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REVIEW

Eradication and containment of non-native forest insects: successes and failures

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Abstract
The problem of forest insect invasions is intensifying. Non-native forest insects are invading virtually every world region, and many are causing severe ecological and economic impacts. Biosecurity programs provide for intervention at various stages of the invasion process in order to mitigate the invasion problem. While preventing initial arrival of non-native insect species is a sound approach, such prevention is not always possible so additional measures are needed to manage invasions. Surveillance coupled with eradication is a valuable strategy for preventing the establishment of many new and potentially damaging species. Once non-native species are established, containment measures can be implemented to stop or slow the spread of these species in their non-native habitat. Here, we review how eradication and containment can be carried out as strategies for managing forest insect invasions. Several hundred programs have been implemented to eradicate non-native forest insects, with most programs proving successful. The vast majority of these eradication programs were implemented from 1970 onward. Pheromone-baited traps play a key role for detection and delimitation in most successful eradication programs. The isolation and synthesis of pheromones provided a key technology that facilitated forest insect eradications starting in the 1970s. Several examples are provided that illustrate both successful and failed eradication and containment programs. Consideration of historical experiences suggests the conditions that may lead to either success or failure of eradication and containment efforts.

Keywords Biological invasion · Biosecurity · Extinction · Barrier zone · Exclusion · Slow the spread

Key messages

- Worldwide, hundreds of programs to eradicate invading forest insect populations have historically been implemented, mostly since 1970.
- While many forest insect eradication efforts have been successful, there have also been many failures; though technological advances have facilitated eradication, there continues to be a need for improved methods.
- The isolation and synthesis of insect semiochemicals has greatly enabled efforts for both eradication and containment of forest insects.
- Slowing the spread of invading forest insect populations can yield economic benefit, but such programs are more practical for certain species.

Introduction

Worldwide, forests are increasingly affected by a variety of human-caused impacts. These include deforestation, air pollution and climate change. In many parts of the world,

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invasions by non-native organisms are also dramatically altering forest ecosystem processes. This often results in a decline in the goods and services that forests provide (Liebhold et al. 2017; Boyd et al. 2013).

During the last two centuries, the problem of invasions by non-native forest insects has been growing (Roques et al. 2009; Aukema et al. 2010; Brockerhoff and Liebhold 2017). Driven primarily by the global movement of wood (including wood packaging material) and plants in trade, a variety of forest insect taxa are being transported outside of their native ranges and establishing in new regions. Most of these non-native species cause little or no noticeable damage; Aukema et al. (2011) report that only ~ 15% of non-native forest insects established in the USA cause reportable damage. However, several of these species have caused severe ecological or economic impacts and represent some of the most serious forest pests (Gandhi and Herms 2010; Boyd et al. 2013).

Managing forest insect invasions can be challenging, but it is crucial to consider the various approaches relative to the known biological invasion phases through which each new invasion passes: arrival, establishment and spread (Liebhold and Tobin 2008). This is a concept described as management across the "Biosecurity Continuum" (Hulme 2014). Preventing arrival has often been identified as the most effective strategy for dealing with invasions (Leung et al. 2002). This is typically accomplished through the use of international quarantines (i.e., bans on the import of specific commodities likely to be contaminated) or phytosanitary treatments (e.g., fumigation) of imported goods (Allen et al. 2017). But often these prevention measures are not totally effective and non-native species may still arrive and establish. In these cases, the next level of species exclusion is accomplished via surveillance (survey to detect newly arrived populations) and eradication (forced extinction of a species from a given area). Eradication may not always be possible, and in these cases some type of containment strategy may be implemented to stop or slow the spread of an invading organism (Sharov and Liebhold 1998a). Once populations become widely established, measures such as biological control or deployment of resistant tree genotypes may be options for mitigating the damage caused by a non-native species.

This paper covers the application of eradication and containment as strategies for managing invading forest and urban tree insect species. The approach taken here is to emphasize case studies that document these management strategies. Relatively little information exists in the literature that covers barrier zones in general, but several recent papers summarize the current state of knowledge on insect eradication (Brockerhoff et al. 2010; Suckling et al. 2014a; Liebhold et al. 2016).

Eradication

The majority of invading populations initially arriving in non-native habitats fail to establish, in part due to habitat unsuitability (e.g., improper climate and lack of host plants), but also because these low-density populations are subject to extinction (Liebhold and Tobin 2008). The two main causes of extinction in low-density populations are stochasticity (both environmental and demographic) and Allee effects (Lande 1998; Kramer et al. 2018). An Allee effect exists when there is decreasing population growth with decreasing density of an organism; a strong Allee effect creates a population density threshold below which populations tend to decline to extinction (Liebhold and Tobin 2008). A variety of mechanisms may cause Allee dynamics, including mate-finding failure, satiation of predators and group feeding (e.g., more successful utilization of hosts by large populations, such as in many bark beetle species). Invading populations that arrive at population densities below Allee thresholds are not likely to establish.

When a strong Allee effect exits, eradication may be achieved without killing all individuals; instead, populations need only be forced below the critical Allee threshold density (e.g., via application of pesticides), and then, they will likely go extinct without further intervention (Liebhold and Tobin 2008; Liebhold et al. 2016). Other approaches to eradication may achieve a similar result by modifying mechanisms that cause Allee effects. For example, mate-finding failure may cause a strong Allee effect in low-density populations of most sexually reproducing insects. Mating disruption treatments will intensify mate-finding failure, shifting the Allee threshold to higher levels and thereby causing extinction in populations that otherwise might persist (Liebhold and Bascompte 2003; Liebhold et al. 2016; Yamanaka and Liebhold 2009). Other treatments that can shift the Allee threshold include male annihilation (i.e., mass trapping of males with sex pheromone-baited traps), predator augmentation and sterile insect releases (Yamanaka and Liebhold 2009; Blackwood et al. 2012).

One general requirement before eradication can even be considered is the availability of a survey tool for initially detecting nascent populations while they are still small and more practically eradicated. Insect attraction to pheromones or host compounds is often exploited for detecting low-density populations by deploying traps baited with synthetic attractants (Suckling et al. 2014a). Analysis of historical insect eradication programs indicates that the availability of a sensitive tool, such as attractant-baited traps, greatly increases the likelihood of successful early detection and eradication of invading populations (Tobin et al. 2014). Availability of sensitive detection tools is not only critical for the early detection of populations, but also key for delimitation of populations being eradicated, facilitating targeting of treatments and also confirming eradication success.

Historical forest insect eradications

There is a long history of both successful and unsuccessful eradications of invading forest insect populations, and this is well documented in the Global Eradication and Response Database (GERDA) (Tobin et al. 2014; Kean et al. 2018). However, Fig. 1 shows that the global implementation of eradications greatly increased considerably in the 1970s. Many insect pheromones were first identified and synthesized beginning in the 1970s and given the key role that insect attractants play in detecting and eradicating populations, this most likely explains this trend.

While the GERDA database indicates that the majority of forest insect eradication projects have been successful (53% successful, 22% failure, 25% unknown outcome), the majority of these have targeted the gypsy moth, *Lymantria dispar*, in N. America (Table 1). If this species is excluded, the success rate is less (40% successful, 27% failures, 33% unknown). The very first known forest insect eradication attempt (possibly the first attempt for all insects) was the failed eradication of the gypsy moth from eastern Massachusetts (USA) (Forbush and Fernald 1896). This species was inadvertently introduced by an amateur naturalist, Étienne Léopold Trouvelot, working at his home near Boston in 1868 or 1869 (Liebhold et al. 1989). Following establishment, populations spread and the first outbreak was noticed in Trouvelot's neighborhood in 1880. Given concern about the damage caused by this insect, the state of Massachusetts implemented a large program to eradicate it. The program utilized a variety of methods for control, including manual removal of life stages, destruction of infested forests and spraying using primitive insecticides (Fig. 2). But ultimately the program was unsuccessful and was abandoned in 1900. It should be noted that even though a female-baited trap had been devised (Fig. 2a) these were not widely implemented as a survey tool.

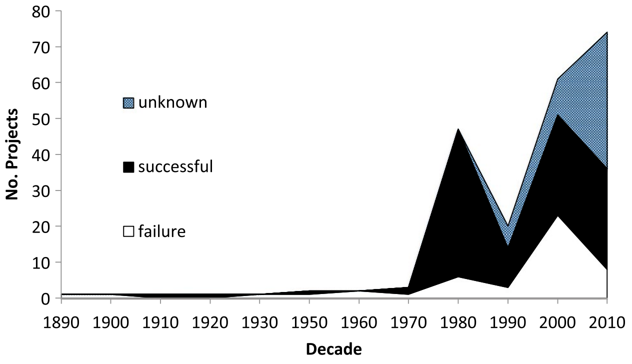

Fig. 1 Numbers of historical forest insect eradication projects by decade. Data extracted from GERDA database (Kean et al. 2018)

More recent efforts to eradicate the gypsy moth have been much more successful. The European strain of the gypsy moth is currently established in northeastern N. America, but every year humans accidentally transport life stages (typically egg masses with household moves) well outside of the generally infested area (Fig. 3). Isolated populations are frequently found as far west as the Pacific coast states. In a cooperative effort between USDA APHIS and state governments, about 100,000 pheromone-baited traps are deployed every year in these uninfested areas to detect new populations (Tobin et al. 2012). Following initial detection, more traps are typically deployed in the following year to confirm the persistence of and delimit populations. If the population still persists, then it is usually treated in the third year. Most gypsy moth eradication programs utilize aerial spraying with *Bacillus thuringiensis* (Hajek and Tobin 2010) though a few programs use ground spraying or mating disruption. Since 1970, there have been > 100 localized gypsy moth eradication programs in the USA and most of these have been successful (Table 1).

It is logical to question why the first gypsy moth eradication program from 1880 to 1900 failed while modern programs are largely successful. The answer probably lies with the availability of tools for detection and treatment. In 1880, scientists knew that female gypsy moths released a pheromone (Fig. 2a), but it could not be synthesized and there was limited knowledge in how to use it for detection and delimitation. Furthermore, treatments available in 1880 were expensive and of limited effectiveness. Thus, the ease with which gypsy moth invasions are currently detected and eradicated in the USA serves to illustrate the importance of technology development to the success of any eradication effort.

As stated earlier, eradication may be difficult to accomplish for species for which sensitive detection tools are lacking, but there are several examples of forest insect species that have been successfully eradicated even though a highly attractive synthetic pheromone is lacking (Table 1). One such case is the successful eradication of the painted apple moth, *Teia anartoides*, an Australian Lymantriidae, using a combination of tactics including host plant removal, aerial application of *B. thuringiensis* and sterile male releases (Suckling et al. 2007). An unusual aspect of this effort was that it was conducted without the use of pheromone-baited traps; the female-produced pheromone was found to be unstable so the program delimited the infestation using traps baited with laboratory-reared live females. Other examples of successful eradication achieved without the availability of synthetic attractant are programs to eradicate the Asian

Table 1 Fifteen forest insect species most frequently appearing in the GERDA eradication database

Species	Common name	Countries	Years	No. of successful	No. of failed	Unknown outcome	Survey methods[a]	Eradication methods[b]
Lymantria dispar	Gypsy moth	Canada, USA	1890–2016	109	10	8	PT, VS	MP, CP, MT, MD
Agrilus planipennis	Emerald ash borer	Canada, USA	2003–2005	1	26	0	VS	HR
Anoplophora glabripennis	Citrus long-horned beetle	Austria, Canada, France, Germany, Italy, Japan, Netherlands, UK, USA	1997–2014	10	0	12	VS	HR, CP
Anoplophora chinensis	Asia long-horned beetle	Croatia, Italy, Lithuania, Netherlands, UK, US	2000–2011	6	0	9	VS	HR
Lymantria dispar asiatiaca	Asian gypsy moth	Canada, USA	1991–2008	17	0	0	PT, VS	MP, CP
Rhynchophorus ferrugineus	Red palm weevil	China, Egypt, Israel, Jordan, Spain, Tunisia	1992–2011	0	2	6	VS	CP, MT, HR
Adelgese tsugae	Hemlock woolly adelgid	USA	2004–2010	2	0	4	VS	HR, CP
Dryocosmus kuriphilus	Oriental chestnut gall wasp	France, Hungary, Netherlands, Slovenia	2005–2010	3	1	2	VS	HR
Epiphyas postvittana	Light brown apple moth	USA	2007–2010	1	1	2	PT	MP, MD
Paysandisia archon	Palm moth	Czech Republic, Italy, Switzerland	2007–2010	1	0	2	VS	HR, CP
Maconellicoccus hirsutus	Pink hibiscus mealybug	Jamaica, USA	2002–2008	1	0	3	VS,	CP
Sirex noctilio	Sirex woodwasp	Australia, Argentina, Chile	1961–2001	1	2	0	HAT, VS	HR
Euproctis chrysorrhoea	Brown-tail moth	Canada, USA	1897–1907	1	1	0	VS	HR
Thaumetopoea pityocampa	Pine processionary moth	Italy, Spain	1983–2007	1	0	1	VS	HR, CP
Haumetopoea processionea	Oak processionary moth	UK	2006–2010	0	1	1	VS	HR, CP

[a] Abbreviations for survey methods: *HAT* host attractant trap, *PT* pheromone traps, *VS* visual searches

[b] Abbreviations for eradication methods: *CP* chemical pesticides, *HR* host removal, *MD* mating disruption, *MP* microbial pesticides, *MT* mass trapping

long-horned beetle (ALB), *Anoplophora glabripennis*, from Chicago, USA (1998–2008), Toronto, Canada (2003–2013), Braunau, Austria (2001–2013) and elsewhere (Haack et al. 2010; Javal et al. 2018). In these programs, delimitation has been accomplished by visual surveys for emergence holes on tree boles. Eradication has been accomplished using removal or pesticide treatments of all trees within a fixed distance (e.g., 400 m) of positive finds (Haack et al. 2010). Virtually all successfully eradicated ALB populations existed in urban habitats, but in the USA there are two sites (Massachusetts and Ohio) where extensive ALB populations have been discovered in continuous natural forests (Dodds and Orwig 2011). These incursions went unnoticed for many years so their populations are more extensive, and given their vast extent, eradication has proved more challenging.

An issue that often arises during eradication programs is the possibility of negative reactions from residents. Urban/suburban habitats are frequent sites for initial arrivals of pests (Paap et al. 2017), so it is no surprise that most forest insect eradication programs operate in such environments.

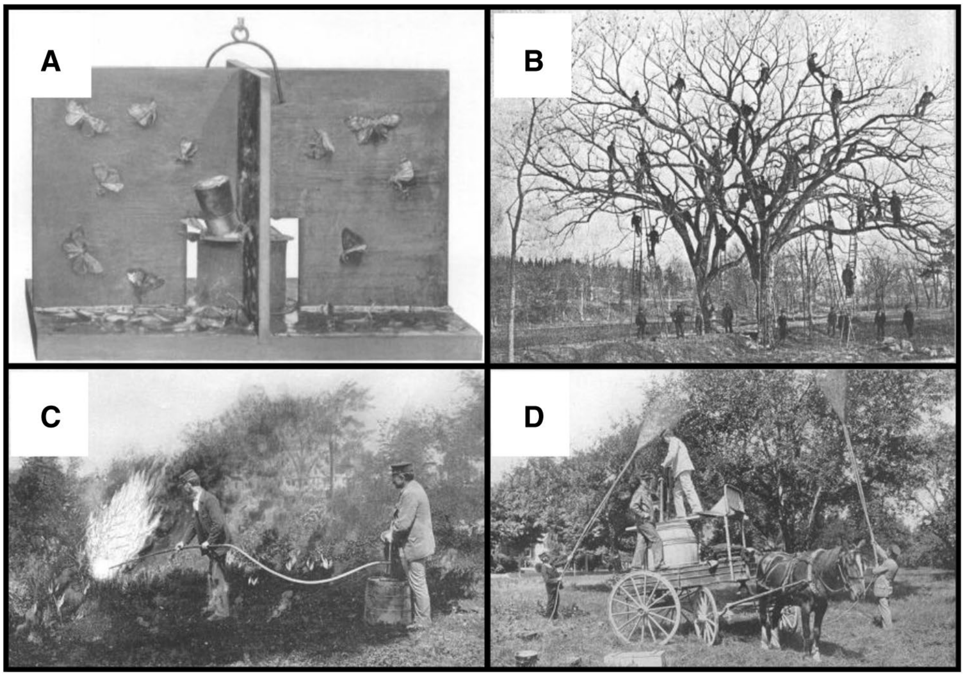

Fig. 2 Scenes from failed attempt to eradicate the gypsy moth, *Lymantria dispar*, from Massachusetts, USA, 1880–1900. **a** Sticky trap baited with live female. Photograph: Forbush and Fernald (1896). **b** Scraping egg masses from large tree. Photograph: USDA. **c** Burning of infested forest. Photograph: Forbush and Fernald (1896). **d** Spraying using primitive insecticides. Photograph: Forbush and Fernald (1896)

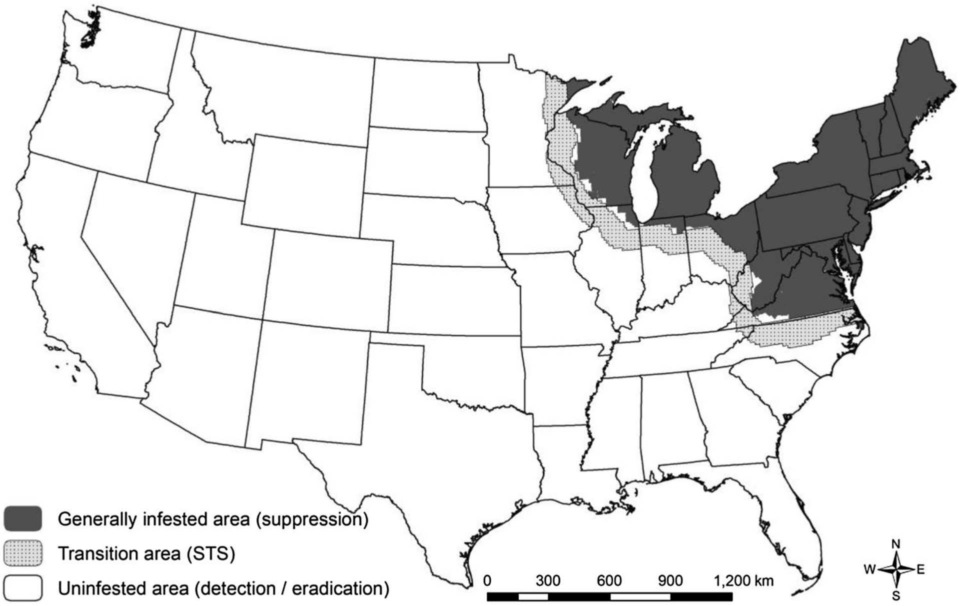

Fig. 3 Map showing the geographical distribution of invading gypsy moth populations in the USA with locations of the generally infested area, the uninfested area and the transition area (location of the gypsy moth Slow the Spread program)

Unfortunately, residents of these areas may perceive eradication treatments, such a tree removal or pesticide applications, as not warranted and/or unhealthy (Liebhold et al. 2016). Consequently, any eradication program should devote considerable resources toward public engagement since there is a need to explain the value of such programs. A good example of the importance of public outreach is provided by the failed eradication of the light brown apple moth, *Epiphyas postvittana*, from California (Suckling et al. 2014b). This damaging Australian Tortricid was discovered in the San Francisco Bay area in 2007, and an eradication effort was initiated. The decision was made to avoid the use of pesticide treatments because of the large residential population in the infested area. Instead, eradication was attempted via aerial treatment using mating disruption. Due to a lack of information, a large segment of the public believed that treatments were being conducted using toxic substances, and this resulted in extensive public outcry which ultimately led the state of California to abandon the eradication effort (Linderman 2013).

Another factor that has contributed to the successful implementation of eradication programs for forest insects has been the development of more effective and environmentally sound treatment technologies. Early eradication programs often relied upon the use of chemical pesticides, but these have largely been replaced by the use of microbial pesticides (Hajek and Tobin 2010) and semiochemical treatments (e.g., mating disruption and mass trapping) (Suckling et al. 2014a). Development of socially acceptable new technologies for more efficiently eradicating invading populations is likely to drive further increases in the frequency and success of eradication attempts.

Containment

Following initial establishment of a non-native species, its populations typically expand into suitable habitats. Invasion spread can be considered the coupling of population growth with dispersal, and thus, any factors that promote either process can be anticipated to promote spread (Liebhold and Tobin 2008). In addition to natural insect dispersal (e.g., airborne flight), insect movement may be facilitated by humans via movement of live plants, infested wood (e.g., firewood) or any object on which insects may become associated (i.e., "hitchhiking").

Given this understanding of the invasion process, strategies to slow or stop the spread of invading species must target reducing either population growth or dispersal. Examples of tactics that have been used to reduce population growth include removal of host plants, suppression of populations via insecticides or enhancement of natural enemy impact. Interruption of natural dispersal has been used as a tactic to contain invasion spread in vertebrate populations (McKnight 1969), but this is not a common strategy applied for containment of invading insects. In contrast to controlling natural dispersal, it is much more practical to interrupt insect movement facilitated by humans, and this may offer tremendous opportunities for limiting their spread. Insects often move domestically on live plants, so inspection and quarantine of plant shipments from nurseries is an important tactic for limiting spread (Davidson et al. 2000). These quarantines may be implemented by national governments or by state/provincial governments but are generally most effective if coordinated at a national level. Within several countries, the movement of wood, particularly firewood, is regulated in order to limit spread of bark and wood-boring insects. For example, Canada prohibits domestic movement of firewood out of areas that are quarantined for pests such as Asian long-horned beetle, brown spruce long-horned beetle (*Tetropium fuscum*), Dutch elm disease, emerald ash borer (*Agrilus planipennis*), gypsy moth and hemlock woolly adelgid (*Adelges tsugae*) (Canadian Food Inspection Agency 2017). Finally, inspection is another approach sometimes implemented in order to contain pest spread. For example, several Australian states maintain border stations where automobiles are inspected for hitchhiking plant pests (Maynard et al. 2004).

One characteristic commonly seen in the spread of invading insect populations is the formation of isolated "satellite populations" ahead of the continuously populated invasion front. This phenomenon results from a process termed "stratified dispersal," in which insects move continuously over short distances but discontinuously over longer distances. These occasional long-distance jumps are recognized to greatly elevate invasion spread (Shigesada et al. 1995; Kovacs et al. 2011). Consequently, any efforts to find and suppress these satellite populations can be an effective strategy for reducing the spread of an invading species.

Historical containment programs

Most eradication programs implement some type of control on movement of potentially contaminated objects out of the eradication area in order to contain the isolated population under eradication. However, there are relatively few examples of efforts to manage the spread of more widely established populations of invasive forest pests. The most common approach to managing spread is the use of quarantines. For example, in the USA and Canada movement of ash wood or nursery stock out of the region infested by the emerald ash borer is prohibited as a measure for limiting the spread of this species (Herms and McCullough 2014). A quarantine on movement of elm wood and nursery stock has been successful at preventing the spread of the European elm bark beetle, *Scolytus multistriatus*, to the South Island of New Zealand from the North Island where it is established (Gadgil et al. 2000).

Another species for which quarantine measures have historically been used to slow spread is the European woodwasp, *Sirex noctilio*. This species has invaded most regions of the southern hemisphere where pines are planted, resulting in considerable tree mortality. For example, in Australia quarantine measures have been in place for many years to restrict the movement of *Sirex*-infested pines into the states of Queensland and Western Australia (Carnegie et al. 2006). Another method that has been implemented for slowing the spread of this species is biological control; in some countries, populations of the pathogenic nematode, *Deladenus siricidicola,* have been augmented along invasion fronts. However, analysis of historical spread in Argentine Patagonia indicates that these efforts sometimes have had little effect on spread (Corley et al. 2014). Releases of natural enemies could conceivably reduce spread via their impacts on host population growth rates (Hilker et al. 2005), but in this case, the impact of the nematode may be diminished by its negative effect on male competitiveness (Corley et al. 2014).

Probably the best example of a successful large barrier zone program targeting a forest insect is the gypsy moth Slow the Spread (STS) program in the eastern USA (Sharov et al. 2002). This program has been fully in place since 1999 and consists of a 100-km band running along the gypsy moth's expanding population front (Fig. 3). Along that band, pheromone traps are deployed in a ~ 3-km grid in order to detect satellite populations ahead of the advancing population front. The STS strategy exploits the stratified dispersal of the gypsy moth; suppression of satellite populations entails treating a relatively small area but has a large benefit in reducing spread (Sharov and Liebhold 1998b). Mating disruption is the primary treatment applied in STS, further limiting its environmental impact. The program has been successful at reducing historical spread by > 50%, and this has been shown to justify the $10 million USD annual cost of the program by delaying the damage and management expenses that begin once an area becomes invaded by the gypsy moth (Sharov et al. 2002).

Other barrier zone efforts have been less successful. Among these, efforts to contain spread of the emerald ash borer (EAB) in N. America have been particularly disappointing. The species probably initially established near Detroit, USA, in the early 1990s but was not discovered until 2002. By this time, populations were so widespread that plans to eradicate the population were quickly abandoned and effort shifted toward containment (Herms and McCullough 2014; Siegert et al. 2014). In 2004, all ash trees were cut in a 10-km band running from Lake Erie to Lake St. Clair just east of the Windsor, Canada, in order to contain EAB spread, but infested trees were subsequently found beyond this ash-free barrier so it was considered a failure and management switched to containing satellite populations (Herms and McCullough 2014; Poland and McCullough 2006). The infested trees found beyond the ash-free barrier were likely colonized before the barrier was cut, and this illustrates the value of early detection for implementing barriers to spread. In late 2005, the Canadian Food Inspection Agency removed ~ 50,000 ash trees within 500 m of a satellite population found near the city of Chatham, but again infested trees were subsequently found beyond this control zone (Marchant 2007). Similar efforts to contain satellite populations failed elsewhere in both Canada and the USA, so currently management focuses only on prohibiting transport of ash firewood and nursery stock out of infested regions. Despite these efforts, this insect has expanded its range at an explosive rate. It appears that the majority of susceptible forests in the eastern USA and Canada are likely to be invaded within the next 5 years. In forest areas where the insect has become established, there has been some success in slowing the rate of ash mortality using girdled trap trees, removal of infested trees and treatment of trees with pesticides (McCullough et al. 2015; Mercader et al. 2015). The failure of the efforts to contain the spread of this damaging insect can be attributed to the lack of effective methods for detecting populations at low density. There is yet no evidence of a long-distance pheromone in this species, and even attraction to host compounds is relatively weak (Silk and Ryall 2015). Without a more sensitive detection tool, EAB typically establishes and spreads over a large area before it is first discovered in an area. This makes both eradication and containment impractical.

Conclusions

The trend of globalization has driven the intensification of the forest insect invasion problem in virtually every world region (Brockerhoff and Liebhold 2017). Given the severe ecological and economic impacts of these invasions, biosecurity takes on an even more important role. Prevention of invasions typically represents a dominant part of biosecurity efforts in most countries, but it may not be practical to prevent all invasions. Consequently, eradication and containment offer opportunities for preventing or delaying the often massive impacts caused by certain non-native forest insects.

Ultimately, decisions whether to implement eradication or containment depend upon both an analysis of the unique features of each non-native species that affect the practicality of eradication or containment along with economic analyses that weigh costs of such efforts against averted impacts (Epanchin-Niell 2017). As mentioned earlier, the single biological feature that is most relevant to the practicality of surveillance, eradication and containment is the availability of an effective attractant that can be used to detect and delimit low-density populations.

There are several economic considerations that play important roles when allocating resources in a biosecurity program and in particular when evaluating the viability of eradication or containment. First, there is typically considerable uncertainty in predicting impacts of any non-native species. Consequently, the science behind pest risk analysis plays a key role in these decisions (Burgman et al. 2014). Second, there is an inherent trade-off between allocation of resources toward surveillance and eradication. High expenditure on surveillance means that invasions are detected early when they are inexpensive to eradicate, but reduction in surveillance effort means that invasions are detected later when eradication is more expensive (Epanchin-Niell et al. 2012). The third consideration is that the timing of an invasion is key to selection of an economically optimal strategy for eradicating it. As an invasion progresses, the optimal strategy often shifts from eradication to containment to no intervention (Sharov and Liebhold 1998a; Olson and Roy 2002). Because future damages are typically discounted back to the moment of intervention (eradication or containment), the delay between establishment and damages may play a key role in determining whether eradication or containment are optimal strategies (Epanchin-Niell and Liebhold 2015). In this context, it should be mentioned that ecologists sometimes fail to understand the economic benefit derived from efforts to slow the spread of an invading species; by delaying the damage into the future, discounted values of impacts may be far less than if they would occur earlier.

Technological advances have driven a rapid increase in the number of successful programs to eradicate forest insect invasions over the last four decades (Fig. 1b). Probably the most significant technology has been the identification and synthesis of insect semiochemicals that can be used to detect populations at low densities. These greatly facilitate the early detection and delimitation of populations prior to eradication. Given that many of these same new technologies can be used in forest insect containment programs, we anticipate that a similar increase in containment may occur in the future when analyses indicate economic value in delaying future impacts.

Author contributions

AML conceived the topic for this paper. JMK designed and assembled the GERDA database. Both authors jointly wrote the manuscript. Both authors read and approved the manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical standard This article does not contain any studies with human participants or animals performed by any of the authors.

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