

Annual Review of Environment and Resources Agrochemicals, Environment, and Human Health

P. Indira Devi,¹ M. Manjula,² and R.V. Bhavani³

¹Department of Agricultural Economics, Kerala Agricultural University, Kerala, India;
email: indiradevi.p@kau.in

²School of Development, Azim Premji University, Bangalore, Karnataka, India;
email: manjula.m@apu.edu.in

³Food and Agriculture Organization of the United Nations, Dhaka, Bangladesh;
email: bhavjoy@gmail.com

Annu. Rev. Environ. Resour. 2022. 47:399–421

First published as a Review in Advance on
June 8, 2022

The *Annual Review of Environment and Resources* is
online at environ.annualreviews.org

<https://doi.org/10.1146/annurev-environ-120920-111015>

Copyright © 2022 by Annual Reviews. This work is
licensed under a Creative Commons Attribution 4.0
International License, which permits unrestricted
use, distribution, and reproduction in any medium,
provided the original author and source are credited.
See credit lines of images or other third-party
material in this article for license information

**ANNUAL
REVIEWS CONNECT**

www.annualreviews.org

- Download figures
- Navigate cited references
- Keyword search
- Explore related articles
- Share via email or social media

Keywords

agrochemicals, environmental impact, human health impact, ecological
assessment, farmer behavior

Abstract

Global consumption of agrochemicals continues to rise, despite growing evidence of their adverse effects on environmental quality and human health. The extent of increase varies across nations, by type of chemical compounds and by severity of the detrimental impacts. The differential impacts are largely attributable to the level of technology adoption and regulation as well as their enforcement and compliance. The article highlights gaps in technical, legal, and social aspects, which include the paucity of holistic and long-term ecological impact assessment frameworks and lack of consideration for the social dimensions of pesticide use in regulatory decisions. Bridging these gaps, establishing global cooperation for regulation and governance, and a regional/national-level monitoring mechanism are suggested. This, complemented with a policy shift from the current approach of productivity enhancement to augmenting agroecosystem services, would encourage sustainable and nature-positive agriculture equipped to meet the multiple challenges of food security, ecological safety, and climate resilience.

Contents

1. INTRODUCTION	400
2. CHEMICALS IN AGRICULTURE: CATEGORIES AND GLOBAL USE PATTERNS	401
3. AGROCHEMICAL USE: FARMER BEHAVIOR AND CROP PRODUCTIVITY IMPACTS	403
4. NATURAL ENVIRONMENT AND HUMAN HEALTH IMPACTS OF AGROCHEMICALS	405
4.1. Environmental Impacts	405
4.2. Human Health Impacts	409
5. CONCLUSION	413

1. INTRODUCTION

The market for agrochemicals—inputs integral to modern agriculture—was estimated to be worth 234.2 billion US dollars (USD) in 2019 and is expected to be more than 300 billion USD by 2025 (1). Advocates of agrochemicals vouch for their potential benefits in improving economic efficiency of agricultural production systems and addressing food security concerns. They are seen as responsible for the large increase in food production that has been witnessed, especially since the 1930s, which saw the beginning of the Green Revolution. Modern agriculture has since come to be associated with the use of chemical fertilizers and pesticides. The trigger may be traced to the discovery of the organochlorine compound dichlorodiphenyltrichloroethane (DDT) in 1939. An insect killer that was widely used in the Second World War by soldiers to fight mosquitoes and fleas, it subsequently came to be widely adopted in agriculture and triggered the development of several chemical formulations to ward off pests. The first herbicide or weed killer—2,4-D—was discovered in 1945 and is the forerunner of atrazine, which came in the 1970s, and glyphosate, which came in the 1980s. In 1947, the US government enacted the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Approximately 10,000 new pesticides were reportedly registered in the following five years.

Application of fertilizers, especially nitrogen and phosphorus, provides nutrients required for enhancing the growth of crops. Similarly, pesticides reduce the risk of loss from plant diseases, insect pests, and weeds on agricultural production. Globally, a little more than one-third (35%) of potential crop yield is reportedly lost to preharvest pest attack (2), making a case for the use of pesticides to ensure food production and food security. It is reported that without pesticide use, 78% of fruit production, 54% of vegetable production, and 32% of cereal production would be lost to pest and disease attack (3). In India, for instance, it was the Green Revolution in the 1960s that warded off doomsday predictions of food shortage and famine. The quantum, intensity, and diversity of agrochemicals used globally has enormously increased since the Green Revolution.

At the same time, there is a large and growing volume of literature on the potential environmental and toxicological risk associated with unscientific use of agrochemicals (4). Questions arise as to the economic rationality of pesticide use when the economic costs of damages on ecosystems and human health are considered in the analysis of profitability and efficiency (5). The 1960s saw increasing attention to the environmental impact of widespread use of chemicals in agriculture. DDT is credited with drawing global attention to the environmental impacts of indiscriminate agrochemical use. Environmental historians date the beginning of the second wave of global environmentalism to 1962, following Rachel Carson's seminal work *Silent Spring* (6). The 1960s also

Agrochemicals:
chemical inputs used
in agricultural
production process to
promote production/
reduce risk; includes
chemical fertilizers,
pesticides, soil
ameliorants, growth
stimulants, and
flowering agents

Silent Spring:
the famous book by
Rachel Carson that
highlighted the
environmental
damages of
indiscriminate
pesticide use

saw a toxic waste spill leading to an outbreak of poisoning on livestock in the United Kingdom, marking what has come to be referred to as the Smarden incident (7). Carson's work saw a surge of public engagement in the hitherto scientific discourses on conservation and environmentalism. This triggered the launch of public-led environmental movements, resulting in the creation of the US Environmental Protection Agency (EPA). The use of DDT for agricultural purposes was banned in the United States in 1972 and the United Kingdom in 1986; however, its use has continued in many developing countries. Since 2001, DDT has been banned for use in agriculture in all the countries that are signatories to the Stockholm Convention on Persistent Organic Pollutants but continues to be used in some developing countries to control vector-borne diseases.

Notwithstanding these early warnings, the use of chemicals in modern agriculture has continued unabated. The uproar created by *Silent Spring* was silenced by the modern technological revolution in agriculture, facilitated by policy support and commercial production of inputs that spread across the globe. Many developing countries were able to make commendable strides in grain production in the 1960s and 1970s. This has, however, not been without serious subsequent concerns regarding the ecological and human impacts of agrochemical use (8, 9). For instance, the increase in food production and the associated food-energy-population dynamics has been facilitated by creation of reactive nitrogen (synthetic fertilizers) from unreactive dinitrogen. The reactive nitrogen from synthetic fertilizers, which spreads through the earth systems, has detrimental consequences for human health, biodiversity, and the natural environment (10). This is further corroborated by the extent of biodiversity loss and alteration in surface heat balance resulting in global warming. Both these phenomena are fallouts of land use intensification for industrial agriculture over the centuries (11). A review by Nielsen et al. (12) also points to the direct impact of agricultural intensification and commercialization on soil biomass. The application of nitrogenous fertilizers in industrial agriculture is said to have had a mixed impact on soil microbial biomass. Increases in bacterial biomass activity and activation of the soil nitrogen cycle were observed in response to nitrogen fertilizer application, while simultaneously being detrimental to nematode diversity and activity of mycorrhizal fungi (12).

This article presents a comprehensive review of the recent trends in agrochemical use patterns, farmer-level behavior, and the detrimental impact of these chemicals on ecosystems and human beings, primarily focusing on evidence from published field-level studies. On that basis, a few suggestions are made: (a) promoting sustainable production systems, (b) strengthening global cooperation in research and development; (c) assessing, monitoring, and regulating the use and management of agrochemicals; and (d) adopting eco-friendly green technologies.

2. CHEMICALS IN AGRICULTURE: CATEGORIES AND GLOBAL USE PATTERNS

The major groups of chemicals in the farming sector are fertilizers, plant growth stimulants, and plant protection chemicals. The technology advancements in the fertilizer manufacturing sector have improved fertilizer formulations from the conventional ones to nanofertilizers. This has also diversified fertilizer materials from macronutrients to micronutrients and soil ameliorants. The application technology of agrochemicals also has undergone changes, from manual methods to use of drones.

Chemical pesticides are broadly categorized as insecticides, fungicides, bactericides, herbicides, and rodenticides. These belong to major chemical groups such as organophosphates, carbamates, organochlorines, triazines, and dithiocarbamates. The latest additions, claimed to be safer alternatives, are pyrethrins and neonicotinoids. The mode of action and ecological and human health effects of the formulations vary according to the chemical groups. Although herbicides account

Stockholm

Convention: a global treaty ratified by 152 countries that came into force in 2004 to protect human health and environment from persistent organic pollutants; the United Nations Industrial Development Organization supports developing and transitioning economies to implement the convention, and the Global Environmental Facility provides an interim financial mechanism

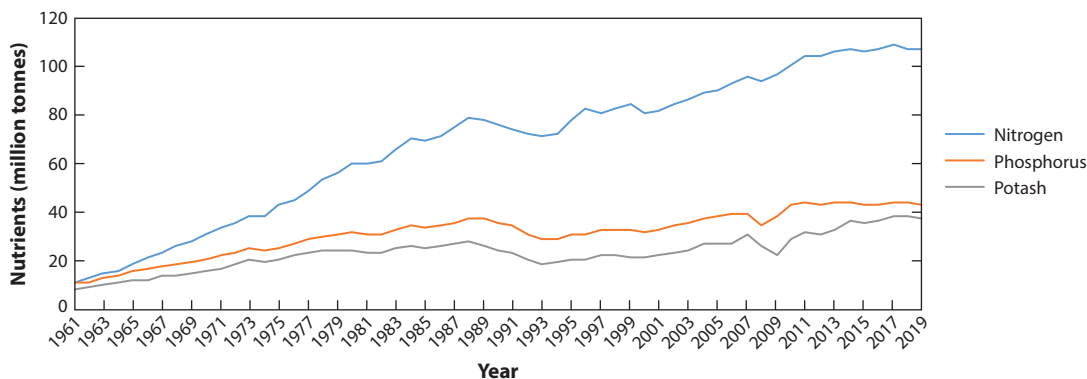


Figure 1

Global fertilizer consumption trend between 1961 and 2019. Nutrients in million tonnes. Data from FAOSTAT (<https://www.fao.org/faostat/en/>).

for the majority of pest control chemicals globally, there are differences in proportion of use of different pesticides across countries. For instance, herbicides are the major group of agrochemicals consumed in the United States, whereas insecticides are the major group in countries like India. This is mainly decided by the cropping pattern, climate, and technology diffusion.

The global consumption of mineral fertilizers in 2019 was 188.54 million tonnes, which was a dramatic increase of more than six times from 30.85 million tonnes in 1961, the pre-Green Revolution period. The global population during the same period increased from 3.1 billion to 7.7 billion. The consumption of nitrogen fertilizers alone saw a massive increase of more than 250% in the five decades between 1969 and 2019 (13). **Figure 1** shows the global trend in use of nitrogen, phosphorus, and potassium (NPK) nutrients in agriculture between 1960 and 2019. Nitrogenous fertilizer accounts for the major share of fertilizer use. Examining the region-wide distribution of its average use during the 2002–2019 period, one finds that Asia accounts for 59.9%, the United States for 21.2%, Europe for 14%, and Africa for just 3.3%.

Figure 2 shows the global trend in use of pesticides and its subgroups during the 1990–2018 period, and, as stated above, herbicides account for the major share. The Food and Agriculture

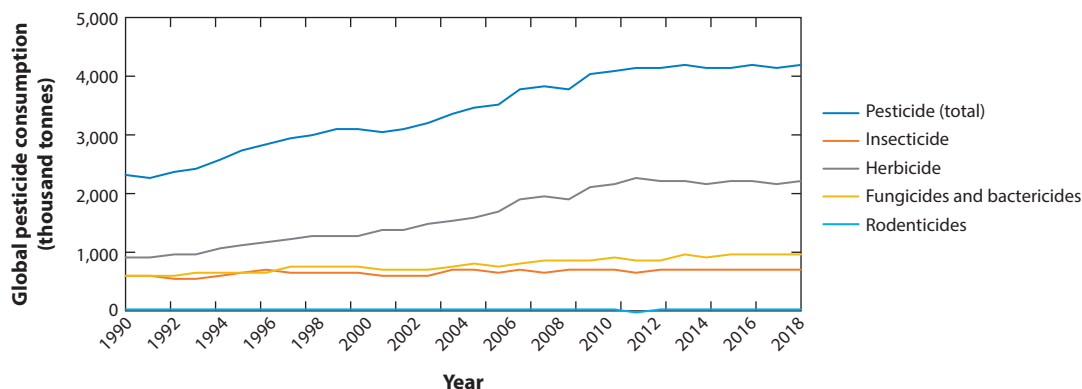


Figure 2

Global pesticide consumption trend between 1990 and 2018. Data from FAOSTAT (<https://www.fao.org/faostat/en/>).

Organization of the United Nations (FAO) data show that, of the 4.2 million tonnes of pesticides used annually in 2019, a little more than half (53%) were herbicides, followed by fungicides and bactericides (23%) and insecticides (17%). The top five pesticide consumers in the world in 2019 were China, the United States, Brazil, Argentina, and USSR (13). The major producers of pesticides in value terms are France, Germany, Poland, Spain, and the United Kingdom, and major exporters are China, the United States, France, and India. Brazil is the largest importer of pesticides, followed by France, the United States, Germany, and Canada.

Intensity of pesticide use: the quantity of pesticide applied per hectare of cropped area

A study examining the consumption of fertilizers and pesticides found that 88 countries on average consumed 110 million tonnes of NPK fertilizers annually during the 1961–2010 period (14). China was the largest consumer, using 21.6 million tonnes/year, followed by the United States at 17.5 million tonnes/year, and 18 countries each used more than one million tonnes/year. With regard to insecticide consumption, average annual consumption from 1990 to 2010 by 82 countries was 342,000 tonnes, with the United States consuming the largest amount at 90,000 tonnes/year, followed by India at 30,600 tonnes/year and 34 countries using more than 1,000 tonnes/year on average. Average annual herbicide consumption of 75 countries during the same period was 566,000 tonnes, with the United States reporting the highest consumption at 201,000 tonnes/year, followed by Mexico at 34,400 tonnes/year and 45 countries using more than 1,000 tonnes/year. In the case of fungicides and bactericides, 353,000 tonnes were consumed annually across 77 countries, with Italy consuming the most at 61,700 tonnes each year, followed by France at 46,400 tonnes/year. Brazil is the second largest consumer of pesticides, after the United States. China is at par with Brazil and is also a major producer of pesticides. Bangladesh and Thailand quadrupled their pesticide use between the early 1990s and early part of the past decade, while newer entrants, such as Ghana, Ethiopia, and Burkina Faso, saw a tenfold increase over the same period (15). The use of pesticides in Africa, although low, was found to be increasing especially in West Africa, following the onslaught of the fall armyworm (FAW) in 2016. Developing countries accounted for only one-quarter of global pesticide use (16).

3. AGROCHEMICAL USE: FARMER BEHAVIOR AND CROP PRODUCTIVITY IMPACTS

Juxtaposing the picture of imbalanced global consumption of fertilizers and pesticides with cereal production, Liu and coworkers (14) reported a positive association. In developed countries, such as those in Europe, where use of agrochemicals was high, the yields and per capita production were also high and increasing over time. Per capita cereal production in most African countries was low; fertilizer and pesticide use in these countries was also low. At the same time, Liu et al. also cite studies that conclude that yields in approximately one-quarter of cereal-growing areas have stagnated or declined. Analysis of pesticide use across countries for the 1990–2009 period shows that a 1% increase in crop output per hectare was associated with a 1.8% increase in pesticide use per hectare (17). The growth in intensity of pesticide use was found to level off as countries reached higher levels of economic development, but did not fall, as decreases in insecticide use were offset by increases in use of herbicides and fungicides. They also found rapid growth in the intensity of pesticide use in the case of middle-income countries, such as Brazil, Mexico, Uruguay, Cameroon, Malaysia, and Thailand.

Comparing data on fertilizer use in China with Brazil, India, Japan, the United States, the European Union (EU), and total for the world, the average chemical fertilizer (NPK) use per hectare of cropland in China was two to four times higher. In pesticide use, it was two to seven times higher (18). The high use of fertilizers and pesticides is, however, not matched by high

yields. The yield of rice, wheat, and maize crops is intermediate compared to the global average, and nitrogen use efficiency is the lowest. Countries with higher per capita GDP were found to use less fertilizer per hectare and have higher fertilizer use efficiency. A field study in Kenya found that returns to fertilizer use start to decline after a threshold level, leading to low yields and low farm incomes (19). This field-level evidence underlines the need for ensuring optimum input use, determined on the basis of economic, environmental, and social dimensions.

Approximately 30% of pesticides marketed in developing countries, particularly in Africa, reportedly do not meet internationally accepted quality standards, posing a serious threat to human health and the environment (2). Older pesticides that have recouped their development cost are generally offered by multinational companies at lower prices, making them attractive to low-income countries. A study commissioned by the EU found export of hazardous pesticides banned within the EU to developing countries, and primarily to countries in Latin America, mainly Brazil. There are also problems of counterfeit imports and illegal mixing and marketing of local variants of pesticides to sell at affordable prices to farmers (16).

Studies have documented that unscientific practices in selection and use of agrochemicals are common, especially in developing economies (16, 20, 21). Regular preventive sprays of pesticides without considering the chances of infestation or threshold of pest population are very common. Issues related to concentration, mixing methods, periodicity of spray, and use of appropriate protective gear are also common. Often, the end users rely on information provided by pesticide retailers in developing countries. The dispensers are also typically not aware of the best practices for use and are driven by a desire to increase the volume of sales—resulting in violations of the laws governing their dispensation and use. There are also reports of certain fertilizers being promoted by private dealers regardless of soil health and specific requirements (19).

The United States, EU, Brazil, and China are four of the largest producers and consumers of agricultural pesticides in the world. However, pesticide-related health damages are reported comparatively less in developed countries (22). This may be due to stricter regulations, compliance, monitoring systems, as well as application of modern technologies. For instance, in the United States, pesticide regulation is enforced by the EPA (<https://www.epa.gov>), under the Federal Food, Drug, and Cosmetic Act and the FIFRA. There is a licensing system for pesticide applicators, both individuals and commercial units. This is issued based on knowledge level, age, and training exposure, to ensure the safety of both the applicator and the public. In 2017, the EPA finalized stronger standards for people who use restricted use pesticides.

Apart from regulations, the compliance level also decides the impacts. According to a 2017 report on pesticide use by the Special Rapporteur on the Right to Food to the UN General Assembly, approximately 25% of developing countries lacked effective laws on distribution and use, and approximately four-fifths of them lacked sufficient resources to enforce existing pesticide-related laws (<https://www.fao.org/agroecology/database/detail/ar/c/473075/>). Despite global scientific prescriptions on code of conduct and legal restrictions for ensuring pesticide efficacy and reducing ecosystem damages, the “adoption of standards and practice of pesticide management has been slow particularly in low- and middle-income countries,” reports a joint WHO-FAO study (23). A study from China reports that technological improvements in application methods reduce pesticide-related health damages. Farm machine use for pesticide application is helping to reduce pesticide application expenses, which in turn lead to a reduction in human and ecological health damages (24). It can be concluded, therefore, that the adverse impacts of chemical pesticides can be considerably reduced through proper legal frameworks, monitoring, and compliance mechanism and application of appropriate technologies, including alternate pest management options (e.g., integrated pest management, botanicals, natural methods).

4. NATURAL ENVIRONMENT AND HUMAN HEALTH IMPACTS OF AGROCHEMICALS

4.1. Environmental Impacts

There are several documented impacts of the indiscriminate use of agrochemicals on the environment and ecology. A recent paper on lessons from the aftermath of the Green Revolution contends that, while agricultural productivity and production increased, the harm caused by indiscriminate use of fertilizers and pesticides is set to have far-reaching consequences (8). Alarming levels of agrochemical residues in air, soil, water, and agricultural produce have been reported from across the globe (25–27). Many of the chemical compounds used in the production of agrochemicals are persistent and prone to bioaccumulation. Arsenic, cadmium, fluorine, lead, and mercury accumulation in soil is associated with excessive use of inorganic fertilizers (4). Overuse of nitrogenous fertilizers results in nitrate leaching into waterbodies, causing eutrophication impacting aquatic life and potability of water (28). Phosphate gets adsorbed onto soil particles and transported to waterbodies through soil erosion. Excess fertilizer use over prolonged periods results in acidification of soils, which impacts soil productivity and soil conservation in the long run (29).

Significant incidents of environmental pollution from pesticides were reported from more than 20% of countries in a global survey on pesticide management in agriculture (23). Herbicides like trifluralin and triazines and nicotine insecticides are said to be detrimental to biodiversity on land and water, even at sublethal doses (30). Excess use of glyphosates—an organophosphate herbicide—has the potential of altering ecosystem functions and impacting biodiversity. Agrochemicals, specifically broad-spectrum pesticides, destroy non-pest, beneficial insects, and general biodiversity, fueling crisis of biodiversity loss and disturbing ecosystem functions (31). Pyrethroids and imidazole fungicides and neonicotinoid insecticides are harmful to honeybees. An estimated 29–36% per annum drop in global honeybee population since 2006 has been reported (32). A fourfold reduction in farm productivity and farm profits was observed in apple farms without honeybees as compared to those with them (33). Loss in productivity and profits was also observed to be twofold lower in farms without bumblebees compared to those with them. The average profit in farms with installed colonies of pollinators was 2.5 times higher than those without pollinators. The loss of predators, which are important agents for biological control of pests, exacerbates pest problems and increases pesticide dosage and quantity, resulting in adverse outcomes for sustainable pest management (34).

Loss of soil biodiversity is also widely attributed to the overuse of chemical control measures in agricultural fields. A 2019 survey of FAO member countries identified pesticide and antibiotic use in agriculture and livestock as a key driver of soil biodiversity loss over the decade (35). A review of 400 studies on the impact of pesticides on 2,842 tested parameters of soil organisms reveals that pesticides impacted 70.5% of the tested parameters on various soil biota (36). The highest impact was from insecticides, followed by fungicides, herbicides, and bactericides, in that order. Soil application of agrochemicals affects beneficial microorganisms—such as nitrogen-fixing rhizobacteria and phosphorus-solubilizing bacteria—by interfering in the molecular interactions necessary for biotransformation of nutrients in the soil. The antagonistic interaction between agrochemicals and the symbiotic nutrient-fixing microbes depends on the chemical composition of the agrochemical. Insecticides, such as monocrotophos, lindane, dichlorvos, endosulfan, malathion, and chlorpyrifos, and most copper-based fungicides and herbicides, such as triazines, alachlor, atrazine, paraquat, and glyphosate, largely alter the symbiotic association of soil microbes with plants, impacting their nutrient-fixing and -solubilizing abilities (37). Organophosphates, namely, phosphamidon, malathion, and parathion, inhibit *Azotobacter* activity. Chlorpyrifos

affects the functioning of *Pseudomonas fluorescens*, *Bacillus subtilis*, *Mycobacterium phlei*, *Trichoderma harzianum*, *Penicillium expansum*, and *Fusarium oxysporum* (38).

Agrochemicals also alter soil enzyme activity and interfere with microbial metabolism. Soil enzymes play a crucial role in biodegradation of agrochemicals in soil. Given their role in maintaining soil equilibrium, soil enzymatic activity is an important bioindicator of soil health and fertility (29, 37). Functions of invertase and dehydrogenase are severely affected by herbicides, atrazine, and metolachlor, respectively. Fungicides, benomyl, mancozeb, thiram, and tridemorph inhibit dehydrogenase, urease, and phosphatase activity. Furthermore, agrochemicals, especially pesticides used to contain certain target soil microorganisms, result in rapid multiplication and flourishing of nontarget microorganisms. Rapid flush in soil bacterial activity reported from regions of fungicide application is indicative of this phenomenon. Intensive application of agrochemicals affects the functional diversity of several nontarget soil microorganisms (37). Fungicides have higher impact on soil biota than herbicides or insecticides. General reductions in soil microbial species richness and soil invertebrates due to excessive pesticide use are also widely reported globally (39, 40).

Soil invertebrates provide key ecosystem services such as maintenance of soil structure, nutrient recycling, mineralization of organic matter, and regulation of pest and diseases and are essential for agricultural sustainability (36). A major threat to soil invertebrates is the neonicotinoid group of insecticides (which accounted for 92% of invertebrate toxicity) and fungicides (41). Substantial impact on mortality, abundance, and biomass due to pesticide use was reported in annelids, nematodes, arthropods, *Bombus* spp., and parasitic wasps (36). Insecticides impacted 60% to 80% of the tested parameters included in the study, while herbicides and fungicides impacted 5% to 100% of the tested parameters. Agrochemical impact on invertebrates adversely affects several links in the soil food web. Earthworms, which constitute more than 80% of the invertebrate population in soil, are impacted by copper-based fungicides and pesticides such as carbamates, chlorpyrifos, and those in the organophosphate group. Combination of insecticides and fungicides causes neurotoxic effects in earthworms.

Spread and persistence of agrochemicals in the environment is another area of concern. A miniscule 0.1% of the total amount of pesticides applied is estimated to reach the target pest or weed (37). The remaining spreads in the environment through spray drift, off-target deposition, and runoff, causing irreversible damage to ecosystems and natural resources (42). Pesticide drift accounts for 2% to 25% of the pesticide loss and pollutes both the local and the global environment. Atmospheric concentration of organochlorine in several regions is attributed to excess use of this compound in the agricultural fields in neighboring areas (43). Pesticides in the environment undergo degradation and produce new chemicals (3). There is wide variation in the environmental behavior of different types of agrochemicals. Organochlorine compounds are persistent, bind strongly to soil particles, and are prone to bioaccumulation (44). They are also more prone to atmospheric dispersion in tropical regions due to volatilization effects of high temperature (37). Volatilization effects of temperature are the reason for higher concentrations of pesticide residue in air during summer than in winter (45). Degraded chlorpyrifos is more toxic and mobile than its parent compound. They are soluble and persistent and are more likely to leach into groundwater and pollute waterbodies, impacting aquatic biodiversity (46). They also affect soil microorganisms, deteriorating soil health (47). Certain organochlorines reportedly suppress symbiotic nitrogen fixation (29). Organophosphates, however, have low persistence but are acutely toxic (48). They undergo different processes of degradation and are subject to leaching effects.

Weather and climatic factors impact agrochemical degradation and dispersion by altering soil characteristics (49). A rise in temperature results in a reduction in organic matter content in soil, resulting in crack formation. This, in turn, accelerates movement of organic and inorganic

chemicals and their subsequent leaching to ground- and surface water (50). Pesticide residue levels are higher in surface water compared to groundwater, as they serve as sinks for surface runoff from farmlands and spray drifts (33). High levels of pesticide contamination are reported in the South Asian river systems, with endosulfan, heptachlor, chlorpyrifos, DDT, and hexachlorocyclohexane being the predominant pollutants (16). Pesticide residues reported in more than 90% of water and fish samples collected from streams in the United States, high glyphosate levels in rivers and seas in China, and herbicide contamination of wetlands in Canada provide more evidence of pesticide leaching to waterbodies (3).

Traces of carbamate and synthetic pyrethroids in water samples tested in peri-urban sites in Nepal are attributed to increasing commercial agricultural activities. Similarly, in Sri Lanka, excess use of chemical fertilizers has resulted in groundwater contamination with high levels of total dissolved salts and nitrates (51). Agrochemical contamination of ground- and surface water sources are detrimental to the survival of aquatic biodiversity. Insecticide carbaryl, chlorpyrifos, endosulfan, and herbicide glyphosate are toxic to amphibians, while herbicide atrazine is toxic to fish populations. Malathion, even in very small concentrations, is reportedly harmful to plankton and periphyton populations, which in turn impacts growth of frog tadpoles. Genetic mutation in amphibians and reduction in reproductive potential of aquatic life forms are reported from atrazine contaminated waterbodies (33). Dead frogs, insects, and worms following pesticide spraying were reported from swamp ecologies of flooded rice farms of Sierra Leone (52).

Another common risk with excessive use of pesticides is development of resistance by target pests and weeds, prompting application of higher doses to contain the population within economic threshold levels (53). Development of pesticide resistance in FAW—a major invasive pest—across America, sub-Saharan Africa, and Asia is a case in point. FAW developed resistance to a wide range of insecticides, including chlorpyrifos, permethrin, pyrethroid, organophosphates, and spinosad (54, 55). Pesticide resistance was a major problem in more than two-thirds of countries that were part of the global survey in pesticide management referred to above (30). Almost 65% of the surveyed countries also reported the absence of special provisions to regulate and restrict the use of highly hazardous pesticides (HHPs).¹

Compounding these effects are methodological shortcomings in ecological risk assessment of agrochemicals. The failure of the current regulatory mechanisms to reduce environmental and ecological damages from pesticide use is attributed to methodological inaccuracies in predictions of both exposure and effect (56). Faulty assumptions of one-time impact from a specific pesticide on organisms, and sufficient recovery periods following long intervals between multiple applications, tend to underestimate the actual risk to biodiversity and ecosystems (57). Organisms are exposed to multiple impacts at short intervals. The assessment framework also underestimates contamination from multiple pesticides (cocktails). The majority of the water and soil samples collected from European orchards reportedly contained traces of more than two pesticides, and a small proportion were even reported to have traces of more than 10 pesticides (58). Bumblebees were found to be susceptible to a cocktail of clothianidin and thiamethoxam, found in pollen and plant nectar (59).

Given this complexity, despite years of evaluation, the scientific and regulatory authorities find it challenging to foresee the long-term negative consequences of persistent use of agrochemicals on the environment (60). The level of pollution, caused by use of approved neonicotinoid and fipronil chemicals, even at prescribed levels, exceeded the permissible limit of concentrations for an array of nontarget species (61). Incorporating ecological, landscape, and management contexts

¹HHPs are agrochemicals that fall under the WHO categories Ia, Ib, and II.

in the test systems and models will make predictions more relevant to real-world scenarios (50). Scientific mechanisms for data collection and reporting on environmental contamination from agrochemicals also remains an underdeveloped field, with just about one-third of the countries reporting some mechanism for this (30). As a result, the known impacts of pesticides can change based on new scientific findings. A development in this direction is the revoking of authorized use of trifluralin, neonicotinoid, clothianidin, thiamethoxam, and imidacloprid in Europe in the early 2010s (61).

An attempt at valuing the external cost imposed by agrochemicals on environment was carried out in Swiss agriculture (62). External costs due to excessive use of nitrogen fertilizers (ammonia and nitrates), pesticides, and the associated pollution of air, soil, water, and impact on biodiversity and habitat were considered. The other external costs included greenhouse gas emissions, soil erosion, habitat deficits, and animal suffering. Using the avoidance cost method, the total cost of avoidance of Swiss agriculture was estimated at 3816.76 USD² per hectare (average avoidance cost) and 5812.53 USD per hectare (highest avoidance cost). The study interprets average avoidance cost as the price that society is currently paying per unit of externality. The highest avoidance cost indicates the cost to avoid one additional unit of externality (marginal cost), given the current level of avoidance measures. The average and marginal avoidance cost of ammonia (units above legal target) was estimated at 97.22 USD and 109.23 USD, respectively. The corresponding figures were 29.49 USD and 436.95 USD, respectively, for excess use of nitrate and fungicide and 764.59 USD and 873.82 USD, respectively, in the case of herbicides.

A similar study on cotton in India estimated the external cost of seed cotton at 4.99 USD per kilogram (63). The cultivation phase accounts for 34% of the external cost. Environmental costs make up 74% of the total external cost in cotton. The major components of environmental costs are water use (35%) and water pollution (17%). Water pollution caused by runoff from nitrogen and phosphatic fertilizers and excess pesticide use is the second largest external cost. Pesticide and fertilizer use in cotton farming results in freshwater and marine water ecotoxicity, eutrophication, and loss of biodiversity.

At a global level, the natural capital impacts from crop production across 40 countries were estimated using materiality assessment approaches (64). The crops included were maize, rice, soybean, and wheat. The total natural capital from crop production was estimated at 1.15 trillion USD, which was 170% higher than the production value. Fertilizer leach into waterbodies was observed to result in significant increases in natural capital cost, as estimated in wheat farming in Germany and rice farming in India and China. The environmental impact of pesticide atrazine was estimated to range from 44,000 to 825,000 USD per tonne, while for fungicide folpet, it was between 38,000 and 721,000 USD. Eutrophication impacts on ecosystems from the emissions of nitrates and phosphates ranges from zero to 82,000 USD and between zero and 818,000 USD per tonne of nitrates and phosphates, respectively. Eliminating pesticide use and reducing fertilizer runoff by using cover crops significantly reduced natural capital costs in farming.

Environmental impact of agrochemicals has been a subject of research across diverse disciplinary domains. Several of these studies have focused on either fertilizers or pesticides, and/or their impact on a single environmental resource like water, soil, or air. Recent decades have witnessed an exponential growth in the research focusing on environmental impact of agrochemicals, and it is expected to grow further. Evans et al. (25) capture the systematic evolution of research in this field by employing information metrology. Using citation analysis, the authors identify three distinct temporal phases in the field of research. The 1990–1999 period, classified as the early

²Non-USD currencies were converted to USD per the exchange rates of October 30, 2021.

stage, largely deals with quantification of pollution concentration, with persistent organic pollutants (POPs) as the primary focus of inquiry. The middle stage, the 2000–2007 period, focused on studying the influence mechanisms. This covered a range of aspects, including source analysis, source-sink relationship, mechanism of pollutant generation, and transmission pathways. A shift to very focused studies on specific agrochemicals, geographies, and agricultural production systems was the hallmark of the late stage, the 2008–2016 period. Variation, if any, in environmental impact of agrochemicals across space, time, cropping systems, and inputs was also a point of analysis in this phase.

Citation-clustering analysis provides insights on the knowledge focus in the field of research on environmental impact of agrochemicals. Impact of pesticides and veterinary drugs and the techniques to monitor their residues were the major focus of the studies. Pesticide exposure impact on wildlife and humans was another area of investigation. The second important category of research in this field pertains to impact of synthetic fertilizer application on agricultural land. Soil acidification and deterioration of soil properties due to excessive fertilizer application on farmlands were aspects of inquiry. The studies also investigate means of shifting to a more sustainable production system in agriculture.

Subsequently, the focus of research expanded to identifying new techniques and methods for environmental monitoring and control. The research studies in this genre focused on techniques to identify sources of pollutants, measure their negative impact, reduce the impact, and identify means to contain the spread of the pollutant. Finally, co-occurrence network analysis reveals organochlorine pesticides and nitrogenous fertilizers to be the chemical compound groups that have been extensively studied within the large family of pesticides and fertilizers. Heavy metal contamination, POPs, and nitrate residues are the pollutant types that generate greatest interest for researchers. Heavy metal residues from agrochemicals are an emerging threat being increasingly reported across the globe (65). As far as sinks are concerned, soil, water, and air account for the environmental objects of interest in the majority of the studies. Groundwater, surface water, wastewater, and sewage sludge are keywords within the broader environmental objects. Eutrophication, leaching, and runoff effects are the focus of these studies. The research aspects covered are monitoring concentration and diffusion of agrochemicals and understanding impact mechanisms on environmental objects.

4.2. Human Health Impacts

The impact of agrochemicals is not limited to nonhuman biota and the environment. Exposure of human beings to agrochemicals can be direct—by accidental, intentional, or occupational factors—or indirect—such as residues in food and the environment. The workers in agrochemical production centers, as well as across other stages of supply chain, retailers, and pesticide applicators are directly exposed. The people who reside or are present near agricultural fields are also impacted. The intentional consumption of chemicals as a means of suicide is also direct exposure, and there are instances of unintended consumption (homicides). The indirect exposure is mainly through pesticide residue in food, water, and air. The exposure is largely through skin contact, ingestion, or inhalation. Once exposed, the chemicals may get metabolized, excreted, stored, or bioaccumulated in body fat. The biomagnification and bioconcentration of the molecules inside the human body have implications for human health. There are several studies that show multiple health problems due to exposure, such as birth defects, cancer, and neurological disorders (66–68). However, the extent of this impact is determined by the individual health status and mitigating behavior (69–74).

Biomagnification refers to the increasing levels of concentration of persistent chemicals at higher levels of the food chain. Living beings at lower levels of the food web contain lower

concentration of the chemicals, which get added up as we move up the food chain. Bioconcentration is the process in which the accumulation of the chemical in an organism occurs from surrounding air or water. For instance, DDT is fat soluble and gets deposited in the fatty tissue (lipids) of fish or human beings. Some other chemicals (e.g., glyphosate) are metabolized and excreted (75, 76). These physiological processes lead to negative health effects, such as dermatological, gastrointestinal, neurological, carcinogenic, respiratory, reproductive, and endocrine impairments. A recent report by the UN Environment Programme observes a significant association between occupational and residential exposure to pesticides and adverse health outcomes, including cancers and neurological, immunological, and reproductive effects (68). A detailed account of the physiochemical, toxicokinetic, and toxicodynamic properties, stages of intoxication, symptoms of poisoning, and remedies pertaining to widely used pesticide has been garnered based on clinical studies under laboratory conditions (41).

However, the severity of health damages due to pesticide use under actual field conditions differs substantially compared to clinical trials. Under field conditions, the extent and severity of impacts are influenced by environmental factors (temperature and wind conditions during spraying), health and behavioral aspects (smoking or alcohol consumption/adoption of personal protection measures, general health conditions), and extent of adherence to scientific practices (choice of the chemical, handling practices, dilution, spray fluid concentration). There is wide divergence from ideal scientific prescriptions in these aspects, especially in most of the developing countries (16, 20, 21). The adoption of precautionary measures and scientific protocols can substantially limit the damage. However, poor health conditions and improper personal habits aggravate the impact (77).

Health damage due to pesticide poisoning has been a public health issue ever since the beginning of widespread use of chemical pesticides in agriculture. The impacts include mortality or morbidity (acute or chronic). The damage can be short term in nature, which is manifested soon after exposure lasting for a few hours or days, or long term, which is experienced after a time lag and lasts for a longer period. The earliest global report on human poisoning by pesticides was by the Task Force of WHO in 1990, which estimated one million cases and a mortality rate of 20,000 per annum (78).

Intentional poisoning with pesticides as a means of suicide is very common, especially in developing countries, due to their easy access. Globally, 110,000–168,000 suicides were reported by this method, annually, over the 2010–2014 period, which accounts for 14–20% of total suicides (79). Suicides are often the immediate response to farm distress in many Indian states. Nearly half of such deaths (48%) are due to pesticide intake, of which 76% are small and marginal farmers (with less than 5 hectares of land holding), relatively young (31 to 60 years), and belonging to socially marginalized sections (80).

According to experts, the decision to commit suicide is often a momentary one, and it can be prevented if immediate and easy access to the method is restricted. There are several instances of professional psychiatric associations demanding a ban on extremely poisonous pesticides as a means to bring down suicide rates. Some of the studies relying on data from India support this view. There was a fall in suicide rates by insecticide ingestion in India during 2011 to 2014, which was related to the nation-wide ban of endosulfan in 2011 (81, 82). The restrictions to access of commonly used HHPs are prescribed as a successful suicide prevention strategy, as it can not only reduce fatality but also lead to reductions in overall suicide rate (79, 83, 84). Pesticide poisoning was the method for more than two-thirds of all suicides in Sri Lanka, one of the countries with the world's highest suicide rates. The country banned paraquat and two other pesticides, leading to a 21% fall in suicide mortality during the 2011–2015 period (84). This saved 93,000 lives, at

a direct government cost of less than 50 USD per life (85). Additionally, in 2020 the Sri Lankan government banned the import of chemical fertilizers, pesticides, and weedicides (86).

It is reported that 0.35 million people globally are victims to accidental fatal pesticide poisoning every year (87). A review of the literature and data from WHO during the 2006–2018 period shows an estimated 385 million cases of poisoning and 11,000 fatalities annually among farmers across 141 countries (83). This accounted for 44% of the 860 million farming population of the world. In Asia and Southeast Asia, the proportion was as high as 54–66%. The World Future Council reports a fatality rate of 300,000 workers per year (86). These estimates reflect only those cases with serious health damages and fatality and do not include those with mild symptoms. Often, the mild symptoms are not taken seriously by farmers and farm workers—and rural populations—and they do not seek formal medical help. Hence, the reported data may be the lower bound of cases.

Although direct contact and exposure as well as the resulting short-term health impacts are directly linked to chemicals, as in the case of occupational or intentional exposure, it is often difficult to link health damages to indirect, long-term exposure to chemicals under real-world situations. This is evident in the cases of residues in food and constant occupational or other types of exposure. The specific cases of endosulfan use in cashew plantations in Kerala, India, and the glyphosate case in the United States are two such instances. The cause–effect relationship was established with high social costs after prolonged investigations and legal interventions.

In 1976, the Plantation Corporation of Kerala, a public sector undertaking in the state of Kerala, India, started the aerial spraying of endosulfan (against the pest tea mosquito) in the 2,200 hectares of cashew plantations they owned in Kasaragod district. This continued for nearly 20 years in 15 villages of the district. By the latter half of the 1980s, there were reports of human health damages like cancer, congenital anomalies, mental and physical retardation, hydrocephalus, and epilepsy in Padre village, one of the villages where the spraying operations were undertaken (88, 89). The news gained media and political attention globally and civil society groups and environmental activists demanded state intervention on the subject. *Down To Earth*, a leading magazine on environmental issues, published a detailed cover story in 2002 that discussed the science and politics of endosulfan use and the ecosystem damages caused by it. In 2001, the government of Kerala legally banned endosulfan use in the state and appointed an expert Commission to study the matter. The National Human Rights Commission entrusted the National Institute of Occupational Health in 2002 to conduct a scientific study. A detailed epidemiological survey was conducted in 2010 by the Government Medical College Calicut, Kerala, in addition to an independent study (90, 91). These studies reported the direct association of aerial spray of endosulfan to the reported cases of health damage in the region.

However, the direct cause–effect relationships were questioned and the findings challenged, on the basis of methodological lapses and lack of scientific rigor (92). The authors alleged opportunistic use of scientific claims and demanded a detailed multidisciplinary epidemiological study. But counterarguments were raised on the grounds of insufficient information on scientific prescriptions regarding use, divergence in actual field practices, environmental and human health effects of exposure, and the limitations in epidemiological studies (93). On the basis of legal directives and political decisions, a compensation package was declared for the victims. An estimated 96.23 million USD compensation package was implemented by different agencies. Dileep Kumar & Jayakumar (94) provide a detailed discussion on the chronology of events leading to the ban of endosulfan and payment of compensation. A recent publication reiterating the inconclusive scientific evidence of higher prevalence of health damage in endosulfan-sprayed villages is the latest addition to the debate (95).

The resource limitations for conducting detailed scientific studies, complexity of socioeconomic conditions, and cultural and behavioral aspects of the population pose challenges in establishing the cause–effect relationship in a conclusive manner. There are no epidemiological studies to disprove the direct link or associate the health damages in the locality with any other causes. The precautionary principle was highlighted in this case by the Supreme Court while issuing directions for the ban of the chemical and for the compensation package (94). The question now is whether the private gains of endosulfan use in cashew farming can be justified when the gains are compared with the long-term social and economic costs incurred by the public and private sectors.

Glyphosate, a herbicide that was introduced in 1974, has been widely used across the world and was projected as a safe chemical. But there were conflicting reports from different agencies. Whereas the EPA reported in 2010 that there was a low risk of carcinogenicity associated with glyphosate, the International Agency for Research on Cancer, France, a subsidiary of WHO, in 2015 classified glyphosate as a probable human carcinogen. Following this, hundreds of lawsuits were filed in courts across the United States against the manufacturer of the chemical. Edwin Hardeman from California, suffering from non-Hodgkin's lymphoma (NHL), a form of cancer, approached the court claiming that glyphosate was responsible for his disease. He had been handling the chemical for nearly 30 years, as part of his occupation. This trial was selected as a bellwether trial (a trial that would inform future litigations), as a series of litigations were filed across the state.

The evidence presented was based on epidemiological studies (to establish the association between agent and outcome), including both case control studies (96–99) as well as meta-analyses (100, 101). The results of an Agricultural Health Study covering more than 57,000 licensed pesticide applicators were also examined (97, 101). On the basis of this evidence, studies on animals, and mechanistic data and testimonials of experts, the court concluded that glyphosate can cause cancer (NHL) in humans. It also ordered the manufacturer to pay a compensation of 90 million USD. A series of litigations on similar lines were filed subsequently. In June 2020, the company agreed to settle nearly 95,000 cases in the United States, for 10 billion USD, reflecting the economic cost of associated health damage.

There are reports on the carcinogenic nature of several extensively used pesticides, although the field-level studies are only indicative in nature. On the basis of a detailed literature review on pesticide exposure and cancer incidence among rural populations, farmers, pesticide applicators, and farm workers, pesticide exposure was associated with NHL, multiple myeloma, prostate cancer, leukemia, and bladder and colon cancers (102). Pesticide exposure is related to blood cancer in children (103); the rate of abdomen cancer was found to be increased in areas of high nitrate concentration and areas with high levels of weed killer contamination (104, 105). However, applying modern methods of epidemiological and toxicological studies with a focus on biological plausibility and mode of toxicological action on humans is recommended, to increase our understanding of the associations between pesticides and cancer (106).

Most of the pest control chemicals that are endocrine disruptors, used to attack the reproductive system of pests, also impact the human reproductive process, leading to infertility. The residues left by endocrine disruptors such as organochlorine and organophosphates lead to lower sperm count, semen volume, and movement, in turn leading to oligospermia (extremely low) or azoospermia (zero count). In the case of women, there are reports of losing good quality eggs at a younger age when compared to previous generations (104).

Pesticide exposure is also attributed with psychiatric problems (107–109). In Mexico, farmers exposed to pesticides showed 25% elevation in depression and depression–anxiety, and 24% showed inhibited enzymatic activity with generalized anxiety (110). Long-term exposure of pesticides as causal agents of Parkinson's and Alzheimer's diseases in addition to various other

reproductive and respiratory disorders has also been reported (105). Occupational exposure to pesticides may also cause cardiovascular diseases (111). Exposure to the organochlorine group of pesticides has been found to be associated with genotoxicity and oxidative stress in pregnant women in India. This in turn results in caesarean deliveries and preterm babies with lower birth weights (112). There are reports of pesticide residues in human breast milk samples and cases of prenatal exposure, which lead to negative health impacts in children (110, 113–114). Postnatal exposure can adversely affect a child's neuropsychological behavior (112, 115).

Exposure through multiple sources, such as air, water, food, and beverages, is very common under real-world situations. Dietary exposure through agrifoods and animal products leads to cocktail residues of different chemicals. This chemical cocktail in human systems may have synergistic effects and exhibit more toxicity than a single molecule (116, 117). Renal damage consistent with chronic kidney disease incidence in Sri Lanka was reported to be linked to the synergistic effects of exposure to glyphosate with other pollutants like paraquat, under stressful physical labor conditions, such as high temperatures in lowland tropical regions (118).

5. CONCLUSION

There is a growing volume of scientific literature on the adverse effects of agrochemical use on both environmental quality and human health. The global production, consumption, and export of chemical pesticides often follow unscientific practices, augmented by aggressive marketing. As a result, even chemicals that are banned in a country get exported to other countries. This is also aided by either poor regulations and/or the lack of enforcement of regulations in the importing countries, which are primarily developing countries. Compounding this are technological advancements, such as herbicide tolerance through genetic modification, which necessitate higher consumption of these chemicals.

Parallely, there has been a global effort to regulate the production, distribution, and use of agrochemicals, which was initiated with the ban on DDT. The Stockholm Convention, a global treaty that came into force in May 2004, is an outcome of such an effort (119). The treaty, which has been ratified by 152 countries, aims to protect human health and environment from POPs. Managing fertilizer and pesticide pollution risk is one of the themes in tracking a nation's progress toward sustainable agriculture under the United Nations Sustainable Development Goals (120). A 2018 global survey on pesticide regulation in agriculture reveals the presence of pesticide legislation in 95% of the countries surveyed (30). There is an internationally applied code of conduct for labeling pesticides, which undergoes periodic revision (121).

There have also been efforts by different countries to ensure scientific use of agrochemicals through different approaches. This includes legal, market-based, and educative interventions. The regulatory authorities of nations approve agrochemicals that are considered tolerable or nonpersistent at the recommended rate of application (27). In India, after more than 50 years, efforts are to replace the Insecticide Act, 1968, with a new Pesticide Management Bill, 2020, to facilitate use of green technologies in crop health management. The shift to a nutrient-based subsidy scheme of fertilizers in India is a price-based approach to encourage balanced fertilizer application. There is empirical evidence linking the earlier Retention Price cum Subsidy Scheme-based and the Maximum Retail Price-based fertilizer pricing policies to the skewed application of nitrogenous fertilizers (122). Furthermore, research in the field of plant health management has resulted in technological solutions for developing safer chemicals and greener alternatives. The Agreement on Agriculture, as part of the World Trade Organization's global trade regulations, specifies produce quality (pesticide residue) as one of the major factors in facilitating global trade in food commodities.

However, existing regulatory and management protocols are based on assessment frameworks that suffer from methodological drawbacks. This has resulted in a consistent increase in global use of agrochemicals deemed harmless by these frameworks. The current assessment frameworks do not account for synergistic long-term ecological impacts and do not capture the impact of agrochemical cocktails. The complex nature of the environmental impact of the agrochemicals and the interlinkages between the sinks in contributing to this impact are often not factored into the assessment. This results in legal use of several agrochemicals that are potentially harmful to both the environment and human health in the long run. This calls for more holistic approaches in scientific assessments of long-term ecological and health impacts. Furthermore, the regulatory framework needs to go beyond the technical to include social, ecological, and economic dimensions of agrochemical impact in order to protect human rights. A global shift to sustainable agriculture and food systems, in the context of natural resource scarcity and the threat of climate change, entails a paradigm shift from productivity enhancement to one that emphasizes and rewards ecosystem service flows from agriculture (123, 124). The UN Food Systems Summit has listed boosting nature-based solutions and nature-positive production systems as one of the priority areas of action. Global dialog about and action toward the transformation of agrifood systems in this direction has to be the way forward.

SUMMARY POINTS

1. Use of agrochemicals globally shows consistent increase, although the intensity of use is lower in developing countries. In 2019, global fertilizer use in agriculture was reported at 188.54 million tonnes, nitrogen being the major nutrient applied. Of the 4.2 million tonnes of pesticides used in 2018, a little over half (53%) were herbicides followed by fungicides and bactericides (23%) and insecticides (17%).
2. The application of pesticides in developing economies is reported to be unscientific at all levels of handling, from choice of pesticides to application methods. Use of pesticide cocktails and spurious products is also very common. A lack of regulations or their poor enforcement, lack of awareness among users, and unethical sales practices aid this status quo.
3. The extensive and unscientific use of agrochemicals has resulted in serious ecosystem damages—through drift, residual, and runoff effects. This has adverse consequences on beneficial organisms, aquatic and terrestrial biodiversity, soil biota, soil functions, and ecological balance. Pesticide residues in food products have serious health implications for humans and animals. Although environmental and human health impacts of agrochemicals are reported from across the globe, the impacts are comparatively more and severe in developing economies. Exposure leads to chronic and acute health impacts in human beings, which manifest in both the short term and long term.
4. Although some of the fungicides and insecticides are reported to be less harmful based on existing scientific assessments and controlled clinical trials, there exists ample field-based scientific evidence of long-term ecological damages that indirectly affect human health and general biodiversity. The health damages include dermatological, gastrointestinal, neurological, carcinogenic, respiratory, reproductive, psychological, and endocrine impairments, which most often are expressed after a time lag. Establishing the cause–effect relations under such circumstances is challenging, given methodological and financial aspects.

5. The human health impact of chemical pesticide use is also linked to the social problem of suicide. Intentional consumption of pesticides, especially highly hazardous pesticides, is a common method of suicide in many countries, and their regulation or ban can help reduce the suicide rate.
6. This can result in inefficient enforcement of scientific prescriptions. Scientific benchmarks could potentially exist at the national level, but distorted market policies driven by several factors, including political lobbying, often act as barriers for implementing such benchmarks.

FUTURE ISSUES

1. Currently, the policy decisions on the regulation and management of agrochemical use are largely based on the criterion of total quantity consumed. However, the toxicity, persistence, and ecological impacts of the agrochemicals should be the basis for policy decisions. Information on chemical group-wise data is required to make meaningful conclusions on the ecosystem and health impacts and to develop scientific benchmarks for management.
2. The complexity of socioeconomic and agroecological systems across time and space, the combined effect of cocktail residues, the synergistic effects of chemical compound groups, and the time lag between exposure and manifestation of symptoms are not currently captured by the existing monitoring and assessment framework. This warrants application of modern scientific tools in the ecological impact assessment framework. Moreover, research is currently concentrated on organochlorine pesticides, nitrogenous fertilizers, and heavy metal contamination. There is a need for intensive research on the negative externalities caused by agrochemicals, which fall under other chemical compound groups.
3. Effective legal and governance systems for ensuring safe use of agrochemicals need to be developed through global consultations and cooperation. Furthermore, there should be global institutional mechanisms for monitoring field-level ecosystem impacts across diverse agroecosystems. This should be in line with the Stockholm Convention on Persistent Organic Pollutants and World Health Organization guidelines. The individual country-level registration policy for each agrochemical should be revised periodically based on outputs from the global monitoring system.
4. Human health impacts are experienced more in developing countries despite comparatively less use of agrochemicals. This is mainly attributed to inadequate legal interventions and improper implementation, poor monitoring, and gaps in scientific prescriptions and farmer practices. This calls for effective regulatory and monitoring systems in all countries that accommodate the social, ecological, and economic dimensions of agrochemical use.
5. The popularization of eco-friendly agriproduction systems such as agroecology and other natural resource-conserving farming systems should be facilitated through policy support. A shift from a productivity enhancement approach to an ecosystem service approach to sustaining global agriculture would go a long way in ensuring productivity increases with minimum ecological harm.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

LITERATURE CITED

1. Statista. 2019. Global agrochemical industry. *Dossier*. <https://www.statista.com/study/37459/agricultural-chemical-industry-statista-dossier/>
2. Popp J, Pető K, Nagy J. 2013. Pesticide productivity and food security. A review. *Agron. Sustain. Dev.* 33:243–55
3. Tudi M, Daniel Ruan H, Wang L, Lyu J, Sadler R, et al. 2021. Agriculture development, pesticide application and its impact on the environment. *Int. J. Environ. Res. Public Health* 18(3):1112
4. Udeigwe TK, Teboh JM, Eze PN, Stietiya MH, Kumar V, et al. 2015. Implications of leading crop production practices on environmental quality and human health. *J. Environ. Manag.* 151:267–79
5. Bourguet D, Guillemaud T. 2016. The hidden and external costs of pesticide use. In *Sustainable Agriculture Reviews*, Vol. 19, ed. E Lichtfouse, pp. 35–120. Cham, Switz.: Springer
6. Guha R. 2016. *Environmentalism: A Global History*. London: Penguin
7. Clark JFM. 2017. Pesticides, pollution and the UK's silent spring, 1963–1964: poison in the Garden of England. *Notes Rec.* 71:297–327
8. John DA, Babu GR. 2021. Lessons from the aftermaths of Green Revolution on food system and health. *Front. Sustain. Food Syst.* 5:644559
9. Somvanshi PS, Pandiaraj T, Singh RP. 2020. An unexplored story of successful green revolution of India and steps towards ever green revolution. *J. Pharmacogn. Phytochem.* 9(1):1270–73
10. Galloway JN, Bleeker A, Erismann JW. 2021. The human creation and use of reactive nitrogen: a global and regional perspective. *Annu. Rev. Environ. Resour.* 46:255–88
11. Ellis EC. 2021. Land use and ecological change: a 12,000-year history. *Annu. Rev. Environ. Resour.* 46:1–33
12. Nielsen UN, Wall DH, Six J. 2015. Soil biodiversity and the environment. *Annu. Rev. Environ. Resour.* 40:63–90
13. FAO (U. N. Food Agric. Organ.). 2021. FAOSTAT Statistical Database. *Food and Agriculture Organization of the United Nations*. <https://www.fao.org/faostat/en/#data>
14. Liu Y, Xubin P, Junsheng L. 2015. A 1961–2010 record of fertilizer use, pesticide application and cereal yields: a review. *Agron. Sustain. Dev.* 35:8383–93
15. Bajak A. 2016. The developing world is awash in pesticides. There may be a better way. *Vox*, July 3. <https://www.vox.com/2016/7/3/12085368/developing-world-pesticides>
16. Sarker S, Dias Bernardes Gil J, Keeley J, Mohring N, Jansen K. 2021. *The use of pesticides in developing countries and their impact on health and the right to food*. Rep., Policy Dep. Extern. Relat. Direct. Gen. Extern. Pol. Union, Eur. Parliam., Strasbourg, Fr. <https://www.europarl.europa.eu/cmsdata/219887/Pesticides%20health%20and%20food.pdf>
17. Schreinemachers P, Tipraqsa P. 2012. Agricultural pesticides and land use intensification in high, middle and low income countries. *Food Policy* 37(6):616–26
18. Wu Y, Xi X, Tang X, Luo D, Gu B, et al. 2018. Policy distortions, farm size, and the overuse of agricultural chemicals in China. *PNAS* 115(27):7010–15
19. Willy DK, Muyanga M, Jayne TS. 2019. Can economic and environmental benefits associated with agricultural intensification be sustained at high population densities? A farm level empirical analysis. *Land Use Policy* 81:100–10
20. Khanal G, Singh A. 2016. Patterns of pesticide use and associated factors among the commercial farmers of Chitwan, Nepal. *Environm. Health Insights* 10(1):1–7
21. Rahaman MM, Islam KS, Jahan M. 2018. Rice farmers' knowledge of the risks of pesticide use in Bangladesh. *J. Health Pollut.* 8(20):181203
22. Devi PI. 2010. Pesticides in agriculture—A boon or a curse? A case study of Kerala. *Econ. Polit. Wkly.* 45(26–27):199–207

23. WHO (World Health Organ.), FAO (U. N. Food Agric. Organ.). 2019. *Global situation of pesticide management in agriculture and public health: report of a 2018 WHO-FAO survey*. Rep., WHO, Geneva. <https://apps.who.int/iris/handle/10665/329971>
24. Zhang J, Wang J, Zhou X. 2019. Farm machine use and pesticide expenditure in maize production: health and environment implications. *Int. J. Environ. Res. Public Health* 16(10):1808
25. Evans AEV, Mateo-Sagasta J, Qadir M, Boelee E, Ippolito A. 2019. Agricultural water pollution: key knowledge gaps and research needs. *Curr. Opin. Environ. Sustain.* 36:20–27
26. Zhang L, Yan C, Guo Q, Zhang J, Ruiz-Menjivar J. 2018. The impact of agricultural chemical inputs on environment: global evidence from informetrics analysis and visualization. *Int. J. Low-Carbon Technol.* 13(4):338–52
27. Zikankuba VL, Mwanyika G, Ntwenya JE, James A. 2019. Pesticide regulations and their malpractice implications on food and environment safety. *Cogent Food Agric.* 5:1601544
28. Khan MN, Mobin M, Zahid A, Alamri S. 2017. Fertilizers and their contaminants in soils, surface and groundwater. *Ref. Module Earth Syst. Environ. Sci.* 5:225–40
29. Mandal A, Sarkar B, Mandal S, Vithanage M, Patra AK, Manna MC. 2020. Impact of agrochemicals on soil health. In *Agrochemicals Detection, Treatment and Remediation*, ed. M Narasimha, V Prasad, pp. 161–87. Oxford, UK: Butterworth-Heinemann
30. Maggi F, Tang F, la Cecilia D, McBratney A. 2019. PEST-CHEMGRIDS, global gridded maps of the top 20 crop-specific pesticide application rates from 2015 to 2025. *Sci. Data* 6(1):170
31. Abbes K, Biondi A, Kurtulus A, Ricupero M, Russo A, et al. 2015. Combined non-target effects of insecticide and high temperature on the parasitoid *Bracon nigricans*. *PLOS ONE* 10(9):e0138411
32. Mahmood I, Imadi SR, Shazadi K, Gul A, Hakeem KR. 2016. Effects of pesticides on environment. In *Plant, Soil and Microbes*, ed. KR Hakeem, M Akhtar, S Abdullah, pp. 253–69. Cham, Switz.: Springer
33. Pérez-Méndez N, Andersson GKS, Requier F, Hipólito J, Aizen MA, et al. 2020. The economic cost of losing native pollinator species for orchard production. *J. Appl. Ecol.* 57:599–608
34. Gill HK, Garg H. 2014. Pesticides: environmental impacts and management strategies. In *Pesticides—Toxic Aspects*, ed. ML Larramendy, S Soloneski, pp. 187–230. London: IntechOpen
35. Gunstone T, Cornelisse T, Klein K, Dubey A, Donley N. 2021. Pesticides and soil invertebrates: a hazard assessment. *Front. Environ. Sci.* 9. <https://doi.org/10.3389/fenvs.2021.643847>
36. Meena RS, Kumar S, Datta R, Lal R, Vijayakumar V, et al. 2020. Impact of agrochemicals on soil microbiota and management: a review. *Land* 9(2):34
37. Virág D, Naár Z, Kiss A. 2007. Microbial toxicity of pesticide derivatives produced with UV-photodegradation. *Bull. Environ. Contam. Toxicol.* 79(3):356–59
38. Newbold T, Hudson LN, Hill SL, Contu S, Lysenko I, et al. 2015. Global effects of land use on local terrestrial biodiversity. *Nature* 520(7545):45–50
39. Forister ML, Pelton EM, Black SH. 2019. Declines in insect abundance and diversity: We know enough to act now. *Conserv. Sci. Pract.* 1(8):e80
40. Mourtzinis S, Krupke CH, Esker PD, Varenhorst A, Arneson NJ, et al. 2019. Neonicotinoid seed treatments of soybean provide negligible benefits to US farmers. *Sci. Rep.* 9:11207
41. Bernardes MFF, Pazin M, Pereira LC, Dorta DJ. 2015. Impact of pesticides on environmental and human health. In *Toxicology Studies—Cells, Drugs and Environment*, ed. AC Andreazza, G Scola, pp. 195–233. London: IntechOpen
42. Chakraborty P, Zhang G, Li J, Sivakumar A, Jones KC. 2015. Occurrence and sources of selected organochlorine pesticides in the soil of seven major Indian cities: assessment of air–soil exchange. *Environ. Pollut.* 204:74–80
43. Debnath M, Khan MS. 2017. Health concerns of pesticides. In *Pesticide Residue in Foods*, ed. M Khan, M Rahman, pp. 103–18. Cham, Switz.: Springer
44. Liu L, Tang J, Zhong G, Zhen X, Pan X, Tian C. 2018. Spatial distribution and seasonal variation of four current-use pesticides (CUPs) in air and surface water of the Bohai Sea, China. *Sci. Total Environ.* 621:516–23
45. Farhan M, Wajid A, Hussain T, Jabeen F, Ishaque U, et al. 2021. Investigation of oxidative stress enzymes and histological alterations in tilapia exposed to chlorpyrifos. *Environ. Sci. Pollut. Res. Int.* 28(11):13105–11

46. Prashar P, Shah S. 2016. Impact of fertilizers and pesticides on soil microflora in agriculture. In *Sustainable Agriculture Reviews*, Vol. 19, ed. E Lichtfouse, pp. 331–61. Cham, Switz.: Springer
47. Ou J, Li H, Ou X, Yang Z, Chen M, et al. 2020. Degradation, adsorption and leaching of phenazine-1-carboxamide in agricultural soils. *Ecotoxicol. Environ. Saf.* 205:111374
48. Srivastava AL. 2020. Chemical fertilizers and pesticides: role in groundwater contamination. In *Agrochemicals Detection, Treatment and Remediation*, ed. M Narasimha, V Prasad, pp. 143–59. Oxford, UK: Butterworth-Heinemann
49. Delcour I, Spanoghe P, Uyttendaele M. 2015. Literature review: impact of climate change on pesticide use. *Food Res. Int.* 68:7–15
50. Sunam R, Mahat A. 2020. *Addressing water pollution from agriculture in South Asia*. Policy Brief, November. https://www.caritas.ch/fileadmin/user_upload/Caritas_Schweiz/data/site/was-wir-tun/engagement-weltweit/klima/Regional_Policy_Brief-SACB-Final-1_Feb_2021.pdf
51. Sankoh AI, Whittle R, Semple KT, Jones KC, Sweetman AJ. 2016. An assessment of the impacts of pesticide use on the environment and health of rice farmers in Sierra Leone. *Environ. Int.* 94:458–66
52. Peterson MA, Collavo A, Ovejero R, Shivrain V, Walsh MJ. 2018. The challenge of herbicide resistance around the world: a current summary. *Pest Manag. Sci.* 74(10):2246–59
53. Zhang D, Xiao Y, Xu P, Yang X, Wu Q, Wu K. 2021. Insecticide resistance monitoring for the invasive populations of fall armyworm, *Spodoptera frugiperda* in China. *J. Integr. Agric.* 20(3):783–91
54. Gutiérrez-Moreno R, Mota-Sanchez D, Blanco CA, Whalon ME, Terán-Santofimio H, et al. 2019. Field-evolved resistance of the fall armyworm (Lepidoptera: Noctuidae) to synthetic insecticides in Puerto Rico and Mexico. *J. Econ. Entomol.* 112(2):792–802
55. Schäfer RB, Liess M, Altenburger R, Filser J, Hollert H, et al. 2019. Future pesticide risk assessment: narrowing the gap between intention and reality. *Environ. Sci. Eur.* 31:21
56. Brühl CA, Zaller JG. 2019. Biodiversity decline as a consequence of an inappropriate environmental risk assessment of pesticides. *Front. Environ. Sci.* 7:177
57. Greenpeace. 2015. *The bitter taste of Europe's apple production and how ecological solutions can bloom*. Rep., Greenpeace Res. Lab., Sch. Biosci., Innov. Cent., Univ. Exeter, UK. <https://www.greenpeace.to/greenpeace/wp-content/uploads/2015/06/TheBitterTasteENG.pdf>
58. Goulson D. 2015. Neonicotinoids impact bumblebee colony fitness in the field: a reanalysis of the UK's Food & Environment Research Agency 2012 experiment. *PeerJ* 3:e854
59. Sánchez-Bayo F, Tennekes HA. 2015. Environmental risk assessment of agrochemicals—a critical appraisal of current approaches. In *Toxicity and Hazard of Agrochemicals*, ed. LL Marcelo, S Soloneski, pp. 7–22. London: IntechOpen
60. van der Sluijs JP, Amaral-Rogers V, Belzunces LP, Bijleveld van Lexmond MF, Bonmatin JM, et al. 2015. Conclusions of the Worldwide Integrated Assessment on the risks of neonicotinoids and fipronil to biodiversity and ecosystem functioning. *Environ. Sci. Pollut. Res. Int.* 22(1):148–54
61. Reuter W, Neumeister L. 2015. *Europe's pesticide addiction: how industrial agriculture damages our environment*. Sci. Rep., Greenpeace, Amsterdam. <https://www.greenpeace.org/static/planet4-international-stateless/2015/10/1a0d04c1-europes-pesticide-addiction.pdf>
62. Schläpfer F. 2020. External costs of agriculture derived from payments for agri-environment measures: framework and application to Switzerland. *Sustainability* 12(15):6126
63. IDH, True Price. 2016. *The true price of cotton from India*. Rep., IDH, True Price, Amsterdam. <https://trueprice.org/the-true-price-of-cotton-from-india/>
64. FAO (U. N. Food Agric. Organ.). 2015. *Natural capital impacts in agriculture: supporting better business decision-making*. Rep., FAO, Rome. https://www.fao.org/fileadmin/templates/nr/sustainability_pathways/docs/Natural_Capital_Impacts_in_Agriculture_final.pdf
65. Mateo-Sagasta J, Marjani SZ, Turrall H. 2017. *Water pollution from agriculture: a global review. Executive summary*. Rep., U. N. Food Agric. Organ. <http://www.fao.org/3/i7754e/i7754e.pdf>
66. CDC (Cent. Disease Control Prev.). 2009. *Fourth national report on human exposure to environmental chemicals*. CDC, U.S. Dep. Health Hum. Serv., Atlanta. <https://www.cdc.gov/exposurereport/pdf/fourthreport.pdf>
67. Nicolopoulou-Stamati P, Maipas S, Kotampasi C, Stamatis P, Hens L. 2016. Chemical pesticides and human health: the urgent need for a new concept in agriculture. *Front. Public Health* 4:148

68. UNEP (U. N. Environ. Progr.). 2021. *Environmental and health impacts of pesticides and fertilizers and ways of minimizing them: envisioning a chemical safe world—summary for policymakers*. Rep., UNEP, Nairobi. <https://wedocs.unep.org/xmlui/bitstream/handle/20.500.11822/34463/JSUNEPPE.pdf?sequence=13>
69. Gupta S, Gupta K. 2020. Bioaccumulation of pesticides and its impact on biological systems. In *Pesticides in Crop Production: Physiological and Biochemical Action*, ed. PK Srivastava, VP Singh, A Singh, DK Tripathi, S Singh, et al., pp. 55–67 Hoboken, NJ: Wiley
70. Hassaan MA, Nemr AE. 2020. Pesticides pollution: classifications, human health impact, extraction and treatment techniques. *Egypt. J. Aquat. Res* 46(3):207–20
71. Sajjad A, Muhammad U, Asif S, Kaiser S, Azhar H. 2021. Environmental and health effects of pesticide residues. *Sustain. Agric. Rev.* 48:311–36
72. Guan KL, Liu Y, Luo XJ, Zeng YH, Mai BX. 2020. Short- and medium-chain chlorinated paraffins in aquatic organisms from an e-waste site: biomagnification and maternal transfer. *Sci. Total Environ.* 708:134840
73. Wang X, Zhong W, Xiao B, Liu Q, Yang L, et al. 2019. Bioavailability and biomagnification of organophosphate esters in the food web of Taihu Lake, China: impacts of chemical properties and metabolism. *Environ. Int.* 125:25–32
74. Zhou S, Pan Y, Zhang L, Xue B, Zhang A, Jin M. 2018. Biomagnification and enantiomeric profiles of organochlorine pesticides in food web components from Zhoushan Fishing Ground, China. *Mar. Pollut. Bull.* 131(A):602–10
75. Katagi T, Tanaka H. 2016. Metabolism, bioaccumulation, and toxicity of pesticides in aquatic insect larvae. *J. Pestic. Sci.* 41(2):25–37
76. Ali S, Ullah MI, Sajjad A, Shakeel Q, Hussain A. 2021. Environmental and health effects of pesticide residues. In *Sustainable Agriculture Reviews*, Vol. 48, ed. Inamuddin, MI Ahamed, E Lichtfouse, pp. 311–66. Cham, Switz.: Springer
77. Mew EJ, Padmanathan P, Konradsen F, Eddleston M, Chang SS, et al. 2017. The global burden of fatal self-poisoning with pesticides 2006–15: systematic review. *J. Affect. Disord.* 219:93–104
78. WHO (World Health Organ.), UNEP (U. N. Environ. Progr.), eds. 1990. *Public health impact of pesticides used in agriculture*. Rep., WHO, Geneva
79. Manjunatha AV, Ramappa KB. 2017. *Farmer suicides: an all India study*. Rep., Dep. Agric. Coop. Farmers Welfare, Gov. India, New Delhi
80. Bonvoisin T, Utyasheva L, Knipe D, Gunnell D, 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
81. Arya V, Page A, Gunnell D, Armstrong G. 2021. Changes in method specific suicide following a national pesticide ban in India (2011–2014). *J. Affect. Disord.* 278:592–600
82. Karunarathne A, Gunnell D, Konradsen F, Eddleston M. 2020. How many premature deaths from pesticide suicide have occurred since the agricultural Green Revolution? *Clin. Toxicol.* 58(4):227–32
83. Boedeker W, Watts M, Clausing P, Marquez E. 2020. The global distribution of acute unintentional pesticide poisoning: estimations based on a systematic review. *BMC Public Health* 20:1875
84. Knipe DW, Chang SS, Dawson A, Eddleston M, Konradsen F, et al. 2017. Suicide prevention through means restriction: impact of the 2008–2011 pesticide restrictions on suicide in Sri Lanka. *PLOS ONE* 12(3):e0172893
85. Utyasheva L, Eddleston M. 2021. Prevention of pesticide suicides and the right to life: the intersection of human rights and public health priorities. *J. Hum. Rights* 20:52–71
86. World Future Council. 2021. Future policy award on protection from hazardous chemicals. *World Future Council*. <https://www.worldfuturecouncil.org/p/2021-protection-from-hazardous-chemicals>
87. Carvalho FP. 2017. Pesticides, environment, and food safety. *Food Energy Secur.* 6(2):48–60
88. Rajendran S. 2002. Pesticide spraying in Kerala—human costs and environmental loss. *Econ. Political Wkly.* 37(23):2206–7
89. Rajendran S. 2003. *Environment and health aspects of pesticide use in Indian agriculture*. In *Proceedings of the Third International Conference on Environment and Health, Chennai, India, 15–17 December, 2003*, ed. MJ Bunch, VM Suresh, T Vasantha Kumaran, pp. 353–73. Dep. Geogr., Univ. Madras, Chennai, Tamil

- Nadu, India/Environ. Stud., York Univ., Toronto, ON, Can. http://www.yorku.ca/bunchmj/ICEH/proceedings/Rajendran_S_ICEH_papers_353to373.pdf
90. Prabhakumari C, Jayakrishnan T, Bina T. 2011. *Epidemiological studies related to health in endosulfan affected areas at Kasaragod district in Kerala 2010–11*. Rep., Dep. Commun. Med., Gov. Med. Coll., Calicut, Ind. <https://www.scribd.com/doc/312236388/Calicut-Medical-College-Full-Report-Endosulfan-Issue>
 91. Embrandiri A, Singh RP, Ibrahim HM, Khan AB. 2012. An epidemiological study on the health effects of endosulfan spraying on cashew plantations in Kasaragod district, Kerala, India. *Asian J. Epidemiol.* 5:22–31
 92. Sreekumar KM, Prathapan KD. 2013. A critique of the epidemiological studies on health in allegedly endosulfan-affected areas in Kasaragod, Kerala. *Curr. Sci.* 104(1):16–21
 93. Mahapatro GK, Panigrahi M. 2014. Endosulfan issue: science versus conscience. *Curr. Sci.* 106:152–55
 94. Dileep Kumar AD, Jayakumar C. 2019. From precautionary principle to nationwide ban on endosulfan in India. *Bus. Hum. Rights J.* 4(2):343–49
 95. Sreekumar KM, Prathapan KD. 2021. An evidence based inquiry into the endosulfan tragedy in Kasaragod, Kerala. *Econ. Political Wkly.* 56(41):45–53
 96. De Roos AJ, Blair A, Ruseicki JA, Hoppin JA, Svec M, et al. 2005. Cancer incidence among glyphosate-exposed pesticide applicators in the Agricultural Health Study. *Environ. Health Perspect.* 113(1):49–54
 97. De Roos AJ, Zahm SH, Cantor KP, Weisenburger DD, Holmes FF, et al. 2003. Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men. *Occup. Environ. Med.* 60(9):e11
 98. McDuffie HH, Pahwa P, McLaughlin JR, Spinelli JJ, Fincham S, et al. 2001. Non-Hodgkin's lymphoma and specific pesticide exposures in men: cross-Canada study of pesticides and health. *Cancer Epidemiol. Biomark. Prev.* 10(11):1155–63
 99. Eriksson M, Hardell L, Carlberg M, Akerman M. 2008. Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis. *Int. J. Cancer* 123(7):1657–63
 100. Schinasi L, Leon ME. 2014. Non-Hodgkin lymphoma and occupational exposure to agricultural pesticide chemical groups and active ingredients: a systematic review and meta-analysis. *Int. J. Environ. Res. Public Health* 11(4):4449–527
 101. Chang ET, Delzell E. 2016. Systematic review and meta-analysis of glyphosate exposure and risk of lymphohematopoietic cancers. *J. Environ. Sci. Health B* 51(6):402–34
 102. Andreotti G, Koutros S, Hofmann JN, Sandler DP, Lubin JH, et al. 2018. Glyphosate use and cancer incidence in the agricultural health study. *J. Natl. Cancer Inst.* 110(5):509–16
 103. Pluth TB, Zanini LAG, Battisti IDE. 2019. Pesticide exposure and cancer: an integrative literature review. *Saúde Debate* 43:906–24
 104. Srivastava AK, Kesavachandran C. 2019. *Health Effects of Pesticides*. London: CRC Press
 105. Sabarwal A, Kumar K, Singh RP. 2018. Hazardous effects of chemical pesticides on human health—cancer and other associated disorders. *Environ. Toxicol. Pharmacol.* 63:103–14
 106. Burns CJ, Juberg DR. 2021. Cancer and occupational exposure to pesticides: an umbrella review. *Int. Arch. Occup. Environ. Health* 94(5):945–57
 107. Faria NM, Fassa AG, Meucci RD, Fiori NS, Miranda VI. 2014. Occupational exposure to pesticides, nicotine and minor psychiatric disorders among tobacco farmers in southern Brazil. *Neurotoxicology* 45:347–54
 108. Buralli RJ, Ribeiro H, Leão RS, Marques RC, Guimarães JRD. 2019. Data on pesticide exposure and mental health screening of family farmers in Brazil. *Data Brief* 25:103993
 109. Buralli RJ, Ribeiro H, Iglesias V, Muñoz-Quezada MT, Leão RS, et al. 2020. Occupational exposure to pesticides and health symptoms among family farmers in Brazil. *Rev. Saúde Pública* 54:133
 110. Serrano-Medina A, Ugalde-Lizárraga A, Bojorquez-Cuevas MS, Garnica-Ruiz J, González-Corral, et al. 2019. Neuropsychiatric disorders in farmers associated with organophosphorus pesticide exposure in a rural village of Northwest México. *Int. J. Environ. Res. Public Health* 16(5):689
 111. Berg ZK, Rodriguez B, Davis J, Katz AR, Cooney RV, Masaki K. 2019. Association between occupational exposure to pesticides and cardiovascular disease incidence: the Kuakini Honolulu Heart Program. *J. Am. Heart Assoc.* 8(19). <https://doi.org/10.1161/JAHA.119.012569>

112. Dwivedi N, Mahdi AA, Deo S, Ahmad MK, Kumar D. 2022. Assessment of genotoxicity and oxidative stress in pregnant women contaminated to organochlorine pesticides and its correlation with pregnancy outcome. *Environ. Res.* 204(B):112010
113. Lu D, Wang D, Ni R, Lin Y, Feng C, et al. 2015. Organochlorine pesticides and their metabolites in human breast milk from Shanghai, China. *Environ. Sci. Pollut. Res. Int.* 22(12):9293–306
114. Buscail C, Chevrier C, Serrano T, Pelé F, Monfort C, et al. 2015. Prenatal pesticide exposure and otitis media during early childhood in the PELAGIE mother-child cohort. *Occup. Environ. Med.* 72(12):837–44
115. González-Alzaga B, Hernández AF, Rodríguez-Barranco M, Gómez I, Aguilar-Garduño C, et al. 2015. Pre- and postnatal exposures to pesticides and neurodevelopmental effects in children living in agricultural communities from South-Eastern Spain. *Environ. Int.* 85:229–37
116. Singh N, Gupta VK, Kumar A, Sharma B. 2017. Synergistic effects of heavy metals and pesticides in living systems. *Front. Chem.* 5:70
117. Roth N, Wilks MF. 2018. *Combination (“cocktail”) effects of pesticide residues in food*. Swiss Cent. Appl. Hum. Toxicol. Rep., Swiss Fed. Food Safety Vet. Off., Basel. [https://www.blv.admin.ch/dam/blv/de/dokumente/lebensmittel-und-ernaehrung/lebensmittelsicherheit/verantwortlichkeiten/bericht-scaht-cocktail-effect-pestizide.pdf.download.pdf/SCAHT%20Report%20for%20FSVO%20-%20Combination%20\(%E2%80%9Ccocktail%E2%80%9D\)%20effects%20of%20pesticide%20residues%20in%20food_DE.pdf](https://www.blv.admin.ch/dam/blv/de/dokumente/lebensmittel-und-ernaehrung/lebensmittelsicherheit/verantwortlichkeiten/bericht-scaht-cocktail-effect-pestizide.pdf.download.pdf/SCAHT%20Report%20for%20FSVO%20-%20Combination%20(%E2%80%9Ccocktail%E2%80%9D)%20effects%20of%20pesticide%20residues%20in%20food_DE.pdf)
118. Gunatilake S, Seneff S, Orlando L. 2019. Glyphosate’s synergistic toxicity in combination with other factors as a cause of chronic kidney disease of unknown origin. *Int. J. Environ. Res. Public Health* 16(15):2734
119. UNIDO (U. N. Ind. Dev. Organ.). 2004. Stockholm Convention. *United Nations Industrial Development Organization*. <https://www.unido.org/our-focus-safeguarding-environment-implementation-multilateral-environmental-agreements/stockholm-convention>
120. UNSTATS (U. N. Stat. Div.). 2021. SDG indicator metadata (harmonized metadata template - format version 1.0). *United Nations Statistical Division*. <https://unstats.un.org/sdgs/metadata/files/Metadata-05-03-01.pdf>
121. FAO (U. N. Food Agric. Organ.), WHO (World Health Organ.). 2015. *International code of conduct on pesticide management: guidelines on good labelling practice for pesticides (revised)*. Rep., FAO, Rome/WHO, Geneva. https://apps.who.int/iris/bitstream/handle/10665/195650/9789241509688_eng.pdf?sequence=1&isAllowed=y
122. Some S, Roy J, Ghose A. 2019. Non-CO₂ emission from cropland based agricultural activities in India: a decomposition analysis and policy link. *J. Clean. Prod.* 225:637–46
123. Manjula M, Venkatachalam L, Mukhopadhyay P, Kumar L. 2019. Ecosystems service approach for revitalizing agriculture in India. *Curr. Sci.* 116(5):723–27
124. Kumar L, Manjula M, Bhatta R, Venkatachalam L, Kumar DS, et al. 2019. Doubling India’s farm incomes: paying farmers for ecosystem services, not just crops. *Econ. Polit. Wkly.* 54(23):43–49