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Review article

Resolving the twin human and environmental health hazards of a plant-based diet

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ABSTRACT

Food can be health-giving. A global transition towards plant-based diets may equally help curb carbon emissions, slow land-system change and conserve finite resources. Yet, projected benefits of such ‘planetary health’ diets imperfectly capture the environmental or societal health outcomes tied to food production. Here, we examine pesticide-related hazards of fruit and vegetable consumption, and list proven management alternatives per commodity, geography and chemical compound. Across countries, pesticide use in these alleged healthful foods is extensive with up to 97% food items containing residues and up to 42% posing dietary risks to consumers. Multiple residues are present in 70–92% of US- and China-grown stone fruit while 58% US cauliflower is tainted with neonicotinoid insecticides. Science-based alternatives and decision-support frameworks can help food producers reduce risks and potential harm by deliberately abstaining from pesticide use. As such, opportunities abound to advance ‘win-win’ diets that simultaneously nurture human health and conserve global biodiversity.

1. Introduction

Food lies at the nexus of human health, nutrition and environmental sustainability (Springmann et al., 2018; Willett et al., 2019). Today’s food system could ensure food security, nurture human well-being, preserve the environment and thereby advance the UN Sustainable Development Goals SDGs (Stafford-Smith et al., 2017), yet it largely fails to deliver on such promises. Worldwide 820 million people are undernourished and about 3 billion people are either micronutrient deficient, overweight or obese, with unhealthy diets exacerbating the global morbidity and mortality burden (Willett et al., 2019). Likewise, food and agricultural production drive environmental change, contributing to greenhouse gas (GHG) emissions, land clearing, overuse of non-renewable resources, agrochemical pollution and biodiversity loss (Tilman & Clark, 2014; Tilman et al., 2017; Kok et al., 2018; Springmann et al., 2018). If unchecked, the ongoing global dietary transitions are bound to deepen those twin human health and environmental impacts (Tilman & Clark, 2014; Springmann et al., 2018).

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Food however can be a restorative force, with dietary change prone to concurrently resolve environmental degradation and foster human health and wellbeing at multiple scales (Willett et al., 2019). A concerted shift to diets centered on plants and plant-based foods can curb GHG emissions by 29–56%, bring about 5–22% reductions in natural resource use or nutrient pollution, and lower vertebrate extinction risk to a small and spatially variable extent (Tilman & Clark, 2014; Springmann et al., 2018). Plant-rich diets can further alleviate worldwide epidemics of diet-related chronic non-communicable diseases, e.g., heart disease or diabetes (Li et al., 2014; Willett et al., 2019). Vegetables, fruits, nuts and pulses are deemed to be core components of these 'planetary health' diets (i.e., diets that substantially benefit human health and keep agri-food production within planetary boundaries; Willett et al., 2019), and their enhanced global intake is expected to mitigate myriad environmental pressures. Yet, while plant-based foods can be health-giving by yielding large quantities of nutrients, vitamins or minerals and help preserve the world's natural capital, benefits of their dietary consumption and farm-level cultivation are invariably offset by agrochemical use.

Though their impacts are usually disregarded in multi-dimensional sustainability assessments (Tilman & Clark, 2014; Fantke & Jolliet, 2016; Bernhardt et al., 2017; Landrigan et al., 2018; Willett et al., 2019), the synthetic pesticides that are used in agri-food production compromise human and environmental health (Geiger et al., 2010; Vigar et al., 2020). Pesticides can inflict substantial human health costs, experience progressively higher usage, spatial coverage, and toxicity loading or 'potency' (Bernhardt et al., 2017; Douglas et al., 2020), and have widespread and often protracted impacts on individual biota or ecosystems (Brühl and Zaller, 2019). Although it may be difficult to gauge the full burden of pesticide residue impacts on human health (Hu et al., 2016), their extensive food-associated usage may disproportionately affect poor and marginalized sections of society, inhabitants of low- and middle-income countries, women, and the more sensitive children, fetuses and infants (Landrigan et al., 2019; Thompson et al., 2017). During their early development, the latter segment of society experiences a window of heightened vulnerability to e.g., neurotoxic pesticides that can have life-long repercussions. Moreover, agro-chemical pollution, poverty and deficient access to safe food (or adequate health care) are closely intertwined (Landrigan et al., 2018). While occupational exposure and pesticide self-poisoning directly imperil the health of 28 million people per year, the most common human exposure pathway is through dietary intake of comparatively small residues in harvested produce and contaminated drinking water (Fantke & Jolliet, 2016). This pathway and its related health impacts however face a paucity of data, particularly for new compounds, pesticide mixtures and generic products (Verger & Boobis, 2013; Cimino et al., 2017; Brühl and Zaller, 2019).

Dietary intake of residues varies substantially between food groups and individual commodities, with elevated pesticide exposure through fruit and vegetable consumption (Boobis et al., 2008; Poulsen et al., 2017). As such, adoption of plant-rich diets can be mirrored in elevated titers of urinary and serum pesticide metabolites (Hu et al., 2016) and high intake of pesticide-tainted fruit and vegetables negatively affects semen quality (Chiu et al., 2015). Considering how pesticide residues in these healthful foods might reduce their demonstrable health benefits (Boobis et al., 2008; Caldas & Jardim, 2012), the 'planetary health' dietary guidelines ideally account for food safety indices or pesticide residue scores. This is particularly important in Latin America, South Asia and Sub-Saharan Africa where pesticide exposure rates are higher than in western countries and dietary guidelines advocate a minimum 39–190% increase in daily intake of fruits and vegetables (Caldas & Jardim, 2012; Springmann et al., 2016). Accounting for pesticide usage or residue levels in harvested produce could more reliably capture the environmental footprint of horticultural production (Praneetvatakul et al., 2013; Fantke & Jolliet, 2016), and possibly help steer current farming practices towards ecologically-based and environmentally-sound measures (Kok et al., 2018; Chaplin-Kramer et al., 2019).

In this study, we use food toxicology profiles to identify, characterize and evaluate hazards of human dietary exposure to pesticide residues in food and to concurrently unveil the extent of farmers' reliance upon synthetic pesticides in global fruit, vegetable and legume cropping. Next, we contrast pesticide residue profiles of individual horticultural produce with the corresponding scientific advances in non-chemical pest management. Given that pesticide dissipation dynamics are shaped by crop parameters e.g., interception area, application times and properties of individual chemical compounds (Fantke and Jolliet, 2016), our approach only yields a fragmentary perspective on the actual in-field pesticide application regimes. Conversely, our findings do permit hazard-based approaches to enhance safety of horticultural produce, enable a grounded assessment of the environmental footprint of fruit and vegetable production, and could facilitate transitions towards ecologically underpinned farming schemes. As such, our work contributes to devising true 'win-win' diets for human health and the environment, and can help propel the 'planetary health' concept from fork to horticulture farm (Willett et al., 2019).

2. Pesticide profiles of horticultural produce

As a first step in our assessment, we compiled pesticide occurrence data for multiple food items, countries or geopolitical entities. While capturing pesticide profiles of diverse horticultural produce globally, a more in-depth analysis was only possible for high-income countries, i.e., European Union (EU) and United States (US). First, we carried out a non-exhaustive review of the global food toxicology literature, including published records from low- and middle-income countries. A core set of peer-reviewed publications post-2010 was compiled, which comprised simultaneous analyses of multiple pesticide classes, reporting residue levels in locally grown horticultural produce. We decided to focus on the last decade to limit the amount of data but also to tie our analyses with current food consumption (and dietary transition) patterns. We are however aware that a vast amount of data is available since the late 1950s when Rachel Carson started to document the impact of pesticides on human health and the environment (Carson, 1962) or University of California (UC) scientists conceptualized, refined and advocated the use of integrated pest management (IPM) and biological control (van den Bosch & Stern, 1962; DeBach & Rosen, 1974; van den Bosch, 1989). For each publication, we extracted and plotted the percentage of samples with any residues, non-compliant samples (i.e., surpassing established maximum residue limits MRL) and those containing more than one pesticide residue (Hu et al., 2016). Data were compiled either for sets of fruits or vegetables separately, or for a diverse set of horticultural produce. Second, we extracted data from the European Food Safety Agency (EFSA) regarding the 2016 occurrence of a broad suite of synthetic pesticides and their metabolites in fresh horticultural produce (i.e., vegetables and fruits) within the EU. For each food item, we noted the percentage samples with detectable residues and those with residue levels above MRL standards. Third, we centered on the world's most popular class of insecticides in terms of sales i.e., neonicotinoid insecticides, and collated data on the occurrence of 7 different compounds in unprocessed fruits and vegetables in the US (Craddock et al., 2019). Data were reported for the following compounds: acetamiprid, clothianidin, dinotefuran, flonicamid, imidacloprid, thiacloprid and thiamethoxam. The breakdown product imidacloprid urea was omitted from analyses. For the three most frequently detected neonicotinoid insecticides in harvested produce (i.e., thiamethoxam, imidacloprid, acetamiprid; Craddock et al., 2019), we compiled their respective detection frequencies (i.e., % samples) in a range of food items.

Pesticide residues in specific food items are only reported whenever their levels are above the analytical limits of detection of each compound. Whether residue levels are compliant with the regulations on food depends on the standards established by individual countries, and while MRLs are mostly observed in food trade, their legal enforcement is rare. As per definition, MRL is termed as the highest level of a given pesticide residue that is legally tolerated in or on a particular food item. Most countries adopt the international food standards of the FAO-WHO *Codex Alimentarius*, which sets MRLs for individual pesticides and food items based on diverse criteria that are not necessarily linked to human health or safety. The main criterion used by FAO-WHO is the acceptable daily intake (ADI), which is based on chronic toxicity data from dietary experiments in laboratory-reared rats. ADI is defined as the maximum amount of a particular compound that can be ingested on a daily basis over a person's entire lifespan without any appreciable health risk. This may or may not be related to MRLs in particular consumed food items. However, countries can choose other criteria to set MRLs on specific commodities, i.e. the lowest bioaccumulation profile in meat products, or the analytical limit of quantitation in Japan. Therefore, the presence of residues below individual MRLs does not mean the food is safe, and countries often adapt their values in response to emerging food safety concerns e.g., the Feb 2020 lowering of MRLs for chlorpyrifos in the EU or the increase of MRLs for neonicotinoids in Japan in 2016 due to farmer non-compliance. The fact that the EU lowered its MRL for chlorpyrifos and chlorpyrifos-methyl to "*the lowest level that can be measured by analytical laboratories*" reflects the important (previously overlooked) safety concerns for these specific compounds. Yet, irrespective of the absence of sufficient basic toxicological information for many popular compounds (e.g., neonicotinoid insecticides), metabolites and pesticide mixtures, MRL compliance is routinely used to inform the general public regarding food safety. For example, in its Pesticide Data Program's 26th Annual Summary, the US Department of Agriculture (USDA) announces "…*reliable data to help assure consumers that the food they feed themselves and their families is safe*", reporting "*over 99% of the products sampled with residues below tolerance levels set by the Environmental Protection Agency EPA*". In many low- and middle-income countries, a proper assessment of food safety is further complicated by the absence of standardized sampling methodologies and routine residue screening, while MRL compliance is often defined by running a suite of (often outdated) analytical assays in underequipped laboratories for a (small) subset of pesticidal compounds. Notwithstanding the above challenges to conduct residue assessments in a credible and comprehensive fashion, the only measure of safety in regard to food is ADI. Also, despite the invaluable information that is encapsulated within some of the above food toxicological metrics, food residue profiles are never used to assess the environmental burden of agri-food production or to gauge the corresponding impacts on farmland biodiversity.

Irrespective of the adopted analytical procedures, screened pesticide compounds or local MRL standards, the residue detection frequency and level of non-compliance of horticultural produce with local regulations varied greatly between countries and geopolitical entities (Fig. 1). While Brazil or the European Union reported 48–52% incidence of pesticide-tainted produce and 3–4% non-compliant samples, respectively, countries such as Nepal reported 97% pesticide-tainted food items and 28% of them above MRL standards. In Bolivia, Morocco or Tanzania, banned or restricted organochlorines and organophosphates were detected in a non-negligible fraction of sampled produce, often representing dietary risks to consumers (Reiler et al., 2015; Thompson et al., 2017). In Colombia, samples of greenhouse tomato exceeded MRLs on average by 356–1375% for multiple chemical compounds (Bojacá et al., 2013). Chlorpyrifos - an organophosphate compound that impacts human vision, causes neurological toxic effects and is linked to developmental disorders in infants (Landrigan et al., 2019) - was recorded at 22–73% frequencies in sampled produce from Argentina, Bolivia, China, Thailand or Nepal (Skretteberg et al., 2015; Skovgaard et al., 2017; Supplementary Table 1). In 20% samples of Bolivian lettuce and 44% of Nepali tomato, this compound surpassed MRLs; chlorpyrifos concentrations in the latter samples were as high as 1772 μg/kg (as compared to the outdated EU MRL standard of 10 μg/kg; Bhandari et al., 2019). Though residue profiles can help ascertain levels of human exposure, they provide an incomplete view on farm-level use of herbicides, seed dressings or compounds that don't reach the harvested produce (Fantke & Jolliet, 2016). Conversely, residue levels in fresh produce cannot be directly translated to actual human dietary intake especially for non-systemic compounds, as many food items are peeled, washed or cooked prior to consumption.

Many fruits and vegetables contained residues of multiple chemical compounds, e.g., 15% Brazilian strawberry, 40% Chinese peach, 79% Nepali tomato, or 83% Saudi Arabian citrus were tainted with > 3 different residues (Pico et al., 2018; Fig. 1; Supplementary Table 1). Multi-residue detection frequency varied between individual countries, farming schemes and sampled produce, yet large shares of lettuce, tomato, apple, peach, pear, citrus or pineapple routinely contained three or more different residues. In the European Union, organically-grown fruits or nuts and vegetables had markedly lower levels of residues than those emanating from conventional production (EFSA, 2018); a respective 16% and 17% of organic produce contained detectable residues (as compared to 71% and 49% from conventional agriculture). The presence of residues in organic food can be explained by on-farm usage of (few) permitted products (del Mar Gómez-Ramos et al., 2020), drift from nearby conventional farms, tainted organic fertilizer, occasional fraud, pesticide leaching into the groundwater (Pérez-Lucas et al., 2018) or the extensive environmental contamination by several popular compounds (imidacloprid in US farmland; Berheim et al., 2019). Multi-residue profiles of some of the above crops differ noticeably between the EU, China and the US, illuminating how pesticide use and/or residue levels are greater in certain geographies irrespective of technological advances in the local agriculture sector (Fig. 1). The above crops are cultivated on large areas worldwide e.g., apple, tomato and citrus fruits are presently grown on 5.2, 4.8 and > 9.2 million hectares (FAOSTAT, 2020), and feature prominently in many human diets. Sequential applications of various biocidal compounds -as reflected in multi-residue profiles- on these crops surely impact biodiversity and upset trophic interactions or broader ecosystem functioning (Pretty et al., 2018), though these effects are poorly understood and rarely quantified (Brühl and Zaller, 2019).

Within the EU, the 30 most pesticide-tainted food items contained residues in 38–85% produce with MRL non-compliance in 4–24% samples (Fig. 2). Rucola, currants and various types of citrus fruit had residue detection frequencies above 75%, while 62% passionfruit was tainted with pesticides (40% of those samples surpassing MRLs). Common vegetables such as parsley or celery had 14–16% samples with residue levels surpassing established MRL standards. Grapefruit, limes, currants, lemon and rucola equally had over 60% samples containing 2 or more residues. The 4 food items with the highest detection frequencies are locally grown on approx. 200,000 ha (FAOSTAT), and their production areas may increase by 2–26% when transitioning towards more plant-based diets (Springmann et al., 2016). Under conventional production schemes, pesticides will continue to be used in those areas either to mitigate actual economic damage by endemic or invasive pests e.g., in berries or cruciferous crops (Zalucki et al., 2012; Rogers et al., 2016), improve cosmetic appeal and market value of harvested produce (Pimentel et al., 1991) or as an ill-guided crop insurance strategy (Waterfield & Zilberman, 2012).

Neonicotinoids, globally applied at approximately 20,000 metric tonnes in 2010, have become omnipresent in harvested fruits and vegetables in a few countries (Lu et al., 2018) and in honey worldwide (Mitchell et al., 2017). Their ubiquitous use poses concern for biodiversity conservation and the maintenance of ecosystem services, inflicting toxic effects on vertebrate wildlife along whole food chains (Berheim et al., 2019) while impacting human beings (Cimino et al., 2017; Zhang et al., 2019). In the US, the 25 food items with the highest neonicotinoid detection frequencies comprised several popular fruits and vegetables (Craddock et al., 2019; Fig. 3). Seven compounds were found at frequencies of 6 ± 3% (average ± SE) in fresh produce, with

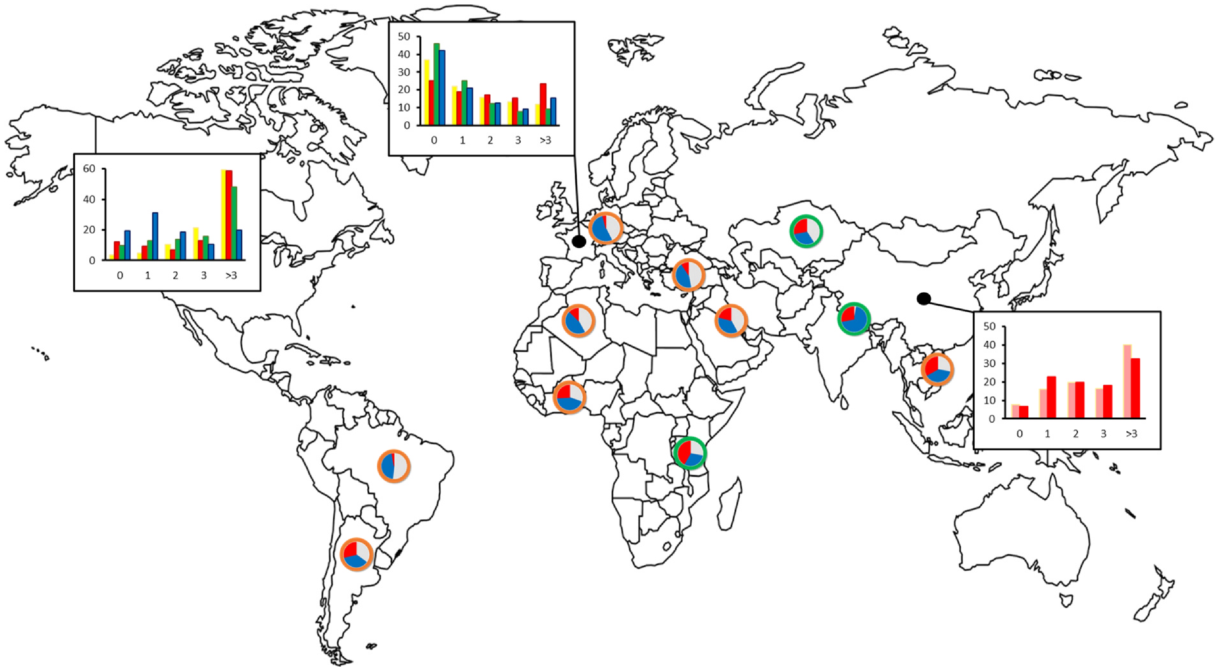

Fig. 1. Country-level pesticide residue profiles for horticultural produce. Pie charts reflect the overall pesticide occurrence frequency for produce within a given country, i.e., total % samples without detectable residues (grey), quantified residues below the MRL (blue) or exceeding established MRLs (red). Note that the analyzed compounds (e.g., metabolites), detection limits and MRL standards vary among countries. Pie charts within an orange or green sphere either depict data for fruits and vegetables or vegetables alone, respectively. For selected countries (i.e., China, USA) or geopolitical entities (i.e., EU), bar charts depict the percentual distribution of samples with multiple pesticide residues (i.e., 0 to > 3; X-axis). The color of individual bars is indicative of the analyzed commodity: peach (pink), pear (red), apple (yellow), tomato (green), lettuce (blue). The above commodities are regularly consumed fruits and vegetables in the study countries. Literature references for each residue profile and corresponding details on -variable- analytical procedures are provided within the Supplementary Information. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

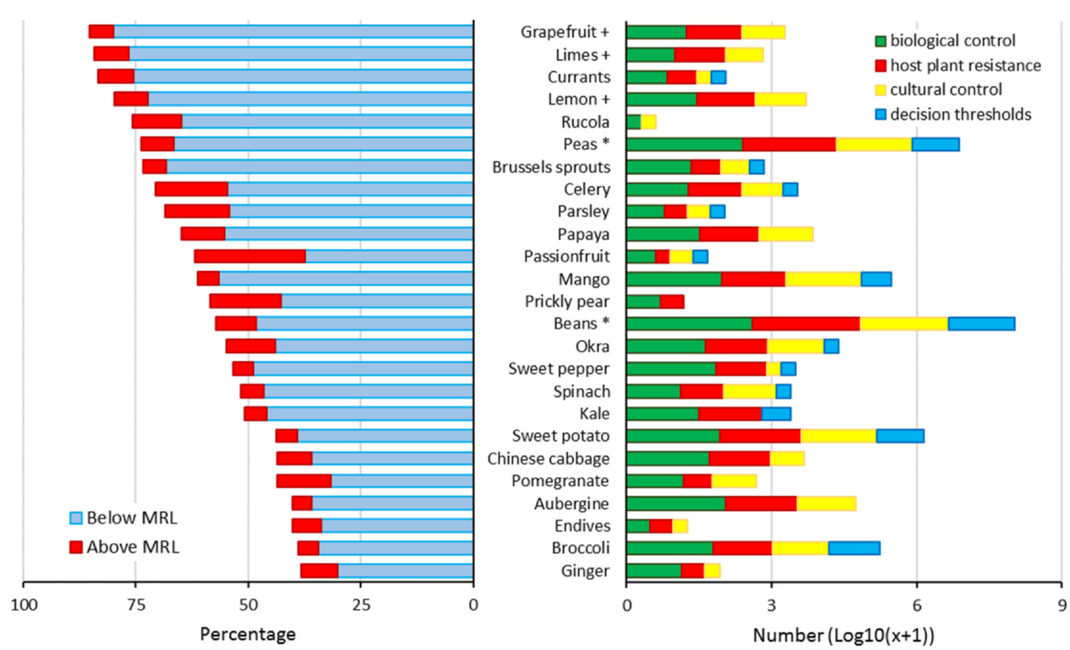

Fig. 2. Commodity-specific listing of key IPM avoidance tactics for common pesticide-tainted food items in the European Union. Food items comprise unprocessed food staples, legumes, spices and diverse horticultural produce, as consumed in 2016 in the European Union (EFSA, 2018). Food items with a '+' or '*' are analyzed with their respective peel or pods. Produce is ranked according to the overall pesticide detection frequency, i.e., total % samples with quantified residues below or at the MRL (left panel; blue) plus those exceeding established MRLs in the EU (left panel; red). The right panel reflects the total scientific attention to various IPM avoidance tactics for a given food item. The log-transformed number of Web of Science citation records is computed separately for each IPM tactic and stacked per food item. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

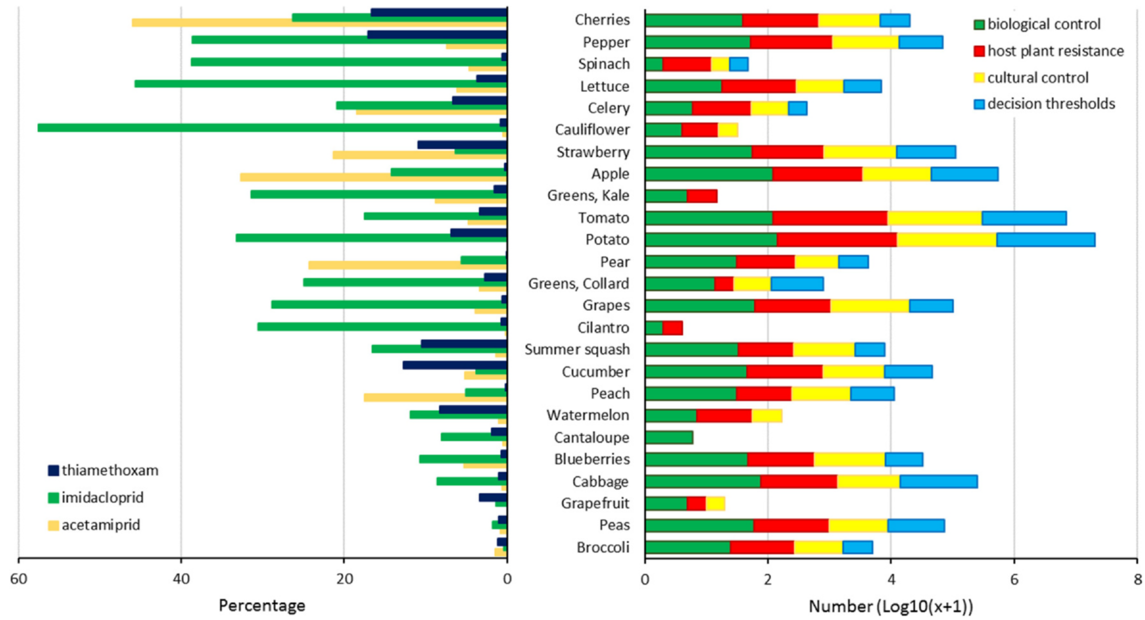

Fig. 3. Commodity-specific listing of key IPM avoidance tactics for common USA food items tainted with neonicotinoid insecticides. Food items comprise unprocessed food staples, legumes and diverse horticultural produce as consumed over 1999–2015 in the United States (USDA Pesticide Data Program; Craddock et al., 2019). Produce is ranked according to the summed detection frequency of 7 different neonicotinoid insecticides, and residue profiles are shown for the three most frequently detected compounds. For each food item, total % samples with quantified residues of thiamethoxam, imidacloprid or acetamiprid is plotted. The right panel reflects the total scientific attention to various IPM avoidance tactics for a given food item (as restricted to US literature). The log-transformed number of Web of Science citation records is computed separately for each IPM tactic and stacked per food item.

imidacloprid (20%), acetamiprid (9%) and thiamethoxam (5%) most commonly recorded. Detection frequencies varied considerably between individual chemical compounds and horticultural produce, e.g., with up to 46% cherries tainted with acetamiprid or 58% cauliflower containing residues of imidacloprid. Among all food items, 5 ± 1% samples contained residues of two or more compounds, with 10–25% pepper, celery and cherries tainted with multiple residues. Three food items with high detection frequencies (i.e., cherries, spinach, lettuce) are currently cultivated on approx. 180,000 ha in the US alone.

In conclusion, health and environmental hazards associated with fruit and vegetable consumption can be pronounced in several low- and middle-income countries (e.g., Argentina, Bolivia, Nepal, Vietnam, Tanzania). Conversely, some low-income countries experience low to moderate pesticide residue levels, while high-income nations (e.g., US) appear unable to drastically lower pesticide usage and incidence of pesticide-contaminated food irrespective of ample technological innovations in pest management science (Schreinemachers & Tipraqsa, 2012).

3. Bridging food toxicology and pest management science

Subsequent analyses centered on the 1970′s concept of IPM, a globally-recognized standard for plant protection, defined as a "*careful integration of appropriate pest control measures that discourage pest population build-up and keep pesticides and other interventions at levels that minimize risks to human health and the environment*" (Kogan, 1998; Barzman et al., 2015). As such, IPM constitutes a broad set of principles to substantially reduce or eliminate the use of synthetic pesticides. Indirect preventative practices, ecological technologies and optimized agronomy underpin crop- or pest-tailored IPM packages, with the relative contribution of these measures and their interrelationships routinely visualized within a so-called IPM 'foundation arch' or 'pyramid'. The basis of such a pyramid is composed of pest or disease avoidance tactics such as host plant resistance (HPR), tailored soil, nutrient and water management, sanitary measures, biological control, reliable diagnostics and a close monitoring of pest populations. Biological control is of particular interest as it provides one of the most economically sound and sustainable IPM tactics (Naranjo et al., 2015). The IPM 'pyramid' further comprises decision criteria to guide pest management interventions (e.g., economic thresholds) while a rational, spatio-temporally confined use of selective, narrow-spectrum synthetic pesticides is explicitly termed a 'measure of last resort'.

To visualize how different IPM avoidance tactics are tailored to specific pesticide-intensive horticultural crops (and associated food items), we carried out a systematic literature review. More specifically, we queried the Web of Science Core Collection database (1900–2019). Queries were run with various Boolean search strings as defined by the authors (Supplementary Table 2). Queries were specifically defined to assess the extent of past scientific attention to constituent measures within the IPM pyramid, i.e., biological control, pest biology and ecology, sampling and monitoring, host plant resistance, cultural control and decision thresholds. Searches were confined to those records that specifically described performance of different IPM measures in field settings, as compared to under laboratory conditions. While certain searches were geographically confined (i.e., covering US scientific literature), others recorded global patterns. Literature searches were further performed for 4 horticultural crops that are characterized by high incidence of pesticide residues in harvested produce such as peach, strawberry, apple and lettuce (EFSA, 2018). These commodities are consumed to variable extent within the EU, with apple and lettuce at a higher dietary intake bracket (i.e., grams per day) as compared to peach and strawberry. For these food items, queries were also run to record the number of scientific studies that simultaneously featured commonly detected pesticides and specific IPM constituent technologies. This allowed quantifying the (crop-specific) extent of scientific attention to either develop or validate IPM alternatives for certain chemical pesticides, to seek integration of non-chemical approaches with pesticide-based tactics or to assess the in-field compatibility of certain pesticides with e.g., biological control.

4. 'Planetary health' solutions space

For all food items, literature records were found that covered at least one of four IPM constituent measures (Fig. 2). For vegetables such as aubergine, sweet potato, peas or beans, 156–658 different literature records were recovered per crop. Fruits with high levels of pesticide contamination, e.g., mango, papaya and lemon, equally had 53–152 records covering one or more IPM constituent measures. Over 60% of records covered biological control of either arthropod pests or plant pathogens, 23% described host plant resistance and 13% cultural control, though only 3% featured decision thresholds for pesticide application. Biological control either comprised the on-farm habitat manipulation to favor resident natural enemies (Landis et al., 2000; Chaplin-Kramer et al., 2019), periodic releases of mass-reared insectivorous organisms or antagonistic fungi (van Lenteren et al., 2018) or the scientifically-guided introduction of exotic natural enemies for control of invasive pests (Bale et al., 2008). Hence, for all pesticide-tainted horticultural produce, scientifically underpinned non-chemical approaches and IPM avoidance tactics are available.

For all neonicotinoid-tainted food items, IPM constituent measures were equally well covered in the scientific literature – even when literature searches were confined to US domestic research, to align with the reported residue profiles (Fig. 3; Craddock et al., 2019). Per food item, an average of 69.5 ± 15.2 literature records covered one or more IPM measures, with biological control featured in 57% of records. For horticultural produce such as cabbage, apple, tomato or potato, a respective 119, 171, 248 and 307 records covered IPM avoidance tactics. Neonicotinoid-tainted produce such as US cherries and pepper had 38–51, 9–11, 16–21 and 2–4 domestic literature records featuring biological control, cultural practices, host plant resistance and decision thresholds, respectively. Hence, measures to replace or reduce usage of neonicotinoid insecticides are well-researched for most pesticide-tainted horticultural produce. More so, in a range of cropping systems and geographies, neonicotinoids could readily be replaced by non-chemical alternatives (Jactel et al., 2019; Veres et al., 2020). Yet, given the neonicotinoid residue profiles in US food items, scientists either appear unable to effectively vulgarize their work, validate it hand-in-hand with farmers or translate it into practice at scale while policy makers fail to act upon a fast-accruing scientific evidence base.

For 4 commodities with high incidence of pesticide residues in harvested produce (i.e., peach, strawberries, apple, lettuce; EFSA, 2018), literature searches revealed diverging scientific interest among the various IPM constituent measures (Fig. 4). Irrespective of the target commodity, most collated literature records covered sampling & monitoring, pest biology & ecology and biological control. These include pheromone-baited traps for codling moth, *Cydia pomonella* in apple (Witzgall et al., 2008), antagonistic fungi and yeasts for suppression of pre- and postharvest diseases in peach (Yánez-Mendizábal et al., 2012), or mass-reared predatory flies for aphid management in California outdoor lettuce (Nelson et al., 2012). Conversely, relatively minor attention was given to HPR, cultural control and decision-support tools. IPM 'pyramids' further revealed a disproportionate amount of scientific attention to the in-field efficacy assessment of synthetic pesticides (Fig. 4).

When quantifying (commodity-specific) scientific attention to IPM measures for routinely detected pesticide residues - as reported by EFSA, IPM 'pyramids' equally proved top-heavy (Supplementary Fig. 1). For example, in peach, 57% publications covered in-field efficacy of tebuconazole – a synthetic compound linked to antifungal resistance (Fisher et al., 2018). Also, for specific compounds (e.g., fludioxonil in peach or apple, propamocarb in lettuce), no literature records were found for most IPM constituent measures. Conversely, ample scientific attention was given to IPM avoidance measures for the legally restricted methyl bromide in lettuce.

A total of 47 synthetic pesticides and selected metabolites were detected at frequencies of 4 ± 1% in all analyzed plant products (EFSA, 2018; Fig. 5), with several fungicides, e.g., boscalid, dithianon or dithiocarbamates recovered from 12 to 15% of sampled produce.

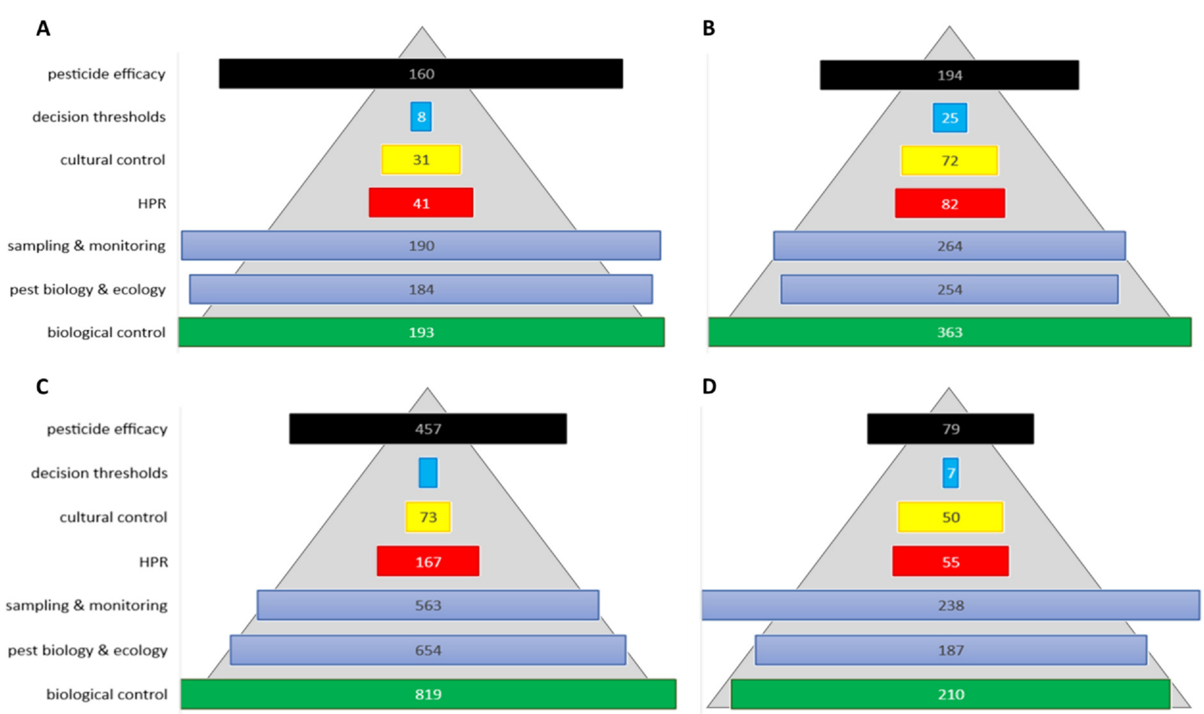

Fig. 4. Comparative extent of global scientific attention to different IPM constituent measures for 4 pesticide-intensive horticultural commodities. For each food item, the number of Web of Science literature records is shown per IPM tactic – broadly ranked according to their relative importance within the IPM 'pyramid' (Kogan, 1998). Graphs depict patterns for a) peach, b) strawberries, c) apple, and d) lettuce. 'HPR' refers to host plant resistance, while 'pesticide efficacy' specifically denotes the field-level screening of synthetic pesticides against crop-inhabiting pest or pathogen targets. For apple (panel c), a total of 28 records for decision thresholds are recorded. Respective search strings for each of the literature queries are included in Supplementary Information.

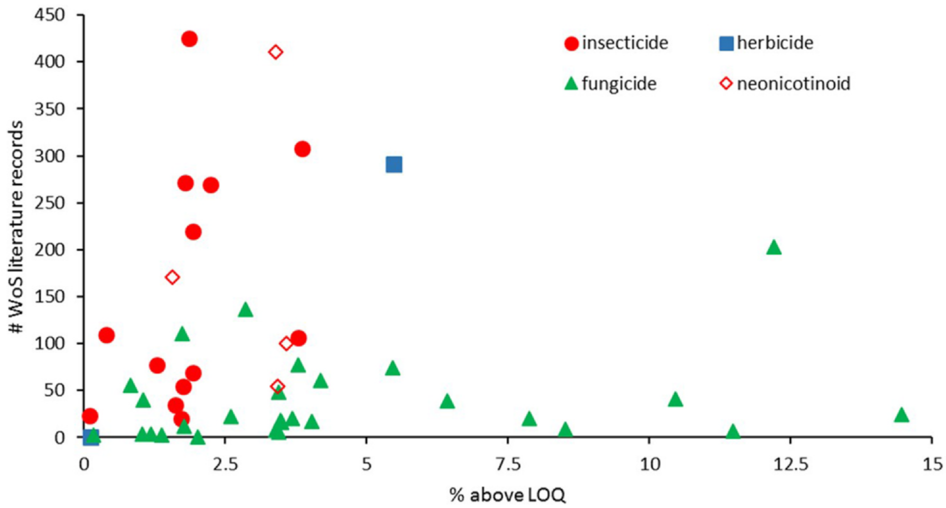

Fig. 5. Extent of global scientific attention to biological control for 47 commonly detected synthetic pesticides. For each pesticide, its overall detection frequency (% samples above limit of quantification, LOQ) in all analyzed plant products within the European Union (EFSA, 2018) is contrasted with the number of Web of Science literature records that list the respective pesticidal compound while also covering its 'biological control' alternatives. The number of samples analyzed per compound ranged from 58 (folpet) to 10,241 (cyprodinil). Patterns for different categories of pesticides, including the specific case of systemic neonicotinoid insecticides, are visualized.

Scientific attention to biological control varied considerably between individual compounds and pesticide classes, with a respective 153 ± 42 and 39 ± 7 literature records per compound for insecticides and fungicides. Concurrent scientific attention to biological control and individual pesticidal compounds was noted for the insecticide deltamethrin (i.e., 425 records) and dithiocarbamate fungicides (203 records). Especially for insecticides, biological control has received ample scientific attention as a non-chemical 'avoidance' tactic within the IPM crop protection toolbox. As such, opportunities abound for food producers, pest management professionals, nutritionists and medical personnel to implement physicians' AD 245 'Hippocratic Oath' to abstain from intentional harm, prioritize non-chemical regenerative practices and thereby safeguard planetary health (Wratten et al., 1997).

5. Human and environmental health 'blind spots'

Interdisciplinary science is crucial to effectively link planetary health (or 'One Health') indices with human food production behavior and consumption patterns (Flandroy et al., 2018; Vandermeer et al., 2018), and a 'food systems' framework lends itself to fuse the above elements (Gordon et al., 2017). By compiling residue profiles at a multi-country scale, we uncover how horticultural food items greatly expand human health hazards of synthetic pesticide use from farm to fork (European Commission, 2020). Overall, our work demonstrates how many widely grown 'healthful' foods are pesticide-intensive, hints at prevailing crop management practices and thus opens a window on the environmental health implications of global fruit and vegetable cropping. In the absence of concerted initiatives to track synthetic pesticide usage and trade (Mitchell et al., 2017; Landrigan et al., 2018) or formal food safety surveillance programs in many countries (Thompson et al., 2017; Skovgaard et al., 2017), our exercise adds to an accruing literature that maps agro-chemical pollution and related human health hazards globally.

To mitigate global risks of cancer, autism and neurological disorders as well as non-communicable diseases (NCD), a reduced exposure to persistent pollutants, toxic substances and endocrine-disrupting chemicals is imperative (Scott et al., 2014; Landrigan et al., 2018). Our data demonstrate that -through regular consumption of plant-based foods- human beings experience extensive exposure to myriad pesticide residues in small but constant doses. Among them, residues of the herbicide glyphosate, systemic fungicides (e.g., boscalid, tebuconazole) and insecticides (e.g., neonicotinoids, carbamates) are most prevalent. With 25–42% samples surpassing MRL standards in Chile, Argentina, Ghana, Kazakhstan, Nepal or Vietnam (Skretteberg et al., 2015; Elgueta et al., 2017), fruit and vegetable consumption may pose health risks especially for those adopting 'planetary health' diets (Caldas & Jardim, 2012; Springmann et al., 2016). While recognizing that MRL standards are set on a precautionary principle (Krimsky & Simoncelli, 2007), we note that actual dietary exposure levels can be extensive, as 100% breast milk samples of mothers in areas of Tunisia or Brazil contain banned, restricted or hazardous pesticides (Caldas & Jardim, 2012; Thompson et al., 2017). Dietary exposure explains the pesticide titers observed in maternal and child urinary samples e.g., in Thailand or among Latino farm-worker families in the US and is further reflected in a heightened incidence of mental development disorders (Eskenazi et al., 2007; Panuwet et al., 2009). Human health risks can be particularly pronounced for vulnerable infants and children or for prenatal exposure (Landrigan et al., 2019), with early-life exposure to low concentrations of pollutants prone to lower cognitive functions, school performance and lifetime earnings. With toxicological data missing for many common active compounds, metabolites and pesticide mixtures (Hernández et al., 2017; Landrigan et al., 2018), it is challenging to reliably predict their protracted health impacts. Furthermore, health hazards aren't exclusively tied to food consumption but equally comprise occupational and non-occupational exposure, the former impacting some 28 million farm workers annually and likely exacerbated among resource-poor smallholders in the tropics, where protective gear is rarely used (Konradsen et al., 2003). In many low-income countries, large fractions of the population are employed in agriculture and the associated health hazards can thus be very substantial (Praneetvatakul et al., 2013). By coupling post-harvest residue profiles with food flow network data, such farm- or landscape-level exposure pathways can also be visualized (Lin et al., 2019). High-resolution pesticide footprints can help map susceptible farmer populations, quantify non-occupational exposure through air and soil or assess elevated risks of (human) antifungal resistance development in horticulture landscapes (Fantke & Jolliet, 2016; Schoustra et al., 2019). These approaches equally permit visualizing how pesticide volatilization patterns contribute to the premature mortality related to air pollution (Lelieveld et al., 2015).

Moreover, residue profiles can help draw pesticide-related 'gray water footprints' tied to certain food environments (Mekonnen & Hoekstra, 2015; Springmann et al., 2018) and quantitatively assess ecological vulnerabilities for aquatic organisms, soil-inhabiting species or airborne biota (Diepens et al., 2014; Mitchell et al., 2017; Silva et al., 2019). These vulnerabilities can be exacerbated in horticultural production settings, as evidenced by the 33% incidence of multiple residues in EU fruits and vegetables. Here, highest multi-residue detection frequencies were for berries (65–86%), hops (82%), grapes (68%) and citrus fruit (73%); (semi-)perennial crops that are cultivated within comparatively stable and biodiversity-rich ecosystems. In those settings, pollinators, bees, arthropod natural enemies and insectivorous vertebrates provide vital ecosystem services (Dainese et al., 2019), yet are negatively impacted by recurrent pesticide applications (Mitchell et al., 2017). Considering how insect pollination secures over € 150 billion in global fruit and vegetable output (Gallai et al., 2009), a comparative valuation of on-farm pesticide sprays and coated seeds vs. foregone ecosystem service delivery and economic returns may be rewarding.

With only 0.1–20% of pesticide active ingredient reaching the focal pest, most pesticides have profound and often prolonged impacts on non-target biota (Pimentel & Levitan, 1986; Sur & Stork, 2003). Environmental impacts aren't confined to ecosystem service-providing organisms within individual farm settings. Pesticides applied through aerial sprays in banana – a crop grown on 5.4 million ha worldwide – reach the Arctic, while other commonly used compounds are found in pristine mountain forests, across the world's oceans or within coral reefs (Daly et al., 2007; Jamieson et al., 2017). Landscape-level habitat diversification is often touted as a way to bolster environmental health and biodiversity-mediated ecosystem services (Karp et al., 2018). However, given the ubiquitous nature and spatial reach of agrochemicals, these actions likely prove futile without an effective reduction in pesticide use (Geiger et al., 2010). On the other hand, pesticide-free and organic farming schemes can help restore species richness and abundance by 30–50% and rebuild their associated ecosystem services (Reganold & Wachter, 2016). When implemented over sufficiently large areas, they can also defuse pesticide-related hazards in surface waters or for highly mobile organisms, including birds, bats and large mammals (Berheim et al., 2019; Eng et al., 2019). Overall, to resolve current pesticide-related hazards to environmental health, a systematic assessment of either global or country-level residue records in harvested horticultural produce can help define vulnerability 'hotspots', prioritize interventions and drive change.

6. Towards lasting agro-ecological transitions

A concerted 'food transformation' could keep the world's food system within planetary boundaries, with an increased global intake of plants and plant-based diets carrying tangible 'win-win' benefits for human health and the environment (Byerlee et al., 2009; Willett et al., 2019). The supplied data however accentuate how this dietary transition cannot stand alone; it won't suffice to stem biodiversity loss, but instead needs to be paired with technological change and pest management innovation to deliver on its promise (Springmann et al., 2018). By systematically listing non-chemical alternatives for specific pesticidal compounds, commodities and geographies, we wish to facilitate endeavors to resolve the widespread use of synthetic pesticides and biocides. Nature-based innovations such as biological control constitute safe, efficacious and cost-effective measures to safeguard human and environmental health in horticulture production landscapes (Lafortezza et al., 2018), while IPM represents a time-tested approach to lower pesticide inputs that result in equal or even higher agricultural yields (Kogan, 1998; Pretty & Bharucha, 2015). Effective scaling of these practices will require action on multiple fronts, involvement of stakeholders across food value chains, tactical use of diverse policy levers, unbiased information, well-designed campaigns and adaptive innovation hand-in-hand with farmers (Springmann et al., 2018; Pretty et al., 2018; Willett et al., 2019). Parallel to this, a major overhaul and serious implementation is needed of both environmental and human health risk assessment for existing and new synthetic pesticides, including for instance the popular neonicotinoids (Boobis et al, 2008; Landrigan et al., 2018; Brühl and Zaller, 2019; Topping et al., 2020).

Nature-based pest control is clearly beneficial to a wide range of stakeholders (Rasmussen et al., 2018; Chaplin-Kramer et al., 2019), representing advantages over conventional, pesticide-based tactics for consumers, farmers and land managers, conservationists or governments (Bale et al., 2008). First and foremost, pesticide-free fruits and vegetables have equal or better profiles of health-promoting nutrients, vitamins and phytochemicals than those that are conventionally grown (Mie et al., 2017; Vigar et al., 2020). Aside from their desirable environmental profile, the on-farm use of IPM tactics helps avert large external costs of agro-chemical pollution on society, mitigates crop yield gaps, bolsters farm-level revenue and thus redirects household savings towards domestic economies instead of transnational corporations (Motzke et al., 2015; Naranjo et al., 2015; Landrigan et al., 2018). For example, among Southeast Asian vegetable growers, current pesticide application regimes entail more than US $300/ha/cycle foregone profit and constitute an undisguised poverty trap (Schreinemachers et al., 2020). Conversely, Nicaraguan cabbage growers that relied on biological control saved $2200/ha and slowed biocide resistance development in local pest populations (Bommarco et al., 2011; Jørgensen et al., 2018). A shift towards non-chemical tactics in horticulture landscapes potentially can help reconstitute broad bundles of ecosystem services, e.g., nutrient cycling, freshwater provisioning and suppression of foodborne pathogens (Vorosmarty et al., 2010; Stehle & Schulz, 2015; Chaplin-Kramer et al., 2019), or even achieve carbon-negative food systems (Heimpel et al., 2013). Lastly, IPM 'avoidance' tactics do not involve pesticide applications and thus do not leave traces of xenobiotic compounds in harvested produce (Vigar et al., 2020). Hence, contrary to prevailing thought, when drawing the 'options space' to safeguard human health from pesticide-related threats, the precautionary principle is entirely practicable because it forces innovation along more sustainable food production trajectories (Pretty et al., 2018).

7. Cleaning out King Augeas' stables

A Herculean task; that's what the decades-long struggle for a biodiversity-friendly agriculture has been. Since the early days of Rachel Carson and University of California pioneers, a lot has been said and written about the relentless chemical intensification of agriculture and its clear threat to planetary health (Carson, 1962; van den Bosch, 1989; Pretty, 2012; Wood and Goulson, 2017; Goulson, 2020). More than half a century ago, Carson's book '*Silent Spring*' succeeded in raising public awareness and ultimately led to a ban on DDT and organochlorine nerve toxins; though such was rapidly followed by the launch of myriad new pesticide classes, some of them equally or more environmentally-damaging (Tennekes & Zillweger, 2010; van der Sluijs et al., 2015). Meanwhile, innumerable scientists and practitioners have built the necessary groundwork for non-chemical crop protection, devised ingenious pest prevention or biological control tactics and joined hands with farmers to transform agri-food production. Yet, given the unrelenting surge in global pesticide use (Bernhardt et al., 2017; Hedlund et al., 2020), one may easily wonder whether Carson's tireless advocacy has been in vain, agro-ecology science has failed to deliver or the "IPM emperor is truly naked" (Orr, 2003; Zalucki et al., 2012; González-Chang et al., 2020). Though UN-backed farmer training programs in the 1990s attained 50–80% pesticide cuts on millions of farms without any yield loss (Gallagher et al., 2009; Bottrell & Schoenly, 2012), these achievements were undone soon thereafter due to political change, dwindling government commitment and agro-industry meddling (Thorburn, 2015). Even while the prophylactic use of neonicotinoid-coated seeds conflicts with globally-valid IPM principles and is not economically justified, it is embraced by farmers across North America for its convenient usage mode (Bredeson & Lundgren, 2015; Mourtzinis et al., 2019; Labrie et al., 2020). It is evident that, in the pursuit of environmentally-sound agriculture, a wide range of perspectives are wielded and multiple roadblocks can be encountered - with agrochemical industry interference playing a nonnegligible role (Bentley & Andrews, 1996; Pretty & Bharucha, 2015; Goulson, 2020). By examining food as a source of toxins and health-giving substances, our work shines new light on the agrochemical pollution issue and can simultaneously advance sustainable agri-food systems and biosphere stewardship. Even if it may sound naive, we list soft and hard policy interventions for further implementation, knowing that these measures will require globe-spanning efforts, a great deal of political will and a responsible attitude (and far more public-spirited commitment) of transnational corporations in order to be effective (Folke et al., 2019; Donley, 2019; European Commission, 2020; Wanger et al., 2020).

Indeed, distributors and processors of plant-based foods can drive change (Duru et al., 2015), and a blend of carefully selected policy levers can engage different stakeholders, reshape supply chains and remediate the current 'planetary health' burden of fruit and vegetable production. Short, decentralized supply chains with few middlemen, rooted in ecologically-intensified, regenerative or organic farming networks across regions offer clear opportunities to bring about positive change at scale (Pretty et al., 2018; Eyhorn et al., 2019). As it's difficult to effectively influence farmer behavior (Kanter et al., 2019; Wyckhuys et al., 2019), 'pressure points' can be identified along agri-food chains and policies can be specifically tailored to certain actors. Soft policy interventions comprise certification schemes, consumer awareness-raising and appropriate food safety labelling. Government-endorsed certification of 'pollution-free' and 'green' food items or retailers' use of 'pesticide footprint' labels may resonate well with individual consumers and be powerful catalysts of farm-level change in developed countries, where there is awareness on these issues (Dou et al., 2015; Kanter et al., 2019). Voluntary certification schemes e.g., GLOBALGAP can be broadened to include clear goals for pesticide reduction. Food processors can opt to source produce (e.g., berries or nuts) from ecologically managed orchards and create further traction with 'honeybee-friendly' brands. Strawberries, oranges, apples or peaches can lend themselves well to such strategies – being sought for their health benefits by young and old, irrespective of their high pesticide load. Notwithstanding the large environmental footprint of pesticide use, food labels that reflect human-health benefits are likely more effective than those referring to a 'biodiversity-friendly' nature of produce (Magnusson et al., 2003). Premium pricing equally carries promise; globally, people are willing to pay US$4.6 trillion to avoid premature death or illness due to pollution, with consumers in countries such as Vietnam keen to pay a 70% higher price for a certified pesticide-free food basket (Landrigan et al., 2018; Larousse et al., 2019). National governments or international bodies can further incentive behavior through 'steward earns' or 'polluter pays' modules, aimed at individual farmers or agro-enterprises. Incentives can also take the form of government subsidies or tax breaks for non-polluting industries, e.g., producers of natural enemies, microbial pesticides, pheromone-based tools or farmer insurance schemes (Furlan et al., 2018; Veres et al., 2020).

Hard policy measures such as conditional financial assistance for farmers who alter their production methods, taxes and more stringent MRL standards can be equally effective in regulating the production, consumption and trade of pesticide-tainted food items. Aside from favoring environmentally-sound farming practices, stricter MRL standards can impart consumer confidence, mitigate biodiversity threats and even facilitate inter-country trade (Drogué and DeMaria, 2012; Lenzen et al., 2012). Taxes can target health-degrading substances such as pesticide residues and create spill-over benefits, in a similar way as those attained following the roll-out of taxes on fat, junk food or sugar-sweetened beverages (Mytton et al., 2012). These measures can only be successful when communicating spill-over benefits and ultimate policy goals, earmarking tax revenues for health- or agriculture-related spending and securing due preparedness on farmers' behalf (Finger et al., 2017). Engaging consumers e.g., in locating residue-free produce or in real-time monitoring of on-farm biodiversity impacts using digital tools, can help tip the balance (Poore & Nemecek, 2018). Overall, *trans*-disciplinary approaches and due attention to social science are key, while large strides need to be taken to sensitize the general public and farmers about pesticide-free forms of agriculture (Röling & van de Fliert, 1994; Rebaudo & Dangles, 2013; Wyckhuys et al., 2019). Conversely, current trends in medical education, crop protection, farming systems research and environmental health science need to be reversed to allow scientists to holistically assess, comprehend and resolve the diet–environment–health trilemma (Warner et al., 2011; Landrigan et al., 2018). "Get green or get out" (Chen, 1995): when policy-makers join scientists' call for a more sustainable agri-food system, transformative change can be enabled. The European Commission's 2030 Green Deal sets clear pesticide reduction targets, commits to a serious implementation of IPM (compulsory since 2014), promotes innovation in e.g., mechanical weeding or crop rotation, and pursues an enhanced use of safe crop protection alternatives. Stepping up an enforcement of the law and roll-out of corrective measures will make sure implementation remains on track, goals are achieved, and words translate into practice (European Parliament, 2019; European Court, 2020).

Packed with decades of (metaphorical) filth and caked-on dirt, the global agrochemical-reduction challenge is easily perceived as an unsurmountable 'Herculean' task from which most scientists back away (Bernhardt et al., 2017). Yet, in order to effectively strive towards a healthier Planet, it is crucial to pick up the shovel, put oneself to the task and make the wheels of (agro-ecology) innovation spin. Thus wielding the full power of science and farmers' innovative capacity while opening all possible (policy) registers, we can profitably grow clean, nutritious farm produce that is protective of human health and cultivated in ways that are respectful to biodiversity and the world's ecosystems.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: KAGW is chief executive officer of Chrysalis Consulting, a firm that provides tailored support to biological control and biodiversity-friendly agriculture initiatives.

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KAGW is chief executive officer of Chrysalis Consulting, a firm that provides tailored support to biological control and biodiversity-friendly agriculture initiatives. Aside from the above, the authors declare no other competing financial or non-financial interests.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2020.106081.

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