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Biological control for One Health

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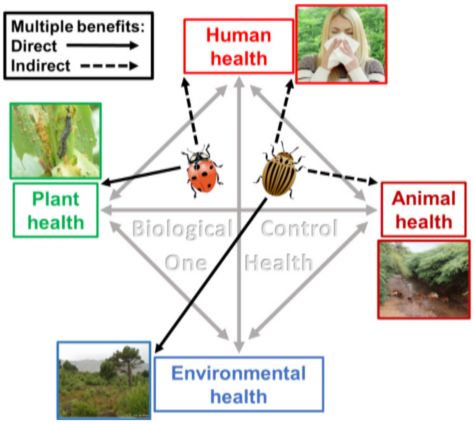
HIGHLIGHTS

- Broader contributions of biological control to One Health remain underappreciated.
- Direct and indirect benefits of biological control help tackle pressing global issues.
- Global contributions of biological control to all dimensions of One Health are highlighted.
- Recommendations to enhance application of biological control in One Health are proposed.

GRAPHICAL ABSTRACT



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ABSTRACT

Biological control has been effectively exploited by mankind since 300 CE. By promoting the natural regulation of pests, weeds, and diseases, it produces societal benefits at the food-environment-health nexus. Here we scrutinize biological control endeavours and their social-ecological outcomes through a holistic 'One-Health' lens, recognizing that the health of humans, animals, plants, and the wider environment are linked and interdependent. Evidence shows that biological control generates desirable outcomes within all One Health dimensions, mitigating global change issues such as chemical pollution, biocide resistance, biodiversity loss, and

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Sustainability
Transdisciplinarity

habitat destruction. Yet, its cross-disciplinary achievements remain underappreciated. To remedy this, we advocate a systems-level, integrated approach to biological control research, policy, and practice. Framing biological control in a One Health context helps to unite medical and veterinary personnel, ecologists, conservationists and agricultural professionals in a joint quest for solutions to some of the most pressing issues in planetary health.

1. Introduction

Global change impacts biodiversity and ecosystem health through multiple, interrelated processes that involve habitat loss, agricultural intensification, invasive species, climate change, and chemical pollution (IPBES, 2019). While the consequences of biodiversity loss are often examined through mono-disciplinary lenses, they are in fact highly complex, dynamic, and multi-dimensional. For example, human, animal, and ecosystem health are closely intertwined, as illustrated by the relationship between biodiversity loss and the increasing prevalence of allergies (Hanski et al., 2012), dietary and nutritional shortfalls (Smith et al., 2022a), and zoonotic and vector-borne disease incidence (Gibb et al., 2020). Disciplinary silos and reductionist approaches hamper our understanding and eventual mitigation of the complex issues that emerge at the food-environment-health nexus. Although other concepts, such as EcoHealth and Planetary Health share overall aims (Adisasmito et al., 2022), the concept of One Health provides a uniquely useful paradigm for gauging the broader implications of environmental change while accounting for the interconnections between people, animals, plants, and their shared environment (One Health Commission, 2023). The One Health framework also underlines how close cooperation between professionals in the human, animal, plant, and environmental health sciences can produce unprecedented societal benefits.

One valuable intervention that merits further attention in the context of One Health is biological control. We define biological control as the suppression of populations of pests, weeds or disease-causing organisms by living organisms i.e., vertebrate or invertebrate animals, plants, microorganisms or viruses (Heimpel and Mills, 2017). While this definition includes strategies such as the use of *Wolbachia* bacteria against disease-vectoring mosquitoes, it omits technologies based on genetic modification of crops or vectors of diseases. Biological control comprises natural biological control that occurs naturally without human intervention as well as nature-based solutions (Sowińska-Świerkosz and García, 2022) delivered by human intervention (Heimpel and Mills, 2017; Stenberg et al., 2021). It not only provides direct benefits through the management of a wide range of pests, weeds and diseases, but additionally contributes indirect benefits through the promotion of biodiversity and human welfare. As compared to many synthetic chemical-based interventions, biological control harnesses biodiversity-driven ecosystem services for sustainable pest, disease, or weed management. The practice has been continually refined since its first records dating from before 300 CE, primarily to increase crop yields (Heimpel and Mills, 2017; Mason, 2021). However, during the second half of the 20th century, agricultural intensification began to decouple agroecosystems from underlying ecosystem services and turned to synthetic pesticides or antibiotics to control pests and diseases (Bernhardt et al., 2017; Nyström et al., 2019). This has resulted in a precipitous decline of farmland biota, critical loss of ecological resilience, and weakened internal feedbacks, as initially brought to light for pesticides by Rachel Carson's *Silent Spring* (Carson, 1962). Along the same lines, over-reliance on chemical antibiotics in the livestock sector has caused rapid increases in antibiotic resistance that directly imperil human society (Jørgensen et al., 2018). Addressing the many environmental challenges stemming from agricultural intensification will require phasing down chemical inputs while actively conserving or restoring biodiverse agricultural landscapes that contain organisms providing critical ecological functions such as nutrient cycling, pollination, and pest control (Dainese et al., 2019; Nyström et al., 2019).

In more recent decades, biological control has also gained momentum beyond the agrifood sector i.e., in public health and environmental protection domains (Van Driesche et al., 2010; Benelli et al., 2016). Yet, despite its proven potential or millennia-long trajectory, biological control continues to face comparatively low rates of adoption and receives marginal attention beyond the disciplinary confines of crop protection science (van Lenteren, 2012; González-Chang et al., 2020). Furthermore, the broader effects of biological control on societal well-being and One Health remain critically underappreciated (but see Ratnadass and Deguine, 2021; Müller-Schärer et al., 2024).

Here we argue that a broader use of biological control can help address multiple One Health challenges. We review how biological control contributes to each of four interrelated One Health dimensions, i.e., environmental, plant, animal and human health (Fig. 1). We examine its direct benefits, such as reduced densities of crop pests or vectors of human diseases, as well as its indirect benefits, including reduced environmental pollution, enhanced habitat conservation, and increased human and livestock health. We first provide a brief history of the different biological control approaches and how they act as cornerstones of integrated pest management in the agricultural domain. Next, while transitioning to human and animal health domains, we outline advances in biological control and examine their social-ecological impacts through a One Health lens. Finally, we discuss ways in which an enhanced uptake of biological control can unlock opportunities for

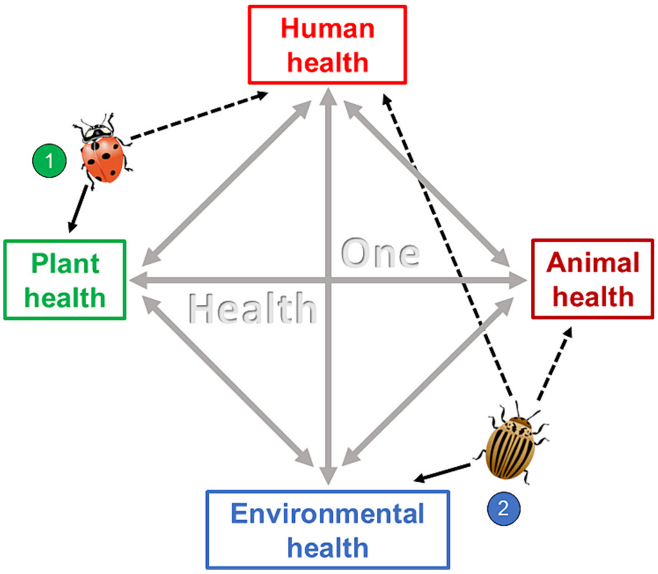

Fig. 1. Hypothetical examples of direct (solid black arrows) and indirect (dashed black arrows) benefits of biological control solutions to different dimensions of the One-Health concept. Example 1 depicts a biological control project against an agricultural pest that directly benefits crop health. By reducing the application of synthetic pesticides, this interaction also indirectly reduces pesticide exposure of humans and thus contributes to improved human health. Example 2 features a biological control project that directly benefits environmental health by reducing densities of a weed which negatively affects native biodiversity. Since the environmental weed increases densities of disease-vectoring insects, reduced weed densities also indirectly contribute to improved animal and human health. The examples illustrate that an overall assessment of biological control should consider its direct as well as its indirect benefits to the four dimensions of the One-Health concept.

transdisciplinary collaboration and help generate a multitude of societal benefits worldwide.

2. Milestones in the science of biological control

Historically, the goal of biological control has been to suppress populations of pests, weeds and disease-causing organisms through the action of living beneficial organisms - or so-called 'natural enemies'- with minimal disturbance to the environment (Heimpel and Mills, 2017). Consequently, the science of biological control is firmly rooted in ecology and based on the dynamics of species interactions within ecological communities (Fig. 2). For >60 years biological control has been the cornerstone of integrated pest management (Mills, 2021), but it has yet to be fully integrated into the One Health framework (Falkenberg et al., 2022). Biological control is implemented through importation, conservation or augmentation of natural enemies, three approaches that can be used independently or in combination as integrated biological control (Gurr and Wratten, 1999).

Importation biological control, the introduction of exotic specialist natural enemies for sustainable management of invasive species, mainly arthropods and weeds, is widely practiced (Heimpel and Mills, 2017). Carefully orchestrated programs have restored ecological balance in invaded ecosystems and greatly reduced the impacts of invasive species (Hoddle, 2004). Since the late 19th century, insect natural enemies have been imported to control 588 insect pest species in 148 different countries leading to satisfactory control of 29 % of target species (Cock et al., 2016b). Similarly, beneficial arthropods and fungi have been deployed against 175 weed species in 90 countries resulting in 66 % partial or complete control (Schwarzländer et al., 2018). Success rates have progressively increased every decade since the 1970s and exotic natural enemies now provide effective, long-term control of multiple high-profile invasive weed and insect species globally (Mason, 2021). Success rates can also be higher in natural areas particularly for the protection of native biodiversity (Van Driesche et al., 2010). While some early biological control releases caused ecological harm through the attack of native non-target species, such risks have been greatly reduced through comprehensive pre-release risk assessments that lead to the release of only specialized biological control agents (Heimpel and Cock, 2018; Hinz et al., 2019). Indeed, recent analyses suggest that the benefits to native biodiversity greatly outweigh risks to native biodiversity (Downey and Paterson, 2016; Novak et al., 2021). Moreover, concepts of invasion biology and population ecology have been implemented to raise establishment and impact rates of biological control agents (Heimpel and Mills, 2017; Blossey et al., 2018). Higher impact translates to lower abundances of both the invasive pest or weed species and the released biological control agents, and thus limits indirect food-web effects stemming from the release of even specialized agents (Pearson and Callaway, 2005). Higher rates of impact on invasive species also produce more favourable outcomes in benefit-risk comparisons (Abram et al., 2024; Heimpel et al., 2024). Although the long-term sustainability of success can potentially be compromised through the evolution of resistance or tolerance to the action of natural enemies, current evidence suggests that such events are rare (Goldson et al., 2014); they are best known in the context of immune responses of vertebrate pests to introduced exotic viruses (Kerr et al., 2021).

In contrast to importation biological control, conservation biological control aims to conserve or enhance the populations of resident natural enemies. This can be attained through crop diversification and habitat

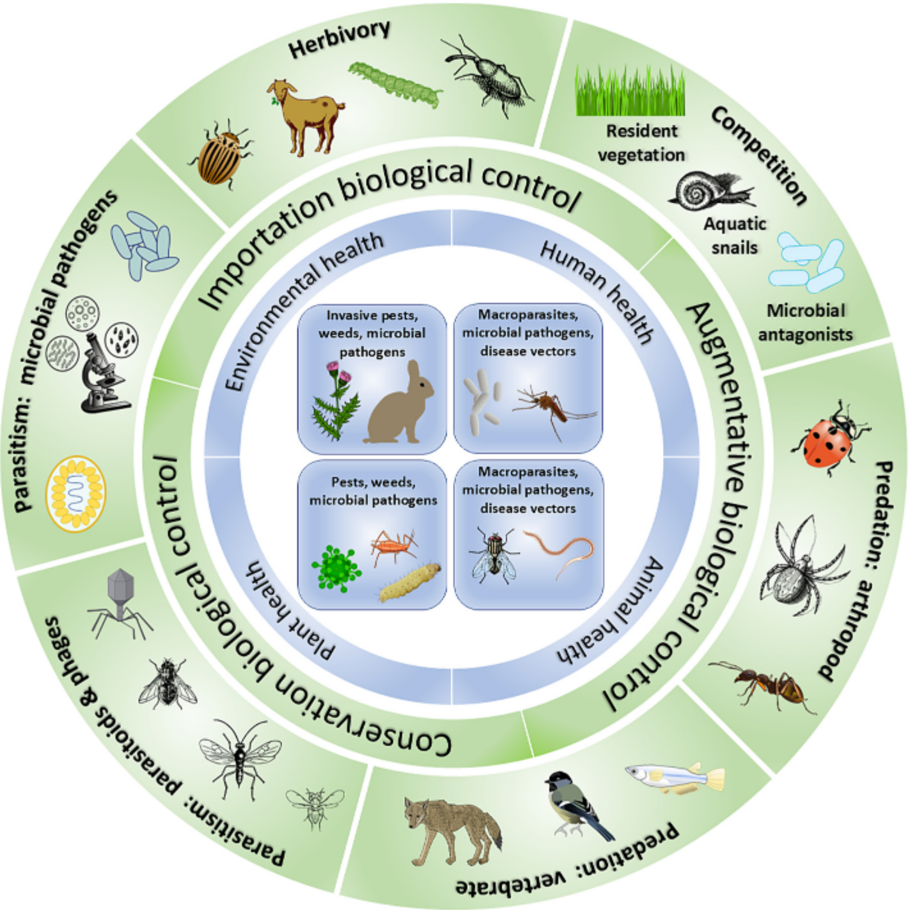

Fig. 2. A schematic representation of the great diversity of natural enemies with different modes of action (outer green ring) that are available to address challenges (blue squares) related to the four dimensions of One Health (blue ring), using one or more of the three approaches to biological control (inner green ring).

manipulation, e.g., by establishing ecological infrastructures such as flower strips, hedgerows, or grass barriers (Gurr et al., 2017). These measures can bolster resilience against crop pests and diseases by retaining abundant, biodiverse natural enemy populations within agroecosystems (Tamburini et al., 2020). This is often achieved by providing food rewards, alternative host or prey species, and shelter at field, farm, or agro-landscape scales. Similarly, integrated pest managent practices such as the targeted application of selective insecticides conserve natural enemies and lower the incidence of pest outbreaks (Bordini et al., 2021). Lastly, by managing plant-soil-microbe interactions and soil microbiota through crop rotation or organic matter addition, one can attain disease-suppressive soils and a lowered incidence of soil-borne crop diseases (Jing et al., 2022).

Augmentative biological control entails the inundative or inoculative release of laboratory-reared biological control agents for immediate or season-long benefits in (natural, or man-made) ecosystems. This approach is widely adopted in greenhouse production systems in Europe and North America (van Lenteren et al., 2018), but mass-reared parasitic wasps and antagonistic fungi are also increasingly employed in field crops such as rice, soybean, sugarcane or maize in Asia and Latin America. Equally, periodic releases of *Wolbachia*-infected mosquitoes greatly reduce dengue fever incidence in Brazil and Indonesia (Dos Santos et al., 2022). Although comparatively high development and production costs have limited current uptake, increased interest in microbial agents and upgraded mass-rearing procedures seem likely to lead to greater implementation in the future.

3. Expanding the benefits of biological control beyond plant production to One Health

Beyond plant-based production systems, an increasing number of case studies demonstrate the benefits of biological control to environmental, animal, and human health. This includes biological control of antibiotic-resistant bacteria, human or animal disease-transmitting arthropods, allergenic weeds, and invasive species threatening natural ecosystems (Table 1 and below). Biological control also contributes to

Table 1
Illustrative examples of contributions of biological control to tackling a wide range of health issues included under the One Health approach (World Health Organization, 2022).

One Health Issue	Biological Control Mechanism	One Health Benefit	Examples
Environmental Health			
Environmental contamination	Replacement of non-selective chemical insecticides with biological control including biopesticides	Reduced environmental contamination and non-target effects, protecting biodiversity and associated ecosystem services	Tang et al. (2021)
Anthropogenic global warming	Replacement of energy-intensive synthetic pesticides with low-carbon solutions	Reduced greenhouse gas emissions from agriculture, bolstered ecological resilience of farmland ecosystems	Heimpel et al. (2013); Wyckhuys et al. (2022)
Ecosystem degradation	Conservation of resident natural enemies in farm settings	Restoration of on- and off-farm ecosystems (across above- and below-ground habitats) and reconstitution of associated ecosystem services	Wubs et al. (2016); Villar (2023); Wyckhuys et al. (2024)
Invasive species affecting environmental integrity	Introduction of natural enemies to reduce populations to new equilibrium	Sustained, long-term control, protecting native biodiversity and restoring ecosystem services	Van Driesche et al. (2010); Arp et al. (2017); Rayamajhi et al. (2019)
Plant Health			
Unsustainable food production	Diverse array of biological control approaches to reduce pest and disease populations	Sustainable control with reduced requirement for pesticides, reducing challenges of resistance evolution	Bale et al. (2008); Burra et al. (2021)
Rangeland productivity and feed security	Biological control of insect pests and weeds that reduce perennial grasses and soil fertility in rangelands	Restoration of rangeland productivity and forage quality, with benefits for livestock and wildlife	Bangsund et al. (1999); Goldson et al. (2020)
Invasive crop pests and diseases	Integration of biological control approaches within pest management	Sustainable crop production, reduced societal exposure to toxins, reduced risks of land degradation	Walker et al. (2017); Wyckhuys et al. (2019b)
Animal Health			
Livestock disease	Deployment of biological control measures against livestock pests, parasites and pathogens	Improved livestock health with reduced reliance upon agrochemical inputs	Weeks et al. (2018); Waller (2006)
Feed hazards and safety	Biological control in pasture and forage production systems	Reduced exposure of livestock to pesticide-tainted feed and forage	Radcliffe and Flanders (1998)
Water quality/pollution	Biological control of aquatic weeds	Restoration of aquatic ecosystems and recovery of fish populations, reduced environmental pollution with benefits for humans	Menzler-Hokkanen (2006); Motitsoe et al. (2020)
Antimicrobial resistance in livestock	Biological control tools to reduce bacterial diseases in animal production systems	Reduction in the use of antibiotics in food production systems, no contamination of water	Nakai and Park (2002)
Human Health			
Vector-borne diseases	Biological pesticides for use in aquatic environments as part of larval source management	Reduction of vector populations with fewer non-target effects and allowing treatment of potable water	Lacey (2007)
Lack of effective chemistry-based strategies against some disease vectors	Biological control tools such as *Wolbachia* to reduce vector competence	Reduced transmission risk and attenuation of insecticide resistance	Dos Santos et al. (2022)
Human malnutrition and diet-related morbidity or mortality	Biological control can protect wild and domesticated pollinators	Mitigated pollination deficit, improving healthy diets and reducing burden of disease	Smith et al. (2022a, 2022b)
Antimicrobial resistance	Biological control solutions such as bacteriophages	Lowered human mortality and morbidity associated with drug-resistant pathogens	Parfitt (2005); Petrovic Fabijan et al. (2023)
Foodborne hazards and food safety	Antagonists to inhibit the growth of toxic fungi such as aflatoxins and spoilage microorganisms	Increased food safety, reduced human and animal intoxication	Konlambigue et al. (2020); Cock et al. (2016a)
Air pollution	Biological control approaches to reduce weeds producing allergenic pollen and pollution due to pesticide drift	Reduced allergies (rhinitis, asthma) and lowered inhalation exposure to pesticides, with cascading health impacts	Kawahara et al. (2005); Schaffner et al. (2020); Tang et al. (2021)

One Health issues that indirectly emanate from pest, weed, or disease control (Fig. 3). In agricultural landscapes, biological control can reduce pollinator exposure to pesticides and thereby enhance pollinator health, with cascading benefits for plant health, human nutrition, and household incomes (Smith et al., 2022b, Garibaldi et al., 2022; Wangithi et al., 2022). Moreover, biological control of invasive alien plant species may halt land degradation and decrease habitat suitability for disease-transmitting vectors such as mosquitoes or tsetse flies, e.g., by removal of sources of nectar (Muller et al., 2017).

Below we review the contributions of biological control to all of the four dimensions of One Health. Our goal is not to provide an in-depth analysis of the details of the complexities of the species interactions or the multitude of individual case studies that underpin biological control, but to focus on the breadth, transdisciplinarity, and global scope of biological control to reveal the underappreciated opportunities and benefits that stem from a One Health perspective. In the sections on human and animal health, we focus on the contribution of biological control towards reducing diseases, disease-transmitting organisms, or other organisms affecting human or animal health. The implications of biological control supporting plant-based nutrition for the physical and mental well-being of humans and animals are explored in the section on plant health.

3.1. *Environmental health*

As a nature-based solution, biological control can improve environmental health by conserving native biodiversity both above and below ground, thereby stabilizing ecosystem functioning. Aboveground this can be achieved by the importation biological control of invasive non-native species that directly threaten native biodiversity. Belowground, environmental health can be bolstered by conservation or augmentation biological control to promote soil microbiome biodiversity. We briefly review these mechanisms here.

Importation biological control has been increasingly used to target invasive alien insect and weed species that have established in natural areas (Van Driesche et al., 2010). At least 15 weed and 12 insect pest species have been controlled in natural habitats through natural enemy introductions with more such species currently targeted. Examples include control of the invasive melaleuca tree (*Melaleuca quinquenervia*) in Florida, which allows restoration of natural vegetation and hydrology in the highly sensitive Everglades wetland ecosystem (Rayamajhi et al., 2019), and control of the cottony cushion scale (*Icerya purchasi*) in the Galapagos Islands, which has saved some species of endemic plants from likely extinction (Hoddle et al., 2013).

As noted above, biological control can be very effective at reducing the need for pesticide use. For example, there is evidence that synthetic pesticide applications do not significantly contribute to a reduction in pest densities when effective natural enemies are present, but by killing the latter they routinely trigger pest resurgence (Janssen and van Rijn, 2021). Given the ubiquitous nature of environmental pesticide contamination (Tang et al., 2021) and the negative effects of this contamination on biodiversity (Geiger et al., 2010; Beketov et al., 2013), the reduction in pesticide use facilitated by biological control can provide protection to native species in both aquatic and terrestrial settings (Heimpel and Wyckhuys, 2021; Pelosi et al., 2021). Curtailing pesticide inputs can also help to reduce greenhouse gas emissions by up to 136 Mt CO_2 equivalents per year (Wyckhuys et al., 2022), and the use (or recognition) of biological control to reduce greenhouse gas-emissions is an aspect of 'climate-smart pest management' (Heeb et al., 2019). This principle was illustrated for insecticide use against the invasive soybean aphid, *Aphis glycines*, in North America, where the actions of naturally occurring biological control agents such as lady beetles resulted in a 5-fold reduction in insecticide usage (Landis et al., 2008). Calculations on the greenhouse gas emissions associated with the manufacture, transport and application of the insecticides used against soybean aphids revealed a reduction of over 200 million kg of CO_2 equivalents per year in the central United States (Heimpel et al., 2013). Similar or greater savings presumably occur in the soybean aphid's native range (China), where natural enemies routinely keep populations under control (Wu et al., 2004; Miao et al., 2007). Given the negative effect of global climate change on biodiversity (Bellard et al., 2012), such savings indirectly protect native species as well.

Biological control can also protect natural habitats from being converted to agricultural habitats, leading to the protection of native biodiversity. This can be achieved by safeguarding crop yields in the face of invasive non-native or native pests, including ones that are favored by climatic upheaval such as spider mites that are triggered by drought stress or elevated temperatures (English-Loeb, 1990; Barnes et al., 2024). Pest-induced yield loss can drive farmers to convert native forests or other habitats to farmland to compensate for those losses, whereas by stabilizing crop yields biological control can prevent the need to do this (Wyckhuys et al., 2019b).

Microbiomes play a pivotal role in promoting soil health in both natural and managed ecosystems with associated benefits that include enhancement of water quality and improvement of plant and animal productivity (van Bruggen et al., 2019). Soil microbiomes can support plant health by facilitating nutrient uptake, promoting plant growth, inducing resistance to pests and diseases, and supporting antagonistic interactions (competition, antibiosis and parasitism) with plant pathogens (Collinge et al., 2022). Historically, biological control of plant diseases has been most effective against soilborne pathogens, as exemplified by the contribution of beneficial microorganisms to disease-suppressive soils in wheat systems (Kwak and Weller, 2013). Although initial attempts to manipulate soil microbiomes using inoculations of single-microbe products have provided inconsistent results in terms of biological control, recent research suggests an alternative that is likely to provide greater potential. For example, precision microbiome management integrates the use of multiple-microbe inoculations with supportive soil management and improved crop varieties to take optimum advantage of beneficial microbe-plant interactions (French et al., 2021). As an important indirect benefit, healthy soils with more diverse microbial communities also suppress soil-borne human pathogens and thus uphold human health (Samaddar et al., 2021).

Considering the benefits of biological control within a One Health framework can significantly affect the economic assessment of pest management options. This can be illustrated with the example of the fungal pathogen *Metarhizium acridum*, a biological control agent against locusts and grasshoppers. The direct costs of locust control tend to be lower for chemical pesticides than for biopesticides. However, biopesticides are highly specific to locusts and grasshoppers, whereas commonly used insecticides have a range of non-target environmental impacts. Economic analysis of a locust control program in Senegal between 2003 and 2005indicated that accounting for these 'externalities' can radically change the benefit-cost ratio of biological control relative to chemicals; adding the indirect environmental and human health costs to the direct costs effectively increased the total cost of chemicals by a factor of 3.8, whereas the indirect costs of biological control, although not evaluated, are likely to be minimal (Leach et al., 2008).

3.2. *Plant health*

Despite increasing pesticide usage, pests, weeds and pathogens inflict crop losses that amount to 40–50 % in developing countries (Oerke, 2006; Bernhardt et al., 2017) and these impacts are likely to worsen due to climate change and pesticide resistance (Deutsch et al., 2018). The global pace of new invasive pest arrivals shows no signs of deceleration (Seebens et al., 2017), and fungal plant diseases are becoming ever harder to control using conventional fungicides, in particular due to increasing resistance to azoles (Stukenbrock and Gurr, 2023). Biological control can substantially and sustainably reduce pest-induced food losses in a cost-effective way, thus meeting the food and nutritional requirements of a surging human population while achieving

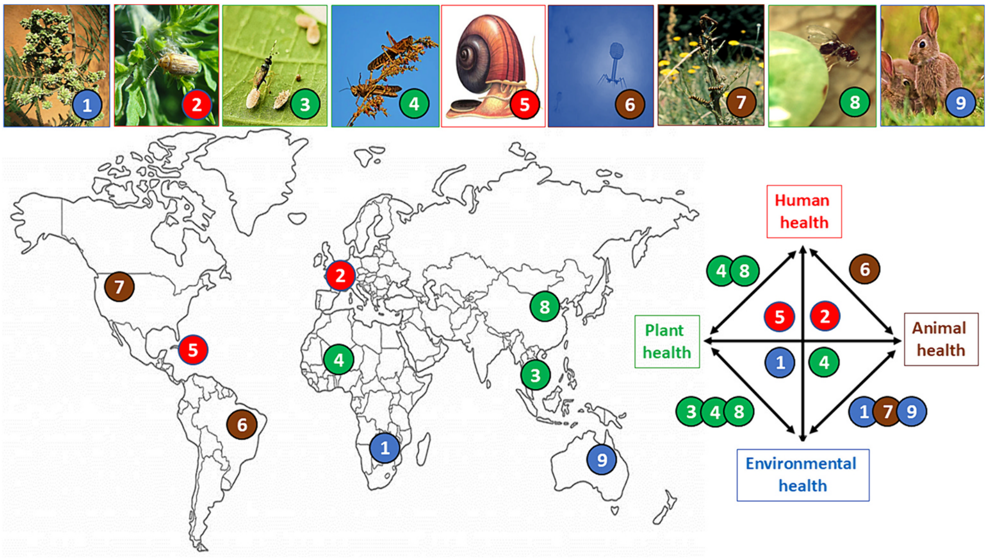

Fig. 3. Compilation of case studies in which biological control (BC) delivers multiple One Health benefits. The color of each dot (i.e., single case study) reflects direct benefits of BC to the correspondingly colored dimension of One Health, while the indirect benefits are shown in the diamond diagram on the right. The dots are positioned next to the lines indicating which dimension of One Health is positively affected by the indirect effects of a particular BC case study. 1. BC of the invasive tree *Acacia mearnsii* was initially implemented to benefit environmental health by restoration of biodiversity hotspots, but it also benefits human health by conserving groundwater and livestock health by protecting grazing habitats (Impson et al., 2021). 2. BC of invasive ragweed directly benefits human health by reducing allergenic pollen by >80 % while indirectly benefiting environmental health by restoring native habitats (Schaffner et al., 2020). 3. BC of the invasive mealybug *P. manihoti* directly benefits plant health through increased cassava production and indirectly benefits environmental health by slowing commodity-driven tropical deforestation by up to 95 % (Wyckhuys et al., 2019b). 4. BC of locusts using the highly specific fungus *Metarhizium acridum* directly benefits plant health but also indirectly benefits human, animal and environmental health by avoiding broad-scale (aerial) insecticide spray applications (Leach et al., 2008). 5. BC of invasive snail vectors directly benefits human health by providing long-lasting control of schistosomiasis, and indirectly benefits environmental health through restored biodiversity of native aquatic habitats (Sokolow et al., 2018). 6. BC of gastrointestinal parasites and diseases directly benefits livestock health and indirectly benefits human health by slowing biocide resistance development (Schmoeller et al., 2021). 7. BC of the toxic weed *Jacobaea vulgaris* directly benefits livestock health by increasing fodder availability and reducing cases of intoxication, and indirectly benefit environmental health by restoring biodiversity and reducing herbicide use (Coombs et al., 1996). 8. Augmentation BC of the Asian corn borer, *Ostrinia furnacalis*, directly benefits plant health through increased crop yield and indirectly benefits human and environmental health by reducing pesticide use regionally (Huang et al., 2020; Zang et al., 2021). 9. BC of invasive rabbits directly benefits environmental health by enabling the recovery of indigenous biodiversity and indirectly benefited animal health, increasing Australia's livestock revenues by more than A$1 billion/year (Kerr et al., 2021).

(Image credits: 1. Brian van Wilgen; 2,7. Urs Schaffner; 3. Charuwat Taekul; 4, 5, 6 and 9. Shutterstock; 8. Dirk Babendreier.)

beneficial human and social livelihood outcomes. For instance, biological control of cereal pests raised aggregate monetary surplus, increased food availability, and lifted over 130,000 people out of poverty in Kenya, Mozambique, and Zambia (Soul-kifouly et al., 2016). Similarly, biological control of the cassava mealybug (*Phenacoccus manihoti*) in Sub-Saharan Africa reconstituted yields of a key staple crop at an estimated benefit-cost ratio of between 200 and 740:1 (Zeddies et al., 2001). Projections reveal how the cassava mealybug campaign generated benefits of up to US$ 123 billion over a 40-year time frame (Raitzer and Kelley, 2008), with a further US$ 3.1–5.6 billion/year generated from a similar campaign in Southeast Asia (Wyckhuys et al., 2020b). Furthermore, biological control of the mango mealybug (*Rastrococcus invadens*) in Benin yielded a benefit-cost ratio of 145:1, with each mango farmer gaining US$328/year for over 20 years (Bokonon-Ganta et al., 2002). In Papua New Guinea, biological control of the invasive banana skipper (*Erionota thrax*) reduced loss of banana yields by 95 % and increased household-level annual food consumption by up to 2.2 % (Bauer et al., 2003). Finally, biological control of the diamondback moth (*Plutella xylostella*) in Kenya's cabbage crop attained a benefit-cost ratio of 24:1, with consumers reaping 58 % of the benefits (Macharia et al., 2005). The food security and nutrition benefits generated from biological control programs regularly deliver societal welfare spill-over gains including improved human health (Burra et al., 2021). Biological control benefits however are not confined to the on-farm stage. While synthetic fungicides are widely used to mitigate postharvest decay, microbial biological control agents – applied at pre- or post-harvest – can extend the shelf-life of food and reduce post-harvest losses (Peles et al., 2021), which are currently estimated to amount to 30–40 % of harvested farm produce (Gustavsson et al., 2011). At the post-harvest stage, popular biological control agents such as *Cryptococcus laurentii*, *Bacillus subtilis* or *Trichoderma harzianum* act through various mechanisms, including competition for nutrients and space, production of antibiotics and direct parasitism (Sharma et al., 2009). For example, when applied on dried red chili at the post-harvest stage, *B. subtilis* inhibits the growth of *Aspergillus flavus* and detoxifies its aflatoxins (Yuan et al., 2023). By immersing harvested lemons in microbial cultures (instead of pesticide baths), bacterial and yeast antagonists form a biofilm that inhibits fungal growth (Wang et al., 2022).

Insect pollinators sustain >85 % of the world's major food crops and 80 % of flowering plants in natural ecosystems (Klein et al., 2007). Recent reports of global declines of insect pollinators, however, have raised concern over the sustainability of pollination services and associated contributions to animal and human health. As pesticide use contributes to the global decline in insect pollinator communities, integrated pest and pollinator management (IPPM) has emerged as a concept to better integrate the management needs of pests, natural enemies, and pollinators in agroecosystems (Lundin et al., 2021). For example, the adoption of IPPM in watermelon crops in the USA lowers insecticide applications by 77 %, enhances pollinator foraging by 62 %, and boosts yields by 49 % (Leach et al., 2022). By safeguarding insect pollination services, one can avert significant economic losses (Lippert et al., 2021) and uphold human health through sustained production of health-giving foods, i.e., fruits, vegetables, nuts or legumes. Poor nutrition is estimated to lead to 500,000 deaths annually worldwide

(Smith et al., 2022a), and the sustainable protection of healthy foods can help to alleviate this problem. More extensive use of biological control could thus boost food security, reduce poverty, and improve human health.

Biological control can also safeguard animal feed security. A multitude of herbivore, pathogen and weed species impact the yield and quality of forage crops; as a consequence, pesticides are now extensively used in the production, storage and transport of animal feed. On Dutch dairy farms for example, animal feed and fodder contain residues of 7–19, 7–14 and 13–17 fungicide, herbicide and insecticide compounds, respectively (Buijs et al., 2022). Pesticide-tainted feed and forage eventually result in an accumulation of chemicals in edible animal tissue, often attaining high levels in selected organs, particularly in developing countries (Tongo and Ezemonye, 2015). To reduce pesticide usage in forage production, augmentation biological control has proven particularly effective. At present, multiple entomopathogenic fungi, bacteria or nematodes (e.g., *Metarhizium anisopliae* and *Serratia entomophila*) are registered for use against prime pasture pests such as whitegrubs (van Lenteren et al., 2018) and spittlebugs (Batista and Auad, 2010). Biological control can also enhance feed and forage quality, e.g., in rangelands that are invaded by noxious weeds or shrubs. For example, in the US Northern Great Plains, importation biological control of the weed leafy spurge (*Euphorbia esula*) yielded total direct economic benefits of US$ 19.1 million/year, which accrued from recovered grazing capacity on rangelands, and from increases in wildlife habitat productivity and soil and water conservation in natural areas (Hinz and Williams, 2016). Equally, intentional and/or accidental introduction of a rust fungus (*Phragmidium violaceum*) partially cleared millions of hectares of Chilean and Australian grasslands from invasive blackberries *Rubus* spp. (Oehrens and Gonzalez, 1977; Gomez et al., 2008).

3.3. Animal health

In addition to a reduction in feed contamination or improvement of forage quality, the potential for biological control of pests and parasites that directly impact animal health is increasingly documented, including research on biting midges, filth flies, ticks, endoparasites and pathogens (Thamsborg et al., 1999; Knipling and Steelman, 2000; Dantas-Torres et al., 2012; Weeks et al., 2018; Alonso-Díaz and Fernández-Salas, 2021). However, on the whole there are few clear examples of highly effective biological control approaches against livestock pests that have attained wide-scale adoption. Given that the pests affecting livestock are taxonomically similar to those in plant-based systems (i.e. insects, parasites, bacteria, etc.), this limitation could be seen as surprising. The nature of certain livestock operations may result in lower economic thresholds or lower profit margins that make biological control agents less cost-effective than chemical or pharmaceutical interventions. Implementation barriers also hamper uptake and diffusion, especially for microbial control agents and biopesticides, where research rarely extends to the product development stage (Thomas, 2018). Nonetheless, given the growing problem of resistance to conventional insecticides and drugs (Kuek et al., 2022) we argue that there ought to be increasing opportunity for biological control in animal health, as indicated by the examples provided below.

Globally, livestock production is impacted by several species of gastrointestinal parasitic helminths, tape- or roundworms, and protozoans. Broad-spectrum veterinary drugs such as avermectins are widely and oftentimes prophylactically used to manage these parasites. Biological control constitutes a prime alternative to resolve the fast-increasing resistance to all three classes of antihelminthic drugs (Waller, 2006). Oral administration of feed pellets inoculated with the nematophagous fungi *Monacrosporium sinense* and *Pochonia chlamydosporia* can lower the load of gastrointestinal nematodes by 86–91 % (de Castro Oliveira et al., 2022) in Brazil. Similar results were obtained in China, after feeding infected sheep with pellets containing the fungus *Duddingtonia flagrans* (Liu et al., 2020). These examples provide clear benefits for animal health, and represent a promising biological control tactic that could circumvent resistance development and pose lower ecotoxicity risks.

The liver fluke (*Fasciola* spp.) is a snail-transmitted trematode that causes fascioliasis in both livestock and humans (Sabourin et al., 2018). Innovative ecological research in Cuba revealed that biological control using competitor snails can markedly reduce population densities of the main intermediate host of the liver fluke, *Galba cubensis,* and thus could potentially become a cornerstone of the country's program to roll back this disease (Rojas et al., 2010). Ascarids or roundworms, including species that infect dogs, cats and pigs are other parasites that can be effectively mitigated through biological control, either through oral administration or environmental application of beneficial fungi or other microbes (Braga and de Araújo, 2014). For example, the oomycete *Pythium oligandrum* exerts ovicidal action against *Toxocara canis* and *T. cati*, and can thus be used for substrate disinfection in sites such as dog pens (Luca et al., 2022). Antagonistic fungi may also regulate gut microbiota or exert direct biological control of protozoan parasites in poultry or pigs. They could become part of an integrated solutions package for avian coccidiosis, a disease that causes US$ 3 billion/year worth in economic losses to global aviculture (Lozano et al., 2022).

The first successes with using bacteriophages to reduce pathogenic infection in fish farming in the 1990s sparked great interest in replacing the use of antibiotics with biological control solutions (Nakai and Park, 2002). Recent evidence suggests that phage therapy has tremendous potential and advantages (Yang et al., 2024) and several companies have now commercialized phage-based products for aquaculture, arguably the fastest-growing sector in the global food industry. While several technical hurdles still bar the way to the global use of phage therapy in aquaculture, Culot et al. (2019) argued that the major obstacles lie in regulations.

3.4. Human health

As compared to the agrifood sector, the use of biological control in the human health domain is far more limited. Nonetheless, the practice currently yields effective control of various human health threats, including vector-borne diseases, pollen-induced allergies, and food safety hazards related to pesticide residues and pathogen contaminants. Biopesticides based on the bacteria *Bacillus thuringiensis* or *B. sphaericus* have been used extensively for treating aquatic breeding habitats of mosquitoes and blackflies (Lacey, 2007). Biological control of adult vectors of human diseases is less well developed, with numerous prospective approaches yet to translate into operational use. As noted above, one promising example is the use of *Aedes aegypti* mosquitoes trans-infected with the endosymbiotic bacteria *Wolbachia*, which blocks development of viruses such as dengue, zika and chikungunya within the mosquito body itself (Dos Santos et al., 2022). Mass-releases of trans-infected mosquitoes can result in the replacement of wild-type populations with transinfected populations and can dramatically reduce transmission rates (Utarini et al., 2021).

Less appreciated is the potential for indirect benefits of biological control on disease transmission. In Africa, invasive trees in the genus *Prosopis* reduce water availability and grazing in both natural and human-altered settings (Shiferaw et al., 2021; Kleinjan et al., 2021) and provide nectar for malaria mosquitoes. Removal of *Prosopis* flowers in rural Mali greatly reduced the abundance of male and female malaria mosquitoes (Muller et al., 2017). Hence, biological control of *Prosopis* spp. or other invasive weeds that provide floral nectar or breeding habitats may yield similar results as pesticide-centred control efforts targeting the mosquito adults or larvae (Stone et al., 2018).

Malarial mosquito control largely relies on the use of chemical insecticides, either via indoor sprays or insecticide treated bed nets (Bhatt et al., 2015). Effectiveness of these tools is now being severely compromised by the development of insecticide resistance (Strode et al., 2014), and the selection for resistance is driven by exposure of the targeted adult mosquitoes. In addition, as the majority of these insecticides are repurposed from agricultural pest control, spill-over of insecticides from agricultural applications into mosquito larval habitats contributes to resistance development (Reid and McKenzie, 2016). By circumventing these issues, biological control can slow down the evolution of resistance in disease vectors and thereby sustain the effectiveness of core public health tools.

Allergies such as allergic rhinitis and allergic asthma are among the most underappreciated societal health problems (Linneberg et al., 2016). In Europe, allergy-related costs are estimated to be € 100 billion (Zuberbier et al., 2014), with those associated with the invasive common ragweed (*Ambrosia artemisiifolia*) amounting to € 7.4 billion (Schaffner et al., 2020). The leaf beetle *Ophraella communa*, an adventive species from North America that was first detected in Europe in 2013, can reduce airborne common ragweed pollen concentrations by >80 %. Based on prospective modelling, *O. communa* is expected to annually reduce Europe-wide health costs by € 1.1 billion once it has colonised its environmental niche (Schaffner et al., 2020). Given that several non-native invasive plant species, such as other *Ambrosia* spp., *Parthenium hysterophorus* and *Broussonetia papyrifera*, are also known to produce highly allergenic pollen, targeted importation biological control can be a tailor-made solution (Winston et al., 2014).

Biological control of (fungal) plant diseases hazardous to human health (Fisher and Denning, 2023) constitutes another example highlighting how a One Health perspective could increase the scope of biological control. Aflatoxins and other *Aspergillus*-derived mycotoxins cause deleterious physiological effects on humans and animals, particularly in tropical and Mediterranean regions (Yu et al., 2007). Biological control methods can give rise to the most effective prevention techniques; for example, treatment of maize and groundnut (peanut) with a biological control product containing atoxigenic *Aspergillus* isolates can lower aflatoxin contamination by 99 % (Agbetiameh et al., 2020). The aflatoxin biological control technology has been adapted and improved for use in Sub-Saharan Africa by the International Institute of Tropical Agriculture (IITA) and the United States Department of Agriculture (USDA) in collaboration with several national and international partners. Several atoxigenic biological control products under the trade name Aflasafe have been developed and are now available for commercial use in Nigeria, Kenya, Senegal, (Konlambigue et al., 2020).

Importantly, biological control can also reduce the human health hazards that result from chemical crop protection. Dietary intake constitutes the most common human exposure pathway to pesticides, especially when consuming food that originates from conventional agriculture (Fantke and Jolliet, 2016). Dietary exposure to pesticides is especially pronounced in some low- and middle-income countries, with up to 97 % of marketed fruits, vegetables, and pulses tainted with pesticides and up to 42 % of produce presenting immediate hazards to human health (Wyckhuys et al., 2020a). A more extensive usage of microbial and invertebrate biological control could mitigate pesticide-related risks and potential harm for consumers (Czaja et al., 2015). In fruit cropping systems, biological control solutions have been validated (Jacas and Urbaneja, 2010; Walker et al., 2017) and can help to phase down pesticide usage in the production of these 'health-giving' foods. Further, the global extent of occupational and non-occupational exposure to synthetic pesticides cannot be disregarded. Recent estimates indicate that 44 % of the world's farmers (or 385 million individuals) annually experience unintentional, acute pesticide poisoning, including 11,000 fatalities (Boedeker et al., 2020). Yet, pesticide mitigation campaigns routinely overlook the true extent of occupational exposure. Non-farming households in rural settings are equally exposed to spray drift and volatilization of pesticides, often far beyond the treated farm area, especially for airplane or drone applications (Dereumeaux et al., 2020). Biological control helps to circumvent these and other adverse health impacts and contributes to delivering safe and nutritious food for producers and consumers alike.

4. Delivering on the promise of biological control

Managing agroecosystems and connected natural habitats while upholding One Health in the face of intertwined and continually deepening stressors, such as climate change, chemical pollution and biodiversity loss, can be seen as a "wicked problem", since the complexity of ecosystems and the inability to foresee all consequences of interventions across spatial and temporal scales do not allow clear-cut solutions (DeFries and Nagendra, 2017) By harnessing nature-based solutions, biological control can help to tackle such wicked problems and bolster the social-ecological resilience of global food and health systems, yet its potential remains unfulfilled.

We propose several avenues for enhancing the understanding and appreciation of biological control, and for promoting its application to all One Health dimensions (Box 1). There is a need for more research to evaluate and document the direct and indirect benefits of biological control of pests, diseases and weeds using multidimensional One Health metrics, and to address and resolve challenges that slow down broad-scale adoption of highly promising approaches. This not only includes technical research and development challenges to optimize biological control tools, but also the development of appropriate research capacity. For example, importation biological control is a key approach in the sustainable management of invasive non-native plant species (Shackleton et al., 2020; Sun et al., 2022). Yet, only a few countries have conducted weed biological control research; most other countries that have intentionally released weed biological control agents have usually done so through collaboration with Australia, New Zealand, South Africa, Canada or USA (Day et al., 2020). Thus, scaling up biological control solutions against invasive non-native plants requires significant capacity building, as well as implementation of regulatory processes that consider potential risks and benefits of importation biological control, in many countries around the globe. Biological control releases against invasive plants or pests cannot go forward without stringent risk assessment (Meurisse et al., 2022). However, improvements are needed in responsibly balancing the potential environmental risks with the expected benefits to be gained through biological control releases across the One Health spectrum (Abram et al., 2024; Heimpel et al., in press).

Science alone, however, is likely to be insufficient to bring about lasting 'real-world' outcomes since end-users such as farmers, livestock producers or environmentalists may be hesitant to adopt certain biological control measures (González-Chang et al., 2020). This may relate to stakeholders' incomplete knowledge of ecological processes and phenomena (Wyckhuys et al., 2019a), an inability to define and assess endpoints relevant to people's primary concerns (Naranjo et al., 2015), and insufficient communication and cooperation between researchers and end-users/beneficiaries. These problems can be addressed using participatory methods that increase knowledge exchange and encourage co-development and co-ownership of solutions (Waddington et al., 2014; Zhang et al., 2016; Costa et al., 2020). These approaches can be further motivated by full-fledged One Health approaches that account for the contribution of biological control in, for example, alleviating food safety risks, lowering carbon emissions, restoring pollination and other ecosystem functions, and retaining antibiotic or pesticide susceptibility (Jørgensen et al., 2018; Wangithi et al., 2022).

Various economic and regulatory pathways could also help scale up biological control (Kleijn et al., 2019). First, while research and outreach efforts can 'push' certain technologies, transformative change across the four One Health dimensions will ultimately transpire through a dynamic interplay among end-users, the full suite of food system actors, scientific disciplines and policymakers (Destoumieux-Garzón et al., 2018; Bedford et al., 2019; Möhring et al., 2020; Rockström et al., 2020). Consumer choice and purchasing can exert considerable 'pull' for preventive, biodiversity-based interventions such as biological control, which can be enacted through traceability protocols. Second, governments and international agencies need to draw upon robust, diverse and effective policy toolkits to mitigate One Health challenges. Soft (e.g. behavioral

Box 1

Broad-scale recommendations to enhance the understanding and application of biological control in One Health.

- **Encourage more research on the diversity of natural enemy types and their diverse modes of action.** Traditional agriculture-based biological control has tended to focus on the direct lethal effects of a relatively limited subset of natural enemies, yet there is a myriad of prospective biological control agents with varied modes of action and potential use strategies.
- **Conduct more rigorous evaluation of the direct and indirect benefits of biological control.** Developing a robust evidence base for decision-making requires systematic outcome tracking using multidimensional One Health metrics across landscapes and sectoral boundaries.
- **Improve economic assessment to take into consideration the full costs and benefits of interventions so that diverse management options can be understood and compared.** All too often decisions are based on direct economic costs of an intervention without consideration of the indirect costs and benefits (the spillovers and externalities).
- **Increase awareness of the value of biodiversity and associated ecosystem services.** This in turn could provide a foundation for mobilizing funding and unlocking novel funding streams, such as re-routing some of the very substantial resources tied in with conventional agricultural subsidies.
- **Increase the use of robust benefit-risk analyses to guide decision-making for biological control importations.** Current practices are based primarily on the assessment of risks to native biodiversity with little regard to protection of biodiversity and ecosystem services that biological control can deliver.
- **Implement a diverse suite of hard and soft policy levers to support One Health goals.** These could include command-and-control regulation, taxation for practices that degrade environmental health, and incentive strategies for sustainable biological control approaches.
- **Streamline regulatory and approval mechanisms to facilitate adoption of biological control tools without compromising necessary data on safety and efficacy.** Current frameworks tend to be slow and overly burdensome, which disincentivizes innovation.
- **Promote transdisciplinary approaches involving multi-sector collaboration and engagement of stakeholders across the value chain.** The One Health paradigm follows an explicit system-level perspective, yet current research and policy tend to be discipline-based, siloed, and top-down.

nudges, certification schemes, food-safety labelling) and hard policy measures such as conditional financial assistance, (differential) taxes or regulatory caps could build critical momentum for biological control (FAO, 2023). For instance, redesigned taxes led to a 16 % reduction of pesticide load in Denmark (Nielsen et al., 2023), and the impacts of such modifications can be leveraged by rerouting tax revenues to multi-stakeholder awareness-raising and promotion of effective non-chemical alternatives. Subsidies and tax breaks for biological control manufacturers are also in order, especially when those are rolled out in parallel with dependable quality assurance systems and distribution networks. To enforce new policies, target subsidies or design insurance policies that encompass One Health risks, transparency and traceability are vital (Davis et al., 2021). This can be achieved with context-appropriate, results-based metrics for One Health that account for biodiversity conservation, soil health, or emerging disease threats (Elmiger et al., 2023). Third, to avoid that policy making falls prey to irrational fears and externally-induced processes of collective belief formation (i.e., so-called availability cascades; Kuran and Sunstein, 1998), decision-making should be guided by careful deliberation while civil servants are properly insulated from public pressure. In this process, scientific expertise serves as a “bulwark against populist excesses” (Kahneman, 2011). Lastly, while biological control constitutes an appealing investment proposition, few funding streams are specifically geared towards this practice. A repurposing of US$ 500 billion/year in farm subsidies that were identified as harmful to biodiversity at COP15 in Montreal, represents an unprecedented opportunity to support the world's farmers in their transition towards biodiversity-based production systems (Wanger et al., 2020; Wyckhuys et al., 2022).

Finally, strengthening the multidimensional scope of biological control and its contribution to One Health requires the inter- or transdisciplinary co-production of knowledge (Chambers et al., 2021). Inter- and transdisciplinary science would support a more effective, global promotion of biological control; a process in which ecologists, agronomists, social scientists, economists, food safety specialists, epidemiologists, medical personnel or veterinarians learn to think and act collectively (Barnett et al., 2020), ideally engaging end-users' perceptions and needs. These changes would be supported by shifts in disciplinary principles, institutional change, amended incentive schemes and long-term commitments.

5. Conclusions

In 1962, Rachel Carson dedicated her book ‘*Silent Spring*’ to the physician Albert Schweitzer, who emphasized humanity's need to foresee and forestall in order to preserve the Earth. Biodiversity-driven pest, weed or disease management, or biological control, can provide a real contribution to forestalling further ecological breakdown and defusing some of the world's most urgent human, animal and environmental threats. We hope that our review – although not exhaustive – provides compelling evidence for the breadth and transdisciplinarity of the biological control approach. We also submit that a One Health perspective reveals underappreciated opportunities for biological control that go beyond its well-known application in plant-based production systems. We advocate a systems-level, integrated approach to biological control research, policy, and practice that considers its direct and indirect benefits for the four dimensions of One Health. The full potential of the biological control approach to tackle some of the major global challenges, including biodiversity loss, environmental pollution or biocide resistance, still remains to be realized. We call upon scientists, practitioners and policy-makers to join hands, transcending disciplinary or sectoral boundaries and ideological differences, to deliver on its One Health promise. The time for action is now.

CRediT authorship contribution statement

Urs Schaffner: Writing – review & editing, Writing – original draft, Visualization, Conceptualization. **George E. Heimpel:** Writing – review & editing, Writing – original draft, Conceptualization. **Nicholas J. Mills:** Writing – review & editing, Writing – original draft, Visualization, Conceptualization. **Beatrice W. Muriithi:** Writing – review & editing, Writing – original draft, Conceptualization. **Matthew B. Thomas:** Writing – review & editing, Writing – original draft, Visualization, Conceptualization. **Yubak D. GC:** Writing – review & editing, Funding acquisition. **Kris A.G. Wyckhuys:** Writing – review & editing, Writing – original draft, Visualization, Conceptualization.

Declaration of competing interest

The authors declare no conflict of interest.

Data availability

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