences of infections with resistant microorganisms can be severe, including longer illnesses, increased mortality, loss of protection for patients undergoing operations and other medical procedures, and increased costs (WHO 2015; WHO 2020e).

AMR in human and animal pathogens is primarily a result of the use, misuse and overuse of antibiotic and antimicrobial drugs to treat infections in humans as well as in animals (e.g., livestock, aquaculture). Although the scale of the problem is driven by human activity, AMR is ancient, predating human use of antimicrobials (D’Costa *et al.* 2011). Many antibacterial drugs are natural products produced by microorganisms and resistance has evolved in environmental microbial populations over evolutionary time. Critically, AMR in human and animal pathogens is not only conferred by mutation but also by acquisition of mobile resistance genes through a process called horizontal gene transfer, whereby resistance genes can be mobilized from harmless soil bacteria to unrelated clinical pathogens. The environment is also contaminated with antimicrobials and antimicrobial-resistant microbes through human and animal faecal wastes, which can accelerate the development and spread of resistance.

Emerging evidence suggests that metals, non-antimicrobial pharmaceuticals and even plant protection products such as herbicides may have previously unknown antimicrobial properties that can contribute to development of AMR (Kurenbach *et al.* 2015; Maier *et al.* 2018). Such contamination can occur from, for example, human and animal wastes (i.e., faeces, manure; see Chapter 9 on the risks of organic fertilizers),

pharmaceutical manufacturing waste, and use of antimicrobial pesticides and other pesticides on crops (Wellcome 2018).

Slowing down antimicrobial resistance development to ensure the continuity of successful treatment and prevention of infectious diseases has become a worldwide priority, with global action plans developed in the human health as well as the agriculture and food sectors (WHO 2015; FAO 2015; EU 2020b; WHO, FAO and World Organization for Animal Health 2020). The United Nations Environment Assembly (UNEA) has also recognized that antimicrobial resistance is an increasing threat to global health, food security and sustainable development, and has underlined the need to further understand the role of environmental pollution in the development of antimicrobial resistance (UNEP 2018).

##### Use of antimicrobial pesticides

Antimicrobials in agriculture are used in terrestrial and aquatic animal and plant production for both treatment and non-therapeutic purposes such as animal growth promotion. The large majority of agricultural uses are as veterinary medicines in livestock production and aquaculture. These uses are not discussed here, as most of them do not fall under the commonly used definition of a pesticide (Chapter 2.2).<sup>8</sup>

Antimicrobials used as pesticides in crops can be broadly categorized as antibiotics (used to control bacterial plant diseases) and fungicides (used to control fungal plant diseases). In some cases these antimicrobials are the same, or closely related to, antimicrobials used in human medicine (Table 4.4-14).

The yearly amount of *antibiotics* used on crops has been considered relatively low in comparison to the quantities used in livestock, with estimates ranging from 0.2 to 0.4 percent of total agricultural

8 In aquaculture many antimicrobials and antibiotics are administered orally (e.g., in food pellets) and would be regarded as veterinary medicines. However, in both treatments of prawn and shrimp and the disinfection of ponds the antimicrobial is applied to the environment of the animals, in which case it could be considered a pesticide.

**Table 4.4-14 Antimicrobials used as both pesticides and human medicines.** Berger *et al.* (2017); Wellcome (2018); WHO (2019); FAO and WHO (2019).

Antimicrobial class	Antimicrobial pesticide	Use as human medicine	WHO CIA List classification (only for antibiotics)
<b>Antibiotics</b>			
Aminoglycosides		Yes	
	streptomycin	Yes	Critically Important
	gentamicin	Yes	High priority, critically Important
	kasugamycin	No (and no known cross-resistance with amino-glycosides used in human medicine)	
Tetracyclines		Yes	
	oxytetracycline	Yes	Highly Important
Quinolones and fluoroquinolones		Yes	
	oxolinic acid	Yes	Highest priority, critically Important
<b>Antifungals</b>			
Azoles		Yes	Not applicable
	e.g. difenoconazole, epoxiconazole, propiconazole, tebuconazole	No; e.g. itraconazole, voriconazole, posaconazole – but observed cross-resistance	

WHO classification of Critically Important Antimicrobials (WHO 2019):

**Critically important:** Antimicrobial classes which are C1 (this class is the sole or one of limited available therapies to treat serious bacterial infections in people) and C2 (this class is used to treat infections in people caused by either bacteria that may be transmitted to humans from non-human sources, or bacteria that may acquire resistance genes from non-human sources)

**Highly important:** Antimicrobial classes which meet the criteria for either classes C1 or C2, above.

**Highest priority:** Antimicrobial agents for which risk management strategies are needed most urgently.

antibiotic consumption (FAO 2015). Historically, the largest use of antibiotics on crops has been to control fire blight of apple and pear, but they are also used to control bacterial diseases in vegetables, fruits and flowers (Stockwell and Duffy 2012; Wellcome 2018). A recent review (Taylor and Reeder 2020) suggests that antibiotics are being recommended far more frequently and on a greater variety of crops than previously thought. The authors found that antibiotics are used in low and middle income countries in all regions of the world except Africa. Rice appears to be the main crop on which antibiotics are used. Streptomycin was the most frequently recommended antibiotic, followed by kasugamycin and tetracycline.

According to Taylor and Reeder (2020), although the quantities of antibiotics used for

crop protection remain relatively low compared with medical and veterinary uses, application concentrations of antibiotics used to treat plant diseases are several orders of magnitude higher than residue concentrations of veterinary and human antibiotics in manures and sludges applied to soils, so that the impact on selection for AMR in the environment may be significant. The study further notes that mixtures of antibiotics with other pesticides are common, and that they have been found to promote cross-resistance or co-selection for antibiotic resistance.

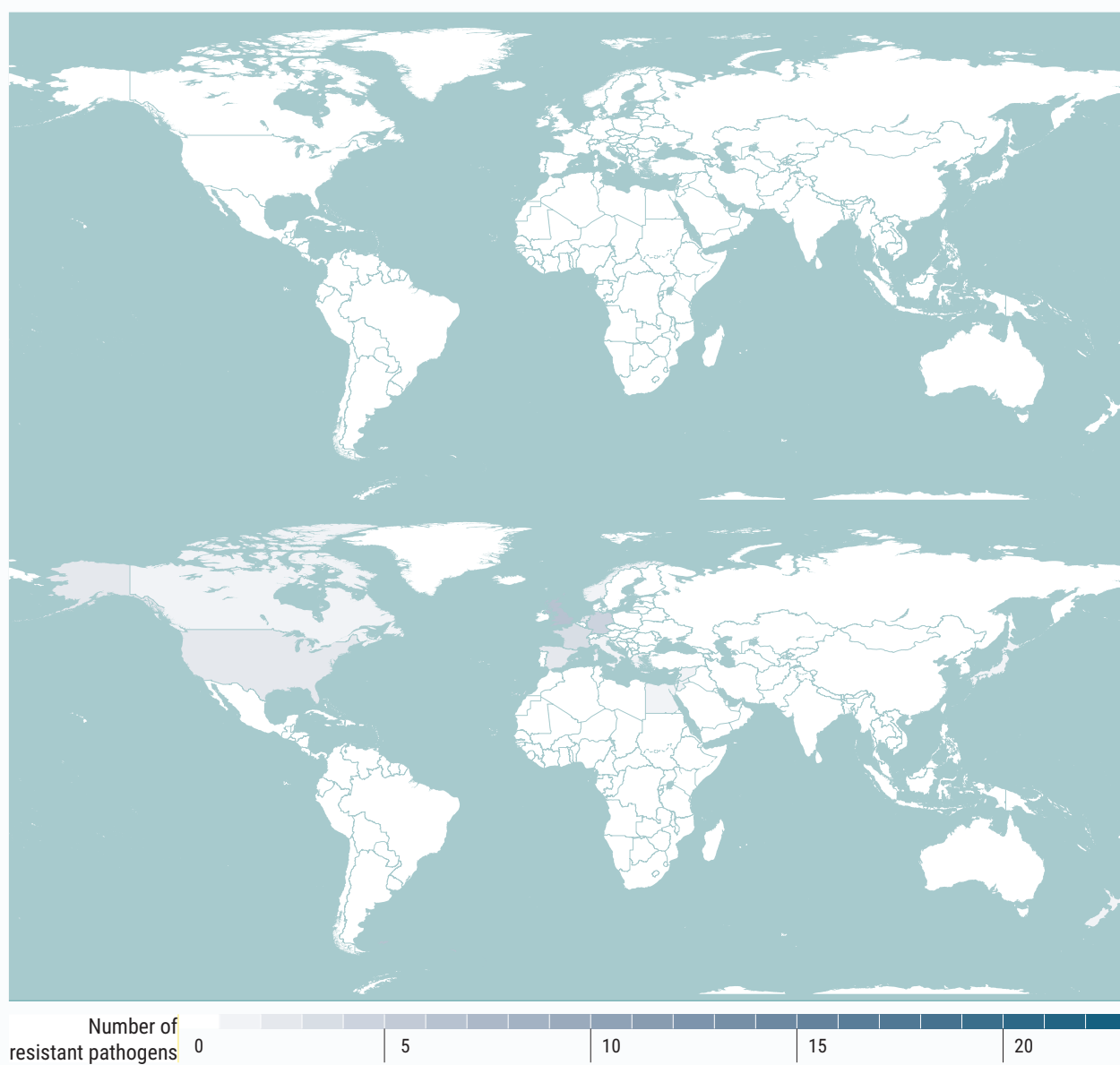
The use of *fungicides* is much higher than that of antibiotics (Chapter 2.3), although many fungicides are not known to be important for AMR development in human health. Of particular relevance are the azole fungicides, which are

among the most used fungicides in the world and are used in both agriculture and human medicine (Berger *et al.* 2017).

In contrast to antibiotic pesticides, copper based compounds are very commonly used on a wide variety of crops to manage bacterial and fungal plant diseases. While copper is not used in human medicine, it has been shown to co-select for resistance in bacteria and so may contribute to resistance development of antimicrobials in human medicine (Wellcome 2018).

*Chemical disinfectants* are included under the definitions of pesticide or biocide in certain countries and may be regulated accordingly. They are of critical importance for food safety to control microbial cross-contamination and ensure general hygiene at many stages of the food value chain. Chemical disinfectants are also used for decontamination and in healthcare facilities, as well as for disinfection of drinking water. Very large volumes of chemical disinfectants are used globally in both the food and the health sectors. The use of certain biocides is being questioned due to the possibility that

► **Figure 4.4-10** The number of fungal species with reported antifungal resistance has been increasing over time, both in agriculture and in human health. Increasing colour intensity reflects a higher number of reports. The plant maps depict records of resistance of crop pathogens to azole fungicides (blue scale).



exposure could select for resistance to different antimicrobials including antibiotic drugs (FAO and WHO 2019).

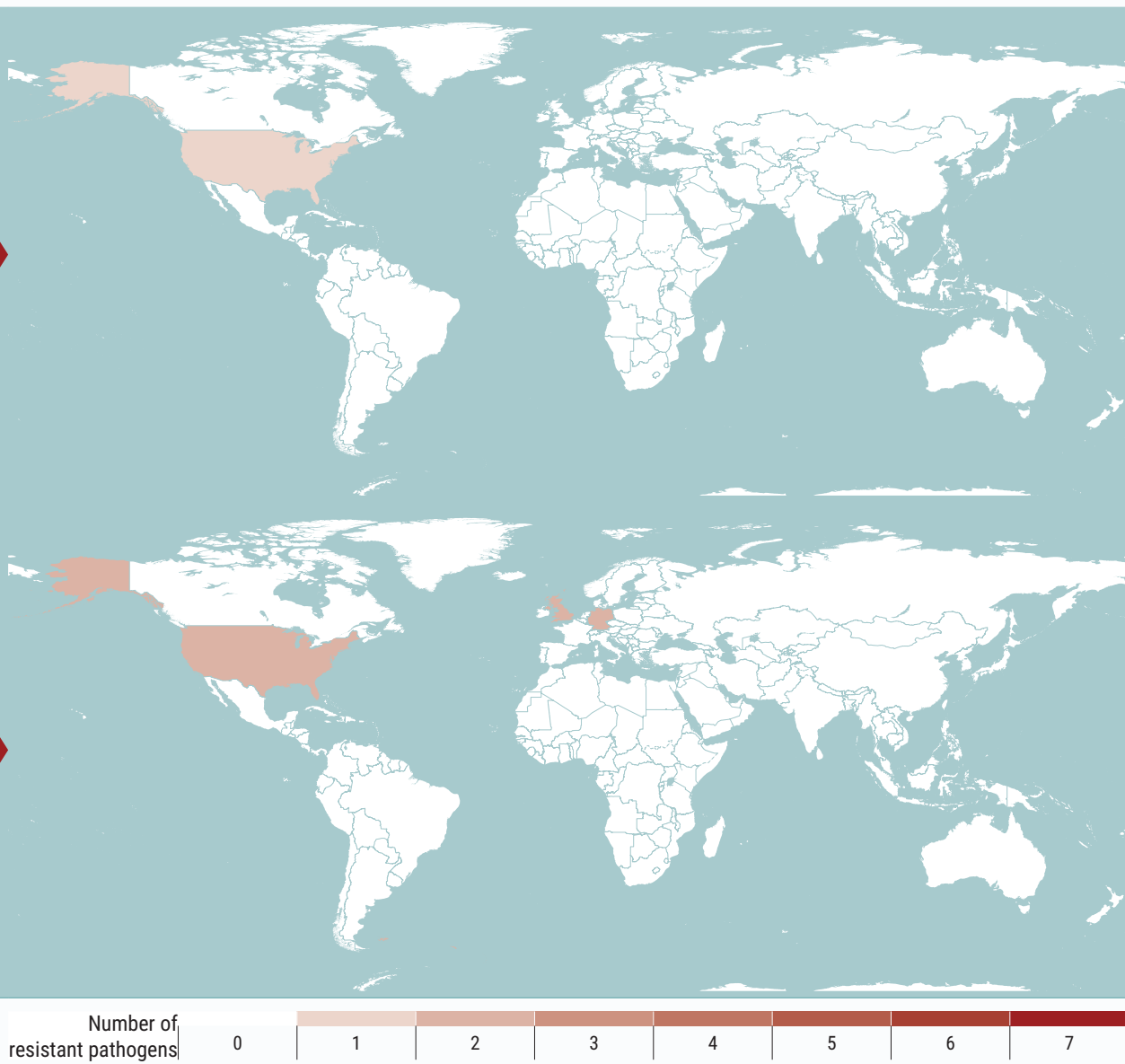
### Impact of pesticide-induced antimicrobial resistance

A recent expert meeting (FAO and WHO 2019) concluded that antimicrobial pesticides may contaminate soils following crop applications, which may lead to augmentation of antimicrobial-resistant bacteria and genes in the environment. However, the extent to which the

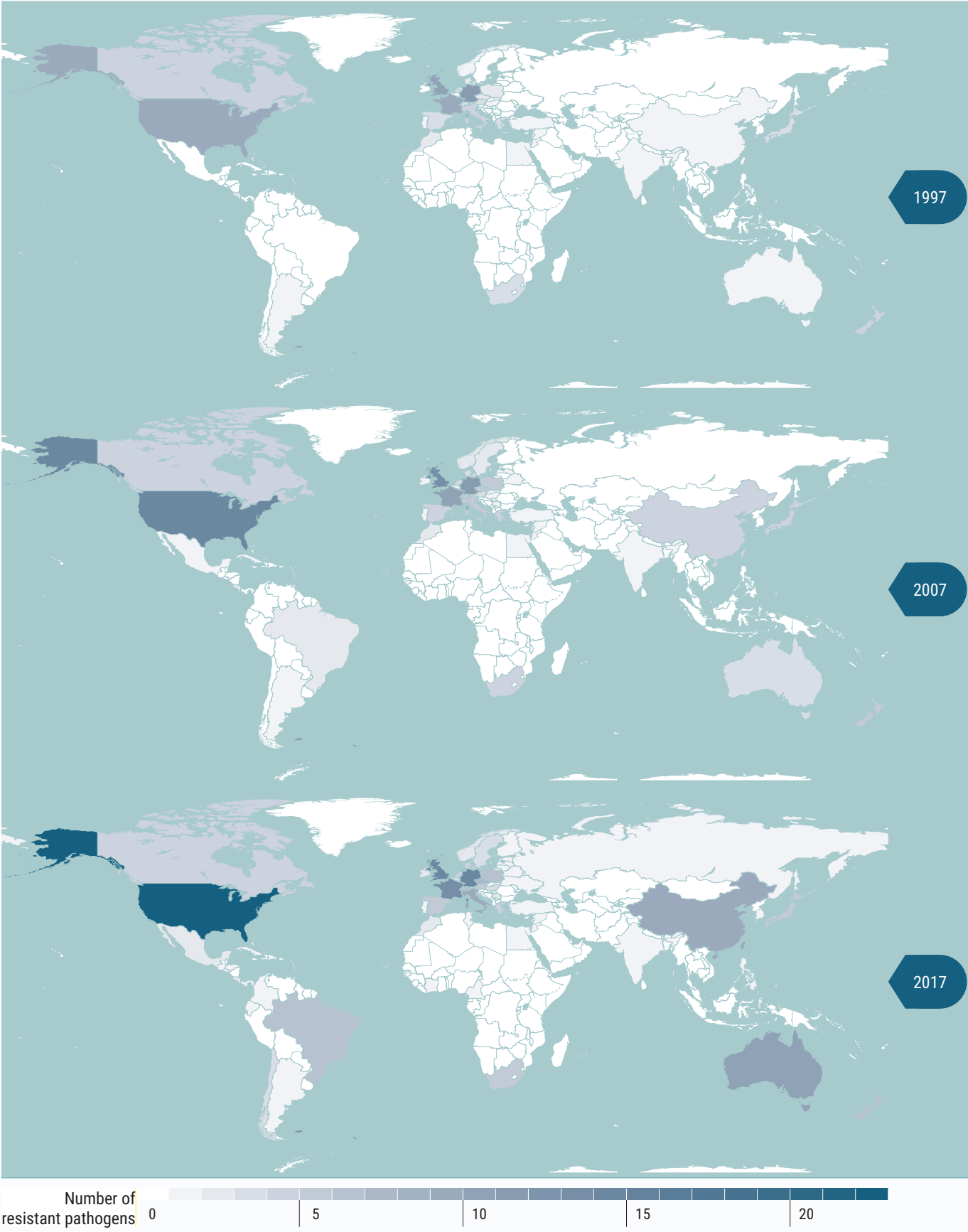
treatment of crops with antimicrobial agents promotes AMR in bacteria found on edible portions of fresh plant produce is uncertain (FAO and WHO 2019).

While further research is needed to determine the effects of antimicrobial based pesticides on human health, there are specific concerns where antimicrobial pesticides are the same as, or closely related to, antimicrobials used in human medicine (Wellcome 2018; WHO 2019). This is the case for the antibiotics belonging to the classes of aminoglycosides, quinolones

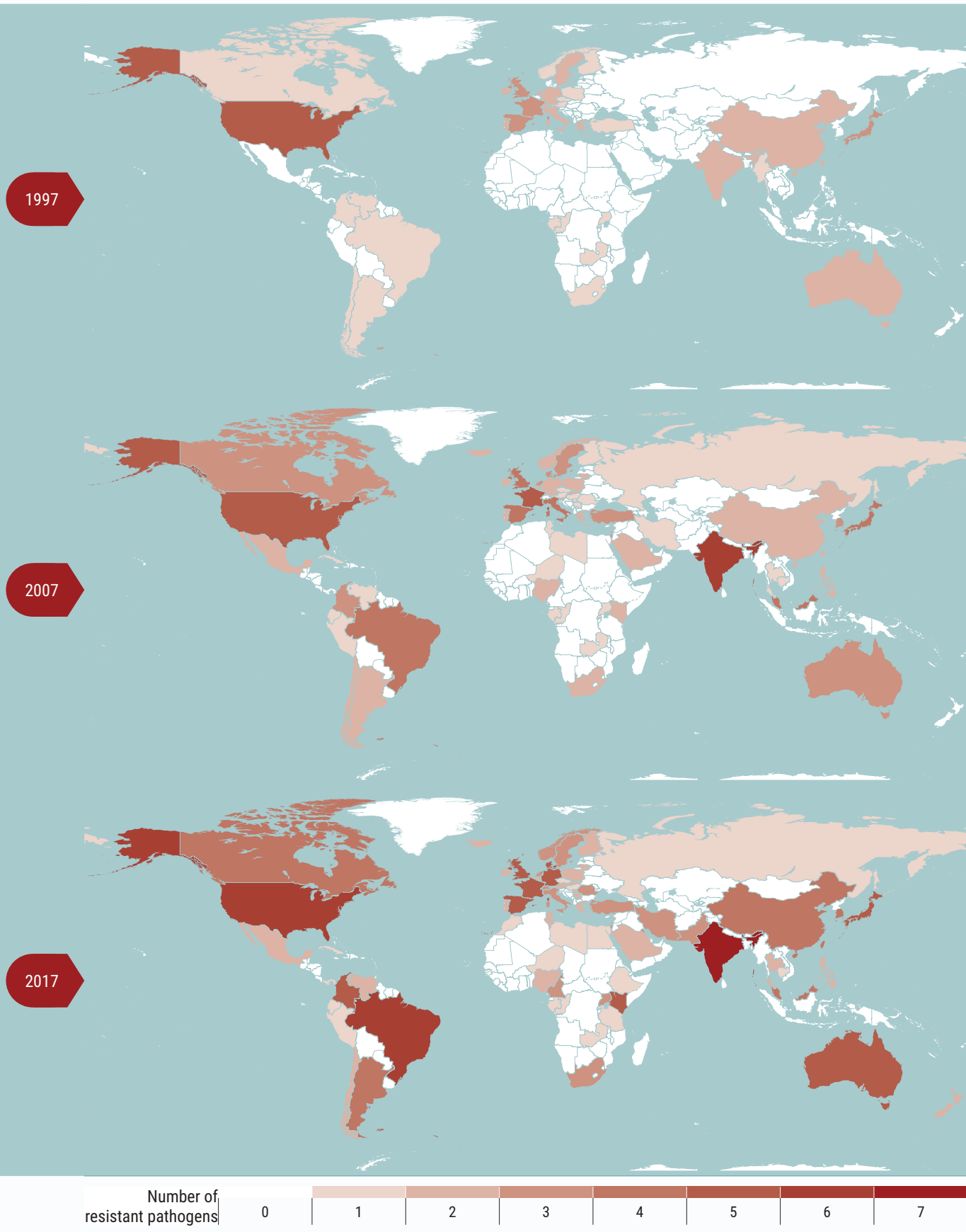
**The human maps depict records of resistance of the human pathogens *Aspergillus fumigatus*, *Candida albicans*, *Candida auris*, *Candida glabrata*, *Cryptococcus gatti* and *Cryptococcus neoformans* to azole medicines (red scale).** From Fisher *et al.* (2018).



The plant maps depict records of resistance of crop pathogens to azole fungicides (blue scale).



The human maps depict records of resistance of the human pathogens to azole medicines (red scale).



and tetracyclines, representatives of which are used in both agriculture and human medicine (Table 4.4-14). Some of them, such as oxolinic acid and gentamicin, are considered of critical importance to human medicine by WHO (2019) and their use in agriculture therefore urgently requires risk management measures.

Of further concern is the possibility of selection of antibiotic-resistant bacteria and genes through the processes of co-resistance, cross-resistance and co-regulation with certain metal ions. Copper resistance is widespread in plant pathogenic bacteria isolated from many continents, and evidence indicates that contamination of soil with copper ions also promotes AMR in soil bacteria (FAO and WHO 2019).

Less well publicized than the antibiotic resistance of bacteria is the rapid emergence of multi-drug resistant pathogenic fungi. Human fungal diseases are currently surging, and the global mortality numbers for fungal diseases have been reported to exceed those for malaria or breast cancer (Fisher *et al.* 2018). Recently there has been growing interest in the fungus *Aspergillus fumigatus*, airborne spores of which can enter the human respiratory system by inhalation and cause severe and possibly fatal invasive mould infections, especially in people who are immunocompromised. The main treatment for these infections currently is with antifungal medicines from the azole class. However, these medications are ineffective against resistant *Aspergillus* strains, leading to higher human mortality (Wellcome 2018).

The number of crop pathogens with reported resistance to azole fungicides has been increasing steadily during the last few decades. A similar expansion of resistance can be seen in human fungal diseases against azole based antifungal medicines (Figure 4.4-10). Infections with *Aspergillus fumigatus* that were resistant to all triazole antifungals were detected first in Europe and are now widespread across the world.

There is increasing evidence that use of azole fungicides in some specific agricultural sectors may be at least partly responsible for resistance selection in *Aspergillus fumigatus* and for

subsequent medical treatment failure. Of particular importance is the fact that many patients with resistant infections did not have previous exposure to medical triazole antifungals, suggesting they became infected with a strain already carrying the mutation. Such strains would have become resistant in the environment following exposure to agricultural or other non-medical azole fungicides (Berger *et al.* 2017; Fisher *et al.* 2018; Wellcome 2018).

Bacteria with increased tolerance to chemical disinfectants have been recovered from food production environments. There is theoretical and experimental evidence that certain microbiocidal agents may co-select for AMR, including antibiotic resistance. Examples include the use of chlorhexidine resulting in colistin resistance, or triclosan inducing isoniazid resistance. However, such evidence is based on laboratory studies and there is an absence of empirical data indicating that use of biocides drives this co-selection under the conditions present in the food production or processing environments (FAO and WHO 2019).

At present, insufficient evidence is available to link biocide use in food production to the development of AMR. However, the identified association between biocide tolerance and resistance and one or more classes of antimicrobials underscores the need for increased awareness and judicious use of these products (FAO and WHO 2019).

### Risk mitigation

The use of antimicrobial pesticides and disinfectants in agriculture and the food industry has either been identified as a driver of antimicrobial resistance, or serious concerns exist that this could be the case. Some countries have therefore taken measures to mitigate such risks and to ensure that antimicrobials can continue to be used effectively in human medicine.

Due to the risk of AMR to human antibiotics, use of antibiotics as bactericides in crop protection has been banned or restricted in certain parts of the world. For example, compounds such as streptomycin, oxytetracycline, gentamicin are no longer registered for use in agriculture in the EU. Some antibiotics are authorized for



use in crop protection in Mexico, New Zealand and the United States, but are fairly strictly regulated. Indeed, limiting the use of antibiotics in agriculture, particularly that of critically important antimicrobials and for prophylactic uses supporting unsustainable farming practices, has been proposed as a direct route for controlling agricultural antibiotic release into the environment, and likely also antibiotic resistance (Pruden *et al.* 2013; Wellington *et al.* 2013). However, in most countries the use of antimicrobials in agriculture is not regulated or monitored and their use may be more frequent than previously thought (Taylor and Reeder 2020).

Copper based fungicides and bactericides are widely used globally. They are often considered relatively low-risk pesticides which can even be used in organic agriculture. More recently copper compounds have come under increased scrutiny, mainly due to environmental persistence and toxicity to soil organisms and processes. Therefore, they have been listed in the EU as a candidate for substitution.

There are strategies for avoiding or limiting the use of medically important antimicrobials as pesticides, including modelling to predict high-risk periods for crop disease, practices that reduce the spread of crop pathogens, integrated pest management (IPM), and alternative treatments that reduce disease. However, these strategies are not always used globally and growers need support to use them, including access to these treatments and training (Wellcome 2018; FAO and WHO 2019).

#### 4.4.8 Knowledge gaps on human health effects of pesticides

Much knowledge has been amassed in the last few decades about the human health effects of pesticides. The European Academies of Science recently reviewed the methods and procedures used in the EU to assess potential harmful effects on human health of the use of plant protection products (SAPEA 2018). They indicated that although the system is precautionary, there is scope for further improvement in the scientific data that underpin pesticide risk assessments and the methods by which such data are analysed.

SAPEA suggested that improvements to the range and quality of data informing risk assessment could come from advances in: toxicology, where newly emerging methods should enable the collection of data more directly relevant to human toxicity; epidemiology, where the development of new biomarkers for pesticide exposure and new study designs could improve surveillance for unanticipated adverse effects of pesticides; and exposure sciences, where there is scope for refining information on the distribution and determinants of personal exposures to pesticides (SAPEA 2018).

Other bodies and scientists have also recently identified gaps in knowledge and priorities for research on the human health effects of pesticides, toxicological testing and risk assessment approaches (Milner and Boyd 2017; European Food Safety Authority Scientific Committee 2019; Liu *et al.* 2019; Robinson *et al.* 2020; United States Environmental Protection Agency [US EPA] 2020c; US EPA 2020d). The Government of Canada has prepared a fact sheet for the consideration of sex and gender in pesticide risk assessments (Government of Canada 2020a; Government of Canada 2020b)

On the basis of these reviews, and of this report, the following gaps in scientific knowledge can be identified which are important for future reduction in human health risks and impacts of pesticide use:

toxicological evaluations of more complex human health outcomes such as immunotoxicity, childhood leukemias, developmental neurotoxicity, chronic neurological diseases like Parkinson's disease, neuropsychological effects and mental illnesses, as well as endocrine disorders such as some hormonal cancers, endometriosis, metabolic syndrome, type-2 diabetes, and reproductive senescence;

- toxicological assessments of co-formulants and of formulated products;
- assessments of detailed mechanisms by which chemicals interact with the body, and the adverse outcome pathways (AOPs) through which they might cause harm;

- new toxicological methods that reduce use of animals in testing, including the application of in vitro toxicogenomics;
- the risk of combined effects from exposure to multiple active substances, either simultaneously or in sequence;
- further development and standardization of methods for cumulative dietary risk assessments;
- ascertain whether prevailing human health risk assessments are sufficiently protective for potentially sensitive populations such as immuno-depressed persons, female farmers and agricultural workers, pregnant and nursing women, and children.
- levels and determinants of exposure, especially of pesticide applicators using handheld or backpack sprayers, and of workers who enter crops that have been treated with pesticides;
- better characterization and quantification of exposure to pesticides in epidemiological studies;
- “real life” behaviours of pesticide operators in regard to the use of equipment and application techniques, and the extent to which such approaches can be used to manage or reduce exposures;
- standardized risk assessment procedures for nanopesticides and for biopesticides;
- the impact of the use of pesticides on the development of antimicrobial resistance;
- consideration of the rapidly growing body of epidemiological evidence, especially when reviewing approvals for products that are already on the market;
- post-marketing surveillance of approved pesticides to (e.g., through establishing or strengthening poison centres) verify that they do not cause unanticipated human health problems.

# References

- Abdou, M. (2015). An assessment of the impact of chemical insecticides used to control desert locust (*Schistocerca gregaria*) (Orthoptera, Acrididae) on Lacertid lizard *Acanthodactylus* spp (Sauria, *Lacertidae*) in Niger. *American Chemical Science Journal* 7(4), 193-200. <http://doi.org/10.9734/ACSj/2015/16556>.
- Adhikari, K. and Hartemink, A.E. (2016). Linking soils to ecosystem services – A global review. *Geoderma* 262, 101-111. <https://doi.org/10.1016/j.geoderma.2015.08.009>.
- Agencia Nacional de Vigilância Sanitária (ANVISA) (Brazil) (2019). Relatório das amostras analisadas no período de 2017 a 2018. Programa de Análise de Resíduos de Agrotóxicos em Alimentos (PARA). <http://portal.anvisa.gov.br/programa-de-analise-de-registro-de-agrotoxicos-para>. Accessed 26 December 2020.
- Agostini, M.G., Roesler, I., Bonetto, C., Ronco, A.E. and Bilenca, D. (2020). Pesticides in the real world: The consequences of GMO-based intensive agriculture on native amphibians. *Biological Conservation* 241, 108355. <https://doi.org/10.1016/j.biocon.2019.108355>.
- Ahrensberg, H., Madsen, L.B., Pearson, M., Weerasinghe, M., Eddleston, M., Jayamanne, S. et al. (2019). Estimating the government health-care costs of treating pesticide poisoned and pesticide self-poisoned patients in Sri Lanka. *Global Health Action* 12, 1692616. <https://doi.org/10.1080/16549716.2019.1692616>.
- Albuquerque, A.F., Ribeiro, J.S., Kummrow, F., Nogueira, A.J.A., Montagner, C.C. and Umbuzeiro, G.A. (2016). Pesticides in Brazilian freshwaters: A critical review. *Environmental Science: Processes and Impacts* 18(7), 779-787. <https://doi.org/10.1039/c6em00268d>.
- Ali, U., Syed, J.H., Malik, R.N., Katsoyiannis, A., Li, J., Zhang, G. and Jones, K.C. (2014). Organochlorine pesticides (OCPs) in South Asian region: A review. *Science of The Total Environment* 476-477, 705-717. <https://doi.org/10.1016/j.scitotenv.2013.12.107>.
- Alix, A., Bakker, F., Baret, K., Brühl, C.A., Coulson, M., Hoy, S. et al. (2012). *ESCORT 3: Linking Non-target Arthropod Testing and Risk Assessment with Protection Goals*. Pensacola, FL: Society for Environmental Toxicology and Chemistry (SETAC). [https://www.researchgate.net/publication/262853453\\_ESCORT\\_3\\_Linking\\_Non-Target\\_Arthropod\\_Testing\\_and\\_Risk\\_Assessment\\_with\\_Protection\\_Goals/link/0deec53c7f2ed12a18000000/download](https://www.researchgate.net/publication/262853453_ESCORT_3_Linking_Non-Target_Arthropod_Testing_and_Risk_Assessment_with_Protection_Goals/link/0deec53c7f2ed12a18000000/download).
- Alli, B.O. (2008). *Fundamental Principles of Occupational Health and Safety. Second Edition*. Geneva: International Labour Office. [https://www.ilo.org/global/publications/ilo-bookstore/order-online/books/WCMS\\_093550/lang-en/index.htm](https://www.ilo.org/global/publications/ilo-bookstore/order-online/books/WCMS_093550/lang-en/index.htm).
- Amaral, M.J., Carretero, M.A., Bicho, R.C., Soares, A.M.V.M. and Mann, R.M. (2012a). The use of a lacertid lizard as a model for reptile ecotoxicology studies: Part 1 – Field demographics and morphology. *Chemosphere* 87, 757-764. <https://doi.org/10.1016/j.chemosphere.2011.12.075>.
- Amaral, M.J., Bicho, R.C., Carretero, M.A., Sanchez-Hernandez, J.C., Faustino, A.M.R., Soares, A.M.V.M. and Mann, R.M. (2012b). The use of a lacertid lizard as a model for reptile ecotoxicology studies: Part 2 – Biomarkers of exposure and toxicity among pesticide exposed lizards. *Chemosphere* 87, 765-774. <https://doi.org/10.1016/j.chemosphere.2012.01.048>.
- Ambrus, A. and Yang, Y.Z. (2016). Global Harmonization of Maximum Residue Limits for Pesticides. *Journal of Agricultural and Food Chemistry* 64(1), 30-35. <https://doi.org/10.1021/jf505347z>.
- American Academy of Pediatrics (2012). Policy statement: pesticide exposure in children. *Pediatrics* 130(6), e1757. <https://pediatrics.aappublications.org/content/pediatrics/130/6/e1757.full.pdf>.
- Ansara-Ross, T.M., Wepener, V., van den Brink, P.J. and Ross, M.J. (2012). Pesticides in South African fresh waters. *African Journal of Aquatic Science* 37(1), 1-16. <https://doi.org/10.2989/16085914.2012.666336>.
- Araújo, C.V.M., Shinn, C., Moreira-Santos, M., Lopes, I., Espíndola, E.L.G. and Ribeiro, R. (2014). Copper-driven avoidance and mortality in temperate and tropical tadpoles. *Aquatic Toxicology* 146, 70-75. <https://doi.org/10.1016/j.aquatox.2013.10.030>.
- Arts, G.H., Buijse-Bogdan, L.L., Belgers, J.D.M., van Rhenen-Kersten, C.H., van Wijngaarden, R.P.A., Roessink, I. et al. (2006). Ecological impact in ditch mesocosms of simulated spray drift from a crop protection program for potatoes. *Integrated Environmental Assessment and Management* 2, 105-125. [https://www.researchgate.net/deref/http%3A%2F%2Fdx.doi.org%2F10.1897%2F1551-3793\(2006\)2%5B105%3AEIIDMO%5D2.0.CO%3B2](https://www.researchgate.net/deref/http%3A%2F%2Fdx.doi.org%2F10.1897%2F1551-3793(2006)2%5B105%3AEIIDMO%5D2.0.CO%3B2).
- Arts, G.H.P., Beltman, W.H.J., Holterman, H.J., van Vliet, P.J.M., Wipfler, E.L. and van de Zande, J.C. (2017). *Including Multistress in the Risk Assessment of Plant Protection Products: Current State of Knowledge, Based on a Literature Review and an Evaluation of Tank Mixture Applications in a Spraying Schedule for Strawberries*. Wageningen, The Netherlands: Wageningen Environmental Research. <https://doi.org/10.18174/408758>.
- Australian Pesticides and Veterinary Medicines Authority (2019). *Risk Assessment Manual – Environment*. [https://apvma.gov.au/sites/default/files/publication/46416-risk\\_assessment\\_manual\\_environment\\_0.pdf](https://apvma.gov.au/sites/default/files/publication/46416-risk_assessment_manual_environment_0.pdf).
- Australian Pesticides and Veterinary Medicines Authority (2020). Listing of chemical reviews. <https://apvma.gov.au/chemicals-and-products/chemical-review/listing>. Accessed 1 December 2020.

- Aziz, M.A., Tollington, S., Barlow, A., Goodrich, J., Shamsuddoha, M., Islam, M.A. and Groombridge, J.J. (2017). Investigating patterns of tiger and prey poaching in the bangladesh sundarbans: implications for improved management. *Global Ecology and Conservation* 9, 70-81. <https://doi.org/10.1016/j.gecco.2016.12.001>.
- Babut, M., Arts, G.H., Barra Caracciolo, A., Carluer, N., Domange, N., Friberg, N. *et al.* (2013). Pesticide risk assessment and management in a globally changing world – report from a European interdisciplinary workshop. *Environmental Science and Pollution Research* 20(11), 8298-8312. <https://doi.org/10.1007/s11356-013-2004-3>.
- Bai, Z., Caspari, T., Gonzalez, M.R., Batjes, N.H., Mäder, P., Bünemann, E.K. *et al.* (2018). Effects of agricultural management practices on soil quality: A review of long-term experiments for Europe and China. *Agriculture, Ecosystems and Environment* 265, 1-7. <https://doi.org/10.1016/j.agee.2018.05.028>.
- Bain, D., Buttemer, W.A., Astheimer, L., Fildes, K. and Hooper, M.J. (2004). Effects of sublethal fenitrothion ingestion on cholinesterase inhibition, standard metabolism, thermal preference and prey-capture ability in the Australian central bearded dragon (*Pogona vitticeps*, Agamidae). *Environmental Toxicology and Chemistry* 23(1), 109-116. <https://setac.onlinelibrary.wiley.com/doi/abs/10.1897/02-555>.
- Baker, N.J., Bancroft, B.A. and Garcia, T.S. (2013). A meta-analysis of the effects of pesticides and fertilizers on survival and growth of amphibians. *Science of The Total Environment* 449, 150-156. <http://dx.doi.org/10.1016/j.scitotenv.2013.01.056>.
- Baldi, I., Gruber, A., Rondeau, V., Lebailly, P., Brochard, P. and Fabrigoule, C. (2011). Neurobehavioral effects of long-term exposure to pesticides: results from the 4-year follow-up of the PHYTONER Study. *Occupational and Environmental Medicine* 68, 108e115. <https://doi.org/10.1136/oem.2009.047811>.
- Battaglin, W.A., Smalling, K.L., Anderson, C., Calhoun, D., Chestnut, T. and Muths, E. (2016). Potential interactions among disease, pesticides, water quality and adjacent land cover in amphibian habitats in the United States. *Science of The Total Environment* 566-567, 320-332. <http://dx.doi.org/10.1016/j.scitotenv.2016.05.062>.
- Begon, M., Harper, J.L. and Townsend, C.R. (1996). *Ecology – Individuals, Populations and Communities*. Third edition. Malden, MA and Oxford, UK: Blackwell Publishing.
- Beketov, M.A., Kefford, B.J., Schäfer, R.B. and Liess, M. (2013). Pesticides reduce regional biodiversity of stream invertebrates. *Proceedings of the National Academy of Sciences of the United States of America* 110(27), 11039-11043. <https://doi.org/10.1073/pnas.1305618110>.
- Berger, S., El Chazli, Y., Babu, A.F. and Coste, A.T. (2017). Azole resistance in *Aspergillus fumigatus*: A consequence of antifungal use in agriculture? *Frontiers in Microbiology* 8, 1024. <https://doi.org/10.3389/fmicb.2017.01024>.
- Bergman, Å, Heindel, J.J., Kasten, T., Kidd, K.A., Jobling, S., Neira, M. *et al.* (2013). The impact of endocrine disruption: A consensus statement on the state of the science. *Environmental Health Perspectives* 121(4), A104-A106. <https://doi.org/10.1289/ehp.1205448>.
- Bicho, R.C., Amaral, M.J., Faustino, A.M.R., Power, D.M., Rêma, A., Carretero, M.A., Soares, A.M.V.M. and Mann, R.M. (2013). Thyroid disruption in the lizard *Podarcis bocagei* exposed to a mixture of herbicides: A field study. *Ecotoxicology* 22, 156-165. <https://doi.org/10.1007/s10646-012-1012-2>.
- Bienentreu, J.-F. and Lesbarrères, D. (2020). Amphibian disease ecology: Are we just scratching the surface? *Herpetologica* 76(2), 153-166. <https://doi.org/10.1655/0018-0831-76.2.153>.
- Bishop, P.J., Angulo, A., Lewis, J.P., Moore, R.D., Rabb, G.B. and Garcia Moreno, J. (2012). The Amphibian Extinction Crisis – what will it take to put the action into the Amphibian Conservation Action Plan? *S.A.P.I.EN.S* 5(2). <http://journals.openedition.org/sapiens/1406>.
- Blair, A., Ritz, B., Wesseling, C. and Freeman, L.B. (2015). Pesticides and human health. Editorial. *Occupational and Environmental Medicine* 72, 81-82. <https://doi.org/10.1136/oemed-2014-102454>.
- Boedeker, W., Watts, M., Clausing, P. and Marquez, E. (2020). The global distribution of acute unintentional pesticide poisoning: Results of a systematic review. *BMC Public Health* 20, 1875 (2020). <https://doi.org/10.1186/s12889-020-09939-0>.
- Boivin, A. and Poulsen, V. (2017). Environmental risk assessment of pesticides: State of the art and prospective improvement from science. *Environmental Science and Pollution Research* 24(8), 6889-6894. <https://doi.org/10.1007/s11356-016-8289-2>.
- Bonita, R., Beaglehole, R., Kjellström, T. and World Health Organization (2006). *Basic Epidemiology*. Second edition. Geneva: World Health Organization. <https://apps.who.int/iris/handle/10665/43541>.
- Bonvoisin T., Utyasheva, L., Knipe, D., Gunnell, D. and Eddleston, M. (2020). Suicide by pesticide poisoning in India: A review of pesticide regulations and their impact on suicide trends. *BMC Public Health* 20, 251. <https://doi.org/10.1186/s12889-020-8339-z>.
- Boobis, A.R., Ossendorp, B.C., Banasiak, U., Hamey, P.Y., Sebestyen, I. and Moretto, A. (2018). Cumulative risk assessment of pesticide residues in food. *Toxicology Letters* 180, 137-150. <https://doi.org/10.1016/j.toxlet.2008.06.004>.
- Bouktif Zarrouk, M., Gharbi, E., Maatouk, I., Leblanc J.-C. and Landoulsi, A. (2020). Dietary exposure of Tunisian adult population aged from 19 to 65 years old to pesticides residues. *Food Additives and Contaminants: Part A* 37(7), 1165-1179. <https://doi.org/10.1080/19440049.2020.1744065>.
- Bouvier, J.-C., Ricci, B., Agerberg, J. and Lavigne, C. (2011). Apple orchard pest control strategies affect bird communities in southeastern France. *Environmental Toxicology and Chemistry* 30(1), 212-219. <https://pubmed.ncbi.nlm.nih.gov/20928901/>.
- Boyd, I.L. (2018). An inside view on pesticide policy. *Nature Ecology and Evolution* 2(6), 920-921. <https://doi.org/10.1038/s41559-018-0557-8>.

- Boye, K., Lindström, B., Boström, G. and Kreuger, J. (2019). Long-term data from the Swedish National Environmental Monitoring Program of Pesticides in Surface Waters. *Journal of Environmental Quality* 48(4), 1109. <https://doi.org/10.2134/jeq2019.02.0056>.
- Boyle, N.K., Pitts-Singer, T.L., Abbott, J., Alix, A., Cox-Foster, D.L., Hinarejos, S. et al. (2019). Workshop on pesticide exposure assessment paradigm for non-*Apis* bees: Foundation and summaries. *Environmental Entomology* 48(1), 4-11. <https://doi.org/10.1093/ee/nvy103>.
- Bradford Hill, A. (1965). The environment and disease: Association or causation? *Proceedings of the Royal Society of Medicine* 58, 295-300. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1898525/>.
- Brain, R.A. and Anderson, J.C. (2019). The agro-enabled urban revolution, pesticides, politics, and popular culture: a case study of land use, birds, and insecticides in the USA. *Environmental Science and Pollution Research* 26, 21717-21735. <https://doi.org/10.1007/s11356-019-05305-9>.
- Brander, S.M., Gabler, M.K., Fowler, N.L., Connon, R.E. and Schlenk, D. (2016). Pyrethroid pesticides as endocrine disruptors: Molecular mechanisms in vertebrates with a focus on fishes. *Environmental Science and Technology* 50, 8977-8992. <https://doi.org/10.1021/acs.est.6b02253>.
- Brevik, K., Schoville, S.D., Mota-Sanchez, D. and Chena, Y.H. (2018). Pesticide durability and the evolution of resistance: A novel application of survival analysis. *Pest Management Science* 74, 1953-1963. <https://doi.org/10.1002/ps.4899>.
- Brittain, C.A., Vighi, M., Bommarco, R., Settele, J. and Potts, S.G. (2010). Impacts of a pesticide on pollinator species richness at different spatial scales. *Basic and Applied Ecology* 11(2), 106-115. <https://doi.org/10.1016/j.baae.2009.11.007>.
- Brock, T.C.M., Alix, A., Brown, C.D., Capri, E., Gottesbüren, B.F.F., Heimbach, F. et al. (eds.) (2010). *Linking Aquatic Exposure and Effects – Risk Assessment of Pesticides*. London and New York: CRC Press. <https://www.routledge.com/Linking-Aquatic-Exposure-and-Effects-Risk-Assessment-of-Pesticides/Brock/p/book/9781138112643>.
- Brodie, J. and Landos, M. (2019). Pesticides in Queensland and Great Barrier Reef waterways – potential impacts on aquatic ecosystems and the failure of national management. *Estuarine, Coastal and Shelf Science* 230, 106447. <https://doi.org/10.1016/j.ecss.2019.106447>.
- Bruce-Vanderpujje, P., Megson, D., Reiner, E.J., Bradley, L., Adu-Kumi, S. and Gardella, J.A. (2019). The state of POPs in Ghana – A review on persistent organic pollutants: Environmental and human exposure. *Environmental Pollution* 245, 331-342. <https://doi.org/10.1016/j.envpol.2018.10.107>.
- Brühl, C.A., Schmidt, T., Pieper, S. and Alscher, A. (2013). Terrestrial pesticide exposure of amphibians: An underestimated cause of global decline? *Scientific Reports* 3, 1135. <https://doi.org/10.1038/srep01135>.
- Brühl, C.A. and Zaller, J. G. (2019). Biodiversity decline as a consequence of an Inappropriate Environmental Risk Assessment of pesticides. *Frontiers in Environmental Science* 7, 2013-2016. <https://doi.org/10.3389/fenvs.2019.00177>.
- Buckle, A. and Prescott, C. (2018). Anticoagulants and risk mitigation. In *Anticoagulant Rodenticides and Wildlife. Emerging Topics in Ecotoxicology (Principles, Approaches and Perspectives) vol 5*. van den Brink, N.W., Elliott, J.E., Shore, R.F. and Rattner, B.A. (eds.). Cham: Springer. 319-355. [https://doi.org/10.1007/978-3-319-64377-9\\_12](https://doi.org/10.1007/978-3-319-64377-9_12).
- Calvert, A.M., Bishop, C.A., Elliot, R.D., Krebs, E.A., Kydd, T.M., Machtans, C.S. and Robertson, G.J. (2013). A synthesis of human-related avian mortality in Canada. *Avian Conservation and Ecology* 8(2), 11. <http://dx.doi.org/10.5751/ACE-00581-080211>.
- Calvert, G.M., Beckman, J., Bonnar Prado, J., Bojes, H., Schwartz, A., Mulay, P. et al. (2016). Acute occupational pesticide-related illness and injury – United States, 2007-2011. United States Centers for Disease Control and Prevention. *Morbidity and Mortality Weekly Report* 63 (55), 11-15. <https://www.cdc.gov/mmwr/volumes/63/wr/mm6355a3.htm>.
- Calvert, G.M., Karnik, J., Mehler, L., Beckman, J., Morrissey, B., Sievert, J. et al. (2008). Acute pesticide poisoning among agricultural workers in the United States, 1998-2005. *American Journal of Industrial Medicine* 51, 883-898. <https://doi.org/10.1002/ajim.20623>.
- Camenzuli, L., Scheringer, M. and Hungerbühler, K. (2016). Local organochlorine pesticide concentrations in soil put into a global perspective. *Environmental Pollution* 217, 11-18. <https://doi.org/10.1016/j.envpol.2015.08.028>.
- Campbell, L.J., Pawlik, A.H. and Harrison, X.A. (2020). Amphibian ranaviruses in Europe: Important directions for future research. *FACETS* 5, 598-614. <https://doi.org/10.1139/facets-2020-0007>.
- Canadian Food Inspection Agency (2019). *Pesticides and Metals in Selected Foods – April 1, 2018 to March 31, 2019. Food chemistry – Targeted surveys – Final Report*. [https://www.inspection.gc.ca/DAM/DAM-food-aliments/STAGING/text-texte/pesticides\\_Metals\\_in\\_Selected\\_Foods\\_2018-2019\\_1596227305870\\_eng.pdf](https://www.inspection.gc.ca/DAM/DAM-food-aliments/STAGING/text-texte/pesticides_Metals_in_Selected_Foods_2018-2019_1596227305870_eng.pdf).
- Canadian Food Inspection Agency (n.d.). *National Chemical Residue Monitoring Program and Chemistry Food Safety Oversight Program Annual Report 2015-2016*. <https://www.inspection.gc.ca/food/chemical-residues-microbiology/food-safety-testing-bulletins/2019-04-17/annual-report-2015-2016/eng/1554904884535/1554905013036>.
- Cardoso, P., Barton, P. S., Birkhofer, K., Chichorro, F., Deacon, C., Fartmann et al. (2020). Scientists' warning to humanity on insect extinctions. *Biological Conservation* 242, 108426. <https://doi.org/10.1016/j.biocon.2020.108426>.
- Castaño-Sánchez, A., Hose, G.C. and Reboleira, A.S.P.S. (2020). Ecotoxicological effects of anthropogenic stressors in subterranean organisms: A review. *Chemosphere* 244, 125422. <https://doi.org/10.1016/j.chemosphere.2019.125422>.

- Cattan, P., Charlier, J.B., Clostre, F., Letourmy, P., Arnaud, L., Gresser, J. and Jannoyer, M. (2019). A conceptual model of organochlorine fate from a combined analysis of spatial and mid- to long-term trends of surface and ground water contamination in tropical areas (FWI). *Hydrology and Earth System Sciences* 23(2), 691-709. <https://doi.org/10.5194/hess-23-691-2019>.
- Cavallaro, M.C., Main, A.R., Liber, K., Phillips, I.D., Headley, J.V., Peru, K.M. and Morrissey, C.A. (2019). Neonicotinoids and other agricultural stressors collectively modify aquatic insect communities. *Chemosphere* 226, 945-955. <https://doi.org/10.1016/j.chemosphere.2019.03.176>.
- Cedergreen, N. (2014). Quantifying synergy: A systematic review of mixture toxicity studies within environmental toxicology. *PLoS One* 9(5): e9658. <https://doi.org/10.1371/journal.pone.0096580>.
- Cha, E.S., Chang, S.S., Gunnell, D., Eddleston, M., Khang, Y.H. and Lee, W.J. (2016). Impact of paraquat regulation on suicide in South Korea. *International Journal of Epidemiology* 45(2), 470-479. <https://doi.org/10.1093/ije/dyv304>.
- Chang, C.-H., MacIntosh, D., Lemos, B., Zhang, Q. and Lu, C. (2018). Characterization of daily dietary intake and the health risk of neonicotinoid insecticides for the US population. *Journal of Agricultural and Food Chemistry* 66(38), 10097-10105. <https://doi.org/10.1021/acs.jafc.8b02982>.
- Chen, Y., Zang, L., Liu, M., Zhang, C., Shen, G., Du, W. et al. (2019). Ecological risk assessment of the increasing use of the neonicotinoid insecticides along the east coast of China. *Environment International* 127, 550-557. <https://doi.org/10.1016/j.envint.2019.04.010>.
- Chiron, F., Chargé, R., Julliard, R., Jiguet, F. and Muratet, A. (2014). Pesticide doses, landscape structure and their relative effects on farmland birds. *Agriculture, Ecosystems and Environment* 185, 153-160. <http://dx.doi.org/10.1016/j.agee.2013.12.013>.
- Chowdhury, F.R., Dewan, G., Verma, V.R., Knipe, D.W., Isha, I.T., Faiz, M.A. et al. (2018). Bans of WHO Class I pesticides in Bangladesh – suicide prevention without hampering agricultural output. *International Journal of Epidemiology* 47(1), 175-184. <https://doi.org/10.1093/ije/dyx157>.
- Close, M.E. and Skinner, A. (2012). Sixth national survey of pesticides in groundwater in New Zealand. *New Zealand Journal of Marine and Freshwater Research* 46(4), 443-457. <https://doi.org/10.1080/00288330.2012.707131>.
- Cloyd, R.A. (2012). Indirect effects of pesticides on natural enemies. In *Pesticides – Advances in Chemical and Botanical Pesticides*. Soundararajan, R.P. (ed.). IntechOpen. Chapter 6. <https://doi.org/10.5772/48649>.
- Coates, P.S., Brussee, B.E., Howe, K.B., Fleskes, J.P., Dwight, I.A., Connelly, D.P. et al. (2017). Long-term and widespread changes in agricultural practices influence ring-necked pheasant abundance in California. *Ecology and Evolution* 7, 2546-2559. <https://pubmed.ncbi.nlm.nih.gov/28428846/>.
- Cochrane Library (2020). About Cochrane Reviews. <https://www.cochranelibrary.com/about/about-cochrane-reviews>. Accessed 20 December 2020.
- Convention on Biological Diversity (1992). Text of the Convention. <https://www.cbd.int/convention/text/>. Accessed 20 December 2020.
- Convention on Biological Diversity (2019). Identification, monitoring, indicators and assessments. <https://www.cbd.int/indicators/>. Accessed 20 December 2020.
- Copplestone, J.F. (1977). A global view of pesticide safety. In *Pesticide Management and Insecticide Resistance*. Watson, D.L. and Brown, A.W.A. (eds.). New York: Academic Press. 147-155. <https://doi.org/10.1016/B978-0-12-738650-8.50014-X>.
- Corriols, M., Marín, J., Berroteran, J., Marina Lozano, L., Lundberg, I. and Thörn, Å. (2008). The Nicaraguan pesticide poisoning register: Constant underreporting. *International Journal of Health Services* 38(4), 773-787. <https://doi.org/10.2190/HS.38.4.k>.
- Coscollà, C. and Yusa, V. (2016). Pesticides and agricultural air quality. In *The Quality of Air. Comprehensive Analytical Chemistry vol 73*. de la Guardia, M. and Armenta, S. (eds.). Elsevier. Chapter 17. <https://www.elsevier.com/books/the-quality-of-air/de-la-guardia/978-0-444-63605-8>.
- Crépet, A., Luong, T.M., Baines, J., Boon, P.E., Ennis, J., Kennedy, M. et al. (2021). An international probabilistic risk assessment of acute dietary exposure to pesticide residues in relation to codex maximum residue limits for pesticides in food. *Food Control* 121, 107563. <https://doi.org/10.1016/j.foodcont.2020.107563>.
- Croft, B.A. (1990). Natural enemies and pesticides: An overview. In *Arthropod Biological Control Agents and Pesticides*. Croft, B.A. (ed.). New York: Wiley and Sons. Chapter 1.
- Croft, B.A. and Theiling, K.M. (1990). Pesticide effects on arthropod natural enemies: A database. In *Arthropod Biological Control Agents and Pesticides*. Croft, B.A. (ed.). New York: Wiley and Sons.
- CropLife International (2020). Resistance management. <https://croplife.org/crop-protection/stewardship/resistance-mangement>. Accessed 20 December 2020.
- Cutler, G.C., Scott-Dupree, C.D. and Drexler, D.M. (2014). Honey bees, neonicotinoids and bee incident reports: The Canadian situation. *Pest Management Science* 70(5), 779-783. <https://pubmed.ncbi.nlm.nih.gov/23873722/>.
- D'Costa, V.M., King, C.E., Kalan, L., Morar, M., Sung, W.W.L., Schwarz, C. et al. (2011). Antibiotic resistance is ancient. *Nature* 477, 457-461. <https://doi.org/10.1038/nature10388>.
- Daam, M.A., Chelinho, S., Niemeyer, J.C., Owojori, O J., De Silva, P.M.C.S., Sousa, J.P. et al. (2019). Environmental risk assessment of pesticides in tropical terrestrial ecosystems: Test procedures, current status and future perspectives. *Ecotoxicology and Environmental Safety* 181, 534-547. <https://doi.org/10.1016/j.ecoenv.2019.06.038>.

- Daam, M.A., Leitão, S., Cerejeira, M.J. and Paulo Sousa, J. (2011). Comparing the sensitivity of soil invertebrates to pesticides with that of *Eisenia fetida*. *Chemosphere* 85(6), 1040-1047. <https://doi.org/10.1016/j.chemosphere.2011.07.032>.
- Dahshan, H., Megahed, A.M., Abd-Elall, A.M.M., Abd-El-Kader, M.A.G., Nabawy, E. and Elbana, M.H. (2016). Monitoring of pesticides water pollution – The Egyptian River Nile. *Journal of Environmental Health Science and Engineering* 14(1), 1-9. <https://doi.org/10.1186/s40201-016-0259-6>.
- Dainese, M., Martin, E.A., Aizen, M.A., Albrecht, M., Bartomeus, I., Bommarco, R. *et al.* (2019). A global synthesis reveals biodiversity-mediated benefits for crop production. *Science Advances* 5(10), eaax0121. <https://doi.org/10.1126/sciadv.aax0121>.
- Dansereau, C., Perez, M., Kegley, S.E., Tupper, K.A. and Wang, A. (2006). *Poisons on the Wind – Community Air Monitoring for Chlorpyrifos in the Yakima Valley*. Seattle and San Francisco: Farm Worker Pesticide Project and Pesticide Action Network North America. <http://www.panna.org/sites/default/files/POW12-20-06YakimaSUM.pdf>.
- Dawson, A.H., Eddleston, M., Senarathna, L., Mohamed, F., Gawarammana, I., Bowe, S.J. *et al.* (2010). Acute human lethal toxicity of agricultural pesticides: A prospective cohort study. *PLoS Medicine* 7(10), e1000357. <https://doi.org/10.1371/journal.pmed.1000357>.
- de Graaff, M.A., Hornslein, N., Throop, H.L., Kardol, P. and van Diepen, L.T.A. (2019). Effects of agricultural intensification on soil biodiversity and implications for ecosystem functioning: A meta-analysis. In *Advances in Agronomy vol. 155*. Academic Press. Chapter 1, 1-44. <https://doi.org/10.1016/bs.agron.2019.01.001>.
- de Souza, R.M., Seibert, D., Quesada, H.B., de Jesus Bassetti, F., Fagundes-Klen, M.R and Bergamasco, R. (2020). Occurrence, impacts and general aspects of pesticides in surface water: A review. *Process Safety and Environmental Protection* 135, 22-37. <https://doi.org/10.1016/j.psep.2019.12.035>.
- de Weert, J., Roex, E., Klein, J. and Janssen, G. (2014). *Establishment of the National Monitoring Network Plant Protection Products in Agriculture and Horticulture*. Delft: Deltares. [http://publications.deltares.nl/1207762\\_008.pdf](http://publications.deltares.nl/1207762_008.pdf). (in Dutch).
- Department of Agriculture, Australia (2019). *National Residue Survey 2018-19 – Annual Summary*. <http://www.agriculture.gov.au/ag-farm-food/food/nrs>.
- Derbalah, A., Chidya, R., Jadoon, W. and Sakugawa, H. (2019). Temporal trends in organophosphorus pesticides use and concentrations in river water in Japan, and risk assessment. *Journal of Environmental Sciences* 79, 135-152. <https://doi.org/10.1016/j.jes.2018.11.019>.
- Dereumeaux, C., Fillol, C., Quenel, P. and Denys, S. (2020). Pesticide exposures for residents living close to agricultural lands: A review. *Environment International* 134, 105210. <https://doi.org/10.1016/j.envint.2019.105210>.
- Deziel, N.C., Beane Freeman, L.E., Graubard, B.I., Jones, R.R., Hoppin, J.A., Thomas, K. *et al.* (2017). Relative contributions of agricultural drift, para-occupational, and residential use exposure pathways to house dust pesticide concentrations: meta-regression of published data. *Environmental Health Perspectives* 125(3), 206-305. <http://dx.doi.org/10.1289/EHP426>.
- Deziel, N.C., Friesen, M.C., Hoppin, J.A., Hines, C.J., Thomas, K. and Beane Freeman, L.E. (2015). A review of nonoccupational pathways for pesticide exposure in women living in agricultural areas. *Environmental Health Perspectives* 123(6), 515-524. <http://dx.doi.org/10.1289/ehp.1408273>.
- Dhiman, R.C. and Yadav, R.S. (2016). Insecticide resistance in phlebotomine sandflies in Southeast Asia with emphasis on the Indian subcontinent. *Infectious Diseases of Poverty* 5, 106 <https://doi.org/10.1186/s40249-016-0200-3>.
- Di Lorenzo, T., Cifoni, M., Fiasca, B., Di Cioccio, A., and Galassi, D.M.P. (2018). Ecological risk assessment of pesticide mixtures in the alluvial aquifers of central Italy: Toward more realistic scenarios for risk mitigation. *Science of The Total Environment* 644, 161-172. <https://doi.org/10.1016/j.scitotenv.2018.06.345>.
- Dirbaba, N.B., Li, S., Wu, H., Yan, X. and Wang, J. (2018). Organochlorine pesticides, polybrominated diphenyl ethers and polychlorinated biphenyls in surficial sediments of the Awash River Basin, Ethiopia. *PLoS ONE* 13(10). <https://doi.org/10.1371/journal.pone.0205026>.
- Dutcher, J.D. (2007). A review of resurgence and replacement causing pest outbreaks in IPM. In *General Concepts in Integrated Pest and Disease Management*. Ciancio, A. and Mukerji, K.G. (eds.). Dordrecht, The Netherlands: Springer. 27-43. <https://www.springer.com/gp/book/9781402060601>.
- Eardley, C., Freitas, B.M., Kevan, P.G., Rader, R., Gikungu, M., Klein, A.M. *et al.* (2016). Background to pollinators, pollination and food production. In *The Assessment Report of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services on Pollinators, Pollination and Food Production*. Potts, S.G., Imperatriz-Fonseca, V.L. and Ngo, H.T. (eds.). Bonn: Secretariat of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services. Chapter 1, 1-25. <https://ipbes.net/assessment-reports/pollinators>.
- Eddleston, M. (2018). Response to Jors *et al.*, *Environmental Health Insights*. *Environmental Health Insights* 12, 1178630218788554. <https://doi.org/10.1177/1178630218788554>.
- Eddleston, M. and Phillips, M.R. (2004). Self poisoning with pesticides. *BMJ* 328, 42-44. <https://doi.org/10.1136/bmj.328.7430.42>.
- Egea-Serrano, A., Relyea, R.A., Tejedo, M. and Torralva, M. (2012). Understanding of the impact of chemicals on amphibians: A meta-analytic review. *Ecology and Evolution* 2(7), 1382-1397. <https://onlinelibrary.wiley.com/doi/full/10.1002/ece3.249>.
- Elibariki, R. and Maguta, M.M. (2017). Status of pesticides pollution in Tanzania – A review. *Chemosphere* 178, 154-164. <https://doi.org/10.1016/j.chemosphere.2017.03.036>.

- Emmerson, M., Morales, M.B., Oñate, J.J., Batáry, P., Berendse, F., Liira, J. *et al.* (2016). Chapter Two – How agricultural intensification affects biodiversity and ecosystem services. *Advances in Ecological Research* 55, 43-97. <http://dx.doi.org/10.1016/bs.aecr.2016.08.005>.
- Encarnação, T., Pais, A.A.C.C., Campos, M.G. and Burrows, H.D. (2019). Endocrine disrupting chemicals: Impact on human health, wildlife and the environment. *Science Progress* 102(1), 3-42. <https://doi.org/10.1177/0036850419826802>.
- Eng, M.L., Stutchbury, B.J.M. and Morrissey, C.A. (2019). A neonicotinoid insecticide reduces fueling and delays migration in songbirds. *Science* 365 (6458), 1177-1180. <https://doi.org/10.1126/science.aaw9419>.
- Eqani, S.A., Malik, R.N., Alamdar, A. and Faheem, H. (2012). Status of organochlorine contaminants in the different environmental compartments of Pakistan: A review on occurrence and levels. *Bulletin of Environmental Contamination and Toxicology* 88(3), 303–310. <https://doi.org/10.1007/s00128-011-0496-4>.
- Ertl, H.M.H., Mora, M.A., Brightsmith, D.J. and Navarro-Alberto, J.A. (2018). Potential impact of neonicotinoid use on Northern bobwhite (*Colinus virginianus*) in Texas: A historical analysis. *PLoS ONE* 13(1), e0191100. <https://doi.org/10.1371/journal.pone.0191100>.
- Estep, A.S., Sanscrainte, N.D., Waits, C.M., Bernard, S.J., Lloyd, A.M., Lucas K.J. *et al.* (2018). Quantification of permethrin resistance and *kdr* alleles in Florida strains of *Aedes aegypti* (L.) and *Aedes albopictus* (Skuse). *PLoS Neglected Tropical Diseases* 12 (10), e0006544. <https://doi.org/10.1371/journal.pntd.0006544>.
- European Agency for Safety and Health at Work (2018). Directive 89/391/EEC - OSH "Framework Directive" of 12 June 1989 on the introduction of measures to encourage improvements in the safety and health of workers at work. <https://osha.europa.eu/en/legislation/directives/the-osh-framework-directive/1>. Accessed 28 December 2020.
- European Chemical Agency and European Food Safety Authority (2018). Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009. *EFSA Journal* 16(6), 5311. <https://www.efsa.europa.eu/en/efsajournal/pub/5311>.
- European Commission (2018). *Technical Guidance for Deriving Environmental Quality Standards*. Guidance Document No. 27, Updated version 2018. <https://circabc.europa.eu/sd/a/ba6810cd-e611-4f72-9902-f0d8867a2a6b/Guidance%20No%2027%20-%20Deriving%20Environmental%20Quality%20Standards%20-%20version%202018.pdf>.
- European Environment Agency (2012). *The Impacts of Endocrine Disruptors on Wildlife, People and their Environments: The Weybridge+15 (1996- 2011) Report*. <https://www.eea.europa.eu/publications/the-impacts-of-endocrine-disruptors>.
- European Environment Agency (2019). Waterbase – water quality IBM. <https://www.eea.europa.eu/data-and-maps/data/waterbase-water-quality-icm>. Accessed 20 December 2020.
- European Food Safety Authority (2009). Guidance document on risk assessment for birds and mammals. *EFSA Journal* 7(12), 1438. <https://doi.org/10.2903/j.efsa.2009.1438>.
- European Food Safety Authority (2013a). Guidance on the risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees). *EFSA Journal* 11(7), 3295. <https://doi.org/10.2903/j.efsa.2013.3295>.
- European Food Safety Authority (2013b). Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. *EFSA Journal* 11(7), 3290. <https://doi.org/10.2903/j.efsa.2013.3290>.
- European Food Safety Authority (2014). Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. *EFSA Journal* 12(10), 3874. <https://doi.org/10.2903/j.efsa.2014.3874>.
- European Food Safety Authority (2015). Scientific Opinion on the effect assessment for pesticides on sediment organisms in edge-of-field surface water. *EFSA Journal* 13. <https://doi.org/10.2903/j.efsa.2015.4176>.
- European Food Safety Authority (2018a). Scientific Opinion on the state of the science on pesticide risk assessment for amphibians and reptiles. EFSA Panel on Plant Protection Products and their Residues: Ockleford, C., Adriaanse, P., Berny, P., Brock, T., Duquesne, S., Grilli, S. *et al.* *EFSA Journal* 16(2), 5125. <https://doi.org/10.2903/j.efsa.2018.5125>.
- European Food Safety Authority (2018b). Conclusion on the peer review of the pesticide risk assessment for bees for the active substance clothianidin considering the uses as seed treatments and granules. *EFSA Journal* 16(2), 5177. <https://doi.org/10.2903/j.efsa.2018.5177>.
- European Food Safety Authority (2018c). Conclusion on the peer review of the pesticide risk assessment for bees for the active substance imidacloprid considering the uses as seed treatments and granules. *EFSA Journal* 16(2), 5178. <https://doi.org/10.2903/j.efsa.2018.5178>.
- European Food Safety Authority (2018d). Conclusions on the peer review of the pesticide risk assessment for bees for the active substance thiamethoxam considering the uses as seed treatments and granules. *EFSA Journal* 16(2), 5179. <https://doi.org/10.2903/j.efsa.2018.5179>.
- European Food Safety Authority (2018e). Use of EFSA pesticide residue intake model. *EFSA Journal* 16(1), 5147. <https://doi.org/10.2903/j.efsa.2018.5147>.
- European Food Safety Authority (2020a). Definitions of EFSA scientific outputs and supporting publications. <https://www.efsa.europa.eu/en/efsajournal/scdocdefinitions>. Accessed 1 December 2020.
- European Food Safety Authority (2020b). The 2018 European Union report on pesticide residues in food. *EFSA Journal* 18(4), e60570. <https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2020.6057>.



- European Food Safety Authority (2020c). Scientific report on cumulative dietary risk characterisation of pesticides that have acute effects on the nervous system. European Food Safety Authority: Craig, P.S., Dujardin, B., Hart, A., Hernandez-Jerez, A.F., Hougaard Bennekou, S., Kneuer, C. et al. *EFSA Journal* 18(4), 6087. <https://doi.org/10.2903/j.efsa.2020.6087>.
- European Food Safety Authority (2020d). Scientific report on the cumulative dietary risk characterisation of pesticides that have chronic effects on the thyroid. *EFSA Journal* 18(4), 6088. <https://doi.org/10.2903/j.efsa.2020.6088>.
- European Food Safety Authority Panel on Plant Protection Products and their Residues (2017). Scientific Opinion of the PPR Panel on the follow-up of the findings of the External Scientific Report "Literature review of epidemiological studies linking exposure to pesticides and health effects". *EFSA Journal* 15(10): 5007 <https://doi.org/10.2903/j.efsa.2017.5007>.
- European Food Safety Authority Scientific Committee (2019). Guidance on harmonised methodologies for human health, animal health and ecological risk assessment of combined exposure to multiple chemicals. *EFSA Journal* 17(3), 5634. <https://doi.org/10.2903/j.efsa.2019.5634>.
- European Parliamentary Research Service (2019). *Endocrine Disruptors: An Overview of Latest Developments at European Level in the Context of Plant Protection Products*. [https://www.europarl.europa.eu/RegData/etudes/STUD/2019/631743/EPRS\\_STU\(2019\)631743\\_EN.pdf](https://www.europarl.europa.eu/RegData/etudes/STUD/2019/631743/EPRS_STU(2019)631743_EN.pdf).
- European Union (1998). Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption. *Official Journal of the European Communities* L(330), 32-34. <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1998:330:0032:0054:EN:PDF>.
- European Union (2000). Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy. <https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32000L0060&from=EN>. Accessed 30 December 2020.
- European Union (2013). Directive 2008/105/EC of the European Parliament and of the Council of 16 December 2008 on environmental quality standards in the field of water policy. Amended by Directive 2013/39/EU of 12 August 2013. <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02008L0105-20130913>. Accessed 20 December 2020.
- European Union (2020a). *Proposal for a Directive of the European Parliament and of the Council on the Quality of Water Intended for Human Consumption (recast) – Political Agreement*. <https://op.europa.eu/en/publication-detail/-/publication/13def1fc-5711-11ea-8b81-01aa75ed71a1/language-en/format-PDF>.
- European Union (2020b). EU action on antimicrobial resistance. [https://ec.europa.eu/health/antimicrobial-resistance/eu-action-on-antimicrobial-resistance\\_en](https://ec.europa.eu/health/antimicrobial-resistance/eu-action-on-antimicrobial-resistance_en). Accessed 28 December 2020.
- Ewald, J.A., Wheatley, C.J., Aebischer, N.J., Moreby, S.J., Duffield, S.J., Crick, H.Q.P. and Morecroft, M.B. (2015). Influences of extreme weather, climate and pesticide use on invertebrates in cereal fields over 42 years. *Global Change Biology* 21(11), 3931-3950. <https://onlinelibrary.wiley.com/doi/abs/10.1111/gcb.13026>.
- Faheem, N., Sajjad, A., Mehmood, Z., Iqbal, F., Mahmood, Q., Munsif, S. and Waseem, A. (2015). Pesticide exposure through fruits and meat in Pakistan. *Fresenius Environmental Bulletin* 24(12B), 4555-4566. <https://www.prt-parlar.de/download/>.
- FAOSTAT (2020). Food and agriculture data. *Food and Agriculture Organization of the United Nations*. <http://www.fao.org/faostat/en/#home>. Accessed 26 December 2020.
- Fenske, R.A., Lu, C., Negrete, M. and Galvin, K. (2013). Breaking the take home pesticide exposure pathway for agricultural families: Workplace predictors of residential contamination. *American Journal of Industrial Medicine* 56, 1063-1071. <https://doi.org/10.1002/ajim.22225>.
- Fisher, M.S., Hawkins, N.J., Sanglard, D. and Gurr, S.J. (2018). Worldwide emergence of resistance to antifungal drugs challenges human health and food security. *Science* 360(6390), 739-742. <https://doi.org/10.1126/science.aap7999>.
- FOCUS (2008). *Pesticides in Air: Considerations for Exposure Assessment. Report Prepared by the FOCUS Working Group on Pesticides in Air*. European Commission (EC) Document Reference SANCO/10553/2006 Rev 2 June 2008. [https://esdac.jrc.ec.europa.eu/public\\_path/projects\\_data/focus/air/docs/FOCUS\\_AIR\\_GROUP\\_REPORT-FINAL.pdf](https://esdac.jrc.ec.europa.eu/public_path/projects_data/focus/air/docs/FOCUS_AIR_GROUP_REPORT-FINAL.pdf).
- Food and Agriculture Organization of the United Nations (2012). *International Code of Conduct on the Distribution and Use of Pesticides: Guidelines on Prevention and Management of Pesticide Resistance*. Rome. <http://www.fao.org/publications/card/en/c/8dcf273c-c907-4e71-b5e5-8753a861de87/>.
- Food and Agriculture Organization of the United Nations (2015). *The FAO Action Plan on Antimicrobial Resistance 2016-2020*. Rome. <http://www.fao.org/3/a-i5996e.pdf>.
- Food and Agriculture Organization of the United Nations (2016). *Submission and Evaluation of Pesticides Residues Data for the Estimation of Maximum Residue Levels in Food and Feed*. 3rd edition. <http://www.fao.org/3/i5452e/i5452E.pdf>.
- Food and Agriculture Organization of the United Nations (2019). *The State of the World's Biodiversity for Food and Agriculture*. Bélanger, J. and Pilling, D. (eds.). <http://www.fao.org/3/CA3129EN/CA3129EN.pdf>.
- Food and Agriculture Organization of the United Nations (2020). List of pesticides that have been evaluated by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) and the Joint FAO/WHO Meeting on Pesticide Specifications (JMPS). <http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/lpe/en/>. Accessed 28 December 2020.
- Food and Agriculture Organization of the United Nations and Intergovernmental Technical Panel on Soils (2015). *Status of the World's Soil Resources (SWSR) – Main Report*. Rome. <http://www.fao.org/documents/card/en/c/c6814873-efc3-41db-b7d3-2081a10ede50/>.

- Food and Agriculture Organization of the United Nations and Intergovernmental Technical Panel on Soils (2017). *Global Assessment of the Impact of Plant Protection Products on Soil Functions and Soil Ecosystems*. Rome. <http://www.fao.org/documents/card/en/c/18168EN/>.
- Food and Agriculture Organization of the United Nations, Intergovernmental Technical Panel on Soils, Global Soil Biodiversity Initiative, Secretariat of the Convention of Biological Diversity and European Commission (2020). *State of Knowledge of Soil Biodiversity – Status, Challenges and Potentialities, Report 2020*. <https://doi.org/10.4060/cb1928en>.
- Food and Agriculture Organization of the United Nations and World Health Organization (2014). *The International Code of Conduct on Pesticide Management*. Rome and Geneva. <http://www.fao.org/3/l3604E/i3604e.pdf>.
- Food and Agriculture Organization of the United Nations and World Health Organization (2019). *Joint FAO/WHO Expert Meeting in collaboration with OIE on Foodborne Antimicrobial Resistance: Role of the Environment, Crops and Biocides – Meeting Report*. Microbiological Risk Assessment Series No. 34. Rome and Geneva. <http://www.fao.org/3/ca6724en/ca6724en.pdf>.
- Forister, M.L., Cousens, B., Harrison, J.G., Anderson, K., Thorne, J.H., Waetjen, D. *et al.* (2016). Increasing neonicotinoid use and the declining butterfly fauna of lowland California. *Biology Letters* 12, 8. <https://doi.org/10.1098/rsbl.2016.0475>.
- Fosu-Mensah, B.Y., Okoffo, E.D., Darko, G. and Gordon, C. (2016). Assessment of organochlorine pesticide residues in soils and drinking water sources from cocoa farms in Ghana. *SpringerPlus* 5, 869. <https://doi.org/10.1186/s40064-016-2352-9>.
- Franz, J.M., Bogenschütz, H., Hassan, S.A., Huang, P., Naton, E., Suter, H. and Viggiani, G. (1980). Results of a joint pesticide test programme by the Working Group: Pesticides and beneficial arthropods. *Entomophaga* 25, 231-236. <https://doi.org/10.1007/BF02371922>.
- Freeman, S., Kaufman-Shriqui, V., Berman, T., Varsano, R., Shahar, D.R. and Manor, O. (2016). Children's diets, pesticide uptake, and implications for risk assessment: An Israeli case study. *Food and Chemical Toxicology* 87, 88-96. <https://doi.org/10.1016/j.fct.2015.11.009>.
- Frisvold, G.B., Bagavathiannan, M.V. and Norsworthy, J.K. (2017). Positive and normative modeling for Palmer amaranth control and herbicide resistance management. *Pest Management Science* 73(6), 1110-1120. <https://doi.org/10.1002/ps.4537>.
- Fuhrmann, S., Staudacher, P., Lindh, C., van Wendel de Joode, B., Mora, A.M., Winkler, M.S. and Kromhout, H. (2019). Variability and predictors of weekly pesticide exposure in applicators from organic, sustainable and conventional smallholder farms in Costa Rica. *Occupational and Environmental Medicine* 77(1), 40-47. <https://doi.org/10.1136/oemed-2019-105884>.
- Gallai, N., Garibaldi, L.A., Li, X., Breeze, T.D., Espírito Santo, M.M., Rodríguez Fernandez, J. *et al.* (2016). Economic valuation of pollinator gains and losses. In *The Assessment Report of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services on Pollinators, Pollination and Food Production*. Potts, S.G., Imperatriz-Fonseca, V.L. and Ngo, H.T. (eds.). Bonn: Secretariat of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services. Chapter 4, 205-273. <https://ipbes.net/assessment-reports/pollinators>.
- Garrigou, A., Laurent, C., Berthet, A., Colosio, C., Jas, N., Daubas-Letourneux, V. *et al.* (2020). Critical review of the role of PPE in the prevention of risks related to agricultural pesticide use. *Safety Science* 123, 104527. <https://doi.org/10.1016/j.ssci.2019.104527>.
- Geiger, F., Bengtsson, J., Berendse, F., Weisser, W.W., Emmerson, M., Morales, M.B. *et al.* (2010). Persistent negative effects of pesticides on biodiversity and biological control potential on European farmland. *Basic and Applied Ecology* 11(2), 97-105. <https://doi.org/10.1016/j.baec.2009.12.001>.
- Gendron, A. (2013). Amphibian ecotoxicology. In *Encyclopedia of Aquatic Ecotoxicology*. Dordrecht: Springer. Féraud, J.F. and Blaise, C. (eds.). [https://doi.org/10.1007/978-94-007-5704-2\\_4](https://doi.org/10.1007/978-94-007-5704-2_4).
- Gibbons, D., Morrissey, C. and Mineau, P. (2015). A review of the direct and indirect effects of neonicotinoids and fipronil on vertebrate wildlife. *Environmental Science and Pollution Research International* 22(1), 103-118. <https://doi.org/10.1007/s11356-014-3180-5>.
- Gibbs, K.E., MacKey, R.L. and Currie, D.J. (2009). Human land use, agriculture, pesticides and losses of imperiled species. *Diversity and Distributions* 15(2), 242–253. <https://doi.org/10.1111/j.1472-4642.2008.00543.x>.
- Gilburn, A.S., Bunnefeld, N., McVean Wilson, J., Botham, M.S., Brereton, T.M., Fox, R. and Goulson, D. (2015). Are neonicotinoid insecticides driving declines of widespread butterflies? *PeerJ* 11, 1-13. <https://doi.org/10.7717/peerj.1402>.
- Godfray, H.C.J., Blacquière, T., Field, L.M., Hails, R.S., Petrokofsky, G., Potts, S.G. *et al.* (2015). A restatement of the natural science evidence base concerning neonicotinoid insecticides and insect pollinators. *Proceedings of the Royal Society B: Biological Sciences* 281, 20140558. <http://dx.doi.org/10.1098/rspb.2015.1821>.
- Gomes, H.O., Jorge Menezes, J.M.C., da Costa, J.G.M., Coutinho, H.D.M., Teixeira, R.N.P. and do Nascimento, R.F. (2020). Evaluating the presence of pesticides in bananas: An integrative review. *Ecotoxicology and Environmental Safety* 189, 110016. <https://doi.org/10.1016/j.ecoenv.2019.110016>.
- Goss, D. and Wauchoppe, R.D. (1990). The SCR/ARS/CES pesticides properties database: II Using it with soils data in a screening procedure. In *Pesticides in the Next Decade: The Challenge Ahead*. Weigmann, D.L. (ed.). Virginia Water Resources Research Center (United States). 471-493. <https://www.nrcs.usda.gov/wps/portal/nrcs/detailfull/national/technical/ecoscience/invasive/?cid=stelprdb1044493>.
- Gould, F., Brown, Z.S. and Kuzma, J. (2018). Wicked evolution: Can we address the sociobiological dilemma of pesticide resistance? *Science* 360(6390), 728-732. <https://doi.org/10.1126/science.aar3780>.

- Government of Canada (2020a). Sex- and gender-based considerations in the scientific risk assessment of pesticides in Canada, 21 January. <https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/fact-sheets-other-resources/sex-and-gender-based-considerations-in-the-scientific-risk-assessment-of-pesticides-in-canada.html>. Accessed 19 January 2022
- Government of Canada (2020b). Consideration of sex and gender in pesticide risk assessment, 21 February. <https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/fact-sheets-other-resources/consideration-sex-gender-pesticide-risk-assessment-infographic.html>. Accessed 19 January 2022
- Grant, S., Thompson, K., Paxman, C., Elisei, G., Gallen C., Tracey, D. *et al.* (2018). *Marine Monitoring Program: Annual Report for Inshore Pesticide Monitoring 2016-2017*. Great Barrier Reef Marine Park Authority. <https://hdl.handle.net/11017/3399>.
- Grilo, A., Moreira, A., Carrapiço, B., Belas, A. and Braz, B.S. (2021). Epidemiological study of pesticide poisoning in domestic animals and wildlife in Portugal: 2014-2020. *Frontiers in Veterinary Science* 7, 1181. <https://doi.org/10.3389/fvets.2020.616293/bibtext>.
- Gross, K. and Rosenheim, J.A. (2011). Quantifying secondary pest outbreaks in cotton and their monetary cost with causal-inference statistics. *Ecological Applications* 21(7), 2770-2780. <https://www.jstor.org/stable/41416693>.
- Group of Chief Scientific Advisors (2018). *EU Authorisation Processes of Plant Protection Products – from a Scientific Point of View*. Scientific Advice Mechanism (SAM), Scientific Opinion 5. Directorate-General for Research and Innovation, European Commission, Brussels. <https://op.europa.eu/en/publication-detail/-/publication/5306df12-79b9-11e8-ac6a-01aa75ed71a1/language-en/format-PDF/source-94583924>.
- Grung, M., Lin, Y., Zhang, H., Steen, A.O., Huang, J., Zhang, G. and Larssen, T. (2015). Pesticide levels and environmental risk in aquatic environments in China – A review. *Environment International* 81, 87-97. <https://doi.org/10.1016/j.envint.2015.04.013>.
- Grzywacz, D., Rossbach, A., Rauf, A., Russell, D.A., Srinivasan, R. and Shelton, A.M. (2010). Current control methods for diamondback moth and other brassica insect pests and the prospects for improved management with lepidopteran-resistant Bt vegetable brassicas in Asia and Africa. *Crop Protection* 29, 68-79. <https://doi.org/10.1016/j.cropro.2009.08.009>.
- Guedes, R.N.C., Beins, K., Navarro Costa, D., Coelho, G. E. and Bezerra, H.S. da S. (2020). Patterns of insecticide resistance in *Aedes aegypti*: Meta-analyses of surveys in Latin America and the Caribbean. *Pest Management Science* 76(6), 2144-2157. <https://doi.org/10.1002/ps.5752>.
- Guida, Y. de S., Meire, R.O., Torres, J.P.M. and Malm, O. (2018). Air contamination by legacy and current-use pesticides in Brazilian mountains: An overview of national regulations by monitoring pollutant presence in pristine areas. *Environmental Pollution* 242, Part A, 19-30. <https://doi.org/10.1016/j.envpol.2018.06.061>.
- Guitart, R., Sachana, M., Caloni, F., Croubels, S., Vandenbroucke, V. and Berny, P. (2010). Animal poisoning in Europe. Part 3: Wildlife. *The Veterinary Journal* 183, 260-265. <https://doi.org/10.1016/j.tvjl.2009.03.033>.
- Gunnell, D., Eddleston, M., Phillips, M.R. and Konradsen, F. (2007). The global distribution of fatal pesticide self-poisoning: Systematic review. *BMC Public Health* 7, 357. <https://doi.org/10.1186/1471-2458-7-357>.
- Gunnell, D., Knipe, D., Chang, S.-S., Pearson, M., Konradsen, F., Lee, W.J. and Eddleston, M. (2017). Prevention of suicide with regulations aimed at restricting access to highly hazardous pesticides: A systematic review of the international evidence. *Lancet Global Health* 5, e1026-37. [http://dx.doi.org/10.1016/S2214-109X\(17\)30299-1](http://dx.doi.org/10.1016/S2214-109X(17)30299-1).
- Hallmann, C.A., Foppen, R.P.B., van Turnhout, C.A.M., de Kroon, H. and Jongejans, E. (2014). Declines in insectivorous birds are associated with high neonicotinoid concentrations. *Nature* 511, 341. <https://doi.org/10.1038/nature13531>.
- Hanson, M.L., Solomon, K.R., Van Der Kraak, G.J. and Brian, R.A. (2019). Effects of atrazine on fish, amphibians, and reptiles: update of the analysis based on quantitative weight of evidence. *Critical Reviews in Toxicology*, 49(8), 670-709. <https://doi.org/10.1080/10408444.2019.1701985>.
- Hardman, J.M., Franklin, J.L., Jensen, K.I.N. and Moreau, D.L. (2006). Effects of pesticides on mite predators (Acari: Phytoseiidae) and colonization of apple trees by *Tetranychus urticae*. *Phytoparasitica* 34, 449-462. <https://doi.org/10.1007/BF02981199>.
- Hasan, M.K., Shahriar, A. and Jim, K.U. (2019). Water pollution in Bangladesh and its impact on public health. *Heliyon* 5(8), e02145. <https://doi.org/10.1016/j.heliyon.2019.e02145>.
- Hayes, T.B., Anderson, L.L., Beasley, V.R., De Solla, S.R., Iguchi, T., Ingraham, H. *et al.* (2011). Demasculinization and feminization of male gonads by atrazine: Consistent effects across vertebrate classes. *Journal of Steroid Biochemistry and Molecular Biology*, 127(1-2), 64-73. <https://doi.org/10.1016/j.jsbmb.2011.03.015>.
- Hayes, T.B., Falso, P., Gallipeau, S. and Stice, M. (2010). The cause of global amphibian declines: A developmental endocrinologist's perspective. *Journal of Experimental Biology* 213, 921-933. <https://doi.org/10.1242/jeb.040865>.
- Health Council of the Netherlands (2020). *Follow-up Advisory Report on Crop Protection and Local Residents*. The Hague The Hague: Health Council of the Netherlands. Full report in Dutch: <https://www.gezondheidsraad.nl/documenten/adviezen/2020/06/29/vervolgadvies-gewasbescherming-en-omwonenden>. Executive summary in English: <https://www.healthcouncil.nl/documents/advisory-reports/2020/06/29/follow-up-advisory-report-on-crop-protection-and-local-residents>.
- Heap, I. (2019). The international herbicide-resistant weed database. [www.weedscience.com](http://www.weedscience.com). Accessed 20 December 2020.
- Hearn, S. and Buffardi, A.L. (2016). *What is Impact?* Methods Lab. London: Overseas Development Institute. <https://cdn.odi.org/media/documents/10352.pdf>.

- Henao, S. and Arbelaez, M.P. (2002). Epidemiological situation of acute pesticide poisoning in Central America, 1992-2000. *Epidemiological Bulletin* 23(3), 5-9. [http://www1.paho.org/english/sha/EB\\_v23n3.pdf?ua=1](http://www1.paho.org/english/sha/EB_v23n3.pdf?ua=1).
- Hertz-Picciotto, I., Sass, J.B., Engel, S., Bennett, D.H., Bradman, A., Eskenazi, B. *et al.* (2018). Organophosphate exposures during pregnancy and child neurodevelopment: Recommendations for essential policy reforms. *PLoS Medicine* 15(10), e1002671. <https://doi.org/10.1371/journal.pmed.1002671>.
- Hill, M.P., MacFadyen, S. and Nash, M.A. (2017). Broad spectrum pesticide application alters natural enemy communities and may facilitate secondary pest outbreaks. *PeerJ* 5, e4179. <https://doi.org/10.7717/peerj.4179>.
- Hladik, M.L. and Kolpin, D.W. (2016). First national-scale reconnaissance of neonicotinoid insecticides in streams across the USA. *Environmental Chemistry* 13(1), 12-20. <https://doi.org/10.1071/EN15061>.
- Hladik, M.L., Main, A.R. and Goulson, D. (2018). Environmental risks and challenges associated with neonicotinoid insecticides. *Environmental Science and Technology* 52(6), 3329-3335. <https://doi.org/10.1021/acs.est.7b06388>.
- Huang, F. (2020). Resistance of the fall armyworm, *Spodoptera frugiperda*, to transgenic *Bacillus thuringiensis* Cry1F corn in the Americas: lessons and implications for Bt corn IRM in China. *Insect Science* 28(3), 574-589. <https://doi.org/10.1111/1744-7917.12826>.
- Huang, F., Andow, D.A. and Buschman, L.L. (2011). Success of the high-dose/refuge resistance management strategy after 15 years of Bt crop use in North America. *Entomologia Experimentalis et Applicata* 140, 1-16. <https://doi.org/10.1111/j.1570-7458.2011.01138.x>.
- Huang, X., Cui, H. and Duan, W. (2020). Ecotoxicity of chlorpyrifos to aquatic organisms: A review. *Ecotoxicology and Environmental Safety* 200, 110731. <https://doi.org/10.1016/j.ecoenv.2020.110731>.
- Huguiet, P., Manier, N., Owojori, O.J., Bauda, P., Pandard, P. and Römbke, J. (2015). The use of soil mites in ecotoxicology: A review. *Ecotoxicology* 24(1), 1-18. <https://doi.org/10.1007/s10646-014-1363-y>.
- Human Rights Watch (2018). "You Don't Want to Breathe Poison Anymore": The Failing Response to Pesticide Drift in Brazil's Rural Communities. [https://www.hrw.org/sites/default/files/report\\_pdf/brazil0718\\_web.pdf](https://www.hrw.org/sites/default/files/report_pdf/brazil0718_web.pdf).
- Humann-Guillemint, S., Binkowski, Ł.J., Jenni, L., Hilke, G., Glauser, G. and Helfenstein, F. (2019). A nation-wide survey of neonicotinoid insecticides in agricultural land with implications for agri-environment schemes. *Journal of Applied Ecology* 56(7), 1502-1514. <https://doi.org/10.1111/1365-2664.13392>.
- Hvězďová, M., Kosubová, P., Košíková, M., Scherr, K.E., Šimek, Z., Brodský, L. *et al.* (2018). Currently and recently used pesticides in Central European arable soils. *Science of The Total Environment* 613-614, 361-370. <https://doi.org/10.1016/j.scitotenv.2017.09.049>.
- Imfeld, G. and Vuilleumier, S. (2012). Measuring the effects of pesticides on bacterial communities in soil: A critical review. *European Journal of Soil Biology* 49, 22-30. <https://doi.org/10.1016/j.ejsobi.2011.11.010>.
- Indian Council of Agriculture Research (ICAR) (n.d.). All India Network Project on Pesticide Residues (AINP-PR). Monitoring of pesticide residues. <https://aicrp.icar.gov.in/pesticide/monitoring-of-pesticide-residues>. Accessed 15 December 2020.
- Institut national de la santé et de la recherche médicale (Inserm) (France) (2013). *Pesticides – effets sur la santé. Collection expertise collective*. <http://www.ipubli.inserm.fr/handle/10608/4819>.
- Instituto Brasileiro do Meio Ambiente e dos Recursos Naturais (Brazil) (2009). *Manual Para Requerimento de Avaliação Ambiental: Agrotóxicos e Afins. Diretoria de Qualidade Ambiental*. Brasília. [http://www.leb.esalq.usp.br/disciplinas/Casimiro/LFN/Leitura\\_complementar/Manual\\_de\\_procedimento%20IBAMA.pdf](http://www.leb.esalq.usp.br/disciplinas/Casimiro/LFN/Leitura_complementar/Manual_de_procedimento%20IBAMA.pdf).
- Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services (2019). *The Global Assessment Report on Biodiversity and Ecosystem Services of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services: Summary for Policymakers*. S. Díaz, J. Settele, E. S. Brondízio E.S., H. T. Ngo, M. Guèze, J. Agard *et al.* (eds.). IPBES Secretariat, Bonn. [https://www.ipbes.net/sites/default/files/2020-02/ipbes\\_global\\_assessment\\_report\\_summary\\_for\\_policymakers\\_en.pdf](https://www.ipbes.net/sites/default/files/2020-02/ipbes_global_assessment_report_summary_for_policymakers_en.pdf).
- International Agency for Research on Cancer (2020a). IARC Monographs on the Identification of Carcinogenic Hazards to Humans. <https://monographs.iarc.fr/monographs-available/>. Accessed 1 December 2020.
- International Agency for Research on Cancer (2020b). AGRICOH: A Consortium of Agricultural Cohort Studies. <https://agricoh.iarc.fr/>. Accessed 15 December 2020.
- International Organization for Biological and Integrated Control – West Palearctic Regional Section (2019). IOBC-WPRS Pesticide Side Effect Database. [https://www.iobc-wprs.org/ip\\_integrated\\_production/Pesticide\\_Side\\_Effect\\_Database.html#:~:text=The%20database%20on%20selectivity%20of,in%20the%20choice%20of%20pesticides](https://www.iobc-wprs.org/ip_integrated_production/Pesticide_Side_Effect_Database.html#:~:text=The%20database%20on%20selectivity%20of,in%20the%20choice%20of%20pesticides). Accessed 20 December 2020.
- International Service for the Acquisition of Agri-Biotech Applications (2019). GM approval database. <http://www.isaaa.org/gmaprovaldatabase/default.asp>. Accessed 20 December 2020.
- International Union for Conservation of Nature (2020). IUCN Red List – Summary Statistics. <https://www.iucnredlist.org/resources/summary-statistics>. Accessed 20 December 2020.
- Ito, H.C., Shiraishi, H., Nakagawa, M. and Takamura, N. (2020). Combined impact of pesticides and other environmental stressors on animal diversity in irrigation ponds. *PLoS One* 15(7), e0229052, <https://doi.org/10.1371/journal.pone.0229052>.

- Ittner, L.D., Junghans, M. and Werner, I. (2018). Aquatic fungi: A disregarded trophic level in ecological risk assessment of organic fungicides. *Frontiers in Environmental Science* 6(105). <https://doi.org/10.3389/fenvs.2018.00105>.
- Jahn, T., Hötter, H., Oppermann, R., Bleil, R. and Vele, L. (2014). *Protection of Biodiversity of Free Living Birds and Mammals in Respect of the Effects of Pesticides*. Dessau-Roßlau: Federal Environment Agency. <https://www.umweltbundesamt.de/en/publikationen/protection-of-biodiversity-of-free-living-birds>.
- Jänsch, S., Frampton, G.K., Römbke, J., Van Den Brink, P.J. and Scott-Fordsmand, J.J. (2006). Effects of pesticides on soil invertebrates in model ecosystems and field studies: A review and comparison with laboratory toxicity data. *Environmental Toxicology and Chemistry* 25(9), 2480-2489. <https://doi.org/10.1897/05-438R.1>.
- Jansen, J.-P. (2013). Pest select database: a new tool to use selective pesticides for IPM. *Communications in Agricultural and Applied Biological Sciences* 78(2), 115-119. <https://www.cra.wallonie.be/en/pest-select-database-a-new-tool-to-use-selective-pesticides-for-ipm-2013>.
- Jensen, B.H., Petersen, A., Nielsen, E., Christensen, T., Poulsen, M.E. and Andersen, J.H. (2015). Cumulative dietary exposure of the population of Denmark to pesticides. *Food and Chemical Toxicology* 83, 300-307. <https://doi.org/10.1016/j.fct.2015.07.002>.
- Jeyaratnam, J. (1990). Acute pesticide poisoning: A major global health problem. *World Health Statistics Quarterly* 43(3), 139-144. <https://apps.who.int/iris/handle/10665/51746>.
- Jørs, E. (2016). *Acute Pesticide Poisoning among Bolivian Small-holder Farmers – Frequency, Risk Factors and Prevention*. Odense: University of Southern Denmark. [https://www.sdu.dk/-/media/files/om\\_sdu/institutter/ist/sundhedsfremme/erikphd.pdf?la=en&andhash=8C6152C8C762A6CCB7E1C426C3A6E2FAA23A2255](https://www.sdu.dk/-/media/files/om_sdu/institutter/ist/sundhedsfremme/erikphd.pdf?la=en&andhash=8C6152C8C762A6CCB7E1C426C3A6E2FAA23A2255).
- Jørs, E., Neupane, D. and London, L. (2018). Pesticide poisonings in low and middle-income countries. *Environmental Health Insights* 12, 1-3. <https://doi.org/10.1177/1178630217750876>.
- Jurado, A., Vázquez-Suñé, E., Carrera, J., López de Alda, M., Pujades, E. and Barceló, D. (2012). Emerging organic contaminants in groundwater in Spain: A review of sources, recent occurrence and fate in a European context. *Science of The Total Environment* 440, 82-94. <https://doi.org/10.1016/j.scitotenv.2012.08.029>.
- Jurado, A., Walther, M. and Díaz-Cruz, M.S. (2019). Occurrence, fate and environmental risk assessment of the organic microcontaminants included in the Watch Lists set by EU Decisions 2015/495 and 2018/840 in the groundwater of Spain. *Science of the Total Environment* 663, 285-296. <https://doi.org/10.1016/j.scitotenv.2019.01.270>.
- K'oreje, K.O., Okoth, M., Van Langenhove, H. and Demeestere, K. (2020). Occurrence and treatment of contaminants of emerging concern in the African aquatic environment: Literature review and a look ahead. *Journal of Environmental Management* 254. <https://doi.org/10.1016/j.jenvman.2019.109752>.
- Kamel, F., Engel, L.S., Gladen, B.C., Hoppin, J.A., Alavanja, M.C.R. and Sandler, D.P. (2007). Neurologic symptoms in licensed pesticide applicators in the Agricultural Health Study. *Human and Experimental Toxicology* 26, 243-250. <https://doi.org/10.1177/0960327107070582>.
- Karalexí, M.A., Tagkas C.F., Markozannes, G., Tseretopoulou, X., Hernández, A.F., Schüz, J. et al. (2021). Exposure to pesticides and childhood leukemia risk: A systematic review and meta-analysis. *Environmental Pollution* 285(117376), 1-12. <https://doi.org/10.1016/j.envpol.2021.117376>.
- Karki, A.J., Cappelli, P., Dirks, C., Pekar, H., Hellenäs, K.E., Rosén, J. and Westerberg, E. (2020). New efficient methodology for screening of selected organic micropollutants in raw- and drinking water from 90 Swedish water treatment plants. *Science of The Total Environment* 724, 138069. <https://doi.org/10.1016/j.scitotenv.2020.138069>.
- Karunaratne, A., Gunnell, D., Konradsen, F. and Eddleston, M. (2019). How many premature deaths from pesticide poisoning have occurred since the agricultural Green Revolution? *Clinical Toxicology* 58(4), 227-232. <https://doi.org/10.1080/15563650.2019.1662433>.
- Kennedy, C.M., Lonsdorf, E., Neel, M.C., Williams, N.M., Ricketts, T.H., Winfree, R. et al. (2013). A global quantitative synthesis of local and landscape effects on wild bee pollinators in agroecosystems. *Ecology Letters* 16(5), 584-599. <https://doi.org/10.1111/ele.12082>.
- Kim, J.-H., Kim, J., Cha, E.S., Ko, Y., Kim, D.H. and Lee, W.J. (2013). Work-related risk factors by severity for acute pesticide poisoning among male farmers in South Korea. *International Journal of Environmental Research and Public Health* 10, 1100-1112. <https://doi.org/10.3390/ijerph10031100>.
- Kirchner, M., Jakobi, G., Körner, W., Levy, W., Moche, W., Niedermoser, B. et al. (2016). Ambient air levels of organochlorine pesticides at three high alpine monitoring stations: Trends and dependencies on geographical origin. *Aerosol and Air Quality Research* 16(3), 738-751. <https://doi.org/10.4209/aaqr.2015.04.0213>.
- Klok, C., de Vries, P., Jongbloed, R. and Tamis, J. (2017). Literature review on the sensitivity and exposure of marine and estuarine organisms to pesticides in comparison to corresponding fresh water species. *EFSA Supporting Publications* 9(11), 357E. <https://doi.org/10.2903/sp.efsa.2012.en-357>.
- Knauer, K. (2016). Pesticides in surface waters: A comparison with regulatory acceptable concentrations (RACs) determined in the authorization process and consideration for regulation. *Environmental Sciences Europe* 28(13), 1-7. <https://doi.org/10.1186/s12302-016-0083-8>.
- Ko, Y., Kim, H.J., Cha, E.S., Kim, J. and Lee, W.J. (2012). Emergency department visits due to pesticide poisoning in South Korea, 2006-2009. *Clinical Toxicology* 50(2), 114-119. <https://doi.org/10.3109/15563650.2012.655281>.

- Köck-Schulmeyer, M., Ginebreda, A., Postigo, C., Garrido, T., Fraile, J., López de Alda, M., and Barceló, D. (2014). Four-year advanced monitoring program of polar pesticides in groundwater of Catalonia (NE-Spain). *Science of the Total Environment* 470-471, 1087-1098. <https://doi.org/10.1016/j.scitotenv.2013.10.079>.
- Köhler, H.-R. and Trieborsk, R. (2013). Wildlife ecotoxicology of pesticides: Can we track effects to the population level and beyond? *Science* 341(6147), 759-765. <https://doi.org/10.1126/science.1237591>.
- Kohlschmid, E. and Ruf, D. (2016). Is the risk for soil arthropods covered by new data requirements under the EU PPP Regulation No. 1107/2009? *Environmental Science and Pollution Research* 23(23), 23884-23891. <https://doi.org/10.1007/s11356-016-7536-x>.
- Komárek M., Čadková, E., Chrástný, V., Bordas, F. and Bollinger, J.C. (2010). Contamination of vineyard soils with fungicides: A review of environmental and toxicological aspects. *Environment International* 36(1), 138-151. <https://doi.org/10.1016/j.envint.2009.10.005>.
- Kouzayha, A., Al Ashi, A., Al Akoum, R., Al Iskandarani, M., Budzinski, H. and Jaber, F. (2013). Occurrence of pesticide residues in Lebanon's water resources. *Bulletin of Environmental Contamination and Toxicology* 91(5), 503-509. <https://doi.org/10.1007/s00128-013-1071-y>.
- Kovács-Hostyánszki A., Li, J., Pettis, J., Settele, J., Aneni, T., Espíndola, A. et al. (2016). Drivers of change of pollinators, pollination networks and pollination. In *The Assessment Report of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services on Pollinators, Pollination and Food Production*. Potts, S.G., Imperatriz-Fonseca, V.L. and Ngo, H.T. (eds.). Bonn: Secretariat of the Intergovernmental Science- Policy Platform on Biodiversity and Ecosystem Services. Chapter 2, 27-149. <https://ipbes.net/assessment-reports/pollinators>.
- Krauss, J., Gallenberger, I. and Steffan-Dewenter, I. (2011). Decreased functional diversity and biological pest control in conventional compared to organic crop fields. *PLoS ONE*, 6(5), 1-9. <https://doi.org/10.1371/journal.pone.0019502>.
- Krieger, R. (2010). *Hayes' Handbook of Pesticide Toxicology, Volumes 1 and 2*. 3rd edition. Krieger, R., Doull, J., van Hemmen, J., Hodgson, E., Maibach, H., Reiter, L., Ritter et al. (eds.). London: Academic Press. <https://www.elsevier.com/books/hayes-handbook-of-pesticide-toxicology/krieger/978-0-08-092201-0>.
- Kurenbach, B., Marjoshi, D., Amáñile-Cuevas, C.F., Ferguson, G.C., Godsoe, W., Gibson, P. and Heinemann, J.A. (2015). Sublethal exposure to commercial formulations of the herbicides dicamba, 2,4-dichlorophenoxyacetic acid, and glyphosate cause changes in antibiotic susceptibility in *Escherichia coli* and *Salmonella enterica* serovar *Typhimurium*. *mBio* 6(2), e00009-15. <https://doi.org/10.1128/mBio.00009-15>.
- La Merrill, M.A., Vandenberg, L.N., Smith, M.T., Goodson, W., Browne, P., Patisaul, H.B. et al. (2020). Consensus on the key characteristics of endocrine-disrupting chemicals as a basis for hazard identification. *Nature Reviews Endocrinology* 16, 45-57 <https://doi.org/10.1038/s41574-019-0273-8>.
- Landrigan, P.J., Fuller, R., Acosta, N.J.R., Adeyi, O., Arnold, R., Basu, N. et al. (2018). The Lancet Commission on pollution and health. *Lancet* 391, 462-512. [http://dx.doi.org/10.1016/S0140-6736\(17\)32345-0](http://dx.doi.org/10.1016/S0140-6736(17)32345-0).
- Larsson, M.O., Sloth Nielsen, V., Bjerre, N., Laporte, F. and Cedergreen, N. (2018). Refined assessment and perspectives on the cumulative risk resulting from the dietary exposure to pesticide residues in the Danish population. *Food and Chemical Toxicology* 111, 207-267. <https://doi.org/10.1016/j.fct.2017.11.020>.
- Leather, S.R. (2018). "Ecological Armageddon" – more evidence for the drastic decline in insect numbers. *Annals of Applied Biology* 172(1), 1-3. <https://doi.org/10.1111/aab.12410>.
- Lee, S.-J., Mehler, L., Beckman, J., Diebolt-Brown, B., Prado, J., Lackovic, M. et al. (2011). Acute pesticide illnesses associated with off-target pesticide drift from agricultural applications: 11 states, 1998-2006. *Environmental Health Perspectives* 119(8), 1162-1169 <https://doi.org/10.1289/ehp.1002843>.
- Lee, Y.Y., Chisholm, D., Eddleston, M., Gunnell, D., Fleischmann, A., Konradsen, F. et al. (2020). The cost-effectiveness of banning highly hazardous pesticides to prevent suicides due to pesticide self-ingestion across 14 countries: An economic modelling study. *The Lancet Global Health*. [https://doi.org/10.1016/S2214-109X\(20\)30493-9](https://doi.org/10.1016/S2214-109X(20)30493-9).
- Lehmann, E., Turrero, N., Kolia, M., Konaté, Y. and de Alencastro, L. F. (2017). Dietary risk assessment of pesticides from vegetables and drinking water in gardening areas in Burkina Faso. *Science of The Total Environment* 601-602, 1208-1216. <https://doi.org/10.1016/j.scitotenv.2017.05.285>.
- Lekei, E., Ngowi, A.V., Kapeleka, J. and London, L. (2020). Acute pesticide poisoning amongst adolescent girls and women in northern Tanzania. *BMC Public Health* 20(303), 1-8. <https://doi.org/10.1186/s12889-020-8374-9>.
- Lekei, E., Ngowi, A.V. and London, L. (2014). Hospital-based surveillance for acute pesticide poisoning caused by neurotoxic and other pesticides in Tanzania. *NeuroToxicology* 45, 318-326. <http://dx.doi.org/10.1016/j.neuro.2014.02.007>.
- Lekei, E., Ngowi, A.V. and London, L. (2016). Underreporting of acute pesticide poisoning in Tanzania: Modelling results from two cross-sectional studies. *Environmental Health* 15(118). <https://doi.org/10.1186/s12940-016-0203-3>.
- Lettoof, D.C., Lohr, M.T., Busetti, F., Bateman, P.W. and Davis, R.A. (2020). Toxic time bombs: Frequent detection of anticoagulant rodenticides in urban reptiles at multiple trophic levels. *Science of The Total Environment* 724, 138218. <https://doi.org/10.1016/j.scitotenv.2020.138218>.
- Leusch, F.D.L., Neale, P.A., Arnal, C., Aneck-Hahn, N.H., Balaguer, P., Bruchet, A. et al. (2018). Analysis of endocrine activity in drinking water, surface water and treated wastewater from six countries. *Water Research* 139, 1018. <https://doi.org/10.1016/j.watres.2018.03.056>.

- Levillain, J., Cattan, P., Colin, F., Voltz, M. and Cabidoche, Y.-M. (2012). Analysis of environmental and farming factors of soil contamination by a persistent organic pollutant, chlordecone, in a banana production area of French West Indies. *Agriculture, Ecosystems and Environment* 159, 123-132. <https://doi.org/10.1016/j.agee.2012.07.005>.
- Levine, R.S. (1986). *Assessment of Mortality and Morbidity due to Unintentional Pesticide Poisonings*. Document WHO/VBC/86.929. Geneva: World Health Organization. <https://apps.who.int/iris/bitstream/handle/10665/59938/WHO-VBC-86.929-eng.pdf;sequence=1>.
- Li, H., Cheng, F., Wei, Y., Lydy, M.J. and You, J. (2017). Global occurrence of pyrethroid insecticides in sediment and the associated toxicological effects on benthic invertebrates: An overview. *Journal of Hazardous Materials* 324 (Part B), 258-271. <https://doi.org/10.1016/j.jhazmat.2016.10.056>.
- Li, J., Li, F. and Liu, Q. (2015). Sources, concentrations and risk factors of organochlorine pesticides in soil, water and sediment in the Yellow River estuary. *Marine Pollution Bulletin* 100(1), 516-522. <https://doi.org/10.1016/j.marpolbul.2015.09.003>.
- Li, Y., Miao, R. and Khanna, M. (2020). Neonicotinoids and decline in bird biodiversity in the United States. *Nature Sustainability* 3, 1027-1035. <https://www.nature.com/articles/s41893-020-0582-x>.
- Li, Y.F. and Macdonald, R.W. (2005). Sources and pathways of selected organochlorine pesticides to the Arctic and the effect of pathway divergence on HCH trends in biota: A review. *Science of The Total Environment* 342(1-3), 87-106. <https://doi.org/10.1016/j.scitotenv.2004.12.027>.
- Liberati, A., Altman, D.G., Tetzlaff, J., Mulrow, C., Gøtzsche, P.C., Ioannidis, J.P.A. et al. (2009). The PRISMA Statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *PLoS Medicine* 6(7), e1000100. <https://doi.org/10.1371/journal.pmed.1000100>.
- Litchfield, M.H. (2005). Estimates of acute pesticide poisoning in agricultural workers in less developed countries. *Toxicological Reviews* 24(4), 271-271. <https://doi.org/10.2165/00139709-200524040-00006>.
- Liu, Z., Huang, R., Roberts, R. and Tong W. (2019). Toxicogenomics: A 2020 Vision. *Trends in Pharmacological Sciences* 40(2), P93-P103. <https://doi.org/10.1016/j.tips.2018.12.001>.
- Lohr, M.T. and Davis, R.A. (2018). Anticoagulant rodenticide use, non-target impacts and regulation: A case study from Australia. *Science of The Total Environment* 634, 1372-1384. <https://doi.org/10.1016/j.scitotenv.2018.04.069>.
- London, L. (2003). Human rights, environmental justice, and the health of farm workers in South Africa. *International Journal of Occupational and Environmental Health* 9, 59-68. <https://doi.org/10.1179/107735203800328876>.
- London, L. and Bailie, R. (2001). Challenges for improving surveillance for pesticide poisoning: Policy implications for developing countries. *International Journal of Epidemiology* 30(3), 564-570. <https://doi.org/10.1093/ije/30.3.564>.
- Lopez, B., Ollivier, P., Togola, A., Baran, N., and Ghestem, J.P. (2015). Screening of French groundwater for regulated and emerging contaminants. *Science of The Total Environment* 518-519, 562-573. <https://doi.org/10.1016/j.scitotenv.2015.01.110>.
- López-Gálvez, N., Wagoner, R., Quirós-Alcalá, L., Van Horne, Y.O., Furlong, M., Avila, E. and Beamer, P. (2019). Systematic literature review of the take-home route of pesticide exposure via biomonitoring and environmental monitoring. *International Journal of Environmental Research and Public Health* 16, 2177. <https://doi.org/10.3390/ijerph16122177>.
- López-Perea, J.J. and Mateo, R. (2018). Secondary exposure to anticoagulant rodenticides and effects on predators. In *Anticoagulant Rodenticides and Wildlife. Emerging Topics in Ecotoxicology (Principles, Approaches and Perspectives) vol 5*. van den Brink, N.W., Elliott, J.E., Shore, R.F. and Rattner, B.A. (eds.). Cham: Springer. Chapter 7, 159-193. [https://link.springer.com/chapter/10.1007/978-3-319-64377-9\\_7](https://link.springer.com/chapter/10.1007/978-3-319-64377-9_7).
- Łozowicka, B., Kaczyński, P., Wolejko, E., Piekutin, J., Sagitov, A., Toleubayev, K. et al. (2016). Evaluation of organochlorine pesticide residues in soil and plants from east Europe and central Asia. *Desalination and Water Treatment* 57(3), 1310-1321. <https://doi.org/10.1080/19443994.2014.996008>.
- Lucas, J.A., Hawkins, N.J. and Fraaije, B.A. (2015). Chapter Two – The evolution of fungicide resistance. *Advances in Applied Microbiology* 90, 29-92. <http://dx.doi.org/10.1016/bs.aambs.2014.09.001>.
- Lundin, O., Rundlöf, M., Smith, H.G., Fries, I. and Bommarco, R. (2015). Neonicotinoid insecticides and their impacts on bees: A systematic review of research approaches and identification of knowledge gaps. *PLoS ONE* 10(8), e0136928. <https://doi.org/10.1371/journal.pone.0136928>.
- Machete, M. and Shadung, J. M. (2019). Detection of selected agricultural pesticides in river and tap water in Letsitele, Lomati and Vals–Renoster catchments, South Africa. *Water SA* 45(4), 716–720. <https://doi.org/10.17159/wsa/2019.v45.i4.7554>.
- Magalhães, A.F.A. and Caldas, E.D. (2018). Underreporting of fatal poisonings in Brazil – A descriptive study using data from four information systems. *Forensic Science International* 287, 136-141. <https://doi.org/10.1016/j.forsciint.2018.03.040>.
- Maier, L., Pruteanu, M., Kuhn, M., Zeller, G., Telzerow, A., Anderson, E.E. et al. (2018). Extensive impact of non-antibiotic drugs on human gut bacteria. *Nature* 555, 623-628. <https://doi.org/10.1038/nature25979>.
- Main, A.R., Webb, E.B., Goyno, K.W. and Mengel, D. (2020). Reduced species richness of native bees in field margins associated with neonicotinoid concentrations in non-target soils. *Agriculture, Ecosystems and Environment* 287, 106693. <https://doi.org/10.1016/j.agee.2019.106693>.

- Malaj, E., von der Ohe, P.C., Grote, M., Kühne, R., Mondy, C.P., Usseglio-Polatera, P. *et al.* (2014). Organic chemicals jeopardize the health of freshwater ecosystems on the continental scale. *Proceedings of the National Academy of Sciences of the United States of America* 111(26), 9549-9554. <https://doi.org/10.1073/pnas.1321082111>.
- Mallinger, R.E., Werts, P. and Gratton, C. (2015). Pesticide use within a pollinator-dependent crop has negative effects on the abundance and species richness of sweat bees, *Lasioglossum* spp., and on bumble bee colony growth. *Journal of Insect Conservation* 19(5), 999-1010. <https://doi.org/10.1007/s10841-015-9816-z>.
- Maltby, L., Blake, N., Brock, T.C.M. and Van Den Brink, P.J. (2005). Insecticide species sensitivity distributions: Importance of test species selection and relevance to aquatic ecosystems. *Environmental Toxicology and Chemistry* 24, 379-388. <https://doi.org/10.1897/04-025R.1>.
- Maltby, L., Brock, T.C.M. and Van Den Brink, P.J. (2009). Fungicide risk assessment for aquatic ecosystems: Importance of interspecific variation, toxic mode of action, and exposure regime. *Environmental Science and Technology* 43(19), 7556-7563. <https://doi.org/10.1021/es901461c>.
- Malyan, S.K., Singh, R., Rawat, M., Kumar, M., Pugazhendhi, A., Kumar, A. *et al.* (2019). An overview of carcinogenic pollutants in groundwater of India. *Biocatalysis and Agricultural Biotechnology* 21, 101288. <https://doi.org/10.1016/j.bcab.2019.101288>.
- Manamsa, K., Crane, E., Stuart, M., Talbot, J., Lapworth, D. and Hart, A. (2016). A national-scale assessment of micro-organic contaminants in groundwater of England and Wales. *Science of The Total Environment* 568, 712-726. <https://doi.org/10.1016/j.scitotenv.2016.03.017>.
- Manuweera, G., Eddleston, M., Egodage, S. and Buckley, N. (2008). Do targeted bans of insecticides to prevent deaths from self-poisoning result in reduced agricultural output? *Environmental Health Perspectives* 116, 492-495. <https://doi.org/10.1289/ehp.11029>.
- Martin, O., Scholze, M., Ermler, S., McPhie, J., Bopp, S.K., Kienzler, A. *et al.* (2021). Ten years of research on synergisms and antagonisms in chemical mixtures: A systematic review and quantitative reappraisal of mixture studies. *Environmental International* 146, 106206. <https://doi.org/10.1016/j.envint.2020.106206>.
- Martyniuk, C.J., Mehinto, A.C. and Denslow, N.D. (2020). Organochlorine pesticides: Agrochemicals with potent endocrine-disrupting properties in fish. *Molecular and Cellular Endocrinology* 507, 110764. <https://doi.org/10.1016/j.mce.2020.110764>.
- Matthiessen, P., Wheeler, J.R. and Weltje, L. (2018). A review of the evidence for endocrine disrupting effects of current-use chemicals on wildlife populations. *Critical Reviews in Toxicology* 48(3), 195-216. <https://doi.org/10.1080/10408444.2017.1397099>.
- Maute, K., French, K., Bull, C.M., Story, P. and Hose, G. (2015). Current insecticide treatments used in locust control have less of a short-term impact on Australian arid-zone reptile communities than does temporal variation. *Wildlife Research* 42(1), 50-59. <http://dx.doi.org/10.1071/WR14194>.
- McManus, S.L., Richards, K.G., Grant, J., Mannix, A., and Coxon, C.E. (2014). Pesticide occurrence in groundwater and the physical characteristics in association with these detections in Ireland. *Environmental Monitoring and Assessment* 186(11), 7819-7836. <https://doi.org/10.1007/s10661-014-3970-8>.
- Meek, M.E., Boobis, A.R., Crofton, K.M., Heinemeyer, G., van Raaij, M. and Vickers C (2011). Risk assessment of combined exposure to multiple chemicals: A WHO/IPCS framework. *Regulatory Toxicology and Pharmacology* 60, S1-S14. <https://doi.org/10.1016/j.yrtph.2011.03.010>.
- Meffe, R. and de Bustamante, I. (2014). Emerging organic contaminants in surface water and groundwater: A first overview of the situation in Italy. *Science of The Total Environment* 481 (1), 280-295. <https://doi.org/10.1016/j.scitotenv.2014.02.053>.
- Menzies, R., Soares Quinete, N., Gardinali, P. and Seba, D. (2013). Baseline occurrence of organochlorine pesticides and other xenobiotics in the marine environment: Caribbean and Pacific collections. *Marine Pollution Bulletin* 70 (1-2), 289-295. <https://doi.org/10.1016/j.marpolbul.2013.03.003>.
- Mew, E.J., Padmanathan, P., Konradsen, F., Eddleston, M., Chang, S.-S., Phillips, M.R. and Gunnell, D. (2017). The global burden of fatal self-poisoning with pesticides 2006-15: Systematic review. *Journal of Affective Disorders* 219, 93-104. <https://doi.org/10.1016/j.jad.2017.05.002>.
- Millennium Ecosystem Assessment (2005). *Ecosystems and Human Well-being: Biodiversity Synthesis*, Washington, D.C. World Resources Institute. <https://www.millenniumassessment.org/documents/document.354.aspx.pdf>.
- Milner, A.M. and Boyd, I.L. (2017). Toward pesticidovigilance – Can lessons from Pharmaceutical monitoring help to improve pesticide regulation? *Science* 357(6357), 1232-1234. <https://doi.org/10.1126/science.aan2683>.
- Mineau P (2013a). Bird impacts from pesticide use. In *Encyclopedia of Environmental Management vol 1*. Jørgensen, S.E. (ed.). Boca Raton, FL: CRC Press. 416-423. [https://www.researchgate.net/publication/260338687\\_Bird\\_impacts\\_from\\_pesticide\\_use\\_Encyclopedia\\_of\\_Environmental\\_Management\\_1st\\_edition\\_SE\\_Jorgensen\\_ed\\_DOI\\_101081E-EEM-120046191\\_Pages\\_416-423\\_Taylor\\_and\\_Francis\\_New\\_York](https://www.researchgate.net/publication/260338687_Bird_impacts_from_pesticide_use_Encyclopedia_of_Environmental_Management_1st_edition_SE_Jorgensen_ed_DOI_101081E-EEM-120046191_Pages_416-423_Taylor_and_Francis_New_York).
- Mineau, P. (2013b). Avian mortality from pesticides used in agriculture in Canada. Unpublished manuscript, provided as an annex to Calvert *et al.* (2013). [https://www.researchgate.net/publication/278212489\\_Avian\\_mortality\\_from\\_pesticides\\_used\\_in\\_agriculture\\_in\\_Canada](https://www.researchgate.net/publication/278212489_Avian_mortality_from_pesticides_used_in_agriculture_in_Canada).
- Mineau, P. and Whiteside, M. (2006). Lethal risk to birds from insecticide use in the United States – a spatial and temporal analysis. *Environmental Toxicology and Chemistry* 25(5), 1214-1222. <https://pubmed.ncbi.nlm.nih.gov/16704051/>.
- Mineau, P. and Whiteside, M. (2013). Pesticide acute toxicity is a better correlate of U.S. grassland bird declines than agricultural intensification. *PLoS ONE* 8(2), e57457. <https://doi.org/doi:10.1371/journal.pone.0057457>.
- Mingo, V., Lötters, S. and Wagner, N. (2016). Risk of pesticide exposure for reptile species in the European Union. *Environmental Pollution* 215, 164e169. <http://dx.doi.org/10.1016/j.envpol.2016.05.011>.



- Mingo, V., Lötters, S. and Wagner, N. (2017). The impact of land use intensity and associated pesticide applications on fitness and enzymatic activity in reptiles—A field study. *Science of The Total Environment* 590-591, 114-124. <http://dx.doi.org/10.1016/j.scitotenv.2017.02.178>.
- Ministry of Agriculture and Farmers Welfare (MAFW) (India) (2019). *Survey Report: Status of Pesticide Residues in India*. [https://fssai.gov.in/upload/advisories/2019/10/5da705b31ca78Letter\\_Report\\_Pesticides\\_MRL\\_16\\_10\\_2019.pdf](https://fssai.gov.in/upload/advisories/2019/10/5da705b31ca78Letter_Report_Pesticides_MRL_16_10_2019.pdf).
- Mishra, K., Sharma, R.C. and Kumar, S. (2012). Contamination levels and spatial distribution of organochlorine pesticides in soils from India. *Ecotoxicology and Environmental Safety* 76(1), 215-225. <https://doi.org/10.1016/j.ecoenv.2011.09.014>.
- Mochungong, P. and Zhu, J. (2015). DDTs, PCBs and PBDEs contamination in Africa, Latin America and South-southeast Asia—a review. *AIMS Environmental Science* 2(2), 374–399. <https://doi.org/10.3934/environsci.2015.2.374>.
- Mohaupt, V., Völker, J., Altenburger, R., Birk, S., Kirst, I., Kühnel, D. et al. (2020). *Pesticides in European Rivers, Lakes and Groundwaters – Data Assessment*. ETC/ICM Technical Report 1/2020. <https://www.eionet.europa.eu/etcs/etc-icm/products/etc-icm-report-1-2020-pesticides-in-european-rivers-lakes-and-groundwaters-data-assessment>.
- Mohr, S., Berghahn, R., Feibicke, M., Meinecke, S., Ottenströer, T., Schmiedling, I. et al. (2007). Effects of the herbicide metazachlor on macrophytes and ecosystem function in freshwater pond and stream mesocosms. *Aquatic Toxicology* 82(1), 73-84. <https://doi.org/10.1016/j.aquatox.2007.02.001>.
- Mohr, S., Feibicke, M., Berghahn, R., Schmiedliche, R. and Schmidt, R. (2008). Response of plankton communities in freshwater pond and stream mesocosms to the herbicide metazachlor. *Environmental Pollution* 152(3), 530-542. <https://doi.org/10.1016/j.envpol.2007.07.010>.
- Montgomery, G.A., Dunn, R.R., Fox, R., Jongejans, E., Leather, S.R., Saunders, M.E. et al. (2020). Is the insect apocalypse upon us? How to find out. *Biological Conservation* 241, 108327. <https://doi.org/10.1016/j.biocon.2019.108327>.
- Morrissey, C.A., Mineau, P., Devries, J.H., Sánchez-Bayo, F., Liess, M., Cavallaro, M.C. and Liber, K. (2015). Neonicotinoid contamination of global surface waters and associated risk to aquatic invertebrates: A review. *Environment International* 74, 291-303. <https://doi.org/10.1016/j.envint.2014.10.024>.
- Mostafalou, S. and Abdollahi, M. (2013). Pesticides and human chronic diseases: Evidences, mechanisms, and perspectives. *Toxicology and Applied Pharmacology* 268(2), 157-177. <https://doi.org/10.1016/j.taap.2013.01.025>.
- Mota-Sanchez, D. and Wise, J.C. (2019). Arthropod Pesticide Resistance Database. *Michigan State University*. <http://www.pesticideresistance.org>. Accessed 20 December 2020.
- Moutinho, M.F., de Almeida, E.A., Espíndola, E.L.G., Daam, M.A. and Schiesari, L. (2020). Herbicides employed in sugarcane plantations have lethal and sublethal effects to larval *Boana pardalis* (Amphibia, Hylidae). *Ecotoxicology* 29, 1043-1051. <https://doi.org/10.1007/s10646-020-02226-z>.
- Nakayama, S.M.M., Morita, A., Ikenaka, Y., Mizukawa, H. and Ishizuka, M. (2019). A review: Poisoning by anticoagulant rodenticides in non-target animals globally. *Journal of Veterinary Medical Science* 81(2), 298-313. <https://doi.org/10.1292/jvms.17-0717>.
- National Academies of Sciences, Engineering and Medicine (2016). *Genetically Engineered Crops: Experiences and Prospects*. Washington D.C.: National Academies Press. <https://doi.org/10.17226/23395>.
- National Poisons Information Service (United Kingdom) (2019). *National Poisons Information Service Report 2018/19*. <https://www.npis.org/Download/NPISAnnualReport2018-19.pdf>.
- National Research Council (2013). *Assessing Risks to Endangered and Threatened Species from Pesticides*. Washington, D.C.: National Academies Press. <https://doi.org/10.17226/18344>.
- Neher, D.A. and Barbercheck, M.E. (2019). Soil microarthropods and soil health: Intersection of decomposition and pest suppression in agroecosystems. *Insects* 10(10), 414. <https://doi.org/10.3390/insects10120414>.
- Nelson, R., Wiesner-Hanks, T., Wissler, R. and Balint-Kurti, P. (2018). Navigating complexity to breed disease-resistant crops. *Nature Reviews Genetics* 19, 21-33. <https://doi.org/10.1038/nrg.2017.82>.
- Nesser, G.A.A., Abdelbagi, A.O., Hammad, A.M.A., Tagelseed, M. and Laing, M.D. (2016). Levels of pesticides residues in the White Nile water in the Sudan. *Environmental Monitoring and Assessment* 188, 374. <https://doi.org/10.1007/s10661-016-5367-3>.
- Netherlands Environmental Assessment Agency (2019). *Geïntegreerde gewasbescherming Nader Beschouwd – Tussenevaluatie van de Nota Gezonde Groei, Duurzame Oogst* (Integrated Pest Management Closer Considered – Interim Evaluation of the Policy for Healthy Growth and Sustainable Yield). The Hague, The Netherlands: Netherlands Environmental Assessment Agency (PBL) (in Dutch). <https://www.pbl.nl/publicaties/geintegreerde-gewasbescherming-nader-beschouwd>.
- New Zealand Food Safety (2020). *Food Residues Survey Programme Final Report – Results for 1 July 2017-30 June 2019 for Plant Based Foods*. <https://www.mpi.govt.nz/dmsdocument/40274-2017-2019-plant-based-foods-survey-final-report>.
- New Zealand Food Safety (n.d.). Food monitoring and surveillance. <https://www.mpi.govt.nz/food-safety/food-monitoring-and-surveillance/>. Accessed 26 December 2020.
- North, A.C., Hodgson, D.J., Price, S.J. and Griffiths, A.G.F. (2015). Anthropogenic and ecological drivers of amphibian disease (Ranavirosis). *PLoS ONE* 10(6), e0127037. <https://doi.org/10.1371/journal.pone.0127037>.

- Ntzani, E.E., Chondrogiorgi, M., Ntritsos, G., Evangelou, E. and Tzoulaki, I. (2013). Literature review on epidemiological studies linking exposure to pesticides and health effects. *EFSA Supporting Publications* 10(10), 497e. <https://efsa.onlinelibrary.wiley.com/doi/abs/10.2903/sp.efsa.2013.EN-497>.
- Ntzani, E.E., Markozannes, G., Tagas, C., Rizos, E. and Karalexi, M. (2020). Epidemiological evidence review report: Exposure to pesticides and fertilizers and human health – Part A. Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina, Greece. Supporting document to this review (*Environmental and Health Impacts of Pesticides and Fertilizers and Ways of Minimizing Them*).
- Nuyttens, D., Devarrewaere, W., Verboven, P. and Foqué, D. (2013). Pesticide-laden dust emission and drift from treated seeds during seed drilling: A review. *Pest Management Science* 69(5), 564-575. [https://www.researchgate.net/publication/235777972\\_Pesticide-laden\\_dust\\_emission\\_and\\_drift\\_from\\_treated\\_seeds\\_during\\_seed\\_drilling\\_A\\_review](https://www.researchgate.net/publication/235777972_Pesticide-laden_dust_emission_and_drift_from_treated_seeds_during_seed_drilling_A_review).
- Nygård, T., Sandercock, B.K., Reinsborg, T. and Einvik, K. (2019). Population recovery of peregrine falcons in central Norway in the 4 decades since the DDT-ban. *Ecotoxicology* 28, 1160-1168. <https://doi.org/10.1007/s10646-019-02111-4>.
- Odendaal, C., Seaman, M.T., Kemp, G., Patterton, H.E. and Patterton, H.G. (2015). An LC-MS/MS based survey of contaminants of emerging concern in drinking water in South Africa. *South African Journal of Science* 111(9-10). [https://www.researchgate.net/publication/282313442\\_An\\_LC-MSMS\\_based\\_survey\\_of\\_contaminants\\_of\\_emerging\\_concern\\_in\\_drinking\\_water\\_in\\_South\\_Africa](https://www.researchgate.net/publication/282313442_An_LC-MSMS_based_survey_of_contaminants_of_emerging_concern_in_drinking_water_in_South_Africa).
- Ogada, D., Botha, A. and Shaw, P. (2016). Ivory poachers and poison: drivers of Africa's declining vulture populations. *Oryx* 50(4), 593-596. <https://doi.org/10.1017/s0030605315001209>.
- Ogada, D., Shaw, P., Beyers, R.L., Buij, R., Murn, C., Thiollay, J.M. et al. (2016). Another continental vulture crisis: Africa's vultures collapsing toward extinction. *Conservation Letters* 9(2), 89-97 <https://conbio.onlinelibrary.wiley.com/doi/full/10.1111/conl.12182>.
- Ogada, D.L. (2014). The power of poison: Pesticide poisoning of Africa's wildlife. *Annals of the New York Academy of Sciences* 1322, 1-20. [https://www.researchgate.net/publication/261476784\\_The\\_power\\_of\\_poison\\_Pesticide\\_poisoning\\_of\\_Africa%27s\\_wildlife](https://www.researchgate.net/publication/261476784_The_power_of_poison_Pesticide_poisoning_of_Africa%27s_wildlife).
- Ohlander, J., Fuhriemann, S., Basinas, I., Cherrie, J.W., Galea, K.S., Povey, A.C. et al. (2020). Systematic review of methods used to assess exposure to pesticides in occupational epidemiology studies, 1993-2017. *Occupational and Environmental Medicine* 77(6), 357-367. <http://dx.doi.org/10.1136/oemed-2019-105880>.
- Ojemaye, C.Y., Onwordi, C.T., Pampanin, D.M., Sydnes, M.O. and Petrik, L. (2020). Presence and risk assessment of herbicides in the marine environment of Camps Bay (Cape Town, South Africa). *Science of The Total Environment* 738, 140346. <https://doi.org/10.1016/j.scitotenv.2020.140346>.
- Oliveira Jardim, A.N., Brito, A.P., van Donkersgoed, G., Boon, P.E. and Caldas, E.D. (2018a). Dietary cumulative acute risk assessment of organophosphorus, carbamates and pyrethroids insecticides for the Brazilian population. *Food and Chemical Toxicology* 112, 108-117. <https://doi.org/10.1016/j.fct.2017.12.010>.
- Oliveira Jardim, A.N., Mello, D.C., Brito, A.P., van der Voet, H., Boon, P.E. and Caldas, E.D. (2018b). Probabilistic dietary risk assessment of triazole and dithiocarbamate fungicides for the Brazilian population. *Food and Chemical Toxicology* 118, 317-327. <https://doi.org/10.1016/j.fct.2018.05.002>.
- Organisation for Economic Co-operation and Development (2004). *OECD Guidelines for the Testing of Chemicals - Test No. 312: Leaching in Soil Columns*. [https://www.oecd-ilibrary.org/environment/test-no-312-leaching-in-soil-columns\\_9789264070561-en](https://www.oecd-ilibrary.org/environment/test-no-312-leaching-in-soil-columns_9789264070561-en).
- Ortiz-Santaliestra, M.E., Maia, J.P., Egea-Serrano, A. and Lopes, I. (2018). Validity of fish, birds and mammals as surrogates for amphibians and reptiles in pesticide toxicity assessment. *Ecotoxicology* 27, 819-833. <https://doi.org/10.1007/s10646-018-1911-y>.
- Orton, F. and Tyler, C.R. (2015). Do hormone-modulating chemicals impact on reproduction and development of wild amphibians? *Biological Reviews* 90, 1100-1117. <https://doi.org/10.1111/brv.12147>.
- Osei-Fosu, P., Donkor, A.K., Nyarko, S., Nazzah, N.K., Asante, I.K., Kingsford-Adabo, R. and Arkorful, N.A. (2014). Monitoring of pesticide residues of five notable vegetables at Agboghloshie market in Accra, Ghana. *Environmental Monitoring and Assessment* 186(11), 7157-7163. <https://doi.org/10.1007/s10661-014-3917-0>.
- Osterman, J., Wintermantel, D., Locke, B., Jonsson, O., Semberg, E., Onorati, P. et al. (2019). Clothianidin seed-treatment has no detectable negative impact on honeybee colonies and their pathogens. *Nature Communications* 10, 692. <https://doi.org/10.1038/s41467-019-08523-4>.
- Pan, L., Sun, J., Li, Z., Zhan, Y., Xu, S. and Zhu, L. (2018). Organophosphate pesticide in agricultural soils from the Yangtze River Delta of China: Concentration, distribution, and risk assessment. *Environmental Science and Pollution Research* 25(1), 4-11. <https://doi.org/10.1007/s11356-016-7664-3>.
- Pannell, D.J., Tillie, P., Rodriguez-Cerezo, E., Ervin, D. and Frisvold, G. (2016). Herbicide resistance: Economic and environmental challenges. *AgBioForum* 19(2), 136-155. [https://www.researchgate.net/publication/316669609\\_Herbicide\\_Resistance\\_Economic\\_and\\_Environmental\\_Challenges\\_AgBioForum\\_19\\_2\\_136-155](https://www.researchgate.net/publication/316669609_Herbicide_Resistance_Economic_and_Environmental_Challenges_AgBioForum_19_2_136-155).
- Park, M.G., Blitzer, E.J., Gibbs, J., Losey, J.E. and Danforth, B.N. (2015). Negative effects of pesticides on wild bee communities can be buffered by landscape context. *Proceedings of the Royal Society B: Biological Sciences* 282, 20150299. <http://dx.doi.org/10.1098/rspb.2015.0299>.
- Parsons, A.E., Escobar-Lux, R.H., Sævik, P.N., Samuelsen, O.B. and Agnalt, A.L. (2020). The impact of anti-sea lice pesticides, azamethiphos and deltamethrin, on European lobster (*Homarus gammarus*) larvae in the Norwegian marine environment. *Environmental Pollution* 264, 114725. <https://doi.org/10.1016/j.envpol.2020.114725>.

- Parsons, K.C., Mineau, P. and Renfrew, R.B. (2010). Effects of pesticide use in rice fields on birds. *Waterbirds* 33 (Special Publication 1), 193-218. <https://doi.org/10.1675/063.033.s115>.
- Pasiani, J.O., Torres, P., Silva, J.R., Diniz, B.Z. and Caldas, E.D. (2012). Knowledge, attitudes, practices and biomonitoring of farmers and residents exposed to pesticides in Brazil. *International Journal of Environmental Research and Public Health* 24(9), 3051-3068. <https://doi.org/10.3390/ijerph9093051>.
- Peakall, D.B. (1993). DDE-induced eggshell thinning: An environmental detective story. *Environmental Reviews* 1(1),13-20. <https://www.jstor.org/stable/envirevi.1.1.13?seq=1>.
- Peeters, F.M., Qu Mengmeng, Piao Xiuying, Valk, H. van der and Tao Chuanjiang (2014). *Environmental Risk Assessment Handbook for Pesticide Registration in China*. Alterra report 2558. Wageningen: Wageningen University and Research Centre. <http://content.alterra.wur.nl/Webdocs/PDFFiles/Alterrarapporten/AlterraRapport2558.pdf>.
- Pelch, K.E., Beeman, J.M., Niebruegge, B.A., Winkler, S.R. and Nagel, S.C. (2011). Endocrine-disrupting chemicals (EDCs) in mammals. *Hormones and Reproduction of Vertebrates* 5(5), 329-371. <https://doi.org/10.1016/B978-0-12-374928-4.10014-8>.
- Pelosi, C., Barot, S., Capowiez, Y., Hedde, M. and Vandenbulcke, F. (2014). Pesticides and earthworms. A review. *Agronomy for Sustainable Development* 34(1), 199-228. <https://doi.org/10.1007/s13593-013-0151-z>.
- Pelosi, C., Bertrand, C., Daniele, G., Coeurdassier, M., Benoit, P., Nélieu, S. et al. (2021). Residues of currently used pesticides in soils and earthworms: A silent threat? *Agriculture, Ecosystems and Environment* 305, 107167. <https://doi.org/10.1016/j.agee.2020.107167>.
- Pérez-Lucas, G., Vela, N., Aatik, A. El, and Navarro, S. (2018). Environmental risk of groundwater pollution by pesticide leaching through the soil profile. In *Pesticides - Use and Misuse and Their Impact in the Environment*. Larramendy, M.L. and Soloneski, S. (eds). London: IntechOpen. Chapter 3. <https://doi.org/10.5772/intechopen.82418>.
- Perry, L., Adams, R.D., Bennett, A.R., Lupton, D.J., Jackson, G., Good, A.M. et al. (2014). National toxicovigilance for pesticide exposures resulting in health care contact – An example from the UK's National Poisons Information Service. *Clinical Toxicology* 52(5), 549-555. <https://doi.org/10.3109/15563650.2014.908203>.
- Persson, H.E., Sjöberg, G.K., Haines, J.A. and Pronczuk de Garbino, J. (1998). Poisoning severity score – Grading of acute poisoning. *Clinical Toxicology* 36(3), 205-213. <https://doi.org/10.3109/15563659809028940>.
- Pesticide Action Network Asia Pacific (2010). *Communities in Peril – Global Report on Health Impacts of Pesticide Use in Agriculture*. [http://www.panna.org/sites/default/files/PAN-Global-Report\\_0.pdf](http://www.panna.org/sites/default/files/PAN-Global-Report_0.pdf).
- Pesticide Action Network UK (2020). *Acute Pesticide Poisoning Among Smallholder Farmers and Farmworkers – A Review of 13 Studies in EECCA and Africa*. <https://www.pan-uk.org/acute-pesticide-poisoning-among-smallholder-farmers>.
- Peters, B., Gao, Z. and Zumkier, U. (2016). Large-scale monitoring of effects of clothianidin-dressed oilseed rape seeds on pollinating insects in Northern Germany: Effects on red mason bees (*Osmia bicornis*). *Ecotoxicology* 25, 1679-1690. <https://doi.org/10.1007/s10646-016-1729-4>.
- Peters, K., Bundschuh, M. and Schäfer, R.B. (2013). Review on the effects of toxicants on freshwater ecosystem functions. *Environmental Pollution* 180. <https://doi.org/10.1016/j.envpol.2013.05.025>.
- Peveling, R. and Demba, S.A. (2003). Toxicity and pathogenicity of *Metarhizium anisopliae* var. *acridum* (Deuteromycotina, Hyphomycetes) and fipronil to the fringe-toed lizard *Acanthodactylus dumerrilli* (Squamata: Lacertidae). *Environmental Toxicology and Chemistry* 22(7), 1437-1447. <https://doi.org/10.1002/etc.5620220704>.
- Peveling, R., McWilliam, A.N., Nagel, P., Rasolomanana, H., Raholijaona, L., Rakotomianina, A. et al. (2003). Impact of locust control on harvester termites and endemic vertebrate predators in Madagascar. *Journal of Applied Ecology* 40, 729-741. <https://doi.org/10.1046/j.1365-2664.2003.00833.x>.
- Pietrzak, D., Kania, J., Malina, G., Kmiecik, E., and Wątor, K. (2019). Pesticides from the EU First and Second Watch Lists in the Water Environment. *Clean Soil, Air, Water* 47(7), 1800376. <https://doi.org/10.1002/clen.201800376>.
- Pirsaheb, M., Hossini, H., Asadi, F. and Janjani, H. (2017). A systematic review on organochlorine and organophosphorus pesticides content in water resources. *Toxin Reviews* 36(3), 210-221. <https://doi.org/10.1080/15569543.2016.1269810>.
- Pisa, L.W., Amaral-Rogers, V., Belzunces, L.P., Bonmatin, J.M., Downs, C.A., Goulson, D. et al. (2015). Effects of neonicotinoids and fipronil on non-target invertebrates. *Environmental Science and Pollution Research* 22, 68-102. <https://doi.org/10.1007/s11356-014-3471-x>.
- Pitt, W.C., Berentsen, A.R., Shiels, A.B., Volker, S.F., Eisemann, J.D., Wegmann, A.S. and Howald, G.R. (2015). Non-target species mortality and the measurement of brodifacoum rodenticide residues after a rat (*Rattus rattus*) eradication on Palmyra Atoll, tropical Pacific. *Biological Conservation* 185, 36-46. <http://dx.doi.org/10.1016/j.biocon.2015.01.008>.
- Plano de Nacional de Controle de Resíduos e Contaminantes (Brazil) (2018). Results of the national plan for control of residues and contaminants – PNCRC / Animal. Ministério da Agricultura, Pecuária e Abastecimento. <https://www.gov.br/agricultura/pt-br/assuntos/inspecao/produtos-animais/plano-de-nacional-de-controle-de-residuos-e-contaminantes/plano-de-nacional-de-controle-de-residuos-e-contaminantes>. Accessed 23 January 2020.
- Plano de Nacional de Controle de Resíduos e Contaminantes (Brazil) (n.d). PNCRC / Vegetal. Ministério da Agricultura, Pecuária e Abastecimento. [http://www.agricultura.gov.br/assuntos/inspecao/produtos-vegetal/copy\\_of\\_pncrc-vegetal](http://www.agricultura.gov.br/assuntos/inspecao/produtos-vegetal/copy_of_pncrc-vegetal). Accessed 23 January 2020.

- Plaza, P.I., Martínez-López, E. and Lambertucci, S.A. (2019). The perfect threat: Pesticides and vultures. *Science of The Total Environment* 687, 1207-1218. <https://doi.org/10.1016/j.scitotenv.2019.06.160>.
- Postigo, C. and Barceló, D. (2015). Synthetic organic compounds and their transformation products in groundwater: Occurrence, fate and mitigation. *Science of The Total Environment* 503-504, 32-47. <https://doi.org/10.1016/j.scitotenv.2014.06.019>.
- Potts, S.G., Imperatriz-Fonseca, V.L. and Ngo, H.T. (eds.) (2016). *Assessment Report of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services on Pollinators, Pollination and Food Production*. Bonn: Secretariat of the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services. <https://ipbes.net/assessment-reports/pollinators>.
- Prado, J.B., Mulay, P.R., Kasner, E.J., Bojes, H.K. and Calvert, G.M. (2017). Acute pesticide-related illness among farmworkers: Barriers to reporting to public health authorities. *Journal of Agromedicine* 22(4), 395-405. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5846675/>.
- Pruden, A., Larsson, D.G.J., Amézquita, A., Collignon, P., Brandt, K.K., Graham, D.W. et al. (2013). Management options for reducing the release of antibiotics and antibiotic resistance genes to the environment. *Environmental Health Perspectives* 121, 878-885. <http://dx.doi.org/10.1289/ehp.1206446>.
- Prüss-Ustün, A., Wolf, J., Corvalán, C., Bos, R. and Neira, M. (2016). *Preventing Disease through Healthy Environments: A Global Assessment of the Burden of Disease from Environmental Risks*. Geneva: World Health Organization. <https://www.who.int/publications/i/item/9789241565196>.
- Puglisi, E. (2012). Response of microbial organisms (aquatic and terrestrial) to pesticides. *EFA Supporting Publications* 9(11), 359E. <https://doi.org/10.2903/sp.efsa.2012.EN-359>.
- Quandt, S.A., Hernández-Valero, M.A., Grzywacz, J.G., Hovey, J.D., Gonzales, M. and Arcury, T.A. (2006). Workplace, household, and personal predictors of pesticide exposure for farmworkers. *Environmental Health Perspectives* 114, 943-952. <https://doi.org/10.1289/ehp.8529>.
- Quinn, N. (2019). Assessing individual and population-level effects of anticoagulant rodenticides on wildlife. *Human-Wildlife Interactions* 13(2), 200-211. <https://doi.org/10.26077/y9tj-ew86>.
- Ranson, H. and Lissenden, N. (2016). Insecticide resistance in African Anopheles mosquitos: a worsening situation that needs urgent action to maintain malaria control. *Trends in Parasitology* 32(2), 187-196. <http://dx.doi.org/10.1016/j.pt.2015.11.010>.
- Rauert, C., Harner, T., Schuster, J.K., Eng, A., Fillmann, G., Castillo, L.E. et al. (2018). Air monitoring of new and legacy POPs in the Group of Latin America and Caribbean (GRULAC) region. *Environmental Pollution* 243, Part B, 1252-1262. <https://doi.org/10.1016/j.envpol.2018.09.048>.
- Rhalem, N., Chaoui, H., Smlali, I., Aoued, L., El Hattimy, F., Aghandous, R. et al. (2012). Exhaustivité des données de toxicovigilance au Maroc – Implication des services de santé publique et de surveillance épidémiologique. *Toxicologie Maroc* 15, 8-15. [https://www.researchgate.net/publication/259467113\\_Exhaustivite\\_des\\_donnees\\_de\\_Toxicovigilance\\_au\\_Maroc\\_Implication\\_des\\_Services\\_de\\_Sante\\_Publique\\_Et\\_de\\_Surveillance\\_epidemiologique](https://www.researchgate.net/publication/259467113_Exhaustivite_des_donnees_de_Toxicovigilance_au_Maroc_Implication_des_Services_de_Sante_Publique_Et_de_Surveillance_epidemiologique).
- Ricci, B., Lavigne, C., Alignier, A., Aviron, S., Biju-Duval, L., Bouvier, J.C. et al. (2019). Local pesticide use intensity conditions landscape effects on biological pest control. *Proceedings of the Royal Society B: Biological Sciences*, 286(1904). <https://doi.org/10.1098/rspb.2018.2898>.
- Richards, N.L., Ogada, D., Buij, R. and Botha, A. (2018). The killing fields: the use of pesticides and other contaminants to poison wildlife in africa. *Encyclopedia of the Anthropocene* 1-5, 161-167. <https://doi.org/10.1016/b978-0-12-809665-9.09995-x>.
- Rico, A., Brock, T.C.M. and Daam, M.A. (2019). Is the effect assessment approach for fungicides as laid down in the European Food Safety Authority aquatic guidance document sufficiently protective for freshwater ecosystems? *Environmental Toxicology and Chemistry* 38, 2279-2293. <https://doi.org/10.1002/etc.4520>.
- Rico, A., Dafouz, R., Vighi, M., Rodríguez-Gil, J.L. and Daam, M.A. (2020). Use of post registration monitoring data to evaluate the ecotoxicological risks of pesticides to surface waters: A case study with Chlorpyrifos in the Iberian Peninsula. *Environmental Toxicology and Chemistry* 40(2), 500-512. <https://doi.org/10.1002/etc.4927>.
- Ripper, W.E. (1956). Effect of pesticides on the balance of arthropod populations. *Annual Review of Entomology* 1, 403-438. <https://doi.org/10.1146/annurev.en.01.010156.002155>.
- Roberts, J. and Reigart, J.R. (2013). *Recognition and Management of Pesticide Poisonings*. Sixth edition. Washington, D.C.: United States Environmental Protection Agency. [https://www.epa.gov/sites/production/files/2015-01/documents/rmpp\\_6thed\\_final\\_lowresopt.pdf](https://www.epa.gov/sites/production/files/2015-01/documents/rmpp_6thed_final_lowresopt.pdf).
- Robinson, C., Portier, C.J., Čavoški, A., Mesnage, R., Roger, A., Clausen, P. et al. (2020). Achieving a high level of protection from pesticides in Europe: Problems with the current risk assessment procedure and solutions. *European Journal of Risk Regulation* 11, 450-480. <https://doi.org/10.1017/err.2020.18>.
- Rohr, J. R. and McCoy, K. A. (2018). A qualitative meta-analysis reveals consistent effects of atrazine on freshwater fish and amphibians. *Environmental Health Perspectives* 118(1), 20-32. <http://www.jstor.com/stable/30249901>.
- Römbke, J., Schmelz, R.M. and Pélosi, C. (2017). Effects of organic pesticides on enchytraeids (Oligochaeta) in agroecosystems: Laboratory and higher-tier tests. *Frontiers in Environmental Science* 5(20), 1-23. <https://doi.org/10.3389/fenvs.2017.00020>.
- Rosic, N., Bradbury, J., Lee, M., Baltrotsky, K. and Grace, S. (2020). The impact of pesticides on local waterways: A scoping review and method for identifying pesticides in local usage. *Environmental Science and Policy* 106, 12-21. <https://doi.org/10.1016/j.envsci.2019.12.005>.

- Roubos, C.R., Rodriguez-Saona, C. and Isaacs, R. (2014). Mitigating the effects of insecticides on arthropod biological control at field and landscape scales. *Biological Control* 75, 28-38. <https://doi.org/10.1016/j.biocontrol.2014.01.006>.
- Ruddle, N., Elston, C., Klein, O., Hamberger, A. and Thompson, H. (2018). Effects of exposure to winter oilseed rape grown from thiamethoxam-treated seed on the red mason bee *Osmia bicornis*. *Environmental Toxicology and Chemistry* 37(4), 1071-1083. <https://doi.org/10.1002/etc.4034>.
- Rusch, A., Valantin-Morison, M., Sarthou, J.-P. and Roger-Estrade, J. (2010). Biological control of insect pests in agroecosystems: Effects of crop management, farming systems, and seminatural habitats at the landscape scale: A review. In *Advances in Agronomy vol 109*. Sparks, D.L. (ed.). Academic Press. Chapter 6, 219-259. <https://www.sciencedirect.com/science/article/pii/B9780123850409000062>.
- Sackaria, M. and Elango, L. (2020). Organic micropollutants in groundwater of India – A review. *Water Environment Research* 92(4), 504-523. <https://doi.org/10.1002/wer.1243>.
- Sánchez-Bayo, F., Goka, K. and Hayasaka, D. (2016). Contamination of the aquatic environment with neonicotinoids and its implication for ecosystems. *Frontiers in Environmental Science* 4(71), 1-14. <https://doi.org/10.3389/fenvs.2016.00071>.
- Sánchez-Bayo, F. and Hyne, R.V. (2011). Comparison of environmental risks of pesticides between tropical and nontropical regions. *Integrated Environmental Assessment and Management* 7(4), 577-586. <https://doi.org/10.1002/ieam.189>.
- Sánchez-Bayo, F. and Tennekes, H.A. (2020). Time-cumulative toxicity of neonicotinoids: Experimental evidence and implications for environmental risk assessments. *International Journal of Environmental Research and Public Health* 17(5), 1629. <https://doi.org/10.3390/ijerph17051629>.
- Sánchez-Bayo, F. and Wyckhuys, K.A.G. (2019). Worldwide decline of the entomofauna: A review of its drivers. *Biological Conservation* 232, 8-27. <https://doi.org/10.1016/j.biocon.2019.01.020>.
- Sapbamrer, R. and Hongsibsong, S. (2014). Organophosphorus pesticide residues in vegetables from farms, markets, and a supermarket around Kwan Phayao Lake of Northern Thailand. *Archives of Environmental Contamination and Toxicology* 67(1), 60-67. <https://doi.org/10.1007/s00244-014-0014-x>.
- Sapbamrer, R. and Thammachai, A. (2020). Factors affecting use of personal protective equipment and pesticide safety practices: A systematic review. *Environmental Research* 185, 109444. <https://doi.org/10.1016/j.envres.2020.109444>.
- Sattler, C., Gianuca, A.T., Schweiger, O., Franzén, M. and Settele, J. (2020). Pesticides and land cover heterogeneity affect functional group and taxonomic diversity of arthropods in rice agroecosystems. *Agriculture, Ecosystems and Environment* 297, 106927. <https://doi.org/10.1016/j.agee.2020.106927>.
- Schäfer, R.B. (2019). Responses of freshwater macroinvertebrates to pesticides: Insights from field studies. *Current Opinion in Environmental Science and Health* 11, 1-7. <https://doi.org/10.1016/j.coesh.2019.06.001>.
- Schäfer, R.B., Liess, M., Altenburger, R., Filser, J., Hollert, H., Roß-Nickoll, M., Schäfer, A. and Scheringer, M. (2019). Future pesticide risk assessment: Narrowing the gap between intention and reality. *Environmental Sciences Europe* 31(21), 1-5. <https://doi.org/10.1186/s12302-019-0203-3>.
- Schäfer, R.B., van den Brink, P.J. and Liess, M. (2011). Impacts of pesticides on freshwater ecosystems. In *Ecological Impacts of Toxic Chemicals*. Sánchez Bayo, F., van den Brink, P.J. and Mann, R.M. (eds.). Bentham Science. Chapter 6, 111-137. <https://www.eurekaselect.com/51450/chapter/impacts-of-pesticides-on-freshwater-ecosystems>.
- Schäfer, R.B., von der Ohe, P.C., Rasmussen, J., Kefford, B.J., Beketov, M.A., Schulz, R. and Liess, M. (2012). Thresholds for the effects of pesticides on invertebrate communities and leaf breakdown in stream ecosystems. *Environmental Science and Technology* 46(9), 5134-5142. <https://doi.org/10.1021/es2039882>.
- Schepker, T.J., Webb, E.B., Tillitt, D. and LaGrange, T. (2020). Neonicotinoid insecticide concentrations in agricultural wetlands and associations with aquatic invertebrate communities. *Agriculture, Ecosystems and Environment* 287, 106678. <https://doi.org/10.1016/j.agee.2019.106678>.
- Schiesari, L. and Corrêa, D.T. (2016). Consequences of agroindustrial sugarcane production to freshwater biodiversity. *GCB-Bioenergy* 8(3), 644-657. <https://doi.org/10.1111/gcbb.12279>.
- Schreiner, V.C., Link, M., Kunz, S., Szöcs, E., Scharmüller, A., Vogler, B. et al. (2021). Paradise lost? Pesticide pollution in a European region with considerable amount of traditional agriculture. *Water Research* 188(116528), 1-10. <https://doi.org/10.1016/j.watres.2020.116528>.
- Science Advice for Policy by European Academies (SAPEA) (2018). *Improving Authorisation Processes for Plant Protection Products in Europe: A Scientific Perspective on the Potential Risks to Human Health*. <https://allea.org/portfolio-item/improving-authorisation-processes-for-plant-protection-products-in-europe-a-scientific-perspective-on-the-assessment-of-potential-risk-to-human-health/?cn-reloaded=1>.
- Secretariat of the Convention on Biological Diversity (2020). *Global Biodiversity Outlook 5*. <https://www.cbd.int/gbo5>.
- Settimi, L., Orford, R., Davanzo, F., Hague, C., Desel, H., Pelclova, D. et al. (2016). Development of a new categorization system for pesticides exposure to support harmonized reporting between EU Member States. *Environment International* 91, 332-340. <https://doi.org/10.1016/j.envint.2016.02.034>.
- Settle, W.H., Ariawan, H., Astuti, E.T., Cahyana, W., Hakim, A.L., Hindayana, D. et al. (1996). Managing tropical rice pests through conservation of generalist natural enemies and alternative prey. *Ecology* 77(7), 1975-1988. <https://doi.org/10.2307/2265694>.

- Shore, R.F. and Coeurdassier, M. (2018). Primary exposure and effects in non-target animals. In *Anticoagulant Rodenticides and Wildlife. Emerging Topics in Ecotoxicology (Principles, Approaches and Perspectives) vol 5*. van den Brink, N.W., Elliott, J.E., Shore, R.F. and Rattner, B.A. (eds.). Cham: Springer. Chapter 6, 135-157. [https://link.springer.com/chapter/10.1007/978-3-319-64377-9\\_7](https://link.springer.com/chapter/10.1007/978-3-319-64377-9_7).
- Shunthirasingham, V., Oyiliagu, C.E., Cao, Z., Gouin, T., Wania, F., Lee, S.-C. *et al.* (2010). Spatial and temporal pattern of pesticides in the global atmosphere. *Journal of Environmental Monitoring* 12, 1650-1657. <https://doi.org/10.1039/C0EM00134A>.
- Siddique, A., Liess, M., Shahid, N. and Becker, J.M. (2020). Insecticides in agricultural streams exert pressure for adaptation but impair performance in *Gammarus pulex* at regulatory acceptable concentrations. *Science of The Total Environment* 722, 137750. <https://doi.org/10.1016/j.scitotenv.2020.137750>.
- Sieke, C., Michalski, B. and Kuhl, T. (2018). Probabilistic dietary risk assessment of pesticide residues in foods for the German population based on food monitoring data from 2009 to 2014. *Journal of Exposure Science and Environmental Epidemiology* 28(1), 46-54. <https://doi.org/10.1038/jes.2017.7>.
- Silva, V., Mol, H.G.J., Zomer, P., Tienstra, M., Ritsema, C.J. and Geissen, V. (2019). Pesticide residues in European agricultural soils – A hidden reality unfolded. *Science of The Total Environment* 653, 1532-1545. <https://doi.org/10.1016/j.scitotenv.2018.10.441>.
- Sjerps, R.M.A., Kooij, P.J.F., van Loon, A. and Van Wezel, A.P. (2019). Occurrence of pesticides in Dutch drinking water sources. *Chemosphere* 235, 510-518. <https://doi.org/10.1016/j.chemosphere.2019.06.207>.
- Skovgaard, M., Renjel Encinas, S., Jensen, O.C., Andersen, J.H., Condarco, G. and Jørs, E. (2017). Pesticide residues in commercial lettuce, onion, and potato samples from Bolivia – A threat to public health? *Environmental Health Insights* 11, 1-8. <https://doi.org/10.1177/1178630217704194>.
- Slama, R., Bourguignon, J.-P., Demeneix, B., Ivell, R., Panzica, G., Kortenkamp, A. and Zoeller, R.T. (2016). Scientific issues relevant to setting regulatory criteria to identify endocrine-disrupting substances in the European Union. *Environmental Health Perspectives* 124(10), 1497-1503. <http://dx.doi.org/10.1289/EHP217>.
- Sonne, C., Siebert, U., Gonnens, K., Desforges, J.-P., Eulaers, I., Persson, S. *et al.* (2020). Health effects from contaminant exposure in Baltic Sea birds and marine mammals: A review. *Environment International* 139, 105725. <https://doi.org/10.1016/j.envint.2020.105725>.
- Spiller, K.J. and Dettmers, R. (2019). Evidence for multiple drivers of aerial insectivore declines in North America. *The Condor: Ornithological Applications* 121(2), 1-13. <https://doi.org/10.1093/condor/duz010>.
- Spillsbury, F.D., Warne, M.S.J. and Backhaus, T. (2020). Risk assessment of pesticide mixtures in Australian rivers discharging to the Great Barrier Reef. *Environmental Science and Technology* 54 (22), 14361-14371. <https://doi.org/10.1021/acs.est.0c04066>.
- Staley, Z.R., Harwood, V.J. and Rohr, J.R. (2015). A synthesis of the effects of pesticides on microbial persistence in aquatic ecosystems. *Critical Reviews in Toxicology* 45(10), 813-836. <https://doi.org/10.3109/10408444.2015.1065471>.
- Stanton, R.L., Morrissey, C.A. and Clark, R.G. (2018). Analysis of trends and agricultural drivers of farmland bird declines in North America: A review. *Agriculture, Ecosystems and Environment* 254, 244-254. <https://doi.org/10.1016/j.agee.2017.11.028>.
- Stehle, S. and Schulz, R. (2015). Agricultural insecticides threaten surface waters at the global scale. *Proceedings of the National Academy of Sciences of the United States of America* 112(18), 5750-5755. <https://doi.org/10.1073/pnas.1500232112>.
- Stehle, S., Bub, S. and Schulz, R. (2018). Compilation and analysis of global surface water concentrations for individual insecticide compounds. *Science of The Total Environment* 639, 516-525. <https://doi.org/10.1016/j.scitotenv.2018.05.158>.
- Stehle, S., Knäbel, A. and Schulz, R. (2013). Probabilistic risk assessment of insecticide concentrations in agricultural surface waters: A critical appraisal. *Environmental Monitoring and Assessment* 185(8), 6295-6310. <https://doi.org/10.1007/s10661-012-3026-x>.
- Stockwell, V.O. and Duffy, B. (2012). Use of antibiotics in plant agriculture. *Revue Scientifique et Technique, World Organization for Animal Health (OIE)*. 31(1), 199-210. <https://doc.oie.int/seam/resource/directMedia/7KydABGWigpmB6PIAoDoAhshrFrZIn-ujsessionid=1d60b632a935cedf58f7088cbd43?binaryFileId=10947&cid=1990>.
- Stokstad, R. (2013). The war against weeds down under. *Science* 341(6147), 734-736 <https://doi.org/10.1126/science.341.6147.734>. In Special Issue: Smarter Pest Control. <https://www.sciencemag.org/site/special/pesticides/index.xhtml>.
- Stone, W.W., Gilliom, R.J. and Ryberg, K.R. (2014). Pesticides in U.S. streams and rivers: Occurrence and trends during 1992-2011. *Environmental Science and Technology* 48 (19), 11025-11030. <https://doi.org/10.1021/es5025367>.
- Storck, V., Karpouzias, D.G. and Martin-Laurent, F. (2017). Towards a better pesticide policy for the European Union. *Science of the Total Environment* 575, 1027-1033. <http://dx.doi.org/10.1016/j.scitotenv.2016.09.167>.
- Sud, M. (2020). *Managing the Biodiversity Impacts of Fertiliser and Pesticide use – Overview and Insights from Trends and Policies across Selected OECD Countries*. OECD Environment Working Paper No. 155. Paris: Organisation of Economic Co-operation and Development. <https://dx.doi.org/10.1787/63942249-en>.
- Sun, J., Pan, L., Tsang, D.C.W., Zhan, Y., Zhu, L. and Li, X. (2018). Organic contamination and remediation in the agricultural soils of China: A critical review. *Science of The Total Environment* 615, 724-740. <https://doi.org/10.1016/j.scitotenv.2017.09.271>.

- Sun, Y., Cao, M., Wan, Y., Wang, H., Liu, J., Pan, F. *et al.* (2020). Spatial variation of 2,4-D and MCPA in tap water and groundwater from China and their fate in source, treated, and tap water from Wuhan, Central China. *Science of The Total Environment* 727, 138691. <https://doi.org/10.1016/j.scitotenv.2020.138691>.
- Székács, A., Mörtl, M. and Darvas, B. (2015). Monitoring pesticide residues in surface and ground water in Hungary: Surveys in 1990-2015. *Journal of Chemistry* 2015, 717948. <https://doi.org/10.1155/2015/717948>.
- Tabashnik, B.E. and Carrière, Y. (2017). Surge in insect resistance to transgenic crops and prospects for sustainability. *Nature Biotechnology* 35(10), 926-935. <https://doi.org/10.1038/nbt.3974>.
- Tabashnik, B.E. and Carrière, Y. (2019). Global patterns of resistance to Bt crops highlighting pink bollworm in the United States, China, and India. *Journal of Economic Entomology* 112(6), 2513-2523. <https://doi.org/10.1093/jee/toz173>.
- Taiwo, A.M. (2019). A review of environmental and health effects of organochlorine pesticide residues in Africa. *Chemosphere* 220, 1126-1140. <https://doi.org/10.1016/j.chemosphere.2019.01.001>.
- Tang, W., Wang, D., Wang, J., Wu, Z., Li, L., Huang, M. *et al.* (2018). Pyrethroid pesticide residues in the global environment: An overview. *Chemosphere* 191 (308), 990-1007. <https://doi.org/10.1016/j.chemosphere.2017.10.115>.
- Tassin de Montaigu, C. and Goulson, D. (2020). Identifying agricultural pesticides that may pose a risk for birds. *PeerJ* 8, e9526. <https://doi.org/10.7717/peerj.9526>.
- Taylor, P. and Reeder, R. (2020). Antibiotic use on crops in low and middleincome countries based on recommendations made by agricultural advisors. *CABI Agriculture and Bioscience* 1, 1. <https://doi.org/10.1186/s43170-020-00001-y>.
- Teyssere, R., Manangama, G., Baldi, I., Carles, C., Brochard, P., Bedos, C. and Delva, F. (2020). Assessment of residential exposures to agricultural pesticides: A scoping review. *PLoS ONE* 15(4), e0232258. <https://doi.org/10.1371/journal.pone.0232258>.
- Thundiyil, J.G., Stober, J., Besbelli, N. and Pronczuk, J. (2008). Acute pesticide poisoning: A proposed classification tool. *Bulletin of the World Health Organization* 86, 205-209. <https://apps.who.int/iris/handle/10665/270154>.
- Toccalino, P.L., Gilliom, R.J., Lindsey, B.D. and Rupert, M.G. (2014). Pesticides in groundwater of the United States: Decadal-scale changes, 1993- 2011. *Ground Water* 52, 112-125. <https://doi.org/10.1111/gwat.12176>.
- Todd, B.D., Willson, J.D. and Gibbons, J.W. (2010). The global status of reptiles and causes of their decline. In *Ecotoxicology of Amphibians and Reptiles*. Third edition. Sparling, D.W., Bishop, C.A. and Krest, S. (eds.). Pensacola, FL: CRC Press. 47-67. <https://www.routledge.com/Ecotoxicology-of-Amphibians-and-Reptiles/Sparling-Linder-Bishop-Krest/p/book/9781420064162>.
- Tomenson, J.A. and Matthews, G.A. (2009). Causes and types of health effects during the use of crop protection chemicals: Data from a survey of over 6,300 smallholder applicators in 24 different countries. *International Archives of Occupational and Environmental Health* 89, 935-949. <https://doi.org/10.1007/s00420-009-0399-4>.
- Topping, C.J., Aldrich, A. and Berny, P. (2020). Overhaul environmental risk assessment for pesticides. *Science* 367(6476), 360-363. <https://doi.org/10.1126/science.aay1144>.
- Trudeau, V.L., Thomson, P., Zhang, W.S., Reynaud, S., Navarro-Martin, L. and Langlois, V.S. (2020). Agrochemicals disrupt multiple endocrine axes in amphibians. *Molecular and Cellular Endocrinology* 513, 110861. <https://doi.org/10.1016/j.mce.2020.110861>.
- Tuck, S.L., Winqvist, C., Mota, F., Ahnström, J., Turnbull, L.A. and Bengtsson, J. (2013). Land-use intensity and the effects of organic farming on biodiversity: A hierarchical meta-analysis. *Journal of Applied Ecology* 51, 746-755. <https://doi.org/10.1111/1365-2664.12219>.
- Tyrell, K., Willis, S., Williamson, S., Vodouhe, D.S. and Youdeowei, A. (2019). Monitoring and minimizing health risks related to pesticides. In *Integrated Management of Insect Pests: Current and Future Developments*. Kogan, M. and Heinrichs, E.A. (eds.). Cambridge, UK: Burleigh Dodds Science Publishing. Chapter 21 <https://shop.bdsublishing.com/store/bds/detail/product/3-190-9781838799564>.
- Uman, L.S. (2011). Systematic Reviews and Meta-Analyses. *Journal of the American Academy of Child and Adolescent Psychiatry* 20(1), 57-59. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3024725/>.
- United Nations Environment Programme (2017a). *Second Global Monitoring Report: Global Monitoring Plan for Persistent Organic Pollutants*. UNEP/POPS/COP.8/INF/38. <http://chm.pops.int/Implementation/GlobalMonitoringPlan/MonitoringReports/tabid/525/Default.aspx>.
- United Nations Environment Programme (2017b). *Overview Report I: Worldwide initiatives to identify endocrine disrupting chemicals (EDCs) and potential EDCs*. Prepared by: The International Panel on Chemical Pollution (IPCP). <https://www.unenvironment.org/explore-topics/chemicals-waste/what-we-do/emerging-issues/scientific-knowledge-endocrine-disrupting>.
- United Nations Environment Programme (2018). *Resolution 3/4 on Environment and Health*. UNEP/EA.3/Res.4. [https://wedocs.unep.org/bitstream/handle/20.500.11822/30795/UNEA3\\_4EN.pdf?sequence=1&isAllowed=y](https://wedocs.unep.org/bitstream/handle/20.500.11822/30795/UNEA3_4EN.pdf?sequence=1&isAllowed=y).
- United Nations Environment Programme (2020). Pesticide poisoning – Data from poison centres and national poisoning statistics. Working document for the UNEP report, *Environmental and Health Effects of Pesticides and Fertilizers and Ways to Minimize Them*; version: 25 January 2021. Supporting document to *Environmental and Health Impacts of Pesticides and Fertilizers and Ways of Minimizing Them*. <https://www.unep.org/resources/report/environmental-and-health-impacts-pesticides-and-fertilizers-and-ways-minimizing>.

- United Nations Environment Programme (2022). *Synthesis Report on Environmental and Health Impacts of Pesticides and Fertilizers and Ways of Minimizing Them*. <https://www.unep.org/resources/report/environmental-and-health-impacts-pesticides-and-fertilizers-and-ways-minimizing>.
- United Nations Environment Programme and World Health Organization (2012). *State of the Science of Endocrine Disrupting Chemicals – An Assessment of the State of the Science of Endocrine Disruptors Prepared by a Group of experts for the United Nations Environment Programme and World Health Organization*. Bergman, Å, Heindel, J.J., Jobling, S., Kidd, K.A. and Zoeller, R.T. (eds.) Nairobi and Geneva. <https://www.who.int/ceh/publications/endocrine/en/>.
- United States Department of Agriculture (2019). *Pesticide Data Program Annual Summary, Calendar Year 2018*. <https://www.ams.usda.gov/reports/pdp-annual-summary-reports>.
- United States Environmental Protection Agency (2016). *Generic Ecological Assessment Endpoints (GAEs) for Ecological Risk Assessment: Second Edition with Generic Ecosystem Services Endpoints Added*. [https://www.epa.gov/sites/production/files/2016-08/documents/geae\\_2nd\\_edition.pdf](https://www.epa.gov/sites/production/files/2016-08/documents/geae_2nd_edition.pdf).
- United States Environmental Protection Agency (2017). DEEM-FCID/Calendex Software Installer. <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/deem-fcidcalendex-software-installer>. Accessed 26 December 2020.
- United States Environmental Protection Agency (2020a). Pesticide chemical search: conventional, antimicrobial and biopesticide active ingredients. <https://ofmpub.epa.gov/apex/pesticides/f?p=chemicalsearch:1>. Accessed 1 December 2020.
- United States Environmental Protection Agency (2020b). Ecological risk assessment for pesticides: Technical overview. <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/ecological-risk-assessment-pesticides-technical>. Accessed 29 December 2020.
- United States Environmental Protection Agency (2020c). New approach methods work plan: reducing use of animals in chemical testing. <https://www.epa.gov/chemical-research/epa-new-approach-methods-work-plan-reducing-use-animals-chemical-testing>. Accessed 26 December 2020.
- United States Environmental Protection Agency (2020d). *Chemical Safety for Sustainability. National Research Program Strategic Research Action Plan 2019-2022*. [https://www.epa.gov/sites/production/files/2020-10/documents/css\\_fy19-22\\_strap-final\\_2020.pdf](https://www.epa.gov/sites/production/files/2020-10/documents/css_fy19-22_strap-final_2020.pdf).
- United States Environmental Protection Agency, Heath Canada Pest Management Agency, and California Department of Pesticide Regulation (2014). *Guidance for Assessing Pesticide Risks to Bees*. [https://www.epa.gov/sites/production/files/2014-06/documents/pollinator\\_risk\\_assessment\\_guidance\\_06\\_19\\_14.pdf](https://www.epa.gov/sites/production/files/2014-06/documents/pollinator_risk_assessment_guidance_06_19_14.pdf).
- United States Food and Drug Administration (2019). *Pesticide Residue Monitoring Program – Fiscal Year 2017 Pesticide Report*. <https://www.fda.gov/food/pesticides/pesticide-residue-monitoring-2017-report-and-data>.
- United States Geological Survey (2020). National Water-Quality Assessment (NAWQA). [https://www.usgs.gov/mission-areas/water-resources/science/national-water-quality-assessment-nawqa?qt-science\\_center\\_objects=0#qt-science\\_center\\_objects](https://www.usgs.gov/mission-areas/water-resources/science/national-water-quality-assessment-nawqa?qt-science_center_objects=0#qt-science_center_objects). Accessed 29 December 2020.
- United States National Institute for Safety and Health (2015). Hierarchy of controls. *Centers for Disease Control and Prevention*. <https://www.cdc.gov/niosh/topics/hierarchy/>. Accessed 28 December 2020.
- van den Brink, N.W., Elliott, J.E., Shore, R.F. and Rattner, B.A. (2018a). Anticoagulant rodenticides and wildlife: Introduction. In *Anticoagulant Rodenticides and Wildlife. Emerging Topics in Ecotoxicology (Principles, Approaches and Perspectives) vol 5*. van den Brink, N.W., Elliott, J.E., Shore, R.F. and Rattner, B.A. (eds.). Cham: Springer. 1-9. [https://doi.org/10.1007/978-3-319-64377-9\\_1](https://doi.org/10.1007/978-3-319-64377-9_1).
- van den Brink, N.W., Elliott, J.E., Shore, R.F. and Rattner, B.A. (eds.) (2018b). *Anticoagulant Rodenticides and Wildlife. Emerging Topics in Ecotoxicology (Principles, Approaches and Perspectives) vol 5*. Cham: Springer. <https://www.springer.com/gp/book/9783319643755>.
- van den Brink, P.J. and Daam, M.A. (2014). Multispecies environmental testing designs, In *Encyclopedia of Toxicology*. Third edition. Elsevier. 399-402. <https://doi.org/10.1016/B978-0-12-386454-3.00569-8>.
- van der Sluijs, J.P., Amaral-Rogers, V., Belzunces, L.P., Bijleveld van Lexmond, M.F.I.J., Bonmatin, J.-M., Chagnon, M. et al. (2015). Conclusions of the Worldwide Integrated Assessment on the risks of neonicotinoids and fipronil to biodiversity and ecosystem functioning. *Environmental Science and Pollution Research* 22, 148-154. <https://doi.org/10.1007/s11356-014-3229-5>.
- Van der Valk, H.C.H.G., Niassy, A. and Bèye, A.B. (1999). Does grasshopper control create grasshopper problems? – Monitoring side-effects of fenitrothion applications in the western Sahel. *Crop Protection* 18(2), 139–149. [https://doi.org/10.1016/S0261-2194\(99\)00012-5](https://doi.org/10.1016/S0261-2194(99)00012-5).
- van Klink, R., Bowler, D.E., Gongalsky, K.B., Swengel, A.B., Gentile, A. and Chase, J.M. (2020). Meta-analysis reveals declines in terrestrial but increases in freshwater insect abundances. *Science* 368(6489), 417-420. <https://doi.org/10.1126/science.aax9931> and Erratum: <https://doi.org/10.1126/science.abf1915>.
- van Wijngaarden, R.P., Cuppen, J.G., Arts, G.H., Crum, S.J., Van Den Hoorn, M.W., Van Den Brink, P.J. and Brock T.C. (2004). Aquatic risk assessment of a realistic exposure to pesticides used in bulb crops: A microcosm study. *Environmental Toxicology and Chemistry* 23, 1479-1498. <https://doi.org/10.1897/03-80>.
- Varea, R., Piovano, S. and Ferreira, M. (2020). Knowledge gaps in ecotoxicology studies of marine environments in Pacific Island Countries and Territories – A systematic review. *Marine Pollution Bulletin* 156, 111264. <https://doi.org/10.1016/j.marpolbul.2020.111264>.
- Vašíčková, J., Hvězdová, M., Kosubová, P. and Hofman, J. (2019). Ecological risk assessment of pesticide residues in arable soils of the Czech Republic. *Chemosphere* 216, 479-487. <https://doi.org/10.1016/j.chemosphere.2018.10.158>.



- Vijver, M.G., Hunting, E.R., Nederstigt, T.A.P., Tamis, W.L.M., van den Brink, P.J. and van Bodegom, P.M. (2017). Postregistration monitoring of pesticides is urgently required to protect ecosystems. *Environmental Toxicology and Chemistry* 36(4), 860-865. <https://doi.org/10.1002/etc.3721>.
- Vorkamp, K. and Rigét, F.F. (2014). A review of new and current-use contaminants in the Arctic environment: Evidence of long-range transport and indications of bioaccumulation. *Chemosphere* 111, 379-395. <https://doi.org/10.1016/j.chemosphere.2014.04.019>.
- Vulliet, E., Tournier, M., Vauchez, A., Wiest, L., Baudot, R., Lafay, F. et al. (2014). Survey regarding the occurrence of selected organic micropollutants in the groundwaters of overseas departments. *Environmental Science and Pollution Research* 21(12), 7512-7521. <https://doi.org/10.1007/s11356-014-2619-z>.
- Wagner, D.L. (2020). Insect declines in the anthropocene. *Annual Review of Entomology* 65, 457-480. <https://doi.org/10.1146/annurev-ento-011019-025151>.
- Wagner, N., Mingo, V., Schulte, U. and Lötters, S. (2015). Risk evaluation of pesticide use to protected European reptile species. *Biological Conservation* 191, 667-673. <http://dx.doi.org/10.1016/j.biocon.2015.08.002>.
- Wang, A., Hu, X., Wan, Y., Mahai, G., Jiang, Y., Huo, W. et al. (2020). A nationwide study of the occurrence and distribution of atrazine and its degradates in tap water and groundwater in China: Assessment of human exposure potential. *Chemosphere* 252. <https://doi.org/10.1016/j.chemosphere.2020.126533>.
- Wang, X., Wang, C., Zhu, T., Gong, P., Fu, J. and Cong, Z. (2019). Persistent organic pollutants in the polar regions and the Tibetan Plateau: A review of current knowledge and future prospects. *Environmental Pollution* 248, 191-208. <https://doi.org/10.1016/j.envpol.2019.01.093>.
- Warner, G.R., Mourikes, V.E., Neff, A.M., Brehm, E. and Flaws, J.A. (2020). Mechanisms of action of agrochemicals acting as endocrine disrupting chemicals. *Molecular and Cellular Endocrinology* 502, 110680. <https://doi.org/10.1016/j.mce.2019.110680>.
- Weir, S.M., Talent, L.G., Anderson, T.A. and Salice, C.J. (2014). Unraveling the relative importance of oral and dermal contaminant exposure in reptiles: Insights from studies using the western fence lizard (*Sceloporus occidentalis*). *PLoS ONE* 9(6), e99666. <https://doi.org/10.1371/journal.pone.0099666>.
- Wellcome (2018). *Initiatives for Addressing Antimicrobial Resistance in the Environment: Current Situation and Challenges: Executive Summary*. Wellcome, United States Centers for Disease Control and Prevention, and UK Research and Innovation Network. London: Wellcome Trust. <https://wellcome.org/sites/default/files/antimicrobial-resistance-environment-summary.pdf>.
- Wellington, E.M.H., Boxall, A.B.A., Cross, P., Feil, E.J., Gaze, W.H., Hawkey, P.M. et al. (2013). The role of the natural environment in the emergence of antibiotic resistance in Gram-negative bacteria. *The Lancet Infectious Diseases* 13, 155-65. [https://doi.org/10.1016/S1473-3099\(12\)70317-1](https://doi.org/10.1016/S1473-3099(12)70317-1).
- Wesseling, C., Corriols, M. and Bravo, V. (2005). Acute pesticide poisoning and pesticide registration in Central America. *Toxicology and Applied Pharmacology* 207(2), 697-705. <https://doi.org/10.1016/j.taap.2005.03.033>.
- Whalon, M.E. (2008). Introduction. In *Global Pesticide Resistance in Arthropods*. Whalon, M.E., Mota-Sanchez, D. and Hollingworth, R.M. (eds.). Wallingford, UK: CAB International. 1-4. <https://www.cabi.org/bookshop/book/9781845933531/>.
- Whitfield, S.M., Lips, K.R. and Donnelly, M.A. (2016). Amphibian decline and conservation in Central America. *Copeia* 104, 351-379. <https://doi.org/10.1643/CH-15-300>.
- Wolfram, J., Stehle, S., Bub, S., Petschick, L.L. and Schulz, R. (2018). Meta-analysis of insecticides in United States surface waters: Status and future implications. *Environmental Science and Technology* 52(24), 14452-14460. <https://doi.org/10.1021/acs.est.8b04651>.
- Wood, T.J. and Goulson, D. (2017). The environmental risks of neonicotinoid pesticides: A review of the evidence post 2013. *Environmental Science and Pollution Research* 24(21), 17285-17325. <https://doi.org/10.1007/s11356-017-9240-x>.
- Woodcock, B.A., Bullock, J.M., Shore, R.F., Heard, M.S., Pereira, M.G., Redhead, J. et al. (2017). Country-specific effects of neonicotinoid pesticides on honey bees and wild bees. *Science* 356(6345), 1393-1395. <https://doi.org/10.1126/science.aaa1190>.
- Woodcock, B.A., Isaac, N.J.B., Bullock, J.M., Roy, D.B., Garthwaite, D.G., Crowe, A. and Pywell, R.F. (2016). Impacts of neonicotinoid use on long-term population changes in wild bees in England. *Nature Communications* 7, 12459. <https://doi.org/10.1038/ncomms12459>.
- World Health Organization (1990). *Public Health Impact of Pesticides Used in Agriculture*. <https://apps.who.int/iris/handle/10665/39772>.
- World Health Organization (2004). *IPCS Risk Assessment Terminology*. <https://apps.who.int/iris/handle/10665/42908>.
- World Health Organization (2014). *Preventing Suicide: A Global Imperative*. <https://www.who.int/publications/i/item/9789241564779>.
- World Health Organization (2015). *Global Action Plan on Antimicrobial Resistance*. <https://apps.who.int/iris/handle/10665/193736>.
- World Health Organization (2019). *Critically Important Antimicrobials for Human Medicine. 6th revision 2018. Ranking of Medically Important Antimicrobials for Risk Management of Antimicrobial Resistance due to Non-human use*. Geneva. <https://apps.who.int/iris/handle/10665/312266>.
- World Health Organization (2020a). *World Malaria Report 2020: 20 Years of Global Progress and Challenges*. Geneva. <https://www.who.int/publications/i/item/9789240015791>.
- World Health Organization (2020b). INTOX tools for harmonized data collection: Poisoning severity score. Appendix 1. In *Poisons Centre Training Manual*. <https://apps.who.int/iris/bitstream/handle/10665/329502/WHO-FWC-PHE-EPE-13.01-eng.pdf?ua=1>.

- World Health Organization (2020c). World directory of poison centres. <https://www.who.int/data/gho/data/themes/topics/indicator-groups/poison-control-and-unintentional-poisoning>. Accessed 26 December 2020.
- World Health Organization (2020d). Global Environment Monitoring System (GEMS) / Food Contamination Monitoring and Assessment Programme. <https://www.who.int/teams/nutrition-and-food-safety/databases/global-environment-monitoring-system-food-contamination>. Accessed 26 December 2020.
- World Health Organization (2020e). Antimicrobial resistance. <https://www.who.int/health-topics/antimicrobial-resistance>. Accessed 26 December 2020.
- World Health Organization and Food and Agriculture Organization of the United Nations (2019a). *Global Situation of Pesticide Management in Agriculture and Public Health: Report of a 2018 WHO-FAO Survey*. Geneva and Rome. <https://apps.who.int/iris/bitstream/handle/10665/329971/9789241516884-eng.pdf?sequence=1&isAllowed=y>.
- World Health Organization and Food and Agriculture Organization of the United Nations (2019b). *Preventing Suicide: A Resource for Pesticide Registrars and Regulators*. Geneva and Rome. <https://www.who.int/publications/i/item/9789241516389>.
- World Health Organization, Food and Agriculture Organization of the United Nations and World Organisation for Animal Health (2020). *International Instruments on the Use of Antimicrobials across the Human, Animal and Plant Sectors*. <https://www.who.int/publications/i/item/9789240013964>.
- Wu, J., Ge, L., Liu, F., Song, Q. and Stanley, D. (2020). Pesticide-induced planthopper population resurgence in rice cropping systems. *Annual Review of Entomology* 65, 409-429. <https://doi.org/10.1146/annurev-ento-011019-025215>.
- Xie, H., Wang, X., Chen, J., Li, X., Jia, G., Zou, Y. et al. (2019). Occurrence, distribution and ecological risks of antibiotics and pesticides in coastal waters around Liaodong Peninsula, China. *Science of The Total Environment* 656, 946-951. <https://doi.org/10.1016/j.scitotenv.2018.11.449>.
- Yadav, I.C., Devi, N. L., Syed, J. H., Cheng, Z., Li, J., Zhang, G., and Jones, K.C. (2015). Current status of persistent organic pesticides residues in air, water, and soil, and their possible effect on neighboring countries: A comprehensive review of India. *Science of The Total Environment* 511, 123-137. <https://doi.org/10.1016/j.scitotenv.2014.12.041>.
- Yeung, M., Kerr, W.A., Coomber, B., Lantz, M. and McConnell, A. (2018). Declining harmonization in maximum residue levels for pesticides. *British Food Journal* 120(4), 901-913. <https://doi.org/10.1108/BFJ-05-2017-0291>.
- Zubrod, J.P., Bundschuh, M., Arts, G., Brühl, C.A., Imfeld, G., Knäbel, A. et al. (2019). Fungicides: An overlooked pesticide class? *Environmental Science and Technology* 53(7), 3347-3365. <https://doi.org/10.1021/acs.est.8b0439>.



