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Ecology

A cocktail of pressures imperils bees

Adam J. Vanbergen

Pollinators are under threat. A meta-analysis reveals that the combination of agrochemicals, parasites and malnutrition has a cumulative negative effect on bees, and that pesticide–pesticide interactions increase bee mortality. **See p.389**

Worldwide, an estimated 20,000 species of wild and managed bees pollinate flowers, aiding plant reproduction[1]. In doing so, they form a key link in the tangled web of species interactions that support biodiverse and healthy ecosystems[1,2]. Moreover, humans enjoy a variety of sociocultural and economic benefits from pollinator biodiversity[2,3], and pollination secures crop yields that supply essential nutrients and healthy, diverse diets[1,4]. On page 389, Siviter *et al.*[5] report a pollinator threat that jeopardizes these benefits.

Pollinators and pollination are threatened by environmental pressures, including many that are a consequence of human activity (Fig. 1). These pressures include land-use and climate change[2,6], intensive agriculture[7], the spread of invasive alien species and problems with pests and disease-causing agents (pathogens)[2,8]. The individual effects of these pressures on pollinators are well established[1,2], raising the question of whether an interplay between these various pressures exacerbates the overall risk that they pose to pollinators and pollination[9–11]. This issue has been recognized by the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services, which stated[2] in 2016 that "many drivers that directly impact the health, diversity and abundance of pollinators … can combine in their effects and thereby increase the overall pressure on pollinators".

Intensive agriculture is a multifactorial source of stress on pollinator populations[1,7,10,11]. Pollinating insects, such as bees, face the physiological challenge of acute or chronic harm from exposure to various agrochemicals, including fungicides and pesticides, that are used to protect crop plants. They also face nutritional stress arising from the lack of pollen- and nectar-providing wild flowers in large-scale, intensive crop monocultures[1,2,7,12]. Moreover, the industrial transport and use of managed high-density colonies of honey bees (*Apis mellifera*) for crop pollination can increase pollinator exposure to parasites or pathogens[2], and might result in disease spillover to wild pollinators[13]. Over the past decade, the lethal or sublethal effect of combinations of agrochemical, pathogenic or nutritional stressors on bees has been tested in many individual experiments[2,9,10].

Siviter *et al.* advance this knowledge through a quantitative meta-analysis of the effect of interactions between agrochemical, pathogenic and nutritional stressors on multiple aspects of bee health and fitness. Their analysis is notable because of the breadth of bee responses considered (for example, foraging behaviour, memory, mortality and colony reproduction), and for comparisons of the interactions of multiple classes of stressor (for example, agrochemical–parasite, parasite–nutrition, agrochemical–agrochemical and parasite–parasite interactions).

The authors conducted a monumental literature search that yielded almost 15,000 relevant individual studies. Siviter and colleagues combed through these publications to focus on the experiments that investigated the combined effect of parasites (microorganisms and invertebrates), agrochemicals and nutritional stressors on bee health. The authors selected studies that used a balanced and replicated experimental design, and that provided accessible data (means, standard deviations and sample sizes) for each treatment. This rigorous focus and quality control resulted in a final set of 90 studies being selected for further analysis.

These studies provide a total of 356 effect sizes (measurements indicating the magnitude of a relationship between factors of interest and a particular outcome) for different stressor and bee-response combinations. The authors accounted for data issues that might have confounded their accurate detection of bee responses. Such challenges included those arising from statistical non-independence of multiple effects reported from a single study, publication biases (for example, the lack of negative results), species skews (honey bee data sets predominated), and how experimental treatments such as pesticide dose compare with what might be realistically encountered in the field (termed field realism).

Siviter and colleagues tested whether the stressor interactions were synergistic, meaning that their combined effect was greater than the sum of their individual effects, as would be the case if the effect of one stressor on a bee elevates the effect of another stressor. The authors also examined alternative scenarios in which the effects of multiple stressors were antagonistic (the effect of one stressor lessens the effect of another) or additive (the combined effect is equivalent to the sum of the individual effects).

A consistent message from their analysis is that bee mortality is increased by a synergistic interaction between multiple stressors — the worst-case scenario, indicating a disproportionate effect of multiple stressors on bee survival. Interactions between different agrochemicals, rather than other stressors, drove this overall effect, and this finding held true when accounting for the field realism of the agrochemical doses. This result confirms that the cocktail of agrochemicals that bees encounter in an intensively farmed environment can create a risk to bee populations[1,2,9,14]. Multi-stressor interactions involving parasites and nutritional stress (including in combination with agrochemicals) produced additive effects on bee mortality overall.

The authors' deeper analysis of the biological complexity, however, revealed large differences between particular parasite groups in terms of the full range of additive, antagonistic and synergistic effects on bee mortality, when considering interactions between different parasites or between different parasites and nutritional stress. This variability in response, together with the lower sample sizes for the interactions involving stressors other than agrochemicals, indicate a caveat to consider and also suggest a need for more research on the combined effects of biological sources of stress.

It is intriguing that Siviter and colleagues found that additive, not synergistic, effects predominated for the non-lethal effects of stressors on fitness proxies (such as

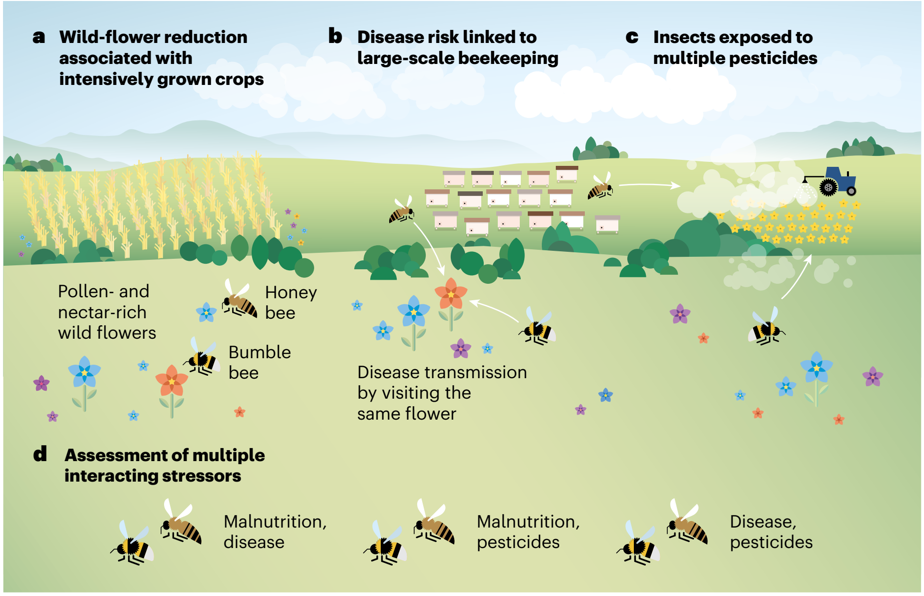

Figure 1 | The effect of multiple stressors on bees. Agricultural intensification has put pollinators under pressure. **a**, Practices associated with intensive farming reduce food availability for pollinators[1,2,7,12]. **b**, Managed high-density bee colonies for crop pollination are associated with these pollinators being at risk of disease and parasite infection[2]. This poses a risk of illness spreading to wild bees. **c**, Exposure to a variety of pesticides poses another risk to pollinators. **d**, Siviter *et al.*[5] present a meta-analysis that indicates the consequences for bees of combinations (some examples shown) of these challenges.

modifications of bee behaviour or reproduction, changes in parasite load or immune function). Such non-lethal changes could ultimately affect bee mortality rates. Consequently, how the observed synergistic effects of agrochemicals on bee mortality arise remains to be established. More work is therefore needed to identify the mechanism that links exposure to behavioural or physiological changes and mortality.

The majority of the studies in the data set were of managed populations of *A. mellifera*, so the authors also separately analysed responses at the level of bee genus (*Apis*, *Bombus*, *Megachile* and *Osmia*). *Apis* mortality was affected by a synergistic multi-stressor interaction qualitatively similar to the full analysis of all bee genera. Other bee genera exhibited additive or antagonistic mortality responses from many fewer studies. This raises an important point. There is a need for research efforts and regulators to widen their focus from *A. mellifera* – a single, mostly managed bee species – to other pollinator model organisms, whose different ecology and evolutionary history might result in different responses to stressors[10].

Siviter and colleagues' findings of the cumulative negative effect of multi-stressor interactions on bees reinforces the call to evaluate such interactions to avoid unforeseen risks to biodiversity and healthy ecosystems[1,9,10]. In some regions of the world, regulatory risk-assessment frameworks for plant-protection products are being developed to deal with sublethal, long-term and potentially synergistic effects among stressors[15] (see go.nature.com/3f4ax5r), but their biological and geographical scope must be extended. The authors acknowledge that the high levels of variability between the studies and parameters investigated demand an appropriately cautious interpretation. However, this highlights the need for worldwide reconsideration of risk-assessment approaches for pesticide regulation.

Given the widespread loss of habitat resources – such as pollen and nectar sources – from intensively managed agricultural landscapes[7,12], nutritional deficits occurred surprisingly infrequently as a mechanism underlying bees' physiological stress (they accounted for only 58 out of the 365 measurements of effect sizes). A greater consideration of how nutritional stress interacts with exposure to pathogens and agrochemicals is therefore an obvious research gap to fill. Moreover, ensuring that experimental treatments are calibrated to simulate realistic environmental conditions would greatly aid risk assessments. This might include three-way combinations of field-realistic chemical doses and parasite levels, and a spatio-temporal dietary diversity similar to that found in semi-natural or highly human-modified landscapes.

"The authors' findings highlight the need for worldwide reconsideration of risk-assessment approaches for pesticide regulation."

The next challenge is to look beyond these parasite–nutrition–agrochemical interactions to consider other risks to pollination. Future studies must ultimately consider, through a combination of correlative and experimental approaches, the interplay of nutrition–pathogen–agrochemical interactions alongside the effects of other human-driven changes (such as climate change, pollution, land-use changes and the spread of invasive species)[1,2,11]. Although such assessments would be non-trivial to carry out, they will be vital for understanding and ranking the relative risks to pollinators and pollination that are coming from multiple combinations of pressures resulting from global changes.

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Correction

This article incorrectly stated that an estimated 20,000 species of wild and managed insects pollinate flowers. It should have said that an estimated 20,000 species of wild and managed bees pollinate flowers.