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What is the evidence that ecosystem components or functions have an impact on infectious diseases? A systematic review protocol

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Abstract

Background: Many infectious pathogens can be transmitted from animals to humans and vice versa, or by animals (especially arthropods) to humans. Such diseases are called zoonotic and/or vector-borne diseases. To control or prevent them, it is often recommended to target population reduction of host or vector species, through preventive culling or insecticide use for example. But these types of destructive interventions have shown several limits altering their efficiency, including acquired resistance of arthropods to insecticides, unpredicted change in the ecology of host populations, unexpected negative functional consequences on ecosystems, as well as economic embrittlement when livestock is concerned. An alternative pathway of action would be to rely on the functioning of ecosystems, and on their careful management, to regulate diseases and thus reduce their impact on human health. In this perspective, a thorough evaluation of the conditions that can potentially promote such a positive regulation of infectious pathogens by ecosystems, and their efficiency, is needed. Here, we present the protocol of a systematic review that will evaluate the scientific evidence existing on potential links between ecosystem components or functions and 14 vector-borne and zoonotic diseases impacting human health.

Methods: We will search for studies that tested the effect of changes in (i) biological communities, and (ii) habitats and landscapes, on diseases. Scientific literature from 5 publication databases will be screened in a 3-rounds process: title, abstract and full-text screening. At each stage, articles will be either rejected or kept for the next round, depending on whether they fall in the exclusion or inclusion criteria. We will present results in two parts: a systematic map and a systematic review. The systematic map will present, for the 14 diseases, the number of publications, their geographical distribution, the type of ecosystem component/function they studied, as well as the host(s) in which epidemiological measurements have been performed. From this systematic map, we will identify groups of articles that allow for critical appraisal, i.e. groups of articles that studied the effect of the same ecosystem component/function on the same disease. Only those articles will be included in the systematic review. The validity of these articles will be assessed by critical appraisal and presented as a narrative synthesis with confidence levels.

Keywords: Ecological function, Landscape, Dilution effect, Regulation, One health, Ecological control, Ecosystem functioning

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Background
About 60% of all infectious diseases infecting humans also infect wild and/or domesticated animals [1]. They are known as zoonotic diseases. Some of them are vector-borne, i.e., their causal infectious agents are transmitted by arthropods (mainly mosquitoes, ticks and sandflies). Zoonotic and vector-borne diseases are due to a variety of pathogens that can be viruses, bacteria and eukaryotes. They all have in common the presence of one or several animal species in their biological cycle. These species are parts of an ecosystem: they are embedded in a trophic network, they live, feed, reproduce in specific habitats or landscapes [2]. This leads to think that ecosystems and landscapes are somehow, positively or negatively, involved in human health [3, 4].

This idea might sound obvious and acceptable, but its integration in health policies, at national and international levels, is quite new [5, 6]. For many decades, health plans aiming to reduce the impact of vector-borne diseases on human health have been mainly focused toward chemical and physical anti-vectorial fight, i.e., destroying vectors and their habitats or micro-habitats [7]. When zoonotic diseases infecting livestock represent a significant threat for the economy [8], crisis mitigation strategies often rely on preventive culling of livestock or of wild hosts to stop the epizooty. France recently went through two epizootic events that illustrated this. Two cases of brucellosis detected in 2012, likely caused by contacts of cows with infected ibex (Capra ibex), led to the slaughter of 200 ibex in the Bargy mountains [9]. In 2016/2017, an epizooty of avian influenza in poultry farms led the authorities to order a 6-weeks swallowing period, and thus the preventive culling of several million of fowls [10].

But these methods have shown their limits. Concerning the use of insecticides, the first cases of mosquitoes resistant to an insecticide were reported within 1 year after the first spraying campaigns [11, 12]. Since then, insecticide resistance of mosquitoes has spread so much that pyrethroid insecticides no longer kill mosquitoes in many places of Africa [13], and that 60 countries among the 78 included in the monitoring program of the WHO reported mosquito resistance to at least one insecticide molecule [14].

For zoonotic diseases, attempts to control an epizooty through the culling of wild hosts can be totally inefficient. Field studies performed 1 year after the above-mentioned culling of ibex, showed that the prevalence of brucellosis in the infected ibex population had not been reduced. In fact, it had even increased in the younger individuals. Moreover, given that males from surrounding non-infected populations came to “fill the blanks” left by the culling, the risk to see the infection spread to other populations was considered as high [9]. Finally, massive preventive culling, such as the one performed in 2017 to stem avian influenza, have huge socio-economical costs, without mentioning the ethical questions raised by the culling of millions of healthy animals. Sociological studies performed in Great Britain to evaluate citizens’ opinions regarding the culling of badgers to control bovine tuberculosis showed a large disapproval of this type of destructive control methods [15]. These limits highlight the need for alternative control methods that would no longer be based on the direct destruction of populations or habitats, but rather on the regulation functions performed by ecosystems.

Several mechanisms have been described to explain how natural changes in species richness and abundance can regulate certain diseases. Among them, the dilution effect has been particularly studied and debated [16–20]. It states that, in an ecosystem with a rich host community, a pathogen would have a lower probability to find a highly competent host, i.e., a host in which it could multiply and, for a vector-borne disease, be transmitted to a suitable vector [21]. Several ecological conditions necessary for this dilution effect to occur have been proposed by Ostfeld and Keesing [21, 22]. One of them is the necessary tolerance of highly competent host species to perturbations, that enable them to become dominant while other species, less competent, decline. Such tolerance to perturbation has been reported for the white-footed mouse Peromyscus leucopus, a highly competent host for Lyme disease [23], and the American robin Turdus americanus, a highly competent host for the West Nile virus [24, 25]. A meta-analysis performed on 345 wetlands by Johnson et al. [26] found that host species highly competent for the parasite Ribeiroia ondatrae, responsible for amphibian limb malformations, dominate in species-poor communities, while richer communities contain more low-competent species, which decreases the overall host competence in the ecosystem.

Among dilution hosts, some species have a competence close to zero, and act as “ecological traps” for the pathogen or the vector. These species are sometimes referred to as “dead-end hosts”. This seems to be the case of the opossum Didelphis virginiana that kills the vast majority of ticks that attach to him [27]. It has also been reported for the roe deer Capreolus capreolus which has the ability to destroy in his bloodstream the spirochetes of Borrelia burgdorferi responsible for Lyme disease, thus preventing the infection of ticks that feed on roe deers [28]. However, the roe deer plays a key-role in the reproduction of Ixodes ticks, vectors of the Lyme disease agent [29], illustrating the complexity of interactions between diseases and ecosystems.
Ecological competition between vector/host species and species that occupy the same ecological niche but are not a vector/host for the pathogen can a priori be seen as a form of dilution effect. However, an experimental study performed by Johnson et al. [30] showed that increasing the diversity of snails reduced transmission of schistosomiasis, even when maintaining a constant density of the snail Biomphalaria glabrata, which was the only host of schistosomiasis in the studied snail community. This result suggests a positive effect of host diversity that would not be mediated by a decrease in the density or abundance of the host.

The regulation of diseases can also occur through predation that can decrease populations of vectors or hosts [31–33]. However, some authors suggest that not all predators are equally efficient in this respect, and that generalist predators can regulate host or vector populations more efficiently than specialized ones [34].

The examination of these various mechanisms leads us to suggest that modifications of habitats or landscapes structure, including by appropriate management, could also lead to changes in diseases incidence, by changing vector or host populations, or altering/enhancing certain population dynamics. This would relate to services provided by the regulation function of ecosystems. For example, a growing proportion of grasslands in agricultural landscapes has been shown to increase echinococcosis, by favoring populations of intermediate hosts, grassland rodents [35], and increasing predation by the red fox Vulpes vulpes, the definitive host of echinococcosis [36]. It is however interesting to notice that these ecological conditions, favorable to echinococcosis, would likely be unfavorable to other diseases such as Lyme disease. Indeed, in this case the red fox Vulpes vulpes is not a definitive host but acts at the contrary as a regulator of rodent hosts, thus potentially decreasing the incidence of the disease [32].

The links between the functioning of ecosystems, their modification, and infectious diseases are thus highly complex, and knowledge on these links is scattered and fragmented. This review has 2 main goals: first, to evaluate how much evidence exists about the links between ecosystem components/functions and 14 vector-borne and zoonotic diseases impacting human health, as preliminary scoping suggests that many knowledge gaps exist. Second, for diseases with existing relevant literature, the strength of those links will be appraised and synthesized.

**Stakeholder engagement**

This systematic review was commissioned by the French Ministry for the Ecological and Inclusive Transition, in the framework of the third National Action Plan for Health and Environment (2015–2019). The Ministry is accompanied by a working group of more than 15 stakeholders (mostly scientifically-oriented) who initially proposed a list of diseases to be assessed. The advancement of the mission is regularly reported to this group. The execution of the review was entrusted to the National Agency for Biodiversity (AFB) and the Foundation for Research on Biodiversity (FRB). The review team was initially composed of a core staff based in FRB/AFB and completed by a panel of experts. These experts were contacted upon consultation of the literature and upon suggestions made by the stakeholders. A total of 26 French-speaking experts from public research institutions or nature management agencies, working on the 5 continents, have accepted to collaborate. They belong to various disciplines such as eco-epidemiology, ecology of pathogens, vectors or hosts. This panel group was associated to the elaboration of the protocol and will participate to the whole review process.

A steering committee validates decisions on the framing on the review, the diseases to include, the experts to associate, etc. It is composed of representatives from 4 French ministries (Ecology, Health, Research, Agriculture), from ANSES,1 and from the National Action Plan.

**Objective of the review**

In this systematic review, we will assess the links between ecosystems and 14 vector-borne and zoonotic infectious diseases that have been identified by the French Ministry for Ecological and Inclusive Transition and the French Ministry for Health and Solidarities as causing, or susceptible to cause, a public health issue in France, including French Overseas Territories (cf. list below in “Definition of the question components”). These 14 diseases cover a large range of types of pathogen organisms (virus, bacteria, protozoan, nematode), with variable life-cycle complexity (single host, multi-hosts, vector-borne), and are linked to different types of ecosystems (aquatic, tropical forests, temperate forests, peri-urban, agricultural).

Our objective is double. First, produce a systematic map whose primary question will be “What knowledge exists on potential effects of ecosystem components or functions on the impact of vector-borne and zoonotic diseases?”. In this map, we aim to present, for 14 diseases, the existing knowledge in term, notably, of number of relevant articles and type of ecosystem function/component studied. Second, conduct a systematic review on the subset of diseases for which existing literature allows for critical appraisal. The question of this systematic review

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1 French Agency for Food, Environmental and Occupational Health & Safety.
will be: “What is the modifying effect of ecosystem components or functions on the impact of vector-borne and zoonotic diseases?”.

**Question definition and components**

The map will address the question: “What knowledge exists on potential effects of ecosystem components or functions on the impact of vector-borne and zoonotic diseases?”

The synthesis will answer to the question: “What is the modifying effect of ecosystem components or functions on the impact of vector-borne and zoonotic diseases?”

The question components are detailed hereafter:

**Population**

Ecosystems, habitats, landscapes, or ecological communities in which the pathogen agent causing one of the 14 selected diseases (i.e. leishmaniasis, schistosomiasis, Lyme disease, Malaria, dengue, chikungunya, Zika, West Nile disease, bovine tuberculosis, avian influenza, brucellosis, leptospirosis, echinococcosis, or cryptosporidiosis) is present.

**Exposure/intervention**

Any type of exposure/intervention susceptible to modify the biological cycle of the pathogen through modifications of habitats, landscapes, or ecological communities.

**Comparator**

Before/after an exposure/intervention; in space between habitats, ecosystems, or landscapes with different levels/intensities of exposure or with/without intervention.

**Outcome**

Any change, at any scale, in the incidence, prevalence, intensity or transmission of the disease in humans and/or vectors and/or animal hosts infected by pathogen agents responsible for the 14 diseases listed above.

**Methods**

**Searches**

**Search strategy**

Our search strategy has been designed to retrieve articles that cover a broad range of ecosystem components/functions and diseases. We will search for publications in 5 bibliographic databases, identified as relevant by the review team and the expert panel, and listed in “Bibliographic databases”. In each database, we will perform one search per disease. We will search in the “topic” section or in the title/abstract/keywords, whenever this option is possible. These databases are either available in open-access, or through a pre-existing subscription of FRB or research institutions of experts. Unpublished research articles will also be searched for, in an effort to minimize publication bias, and scientists from the expert panel and the enlarged committee have been asked to share unpublished articles.

Grey literature will be collected, and we will put effort in collecting reports from local initiatives (through environmental NGOs) or management practices (i.e. through national and regional natural parks). Institutional websites will also be searched for grey literature (see details in “Organizational websites”), but because they rarely allow complex searches, we will only use disease names as search terms.

**Search string**

The search string has been built based on a scoping exercise conducted on Web of Science in May–June 2018. This search string is structured into 3 elements related to Population and Outcomes. We chose not to use Intervention- or Exposure-related search terms, as it seemed impossible to exhaustively list them and thus retrieve all the possible range of them.

The 1st element targets articles mentioning the required disease or pathogen agent(s). It is the only part of the search string that will differ between searches for different diseases. Synonyms of disease names, including vernacular names, were listed using the Mesh database and Google and will be included in the search string. This list can be found in Additional file 1, along with the list of pathogen agents identified for each disease. The 2nd element contains keywords related to the structure and the functioning of ecological communities. The 3rd element contains altogether generalist keywords related to ecosystems or ecology (part 3a) and a list of habitat types (part 3b) in order to try retrieve specific field studies that do not mention the generalist keywords. This list of habitats has been built based on the habitat classification from UICN [37], from which we selected first-level habitats relevant for the 14 diseases included in the review (i.e. all habitats except marine habitats, rocky areas and deserts) and added synonyms.

The 3 elements will be combined using the Boolean operators AND (both terms must be found) and OR (at least one term must appear), as follow: 1 AND 2 AND (3a OR 3b).

The operator NEAR/5 (both terms must appear, with 5 words maximum between them) will be used inside the 2nd element. The “*” wildcard will allow to retrieve plurals and words sharing the same root such as the words “predator”, “predation”, “predated” (etc.) from the single word predat*.

Detailed search string, as designed for the Web of Science database:
(Name(s) of the disease OR name(s) of the pathogen agent(s)) AND
((species OR vector OR host OR community OR population OR prey) NEAR/5 (compos* OR structure* OR divers* OR density* OR rich* OR abundance* OR dynamic* OR increase* OR decrease* OR change* OR homogen* OR heterogen*)) AND
((land* OR habitat OR ecology* OR ecosystem* OR predator* OR wildlife OR “wild life” or “wild animals” OR “wild fauna” OR biodiversity OR “dilution effect”) OR
(forest* OR shrub* OR scrub* OR wood* OR grass* OR pasture* OR arable* OR wetland OR peat* OR grove OR hedgerow OR mangrove OR savanna* OR bush OR bushes OR ricefield OR “rice fields” OR paddy OR plantation OR tundra OR pond OR canal OR ditch OR river OR stream OR creek OR bog OR marsh OR swamp OR fen OR lake OR oases OR delta OR mountain OR cave OR estuary OR dune OR lagoon OR island OR garden OR park OR "green areas")

This search string was validated by the expert panel. It will be adapted to the specific requirements of each bibliographic database (Boolean operator accepted, maximum number of words). If it must be reduced, priority will be given to the 1st and 2nd elements of the search string. The search string used in each database will be reported in an Additional file attached to the systematic review to ensure replicability and facilitate future upgrading.

Language
For most diseases, we will search for literature written in English and in French. This should allow to screen most of the peer-reviewed scientific literature as well as research published in French and adapted to the French context. For leishmaniasis and schistosomiasis, two diseases that marginally affect mainland France, but that are a major concern in French Guiana and French Caribbean islands, we will also search for literature in Spanish, to include studies performed in south/central America and in the Caribbean islands.

The potential sources of grey literature that we identified are either international institutions, or French institutions, so we will perform the search in English and French.

Bibliographic databases
Publications will be collected from the following databases:

- PubMed
- Science Direct
- Scopus
- Web of Science Core Collection

Web-based search engines
Internet searches were used only at the scoping stage, to start building the test-lists. We limited our search to the results contained in the first 3 pages in:

- Google scholar (https://scholar.google.com)
- Google (https://www.google.com)

Organizational websites
The 13 organizations whose websites will be searched are listed below:

- World Health Organization (https://www.who.int)
- World Organization for Animal Health (https://www.oie.int)
- Centers for Disease Control and Prevention (https://www.cdc.gov)
- European Center for Disease Prevention and Control (https://www.ecdc.europa.eu)
- EcoHealth (https://www.ecohealthalliance.org)
- European Commission for Environment (https://www.ec.europa.eu/environment/index_en.htm)
- Food and Agriculture Organization (https://www.fao.org)
- French Ministry for the Ecological and Inclusive Transition (https://www.ecologique-solidaire.gouv.fr)
- French Ministry for Solidarity and Health (https://www.social-sante.gouv.fr)
- French Ministry for Agriculture and Alimentation (https://www.agriculture.gouv.fr)
- National Agency for Sanitary Security of Food, Environment and Work (https://www.anses.fr)
- Public Health France (https://www.invs.publiquefrance.fr)
- National Office for Hunting and Wild Fauna (http://www.oncfs.gouv.fr)

Estimating the comprehensiveness of the search
To evaluate the performance of our search (see Additional file 2), we used test-lists built by the expert panel and the project leader. These test-lists are composed of articles identified as key-articles by the expert panel or by the review team, and collected using personal knowledge, private bibliographic files, searches on Google and Google scholar. Relevant reviews identified were not
included in the test-lists, but the bibliographic references they contained were investigated to find other key-articles, using the snow-balling method.

For 5 of the 14 diseases, the number of relevant articles initially found ranged between 22 and 4, respectively for Lyme disease (n = 22), West Nile virus (n = 15), echinococcosis (n = 12), schistosomiasis (n = 6) and malaria (n = 4). The number of articles from these 5 test-lists retrieved by our bibliographic search are reported in Additional file 2.

For the other diseases, we were either not able to identify any relevant article (cryptosporidiosis, leishmaniasis, avian influenza, Zika, bovine tuberculosis), only 1 article (Chikungunya, dengue virus, brucellosis) or only 2 articles (leptospirosis). This quasi-emptiness of 9 test-lists is likely to reflect the scarcity of existing literature on what is a quite new research topic for many diseases. The non-empty test-lists can be consulted in the Additional file 2.

Search update
We will provide the date of the searches performed in each database as well as the exact search string to facilitate a future upgrading of the work.

Given that we will present both a systematic map and a systematic review, the subsequent part of this protocol is divided in two: the sections “Article screening and study inclusion criteria”, “Study validity assessment”, “Data coding strategy”, “Study mapping and presentation” detail the protocol for the systematic map, and the sections “Study inclusion criteria”, “Critical appraisal”, “Data extraction”, “Potential effect modifiers/reasons for heterogeneity”, “Data synthesis and presentation” describe the protocol for the systematic review.

Systematic map
Article screening and study inclusion criteria
Using the reference management software Zotero®, all exported articles and documents will be organized into separate collections, one for each disease. Once the searches completed (one per disease and per database), references for each search will be archived in a unique database, and duplicates will be removed.

Articles retrieved by the bibliographic search will be screened as detailed below to keep only those relevant for the map. An additional step of eligibility (detailed in the “Eligibility criteria” section of the “Systematic review” part of the protocol), will be performed to select the subset of articles included in the synthesis.

Screening strategy
The screening of titles, abstracts and full-texts will be performed by 3 members of the review team. Eligibility criteria have been proposed by the review team and validated by the expert panel.

Consistency checking
Prior to the beginning of the screening, the 3 persons from the review team will screen the titles of 42 articles (3 per disease) randomly extracted from those retrieved by the search equation. The Kappa scores should be larger than 0.6. Differences in screening decisions will be discussed, the eligibility criteria refined, and the screening test performed on 42 different articles, with the aim at improving the Kappa scores, if needed.

The same exercise will be conducted on 28 abstracts (2 per disease).

At the full-text stage, a double-checking of all articles rejected will be performed by the project leader.

Eligibility criteria
Different eligibility criteria will be applied at the 3 steps of the screening: title, abstract, and full-text. If the information provided by the title or abstract is not enough to reject or retain the article with certainty, it will be retained and examined at the next eligibility stage.

Title
Inclusion criteria: presence of the name of the disease or of the pathogen agent responsible for this disease, or presence of a generic term related to infectious diseases or pathogens (to ensure we do not reject relevant papers when the title is not precise enough). In the case of vector-borne diseases, the title may not contain any of the above criteria but would still be eligible if it contains the name of the vector or a generic term related to vectors (e.g. mosquitoes, ticks, vectors). The list of pathogen agents and vectors identified for each disease can be found in Additional file 1.

Exclusion criteria: absence of the above-mentioned elements; or indication that the article is a review, a meta-analysis, an opinion paper, ex situ studies or theoretical modelling. Relevant reviews and meta-analysis will be kept in a separate collection for use in the discussion of our work.

Abstract
Inclusion criteria: presence of words related to ecosystem components, functioning, or management.

Exclusion criteria: similar as for title or elements showing that the paper is a descriptive study (no exposure/intervention, no comparator); destructive intervention targeted towards a vector or a host; intervention non-related to ecosystems, such as individual prophylaxis, micro-habitats removal (tires, flower pots), spraying of
organic insecticides, genetical modifications of vectors, etc.

**Full text**
Inclusion criteria: the outcome has been obtained from field data (e.g. vector/host collection on the field, epidemiological database collected in hospitals); presence of all PECO elements detailed in the section “Definition of the question components”.

Exclusion criteria: similar to those applied for title or abstract screening, or elements informing that the outcome is the output of a model, or has been obtained ex situ (e.g. in laboratory).

**Reasons for exclusion**
The list of articles excluded at full-text will be provided, with reason for their exclusion.

**Study validity assessment**
Critical appraisal will be limited to the identification of research design, but susceptibility to bias will not be assessed. The type and diversity of research designs will be reported in the narrative synthesis accompanying the systematic map. We expect to find research designs such as: post hoc surveys, cross-sectional studies, time-series, and maybe a few before-after studies.

**Data coding strategy**
Meta-data extraction for mapping will be performed by the 3 members of the review team. Meta-data will be extracted from all articles retained after the screening process. From the full-text of these articles, we will extract and store in an Excel database the following information:

- Title
- First author
- Year of publication
- Country
- Continent
- Disease
- Study design
- Type of ecosystem component/function
- Outcome measured in vector (yes/no)
- Outcome measured in intermediate host (yes/no)
- Outcome measured in non-human final host (yes/no)
- Outcome measured in human (yes/no)

In the “Country” column, the name of the country/countries in which field study was performed or data collected will be written. Studies performed at the global scale will be attributed the code “global”.

For the name of the disease, the coding will follow the list presented in the section Question components.

We will code study designs as follow: PH for post hoc surveys, CS for cross-sectional studies, TS for time-series, and BA for before-after studies.

We expect to describe ecosystem components/function with the following list established during scoping: predation, competition, dilution (includes host species richness/diversity), host density/abundance, community composition, landscape composition, landscape structure, habitat type, vegetation measurement (NDVI, % of vegetation cover), habitat perturbation, distance to habitat, habitat management. This list may be revised as appropriate if other components/functions are identified during examination at full-text.

To facilitate the use of the map, epidemiological outcomes will be coded in 4 different columns, signaling where measurements have been conducted.

**Study mapping and presentation**
The systematic map will be reported as an Excel spreadsheet. A geographical map will present for each disease the geographical distribution of publications. Then, we will analyse for each disease the characteristics of publications per type of ecosystem component/function (i.e. Exposure), and per type of epidemiological measurement (i.e. Outcome). These results will be presented in tables (one per disease) to highlight knowledge gaps and trends in research orientations, and as a narrative description.

**Systematic review**
**Study inclusion criteria**
From the systematic map table, we will identify group(s) of at least 2 articles that have in common a) the same disease AND b) the same ecosystem component/function (listed in the “Data coding” section). Within each group, we will perform critical appraisal and metadata extraction, and synthesize the outcome.

Articles that are not part of any group will be only reported in the systematic map section.

**Critical appraisal**
**Critical appraisal strategy**
Each study included in synthesis will be critically appraised. Expert consultation allowed us to identify and prioritize criteria for critical appraisal. As this can vary between diseases, one critical appraisal grid will be produced for each disease, and presented as an additional file to the final manuscript. Each of these grids will list the different aspects of the studies that need to be considered to estimate the risk of bias considering the specificities of each disease. It will be composed of elements related to both internal and external validity. Each study
will be assessed against each criterion and will obtain a high, medium/high, medium/low or low rank regarding its risk of bias. We will present these grids in the systematic review (see also criteria in section below).

**Critical appraisal used in synthesis**

Results from papers with a low and medium/low risk of bias will be synthesized first. We will report whether they are consistent or heterogeneous and hypothesis will be made regarding reasons for heterogeneity. Results from studies with a medium/high risk of bias will be examined subsequently to determine whether they are consistent with results from papers with a low and medium/low risk of bias and convene extra possible explanations for heterogeneity. Studies with an unclear or high risk of bias will be excluded from the synthesis, unless they compose the majority of the relevant literature. In this case, the emphasis will be put on the reasons why biases are high and how to possibly remediate to this in future research. The list of papers with a high risk of bias will be provided with reasons for their exclusion.

**Critical appraisal criteria**

The grid that will be used to critically appraise each study may list the following elements:

**A. To assess internal validity:**

- Duration of the study: Many diseases that have one or several animal hosts in their cycle show a marked inter-annual variation due to population dynamics, masting etc. Post-intervention/exposure effects might also take some time before being measurable, or at the contrary be very transient and disappear quickly. We will thus consider that long studies would increase the sustainability of results, although measurements could have more chance to be affected by variations of the environment independent of the intervention/exposure initially examined.

- Distance between replicates of between treatment and control: depending of the biology of each disease, a "buffer distance" between replicates or between treatment and control sites might be relevant and established. Trade-off with the interest of having replicates in the same ecosystem, to ensure having similar conditions, will be discussed with the expert panel.

- Study design: before-after intervention/exposure studies may be obtained although we do not expect to find BACI-designs. We expect to find mostly longitudinal studies, cross-sectional studies, and possibly time-series.

- Randomization: may be found when choosing sampling plots.

- Sampling methodology: here we will examine how the intervention(s)/exposure(s) has been described, the outcomes(s) measured, and elements of robustness will be established by the expert panel.

- Accuracy of measurements: replication of measurements or analysis may be a way to minimize errors or hazardous results.

- Potential effect modifiers: we will assess if they have been identified and/or accounted for (see details in “Potential effect modifiers/reasons for heterogeneity”).

**B. To assess external validity:**

- Replications in sites with contrasted conditions (e.g. intervention performed in different regions) would be highly valuable.

Biases identified and/or reported by the authors of the articles will be added to this list when reading papers at full-text stage, if considered relevant for our question.

**Consistency checking**

Prior to beginning the critical appraisal, 2 persons from the review team will evaluate a sample of 5 randomly-extracted articles, using the same critical appraisal grid. We will discuss potential differences, and if necessary refine the grid and repeat the exercise on 5 new articles.

**Data extraction**

**Meta-data extraction and coding strategy**

Groups or articles studying the same disease and the same ecosystem component/function will be identified from the map, and submitted to critical appraisal. Then, meta-data extraction for synthesis will be performed by the 3 members of the review team. Meta-data will be extracted from articles with a low, medium/low and medium/high risk of bias.

The same data extraction table will be used for all diseases, but reporting will be limited to variables that are relevant to each disease (for instance, not reporting vector-related information for non-vector-borne diseases). Below are listed the meta-data that will be extracted, related to the context of studies, and the PECO elements. This list will be implemented during a meeting of the expert panel that will take place prior to meta-data extraction.

**Context**

- Country, city
- GPS coordinates of study site
- Temperate/tropical climate
• Publication date

Population
• Type of ecosystem
• Type(s) of habitat(s)
• Pathogen(s)
• Vector(s)
• Host(s)
• Ecosystem component/function
• Ecosystem-related variables measured (abundance, diversity, richness…)
• Taxonomic group in which the measure was made (i.e. rodents, birds, known hosts, predators, one particular species…)
• Data collection (on field, from database)

Intervention/exposure
• Description of the intervention
• Description of the exposure
• Date of the intervention/exposure

Comparator
• Type of study design
• Duration of follow-up (if before/after or time series)
• Number of sites
• Number of replicates per site
• Distance between sites, between replicates

Outcome
• Date of outcome measurements
• Measured epidemiologic variable (incidence, prevalence, transmission…)
• Species (human, vector, host)
• Number of individuals tested for infection
• Protocol for vector collection or sampling (stage (larvae, nymph, adult), with/without human bait)
• Method used to test for infection
• Ratio of females/males for mosquitoes and sand-flies
• Source of human epidemiologic data (field measures, hospital data, national database…)

Data extraction strategy
Data will be extracted from the narrative or figures/tables of each article. Priority will be given to primary datasets if considered useful for subsequent analysis, or to descriptive statistics (means, medians, standard deviations).

Approaches to missing data
In the case of missing meta-data, NA will be mentioned in the table. Missing data will be reported as such if they represent an attrition bias.

Consistency checking
The 3 members of the review team will read the same 5 articles and fill the same meta-data extraction grid. Results will be compared, and the grid refined if needed. A random sample of 20 studies will be double-checked by the project leader.

Potential effect modifiers/reasons for heterogeneity
We will identify the potential effect modifiers in order to better understand the different effects that a similar management option could have in different studies.
We anticipate that these potential effects modifiers will be very important for certain diseases that have a very large geographical area, thus occurring in extremely various ecosystems, and that can infect or be vectored by different species.

• Study location
• Climatic conditions
• Non-biological changes associated with intervention/exposure (change in temperature, shadow, hydrological micro-conditions…)
• Time and period of specimen collection for vectors/hosts in relation with their known daily and seasonal activity.
• Type of ecosystem
• History of the ecosystem (past modifications etc.)
• Time since intervention, in the case of before/after study design.
• Socio-economical context (proximity with animals (potential hosts such as rodents, but also zooprophylaxis), use of prophylaxis…)
• For zoonoses affecting livestock: breeding practices (size of herds, breeds, transhumance, veterinary surveillance and treatments…)

Data synthesis and presentation

Type of synthesis
The synthesis will focus on the subset of diseases for which relevant literature is available and allows for critical appraisal. This review will mostly be presented as a narrative synthesis with confidence levels.
Narrative synthesis strategy
The eligible literature will be synthesized in a narrative format including confidence levels based on the quality assessment of each article. Contradictory results will be resumed, with an attempt to provide an explanation of the reason(s) for their differences.

Quantitative synthesis strategy
We do not expect to have enough compatible datasets (i.e. enough publications studying the same disease, the same ecosystem component, and the same outcome) to perform meta-analysis.

Qualitative synthesis strategy
As mentioned in the “Eligibility criteria” section, we will only retrieve articles in which the outcome has been measured and is thus quantitative. Qualitative outcomes, such as a change in the perceived risk of disease by a population are not eligible. Thus, we do not expect to find any qualitative data in this review.

Assessment of risk of publication bias
The risk of publication bias is taken in account by looking for grey literature directly on institutional websites, and for unpublished articles through solicitation of experts.

Knowledge gap identification strategy
Identification of knowledge gaps will be conducted at various stages of the review: once literature is screened and mapped, absence of articles related to Population, Intervention/Exposure or Outcome may be reported. During the narrative synthesis, gaps in research designs or specific measurements (including that of biases) might be highlighted as well.

Demonstrating procedural independence
The screening process will be done by 3 members of the review team that have no particular expertise on any of the 14 diseases and are not author or co-author of any article potentially retrieved by the bibliographic search. Experts will join the review process once the screening is completed, to participate to the extraction of meta-data and the critical appraisal.

Additional files

**Additional file 1.** Names of the (I) diseases, (II) pathogen agents, and (III) vector species.

**Additional file 2.** Test lists, and number of articles from the test lists retrieved by the bibliographic search.

Authors’ contributions
This systematic review protocol is based on a draft written by LL, and all co-authors contributed to its elaboration. BL, CM, VR, SL and MdGW contributed to improve the manuscript. All authors read and approved the final manuscript.

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Competing interests
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References
1. Taylor LH, Latham SM, Woolhouse ME. Risk factors for human disease emergence. Philos Trans R Soc Lond B Biol Sci. 2001;356(1411):983–9. https://doi.org/10.1098/rstb.2001.0888.

2. Horwitz P, Wilcox BA. Parasites, ecosystems and sustainability: an ecological and complex systems perspective. Int J Parasitol. 2005;35(7):725–32. https://doi.org/10.1016/j.ijpara.2005.03.002.

3. Keesing F, Belden LK,Daszak P, Dobson A, Harvell CD, Holt RD, et al. Impacts of biodiversity on the emergence and transmission of infectious diseases. Nature. 2010;468(7324):647–52. https://doi.org/10.1038/nature09575.

4. Wood CL, Lafferty KD, DeLeo G, Young HS, Hudson PJ, Kuris AM. Does biodiversity protect humans against infectious disease? Ecology. 2014;95(4):817–32. https://doi.org/10.1890/13-1041.1.

5. CBD-WHO, 2015. https://www.cbd.int/health/SOK-biodiversity-en.pdf. Accessed 17 July 2018.

6. PNSE3, 2014. http://solidarites-sante.gouv.fr/IMC/pdf/pnse3_v_finale.pdf. Accessed 17 July 2018.

7. Becker N, Petrić D, Boase C, Lane J, Zgomba M, Dahl C, Kaiser A. Mosquitoes and their control. New York: Springer. 2003;2:441–481. https://doi.org/10.1007/978-3-540-92874-4.

8. World Bank. 2010. People, pathogens, and our planet: Volume one: towards a one health approach for controlling zoonotic diseases (English). Washington, DC: World Bank. http://documents.worldbank.org/curated/en/21470146833893565/Volume-one-towards-a-one-health-approach-for-controlling-zoonotic-diseases. Accessed 17 July 2018.

9. Anses. Mesures de maîtrise de la brucellose chez les bovins de la France. 2015. https://www.anses.fr/fr/system/files/SANT2014sa0218Ra.pdf. Accessed 17 July 2018.
10. Anses. Avis relatif au périmètre optimal de dépeuplement préventif influenza aviaire IA HP H5N8. 2017. https://www.anses.fr/fr/system/files/SABA2017SA0011.pdf. Accessed 17 July 2018.

11. Brown AW. Insecticide resistance in mosquitoes: a pragmatic review. J Am Mosq Control Assoc. 1996;2(2):123–40.

12. Hemingway J, Ranson H. Insecticide resistance in insect vectors of human disease. Annu Rev Entomol. 2000;45(1):371–91. https://doi.org/10.1146/annurev.ento.45.1.371.

13. Hemingway J, Ranson H, Magill A, Kolaczinski J, Fornadel C, Gimnig J, et al. Averting a malaria disaster: will insecticide resistance derail malaria control? Lancet. 2016;387(10029):1785–8. https://doi.org/10.1016/S0140-6736(15)00417-1.

14. World Health Organization. World malaria report 2015. World Health Organization. http://apps.who.int/iris/bitstream/handle/10665/20018/9789241565158_eng.pdf?sequence=1. Accessed 17 July 2018.

15. Bennett R, Willis K. Public opinions on badger populations and the control of tuberculosis in cattle in the uk. Vet Rec. 2007;160(8):266–8. https://doi.org/10.1136/vr.160.8.266.

16. Schmidt KA, Ostfeld RS. Biodiversity and the dilution effect in disease ecology. Ecology. 2001;82(3):609–19. https://doi.org/10.1890/0012-9658(2001)082%5b0609:BDTEID%5d2.0.CO;2.

17. LoGiudice K, Ostfeld RS, Schmidt KA, Keesing F. The ecology of infectious disease: effects of host diversity and community composition on Lyme disease risk. Proc Natl Acad Sci. 2000;100(2):567–71. https://doi.org/10.1073/pnas.0323733100.

18. Johnson PTJ, Thieltges DW. Diversity, decays and the dilution effect: how ecological communities affect disease risk. J Exp Biol. 2010;213(6):961–70. https://doi.org/10.1242/jeb.037721.

19. Randolph SE, Dobson ADM. Pangloss revisited: a critique of the dilution effect and the biodiversity-buffers-disease paradigm. Parasitology. 2012;139(7):847–63. https://doi.org/10.1017/S0031182012000200.

20. Civitello DJ, Cohen J, Fatima H, Halstead NT, Liriano J, McMahon TA, et al. Biodiversity inhibits parasites: broad evidence for the dilution effect. Proc Natl Acad Sci. 2015;112(28):8667–71. https://doi.org/10.1073/pnas.1506279112.

21. Ostfeld RS, Keesing F. The function of biodiversity in the ecology of vector-borne zoonotic diseases. 2000;178.

22. Ostfeld RS, Keesing F. Effects of host diversity on infectious disease. Annu Rev Ecol Syst. 2012;43(1):157–82. https://doi.org/10.1146/annurev-ecolsys-102710-145022.

23. Allan BF, Keesing F, Ostfeld RS. Effect of forest fragmentation on Lyme disease risk. Conserv Biol. 2003;17(1):267–72. https://doi.org/10.1111/j.1523-1739.2003.01260.x.

24. Marm Kilpatrick A, Daszak P, Jones MJ, Marra PP, Kramer LD. Host heterogeneity dominates West Nile virus transmission. Proc Biol Sci. 2006;273(1599):2327–33. https://doi.org/10.1098/rspb.2006.3575.

25. Kilpatrick AM. Globalization, land use and the invasion of West Nile virus. Science. 2011;334(6054):323–7. https://doi.org/10.1126/science.1210100.

26. Johnson PTJ, Preston DL, Hoverman JT, Richgels KLD. Biodiversity decreases disease through predictable changes in host community competence. Nature. 2013;494(7436):230–3. https://doi.org/10.1038/nature11883.

27. Keesing F, Brunner J, Duerer S, Killiela M, LoGiudice K, Schmidt K, et al. Hosts as ecological traps for the vector of Lyme disease. Proc R Soc B Biol Sci. 2009;276(1675):3911–9. https://doi.org/10.1098/rspb.2009.1159.

28. Jaenson TGT, Tälleklint L. Incompetence of roe deer as reservoirs of the Lyme borreliosis spirochete. J Med Entomol. 1992;29(5):813–7. https://doi.org/10.1093/jmedent/29.5.813.

29. Kiffner C, Lodice C, Alings M, Vor T, Ruhe F. Attachment site selection of ticks on roe deer, Capreolus capreolus. Exp Appl Acarol. 2011;53(1):79–94. https://doi.org/10.1007/s10493-010-9378-4.

30. Johnson PT, Lund PJ, Hartson RE, Yoshino TP. Community diversity reduces Schistosoma mansoni transmission, host pathology and human infection risk. Proc R Soc B Biol Sci. 2009;276(1662):1657–63. https://doi.org/10.1098/rspb.2008.1718.

31. Reiskind MH, Wund MA. Experimental assessment of the impacts of northern long-eared bats on ovipositing Culex (Diptera: Culicidae) mosquitoes. J Med Entomol. 2009;46(5):1037–44. https://doi.org/10.1603/033.046.0510.

32. Leit V, Kilpatrick AM, Mangel M, Wilmers CC. Deer, predators, and the emergence of Lyme disease. PNAS. 2012. https://doi.org/10.1073/pnas.1204536109.

33. Sokolow SH, Hutteringer E, Jouanard N, Hield MH, Lafferty KD, Kuris AM, et al. Reduced transmission of human schistosomiasis after restoration of a native river prawn that preys on the snail intermediate host. Proc Natl Acad Sci. 2015;112(31):9650–5. https://doi.org/10.1073/pnas.1502651112.

34. Ostfeld RS, Holt RD. Are predators good for your health? Evaluating evidence for top-down regulation of zoonotic disease reservoirs. Front Ecol Environ. 2004;2(1):13–20. https://doi.org/10.1890/1540-2696(2004)02%5b0013:APGFYH%5d2.0.CO;2.

35. Giraudoux P, Craig PS, Delattre P, Bao G, Bartholomot B, Harraga S, et al. Interactions between landscape changes and host communities can regulate Echinococcus multilocularis transmission. Parasitology. 2003;127(7):S119–29. https://doi.org/10.1017/S0031182003003512.

36. Weber JM, Aubry S. Predation by foxes, Vulpes vulpes, on the fossorial rodent, Cricetus cricetus, in Spain. J Zool. 1993;229(4):553–9. https://doi.org/10.1111/j.1469-7998.1993.tb02656.x.

37. UICN (2012). http://xml.awomens.com/ucmediclist/newcms/staging/public/attachments/3125/dec_2012_guidance_habitats_classification_scheme.pdf. Accessed 17 July 2018.