Goals, Study Design Considerations and Implementation:
Establishing and moving toward the goals (Lyme disease)

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Integrated Tick Management Symposium

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Ultimate goals

- Reduce human bites by vector ticks

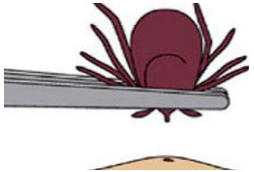
- Reduce the burden of Lyme disease and other tick-borne diseases

Chain of events for a Lyme disease case to occur

Host-seeking infected tick

Bite by infected tick

Tick feeding long enough to transmit spirochetes



If you remove a tick quickly (within 24 hr) you can greatly reduce your chances of getting Lyme disease.

Lyme disease case

Risk measures to predict Lyme disease cases

Density of host-seeking infected ticks

↑ **Human behavior / Personal protection**

No. known bites by infected vector ticks

↑ **Tick detection and removal**

No. known bites by infected vector ticks (>48 hr)

↑ **Transmission efficiency**

Lyme disease incidence

Personal protective measures and environmentally-based tick/pathogen control methods

PERSONAL PROTECTIVE MEASURES	LANDSCAPE / VEGETATION MANAGEMENT	KILLING OF HOST-SEEKING TICKS	RODENT-TARGETED APPROACHES	DEER-TARGETED APPROACHES
Avoid tick habitat	Xeriscaping / Hardscaping	Synthetic chemical acaricide	Topical acaricide	Deer fencing
Physically protective clothing	Keep grass short, remove weeds	Natural product-based acaricide	Oral tick growth regulator/acaricide	Deer reduction
Regular tick checks & Prompt tick removal	Remove leaf litter and brush	Biological fungal acaricide	Oral antibiotic	Topical acaricide
Synthetic repellent	Remove rodent harborage	Acaricides enhanced by tick arrestment pheromones	Oral Lyme disease vaccine	Oral tick growth regulator/acaricide
Natural product repellent	Do not use plants that attract deer			Deer anti-tick vaccine (disrupting tick feeding or reproduction)
Permethrin-treated clothing	Move play structures to low risk areas in the yard			
Antibiotic prophylaxis after tick bite	Ecotone barrier to tick movement			
Natural product acaricidal soap/lotion				
Human Lyme disease vaccine				
Human anti-tick vaccine (disrupting tick feeding)				

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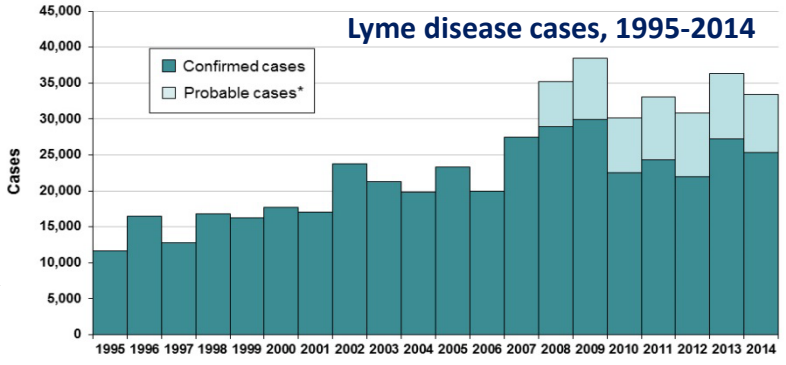
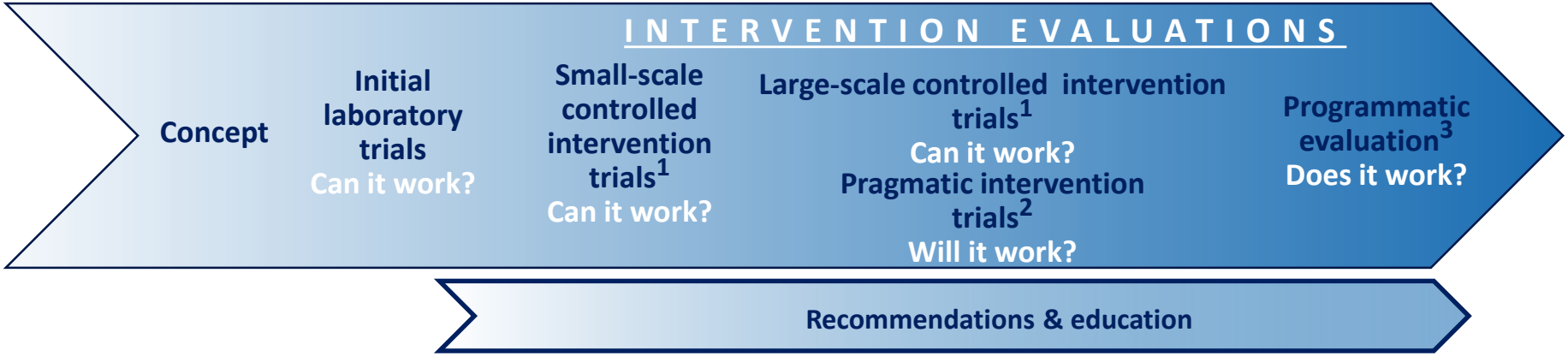


Development and evaluation of tick-borne disease prevention interventions

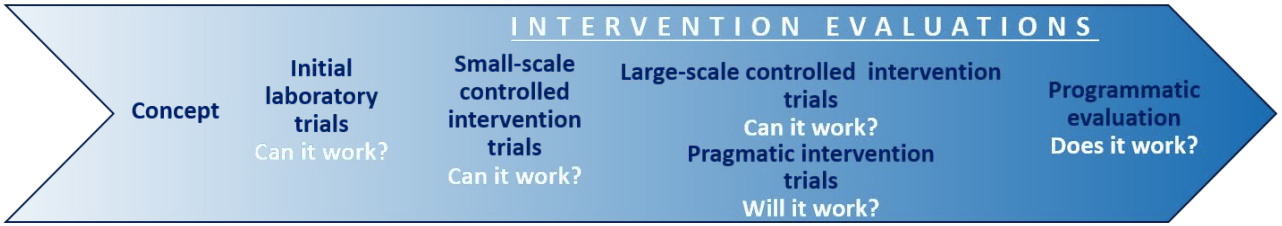


[1]Controlled intervention trial	• Optimal execution of the intervention
[2]Pragmatic intervention trial	• Real-world execution of the intervention
[3]Programmatic evaluation	• Impact on knowledge, attitudes, behaviors, and disease burden

Example 1:

Spray-on repellent

(personal protective measure)



Laboratory trials with *I. scapularis* (synthetic and natural product repellents): Carroll et al. 1989, 2004, 2005, 2007, 2010, 2011; Dietrich et al. 2006; Carroll 2008; Bissinger et al. 2009, 2014; Feaster et al. 2009; Zhang et al. 2009; Dolan and Panella 2011; Büchel et al. 2015

Small-scale controlled intervention trials with human-*I. scapularis* contact outcome (synthetic & natural repellents): Schreck et al. 1986, Evans et al. 1990, Schulze et al. 2011, Jordan et al. 2012; **typically >90% reduction in tick contacts**

Large-scale controlled intervention trials: Still lacking

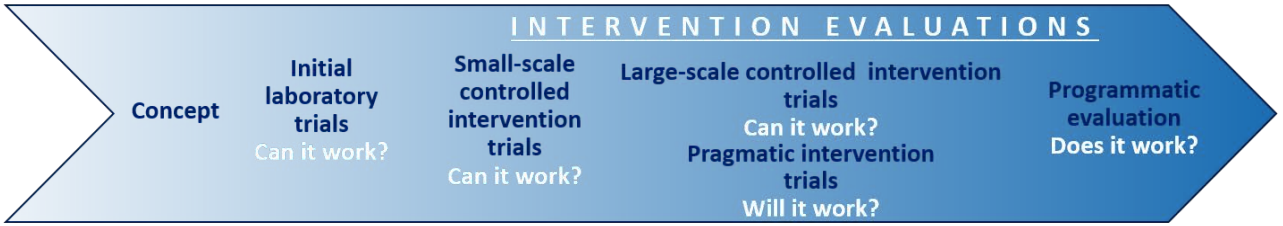
Pragmatic intervention trials with Lyme disease outcomes (case-control studies or cross-sectional studies): Smith et al. 1988, Schwartz and Goldstein 1990, Klein et al. 1996, Orloski et al. 1998, Armstrong et al. 2001, Phillips et al. 2001, Smith et al. 2001, Vázquez et al. 2008, Connally et al. 2009, Finch et al. 2014; **no more than moderate reduction in Lyme disease cases for only 3 of 10 studies**

Programmatic evaluation:

- Lyme disease cases have increased despite long-standing recommendations for repellent use to prevent tick bites

- Hook et al. (2015) found that ~25% of respondents routinely use repellent in Lyme disease endemic regions

Example 2:
Synthetic pyrethroid to kill host-seeking ticks



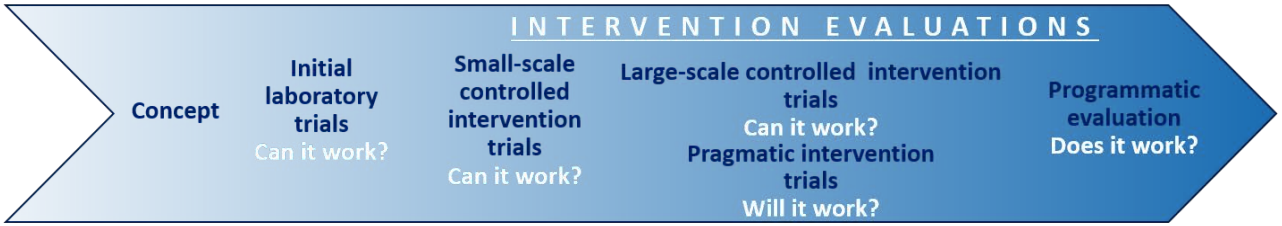
Laboratory trials with *I. scapularis*: Maupin and Piesman 1994; previous trials in the 1980s with several other tick species

Small-scale controlled intervention trials with *I. scapularis* abundance outcome: Solberg et al. 1992; Curran et al. 1993; Schulze et al. 2001b, 2005; Rand et al. 2010; Stafford and Allan 2010; Elias et al. 2013; **>85% control of host-seeking *I. scapularis* nymphs up to 7 wk regardless of application method, spray pressure, or woodland versus residential setting**

Large-scale controlled intervention trials / Pragmatic intervention trials with tick- and disease-based outcomes: Hinckley et al. 2016; **45-69% reduction of *I. scapularis* nymphs in residential ecotones (from barrier spraying) did not reduce either tick bites or Lyme disease cases**

Programmatic evaluation: Hook et al. (2015) found that <10% of respondents currently use yard-based pesticides in Lyme disease endemic regions

Example 3: Integrated tick / pathogen management



Laboratory trials: Based on combinations of single methods already proven in lab trials (if applicable)

Small-scale controlled intervention trials with *I. scapularis* abundance outcome:

- Schulze et al. (2007, 2008); integrated use of barrier spraying with pyrethroid (Yr 1 only) and topical acaricides for rodents (Yrs 1-2 only) and deer (Yrs 1-3); **abundance of host-seeking nymphs reduced by 86% in the year after the intervention was put in place and by 86–94% in the two following years**
- Additional studies are nearing completion (Mather, Stafford); final results still pending

Large-scale controlled intervention trials / Pragmatic intervention trials with tick- and disease-based outcomes: Still lacking but one study about to start (Ostfeld/Keesing; tentatively fungal acaricide to kill host-seeking ticks combined with rodent-targeted acaricide)

Programmatic evaluation: Not yet applicable

Integrated tick/pathogen management: ITM component options

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Selection of ITM combinations to move forward in pipeline:

- **Acceptability**
- **Cost**
- **Single household *vs* Neighborhood/Community**
- **Potential for reducing Lyme disease (hard data, simulation modeling)**

Moving forward

- Prioritization of single and integrated prevention/control approaches to move through the development/evaluation pipeline
  - Weak evidence bases for most approaches, single or ITM, even in small scale intervention trials
  - Only very limited numbers of ITM approaches can realistically be evaluated in large scale intervention trials with Lyme disease outcomes
  - Investment in programmatic implementation will be driven by evidence for disease reduction
- Maintaining expertise to conduct intervention evaluation studies
- Design of intervention evaluation studies – Alison Hinckley
- Study outcome measures – Howie Ginsberg
- Responsible implementation parties / end user engagement – Tom Mather
- Finding the funds (order of magnitude increase needed) – Ben Beard

With thanks to the “pipeline group”
Ben Beard, Marc Dolan, Rebecca Eisen, Ken Gage, Alison Hinckley,
Sarah Hook, Kiersten Kugeler, Paul Mead, Christina Nelson, Anna Perea,
and others……

For more information, contact CDC
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