

Review

Human Health and Soil Health Risks from Heavy Metals, Micro(nano)plastics, and Antibiotic Resistant Bacteria in Agricultural Soils

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Abstract: Humans are exposed to agricultural soils through inhalation, dermal contact, or the consumption of food. Human health may be at risk when soils are contaminated; while some soil contaminants such as heavy metals (HMs) have been extensively studied, others such as micro(nano)plastics (MNPs) or antibiotic-resistant bacteria (ARB) pose novel threats. This paper investigates the linkages between soil contamination and human health risk by reviewing the state of knowledge on HMs, MNPs, and ARB in agricultural soils. A keyword-based search in Web of Science, Scopus, and Google Scholar was conducted, complemented with a backward snowball search. We analysed main sources of contamination for agricultural soils, risks to human health differentiated by uptake pathway (ingestion, inhalation, dermal), and interactions of contaminants with microorganism, soil fauna, and plants. Results show that the emergence and spread of ARB and antibiotic resistant genes from agricultural soils and their contribution to antibiotic resistances of human pathogens is recognized as a significant threat. Likewise, a growing body of evidence indicates that MNPs are able to enter the food chain and to have potentially harmful effects on human health. For HM, knowledge of the effects on human health is well established. Multiple agricultural practices increase HM concentrations in soils, which may lead to adverse health effects from the ingestion of contaminated products or inhalation of contaminated soil particles. Severe knowledge gaps exist about the pathways of the contaminants, their behaviour in soil, and human uptake. Little is known about long-term exposure and impacts of MNPs, antibiotics and ARB on human health or about the possible combined effects of MNPs, ARB, and HMs. Missing monitoring systems inhibit a comprehensive assessment of human health risks. Our research demonstrates the need for human health risk assessment in the context of agricultural soils, in particular to be able to assess risks related to measures reinforcing the concept of the circular economy.

Keywords: heavy metals; micro(nano)plastics; antibiotic resistant bacteria; soil health; soil contamination; human health; plastic source; trace metal; food chain



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1. Introduction

Soils play a fundamental role in human health and well-being [1]. However, population growth and increasing food demand have led to an intensification of agricultural production systems, putting stress on soils and increasing exposure of humans to soil contaminants [2]. The connections between soil health and human health are starting to emerge [3] and gain attention in scientific research [4]. Some human-induced contaminants, such as heavy metals (HMs), are well-known and have been present in agricultural soils for a long time. Others, such as micro(nano)plastics (MNPs) or antibiotic-resistant bacteria

(ARB) represent emerging and novel threats. Consequently, early studies on soil contamination have mostly focused on HMs, while research into MNPs and ARB has increased exponentially in recent years [5].

The term “heavy metals” refers to metals (e.g., Cd, Co, Hg, Pb) and metalloids (e.g., Se, Sb, As) with an atomic number greater than 20 [6] and a density greater than 5 g/cm^{-3} ; the term is often associated with contamination and potential toxicity or ecotoxicity [7,8]. Naturally HMs occur at low concentrations in soils, and some of them are essential micronutrients for plants, animals, and humans (e.g., Fe, Zn, Ni, Cu, Mn) [9]. However, as a consequence of different agricultural practices, high concentrations of HMs in soil can cause toxic effects. HMs are persistent and non-biodegradable, and some of them are toxic at low concentrations. Where they are bioavailable, they pose a major threat to both soil health and human health. HMs accumulated in soils can be taken up by plants and enter the food chain and the human body [10]. Additionally, they can be inhaled together with soil particles or, in specific cases or at high concentrations, absorbed through the skin. There is evidence linking mutagenic, teratogenic, and carcinogenic effects in humans with HMs exposure [10,11]. So far, various reviews have addressed different aspects of HMs in the plant–soil context, such as transport and redistribution processes in plants [12]; HM inputs and outputs to and from agricultural soils [13]; smart sensing for HM monitoring in agricultural soils [14]; HM toxicity in agricultural soils [15], and evaluation of HMs in agricultural lands [16].

Microplastics (MPs) (1 μm –5 mm) or nanoplastics (NPs) ($\leq 1 \mu\text{m}$) represent fragmented plastic particles (due to microbial activities, photodegradation, and mechanical forces) [17,18]. MNPs are persistent contaminants that are ubiquitous in the soil environment [19]. They are of particular concern, as the use of plastic materials in agriculture is expected to further increase [20]. Though MNPs have been extensively studied in aquatic systems, their presence and fate in agricultural systems are still insufficiently understood. Most of the studies suggest that the main risk of MNPs for human health arises from the release of additives which are known to be endocrine disruptors or carcinogenic (e.g., bisphenol A, phthalates) [21], or from their ability to sequester co-pollutants from the environment (e.g., HMs, ARB), enhancing their transfer and uptake [22,23]. The presence of MNPs in agricultural soils leads to increased human uptake with food. This has been suggested to affect human health (oxidative stress, inflammation processes, genotoxicity, neurotoxicity, mitochondrial function) [24,25]. However, mechanisms of MNP toxicity in humans require further investigation, particularly regarding the long-term fate of the ingested MNPs [23,26]. Recent reviews of MNPs have addressed the state of knowledge regarding the sustainable use of plastic nets in agriculture [27]; MPs’ effects on crops [28]; the uptake and accumulation of MPs and NPs in plants [29]; MP pollution and remediation [30], and MPs in agricultural systems in relation to soil quality and crop yield [31].

Resistance development against chemical agents is a natural phenomenon, yet the presence of antibiotic (AB) residues in agricultural soils can accelerate both the development and proliferation of resistant bacteria strains [32]. It is well acknowledged that the expansion of resistances against ABs poses a growing risk to public health [33]. However, the emergence and spread of ARB and antibiotic-resistant genes (ARGs) from agricultural systems and their contribution to the resistance of human pathogens are complex processes that are not yet well understood [34]. Studies have reported that low level concentrations of ABs (below minimum inhibitory concentrations), which can be found in food crops, might impact bacterial resistance selection, contributing to resistance enrichment [32]. Uncertainties therefore remain regarding the linkages between soil ARB and human health, transmission pathways, and mechanisms of ARB in agricultural ecosystems [33]. Recent reviews concerning ARBs have also addressed sources of ARBs in the soil and the connection to human health risks [35] and contamination of fresh fruits and vegetables products by ARBs with further implications to human health risks [36].

While previous reviews have analysed specific aspects of HMs, MNPs, and ARB in agricultural soils, this paper aims to provide an overview on the state of knowledge of all

three contaminants in agricultural soils with a specific focus on linkages to human health risks. In particular, our objectives are to:

- (1) Investigate agriculturally related sources of contamination with HMs, MNPs, and ARB.
- (2) Analyse their effects on human health differentiated by uptake pathway (i.e., oral, respiratory, dermal), as well as interactions with soil microorganisms, fauna, and plants.
- (3) Identify current knowledge gaps relevant for assessing the linkages between soil contamination and human health.

We focus our analysis on contaminants introduced by humans and present in agricultural fields all over the world. Soil-related human health risks of natural origin or those only relevant in specific, locally isolated contexts were not considered. Natural health risks include HMs originating from elevated concentrations in parent rock, radionuclides, viruses, enteric bacteria, fungi, or parasites. Locally relevant contaminants include chemicals released by warfare activities [5] or chemicals released in accidents and spillages. Furthermore, we did not investigate the movement of contaminants through the soil or possible combined effects of multiple contaminants on human health.

In the following section, we provide details on our methodology. In Section 3 we present our results and discuss their implications, and in Section 4 we highlight the diverse state of the knowledge regarding the three contaminants and their pathways into the soil, their behaviour in the soil, and the potential risks to human health, while Section 5 presents our conclusions.

2. Material and Methods

We searched the Web of Science Core Collection (Article title, Abstract, Keyword), Scopus (All Fields), and Google Scholar for peer-reviewed publications on HMs, MNPs, and ARB in agricultural soils. Keywords combined the three contaminant groups with human health and agricultural soils (Table 1). Publications not addressing all three themes were therefore not selected. This excluded, for example, the huge body of literature addressing the contaminants in agricultural soils but without any relation to human health. Only publications in English were included in this review, and the publication date range was not restricted. For governance-related issues such as the regulation of contaminant inputs and monitoring, we focused on Europe. The keyword-based search was complemented with a backward snowball search, where selected references cited in the reviewed articles were then reviewed as well. The review was conducted between November 2021 and June 2022.

Table 1. Search terms used in the keyword search. All search strings were a combination of a contaminant term AND a human health term AND an agricultural soils term.

<i>Search String:</i>		
<i>Contaminant Term AND Human Health Term AND Agricultural Soils Term</i>		
<i>Contaminant Term (OR)</i>	<i>Human Health Term (OR)</i>	<i>Agricultural Soils Term (OR)</i>
<i>"heavy metal*" "trace metal*"</i>	<i>"human health*"</i>	<i>"agricultural soil*" "soil ecosystem*" "agricultural*" "vegetable*" "food crop*" "plant*"</i>
<i>"antibiotic resistant bacteria*" "antibiotic resistant genes*" "antibiotic resistance" "antibiotic*"</i>	<i>"human health*"</i>	<i>"agricultural soil*" "agroecosystem*" "agricultural*"</i>
<i>"microplastic*" "nanoplastic*"</i>	<i>"human health*"</i>	<i>"agricultural soil*" "agroecosystems*" "agricultural*"</i>

To create an overview about the spatial distribution research, we extracted the country of origin from the reviewed articles. For field studies, we used the country where the analysis was performed, and for desktop studies, we used the country of the first author’s institution. In total, we reviewed 134 articles, 51 of which addressed HMs, 52 MNPs, and 31 ARB (Table 2). The distribution was mapped using the ESRI software ArcGIS Pro 2.7.3 (Figure 1).

Table 2. The total number of reviewed field and desk studies.

	Heavy Metals	Micro(nano)plastics	Antibiotic-Resistant Bacteria
Field Study	18	12	10
Desk Study	25	31	20
Total	51	52	31

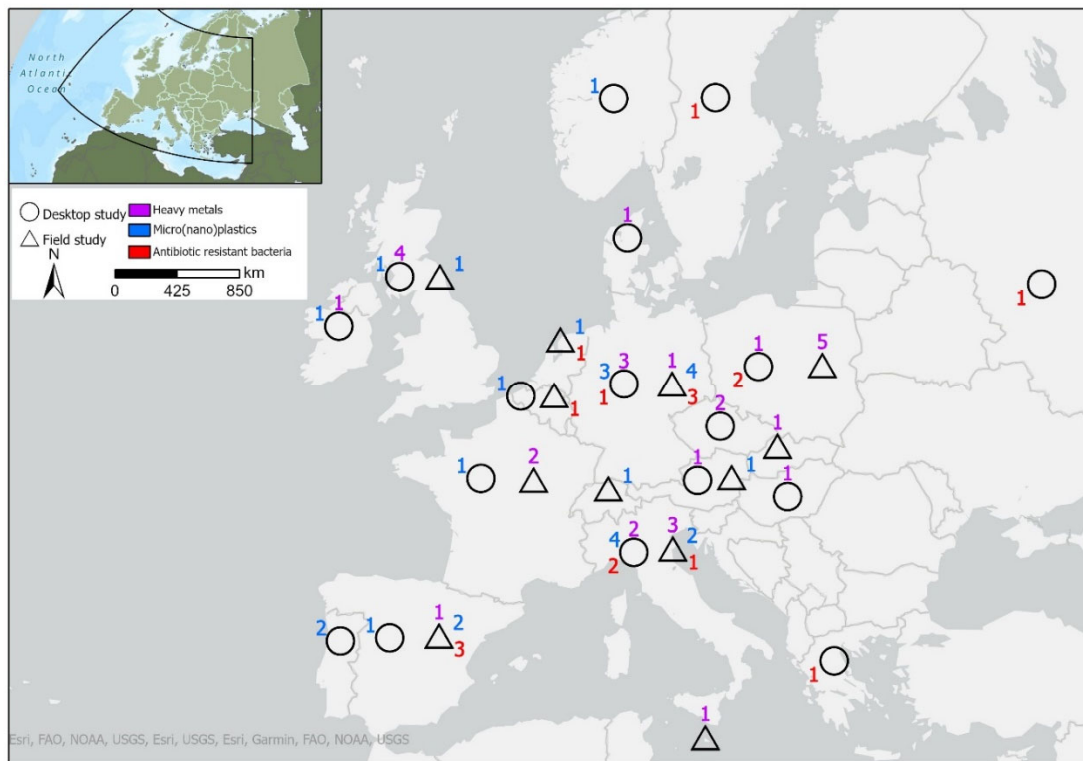


Figure 1. Europe: Number of studies on heavy metals, micro(nano)plastics, and antibiotic-resistant bacteria considered in our review, per country. Field studies were counted for the country where the analysis was performed, desk studies were counted for the country of the first author’s institution.

The vast majority of the studies—90% of HMs, 96% of MNPs, and 93% of ARB studies—originated from Europe (Figure 1), Asia (Figure 2), and North America (Figure 3).

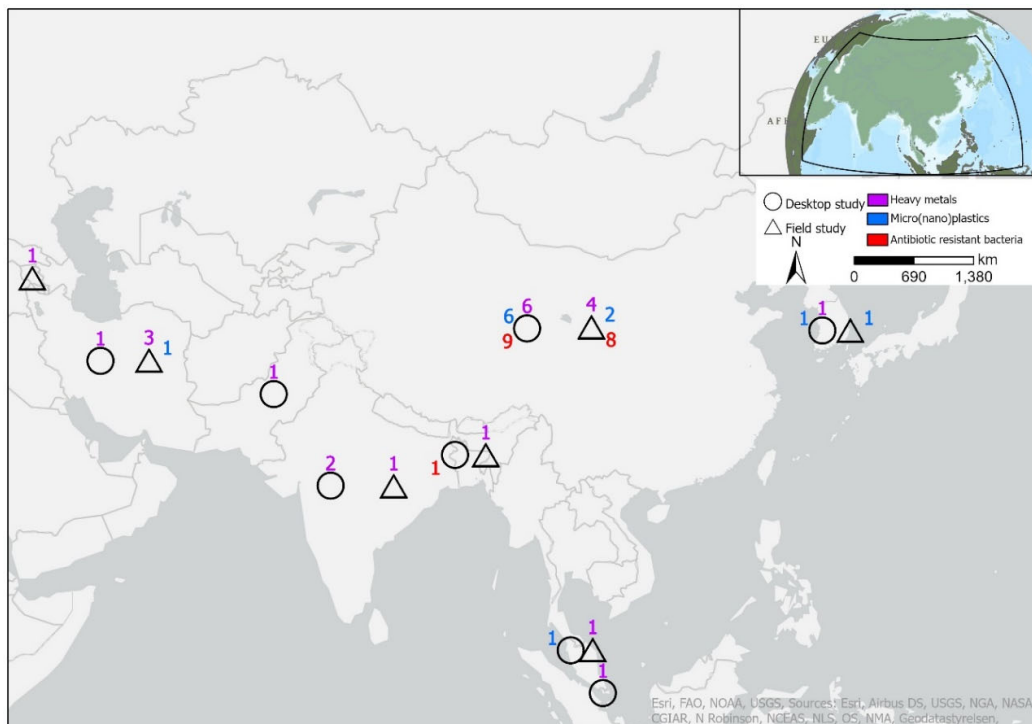


Figure 2. Asia: Number of studies on heavy metals, micro(nano)plastics, and antibiotic-resistant bacteria considered in our review, per country. Field studies were counted for the country where the analysis was performed, desk studies were counted for the country of the first author’s institution.

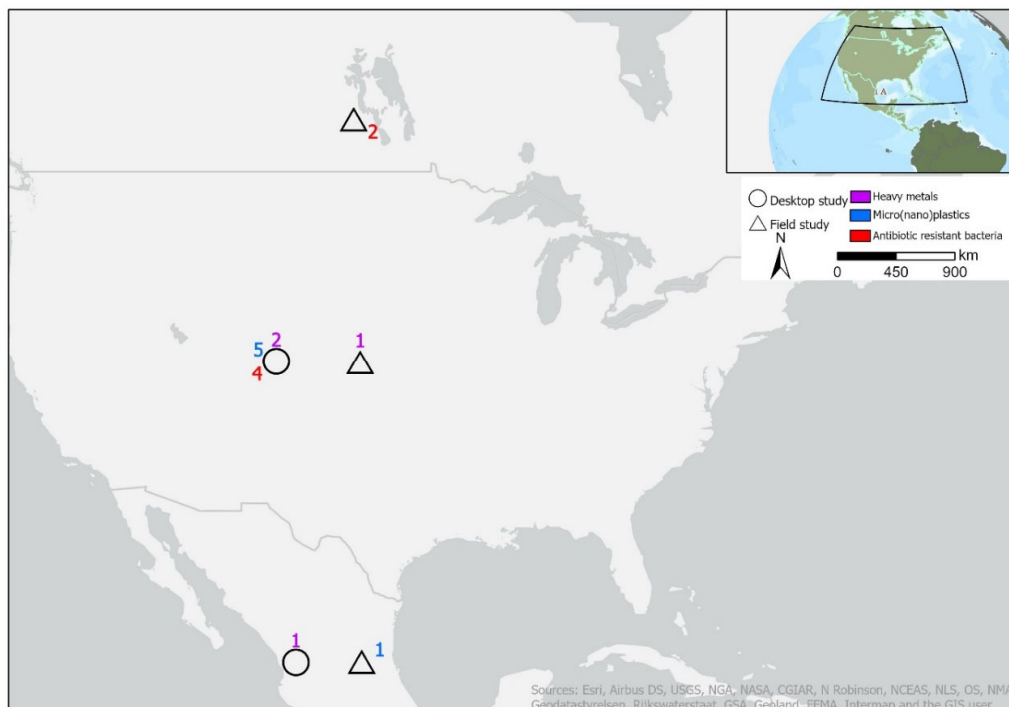


Figure 3. North America: Number of studies on heavy metals, micro(nano)plastics, and antibiotic-resistant bacteria considered in our review, per country. Field studies were counted for the country where the analysis was performed, desk studies were counted for the country of the first author’s institution.

3. Results and Discussion

In this section, we present and discuss findings on heavy metals, micro(nano)plastics, and antibiotic-resistant bacteria. We provide an overview of sources, linkages with human health, and behaviour in soils, including effects on microorganisms, soil fauna, and plants.

3.1. Heavy Metals

3.1.1. Sources of HMs in Agricultural Soils

Sources of elevated HM concentrations in agricultural soils are mainly intentional applications of compounds containing high levels of HMs. These can be fertilizers (e.g., phosphate or nitrate fertilizers, livestock manure, composts, biosolids, or sewage sludge), lime, pesticides, or wastewater for irrigation [15,37–41].

Phosphate (P)-based fertilizers can be a source of diverse HMs (e.g., Zn, Cd) [39] and may cause soil pollution, crop uptake, and bioaccumulation along the food chain, resulting in environmental and human health risks [42]. P fertilizers are estimated to contribute 45% to the total Cd-load in European croplands, and 55% of the total dietary intake of Cd by average consumers is associated with Cd accumulation in soils [43]. This problem is likely to increase, as global production and application of P fertilizers are on the rise, and demand for P-rich rock is growing [44]. More efficient use, recovery, and recycling of P [45] from sewage sludge or ash [46] could help to overcome shortages while alleviating HM pollution [42]. However, risks of regenerated P fertilisers require further assessments [47].

While manure is recognised as a valuable fertiliser, its long-term utilization can lead to accumulation of HMs in soils [46]. The content of HMs in manure varies between animal species and diets, with some HMs (e.g., Cu and Zn) fed as mineral supplements to increase animal performance or to provide protection against bacterial infections [48]. However, application of manure or sewage sludge is also an effective strategy for immobilizing HMs to reduce plant uptake through complexation with organic matter components [48]. The mobility and bioavailability of HMs is strongly influenced by soil conditions. Field studies indicate that the toxicity of potentially toxic elements may decrease over time because of fixation processes in the bulk soil [40]. However, since such phenomena are subject to soil properties and are therefore highly variable, detailed risk assessments are necessary if potentially contaminated material is to be applied to soil [41].

A study conducted by Provolò et al. [48] indicates that soil characteristics play a major role in this regard, as slurry application caused strong interactions with the soil and reduced the content of Cu, Mn, and Zn in plant shoots. Nevertheless, these authors caution against the long-term utilization of manure with high contents of HMs, particularly Cu and Zn, due to potential negative human health impacts.

Mitigating the risk of soil pollution with HMs includes avoidance of excessive fertilizer use [49], monitoring of fertilizer composition [38,48], and periodic soil sampling and testing to assess the concentration and bioavailability of HMs [49]. Since HMs in animal manure originate from livestock feed, feed should be controlled and intentional feeding with HMs restricted to optimal doses rather than maximum permitted levels [14].

3.1.2. Linkages between HMs and Human Health

As HMs can be absorbed by food plants or aerially deposited on their surface, the food chain has been reported to account for approximately 90% of total HM intake [6]. It is important to note that the chemical species or compounds in which HMs occur determine their toxicological impact and may be more important than the total uptake. When HMs are ingested, the human digestive system can absorb them along with the food [6]. HMs are retained and can accumulate in a variety of tissues and organs of the human body [50]; following their accumulation, toxic mechanisms of HMs include the generation of free radicals, enzyme inactivation, oxidative stress, and suppression of the antioxidant defence [50,51]. Additionally, some HMs are able to bind to specific macromolecules (proteins, lipids, nucleic acids) [50], thus causing cellular and tissues damage as well as defects in DNA synthesis and repair [50,52]. Studies report that HMs can impair neurological,

cardiovascular, urogenital, endocrine, immune, digestive, respiratory, and detoxification functions of the body, causing a variety of health problems [2,50,52,53]. Additionally, some HMs (e.g., As, Cd, Cr, Ni) have carcinogenic effects [2,50]. HM concentration, exposure duration, and ingestion rate, as well as nutritional status and immune system and individual detoxification organ strength are factors affecting human health impacts [6,52]. Women and children, especially during the prenatal development period and infancy, may be more susceptible to adverse health effects from HMs [54,55]. Approaches proposed to reduce human health impacts through food ingestion are to reduce the concentration of HMs at their sources (i.e., agricultural soil inputs), as well as to reduce their bioavailability. Additionally, the peeling and washing of food can reduce HM concentrations [56].

HMs can also enter the human body through the inhalation of mobilized soil dust and particles containing HMs [57]. Please note that soil dust is only one of several sources, and that HM containing particles created by fossil fuel combustion may pose a larger health risk. Smaller particles are considered more dangerous, as they penetrate the respiratory tract more deeply and deposit there at a higher rate [58]. Inhaled HM-PM has been suggested as causative agents for adverse respiratory health effects [59]. They can diffuse through the alveolar wall into the blood circulation and accumulate in different parts of the body [58,59]. In vivo and in vitro studies have also shown that some HM-PM (e.g., Pb, Cd, Cr, Ni), even in low concentrations, can exhibit genetic toxicity [59]. The effects of HM-PM exposure depends on individual susceptibility and physical characteristics (e.g., breathing mode, rate, and volume of a person) [58], as well as on the HM concentrations and their chemical and physico-chemical forms [52]. However, research about the metabolic distribution of HM-PM to the major organs is still insufficient [59]. Agricultural management practices aimed at controlling wind erosion (e.g., reduced tillage, cover crops, wind breaks, adjusting the time of tillage) help to reduce HM-PM exposure risk.

Dermal contact with HM-contaminated agricultural soils represents only a small percentage of uptake [6]. Farmers working closely with agricultural soils have an above-average risk of dermal exposure [3], and the continuous use of personal protective equipment (gloves) is therefore recommended [60].

3.1.3. Behaviour of HMs in Soils

HM accumulation can reduce a soil's biological activity, causing reduced fertility and plant growth, loss of soil organic matter [61], loss of soil structure, and soil acidity [15]. HMs incorporated within agricultural particulate matter [59] can be extensively dispersed throughout the atmosphere [52]. The lifetime of HM-carrying particulate matter (HM-PM) and their possible toxicity is a function of their size. Generally, the smaller and lighter a particle is, the longer it will stay in the atmosphere, while larger particles (>10 µm in diameter) tend to be deposited by gravity in a matter of hours [52].

3.1.4. HM Effects on Flora and Fauna

Effects on Plants

Some HMs are nutrients of which low amounts are required for plant development, though exposure to excess concentrations can cause damage [15]. Other HMs serve no function in plants. HMs in soils can induce oxidative stress in plants, affect their photosynthetic process, their respiration and transpiration, as well as the uptake and transport of essential micronutrients. Hence, they may inhibit plant development and growth, including germination and root elongation, resulting in a decrease in biomass and a potential reduction in productivity and yields [38,42,54,61,62]. High concentrations of HMs can also cause plant death and motivate the selection species with resistance mechanisms and high HM tolerances [42].

HMs can accumulate in different concentrations in roots, leaves, and fruits [39]. However, few plants translocate high concentrations from the soil to the shoot, and studies have consequently reported the highest concentrations in plant roots, with only a minor fraction translocated and accumulated in the shoot [48,63]. To what extent HMs will be absorbed

by plants depends on HM type, concentration, and bioavailability [54,61]. Additionally, HMs uptake by plants depends on plants species, as different plants have different uptake rates of specific metals [54,64]. Studies report that leafy and root vegetables show the highest accumulation of HMs [49,65], in contrast to legumes or solanaceous fruits [66,67]. Plants with either high or low HM uptake rates provide management opportunities for soils contaminated with HMs. Restricting cultivation on these soils to plant species with low HM accumulation rates increases the safety of food production [66]. Additionally, the application of organic amendments (e.g., manure, compost, straw) or inorganic amendments (e.g., lime, zeolites) in order to maintain high pH and organic matter content have been proposed as measures to reduce HM bioavailability and plant uptake [66,68]. On the other hand, plants with high HM accumulation rates can be used for phytoremediation [69,70] to improve polluted soils and stabilize soil fertility [69,71,72]. While in this case they cannot be used for human consumption, their cultivation represents a cost-effective practice that contributes to other food crops growing free of HMs and thus safeguards human health [39].

Effects on Microorganisms and Soil Fauna

Studies show that HMs in soils can have inhibitory effects on soil microbial and enzymes activities, microbial biomass, populations, growth, and metabolic processes [15,38]. Therefore, the abundance, diversity, and structure of the microbial communities can be affected [73], potentially causing functional changes in soil flora with implications for C or N cycling [74]. However, despite the toxic effect of HMs, microorganisms such as bacteria, fungi, or algae can survive in their presence thanks to several evolutionary strategies enabling them to reduce or tolerate HM toxicity. Multiple mechanisms of microbial detoxification can be applied in bioremediation strategies, which represents an economic, efficient, and eco-friendly approach [75]. However, studies providing a comprehensive analysis of the most effective microbial resources for bioremediation or bacterial-assisted phytoremediation are lacking [75].

Studies indicate that HMs in soils can affect the mortality, reproduction, and growth rate of soil organism [74], thus affecting the density, diversity, and structure of the faunal community [76]. The HM concentrations at which this occurs are a complex combination of the bioavailability of the metals, exposure pathways, duration of exposure, and soil physicochemical properties [74]. However, the presence of HMs can also stimulate soil organisms (e.g., earthworms, nematodes, isopods, snails) to produce chemicals capable of protecting them from damage (e.g., metallothioneins) or repairing damage once it occurs (e.g., heat shock proteins). HMs in soil can act as evolutionary drivers, as studies show the ability of soil organisms to develop mechanisms by which they can tolerate or resist the effects of HM-induced stress (e.g., acclimation and adaptation) [74].

3.2. *Micro(nano)plastics*

3.2.1. Sources of MNPs in Agricultural Soils

The prevalence of MNP particles in agricultural soils is due to multiple sources. These include the use of plastic materials such as mulching films [77,78], greenhouse or tunnel materials, silage films, boxes, packaging materials, harvesting nests, plastic reservoirs, or irrigation tubes [79–82]. Other sources are the application of MNP-contaminated substances such as sewage sludge, biosolids, or organic fertilizers, irrigation with treated wastewater or contaminated freshwater [78,83], or the application of substances intentionally containing plastics such as polymer-based slow-release fertilizers or pesticides [19]. All these sources are due to uses of the initial materials in agriculture. Tire debris from agricultural mechanization may also add MNPs to soils. Plastic particles that contaminate soil systems may be very difficult to remove due to their small sizes. In the field, they may break down further, consequently contaminating soils with MNPs [84].

Plastic mulching, mostly made by low-density polyethylene and polypropylene, has become a globally applied practice for plant protection from harsh climatological con-

ditions [81]. It is considered one of the major causes of MNP pollution in agricultural soils [20,81]. About 83,000 tons of mulch films were sold in Europe in 2019 [22], with projections that the global market will grow until 2030 at a rate of 5.6% per year [20].

Recently, biodegradable plastic mulches (BDMs) have been proposed as an environmentally sustainable alternative [85]. According to international standard ISO 17556, biodegradable plastic mulches should be degraded by at least 90% after 2 years in the soil [86]. However, plastic fragments (e.g., high in molecular weight) may reside in agricultural soils for years [87]. MNPs derived from BDMs have been detected in agricultural fields, thus leading to uncertainty about long-term impacts of BDMs constituents on soil ecosystems, properties, crop productivity, and human health [85,87]. More research is needed, especially since due to an increasing demand for environment-friendly substitutes for plastic mulching films, it is expected that the global market for BDMs continues to grow [85]. Plastic-free organic-based mulches, which consist of plant residues (e.g., straws, husks, grasses, saw dust, woodchips) or cover crops constitute environment-friendly alternatives [86,88].

Besides plastic mulches, sewage sludge as fertilizer is also a globally applied practice in agriculture. However, based on studies analysing the efficiency of wastewater treatment plants, it is suggested that most MNPs remain in the sludge [78]. It is estimated that in Europe, about 50% of total sewage sludge is spread on agricultural fields [78]. This widespread application to farmlands likely represents a significant input of MNPs into agricultural soils, with unknown consequences for food security [89] and human health. Since sewage sludge is known to contain several pollutants, its application in the EU is intensively regulated, including limits for contents of pathogens, heavy metals, and several organic substances [78,89]. However, the European Sewage Sludge Directive (EU 86/278/EEC) does not consider plastic as a potential, unwanted element [78,89], though an update of this directive is planned for the near future. Moreover, most countries allow a certain amount of “foreign” matter such as plastics in fertilizers. For example, up to 0.1 weight percent of plastics are permitted to remain in fertilizers in Germany, while particles smaller than 2 mm are not even considered [90].

3.2.2. Linkages between MNPs and Human Health

Only limited evidence confirming the effects of micro- and nanoplastics on human health is available. However, a potential threat could occur through uptake with ingestion of agricultural products, as a growing body of evidence indicates that MNPs are able to enter the food chain [83,91]. NPs were recently found to accumulate in crops [92], fruits, and vegetables, with the highest concentrations found in apples and carrots [93]. Furthermore, owing to their tendency to adsorb other chemicals or soil constituents, plastic particles could cause bioaccumulation and bioamplification phenomena by adsorbing persistent organic pollutants, agrochemicals, heavy metals, antibiotics resistance genes, or pathogenic microorganisms. This significantly increases their potential environmental and health threat [18,83,94]. Likewise, intentionally added chemicals such as flame retardants and plasticizers (i.e., additives) in plastic products, which subsequently become MNPs, should be considered [19,23]. For example, chemicals such as bisphenol A and phthalates, which are endocrine disruptors and can be hazardous for humans, are often found in association with MPs [23,77,81,95]. The fate of MNP particles in the human gut lumen following ingestion is not yet clear [77], as MNP toxicity is influenced by exposure concentration, particle properties, adsorbed contaminants, tissues involved, and individual susceptibility, and the state of knowledge is still limited [96]. However, recent studies have found that MNPs can be accumulated in the human intestines [92]. This may cause gastrointestinal issues such as local inflammation and destroy the community composition and diversity of intestinal microbes [92,97,98]. Additionally, MNPs further have the ability to pass through the intestinal barrier and enter the circulatory system, including the spleen and liver [92,98]. Please note that studies on the fate and effect of MNPs in the human body are not specific for MNPs from agricultural soils. Currently, it is impossible to estimate human exposure to

MNPs through food consumption due to the scarcity of validated methods (and certified reference materials) and due to the lack of standardisation across the analytical procedures used in reporting [91]. More research is therefore required on the extent of MNP intake and the potential effect on human health, including rigorous clinical studies [99,100].

The effects on human health of inhaling MNPs is little understood [99]. It has been suggested that the majority of MNP particles can be cleared from the respiratory system, though some are expected to be able to induce lesions, particularly in individuals with compromised clearance mechanisms [99]. Effects are suggested to be dependent on individual susceptibility and particle properties such as size and density, with less dense and smaller particles reaching deeper into the lungs [96]. The potential transmission of toxic substances and pathogens through MNPs should not be overlooked, as they could reach the lung in this way and pose a threat of infection [23]. Human studies investigating health effects of MNP inhalation are scarce, and future research should address this knowledge gap [99].

Dermal contact with MNPs is regarded as a less significant route of exposure, although it has been suggested that particles lower than 100 nm could transverse the dermal barrier [96]. Since people in professions that work closely with soils (i.e., farmers) may be exposed to greater risks [3], continuous use of personal protective equipment is recommended as a precautionary measure. However, studies to quantify dermal exposure to MNPs and the potential effects are lacking [101].

3.2.3. Behaviour of MNPs in Soils

Though soils, particularly agricultural soils, have been recognized as a major sink of MNPs, the impacts of MNPs on soil ecosystems remain uncertain [102]. Depending on the concentration of MNPs and on their size and shape, MNPs affect physical and chemical soil properties. They can decrease soil bulk density, change water availability, and increase soil pH and dissolved organic matter [103]. Likewise, microbial and enzyme activities, soil fauna, and plant growth can be affected [104]. Soil texture has been suggested as a factor determining the impact of MNPs on soil properties, but more studies are needed to test this hypothesis [104]. MNPs that adhere to small soil particles may easily be mobilized [77] and carried by wind. Uptake through inhalation may therefore occur far beyond its original source [105]. To better understand actual transport rates and assess the mechanism of wind erosion in transporting MNPs, further studies under laboratory and field conditions are needed [105].

Because of the minute size of MNPs, it is difficult to separate and isolate them from soil samples, hampering identification and observation procedures. Hence, future studies should focus on finding standardized analytical methods to estimate MNPs in soil samples as a basis for identifying and closing knowledge gaps about the effects of MNPs in the soil environment [24].

3.2.4. MNP Effects on Flora and Fauna

Effects on Plants

Very few studies have investigated the effects of MNPs on the growth of plants. Observations suggest that MNPs may be able to delay germination, affect both vegetative and reproductive growth of plants, exert eco- and genotoxicity to plants [104], or promote roots and plant growth and higher total biomass. Furthermore, they may enhance the colonization of roots by soil microbes [106], as well as accumulate in the roots of plants and then be transported to their leaves, flowers, and fruits [107]. Overall, neither a generally positive or negative effect of MNPs on plants can be postulated at present [106,108]. Different MNPs may trigger different responses in soils and plants [106].

In agricultural settings, the potential accumulation of MNPs and harmful compounds in plants tissue may have implications for the production and quality of plants, as well as for human health [102]. Effects likely depend on concentration, size, or type of plastic particles; plant species; and environmental conditions [104,106], though further research on this is needed.

Effects on Microorganisms and Soil Fauna

Fungi and bacteria can promote the degradation of plastics [109], though the persistent and pervasive nature of MNPs in the soil environment has been confirmed [19]. MNPs in soils can alter soil microbial community diversity, as well as the activity of soil microbiota and enzymes. They may hence disturb microbial ecosystems and affect soil nutrient cycles [104]. However, these effects display great variability [110] and may depend on MNP type, shape, size, concentration, and composition, as well as on soil characteristics such as texture [104,110]. Negative effects exerted by MNPs may also be related to concomitant pollutants found on MNPs [104]. Furthermore, MNPs in soils can be a habitat for microorganisms. Studies report that the bacterial community on a plastic substrate shows obvious differences compared to that in the surroundings areas, with some bacteria groups mainly detected on plastic debris (e.g., Vibrionaceae or Pseudoalteromonadaceae) [109,110]. These different microbiota found on the surfaces of MNPs may change fundamental ecological functions and biogeochemical processes in the soil environment [110]. Due to stress exerted on soil flora, the adaptation and evolutionary response of soil microorganisms to MNPs in soil should be addressed in future research [104].

Ingestion of MNPs can decrease the growth rate and cause weight loss of earthworms, decrease the survival rate, body length, and reproduction of nematodes, and reduce collembolan growth [104,107]. However, an increase in gut bacteria diversity of collembolan was observed as well [107]. Causes for these differences are still uncertain, though the feeding selectivity of animals as well as properties and exposure concentrations of MNPs have been proposed as possible reasons [107]. Furthermore, the uptake of MPs by earthworms can lead to a size reduction into NPs due to activity of the earthworm's gut microbiome. These NPs will then be excreted and released into the soil [111,112]. However, it should be noted that most of the studies cited above were conducted in artificial environments rather than in the field, so that experimental and environmental concentrations of MNPs are not comparable. The effect of MNPs on soil fauna under real-life conditions is still poorly understood [104].

3.3. Antibiotic-Resistant Bacteria

3.3.1. Sources of ARB in Agricultural Soils

Agricultural soils are natural reservoirs of antibiotics (AB) and therefore also of ARB and ARGs [113]. Elevated levels of ARB in agricultural soils are mainly caused by the continuous application of manure from animals that were given antibiotics for therapeutic or non-therapeutic purposes, the application of contaminated sewage sludge or biosolids, or irrigation with contaminated water or reclaimed wastewater [113,114]. Additionally, some ABs are used as pesticides in crop production [115].

Animal manure is considered a major source of ARB and ARGs in agricultural soils [116], as more than 50% of ABs in Europe are administered to livestock [117]; 30–90% of these ABs are estimated to be excreted again by the animals, largely unmetabolized, resulting in commonly high residual AB concentrations in animal manure [118–120]. Still, the global amount of manure application to agricultural soils is persistently increasing due to rising livestock production [121]. Additionally, the utilization of manure as an organic fertilizer is promoted by the EU, both in the context of expanding organic food production and as part of a circular economy [122]. This could further exert selection pressure for antibiotic resistance [119]. Sewage sludge is another important reservoir of antibiotics, ARB, and ARGs, and its application can promote resistances against antibiotics in the soil [113]. Chen et al. [116], observed an enhanced diversity of ARGs in soils after long-term sewage sludge application. However, the fate of ARGs in agricultural soils following the application of sewage sludge remains insufficiently understood [116].

Composting and anaerobic or aerobic digestion have been proposed as effective methods for reducing ARG concentrations in manure and sludge. However, some ARGs were found to decline during these processes, while others increased, indicating that factors and underlying mechanisms determining decay rates require further investigation [113].

Additionally, ensuring a suitable offset time between manure or sludge application and harvest of fresh produce can reduce ARB soil contamination and human health risks [113,123], though the risk of ARG transmissions cannot be completely eliminated [33].

3.3.2. Linkages between ARB and Human Health

As ARB and ARGs can be absorbed by plants or be found on their surface, the food chain has been suggested as a major pathway for human exposure [33,120]. Ingestion of plants carrying ARB or ARGs may alter the human microbiome and promote the emergence of and selection for resistant bacteria inhabiting the human body [118,124]. This could reduce the efficiency of therapeutic antibiotics, increase the duration and seriousness of infections, and ultimately result in treatment failures or even mortality [124,125]. However, the emergence and spread of ARB and ARGs from agricultural systems and their contribution to the resistance of human pathogens are complex processes that are not yet fully understood [34]. More research is needed to quantify the risk of human exposure to antibiotics, ARB, and ARGs [115], particularly the risk of long-term consumption of low doses [114,122]. Additionally, little knowledge exists about AB transformation products, their metabolites, mixtures, and associated resistance selection [32]. Crops, when consumed raw or minimally processed, may allow ARB to survive and easily reach the human gastrointestinal system [36]. Cooking food can destroy ARB or reduce their levels [114]. Likewise, washing and peeling can reduce the uptake of ARB found on the surface of raw food crops [123].

A potential pathway for human exposure is the atmospheric dispersal of ARB and ARGs via dust or particulate matter (PM) that arise from agricultural soils treated with contaminated organic fertilizers such as manure or sewage sludge [117,121]. Airborne ARB may be contributing to enhanced antibiotic resistances in humans. Moreover, respiratory viral–bacterial co-infection should be considered, as with acquired AR, they are expected to be more difficult to treat [126]. However, understanding how transmitted ARB influence their counterparts in the respiratory system and exchange ARGs upon inhalation is insufficiently understood [126,127].

Skin absorption following contact with contaminated crops or soils presents a possible uptake pathway [128], which may be relevant for farmers, as they may work in close contact with ARB-containing soils and plants [3]. The continuous use of protective equipment is therefore suggested. However, dermal absorption of ARB is not well understood.

3.3.3. Behaviour of ARB in Soils

Soils are natural reservoirs of ARB and ARGs [34], thus contributing to the emergence of resistances without previous exposure to antibiotics (i.e., intrinsic resistance) [120]. However, anthropogenic inputs of antibiotics promote the prevalence of acquired resistances in a variety of clinically relevant bacteria in soil. Therefore, soils may represent a reservoir of both intrinsic and acquired ARGs [120].

When introduced into agricultural soils, antibiotics may be subjected to different processes, including transformation, sorption, plant uptake, removal with runoff, or transport into groundwater [9,129,130]. Fertilization with ARB-containing manure significantly contributes to airborne PM emergence [121]. These particles are small and light enough to be transported over extended distances, posing a potential risk for ARB dispersal to areas remote from the primary source [117,121]. Wind erosion, particularly when accelerated by agricultural operations such as tillage, further contributes to the emissions of ARB to the atmosphere [117,121]. These dynamic processes, which define the spatial–temporal distribution and thus human health risks of antibiotics, are closely interrelated [130] and influenced by soil properties, climate factors, and physicochemical properties of antibiotics [114,115,129,131]. In particular, the emergence of airborne ARB from agricultural soils, their dispersal patterns, and airborne processes by which they find their way into humans are still insufficiently understood. Though distribution processes may reduce AB concentrations in soil, an increase in resistant bacteria was observed even when concentrations of

antibiotics were low [9]. Additionally, sequestration processes result in reduced toxicity but prolonged residence time of ABs in soil, resulting in a continuous release of small amounts of antibiotics back into the soil solution [34].

In addition, contaminants discharged by human activities (e.g., heavy metals, persistent organic pollutants, microplastics, pesticides) may contribute to the selection and dissemination of resistances against antibiotics [113,120,132], making it very difficult to predict the evolution of ARB in polluted soils [9].

3.3.4. ARB Effects on Flora and Fauna

Effects on Plants

In soils contaminated with antibiotics, root uptake is considered an important route of exposure for plants. Studies indicate the accumulation and selection of ARG in different plant tissues such as leaves, stem, or fruits [114,120]. This suggests that plants may contribute to the acquisition of antibiotics resistances in humans [130]. Moreover, residues of antibiotics may affect seed germination, photosynthesis, plant development, and productivity [9,114,133,134]. However, depending mainly on the concentration of antibiotics, both inhibitory and stimulatory effects have been reported [114,134].

The understanding of uptake mechanisms for antibiotics by plants, their phytotoxicity, translocations in plants, as well as of their corresponding environmental and human exposure risks remains limited [114]. Future research should focus on long-term field studies, involving correlations with crop types, antibiotic classes, and concentrations [134,135].

Effects on Microorganisms and Soil Fauna

Antibiotics may change the abundance of soil microorganisms, the microbial biomass, as well as overall microbial and enzyme activity [129], which in turn may disturb various soil processes mediated by microorganisms [34,129]. They can significantly change the structure of soil microbial communities [120], particularly bacteria [130], generating an environment for selection and outgrowth of ARB, which results in changes of entire microbial populations to ABs sensitivity [129]. Studies suggest that low concentrations of antibiotics (below the minimum inhibitory concentration) are able to induce genetic changes in bacterial genomes, even between distantly related bacterial species [129]. However, the effects on soil microbial communities may be transient, thus favouring recovery of the original microbial composition [34,129]. However, numerous studies with ambiguous results indicate that an accurate estimation of impacts on the activity and diversity of soil microbial communities is a challenge [129]. In many studies, effects were depended on the type of antibiotics and length of exposure [129].

In a study of exposure to antibiotics, the diversity and abundance of ARGs in the gut resistome of collembolans notably increased, indicating a significant and underappreciated role of soil fauna on ARGs accumulation and diffusion [1,120]. Diverse and abundant ARGs have been identified in earthworm guts as well, characterising them as hospitable micro-environment for ARB colonization [120]. Disturbances caused by human activities can have a considerable influence on the distribution of ARGs in the gut microbiomes of soil fauna [1]. Synergistic effects of heavy metals and antibiotics were found to increase the abundance of gut-associated ARGs, while silver nanoparticles were found to reduce them [1,120]. There is a need for further research, particularly on the influences of different pollutants on the distribution of ARGs in the gut microbiome of soil fauna [1].

4. Synthesis

Our findings highlight the diverse state of knowledge regarding the three contaminants groups, their pathways into the soil, their behaviour in the soil and the potential risks to human health (Table 3). While knowledge about HMs in agricultural soils is well established and monitoring systems are in place, knowledge is scattered for MNPs and ARB. This is a worrying result, in particular since risks to human health of MNPs and ARB cannot be excluded with the current state of knowledge. The sources of these contami-

nants are well known, though the relative contributions of different sources are not well understood [113,122]. Likewise, available data on the sources and fate of MNPs in the soil environment are limited [19]. Long-term field studies on MNPs under real-life conditions could bring very valuable knowledge in this respect [110]. The lack of standardised protocols to isolate, quantify, and characterize MNPs from the soil environment constitutes an obstacle for comprehensive research and monitoring. Self-contamination due to plastic devices during sampling and experimentation is a risk [25]. Future standards or protocols will also need to take into account differences in shape, size, origin, and composition of MNPs, as well as differences in soil characteristics [19].

Table 3. Available knowledge relevant for human health risk assessment of soil-related contaminants.

	HM _s	MNP _s	ARB
Sources of contamination	++	+	++
Environmental fate and behaviour	++	+	+
Human exposure	++	+/-	+/-
Human health risk	++	-	+
Status of current soil-related monitoring	++	-	-

Legend: established ++; emerging +; emerging/unavailable +/-; unavailable -.

Continuous measurement and assessment of the use of antibiotics, their residues, and emerging resistance through a standardized monitoring network is advisable [113,124]. Research is needed to quantify the linkages between the concentration of antibiotics in agricultural soils and the development of resistances, as well as to determine the influence of soil characteristics [5]. Likewise, the dose–response relationship between ARB and various infectious diseases needs to be established [124]. A better understanding of mechanisms controlling the capture and dissemination of ARGs in bacterial populations is essential to develop effective counter-strategies [113].

There may be combined effects of MNPs, ARB, and HM_s. For example, the co-contamination with antibiotics, HM_s, and MNPs is presumed to have a synergetic effect on the development, persistence, transport, and ecology of ARB in agricultural soils [17,136]. Studies report that the co-selection pressure of HM_s and antibiotics is a crucial driver of ARG spread in soil. MNPs can affect the migration and fractions of ABs and HM_s in the soil by serving as a vector for contaminants [136]. Long-term impacts of MNP contamination on the development of resistances against antibiotics are still insufficiently studied, but the retention of antibiotics, ARG presence, and exchange through horizontal gene transfer among bacteria on MNPs have been shown [17]. Ingestion of MNPs may increase the release of antibiotics and the development of ARB in the human body [25]. HM_s could be introduced in the human body by MNP uptake as well [23]. This raises the question about interactions of MNPs and other contaminants and the environmental aging effects of MNPs in agricultural soils on the long-term risks to human health [107]. In addition to this, it is crucial to identify critical thresholds for the investigated contaminants in the soil, above which a risk to human health can be assumed [5].

5. Conclusions

Agricultural practices have led to increased concentrations of HM_s, MNP_s, and ARB in soils all over the world. Contaminants are absorbed by plants or are found on their surface. This may lead to adverse human health effects from the ingestion of contaminated products, inhalation of contaminated soil particles, or through dermal contact with contaminated soils.

HM_s are well-known contaminants and have been extensively studied, and MNP_s and ARB represent emerging and novel threats that are insufficiently understood. Knowledge is required on the effects of the long-term, low dose consumption of antibiotics and ARB from agricultural systems as well as on the interactions between ARB and contaminants present in agricultural soil that could contribute to the emergence of bacterial resistances. MNP

research should be directed at elucidating different mechanisms by which harmful effects of MNPs on human health could occur, taking into consideration the behaviour of MNPs in soils and how soil properties affect such behaviour. Extraction and sampling methods, as well as reporting mechanisms lack harmonisation, which impairs MNP research.

While agricultural soils may not be responsible for the highest share of human uptake of MNPs and possess mechanisms that can reduce mobility and toxicity of certain HMs, the contamination of soils with the contaminant groups analysed in our study is still an issue of utmost concern, as remediation is extremely costly, time consuming, and in many cases not possible with the technology available today. Rising energy costs and the political call for implementing measures in favour of the circular economy such as, e.g., the use of sewage sludge or fertilizers from recycled materials, may in the future increase the input of contaminants. We recommend to better monitor and regulate the introduction of contaminants into agricultural soils, creating an evidence base for reducing the input of contaminants, setting up thresholds, and implementing effective legislation and better management. Furthermore, to also address the root of the problem, the use of antibiotics in animal husbandry and the use of plastic materials in agriculture and elsewhere should be reduced.

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