

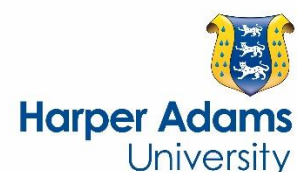
Evidence for the effects of neonicotinoids used in arable crop production on non-target organisms and concentrations of residues in relevant matrices: a systematic map protocol

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SYSTEMATIC MAP PROTOCOL

Open Access



Evidence for the effects of neonicotinoids used in arable crop production on non-target organisms and concentrations of residues in relevant matrices: a systematic map protocol

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Abstract

Background: Neonicotinoid insecticides (NNIs) have been routinely used in arable crop protection since their development in the early 1990s. These insecticides have been subject to the same registration procedures as other groups of pesticides, thus meet the same environmental hazard standards as all crop protection products. However, during the last 10 years the debate regarding their possible detrimental impact on non-target organisms, particularly pollinators, has become increasingly contentious and widely debated. Against this background, legislators and politicians in some countries, have been faced with a need to make decisions on the future registration of some or all of this class of insecticides, based on published evidence that in some areas is incomplete or limited in extent. This has created much concern in agricultural communities that consider that the withdrawal of these insecticides is likely to have significant negative economic, socio-economic and environmental consequences.

Methods: The proposed systematic map aims to address the following primary question: What is the available evidence for the effects of neonicotinoids used in arable crop production on non-target organisms and concentrations of residues in relevant matrices? The primary question will be divided into two sub-questions to gather research literature for (1) the effect of NNIs on non-target organisms (2) the occurrence of concentrations of NNIs in matrices of relevance to non-target organisms (i.e. exposure routes). The systematic map will focus on NNIs used in arable crop production: imidacloprid, clothianidin, thiamethoxam, acetamiprid, thiacloprid and dinotefuran. Separate inclusion criteria have been developed for each sub-question. Traditional academic and grey literature will be searched for in English language and a searchable databases containing extracted meta-data from relevant included studies will be developed.

Keywords: Imidacloprid, Clothianidin, Thiamethoxam, Acetamiprid, Thiacloprid, Dinotefuran, Non-target organism, Exposure, Effects

Background

The impacts of pesticides on the natural environment have long been a focus of public and scientific concern, with opinion ranging from support for their continued use under current testing and registration procedures, to

a call for pesticide free production. Neonicotinoid insecticides (NNIs) have been subject to the same registration procedures as other groups of pesticides, and thus meet the same environmental hazard standards as all crop protection products. However, during the last 10 years the debate regarding their possible detrimental impact on the environment, particularly pollinators, has become increasingly contentious [1].

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NNIs are broad-spectrum, systemic insecticides with a wide range of uses, from crop protection to urban pest and veterinary ecto-parasite control [2]. When applied to crops, regardless of application route, NNIs translocate within the plant suppressing direct damage by herbivorous insects and indirect damage by insect transmitted viruses [3].

In arable crop protection, imidacloprid, clothianidin, thiamethoxam are often used as seed dressings for crops, for example maize, sunflower, oilseed rape, soyabean and cereals [3, 4]. Thiacloprid, acetamiprid and dinotefuran are more often applied as foliar sprays [4]. The unique physicochemical properties of these NNIs means they are used to protect a wide variety of crops against a broad spectrum of economically important pests, such as aphids, wireworms and flea beetles, with single applications simultaneously protecting against multiple threats obviating the need for multiple applications of other products [2]. NNIs in general are also relatively persistent offering long-lasting residual crop protection further reducing the need for multiple applications of insecticide, water soluble and therefore easily taken up by plants, selectively more toxic to insects than vertebrates increasing operator safety for example compared to organophosphates, and versatile in terms of application method (e.g. foliar sprays, soil and seed treatments) compared to other classes of insecticide [2, 5]. NNIs were first introduced to the market in the 1990s and were regarded as an important alternative to organophosphate, carbamate and pyrethroid insecticides, to which there was growing pest resistance [2]. Set against this backdrop, NNIs have been rapidly adopted as plant protection products and in 2014 the market share of NNIs was more than 25 % of global insecticide sales [6].

In parallel with the recorded increase in use of NNIs, there have been increasing concerns raised about the potential negative effects of these broad-spectrum insecticides on non-target organisms, particularly bees. Managed and wild bees are important pollinators of agricultural crops and wild plants and therefore any declines are a cause for economic and environmental concern [7–9]. Bees, especially honeybees, have declined in number in many European countries and the US, and whilst there are many potential drivers for these declines (e.g. habitat loss and fragmentation, climate change, pesticides, pathogens, alien species and the interactions between them [9]), NNIs are thought by many to be a contributing factor [10]. In other areas of the world however where NNIs are routinely used, for example Australia, honeybee numbers have not declined [11, 12]. It has also been noted that the recorded declines of wild bees in Europe commenced many years before the introduction of NNIs

[13], and that although wild bees contribute significantly to production of insect pollinated crops, this service delivery is limited to a small subset of known bee species many of which are not considered threatened species [14].

NNIs are known to be toxic to bees, with imidacloprid, clothianidin and thiamethoxam (nitro-substituted neonicotinoids) being generally more toxic to honeybees than acetamiprid and thiacloprid (cyano-substituted neonicotinoids) [15, 16]. NNI seed treatments were introduced partly to offer an option with lower risk of exposure of many non-target organisms. However, when NNIs were first marketed seed treatment dust generated during the drilling of maize resulted in a number of large scale honeybee losses in the United States, Germany, Italy and Slovenia [17–22]. Legislators acted swiftly to address the risk with additional registration requirements limiting dust generation and requiring use of deflectors to reduce contamination of surrounding vegetation with airborne dust [23] to safeguard bee populations. Manufacturers also improved seed coating adherence [24].

Concern about the potential lethal and sub-lethal effects (e.g. behavioural changes, reduced immunity, etc.) of NNIs on both foragers and the bee colony (via NNI residues in hive matrices such as wax, bee bread and royal jelly [25]) persisted after these changes, particularly as a result of systemic activity in crop, and potentially non-crop plants, leading to presence in nectar, pollen and guttation fluid [19, 26–28].

Evidence is also emerging about the potential direct (e.g. ingestion of seed, direct contact with pesticide dust, spray, etc.) and indirect (e.g. reduction in prey or through soil, plant and water matrices) adverse effects of NNIs on non-target organisms other than bees, for example: beneficial predatory invertebrates via the consumption of crop pests [29, 30] and parasitic wasps through nectar feeding [31], birds through the consumption of treated seed [32–34] or reduction in insect food [35], aquatic invertebrates via leaching of NNIs into water bodies [36–40], and non-target soil organisms via NNI treated seed or soil drenches [28]. A number of studies have also investigated the potential risk to non-target organisms, including pollinators, from the breakdown products (metabolites) of NNIs [15, 37, 41].

Many regulators and scientists, however, have questioned the applicability of laboratory findings to conditions in the field, because concentrations of NNIs tested do not necessarily reflect field-realistic residues [42, 43]. In addition, studies relating to the effects of NNIs on bees have focussed predominantly on the western honeybee *Apis mellifera* and imidacloprid [1, 27, 42, 44]. There is growing evidence, however, that bee taxa respond

differently to NNI exposure [45] and it is not possible to extrapolate the effects of one NNI to another due to differences in the characteristics of their active ingredients [42, 46].

Against this background, legislators and politicians have been faced with a need to use the best available evidence to establish whether registration of some or all of this class of insecticides should continue. A decision to impose a 2-year moratorium in EU countries on the use of imidacloprid, clothianidin and thiamethoxam as seed treatments on bee-attractive crops (commencing in December 2013) has been imposed, during which period further consideration can be given to relevant issues [47]. Ontario in Canada is also restricting the use of NNIs, with a policy to reduce the use of the same three insecticides as seed treatments for maize and soy by 80 % from 2014 levels [48]. Furthermore, the United States Environmental Protection Agency (US EPA), is also in the process of reviewing neonicotinoid insecticide registrations, which is expected to conclude in 2018 [49].

These policy decisions have caused widespread concern in the agricultural community. Recent studies investigating the socio-economic consequences of a non-NNI crop production scenario have forecast significant negative implications for livelihoods, national economies, agricultural markets and food security [4, 50, 51]. Experts have pointed towards the current difficulties of growing oilseed rape in the UK without making a financial loss and the Danish Government decision to apply for a derogation for the use of these products on the whole of their oilseed rape hectareage in 2016 [52]. In contrast, a report by the US Environmental Protection Agency concluded that seed treatments provide little or no benefit for soya bean production (yield) [53] and a review by Goulson [54] questioned the economic and yield benefits of using NNIs concluding that more research is needed.

The consequences for non-target organisms and the wider environment of a ban on NNI use is also a subject of current debate. Projected changes in insecticide use suggest a greater reliance on insecticides such as pyrethroids and organophosphates [4], which also have potentially adverse implications for non-target organisms [55, 56]. In terms of the wider environment, in the EU for example, non-NNI crop production has been predicted to lead to a reduction in acreage of some crops (where there are no alternative options for pest control due to pyrethroid resistance) perhaps illustrated by the significant reduction in the area of oilseed rape grown in the UK since the introduction of the ban [e.g. 57]. This may result in a greater reliance on imports from countries outside of the EU and an increase in land conversion to arable in these exporting countries. Both imports and land conversion could have potentially adverse

environmental costs (e.g. biodiversity loss, greenhouse gas emissions) [51].

Decision-makers require unbiased up-to-date evidence on all the relevant issues on which to base their decisions concerning the continued registration of some or all of this class of insecticides. This systematic map will form a preliminary step in this process by gathering and collating the available evidence for the effects of NNIs used in arable crop production on non-target organisms and exposure to NNI residues through relevant matrices.

Topic identification

This topic is of particular relevance to scientists, legislators and policy-makers in the EU and other countries (e.g. US and Canada), where the future registration of some NNIs, particularly those used in NNI seed-treatments, is currently under review.

In recent years, there have been a number of reviews published concerning the potential environmental impacts of NNIs [26–28, 44, 46, 54, 58]. However, many of these have focussed solely on bees [27, 44, 46, 59] or specific NNIs [44] and the majority have not been conducted using systematic methodology [26, 28, 46, 54, 58, 59]. Furthermore, few reviews have extracted meta-data from studies to enable an assessment to be made of the robustness and relevance of the evidence and the one review that has addressed this issue focused purely on bees [44].

Evidence synthesis methods [60] follow rigorous, objective and transparent processes that, unlike traditional literature reviews, reduce reviewer selection bias and publication bias. They make the decision criteria regarding inclusion and appraisal of identified research, and how conclusions have been reached transparent and readily understood. We therefore, consider this systematic map to be a vital exercise to bring together the available evidence for the effects of NNIs used in arable crop production on all non-target organisms and concentrations of residues found in relevant matrices.

Objective of the map

The objective of this systematic map is to provide an overview of the available evidence about the effects on non-target organisms of NNIs used in arable crop production and the occurrence of concentrations of these NNIs in matrices of relevance to non-target organisms in arable systems. The systematic map will describe the volume and key characteristics of the evidence base, identify evidence clusters and knowledge gaps. Sub-topics that may be suitable for full systematic review will also be identified. The searchable map database will provide a catalogue of evidence for stakeholders interested in the topic to interrogate.

Primary question

What is the available evidence for the effects of neonicotinoids used in arable crop production on non-target organisms and concentrations of residues in relevant matrices?

This primary question will be divided into two sub-questions:

1. What is the available evidence for the effects on non-target organisms of imidacloprid, clothianidin, thiamethoxam, acetamiprid, thiacloprid and dinotefuran used in arable crop production?

Population Any non-target organism in arable systems.

Exposure Direct or indirect exposure to imidacloprid, clothianidin, thiamethoxam, acetamiprid, thiacloprid and dinotefuran used in arable crop protection.

Comparator No NNI, alternative insecticide.

Outcome Acute, chronic, lethal, sub-lethal (e.g. survival, foraging, colony development, reproduction, etc.) effects of exposure to the named NNIs.

2. What is the available evidence for the occurrence of concentrations of imidacloprid, clothianidin, thiamethoxam, acetamiprid, thiacloprid and dinotefuran in matrices of relevance to non-target organisms in arable crop production systems?

Population Any matrix of relevance to non-target organisms (e.g. nectar, pollen and guttation fluid, beebread, soil, water) associated with arable farming systems.

Occurrence Concentrations of imidacloprid, clothianidin, thiamethoxam, acetamiprid, thiacloprid and dinotefuran authorised for use (i.e. seed treatments, foliar sprays) in arable crop protection, in any matrix of relevance to non-target organisms.

Methods

Searches

The review team conducted a scoping search to validate the search terms and test them against articles of relevance (Additional file 1). Using the results of the scoping search the team decided that the best approach for this broad topic is to use only the NNI exposure keywords as search terms to ensure a comprehensive and sensitive search. Relevant articles will be extracted for each sub-question. The following search terms will be used:

Neonic*, neo-nic*, imidacloprid*, clothianidin*, thiamethoxam*, acetamiprid*, thiacloprid*, dinotefuran*

Wildcards ('*') will be used to pick up multiple word endings, '?' and '\$' will be used to pick up differences in

spellings and the search terms will be combined using the Boolean operator 'OR', where accepted by a database or search engine. Where databases or search engines do not accept wildcards or long search strings the search terms will be customised e.g. neonic* to neonicotinoid. Final search terms will be recorded for each search in an appendix.

Database searches will be conducted in the English language with no date restrictions. Articles with only abstracts in English but full texts in other languages that are of that are of potential importance will be recorded separately in an Additional file 1. Articles in other languages will be translated where resources are available.

A comprehensive search will be undertaken using multiple information sources in attempt to capture an unbiased sample of literature. The search strategy has been developed to identify traditional academic and grey (e.g. theses, organisation reports, government papers, consultancy documents, etc.) literature.

The results of each search string for each database will be imported into a separate EndNote X7.5 library file. All the database libraries will be incorporated into one library, recording the number of references captured. Using the automatic function in the EndNote X7.5 software any duplicates will be removed. A record of each search will be made to enable a re-run of the search if needed. The following data will be recorded: date the search was conducted, database and platform name, institutional subscription used to access the database, search term, number of hits and notes.

The following online publication databases will be searched:

Science Direct [<http://www.sciencedirect.com>].

Thomson Reuters Web of Science [<http://ipscience.thomsonreuters.com>].

Wiley Online [<http://onlinelibrary.wiley.com>].

Pubmed [<http://europepmc.org>].

CAB abstracts [<http://www.cabi.org/>].

AgEcon Search [<http://ageconsearch.umn.edu>].

BioOne [<http://www.bioone.org>].

Business Source Complete [<https://www.ebscohost.com/academic/business-source-complete>].

Food Science Source [<https://www.ebscohost.com/corporate-research/food-science-source>].

Greenfile [<https://www.ebscohost.com/academic/greenfile>].

AGRIS [<http://agris.fao.org/agris-search/index.do>].

AGRICOLA [<http://agricola.nal.usda.gov>].

Scopus [<http://www.scopus.com>].

Ethos [<http://ethos.bl.uk/Home.do>].

In addition, internet searches will be performed using the search engines:

Google [<https://www.google.com>].

Google Scholar [<https://www.scholar.google.com>].

The first 1000 hits (.doc.txt, xls and.pdf documents where this can be separated) from each data source will be examined for appropriate studies. No further links from the captured website will be followed unless to a document/pdf file. Both 'full text' and 'title only' searches will be performed in Google Scholar, with title searches shown to be more fruitful if searching for grey literature [61].

Websites of the specialist organisations listed below will be searched for links or references to relevant publications and data, including grey literature:

UK Department for Environment, Food and Rural Affairs [<https://www.gov.uk/government/organisations/departments-for-environment-food-rural-affairs>].

European Food Safety Authority [<http://www.efsa.europa.eu/>].

Food Standards Agency [<http://www.food.gov.uk/>].

Welsh government—Environment and Countryside [<http://gov.wales/topics/environmentcountryside/?lang=en>].

Scottish government [<http://www.gov.scot/>].

Department of Agriculture and Rural Development Northern Ireland [<https://www.dardni.gov.uk/>].

Natural Environment Research Council (NERC) Insect Pollinators Initiative.

[<http://www.nerc.ac.uk/research/funded/programmes/pollinators/>].

Swedish Environmental Protection Agency [<http://www.swedishepa.se/>].

Swedish Board of Agriculture [<http://www.jordbruksverket.se/>].

Finnish Environment Institute [<http://www.environment.fi/>].

Danish Environmental Protection Agency [<http://eng.mst.dk/>].

German Environment Agency [<https://www.umweltbundesamt.de/>].

The Julius Kühn Institute [<http://www.jki.bund.de/>].

United States Environmental Protection Agency [<http://www3.epa.gov/>].

New Zealand Environmental Protection Agency Te Mana Rauhi Taiao [<http://www.epa.govt.nz/Pages/default.aspx>].

European Commission [<http://ec.europa.eu/>].

Australian Pesticides and Veterinary Medicines Authority [<http://apvma.gov.au/>].

Health Canada [www.hc-sc.gc.ca].

Government of Ontario [<http://www.ontario.ca/>].

Growing Matters [<http://growingmatters.org/>].

UK Pollinator Initiative [<https://wiki.ceh.ac.uk/display/ukipi/Home>]

NERC Open Research Archive [<http://nora.nerc.ac.uk/>].

European Environmental Agency [<http://www.eea.europa.eu/>].

Other specific/specialised databases will be searched where identified on an iterative basis.

The reference lists of all identified and retrieved review articles will be checked to ensure that all relevant articles have been captured and included into the search record. Recognised experts and practitioners will also be contacted for further recommendations and for provision of relevant unpublished material.

Article screening and study inclusion criteria

All articles retrieved by the searches will be assessed at three successive levels (title, abstract and full text) against study inclusion criteria to ensure article relevancy. A subset of 10 % of the total results retrieved by the searches will be checked against the inclusion criteria at title and abstract level by two independent reviewers and a kappa test used to determine agreement, with a score of 0.6 or above indicating substantial agreement. Any disagreements will be discussed and any definitions that require clarifying will be adjusted accordingly. Reviewers involved in this review that are also authors of relevant articles will not be included in the decisions connected to inclusion and critical appraisal of these articles.

Endnote files for articles excluded at title and abstract stage will be supplied in an Additional file. A list of excluded studies at full text and reasons for exclusion will also be recorded in an Additional file.

Due to the complexity of this systematic map study, inclusion criteria have been developed for each separate sub-question.

Arable crops are defined here as: potatoes, maize, wheat, oats, barley, oilseed rape, turnip, swede, kale, sugar beet, peas, field beans, sunflowers, alfalfa, turnip rape, mustard, fodder beet, triticale, linseed, rye, cotton, sorghum, soybean (vegetables other than field beans and peas will be excluded for example, cauliflower, cabbage, onions, carrots, hops, artichoke, celeriac, pumpkin, squash, courgette). Any studies not relating to arable systems, for example: horticulture, ornamentals, turf, forestry/agro-forestry, tree nursery and paddy systems, veterinary medicine, urban pest control will be excluded. Following Köppen–Geiger climate classification zones [62] we will include studies from the whole of the United States of America, Canada, Europe and New Zealand and regions climate zones Bsk, Csa, Cfa, Cfb, Cfc, Csb, Csc, Dfa, Dfb, Dfc. These crops and zones were chosen because they are of particular relevance to the current debate on NNIs.

Non-target organisms are defined as any animal, fungi or plant (including crops, weeds, succeeding crops, field margin flora) that are not crop pests (e.g. aphids

or wireworms etc.). Non-target organisms will only be included if they are relevant arable cropping systems and within the regions described above.

Sub-question 1: What is the available evidence for the effects on non-target organisms of imidacloprid, clothianidin, thiamethoxam, acetamiprid, thiacloprid, and dinotefuran used in arable crop production?

Relevant population Non-target organisms.

Relevant types of exposure Studies that investigate the effect on non-target organisms from the direct or indirect exposure of at least one of the following NNIs: imidacloprid, clothianidin, thiamethoxam, acetamiprid, thiacloprid or dinotefuran. Studies captured that investigate the impact of metabolites of these named NNIs on non-target organisms will also be included.

Relevant types of comparator No exposure or alternative non-NNI insecticide. Before exposure.

Relevant study designs Before and after studies (BA), before and after control impacts studies (BACI), randomised controlled trials (RCTs), Randomised split block design, exposure versus no exposure/control impacts (CI), correlative.

Relevant types of outcome Any acute, chronic, lethal, sub-lethal effects on non-target organisms from exposure to the named NNIs above. We will exclude studies that report insecticide resistance or efficacy of neonicotinoids for controlling crop pests.

Sub-question 2: What is the available evidence for the occurrence of concentrations of imidacloprid, clothianidin, thiamethoxam, acetamiprid, thiacloprid and dinotefuran in matrices of relevance to non-target organisms in arable crop production systems?

Relevant population Any matrix relevant to non-target organism associated with arable farming systems. Matrices may include: the non-target animal (e.g. bee, earthworm, bird etc.), plant material (e.g. leaves, pollen, nectar, guttation fluid, NNI treated-seed), dust, soil, water, bee products (e.g. comb, wax, propolis, beebread, honey). Concentrations of NNIs in target pest species will only be included where the aim of the study is to examine the impact on non-target organisms from ingestion of these pests (e.g. ladybirds preying on aphids). Where concentrations of NNIs are recorded in soils or water (e.g. puddles, ponds, lakes, rivers, streams, groundwater, territorial and coastal waters, surface water) these must be clearly associated with NNI inputs from arable systems.

Relevant outcomes Concentrations of authorised use of imidacloprid, clothianidin, thiamethoxam, acetamiprid, thiacloprid and dinotefuran (i.e. as seed treatment or foliar spray) applied as plant protection to arable crops, in matrices of relevance to non-target-organisms. Studies

captured that investigate the metabolites of the above NNIs will also be included.

Relevant type of study Any primary research field or mesocosm (i.e. tunnel tests, cages in fields) study.

Relevant study designs Before and after studies (BA), before and after control impacts studies (BACI), randomised controlled trials (RCTs), randomised split block design trial, exposure versus no exposure/control impacts (CI).

Studies that do not address the primary question but that may help put the collated evidence into context regards the current debate on NNIs (e.g. methods to mitigate the impacts of NNIs on non-target organisms or the potential economic and environmental consequences of a ban on use of NNIs) will be recorded in a separate library to help inform conclusions.

Critical appraisal of studies

Full critical appraisal of included studies will not be carried out in this systematic map because the breadth of the topic and the highly heterogeneous nature of the studies would make this incredibly complex and difficult. Study setting and experimental design meta-data from included studies will be extracted to provide a very basic overview of the robustness and relevance of the evidence. However, the primary aim of extracting this meta-data is to aid future more in depth critical appraisal and synthesis of studies on sub-topics of interest.

In addition to extracting meta-data (e.g. degree of replication, number of treatments, etc.) a checklist of questions (Additional file 2) will also be applied to each included study for sub-questions 1 and 2. The checklist will report compliance of each study with each question using ratings 'yes', 'no' and 'unclear' which correspond to low, high and unclear risk of bias respectively. An additional rating of 'not applicable' will also be included. This enables the construction of risk of bias for individual studies, and an overview describing the overall compliance of a body of evidence for each quality. This approach is used in Cochrane reviews and risk of bias for each study is often summarised as a figure and a graph which shows an overview of study quality within the whole review [63]. The checklist of questions used in this systematic map is based on the critical appraisal skill programme (CASP) randomised controlled trial checklist [64] and the Environmental-Risk of Bias Tool adapted from the Cochrane Collaboration's Risk of Bias Tool [65]. This checklist will form part of the coding in the database.

Compliance with the questions in the checklist will not be used to exclude studies from the systematic map.

Data coding strategy

Coding of studies will be undertaken on full texts and may be expanded in the mapping process depending on the variety of included studies. Coding variables for each sub-question are detailed in Additional file 3. Fifty articles will be checked for coding consistency between reviewers and any disagreements discussed and resolved.

Individual lines within the database represent a unit of one study-article, i.e. each individual reporting of a study. Multiple studies reported within one article are entered as independent lines in the database. Separate articles that report different outcomes from one study are entered as separate lines. This is to reflect the possible differences in reporting between different articles on the same study. These linked articles will be highlighted as such, however, and will be treated as one study unit.

Some studies may report both effects and concentrations of NNIs in non-target organism matrices. In these cases the relevant study and meta-data will be catalogued for each sub-question and the articles linked as effect/exposure studies. Information regarding the location, latitude and longitude (where possible) of each study will also be coded for to enable an online geographical information system (GIS) displaying the contents of the systematic map databases to be generated. The active ingredients of the included NNIs differ in their characteristics, each NNI will therefore also be coded as either nitro-substituted neonicotinoids (imidacloprid, clothianidin, dinotefuran and thiamethoxam) or cyano-substituted neonicotinoids (acetamiprid and thiacloprid).

Study mapping and presentation

All included studies and their meta-data will be catalogued in Access databases, and/or Excel files. The searchable database will enable users to select studies relevant to sub-topics of interest. Studies and study meta-data will also be presented as an interactive GIS world map.

The systematic map will include:

- Searchable database, cataloguing studies and meta-data for each sub-question.
- An open access, online geographical information system (GIS) displaying the contents of the systematic map database as independent layers.
- A narrative report detailing methodology, results (generic and topic specific trends, quality summaries, knowledge gaps and clusters) and implications for research, policy and practice.

Additional files

- Additional file 1.** Search term scoping and evolution.
Additional file 2. Critical appraisal for sub-questions 1 and 2.
Additional file 3. Coding variables for sub-questions 1 and 2.

Authors' contributions

KJ, NR and KW conceived the systematic map question. KJ, NR, KW, NH and ML drafted the protocol. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

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References

1. Walters KFA. Data, data everywhere but we don't know what to think? Neonicotinoid insecticides and pollinators. *Outlooks Pest Manag.* 2013;24(4):151–5.
2. Jeschke P, Nauen R, Schindler M, Elbert A. Overview of the status and global strategy for neonicotinoids. *J Agric Food Chem.* 2011;59:2897–908.
3. Simon-Delso N, Amaral-Rogers V, Belzunces LP, Bonmatin JM, Chagnon M, Downs C, Furlan L, Gibbons DW, Giorio C, Girolami V, Goulson D, Kreutzweiser DP, Krupke CH, Liess M, Long E, McField M, Mineau P, Mitchell EAD, Morrissey CA, Noome DA, Pisa L, Settele J, Stark JD, Tapparo A, Van Dyck H, Van Praagh V, Van der Sluijs JP, Whitehorn PR, Wiemers M. Systemic insecticides (neonicotinoids and fipronil): trends, uses, mode of action and metabolites. *Environ Sci Pollut Res.* 2015;22:5–34.
4. Mitchell PD. The value of neonicotinoids in North American agriculture: estimated impact of neonicotinoid insecticides on pest management practices and costs for US Corn, Soybean, Wheat, Cotton and Sorghum Farmers. 2014. http://growingmatters.org/wp-content/themes/growing-matters/pdf/FINAL_AgInfomatics_EstimatedImpact_2014.pdf. Accessed 12 Jan 2016.
5. Jeschke P, Nauen R. Neonicotinoid Insecticides. In: Gilbert LI, Gill SS, editors. *Insect control: biological and synthetic agents*. London: Academic Press; 2010. p. 61–119.
6. Bass C, Denholm I, Williamson MS, Nauen R. The global status of insect resistance to neonicotinoid insecticides. *Pestic Biochem Phys.* 2015;2015(121):78–87.
7. Klein A-M, Vaissière BE, Cane JH, Steffan-Dewenter I, Cunningham SA, Kremen C, Tscharntke T. Importance of pollinators in changing landscapes for world crops. *Proc Biol Sci.* 2007;274(1608):303–13.

8. Garibaldi LA, Steffan-Dewenter I, Winfree R, Aizen MA, et al. Wild pollinators enhance fruit set of crops regardless of honey bee abundance. *Science*. 2013;339:1608–11.
9. Potts SG, Biesmeijer JC, Kremen C, Neumann P, Schweiger O, Kunin WE. Global pollinator declines: trends, impacts and drivers. *Trends Ecol Evol*. 2010;25:345–53.
10. Bijleveldlexmond M, Bonmatin JM, Goulson D, Noome DA. Worldwide integrated assessment on systemic pesticides. Global collapse of the entomofauna: exploring the role of systemic insecticides. *Environ Sci Pollut Res*. 2015;22:1–4.
11. Australian pesticides and veterinary medicines Authority (APVMA). Australian Pesticides and Veterinary Medicines Authority. Australian Government. Neonicotinoids and the Health of Honey bees in Australia. Overview report. 2014. https://archive.apvma.gov.au/news_media/chemicals/bee_and_neonicotinoids.php. Accessed 12 Jan 2016.
12. Fairbrother JP, Anderson T, Fell R. Risks of neonicotinoid insecticides to honeybees. *Environ Toxicol Chem*. 2014;33(4):719–31.
13. Carvalheiro LG, Kunin WE, Keil P, Aguirre-Gutiérrez J, Ellis WN, Fox R, Groom Q, Hennekens S, Van Landuyt W, Maes D, van de Meutter F, Rasmond P, Michez D, Ode B, Potts SG, Reemer M, Roberts SP, Wallis DeVries MF, Schaminée J, Biesmeijer JC. Species richness declines and biotic homogenisation have slowed down for NW-European pollinators and plants. *Ecol Lett*. 2013;16:870–8.
14. Kleijn D, Winfree R, Bartomeus I, Carvalheiro LG, et al. Delivery of crop pollination services is an insufficient argument for wild pollinator conservation. *Nature*. 2015. doi:10.1038/ncomms8414.
15. Iwasa T, Motoyama N, Ambrose JT, Roe RM. Mechanism for the differential toxicity of neonicotinoid insecticides in the honey bee, *Apis mellifera*. *Crop Prot*. 2004;23(5):371–8.
16. Laurino D, Porporato M, Patetta A, Maninot A. Toxicity of neonicotinoid insecticides to honey bees: laboratory tests. *Bull Insectol*. 2011;64(1):107–13.
17. Bortolotti L, Sabatini AG, Mutinelli F, Astuti M, Lavazza A, Piro R, et al. Spring honey bee losses in Italy Proceedings of Hazards of pesticides to bees—10th International Symposium of the ICP-Bee Protection Group Bucharest (Romania) 2008. *Julius Kuhn-Arch*. 2009;423:148–52.
18. Forster R. Risk mitigation measures for seed treatments using neonicotinoids. Proceedings of 11th 468 International Symposium of the IC-PBR Bee Protection Group, Wageningen (The Netherlands), 2011. *Julius-Kühn-Arch*. 2012;437:63–68; doi: <http://dx.doi.org/10.5073/jka.2012.437.013>. Accessed 12 Jan 2016.
19. Krupke CH, Hunt GJ, Eitzer BD, Andino G, Given K. Multiple routes of pesticide exposure for honey bees living near agricultural fields. *PLoS One*. 2012; doi: <http://dx.doi.org/10.1371/journal.pone.0029268>. Accessed 12 Jan 2016.
20. Gross M. Pesticides linked to bee deaths. *Curr Biol*. 2008;18:684.
21. Marzaro M, Vivan L, Targa A, Mazzon L, Mori N, Greatti M, Petrucco Toffolo E, Di Bernardo A, Giorgio C, Marton D, Tapparo A, Girolami V. Lethal aerial powdering of honey bees with neonicotinoids from fragments of maize seed coat. *Bull Insectol*. 2011;64(1):119–26.
22. Rosenkranz P, Wallner K. The chronology of honey bee losses in the Rhine valley during spring 2008: an example of worst case scenario. Proceedings of 3rd European Conference on Apidology, 8–11 September, Belfast, UK, 2008. 94–95.
23. Commission Directive 2010/21/EU of 12 March 2010 amending Annex I to Council Directive 91/414/EEC as regards the specific provisions relating to clothianidin, thiamethoxam, fipronil and imidacloprid. *Official Journal of the European Union L 65/27*. (2010).
24. Nuyttens D, Devarewaere W, Verboven P, Foque D. Pesticide-laden dust emission and drift from treated seeds during seed drilling: a review. *Pest Manag Sci*. 2013;69:564–75.
25. Giroud B, Vauchez A, Vulliet E, Wiest L, Buleté A. Trace level determination of pyrethroid and neonicotinoid insecticides in bee bread using acetonitrile-based extraction followed by analysis with ultra-high-performance liquid chromatography–tandem mass spectrometry. *J Chromatogr A*. 2013;1316:53–61.
26. Bonmatin JM, Giorio C, Girolami V, Goulson D, Kreuzweiser DP, Krupke C, Liess M, Long E, Marzaro M, Mitchell EAD, Noome DA, Simon-Delso N, Tapparo A. Environmental fate and exposure; neonicotinoids and fipronil. *Environ Sci Pollut Res*. 2015;22:35–67.
27. Lundin O, Rundlöf M, Smith HG, Fries I, Bommarco R. Neonicotinoid insecticides and their impacts on bees: a systematic review of research approaches and identification of knowledge gaps. *PLoS ONE*. 2015. doi:10.1371/journal.pone.0136928.
28. Pisa LW, Amaral-Rogers V, Belzunces LP, Bonmatin JM, Downs CA, Goulson D, Kreuzweiser DP, Krupke C, Liess M, McField M, Morrissey CA, Noome A, Settele J, Simon-Delso N, Stark JD, Van der Sluijs JP, Van Dyck H, Wiemers M. Effects of neonicotinoids and fipronil on non-target invertebrates. *Environ Sci Pollut Res*. 2015;22:68–102.
29. Moser SE, Obrycki JJ. Non-target effects of neonicotinoid seed treatments; mortality of coccinellid larvae related to zoophytophagy. *Biol Control*. 2009;51:487–92.
30. Douglas MR, Rohr JR, Tooker JF. Neonicotinoid insecticide travels through a soil food chain, disrupting biological control of non-target pests and decreasing soya bean yield. *J Appl Ecol*. 2015;52(1):250–60.
31. Krischik VA, Landmark AL, Heimpel GE. Soil-applied imidacloprid is translocated to nectar and kills nectar-feeding *Anagrus pseudococci* (Girault) (Hymenoptera: Encyrtidae). *Environ Entomol*. 2007;36(5):1238–45.
32. Berny PJ, Buronfosse F, Videmann B, Buronfosse T. Evaluation of the toxicity of imidacloprid in wild birds. A new high performance thin layer chromatography (HPTLC) method for the analysis of liver and crop samples in suspected poisoning cases. *J Liq Chrom Rel Technol*. 1999;22:1547–59.
33. Lopez-Anita A, Ortiz-Santaliestra ME, Mougeot F, Mateo R. Imidacloprid-treated seed ingestion has lethal effect on adult partridges and reduces both breeding investment and offspring immunity. *Environ Res*. 2015;136:97–107.
34. Mineau P, Palmer C. The impact of the nation's most widely used insecticides on birds. *American Bird Conservancy, USA*; 2013. http://abcbirds.org/wp-content/uploads/2015/05/Neonic_FINAL.pdf. Accessed 12 Jan 2016.
35. Hallmann CA, Foppen RP, van Turnhout CA, de Kroon H, Jongejans E. Declines in insectivorous birds are associated with high neonicotinoid concentrations. *Nature*. 2014;511(7509):341–3.
36. Anderson JC, Dubetz C, Palace VP. Neonicotinoids in the Canadian aquatic environment: a literature review on current use products with a focus on fate, exposure, and biological effects. *Sci Total Environ*. 2015;505:409–22.
37. Malev O, Klobucar RS, Fabbretti E, Trebse P. Comparative toxicity of imidacloprid and its transformation product 6-chloronicotinic acid to non-target aquatic organisms: microalgae *Desmodesmus subspicatus* and amphipod *Gammarus fossarum*. *Pestic Biochem Phys*. 2012;104(3):178–86.
38. Morrissey CA, Mineau P, Devries JH, Sanchez-Bayo F, Liess M, Cavallaro MC, Liber K. Neonicotinoid contamination of global surface waters and associated risk to aquatic invertebrates: a review. *Environ Int*. 2015;74:291–303.
39. Van Dijk TC, Van Staalduinen MA, Van der Sluijs JP. Macro-invertebrate decline in surface water polluted with imidacloprid. *PLoS ONE*. 2013;8(5):e62374.
40. Vijver MG, van den Brink PJ. Macro-invertebrate decline in surface water polluted with imidacloprid: a rebuttal and some new analyses. *PLoS ONE*. 2014;9(2):e89837.
41. Nauen R, Ebbinghaus-Kitschner U, Schmuck R. Toxicity and nicotinic acetylcholine receptor interaction of imidacloprid and its metabolites in *Apis mellifera*. *Pest Manag Sci*. 2001;57(7):577–86.
42. Blacquièrre T, Smagghe G, Van Gestel CA, Mommaerts V. Neonicotinoids in bees: a review on concentrations, side-effects and risk assessment. *Ecotoxicology*. 2012;21:973–92.
43. Defra. An assessment of key evidence about Neonicotinoids and bees. 2013. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/221052/pb13937-neonicotinoid-bees-20130326.pdf. Accessed 20 June 2016.
44. European Food Safety Authority (EFSA). Statement on the findings in recent studies investigating sub-lethal effects in bees of some neonicotinoids in consideration of the uses currently authorised in Europe. 2012. http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/2752.pdf. Accessed 12 Jan 2016.
45. Rundlöf M, Andersson GKS, Bommarco R, Fries I, Hederström V, Herbertsson L, Jonsson O, Klatt BK, Pedersen TR, Yourstone J, Smith HG. Seed coating with a neonicotinoid insecticide negatively affects wild bees. *Nature*. 2015;521(7550):77–80.

46. 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*. 2014;281:1786.
47. EC Commission implementing regulation (EU) No 485/2013 of 24 May 2013 amending Implementing Regulation (EU) No 540/2011, as regard the conditions of approval of the active substances clothianidin, thiamethoxam and imidacloprid, and prohibiting the use and sale of seed treated with plant protection products containing those active substances. *Official Journal of the European Union* 139:12–26.
48. Ministry of the environment and climate change neonicotinoid regulations. 2015. <http://www.ontario.ca/environment-and-energy/neonicotinoid-regulations>. Accessed 12 Jan 2016.
49. US environmental protection agency schedule for review of neonicotinoid pesticides. 2016. <http://www.epa.gov/pollinator-protection/schedule-review-neonicotinoid-pesticides>. Accessed 12 Jan 2016.
50. Ionel II. Regulation implications on banning the treatment of seeds with neonicotinoid insecticides on the seed market in Romania. *Lucafrafi e tiine ifice Manag Agricol*. 2014;16(2):223–8.
51. Noleppa S, Hahn T. The value of neonicotinoid seed treatment in the European Union. A socio-economic, technological and environmental review. Research report. Humbolt Forum for Food and Agriculture e.V. HFFA working paper 01/2013. http://www.hffa.info/files/wp_1_13_1.pdf. Accessed 12 Jan 2016.
52. Dewar AM, Walters KFA. Can we continue to grow oilseed rape? *Outlooks Pest Manag*. 2016;27:65–9.
53. United States Environmental Protection Agency. Benefits of Neonicotinoid Seed Treatments to Soybean Production, United States Environmental Protection Agency Report. 2014. <http://www2.epa.gov/pollinator-protection/benefits-neonicotinoid-seed-treatments-soybean-production>. Accessed 20 June 2016.
54. Goulson D. Review: an overview of the environmental risks posed by neonicotinoid insecticides. *J App Ecol*. 2013;50(4):977–87.
55. Dai P-L, Wang Q, Sun JH, Liu F, Wang X, Wu YY, Zhou T. Effects of sublethal concentrations of bifenthrin and deltamethrin on fecundity, growth, and development of the honeybee *Apis mellifera* ligustica. *Environ Toxicol Chem*. 2009;29(3):644–9.
56. Frampton GK, van den Brink PJ. Collembola and macroarthropod community responses to carbamate, organophosphate and synthetic pyrethroid insecticides: direct and indirect effects. *Environ Pollut*. 2007;147(1):14–25.
57. Scott C, Bilsborrow P. An interim impact assessment of the neonicotinoid seed treatment ban on oilseed rape production in England 2015. A report for Rural Business. 2015. <http://www.fbpartnership.co.uk/documents/Interim%20Assessment%20of%20Neonicotinoid%20Ban%20on%20Oilseed%20Rape.pdf>. Accessed 16 March 2016.
58. Gibbons D, Morrissey C, Mineau P. A review of the direct and indirect effects of neonicotinoids and fipronil on vertebrate wildlife. *Environ Sci Pollut Res*. 2015;22:103–18.
59. Godfray HCJ, Blacquière T, Field LM, Hails RS, Potts SG, Raine NE, Vanbergen AJ, McLean AR. A restatement of recent advances in the natural science evidence base concerning neonicotinoid insecticides and insect pollinators. *Proc R Soc B*. 2015;282:1818.
60. Collaboration for Environmental Evidence. 2013. Guidelines for Systematic Review and Evidence Synthesis in Environmental Management. Version 4.2. Environmental Evidence: www.environmentalevidence.org/Documents/Guidelines/Guidelines4.2.pdf. Accessed 20 June 2016.
61. Haddaway NR, Collins AM, Coughlin D, Kirk S. The role of Google Scholar in evidence reviews and Its applicability to grey literature searching. *PLoS ONE*. 2015. doi:10.1371/journal.pone.0138237.
62. Kottek M, Grieser J, Beck C, Rudolf B, Rubel F. World map of the Köppen–Geiger climate classification updated. *Meteorol Z*. 2006;15(3):259–63.
63. Higgins JPT, Altman DG, Sterne JAC. Chapter 8. Assessing risk of bias in included studies. In: Higgins JPT, Green S, editors. *Cochrane handbook for systematic reviews of interventions*, version 5.1.0. pp. The Cochrane Collaboration. 2011; http://handbook.cochrane.org/chapter_8/8_assessing_risk_of_bias_in_included_studies.htm. Accessed 12 Jan 2016.
64. Critical Appraisal Skills Programme (CASP). CASP Checklists 2014. Oxford. CASP. <http://www.casp-uk.net>. Accessed 12 Jan 2016.
65. Bilotta GS, Milner AM, Boyd IL. Quality assessment tools for evidence from environmental science. *Environ Evid*. 2014;3:14.

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