Mancini, Francesca; Woodcock, Ben A.; Isaac, Nick J.B. 2019.
Agrochemicals in the wild: identifying links between pesticide use and declines of nontarget organisms.

Agrochemicals in the wild: identifying links between pesticide use and declines of non-target organisms

Francesca Mancini*[a], Ben A. Woodcock[a], Nick J. B. Isaac[a]

[a]Centre for Ecology & Hydrology, Maclean Building, Benson Lane, Crowmarsh Gifford, Wallingford, OX10 8BB UK

*Corresponding author: Centre for Ecology & Hydrology, Maclean Building, Benson Lane, Crowmarsh Gifford, Wallingford, OX10 8BB UK. Email: framan@ceh.ac.uk

Agricultural pesticides are a key component of the toolbox of most agricultural systems and are likely to continue to play a role in meeting the challenge of feeding a growing global population. However, pesticide use has well documented and often significant consequences for populations of native wildlife. Although rigorous, regulatory processes for the approval of new chemicals for agronomic use do have limitations which may fail to identify real world negative effects of products. Here, we describe a possible approach to complement the existing regulatory process, which is to combine long-term and national-scale data sets on native wildlife with pesticide use data to understand long-term and large-scale impacts of agrochemicals on wildlife populations.

Keywords: Occupancy-detection models; pollinators; sustainable agriculture; biological recording; pesticide surveillance

1 Introduction

Agricultural pesticides have an important role in feeding a rapidly growing human population [1], but their use has important consequences for the environment [2]. Pesticides can cause declines in populations of non-target organisms exposed to them [2–7], with potential knock-on consequences for the ecosystem services they provide, including pollination and natural pest control [8–10]. Internationally, there is enormous variation in the approach to pesticide regulation, in standards of implementation and extent of enforcement [11,12]. In most developed countries, laboratory and field tests are conducted to ensure acceptable thresholds of risk are met based on chemical toxicology, fate and behaviour in the environment [13] (Fig. 1). After approval from the regulatory authority, the chemical is licenced under specific limitations (e.g. approved concentrations) for the duration of the licence, typically 10-15 years in Europe and the United States [11,14]. Whilst rigorous, this process has limited potential to assess the impacts of large-scale use of chemicals on wildlife populations. The most significant limitations are: 1) a focus on time scales (days) much shorter than population level processes responding to environmental drivers (years) [15,16]; 2) failure to capture the fact that, as the pesticide becomes more common, its landscape-scale dose increases and so does wildlife exposure, despite the application per unit area remaining the same [14,17]; 3) assays are performed on a small number of model species [15]; and 4) an absence of post approval monitoring under real world conditions where species are exposed to a cocktail of agrochemicals that may interact in unexpected ways [8–10,14].

Here, we assess the practicalities, limitations and best practices for linking long term wildlife population changes to pesticide exposure risks at national scales. By making the most of available large-scale datasets and sophisticated statistical methods it is possible to gain new insights to augment the existing regulatory assessments in a manner not possible under current frameworks. Specifically, we argue for systematic post-approval monitoring of real-world impacts of pesticide use on wildlife populations (Fig. 1). We focus on terrestrial agroecosystems, which represent the direct interface between agriculture and wildlife populations. Our goal is to provide a framework that can be applied to link the use and regulation of agrochemicals to long term declines in populations of non-target organisms.

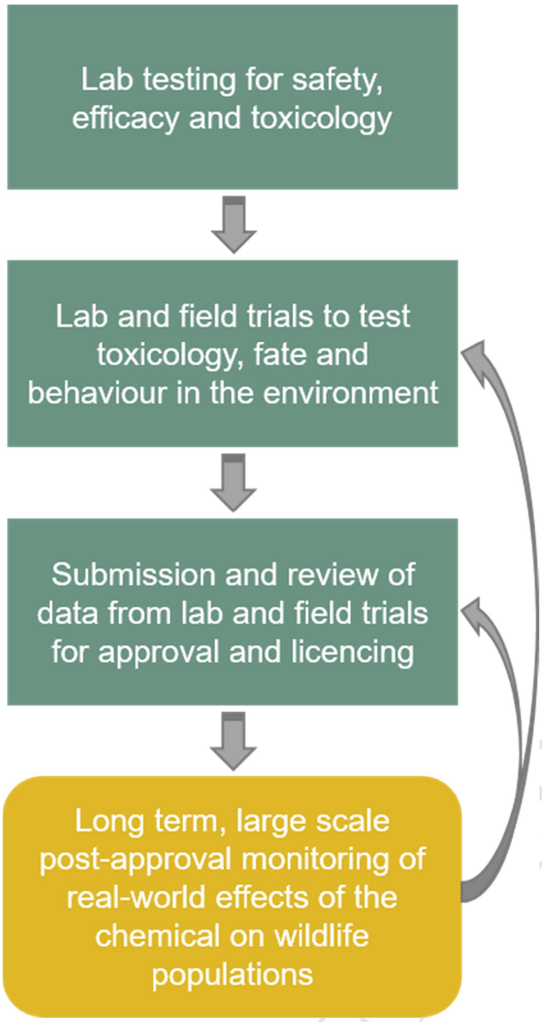

Figure 1. Proposed modification to the regulatory framework to evaluate large-scale and long-term impacts of pesticides on non-target organisms. The three green boxes represent the main steps of the approval procedure for a new pesticide [14]. First the substance is tested using both in vitro and in vivo trials in the lab to determine its efficacy, safety and toxicology. Then lab and field trials are conducted to determine the chemical's toxicology, fate and behaviour in the environment. The data from these tests is submitted to the regulatory body, where the information is reviewed, and the substance can be approved for use under licenced conditions. The last box in yellow represents the missing step in this regulatory framework, a post-approval surveillance system that monitors real-world effects of the chemical's use on a commercial scale on non-target wildlife populations. The results from this monitoring step can either provide reassurance that the chemical is safe to use or early warning signs of impacts on wildlife, therefore providing important feedback for a review of licencing conditions, which, as a result, could become more or less stringent.

Box 1. Neonicotinoid insecticides were approved and introduced in the 1990s after laboratory and field testing determined they were safe to non-target organisms. By 2013, there was substantial published research evidence linking the use of neonicotinoids to impacts on bees [18,19]. This evidence was deemed sufficiently compelling for the European Commission to issue a moratorium on their use in mass-flowering crops, but falling short of an outright ban [20]. Most of the evidence for the effect of neonicotinoids on pollinators was provided by small-scale and short-term laboratory or semi-field experiments on honey bees, bumble bees and some solitary bees [8,18,19]. The sole landscape-scale experiment showed reduced wild pollinator survival and reproduction following actual field exposure to a combined neonicotinoid and pyrethroid treatment [21]. Employing long-term, spatially explicit data collected by citizen scientists on the distribution of 62 wild bee species, allied with Bayesian multi-species statistical modelling techniques, Woodcock et al [15] tested whether the commercial use of these pesticides was linked to population loss through dietary exposure. They found evidence of increased wild bees' population extinction rates in response to neonicotinoid use (Figure 2a). The effect was three times stronger for species known to forage on treated crops (Figure 2a&b). This study provided the first evidence that sub-lethal effects of neonicotinoids may have contributed to the observed declines in wild bee populations [8].

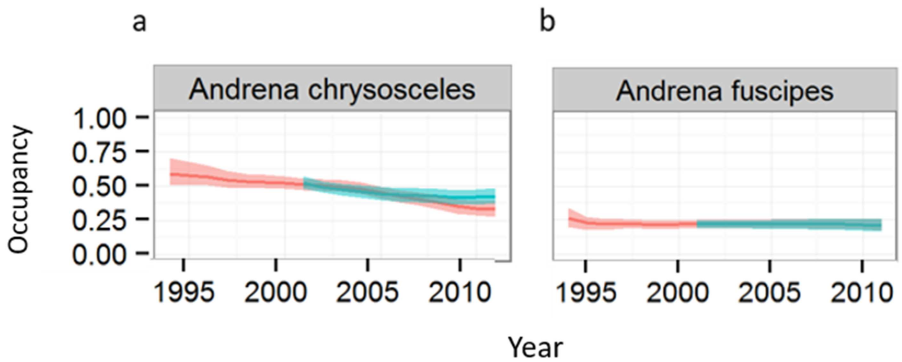

Figure 2. Modelled impact of neonicotinoid exposure to a) *Andrena chrysosceles* (species known to forage on treated crops) and b) Andrena fuscipes (species not known to forage on treated crop) population, two of 62 considered wild bee species. Red line shows actual populations at a national scale, the blue line shows the predicted trend if neonicotinoids were benign and/or had not been used. (from ref [15])

2 Limitations of the agricultural pesticide regulatory process

After a chemical has passed laboratory and field toxicity tests, it is certified to be safe for use given specific restrictions. There are, however, numerous cases where unexpected and significant environmental consequences have subsequently been identified, leading to the ban of that chemical, for example neonicotinoids ([15] Box 1) and DDT [22]. Unexpected consequences from commercial use of approved pesticides can occur for multiple reasons, including chronic/sub-lethal effects [23], unexpected synergistic interactions with existing chemicals [24] or species-specific toxicokinetic and toxicodynamic responses to chemical exposure [25]. As the majority of regulatory approaches, for practical reasons, focus on a small number of model organisms [26], the consequences of pesticide use on real world ecological communities are hard to predict. Behaviours rarely seen under laboratory conditions may also affect responses to chemicals when used in spatially complex agricultural systems. Importantly, as the landscape-scale dose of a pesticide increases with its use becoming more widespread [14], the exposure of organisms that are long-distance foragers (for example honeybees) also increases, despite the application rate per unit area remaining largely the same [17]. Even when chronic effects of pesticide exposure are assessed, the time scale of laboratory or semi-field experiments does not permit an assessment of the consequences of chemical exposure on long term population dynamics.

For all these reasons, there is a strong argument for ongoing monitoring of agrochemical impacts after approval to ensure any emerging risks are identified [14]. Such monitoring has potential benefits both for wildlife as well as the agricultural and agrochemical industries: early warning of adverse impacts could be mitigated through control measures, thus avoiding more restrictive legislation such as an outright ban. The gold standard approach for monitoring such impacts is a Before-After-Control-Impact (BACI) design [27]. However, this may not be possible, especially if the goal is to make such assessments at large scale, where the cost would likely be prohibitive and where replication would be challenging [16]. Moreover, the 'before' component of a BACI design is impossible for agrochemicals already in use. An alternative is to link large scale monitoring of wildlife populations to temporal and spatially explicit data on exposure risk to pesticides. This approach has considerable potential to complement the existing regulatory process, but there are significant issues that need to be addressed for its robust implementation. We discuss these below.

3 Data

3.1 Wildlife data

Wild populations persist in highly variable systems, so the level of replication required to detect a signal may be hard to achieve under a field experimental settings, especially when large-scale, long-term impacts need to be assessed [16]. Structured monitoring schemes that derive quantitative site specific data exist in many countries, e.g. there are more than ten national Butterfly Monitoring Schemes in Europe. Opportunistic data, including occurrence records submitted by volunteer citizen scientists, provide a vast source of information about biodiversity, but modelling change is complicated due to the lack of formal protocols [28]. Both monitoring schemes and opportunistic datasets span long periods of time (potentially prior to chemical exposure) and are collected from many sites exposed to different levels of pesticides, thus approximating a BACI design. Therefore, observational data on wildlife populations can be used to link trends in biodiversity to the use of chemicals, in spite of the fact that surveys were not designed specifically to detect such impacts.

3.2 Pesticide data

To quantify the exposure to plant protection products, such as pesticides, spatiotemporal data on their use is needed. Because there is no global governance for the use of these products and different countries have very different regulatory standards [11], data on their use remain scattered and not necessarily publicly available. However, the European Union requires (Regulation (EC) No 1185/2009) that member countries collect data on pesticide use. For example, the United Kingdom's Pesticide Usage Survey (PUS; [29]) collects data every two years from 1200 farms, stratified by region and size. However, obtaining these data at fine spatial resolution is difficult, in part due to legal protection of the identity of individual farmers. A snapshot of recent PUS data at 1km resolution has been recently published [30]; to date time-series have been available only at the resolution of English regions [15]. Another example is California's Pesticide Use Reporting programme [31] which is accessible directly from the California Pesticide Information Portal for the period 1974-2016 and at a spatial resolution of roughly 2.6 Km^2. Both of these reporting schemes collect information on the product used, the application rate and the area of crop treated. These data, combined with published information about mechanisms of exposure (e.g. dietary – direct or indirect through poisoned prey – or contact) provide an opportunity to estimate wildlife exposure risk, although not as precisely as would be possible with experimental data. For example, large scale data is not available on the mode of application or the fate of chemicals (and their metabolites) in the environment [26], therefore this kind of data described here will not provide a true measure of exposure, but only an approximation.

3.3 Other relevant covariates

Because wild populations are exposed to multiple stressors simultaneously it is valuable, where data allows, to quantify other major environmental drivers of biodiversity change, including land use change, landscape structure, agricultural practices, and weather [8,10]. These factors can either account for unexplained variation , act as confounding variables or interact with pesticide exposure to produce unexpected effects [32–34]. As ever data limitation at the appropriate spatial and temporal scales can limit the capacity of studies to include such information.

4 Statistical approaches

Spatiotemporal data of wildlife populations tends to include a number of significant biases. This is a result of the fact that in most cases distribution or population data is not collected with the goal of investigating the impact of pesticides on wildlife population. As such the selection of sites surveyed, the frequency or timing of the site visits might not be optimal. Uneven sampling in space is common to many biodiversity datasets, including structured monitoring schemes, however, it is possible to account for such issues statistically, e.g. by the addition of terms to stratify the analysis spatially. Having added such terms, it becomes possible to model biological parameters (e.g. population growth rates) as a function of pesticide exposure using standard statistical approaches (e.g. Generalised Linear Models).

Due to their opportunistic nature, unstructured species records (e.g. most citizen science datasets) contain three additional biases: uneven recording intensity over time, uneven sampling effort per visit and uneven detectability across time and space [28]. Without appropriate statistical approaches there is a significant risk of both false positive or negative effects being detected. Occupancy-detection models derived from capture-recapture theory [35], are robust to many of the biases in opportunistic data [36,37] because they explicitly model the detection process to correct for observation, reporting and detection bias. Occupancy-detection models are so-called because they incorporate both the occupancy process (presence/absence) and the detection process (detected/non-detected) in two hierarchically coupled sub-models. Within this modelling framework, covariates on pesticide use can be added to the occupancy sub-model described above. When fitted in a Bayesian framework, it is possible to add variables providing mechanistic explanations for chemical impact, such as species traits that predispose them to high or low risk, e.g. species commonly found in a treated crop are considered to have high risk. This approach has been used to link application of neonicotinoids to oilseed rape crops to population declines of wild bee species across England (Box 1 [15]).

5 Conclusions, challenges and limitations

Laboratory and field tests conducted under the current pesticide regulatory framework can achieve high resolution assessments of the toxicity of a chemical by identifying causal effects of pesticide exposure on individuals and determining safe concentrations. However, current toxicology testing regimes are unable to detect the entire range of toxicity effects that could emerge when the chemical is used at large-scales and over long periods. Therefore, a post-approval monitoring of the long-term population effects of large-scale pesticide use on non-target wildlife is necessary to make the pesticide regulatory framework relevant to real world situations. Ultimately, evidence provided by the current regulatory framework would be complemented by long-term assessments of wildlife persistence linked to large scale pesticide exposure (Fig. 1). The approach would mirror the type of ongoing post approval monitoring used in the regulation of pharmaceuticals [14].

When other major factors of environmental change have been accounted for in the models, as well as potentially evidence on toxicity derived from controlled laboratory experiments, this type of analysis is capable of providing strong correlative evidence of a link between pesticide use and ongoing risks to wildlife populations. The main limitation of this approach is the complexity of the system, as it will be impractical to measure all potentially confounding effects or covariates. Wildlife monitoring schemes and citizen science programmes, however, produce big datasets characterised by high spatial and temporal replication. This scale can help to minimise false positives, because the larger the sample size the more representative it will be of the real population, and false negatives, by increasing statistical power. The inclusion of other possible confounding variables (e.g. landscape structure) would further reduce the chance of type I errors, although availability of this data may be an issue. A further final point to consider is the strong temporal component of use for many chemicals, which can rapidly go from zero, before approval, to almost complete usage for some products after several years. This strong time signal and possible lags between pesticide application and detectable impacts on wildlife, can influence our ability to identify a link between pesticide use and declines in wildlife populations.

As with any modelling, data quality is crucial. There is an ethical argument at the heart of the issue with pesticide data availability. On the one hand, pesticide use affects ecosystem goods and services positively and negatively and agriculture receives a substantial amount of public subsidies. However, data protection regulations require that individual farms and farmers should not be identifiable from the data, leading to information on pesticide use being often only available at very coarse regional resolutions. Ethical considerations aside, the value of this approach can only be improved by open access efforts to collect detailed information on pesticide use at an international level, following the example of freshwater quality or pharmaceuticals monitoring programmes (e.g. World Health Organization Programme for International Drug Monitoring [14]). For example, water quality is monitored systematically by testing for the presence of different chemicals. In a similar way, a pesticide monitoring scheme for terrestrial systems could be implemented, including collection of soil and plant samples from farms to detect exact concentrations of chemicals in the field. These data could then be linked to data from wildlife monitoring programmes through the modelling approaches described here. This would establish a post-approval pesticide surveillance system that could provide either reassurance that the chemical is safe for the non-target organisms tested or early warning signs of impacts on wildlife populations [14].

6 Acknowledgements

This work was supported by the Natural Environment Research Council [NERC grant reference number NEC06550].

7 References

1. Godfray HCJ, Beddington JR, Crute IR, Haddad L, Lawrence D, Muir JF, Pretty J, Robinson S, Thomas SM, Toulmin C: **Food security: the challenge of feeding 9 billion people.** *Science* 2010, **327**:812–8.

2. Köhler HR, Triebskorn R: **Wildlife ecotoxicology of pesticides: Can we track effects to the population level and beyond?** *Science (80-)* 2013, **341**:759–765.

3. Colborn T, vom Saal FS, Soto AM: **Developmental effects of endocrine-disrupting chemicals in wildlife and humans.** *Environ Health Perspect* 1993, **101**:378–84.

4. Mañosa S, Mateo R, Guitart R: **A Review of the Effects of Agricultural and Industrial Contamination on the Ebro Delta Biota and Wildlife**. *Environ Monit Assess* 2001, **71**:187–205.

5. Hamlin HJ, Guillette LJ: **Birth Defects in Wildlife: The Role of Environmental Contaminants as Inducers of Reproductive and Developmental Dysfunction**. *Syst Biol Reprod Med* 2010, **56**:113–121.

6. Kendall MD, Safieh B, Harwood J, Pomeroy PP: **Plasma thymulin concentrations, the thymus and organochlorine contaminant levels in seals infected with phocine distemper virus**. *Sci Total Environ* 1992, **115**:133–144.

7. Bandouchova H, Pohanka M, Kral J, Ondracek K, Osickova J, Damkova V, Vitula F, Treml F,

Pikula J: **Effects of sublethal exposure of European brown hares to paraoxon on the course of tularemia**. *Neuroendocrinol Lett* 2011, **32**:77–83.

8. IPBES: *The assessment report on pollinators, pollination and food production*. IPBES; 2016.

9. Pisa LW, Amaral-Rogers V, Belzunces LP, Bonmatin JM, Downs CA, Goulson D, Kreutzweiser DP, Krupke C, Liess M, Mcfield M, et al.: **Effects of neonicotinoids and fipronil on non-target invertebrates**. *Environ Sci Pollut Res* 2014, **22**:68–102.

10. Potts SG, Imperatriz-Fonseca V, Ngo HT, Aizen MA, Biesmeijer JC, Breeze TD, Dicks L V., Garibaldi LA, Hill R, Settele J, et al.: **Safeguarding pollinators and their values to human well-being**. *Nature* 2016, **540**:220–229.

11. Handford CE, Elliott CT, Campbell K: **A review of the global pesticide legislation and the scale of challenge in reaching the global harmonization of food safety standards**. *Integr Environ Assess Manag* 2015, **11**:525–536.

12. Matthews G, Zaim M, Yadav RS, Soares A, Hii J, Ameneshewa B, Mnzava A, Dash AP, Ejov M, Tan SH, et al.: **Status of legislation and regulatory control of public health pesticides in countries endemic with or at risk of major vector-borne diseases**. *Environ Health Perspect* 2011, **119**:1517–1522.

13. European Food Safety Authority: **Guidance on the risk assessment of plant protection products on bees (Apis mellifera, Bombus spp. and solitary bees)**. *EFSA J* 2013, **11**.

14. Milner AM, Boyd IL: **Toward pesticidovigilance Can lessons from pharmaceutical monitoring help to improve pesticide regulation?** *Science (80-)* 2017, **357**:1232–1234. The authors argue for the creation of a pesticide surveilance system analogous to the pharmacovigilance programme developed to ensure the safety and effectiveness of medicines for large-scale use. Such a monitoring system of pesticide use would improve decisions regarding the approved use of agrochemicals and it would be a foundation for defining best practice in the

regulatory process.

15. Woodcock BA, Isaac NJB, Bullock JM, Roy DB, Garthwaite DG, Crowe A, Pywell RF: **Impacts of neonicotinoid use on long-term population changes in wild bees in England**. *Nat Commun* 2016, **7**:12459. Using large-scale citizen science data on 62 wild bee species and sophisticated statistical techniques, the authors showed a link between the large-scale use of neonicotinoid insecticides and declines in wild bee populations in the UK over a period of 18 years. This was the first time that sub-lethal effects of neonicotinoids were shown to scale up to cause losses in wild bee populations.

16. Woodcock BA, Heard MS, Jitlal MS, Rundlöf M, Bullock JM, Shore RF, Pywell RF: **Replication, effect sizes and identifying the biological impacts of pesticides on bees under field conditions**. *J Appl Ecol* 2016, **53**:1358–1362. The amount of replication needed to detect a 7% effect size change in bee colony size, as stated in the European Food Safety Authority regulations, might be too costly or impractical to achieve in a field trial setting. The authors argue for a strategy that will use experimental as well as simulation approaches to define biologically meaningful threshold effects, power testing to determine the level of replication required to detect such effects and focus on examining the long-term impacts of pesticides on bee populations.

17. Sponsler DB, Johnson RM: **Mechanistic modeling of pesticide exposure: The missing keystone of honey bee toxicology**. *Environ Toxicol Chem* 2017, **36**:871–881.

18. van der Sluijs JP, Simon-Delso N, Goulson D, Maxim L, Bonmatin J-M, Belzunces LP: **Neonicotinoids, bee disorders and the sustainability of pollinator services**. *Curr Opin Environ Sustain* 2013, **5**:293–305.

19. Godfray HCJ, Blacquière T, Field LM, Hails RS, Petrokofsky G, Potts SG, Raine NE, Vanbergen AJ, McLean AR: **A restatement of the natural science evidence base concerning**

neonicotinoid insecticides and insect pollinators. *Proc R Soc B Biol Sci* 2014, **281**:20140558.

20. Gross M: **EU ban puts spotlight on complex effects of neonicotinoids**. *Curr Biol* 2013, **23**:R462–R464.

21. Rundlöf M, Andersson GKS, Bommarco R, Fries I, Hederström V, Herbertsson L, Jonsson O, Klatt BK, Pedersen TR, Yourstone J, et al.: **Seed coating with a neonicotinoid insecticide negatively affects wild bees**. *Nature* 2015, **521**:77–80.

22. Carson R, Wilson EO, Lear LJ, Darling L, Darling L: *Silent spring*. Houghton Mifflin; 2002.

23. Sandrock C, Tanadini LG, Pettis JS, Biesmeijer JC, Potts SG, Neumann P: **Sublethal neonicotinoid insecticide exposure reduces solitary bee reproductive success**. *Agric For Entomol* 2014, **16**:119–128.

24. Cedergreen N: **Quantifying Synergy: A Systematic Review of Mixture Toxicity Studies within Environmental Toxicology**. *PLoS One* 2014, **9**:e96580.

25. Robinson A, Hesketh H, Lahive E, Horton AA, Svendsen C, Rortais A, Dorne J Lou, Baas J, Heard MS, Spurgeon DJ: **Comparing bee species responses to chemical mixtures: Common response patterns?** *PLoS One* 2017, **12**:e0176289.

26. European Commission: **Commission Regulation (EU) No 284/2013**. 2013,

27. Eberhardt LL: **Quantitative ecology and impact assessment**. *J Environ Manage* 1976, **4**:27–70.

28. Isaac NJB, Pocock MJO: **Bias and information in biological records**. *Biol J Linn Soc* 2015, **115**:522–531.

29. FERA: **PUS STAT: Pesticide Usage Surveys**. 2014,

30. Jarvis SG, Henrys PA, Redhead JW, Da Silva Osório BM, Pywell RF: **CEH Land Cover plus: Pesticides 2012-2016 (England and Wales).** 2019, doi:https://doi.org/10.5285/a72f8ce8-

561f-4f3a-8866-5da620c0c9fe.

31. California Department of Pesticide Regulation: **Pesticide Use Reporting: An Overview of California's Unique Full Reporting System. Sacramento:California Department of Pesticide Regulation**. 2000,

32. Dinh Van K, Janssens L, Debecker S, Stoks R: **Temperature- and latitude-specific individual growth rates shape the vulnerability of damselfly larvae to a widespread pesticide**. *J Appl Ecol* 2014, **51**:919–928.

33. Dinh K V., Janssens L, Stoks R: **Exposure to a heat wave under food limitation makes an agricultural insecticide lethal: a mechanistic laboratory experiment**. *Glob Chang Biol* 2016, **22**:3361–3372.

34. Bednarska AJ, Laskowski R: **Environmental conditions enhance toxicant effects in larvae of the ground beetle Pterostichus oblongopunctatus (Coleoptera: Carabidae)**. *Environ Pollut* 2009, **157**:1597–1602.

35. MacKenzie DI: *Occupancy estimation and modeling : inferring patterns and dynamics of species occurrence*. Academic Press, Burlington, Massachusetts,USA; 2006.

36. Isaac NJB, van Strien AJ, August TA, de Zeeuw MP, Roy DB: **Statistics for citizen science: Extracting signals of change from noisy ecological data**. *Methods Ecol Evol* 2014, **5**:1052–1060.

37. Van Strien AJ, Van Swaay CAM, Termaat T: **Opportunistic citizen science data of animal species produce reliable estimates of distribution trends if analysed with occupancy models**. *J Appl Ecol* 2013, **50**:1450–1458.

- Agricultural pesticides can be harmful to non-target wildlife populations
- Current regulatory processes often fail to identify impacts on real world systems
- Large-scale long-term data can help identify these impacts
- Sophisticated statistical tools are necessary to deal with the biases in the data
- This approach can complement the regulatory process to prevent impacts on wildlife

Declarations of interest: none.