

SYSTEMATIC REVIEW

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A systematic review of the effectiveness and utility of Lyme disease prevention measures in Canada, the United States, and Europe

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Abstract

Background This systematic review aimed to assess the effectiveness of interventions which reduce human-tick encounters, prevent tick bites, and reduce the risk of *Borrelia burgdorferi* transmission, and to evaluate knowledge on the cost, environmental impact, social impact and acceptability, and public health impact of these interventions.

Methods The search was conducted in Medline, Embase, Global Health, CAB Abstracts, Cochrane CENTRAL, Scopus, and Econlit for relevant literature in March 2022 and was updated in November 2024 and followed PRISMA guidelines for systematic reviews. Inclusion was applied at citation and full text, after which articles were assessed for risk of bias and data was extracted by two independent reviewers. Studies were summarized by intervention type (landscape management, host animal parasitism and movement, chemical/natural/botanical applications, personal protection) and a multi-study synthesis of tick suppression effects was conducted for interventions that reported the density of infected nymphs as the primary outcome.

Results One hundred and twenty-seven studies published between 1977 and 2024 were included in this systematic review. Most studies ($n=62$) were classified as host-targeted interventions. Twenty-five studies were included in the multi-study synthesis of tick suppression effects, which suggested that chemical tick control methods are the most effective and consistent intervention type with 93.8% mean suppression of questing nymphs.

Conclusion While some strategies such as chemical acaricides were shown to have greater effectiveness, factors such as social acceptability and resistance, environmental impact, cost, and feasibility should be considered when selecting the most appropriate intervention to maximize the utility of the intervention.

Keywords Systematic review, Tick control, Lyme disease control, Multi-study synthesis, Feasibility, Utility, Effectiveness

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Introduction

LD is the most common vector-borne disease in the northern hemisphere with the risk of transmission to humans intensifying and expanding as vector tick populations for *B.burgdorferi* spirochetes expand their geographic range [1–4]. Lyme disease (LD) is caused by several bacterial genospecies belonging to the *Borrelia burgdorferi* sensu lato (s.l.) complex, including *Borrelia burgdorferi* sensu stricto (s.s.), *Borrelia mayonii*, *Borrelia afzelii*, and *Borrelia garinii*, (*B.burgdorferi*) that are transmitted to humans by several species of *Ixodes* ticks found in the Northern Hemisphere, particularly in the North America (primarily United States and Canada), Central and Eastern Europe, as well as Asia (including parts of China, Japan, and Russia) [5]. In its early stage, LD is associated with febrile illness and rash which, if untreated, may progress to neurologic and myocardial abnormalities [6]. Untreated patients with late-stage symptoms may present with arthritis and chronic central nervous system abnormalities, which may also manifest after clinically successful treatment of the early stage [6]. Changing climactic conditions along with factor such as urbanization, landscape fragmentation, and population growth have contributed to this increasing risk of disease transmission in recent years [7–11].

In North America, including Canada, LD is primarily caused by the genospecies *Borrelia burgdorferi* sensu stricto (s.s.) [12]. The main vector ticks of the *B.burgdorferi* spirochetes in North America are *Ixodes scapularis* and *Ixodes pacificus* [12]. Across Canada, active and passive surveillance efforts have revealed variations in the distribution of the two species: *Ixodes scapularis* is found primarily in central and eastern Canada, while *Ixodes pacificus* is mainly confined to British Columbia [13]. In the United States, current data indicate that *Ixodes scapularis* is widely established across all four cardinal regions, whereas *Ixodes pacificus* is predominantly reported in the Pacific Coast states [14]. The incidence of LD in Canada has increased to 8.2 cases per 100,000 people in 2021 from 0.8 cases per 100,000 in 2011; with the majority of these cases (95.6%) from the provinces of Ontario, Nova Scotia, and Quebec [15]. The incidence of LD in the United States was 18.8 per 100,000 in 2022 after the implementation of a new (more sensitive) case definition, and LD incidence is primarily focused in the Northeast and parts of the Midwestern region of the country. In both Canada and the United States, there is significant under-reporting of LD due to i) under-ascertainment, and ii) under-diagnosis [16, 17].

Ixodes scapularis and *I. pacificus* complete their life cycle over two and three-year periods, respectively [18]. *Ixodes scapularis* ticks, the primary vector of interest, seek bloodmeals from small or medium-sized mammals

or birds, in their first two life stages, with the white footed mouse (*Peromyscus leucopus*) often considered as the primary reservoir of *B. burgdorferi*. Adult *I. scapularis* and *I. ricinus* ticks actively seek out their primary reproductive host, the white-tailed deer in North America (*Odocoileus virginianus*) and roe deer (*Capreolus capreolus*) in Europe which play an important role in the establishment and growth of tick populations [19]. Forested areas with deciduous trees and higher levels of leaf litter, or low-lying vegetation and shrubs, promote the survival of vector ticks and constitute suitable habitats for many of their wildlife hosts, such as deer, small mammals, and birds [20, 21]. Furthermore, ecotones between forested areas and other habitat types have been identified as high-risk areas for tick-host interactions [22].

The complex ecology and life cycle of the vector tick and the bacteria causing LD calls for a diverse and multifaceted approach when it comes to controlling LD spread and transmission. Existing strategies can be broadly divided into four approaches: 1) landscape management; 2) host-targeted management of wildlife parasitism, infection, movement, and density; 3) chemical insecticides, biological control agents, natural tick control products applied to the environment; and 4) personal protection methods. With increasing rates of LD in Canada, there is a need for efficacious and locally relevant control strategies for both the LD bacterium and its vector. Furthermore, there is increasing evidence to support the use of multiple strategies in an integrated approach to tick control and LD transmission, despite there being relatively few studies on these combined approaches [23].

Landscape management strategies aim to reduce landscape features which either support the growth of tick populations (like invasive barberry and deep leaf litter), or successful tick questing opportunities (such as long grasses and other low-lying shrubs) [24]. Landscape management can consist of strategies feasible and accessible to many home and property owners such as mowing long grasses and leaf litter removal, or more involved strategies such as woodland ecotone modification using substrates, controlled burns, or vegetation clearing using manual or chemical strategies [24].

Chemical insecticides, biological control agents, and naturally derived tick control products are typically applied to the environment in areas of tick habitat. Chemical insecticides like organophosphates, carbamates, and pyrethroids have been successfully applied in many vector control research studies in the past and present [24], however due to concerns on environmental sustainability and their impact on non-target species, there is growing demand for natural alternatives [25]. Biological control and natural products include many plant-derived products such as garlic (Mosquito

Barrier ©) and Alaskan cedar (Nootkatone) [26]. Other control measures are natural or biological control agents such as entomopathogenic fungi, bacteria, and nematodes [26]. Both plant-derived products, and biologic agents are either used to reduce tick survival or fitness to quest for a bloodmeal and reproductive capabilities [27]. Additionally, there have also been some studies examining the impact of natural predators, namely wolf spiders *Lycosidae spp.* on tick activity and survival [28, 29].

Strategies that incorporate host-targeted management of wildlife parasitism, infection, movement, and density can function through several pathways. These strategies can reduce tick population density through targeting their primary reproductive hosts, white-tailed or roe deer (*Odocoileus virginianus* or *Capreolus capreolus* respectively), with products aimed to kill attached ticks, reducing the number of ticks that successfully reproduce. Host-targeted strategies often use bait methods, such as 4-Poster devices that allow deer to self-treat with topical acaricide while feeding at the device [30]. For rodent reservoirs, primarily the white footed-mouse (*Peromyscus leucopus*), strategies often utilize bait boxes that deliver oral or topical acaricides to small mammals that cause/induce mortality in attached ticks [31, 32]. Treated nesting materials are often used in studies to reduce tick abundance on small mammals, accomplished through permethrin-treated cotton placed in cardboard applicator tubes referred to as tick tubes. This cotton material is collected by rodents and brought back to their nests, allowing for the transfer of a topical dose of acaricide, killing ticks that are present in the nesting environment [32]. Additionally, there are some approaches in this category that reduce enzootic transmission without impacting tick populations through prophylaxis treatments (such as doxycycline) or vaccination (oral or injectable) of small mammal reservoirs. Finally, restriction of host movement or host reduction strategies target deer using fencing to restrict deer movement through areas where humans often encounter ticks such as gardens and personal property. Other host reduction strategies are often accomplished through controlled hunting programs for white-tailed deer [26].

Personal protection strategies consist of actions taken on an individual level to protect oneself from either tick encounters, tick bites, or disease transmission. These include measures such as avoiding tick habitat areas, checking oneself for ticks after time spent outdoors, making certain clothing choices, or using a government-approved insect repellent effective on ticks (e.g. icardin or DEET) designed for use on either an individual's skin or clothing [33].

In North America, most research to date on LD and its associated tick vectors has been concentrated in the

Northeast United States. While many environmental and ecological factors that are suitable for the establishment of tick populations are comparable between the Northeast United States and Eastern Canada [34], there are some differences in policy and public acceptability that need to be considered when implementing novel tick control strategies, specifically regarding control of wildlife populations, and environmental acaricide application [25]. The objective of this systematic review was to perform a comprehensive assessment of the effectiveness of interventions, in countries where there is known transmission of LD, that are most applicable to a Canadian setting (i.e. most similar host animals) which reduce human-tick encounters, prevent tick bites and reduce the risk of LD and to evaluate the current state of knowledge on the economic cost, environmental impact, social impact and acceptability, as well as public health impacts of these interventions. This assessment will identify which global interventions have been shown to be effective and where knowledge gaps exist to inform LD and tick control options that may be applicable to both the natural and political environment in Canada.

Methods

This systematic review adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for systematic reviews (PRISMA) [35]. The protocol was developed a priori and is registered with PROSPERO: CRD42022335612.

Review question and eligibility criteria

The primary objective of our review was to address the question: "What is the effectiveness of interventions to reduce human-tick encounters, prevent tick bites and reduce the risk of LD in a global context, that are most applicable to a Canadian setting?". The secondary objective was to evaluate the current state of knowledge on the economic cost, environmental impact, social impact and acceptability, as well as public health impacts of these interventions. Articles included in the data extraction phase met the following inclusion criteria: 1. Studies focused on LD bacteria vector ticks (ticks who are competent vectors of *Borrelia burgdorferi* (s.l.) or LD focused interventions (including landscape management, management of host parasitism and movement, chemical/biological/natural control agents, or community or population level interventions aiming at increasing personal protective behaviors)), 2. Were written in French or English languages, and 3. Were published in any year.

We excluded case reports, case series, and single-cross-sectional study designs to increase the robustness of causality hypothesis and clearly attribute the risk reduction to the intervention via temporality. Studies

that were conducted in a laboratory setting and were not field applied were excluded from the study to optimize our results for interventions that have been field tested. We also excluded LD interventions that did not focus on wildlife hosts applicable to the Canadian context (i.e. wildlife hosts not found in Canada such as lizards), or which only addressed LD prevention in livestock or domestic animals and did not also have an aim of protecting human populations in their proximity. Finally, we excluded studies that medically or pharmaceutically targeted human populations to prioritize upstream prevention activities that aimed to reduce environmental tick indices or *B.burgdorferi* bacterial infection rates in ticks or reservoir hosts, or activities to reduce human-tick encounters or promote the detection and removal of encountered/attached ticks.

Search strategy

The search strategy was developed in consultation with librarians from the University of Ottawa and the Public Health Agency of Canada and was implemented in March 2022 and updated in November of 2024. We completed our electronic query of seven databases including Medline, Embase, Global Health, CAB Abstracts, Cochrane CENTRAL, Scopus, and Econlit using the following general keywords: tick*, *Ixodes scapularis*, *Ixodes pacificus*, *Ixodes ricinus*, blacklegged tick, deer tick, tickborne disease*, tick bite, Lyme Disease, LD, *Borrelia burgdorferi*, *Borrelia mayonii*, intervention*, implementation, control program*, control practice*, tick reduction. The detailed search strategy can be found in (Supplemental file 2). We verified our search strategy using backwards and forwards citation searching as well as reviewing the citations of previous relevant systematic reviews. We used Covidence, a systematic review management application to review studies and remove duplicates [36].

Selection of studies

Studies identified through the search algorithm were imported into Covidence, where the reviewers (KO, MN, AD, CD, OF, TC) then assessed the relevance of each title and abstracts followed by full texts in duplicate to verify that each article met the inclusion criteria using a predefined and piloted screening tool (Supplemental file 1). Any discordance in the inclusion or exclusion of studies was discussed among all reviewers and if no consensus was reached an additional reviewer was consulted. The screening tools are outlined in detail in Supplemental file 1.

Study characteristics and data extraction

We developed the extraction form a priori in Covidence which was then independently tested by all reviewers.

Data were extracted from the included studies in Covidence and verified by a second reviewer. Conflicts were reviewed as a team to achieve consensus. We extracted data on descriptive characteristics of the study (title, author, year, location of study, targeted tick species and/or *B.burgdorferi* bacteria, intervention setting, type of intervention (Table 1), and outcome measures associated with intervention effectiveness, such as reduction of questing ticks, or reduced infection prevalence in hosts or ticks etc.) and key information on the feasibility, impact, and acceptability of interventions along with any cost effectiveness data available (Supplemental file 1).

In addition, we captured data on integrated tick control approach implementation if applicable, whether implicitly or explicitly. This was defined as a study that used multiple tick control products or approaches within or between intervention classifications.

Multi-study synthesis of nymphal tick suppression effects

Recognizing the wide heterogeneity across studies in terms of design and reporting of outcomes that limited our potential to undertake a meta-analysis, we performed a multi-study synthesis on a subset of studies that reported on the most commonly occurring outcome type, density of questing nymphs, that spanned a breadth of intervention types. This was determined after data extraction was complete. Studies were included if they contained comparable information with regards to two main criteria: (1) timing of the measurements (post-intervention), and (2) density calculations (performed per distance in m^2 , rather than density per time unit). This was done to ensure the results between included studies were comparable in terms of the reported effect size. We organized the primary outcome synthesis results into five intervention groupings (chemical acaricide, natural acaricide, deer fencing, 4-Poster devices, and tick tubes) ensuring each category had at least two studies which met the inclusion criteria. In assessing studies and outcome measurements for inclusion, we accounted for differences in intervention timelines which typically vary by intervention type (i.e. our time-range for synthetic or natural acaricides (9–15 days vs 14–21 days post application respectively) differs from host-targeted interventions which have a much longer time of treatment or post-intervention time lag before effectiveness of the intervention on nymphal tick suppression can be measured (deer fence 1 year, 4-Poster 4 years, tick tubes 1–2 years)).

Risk of bias appraisal and certainty of evidence for multi-study synthesis

For the multi-study synthesis based on a subset of comparable studies, we performed a risk of bias assessment using ROBINS-I and ROB 2.0 for non-randomized studies and

Table 1 Classification of different tick control strategies

<p>Landscape management</p> <ul style="list-style-type: none"> ● Vegetation clearing (e.g. Japanese barberry) ● Vegetation burning ● Barrier approaches (e.g. ecotone modification, substrates, woodchip borders, hardscaping)) <p>Chemical insecticides, and natural tick control products applied to the environment</p> <ul style="list-style-type: none"> ● Chemical control <ul style="list-style-type: none"> ○ Organophosphates ○ Carbamates ○ Pyrethroids ● Natural products <ul style="list-style-type: none"> ○ Botanically derived chemical alternatives ○ Natural enemies <ul style="list-style-type: none"> ■ Wolf spiders etc ○ Biological agents <ul style="list-style-type: none"> ■ Entomopathogenic bacteria ■ Entomopathogenic fungi ■ Nematodes 	<p>Host-targeted management of wildlife parasitism, infection, movement, and density</p> <ul style="list-style-type: none"> ● Deer Management <ul style="list-style-type: none"> ○ Deer exclusion (fencing) ○ Deer reduction (culling; birth control) ○ Deer parasitism suppression (4-Poster [topical acaricide treatment], oral vaccine bait) ● Small mammal management <ul style="list-style-type: none"> ○ Rodent parasitism and pathogen infection suppression <ul style="list-style-type: none"> ■ Acaricide-treated nesting material ■ Bait boxes (deliver oral or topical acaricides, or prophylaxis) ○ Rodent reduction ○ Oral vaccine bait <p>Personal protection (at a community or population level)</p> <ul style="list-style-type: none"> ● Community-targeted communication or empowerment involving: <ul style="list-style-type: none"> ○ Permethrin treated clothing/uniforms ○ Application of spray repellents to skin or clothing ○ Exposure and preventive behaviors or individual behavior changes <ul style="list-style-type: none"> ■ Habitat avoidance ■ Checking for ticks ■ Showering/bathing
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randomized control trials, respectively [37, 38]. These are preferred tools to be used in Cochrane reviews for non-randomized and randomized studies to evaluate comparative effectiveness of interventions, they are primarily designed for healthcare studies but are readily adaptable to other contexts [38, 39]. This was followed by an appraisal of the certainty of the evidence using GRADE (Grading of Recommendations, Assessment, Development, and Evaluations), for the outcomes in our data synthesis and summarized in a GRADE Table [40, 41]. The GRADE tool is also a preferred tool for Cochrane reviews to evaluate the certainty of the evidence using a validated domain-based tool that considers study design, risk of bias, publication bias, as well as the inconsistency, indirectness and imprecision of included effect estimates [42]. These appraisal tools

achieved, a third reviewer was included in the discussion to achieve consensus.

Multi-study synthesis analysis

For the multi-study synthesis on a subset of comparable studies, where necessary we calculated a percent reduction estimate for those studies that did not already provide one, and which had results available for before and after intervention implementation at comparable time points. We completed the multi-study synthesis of tick suppression effects in Excel as an overall summary of the various effect sizes by summarizing the data in a forest plot using percent reduction in density of questing nymphs as the most comparable outcome present in the literature.

$$Percent\ reduction = \left[\frac{pre\ intervention\ density - post\ intervention\ density}{pre\ intervention\ density} \right] * 100$$

help to assess limitations of the studies included in systematic reviews and inform interpretation of the strength of review conclusions [35]. All tools were pretested by all reviewers prior to proceeding with appraisals performed by a single reviewer and verified by a second. All conflicts were resolved between reviewers; if consensus was not

Since 95% confidence intervals for percent reduction or percent change are not often presented in the literature, we only used effect sizes in our synthesis to best reflect the data available in the literature. The risk of bias and GRADE tools were used by the team to inform the overall confidence in the evidence for the main outcome

of interest to evaluate effectiveness. For other outcomes a narrative synthesis was performed, and effectiveness outcomes were tabulated in Table 2 using study by study conclusions on effectiveness at a $p < 0.05$ level.

Results

Characteristics of included studies

Our search strategy identified 9,231 studies which were screened for relevance. A total of 127 studies were deemed eligible for inclusion in the main review, data extraction and risk of bias assessment (Fig. 1). Included articles spanned the years 1977 to 2024 and were all written in English. Most of the studies used an experimental study design ($n = 120$) followed by observational ($n = 6$) and mixed methods ($n = 1$) study designs (Table 2). Most studies were conducted in North America ($n = 114$), of which only four studies were from Canada and the rest were from the United States [43–46]. The remaining 13 studies were conducted in Europe [47–59].

Most studies targeted LD vector ticks, either in the environment or on parasitizing wildlife hosts ($n = 94$), rather than the bacteria ($n = 6$) or a combination of the two ($n = 28$). The majority of the studies were focused on reducing LD vector ticks or bacteria via host targeted strategies ($n = 62$), followed by environmentally applied acaricides (chemical and naturally derived options, $n = 49$), landscape targeted intervention studies ($n = 21$), and personal protection strategies ($n = 7$). Some of these studies crossed multiple classifications using integrated intervention strategies so the total N does not equal 127 studies (Fig. 2).

Of the included studies, 107 measured at least one entomological outcome (e.g. questing tick density, tick infection prevalence, etc.), of which 84 reported reductions in questing tick density, while 45 included at least one host-related outcome (e.g. host parasitism or *B. burgdorferi* host seroprevalence, etc.) and 12 investigated other outcomes such as qualitative or human outcomes.

Primary objective: effectiveness for all study types and outcome measures

Studies featuring chemical strategies had the greatest proportion of effective strategies (91%) according to study results and conclusions reported by the authors. Amongst host targeted strategies, deer targeted 4-Poster strategies had the greatest proportion of studies that reported effective strategies (89%) when compared to tick tubes, oral treatments and deer exclusion or deer reduction (Table 2). Host and landscape targeted strategies had the most variation in reported effectiveness with 16% with no effectiveness and 23% with mixed effectiveness

within the host targeted strategies, and 25% with no effectiveness and 25% mixed effectiveness in landscape targeted strategies (Table 2). Information on the study-by-study effectiveness results, and the various included outcome types for all 127 studies can be found in (Supplemental file 3).

Multi-study synthesis of questing nymphal density

We included 25 studies that evaluated the effectiveness of interventions against questing nymphal stage ticks in the data synthesis. Of these studies, 8 evaluated a chemical acaricide, 10 evaluated a natural acaricide, 2 evaluated deer fencing, 3 evaluated 4-Poster devices, and 3 evaluated tick tubes (Fig. 3). All of the included studies within each category reported a comparable timing of the outcome measurements (post-intervention), as well as comparable density calculations (performed per distance in m^2 , rather than density per time unit).

Risk of bias and certainty of the evidence for studies in the multi-study synthesis

Our risk of bias assessment revealed that most studies had either moderate to serious risk of bias; and that studies often suffered from issues related to potential sources of confounding that were not appropriately controlled for ($n = 24$) (Fig. 4). The source of many of these study limitations were either restrictions placed on the studies by the resources available, or the environment itself.

Grading of the evidence of studies in this multi-study synthesis revealed that most study classifications (i.e. intervention types) had low or very low certainty of evidence with the exception of the effectiveness of environmentally broadcasted chemical acaricides against questing nymphal stage ticks (Table 3). Though this intervention classification also suffered from limitations in the risk of bias assessment, it was graded up for large effect sizes (percent reduction of questing nymphal tick density) and had no detected inconsistency or indirectness according to the GRADE guidelines [60] (Table 3). All the other intervention classifications suffered from limitations due to the risk of bias across studies, and inconsistency of the results (Table 3).

Multi-study synthesis analysis

In the multi-study synthesis of 25 studies, despite the wide variety of products and formulations used in the chemical tick control studies, which often used varied approaches between sites of a single study, the results had consistently strong effect sizes. This finding suggests that these approaches remain the most consistently reliable of all tick control methods included in this analysis. 4-Poster interventions also had high certainty of evidence, as well as relatively consistent effect sizes

Table 2 Overall effectiveness of the included study outcomes (all types) by intervention categories, according to study conclusions (informed by outcome significance p -value < 0.05)

Intervention	Overall effectiveness of the program on all outcomes available in study (questing ticks (any stage), host or human parasitism, tick mortality, or entomological/etiologic risk)*	List of studies included, and design Experimental (non-RCT)** Experimental (RCT) ^a Observational ^b Other ^c **All un-annotated studies are non-randomized experimental design
Management of wildlife host parasitism, movement, and density		
Tick tubes	Yes	Mather 1988, Mejlon 1995, Tiffin 2024
	No	Leprince 1996, Hornbostel 2005
	Mixed results	Mather 1987, Daniels 1991, Stafford 1991
Bait box	Yes	Lane 1998, Dolan 2004, Barrile 2005, Dolan 2011, Schulze 2017, Pelletier 2022
	No	Hinckley 2021 ^a , Pelletier 2024
	Mixed results	No studies applicable
4-Poster	Yes	Solberg 2003, Carrol 2009 (1) ^a , Carrol 2009 (2), Daniels 2009 ^b , Hoen 2009, Miller 2009, Schulze 2009, Stafford 2009
	No	No studies applicable
	Mixed results	Greer 2014
Deer or rodent removal	Yes	Delinger 1993 ^b , Wilson 1998
	No	Jordan 2007, Kiran 2024 ^a
	Mixed results	Stafford 2003, Rand 2004, Martin 2023 ^b
Oral antibiotic treatments/Oral or injection host vaccine/Other	Yes	Tsao 2004, Richer 2014, Contreras 2020 ^a , Stafford 2020 ^a , Vanier 2022
	No	No studies applicable
	Mixed results	Rand 2000
Deer exclusion (deer fencing)	Yes	Daniels 1993 ^b , Fabbro 2015
	No	Perkins 2006
	Mixed results	Stafford 1993, Daniels 1995
Chemical/natural/botanical		
Chemical	Yes	Rupes 1977, Schulze 1987, Schulze 1991, Stafford 1991, Schulze 1992, Curran 1993, Schulze 1994, Schulze 1995, Monsen 1999, Schulze 2000, Schulze 2001(1), Schulze 2001(2), Schulze 2005, Schulze 2008, Jurisic 2010, Jordan 2017, Bron 2020, Schulze 2020 ^a , Jurisic 2023, Williams 2024 ^a
	No	No studies applicable
	Mixed results	Stafford 1990, Hinckley 2016 ^a
Botanical/Fungal	Yes	Patrican 1995 ^a , Benjamin 2002 ^a , Hornbostel 2004 ^a , Dolan 2009, Greengarten 2011, Elias 2013
	No	Hornbostel 2005 ^a , Schulze 2023
	Mixed results	Allan 1995, Bharadwaj 2010, Bharadwaj 2015 ^a
Landscape Management		
Vegetation clearing	Yes	Wilson 1986, Schulze 1995, Hubalek 2006, Williams 2009, Williams 2010, Williams 2017, Conte 2021
	No	Tack 2013, Elias 2024 ^a , Lee 2023
	Mixed results	Linske 2018, Jordan 2020
Vegetation burning	Yes	No studies applicable
	No	Padgett 2009
	Mixed results	Mather 1993, Stafford 1998
Barrier approaches (ecotone modification etc.)	Yes	Mckay 2020 ^a
	No	No studies applicable
	Mixed results	No studies applicable

Table 2 (continued)

Intervention	Overall effectiveness of the program on all outcomes available in study (questing ticks (any stage), host or human parasitism, tick mortality, or entomological/etiologic risk)*	List of studies included, and design Experimental (non-RCT)** Experimental (RCT) ^a Observational ^b Other ^c **All un-annotated studies are non-randomized experimental design
Personal Protection		
Permethrin clothing or repellent program	Yes	Faulde 2015, Nadolny 2024 ^b
	No	No studies applicable
	Mixed results	Staub 2002 ^a , Miller 2011 ^a , Richards 2015
Behaviour change program	Yes	Potes 2023 ^c
	No	No studies applicable
	Mixed results	Beaujean 2016
Integrated Tick Control		
Integrated program or multiple classifications (within or between classification categories) *	Yes	Deblinger 1991, Schulze 2007, Dolan 2009, Rand 2010 ^a , Jordan 2011, Bharadwaj 2012, Gilbert 2012, Del Fabbro 2015, Burtis 2017 ^{ac} , Dolan 2017, Williams 2017, Dolan 2018, Fischhoff 2018 ^a , Jordan 2019, Williams 2018 ^a , Potes 2023 ^c
	No	Linske 2021 ^a , Mandli 2021, Ostfeld 2023 ^a , Linske 2024
	Mixed results	Stafford 2010, Garnett 2011, Little 2020, Dyer 2021 ^a , Schulze 2021 ^a , Keesing 2023 ^a , Ostfeld 2023 ^a , Ostfeld 2024 ^a

See more information on integrated tick control combinations and classifications in the section 'Secondary objectives: integrated tick control'. *Effectiveness was determined by study results on their presented outcomes. Yes = intervention was effective on all outcomes measured. No = the intervention was not effective on outcomes measured. Mixed results = the intervention was effective on some of the outcomes measured but not all. Studies with many outcome measurement types may be more likely to be classified as 'mixed' effectiveness than studies with one or two key outcome measurements. **All un-annotated studies are non-randomized experimental design

(63.4–80% reduction in density of questing nymphs) when measured at the 4-year mark of study measurement. Natural and botanical approaches, deer fencing, and tick tubes all had lower certainty of evidence as well as inconsistent effect sizes among the included studies (Fig. 3). These findings are consistent with the descriptive portion of this systematic review which suggested that most studies in the corresponding intervention classifications reduced some measure of LD risk with most mixed or negative results being present in the literature relating to tick tubes (Table 2).

Secondary outcome: host-targeted management of wildlife parasitism, infection, movement and density

Of 62 articles which featured host targeted strategies, 56.5% and 40.3% were set in rural and residential settings, respectively. Within this classification, 25 were deer targeted, 33 were rodent targeted, and four were mixed (largely a combination of deer removal and rodent bait boxes) (Table 2). Fifteen of the studies indirectly addressed environmental impact, most (n = 9) of these presented their host targeted approach as a way to reduce reliance on environmentally broadcasted acaricides and impact on non-target species; none of these

studies performed direct measurements of environmental impact [48, 56, 61–67].

Ten studies [44, 56, 63, 65, 68–73] indirectly addressed the social acceptability of the intervention, but only one study that used permethrin tick tubes included an anecdotal measurement by noting complaints by visitors to the study area became rare after treatment [65]. Eight studies considered social resistance of the intervention which were mostly captured in studies of deer targeted interventions, which faced concerns over the implications of attracting deer with supplemental feedings [74–76]. Additionally, one study removed several 4-Poster devices during their study during a conflict with landowners [77], while another faced concerns from divided stakeholders over deer culling [48]. Rodent targeted studies faced concerns that there could be unintentional non-target animal ingestion of the treated material [61, 78], and one study anticipated public pushback over the delayed effect of host targeted strategies [79]. None of the studies presented any direct measurement of social resistance or acceptability. Many (33.9%) of the host targeted studies anecdotally reported on feasibility. Using rodent targeted bait boxes and other interventions using rodent applied acaricides had mixed conclusions; five

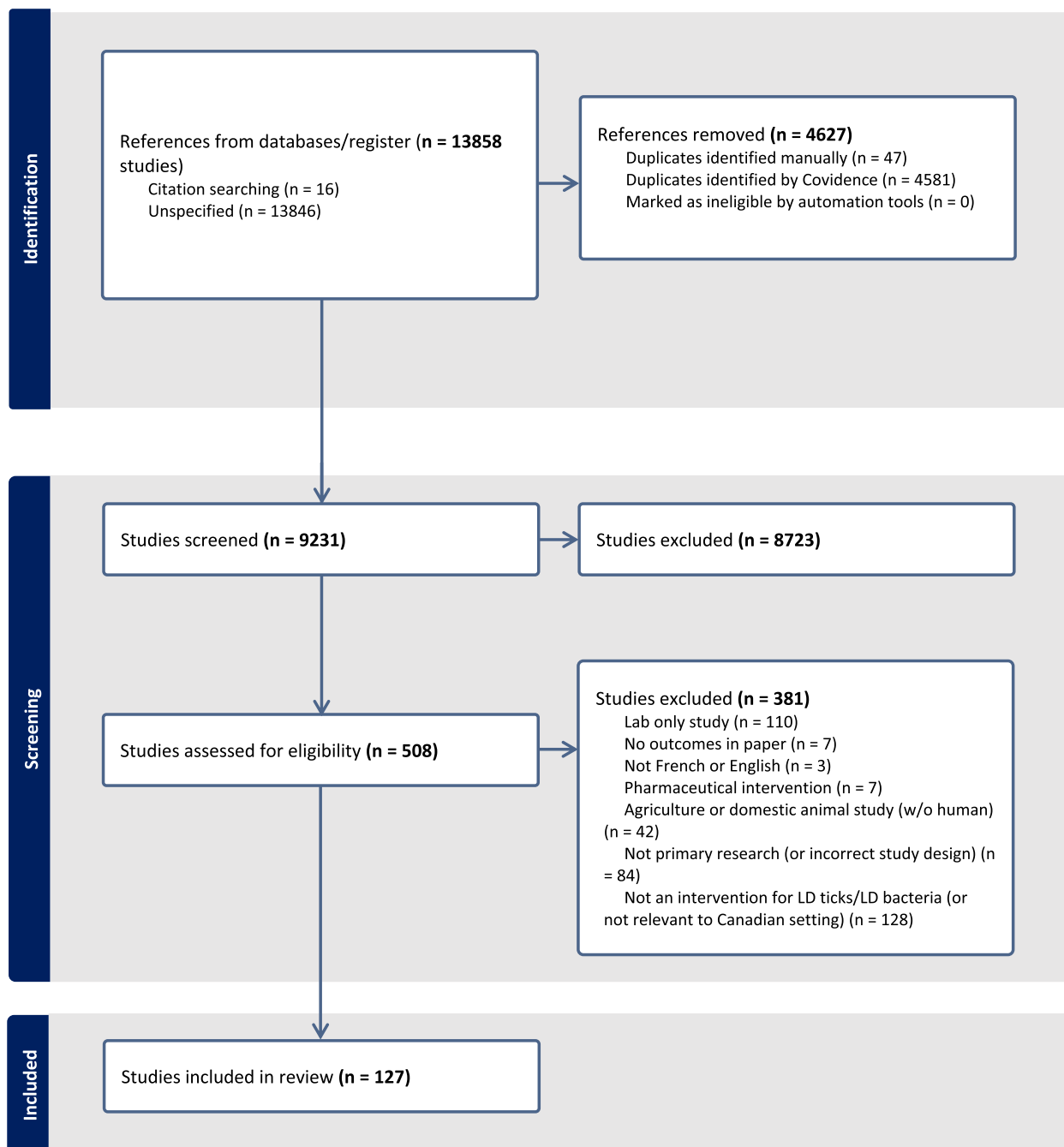


Fig. 1 PRISMA diagram for selection of relevant articles for data extraction

studies identified the level of human resources needed was a barrier to making these approaches highly feasible interventions [50, 64, 68, 80, 81]; two other studies faced challenges with bait predation from non-target species [61, 82]. The deer reduction programs noted the programs were highly labor intensive [61, 70, 74]. Similarly, all of the articles that used 4-Poster devices or corn feed

and discussed feasibility excluding [63] noted challenges faced by the staff who were sometimes required to walk long distances to refill feed stations or perform maintenance on the 4-Poster devices [61, 76, 83, 84]. There were three studies which addressed deer fencing; one of which assigned high feasibility to the intervention and its scalability to small treatment areas [56], the other two faced

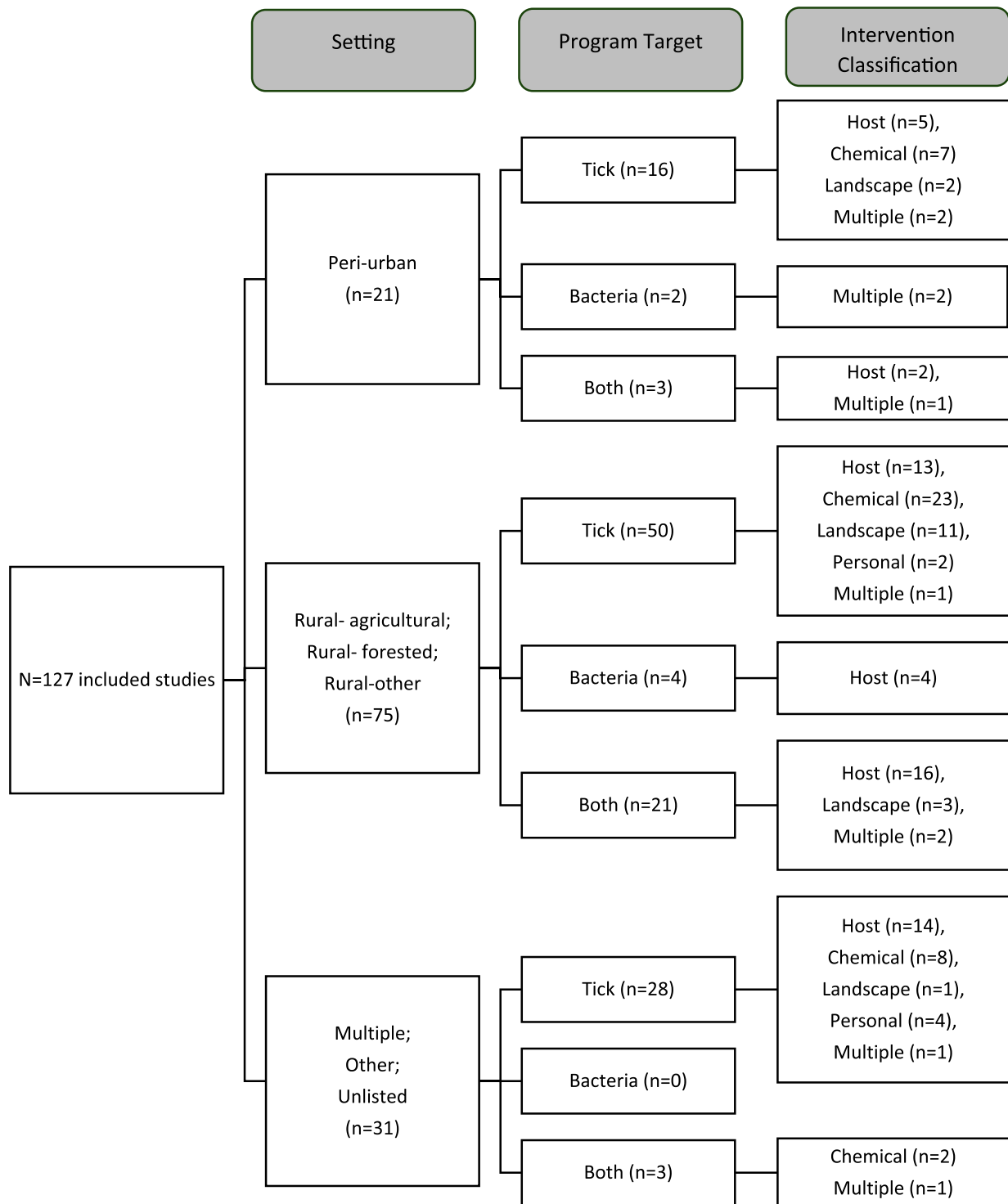


Fig. 2 Descriptive characteristics of the included studies (N= 127). Figure 2 legend: Program targets include 'Tick' defined as programs which aim to reduce or repel LD vector tick species, 'Bacteria' is defined as programs which aim to eliminate or reduce bacteria amplification or transmission, and 'Both' which are programs that target both LD vector ticks and bacteria simultaneously. *Chemical studies include the study classification of chemical and natural control interventions. **Multiple classification includes integrative studies spanning multiple classification types, see Table 1 for more information on classifications

Synthesis of the effectiveness of interventions at the optimal follow-up point on percent suppression of questing nymphal density by product and/or study site (n=25)

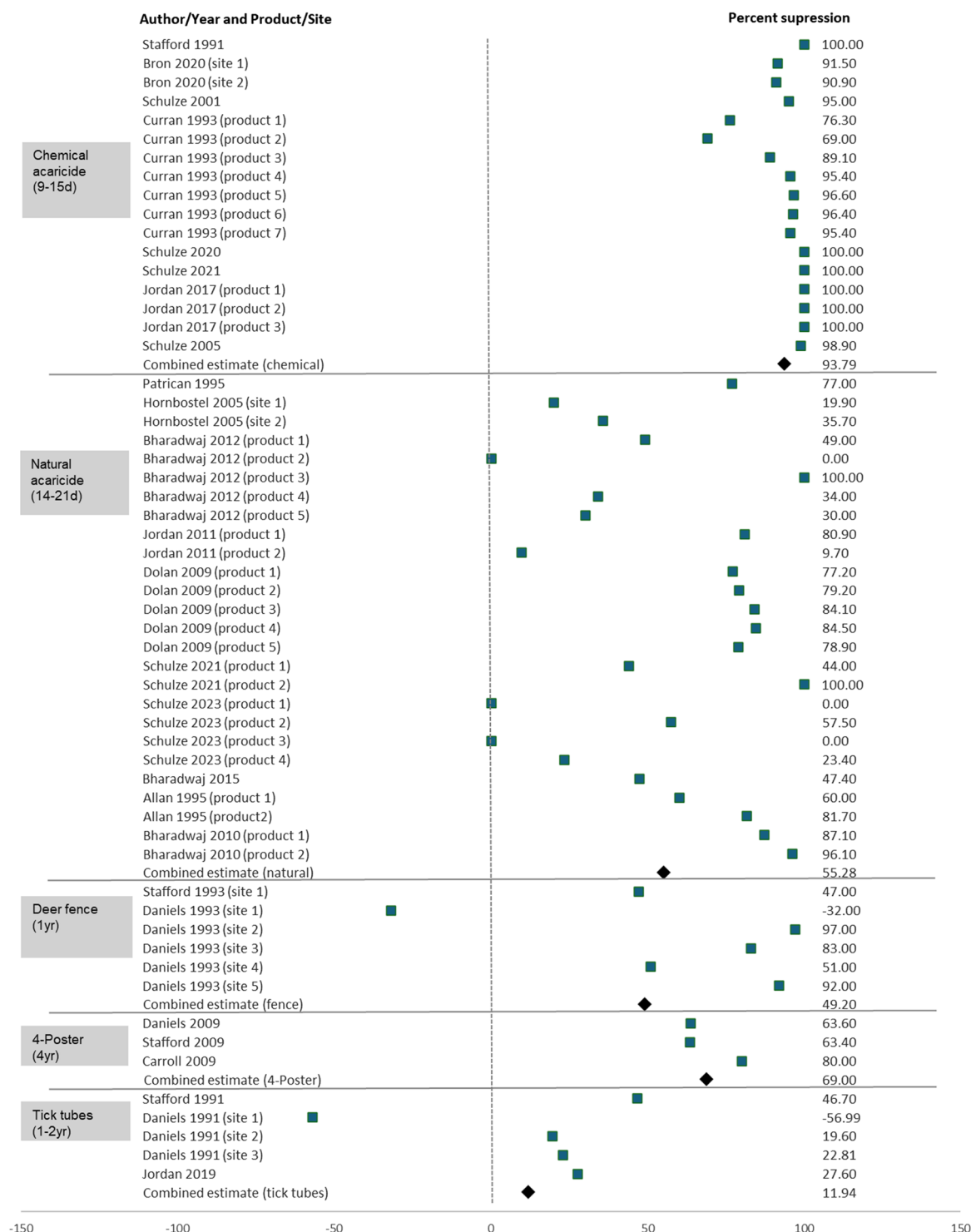


Fig. 3 Data synthesis of the effectiveness of the intervention on percent suppression of questing nymphal density (n = 25) with site and product descriptions found in (Supplementary Material 4)

Study	Tool used	Confounding	Classification of intervention	Departure from interventions	Missing Data	Measurement of the outcome	Reported results	Overall
Chemical Acaricide								
Stafford 1991 (1176)	ROBINS	Yellow	Green	Green	Green	Green	Green	Yellow
Bron 2020	ROBINS	Green	Green	Green	Green	Green	Green	Green
Schulze 2001	ROBINS	Red	Green	Green	Green	Green	Green	Red
Curran 1993	ROBINS	Yellow	Green	Yellow	Green	Green	Green	Yellow
Schulze 2005	ROBINS	Red	Green	Green	Green	Green	Green	Red
Schulze 2020	ROB	Yellow	NA	Green	Green	Green	Green	Yellow
Schulze 2021	ROB	Yellow	NA	Green	Green	Green	Green	Yellow
Jordan 2017	ROBINS	Yellow	Green	Green	Green	Green	Green	Yellow
Botanical and Natural Acaricides								
Patrican 1995	ROB	Yellow	NA	Green	Green	Green	Green	Yellow
Hornbostel 2005	ROB	Green	NA	Green	Green	Red	Green	Red
Bharadwaj 2012	ROBINS	Yellow	Green	Green	Green	Green	Green	Yellow
Jordan 2011	ROBINS	Red	Red	Green	Green	Green	Green	Red
Dolan 2009	ROBINS	Yellow	Yellow	Green	Green	Green	Green	Yellow
Bharadwaj 2010	ROBINS	Red	Yellow	Yellow	Green	Yellow	Green	Red
Bharadwaj 2015	ROB	Green	NA	Yellow	Green	Green	Green	Yellow
Allan 1995	ROB	Green	NA	Yellow	Green	Green	Green	Yellow
Schulze 2023	ROB	Green	NA	Green	Green	Yellow	Green	Yellow
Schulze 2021	ROB	Yellow	NA	Green	Green	Green	Green	Yellow
Fence								
Stafford 1993 (1098)	ROBINS	Yellow	Green	Yellow	Red	Green	Green	Red
Daniels 1993	ROBINS	Yellow	Green	Green	Green	Green	Green	Yellow
4-Poster								
Daniels 2009	ROBINS	Red	Green	Green	Green	Green	Green	Red
Stafford 2009	ROBINS	Red	Green	Green	Red	Green	Green	Red
Carroll 2009	ROBINS	Red	Green	Green	Green	Green	Green	Red
Tick Tubes								
Stafford 1991 (1165)	ROBINS	Red	Green	Green	Green	Green	Green	Red
Daniels 1991	ROBINS	Red	Green	Green	Yellow	Green	Green	Red
Jordan 2019	ROBINS	Yellow	Yellow	Yellow	Green	Yellow	Green	Yellow

Fig. 4 Risk of bias results from ROBINS-I and ROB2.0: studies reporting most common outcome (questing nymphal density). legend: Color coding represents different levels of bias risk, green = low risk of bias, yellow = some concerns and red = high risk of bias for each of the assessment tools

challenges with human resources, fence placement, or the lag time needed between installation and effect [48, 69]. Finally, two studies focusing on rodent targeted oral vaccines noted high feasibility compared to injection vaccines [71, 85], while the other noted challenges faced to ensure proper dosage of orally delivered vaccines [86].

Three studies considered the development of tick or bacterial resistance to the product used in their intervention. In one study, the team first tested the lowest concentration of doxycycline laden rodent-targeted bait needed to achieve complete spirochete suppression before deployment of their intervention [87]. After which they found that the use of the same doxycycline bait could be controversial due to the potential for the development of bacterial resistance in an antibiotic commonly used in human populations [88]. Another study justified their use of a bio-control agent, *Metarhizium anisopliae*, by noting an advantage of bio-control agents in reducing likelihood of resistance development, since there is often

competition between the agent and target in the evolutionary process [66].

Six studies presented explicit information on cost; the most recently published studies used tick tubes (\$75 for 24 tick tubes) and bait boxes (\$40 and \$45 per bait box), all of which were rodent targeted strategies [68, 72, 81]. Three other studies also included some cost estimates for their deer targeted strategies including the cost of corn and 4-Poster device initiation [61, 84, 89]. Additionally, one study provided cost estimates for sharpshooting services for a deer reduction strategy of \$600 USD per deer [90]. Sixteen other studies provided the product name and concentration, and five studies mentioned cost as a possible limitation of the approach [48, 63, 74, 75, 85].

Secondary objectives: chemical insecticides, biological control agents, natural tick control products

Our search resulted in 49 studies that focused on chemical insecticides, biological control agents, and natural tick control products of which 19 and 25 were set in

Table 3 GRADE table: the effectiveness of the intervention on the density of questing nymphs. Overall confidence in the estimates of effects

No. of studies	Risk of bias (ROB 2.0, ROBINS-I)	Inconsistency	Indirectness	^a Imprecision	Publication bias	Other considerations	Certainty of evidence
The effectiveness of chemical acaricides against questing nymphal stage ticks							
8 (6/8 non-randomized)	Serious	None detected	None detected	NA	None detected	+ 1 (upgrade for large effect sizes)	High (++++)
The effectiveness of natural acaricides against nymphal stage ticks							
8 (3/8 non-randomized)	Very serious	Very serious	None detected	NA	None detected	+ 1.5 (upgrade for randomized studies, confounding present likely underestimated the true effect size)	Low (++)
The effectiveness of deer fencing against questing nymphal stage ticks							
2 (2/2 non-randomized)	Very serious	Serious (-1.5)	None detected	NA	None detected	None	Very low (+)
The effectiveness of 4-Poster devices against questing nymphal stage ticks							
3 (3/3 non-randomized)	Serious	Moderate (-0.5)	None detected	NA	None detected	None	Low (++)
The effectiveness of rodent host targeted tick tubes against questing nymphal stage ticks							
3 (3/3 non-randomized)	Very serious	Very serious	None detected	NA	None detected	None	Very low (+)

^a Unable to Grade based on imprecision due to lack of confidence intervals in the study results included in the multi-study synthesis of tick suppression effects, none of the included studies were Graded down based on imprecision. GRADING should be interpreted with caution due to the heterogeneity of methods found within intervention classifications

residential or rural settings, respectively. Of the 49 studies, 49% evaluated chemical acaricides like carbaryl, 47% evaluated natural alternative acaricides like *Metarhizium* based products (i.e., Met 52) or Nootkatone, one of which also included a chemical comparison [91], and 4% evaluated biological control measures (e.g., natural predators such as wolf spiders). Twenty-four studies addressed environmental impacts in the text [49, 52, 55, 61, 62, 64, 69, 91–107]. Many of these studies justified their use of natural or botanical acaricide approaches to reduce impact on the environment or non-target arthropods. Three of these natural or botanical studies indirectly stated there were still concerns over impacts on non-target organisms or a possible need for more research on environmental impact [96, 99, 108]. Two studies directly measured impacts on non-target organisms, finding that *Metarhizium brunneum* spores did yield considerable yellow-mealworm mycosis after application [94, 108]. Additionally, three studies measured the impact of their intervention on non-target species abundance and diversity. The first found that their use of Eco-Exempt IC2 (a plant-derived acaricide) temporarily reduced some non-target species, but they rebounded within a few weeks [97]. The other two studies found that their use of granular Carbaryl had detectable effects

on non-target species over the study period [91], while the use of granular deltamethrin only had a temporary effect on non-target species before rebound [102].

We found six studies which addressed public or social acceptability, most of which cited a higher acceptance of natural or botanical products over chemical products due to health or environmental concerns [91, 92, 95, 96, 109, 110]. We found only one study, which studied the effectiveness of Nootkatone (a natural tick control product derived from Alaskan yellow cedar (*Cupressus nookatensis*)), that directly addressed public or social acceptability which found that many residents in the study area would consider using a natural 'alternative' acaricide to control ticks if they were more available [92]. Two of these studies provided indirect measurements of acceptability by referring to previous studies that provided direct acceptability measurements [109, 110]. Similarly, seven studies indirectly addressed potential social resistance, many of which focused on synthetic acaricides citing environmental or health concerns [61, 73, 101, 103, 106, 111, 112], while one of these faced social resistance when it came to cost and availability [112]. Seven studies addressed concerns surrounding the feasibility of their proposed intervention relating to acaricides; two stated the natural products used in their study were easily

purchased making them an accessible and minimal risk option for tick control [95, 111], and another made sure that the fungal product they chose to test was able to be easily cultured in a laboratory setting to increase real world feasibility [93]. Most others mentioned the cost and availability of the products to be potential barriers to their approach being feasible [61, 96, 103]. Finally, one study mentioned that their demonstrated use of bifenthrin outside its typical application season increased the feasibility of their design [104]. Two of the 49 studies in this intervention category indirectly addressed the potential for tick or bacterial resistance to their proposed product use citing the need for products with strong residual activity, or improved efficacy and selectivity [49, 55].

Seven studies included information on the cost of acaricides, six of these studies provided direct measurements. The first stated that, at the time of the study, the cost of the intervention was roughly 26\$/backyard application of granular acaricide, Spectracide Triazicide, featuring Gamma-cyhalothrin as the active ingredient [113]. Similarly, another study found that applications of synthetic granular formulations: \$25–125/0.20 ha (0.5 acres) of tick habitat while applications of liquid formulations: \$75–185/0.20 ha (0.5 acres) of tick habitat [109]. Two other studies listed acaricide application costs between \$325–350 [61, 103]. Another noted the cost of Nootkatone during the study was \$3,481/kg of product [93]. Finally, one study cited a previous survey which found most companies would charge between (\$100–200 per application per 0.4 ha) [91].

Secondary objectives: landscape management

We identified a total of 21 studies that focused on landscape management to reduce tick or LD risk to humans. Five were set in recreational settings, three were in residential settings, and others were either unlisted or in generally forested areas ($n = 13$). Seven studies framed their interventions as part of a tick control approach which would reduce environmental impact. Of these, one assessed the effects of fencing and vegetation mowing as an environmentally low risk intervention to reduce ticks in high density areas [56], whereas another used active forest management techniques to control ticks as part of an environmentally sound strategy [114]. Two others used vegetation management and/or ecotone modification to control questing ticks [115, 116]. Additionally, four studies mentioned the importance of this type of intervention in reducing the presence of invasive barberry and its effects on both forest health and tick populations [117–120]. Finally, two studies mentioned concerns that their landscape approach may in fact have unintended consequences for the environment through potentially increasing deer populations during controlled

burns [121] or reducing overwintering habitat for pollinators by removing leaf litter [122].

Only two studies mentioned social acceptability or resistance as justification for their type of intervention, one of which proposed fencing and vegetation mowing as a more acceptable intervention when compared to area wide application of acaricides [56], while the other cited a growing interest in non-chemical options to tick control according to a previous telephone survey study [110]. Five of the 21 studies attempted to address feasibility indirectly, often as part of the rationale supporting the use of their tick suppression approach. One suggested vegetation removal is an approachable “do it yourself” friendly strategy to tick reduction [82], while another used ecotone modification using materials (woodchips) from an existing forest management program in the Ottawa area [45], a third study mentioned fencing and mowing are easily scalable approaches [56], and finally one study hoped their Japanese barberry approach would be a low cost option compared to other landscape approaches [117]. Two other studies had concerns over feasibility, one faced study challenges removing decayed leaf litter layers [122], the other mentioned that their approach to vegetation management in control segments may in fact reduce the effectiveness of their sampling technique reducing study feasibility [116]. None of the studies in this classification mentioned tick or bacterial resistance as a concern or benefit of their intervention approach.

We found that two studies directly provided cost estimates for their intervention in this classification. The first provided the cost for some components of their integrative approach (tick tubes) at \$75/24 tick tubes [82], and the second listed their overall cost at \$3800/50 m³ of woodchips, used to treat 500 m of trail, primarily occurred for transportation and labor costs [45]. Finally, one study indirectly addressed cost, by mentioning that removing all layers of leaf litter in order to reduce tick habitat was very labor intensive and could be quite costly if the approach was scaled up [122].

Secondary objectives: personal protection

Seven studies were included for analysis that focused on personal protection strategies at a community level. Most ($n = 4$) of these studies examined the effectiveness of permethrin treated clothing or uniforms in reducing tick encounter or tick bites. Three of these studies focused on occupational exposure [57, 123, 124], while the other focused on a program for a high-risk community in Rhode Island [125]. One study in Canada, used a repeated cross-sectional mixed methods design to evaluate a motivational interviewing technique to increase personal protection measures in a high-risk community, combined with a rodent-targeted strategy [44]. Another

study from Switzerland examined the effectiveness of a spray repellent containing DEET and EBAAP (both of which are commonly used insect repellents) in forestry workers [53]. The final study from the Netherlands used randomized study design to compare education strategies using leaflets or video games, compared to controls, to increase knowledge, attitudes, and practices surrounding ticks and LD [126]. None of these studies focused on the environmental impacts or benefits of their strategy.

Two of these studies mentioned social acceptability or resistance, one of which applied specific methods to ascertain the social acceptability of their strategy and community engagement; they found that participants with higher engagement in the program found it to be more efficacious and acceptable than those who didn't participate. They also noted that qualitative outcomes suggested that the participant and research team collaboration was well received [44]. The other study mentioned that during participant recruitment, negative perceptions of permethrin-treated clothing contributed to lack of interest in the program [124]. Three studies measured feasibility or complexity of their intervention. To this end, the first study noted the importance of treating all layers of clothing with permethrin, as untreated outer layers seemed to reduce the effectiveness of the intervention [57]. While the other study found that community building activities were complicated by disruptions due to the COVID-19 [25]. The research team noted that longer periods of study are required to evaluate the long-term feasibility and sustainability of this intervention type [44]. The final study noted that effectiveness may increase if the method of intervention was tailored to individual preferences and outcome measures may have been more accurate if they had included a separate survey for parents [126]. One of the studies mentioned that there was some concern over tick species resistance to the lethal effects of permethrin [123]. Finally, none of the seven studies included information on cost.

Secondary objectives: integrated tick control

Integrated tick control strategies were strongly supported by the literature. Of the included studies, we found that 40 studies either used or called for an integrated approach to tick control, while 28 of these used an integrated approach (Table 4). Most of the studies which used integrated approaches that spanned multiple intervention classifications ($n = 13$) used a combination of host targeted interventions with chemical or natural tick control strategies. Only five of the studies involved landscape management or personal protection approaches. Of the strategies that used multiple tactics within the same intervention classification ($n = 15$), most ($n = 7$) used a combination of host targeted approaches, while

the remaining studies used chemical, biological, or natural tick control strategies (Table 4).

Discussion

This systematic review of tick and LD prevention strategies provides an overview of the main categories of interventions that have been evaluated in field studies to date and the effectiveness of these strategies against a wide range of outcomes. Our review highlights that most of the 127 included studies evaluated host targeted strategies, followed by chemical/natural/botanical acaricide approaches, landscape management, and personal protection strategies, respectively. A minority of the studies ($n = 28$) employed an integrative approach to tick control, despite support in the literature for increasing the number of tick control studies using a multifaceted approach [129]. Indeed, the authors of 12 of the included studies called for increased adoption of integrative approaches to tick control in the future, highlighting a need for more research conducted in this area.

Overall, the reporting of entomological outcomes (e.g. questing tick density, tick infection prevalence, etc.) was most common across studies, while fewer studies reported host-related outcomes (e.g. host parasitism or *B. burgdorferi* host infection prevalence, etc.), and a minority of studies investigated other outcomes such as qualitative or human outcomes. The most commonly reported outcome across all tick and LD prevention studies was the density of questing nymphal ticks, allowing some synthesis of effectiveness results for this outcome, despite wide variability in study design and reporting, in addition to varied outcome definitions and assessment methods.

According to the data synthesis, chemical tick abatement using varied products and formulations yielded the most efficacious and consistent results in reducing questing nymphal tick density and this effect was consistent at different scales and in different settings. This was followed by 4-Poster devices in their efficacy and consistency. All other interventions included in the data synthesis had varied results and outcomes, although most did have positive tick suppression effects. Amongst host targeted strategies, deer targeted 4-Poster strategies had the greatest proportion of studies with effective strategies according to study conclusions when compared to tick tubes, oral treatments and deer exclusion or deer reduction. Host and landscape targeted strategies had the most variation in effectiveness with 16% and 25% of studies in these categories, respectively, reporting no effectiveness, and roughly a quarter in both categories with mixed effectiveness. This suggests that while chemical abatement strategies may be the most consistently successful programs in reducing the density of questing nymphal ticks, depending on the local context and environment

Table 4 Studies using an integrated tick control strategy by classification (N= 28)

Author	Study/intervention target strategy	Description
Integrated effort occurred across multiple intervention classifications (n = 13)		
Burtis 2017 [127]	1. Landscape management; 2. Chemical, biological, natural tick control	Biological control (natural predator) with landscape management (vegetation removal)
Del Fabbro 2015 [56]	1. Management of host parasitism & movement (Deer targeted); 2. Landscape management	Deer exclusion with vegetation mowing
Keesing 2023 [69]	1. Management of host parasitism & movement (Rodent targeted); 2. Chemical, biological, natural tick control	Natural acaricide -environment (entomopathogenic fungi) and rodent targeted acaricide (bait box)
Little 2020 [64]	1. Management of host parasitism & movement (Rodent and deer targeted); 2. Chemical, biological, natural tick control	Deer removal, natural acaricide- environment (Met52), and rodent targeted acaricide (bait boxes)
Mandli 2021 [82]	1. Landscape management; 2. Management of host parasitism & movement	Vegetation removal and rodent targeted acaricide (tick tubes)
Ostfeld 2023 [62]	1. Management of host parasitism & movement (Rodent targeted); 2. Chemical, biological, natural tick control	Rodent targeted acaricide application (bait box-fipronil); natural acaricide-environment (Met52)
Ostfeld 2023 [62]	1. Management of host parasitism & movement (Rodent targeted); 2. Chemical, biological, natural tick control	Rodent targeted acaricide application (bait box); natural acaricide- environment (Met52)
Ostfeld 2024 [128]	1. Management of host parasitism & movement (Rodent targeted); 2. Chemical, biological, natural tick control	Rodent targeted acaricide application (bait box-fipronil); natural acaricide-environment (Met52)
Potes 2023 [44]	1. Management of host parasitism & movement (Rodent targeted); 2. Personal protection (population level)	Rodent targeted acaricide (fluralaner) and personal protection -community targeted
Schulze 2007 [61]	1. Management of host parasitism & movement (Rodent and deer targeted); 2. Chemical, biological, natural tick control	Deer targeted acaricide application (4-Poster); Rodent targeted acaricide application (bait box); chemical acaricide- environment (granular deltamethrin)
Stafford 2010 [110]	1. Landscape management; 2. Chemical, biological, natural tick control	Natural acaricide- environment (entomopathogenic fungi <i>Beauveria bassiana</i>), with or without woodchip borders
Williams 2017 [129]	1. Management of host parasitism & movement (Rodent and deer targeted); 2. Chemical, biological, natural tick control	Natural acaricide- environment (Met52), rodent-targeted bait boxes (fipronil), deer removal
Williams 2018 [73]	1. Management of host parasitism & movement (Rodent and deer targeted) 2. Chemical, biological, natural tick control	Deer removal; natural acaricide- environment (Met52); rodent targeted bait boxes-topical acaricide
Integrated effort occurred within the same intervention classification (n = 15)		
Bharadwaj 2012 [93]	Chemical, biological, natural tick control	Natural acaricide- environment (Met52, Nootkatone)
Deblinger 1991 [66]	Management of host parasitism & movement (Rodent and deer targeted)	Rodent and deer targeted host interventions
Dolan 2009 [113]	Chemical, biological, natural tick control	Multiple chemical acaricides -environment
Dolan 2017 [81]	Management of host parasitism & movement (Rodent targeted)	Rodent targeted- topical fipronil and oral doxycycline
Dolan 2018 [89]	Management of host parasitism & movement (Rodent targeted)	Rodent targeted- topical fipronil and antibiotic (ATB) treatment against infection
Dyer 2021 [96]	Chemical, biological, natural tick control	Natural and chemical acaricide- environment (multiple products)
Fischhoff 2018 [28]	Chemical, biological, natural tick control	Natural acaricide application-environment (entomopathogenic fungi) and natural predator control- environment
Garnett 2011 [130]	Management of host parasitism & movement (Deer targeted)	Deer removal and deer targeted acaricide application (4-Poster)
Gilbert 2012 [48]	Management of host parasitism & movement (Deer targeted)	Deer exclusion and deer removal

Table 4 (continued)

Author	Study/intervention target strategy	Description
Jordan 2011 [114]	Chemical, biological, natural tick control	Multiple natural acaricides-environment
Jordan 2019 [68]	Management of host parasitism & movement (Rodent targeted)	Rodent targeted acaricide (bait boxes and tick tubes)
Linske 2024 [116]	Landscape management	Vegetation management and ecotone modification
Linske 2021 [131]	Management of host parasitism & movement (Rodent targeted)	Bait-boxes (fipronil), 4-Poster treatment (permethrin), bait-boxes (Met 52)
Rand 2010 [100]	Chemical, biological, natural tick control	Natural acaricide- environment, and chemical acaricide -environment
Schulze 2021 [91]	Chemical, biological, natural tick control	Natural and chemical acaricide- environment (multiple products)

of the intervention, other available options could be considered to reduce LD risk depending on the feasibility, social acceptability, and cost needs of implementation in a given community.

Importantly, because of the environmentally dependent nature and other contextually important factors that influence study design choices for tick and LD prevention studies, the measurement and reporting of results across these studies is highly heterogeneous. This prevents functional synthesis of the data in a robust meta-analysis and is an issue that warrants consideration in future studies. Specifically, our systematic review identified variations in dosage, number of treatments, timing of treatments and measurement ascertainment, and delays between interventions and evaluation. Future research in this field may benefit from the development of guidance on standards for collection of data and reporting of results in published literature in order to optimize comparability with other studies, and consequently uptake of the intervention in other contexts. This could take the form of new or adapted reporting guidelines and quality assessment tools for tick-borne disease intervention studies, which offer flexibility depending on study context. Furthermore, future review studies aiming to conduct a meta-analysis would benefit from the development of guidance on the most appropriate way to synthesize heterogeneous data in this field of study, considering different outcome definitions and assessment timepoints.

In addition to evaluating the effectiveness of tick and LD control initiatives, this review summarized evidence on a range of secondary outcomes such as environmental impact, social acceptability, social resistance, feasibility, tick or biological resistance, and cost. Aside from the overall effectiveness of these studies in reducing LD risk, these factors are essential in determining successful selection, implementation, and scalability of these approaches across a variety of risk settings, and varying community needs. While these are certainly important

outcomes to consider, we found that a majority of the included studies lacked information on these outcomes and that most of the included information was provided indirectly (i.e. there were no measurements of these factors) in a descriptive manner.

Few of the included studies explicitly measured the environmental impact of an intervention despite this being the chief concern that arose surrounding social acceptability or social resistance. Studies evaluating chemical, biological, and natural tick control approaches were the most likely to feature information on environmental impact, with almost half of papers in this category including some discussion or measurement of this secondary outcome. Most of this information was presented in an indirect manner, citing environmental concerns as justification for a certain approach to product application, or the use of a non-synthetic alternative. This category of control was also the most likely to directly measure environmental impact using non-target species evaluation, or an analysis of residual products found in the environment [94, 97, 102, 132]. One third of landscape management studies and a quarter of studies on host targeted approaches also provided some discussion on environmental impacts of their interventions, however none of these studies provided direct measurements such as those found in the chemical/natural/botanical acaricide studies.

There were very few direct or indirect discussions regarding social acceptability or social resistance in any of the reviewed studies, with landscape management studies being the least likely to feature any discussion on these elements. Host targeted strategies were the most likely to highlight issues surrounding social acceptability of their programs, while personal protection strategies were most likely to discuss both social acceptability and resistance in their papers.

Feasibility was mentioned most consistently across all intervention categories, in the form of discussion of

challenges authors faced over the course of the study, or issues that arose regarding cost, scalability, and accessibility of the products or approaches they used. Almost half of the personal protection strategy studies included discussion of feasibility; followed by one third of studies evaluating host targeted strategies, which often faced challenges with non-target animal predation of their products (such as bait boxes), and difficulty maintaining the systems (often referring to 4-Poster devices) [61, 76]. Issues surrounding the feasibility of 4-Poster devices were examined in more depth in another recent study where the authors found that operation was feasible, with strategies available to minimize maintenance time [133].

While acaricide resistance is a growing concern in many vector control programs, very few reviewed studies included a discussion of this issue. A recent review which investigated tick resistance to common acaricides as it relates to both agricultural and pathogen transmission research, found widespread challenges to efficacy for all available acaricides due to the development of tick resistance [134]. The study highlighted a range of products, many that were featured in this systematic review within the chemical/botanical/natural acaricides category, and host targeted category; primarily concerning topical application acaricides (including products like fipronil, organophosphates, pyrethroids etc.). Despite this issue being highlighted as an important issue in the literature, studies on personal protection approaches were most likely to mention this topic, while studies on host targeted and chemical strategies were unlikely to mention issues surrounding tick or bacterial resistance to their products.

Furthermore, most studies did not include any information on the cost of the intervention, hampering the ability to make any strong conclusions on the feasibility of these methods moving forward with scalable community programming. However cost information was provided, this often included direct measurements within the context of the study. Our findings are consistent with findings from a recent study which found that most articles related to tick or LD control programs lacked cost estimates [135]. In addition, the authors conducted key informant interviews of pest control and landscape firms in their study area (Monmouth County, New Jersey) investigating the cost of some tick control products that could be applied on a residential scale. They found that most of the tick control options in their area exceeded the \$100–150 that homeowners are willing to spend per year to treat their residential property [135]. Increasing direct measurement or including more explicit discussion within future studies regarding factors such as feasibility, social acceptability, social resistance, environmental impacts, cost,

and biological resistance potential would help inform the uptake of these interventions by decision makers looking for relevant and feasible tick or LD control programs for their jurisdictions.

Strengths and limitations

While our search strategy was developed in collaboration with a library specialist, it is possible that even with a comprehensive search strategy some relevant studies may not have been identified. While the search was conducted in English, there were no limits placed on the search and no relevant studies were excluded due to language. In addition to measures of intervention effectiveness we included a wide range of outcomes on environmental impact, social acceptability, social resistance, feasibility, tick or bacterial resistance to the intervention, and cost. It is important to note that different categories of intervention are typically implemented on different scales, however this information was not consistently provided in the included studies which somewhat limits the comparability of factors such as cost and protective effect.

Because this systematic review included only personal prevention strategies that were distributed at a community or population level and it excluded studies which were single cross-sectional in their design, there were a limited number of studies in this intervention classification. These findings are consistent with a previous systematic review examining personal protective behaviors in the context of a widespread campaign [136]. This review, published in 2012, identified very few ($n = 9$) studies which met their inclusion criteria while including any study design, only three of which used a randomized design [136].

Risk of bias tools were applied to studies included in the data synthesis, which focused on studies with the most commonly reported outcome measure (density of questing nymphal ticks). ROBINS-I and ROB2.0, while robust tools, are designed to measure the risk of bias of studies with clinical or human outcomes, therefore they may not have been ideal instruments to assess studies in this systematic review; however, there is a lack of tools available for use on primarily environmental outcomes. To improve the applicability of these tools in our context, we followed recommendations from Bilotta et.al. and the modified ROBINS-I and ROB2.0 tools, as well as GRADE, were applied to our largely environmental outcomes [137].

This systematic review identified a lack of homogeneity in the way that results of tick and LD interventions were presented across different studies. This is consistent with previous reviews that have noted challenges in conducting meta-analyses related to this topic due to the

heterogeneity of methods and outcome measures used in this field of study [138]. Paired with the differences in field implementation, variety, density, and formulation of products and methods used, the quantitative data synthesis and effectiveness results should be interpreted with caution and may be most useful for descriptive purposes to compare the effects between intervention categories, not for the purpose of direct comparison of specific products or approaches. This is reflected in both the overall evaluation of effectiveness using paper-by-paper outcomes as well as the synthesis presented in this paper. In the data synthesis, we analyzed data on the most comparable outcomes between studies and the most comparable time points; therefore, some studies were excluded from the analysis because the outcomes were not sufficiently similar to the included studies in that intervention classification. We chose to retain site-specific estimates in the synthesis, rather than using mean estimates to retain environmental variation as an important factor in tick control methods. This means that sample sizes in the site-by-site estimates should be interpreted with caution given potential reductions in study power for these estimates. Additionally, although the use of the density of questing nymphs provides a good method for comparing interventions, this metric is only one component of acarological risk; some risk mitigation strategies which may be effective at reducing infection prevalence and which were not highlighted in our synthesis could also contribute to LD risk reduction. Notably, because most comparable studies reported the percent reduction or percent suppression of questing nymphs as the main outcome, there were no included confidence intervals presented in the articles, limiting our ability to use the GRADE tool to its full potential.

Conclusion

Overall, this systematic review included studies with a wide range of interventions and outcome types relating to tick or LD risk reduction that were applicable to a Canadian context with regards to wildlife hosts and environmental factors. While some strategies such as chemical acaricides were shown to have greater effectiveness, factors such as social acceptability and resistance, environmental impact, cost, and feasibility should be considered when selecting the most appropriate intervention. The consideration of these contextual factors is important to maximize the utility of the intervention for reducing LD risk in different settings.

Abbreviations

LD	Lyme disease
GRADE	Grading of Recommendations, Assessment, Development, and Evaluations
ROBINS-I	Risk Of Bias In Non-randomised Studies—of Interventions
ROB2.0	Risk-of-bias tool for randomized trials

Supplementary Information

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Supplementary Material 1
Supplementary Material 2
Supplementary Material 3
Supplementary Material 4

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Authors' contributions

K.O. wrote the main manuscript text and prepared all figures and tables. K.O., A.D., T.C., L.W., K.Z., J.P.R., C.B., C.A., and M.K., were involved in the conceptualization and methodology for this project. K.O., M.N., A.D., R.S., C.D., and O.F., were responsible for the analysis. A.K., C.F., and M.K. supervised the project and contributed to the conceptualization. All authors reviewed and edited the manuscript.

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Data availability

All included studies and data were extracted from an online query and extraction guide. These materials are provided in the supplemental materials of this article.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

The authors declare no competing interests.

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