ADVANCES IN INTEGRATED TICK MANAGEMENT RESEARCH FOR AREA-WIDE MITIGATION OF TICK- BORNE DISEASE BURDEN

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SUMMARY

In some parts of the world, ticks are the most dangerous animals followed by mosquitoes as ectoparasites and vectors of infectious agents, causing morbidity and mortality in domestic animals including wildlife and humans. The majority of tick-borne diseases are zoonotic. The global importance of ticks and tick-borne diseases in veterinary medicine and public health keeps growing. Some ticks are invasive and transmit pathogens causing transboundary diseases of high consequence for populations of domestic animals and humans. Integrated management pursues the optimized use of compatible methods to manage pests in a way that is safe, economically viable, and environmentally sustainable. The area-wide approach augments and expands the benefits of integrated pest management strategies. Issues challenging the implementation, adoption, and viability of area-wide tick management programmes include funding and socio-political aspects, the availability of support systems related to extension and veterinary services, and stakeholder involvement. Management strategies need to adapt and integrate novel technologies to decrease significantly the use of pesticide and address the complex problem of ticks and tick-borne diseases effectively. Applying the *One Health* concept, the strategy to optimize health outcomes for humans, animals, and the environment, facilitates research on the interplay between climate, habitat, and hosts driving tick population dynamics. It enhances our understanding of the epidemiology of tick-borne diseases and advances their management. This overview of research for adaptive area-wide integrated management concentrates on ticks affecting livestock. Examples focus on *Rhipicephalus microplus* (Canestrini) as one of the tick disease vectors most studied worldwide. Highlights of integrated management research for ticks

of public health importance transmitting zoonotic diseases are reviewed to document opportunities for integrated control that mitigate the health burden of tick-borne diseases on humans, domestic animals, and wildlife. Implementation of the research conducted so far is needed to accelerate advancements in area-wide management of tick populations that can be applied to improve prevention across tick-borne diseases, while decreasing pesticide application and contributing to vector control globally.

Key Words: Acari, *Rhipicephalus annulatus*, *Rhipicephalus microplus*, babesiosis, ectoparasites, disease vectors, tick-borne pathogens, acaricides, resistance, cattle fever tick reservoirs, livestock vaccination, area-wide tick management, integrated tick-borne disease prevention, One Health, global change, invasive

1. INTRODUCTION

In some parts of the world, ticks (Acari) are the most dangerous animals followed by mosquitoes as ectoparasites and vectors of infectious agents causing morbidity and mortality in domestic animals, wildlife and humans (Ahmed et al. 2007; Socolovschi et al. 2008; Heyman et al. 2010; Barker et al. 2014; Paddock et al. 2016). Approximately 80% of the cattle in tropical and subtropical regions of the world are affected by economically important ticks and tick-borne pathogens (McCosker 1979; de Castro 1997). In addition, estimates indicate that Lyme disease and other diseases caused by tick-borne pathogens could burden over 30% of the global human population by 2050 (Davidsson 2018; Sakamoto 2018). Most tick-borne diseases affecting people are zoonotic because they can be transmitted from wild and domestic animals to humans through the bite of an infected tick (Lorusso et al. 2016; Ojeda-Chi et al. 2019).

Life history traits afford ticks considerable importance as pests and vectors of pathogens. Ticks are ancient arthropods that parasitize vertebrate hosts by feeding on blood to be able to complete their life cycle (Mans et al. 2011; Peñalver et al. 2018). Tick-borne pathogens include protozoa, bacteria, and viruses that co-infect their vectors and hosts (Brites-Neto et al. 2015; Talactac et al. 2018; Wikel 2018). Being local specialists and global generalists in their host associations underlie the global distribution of ticks and their ability to adapt to diverse environmental niches (McCoy et al. 2013; de la Fuente et al. 2015b; Beati and Klompen 2019).

There are ca. 920 described tick species in the world, but the diversity of ticks remains to be fully established (Dantas-Torres 2018; Mans et al. 2019). The so-called hard ticks belong to the Ixodidae family that have a sclerotized scutal plate in their dorsum (Sonenshine and Roe 2014). By comparison, soft ticks in the family Argasidae lack the scutum and have a flexible leathery cuticle (Uspensky 2008). Depending on the tick species, the parasitic larva, nymph, and adult stages are completed in one, two, or three hosts (Estrada-Peña 2015). After blood-engorged, females that mated on the host, then drop off and lay their eggs in the environment (Needham and Teel 1991).

Some ticks are invasive and transmit pathogens causing transboundary diseases of high consequence for populations of domestic animals and humans (Minjauw and McLeod 2003; Burridge 2011; Fernández and White 2016; Higgs 2018; Robles et al. 2018; Spengler et al. 2018).

Non-anthropogenic and anthropogenic factors associated with global change, including environmental disturbance and climate variability (Benavides Ortiz et al. 2016; Ogden and Lindsay 2016; Singer and Bulled 2016), increased international trade and travel (Abdullah et al. 2018; Hansford et al. 2018), and the wildlife-livestock-human interface (Gortazar et al. 2015), have increased tick densities resulting in a greater prevalence of tick-borne disease cases (Gasmi et al. 2018; Rasi et al. 2018; Sonenshine 2018). Furthermore, several of the newly discovered tick-borne microbes are pathogenic to humans and domestic animals (Mansfield et al. 2017; Harvey et al. 2019).

Discoveries by Smith and Kilborne (1893), documenting that *Rhipicephalus annulatus* Say was a vector of *Babesia bigemina* (Smith et Kilborne 1893), were important in the history of science by showing for the first time that arthropods can transmit pathogens to their hosts (Smith and Kilborne 1893; McCosker 1993; Egerton 2013).

Smith and Kilborne (1893) suggested the destruction of all *R. annulatus* infesting cattle to treat the disease after noting that outbreaks of bovine babesiosis, caused by *B. bigemina*, also known as redwater or cattle tick fever, and considered to be the most economically important arthropod-borne disease of cattle worldwide (Bock et al. 2008), could not happen without tick parasitism. In retrospect, this research association is an example of the One Health concept described below because T. Smith was a physician and F. L. Kilborne a veterinarian (Schultz 2008).

By 1893, cattle in the USA, Australia, and parts of Africa were already immersed in dipping vats containing various chemical pesticides active against ticks commonly referred to through time as tickicides, ixodicides, or acaricides, to manage infestations associated with what we now know are tick-borne diseases (Angus 1996; George 2000; Alonso-Díaz et al. 2006). The term acaricide used here refers to pesticides used to kill ticks of veterinary and public health importance following the conventions of most literature published on the topic. Vaccination against the pathogen is another approach to prevent and control tick-borne diseases. Attempts by Connaway and Francis (1899) to protect cattle from bovine babesiosis were among the first ones to vaccinate against a tick-borne disease. Several vaccines are commercially available in Europe to prevent tick-borne encephalitis (Riccardi et al. 2019). Nevertheless, the need remains for improved and cost-effective vaccines to prevent tick-borne diseases affecting humans (Smit and Postma 2016; Reece et al. 2018), as well as domestic animals (Perry 2016; Pruneau et al. 2018; Suarez et al. 2019).

Effective and safe tick and tick-borne disease management requires integration of rational tactics involving multiple biological, chemical, physical and vaccine technologies on and off hosts. They can include the judicious application of safer acaricides to address the concerns with chemical treatments (de Meneghi et al. 2016; Pfister and Armstrong 2016; Ginsberg et al. 2017).

Here we review highlights of integrated management research for ticks of public health importance transmitting zoonotic diseases to document opportunities for combined interventions that mitigate the health burden of tick-borne diseases, benefitting humans, domestic animals, and wildlife (Drexler et al. 2014; Khamesipour et al. 2018; Wang et al. 2018).

2. AREA-WIDE TICK MANAGEMENT AND RESEARCH

2.1. *Research Needs for Integrated Area-wide Tick Management*

This overview concentrates on research to enable the area-wide integrated management of livestock ticks. Examples focus on *Rhipicephalus microplus* (Canestrini), a one-host tick commonly known as the Asian blue tick or southern cattle fever tick, originally described as *Haemaphysalis micropla* by Canestrini (1887). It is one of the ticks most studied worldwide as it is a vector of *B. bigemina* and *B. bovis* Babes causing bovine babesiosis (Pérez de León et al. 2014b; Gray et al. 2019), and *Anaplasma marginale* Theiler causing anaplasmosis (Atif 2015). *R. microplus* is an invasive species considered the most economically important ectoparasite of livestock globally (Rodríguez-Vivas et al. 2017a; Betancur-Hurtado and Giraldo-Rios 2018; Sungirai et al. 2018).

The synonym concepts of area-wide integrated pest management, system-, or area-wide pest management, convey the need for research that can be applied to address the complex problem with ticks and tick-borne diseases (Brévault and Bouyer 2014; Pérez de León et al. 2014a; Bourtzis et al. 2016). Efficiency and cost-effectiveness are fundamental to area-wide approaches dealing with societal problems for centuries, including those related to tick disease vectors (Hendrichs et al. 2007; Koul et al. 2008; Shepard et al. 2014).

The goal of integrated pest management is to optimize the use of compatible methods in a way that is safe, economically viable, and ecologically sustainable (Jørs et al. 2017; Mullens et al. 2018). The area-wide approach augments and expands to the population level the benefits of integrated pest management strategies. Tick suppression and eradication can be considered as a continuum in the spectrum of area-wide strategies to manage tick-borne diseases. Approaches for sustainable area-wide control of tick populations recognize the need for translational research to develop new and improved technologies before eradication can be contemplated (Bram and Gray 1979; Pegram et al. 2007; Pluess et al. 2012; Suckling et al. 2014). A common theme for these strategies is the continued need to re-evaluate our understanding of tick biology and ecology (Tatchell 1992; Schmidtman 1994; Esteve-Gassent et al. 2016; Canevari et al. 2017).

2.2. *Unifying Area-wide Tick-borne Disease Mitigation and One Health through Integrated Tick Management Research*

Applying the One Health concept, i.e. a strategy to optimize health outcomes for humans, animals, and the environment, facilitates research on the interplay between climate, habitat, and hosts driving tick population dynamics. It enhances our understanding of the epidemiology of tick-borne diseases and advances their management (Dantas-Torres et al. 2012; Vayssier-Taussat et al. 2015; Laing et al. 2018; World Bank 2018) (Fig. 1).

Figure 1. Suggested research and implementation framework toward sustainable area-wide integrated tick management to prevent tick-borne diseases in the context of global change and the One Health approach (*adapted from Pérez de León et al. 2012).

Previous efforts indicate socio-economic and cultural aspects must be considered in the planning and evaluation of area-wide tick management programmes (Pegram et al. 2000; Hendrichs et al. 2007; Rushton 2009; Mutavi et al. 2018). This can be done using algorithms to select area-wide tick management interventions where the evidence thus generated is used to enhance model predictions that improve area-wide tick management practices (Sutherst et al. 2007; Wang et al. 2017).

Ideal characteristics of technologies for broad acceptability and integrated use against ticks include low cost, minimal effort required for their application, spectrum of efficacy covering as many tick species as possible, and residual activity (Graf et al. 2004; Playford et al. 2005; Eisen and Eisen 2018). Control technologies can target ticks on or off the host.

In addition to acaricides, parasitoids and predators, alteration of the environment, and physical methods were identified for off-host tick control (FAO 1961). The Sterile Insect Technique, botanical repellents and acaricides, host resistance, pheromone-based approaches, and anti-tick vaccines are potential approaches to be integrated for the control of ticks infesting hosts (IAEA 1968; Ghosh and Nagar 2014; de Oliveira Filho et al. 2017). However, reducing to practice the integration of acaricides with other technologies in area-wide tick management remains to be fully accomplished (Jonsson 2004; de la Fuente et al. 2015a).

Adequate protocols and implementation research to evaluate technologies under field conditions are needed to generate the scientific evidence required to justify the investment of resources for area-wide tick management programmes (Piesman and Eisen 2008; Bautista-Garfias and Martínez-Ibañez 2012).

The adoption and viability of these programmes require attention to resource allocation and socio-political aspects, the availability of support systems related to extension and veterinary services, and the engagement of stakeholders (Walker 2011; Estrada-Peña and Salman 2013; Bugeza et al. 2017; Kerario et al. 2018; Mihajlović et al. 2019).

2.3. *Alternatives to Acaricide Use and Strategies to Solve Resistance to Chemical Treatments*

Chemical treatment practices in livestock production systems are under scrutiny because of the impact acaricides and endectocides like ivermectin have on public health, the environment, and the international trade of livestock and animal products (González and Hernández 2012; Ariseto-Bragotto et al. 2017; Miraballes and Riet-Correa 2018).

Intense chemical treatment of infested hosts exerts strong selection pressure for acaricide resistance among tick populations (Guerrero et al. 2014b; de Miranda Santos et al. 2018; Rodríguez-Vivas et al. 2018). Resistance to multiple classes of acaricides keeps spreading among tick populations due to intensive application (Miller et al. 2013; Cuore et al. 2015; Klafke et al. 2017b; Vudriko et al. 2018).

Acaricide resistance resulting from chemical treatment intended to control other parasites can exacerbate the problem with ticks and tick-borne diseases (Foil et al. 2004). Ivermectin used to treat gastrointestinal parasitic infections in cattle simultaneously infested with *R. microplus* selected for resistance due to exposure of the ticks to sublethal doses of that endectocidal drug (Alegria-López et al. 2015). *R. microplus* ranks sixth among the arthropods most resistant to pesticides in the world (Whalon et al. 2008).

Resistance to organophosphates, pyrethroids, amitraz, and ivermectin was reported in the brown dog tick, *Rhipicephalus sanguineus* sensu lato (Latreille) (Klafke et al. 2017a, Rodríguez-Vivas et al. 2017b).

Amblyomma cajennense s.l. (Fabricius) is another three-host tick that was found to be resistant to organophosphates and amitraz in Mexico (Alonso-Díaz et al. 2013). Different acaricide resistance profiles have been reported for two- and three-host tick species parasitizing cattle in South Africa (Ntondini et al. 2008). Widespread resistance to commonly used acaricides has not been reported for other important vectors of zoonotic tick-borne diseases parasitizing humans in the USA and Europe (Coles and Dryden 2014; EMA 2018).

Strategies to diminish acaricide use in domestic animals need to consider the concept of integrated parasite/vector management to maximize the contributions of veterinary public health towards sustainable development (Henrioud 2011; Scasta 2015; Narladkar 2018).

The commercial availability of a technology based on the recombinant protein Bm86 in the 1990s to vaccinate cattle against *R. microplus* represented a significant research achievement towards sustainable area-wide tick management (de la Fuente et al. 2007; Willadsen 2008). Integrating the use of a Bm86-based anti-*R. microplus* vaccine in an area-wide management programme confirmed that this approach decreases the frequency of acaricide treatments and diminishes the amount of chemicals used to control infestations, while reducing tick-borne cases in a cost-effective manner (de la Fuente et al. 1998; Redondo et al. 1999; Valle et al. 2004; Suarez et al. 2016). This is a rational and environment-friendly approach to manage *R. microplus* populations that are resistant to multiple classes of acaricides. Various research efforts to develop vaccines against other hard and soft ticks and the application of an anti-tick vaccine to protect humans, domestic animals, and wildlife from tick-borne diseases are ongoing (Évora et al. 2017; Almazán et al. 2018; de la Fuente et al. 2018).

Collaborative partnerships established to improve efficiencies in the research and development process of those anti-tick vaccines are examples of how global efforts could fully realize the benefits of international cooperation to enable breakthroughs allowing the adaptation of area-wide tick management practices to protect livestock and humans from tick-borne diseases (Sprong et al. 2014; Schetters et al. 2016; Rodríguez-Mallon et al. 2018; Ybañez et al. 2018). These joint international efforts have also resulted in the sequencing the genome of *R. microplus* to mine the information therein for the innovation of management technologies (Barrero et al. 2017).

Integrative taxonomy studies reinstated *Rhipicephalus australis* as a species and revealed that *R. microplus* consists of 3 clades (Estrada-Peña et al. 2012; Roy et al. 2018). Furthermore, some of the new microbes found to be associated with *R. microplus* are known livestock pathogens, while the pathogenicity of others remains unknown (Andreotti et al. 2011; Biguezoton et al. 2016; de Souza et al. 2018; de Oliveira Pascoal et al. 2019).

3. RESEARCH FOR ADAPTIVE AREA-WIDE TICK MANAGEMENT

3.1 *Eradication Efforts Exemplify Challenges with Tick Management in the Context of Global Change*

In 1906 the USA established the Cattle Fever Tick Eradication Program (CFTEP) to eliminate bovine babesiosis by exterminating the tick vectors of the disease based on the scientific evidence generated by the research of Curtice (1891) and Smith and Kilborne (1893) (Curtice 1910). In the context of complex socio-economic dynamics (Strom 2010), the CFTEP efforts has involved cooperation between federal, state governments, and the livestock industry. In 1943, with the exception of a Permanent Quarantine Zone along the Rio Grande in south Texas at the border with Mexico, the USA was declared free of the tick vectors (Graham and Hourigan 1977).

The cattle fever ticks *R. annulatus* and *R. microplus* remain widespread in Mexico (Bautista-Garfias and Martínez-Ibañez 2012), and incursions from Mexico into the free zone, which comprises the rest of the continental USA, are buffered by the Permanent Quarantine Zone (George 1989; Klassen 1989). After 112 years of operations, events related to global change, such as land use changes, livestock-wildlife interface intricacies, and climate variability, complicate efforts by the CFTEP to keep the USA cattle fever tick-free (George 2008; Esteve-Gassent et al. 2014; Rutherford 2019).

A surge of cattle fever tick outbreaks in the free zone during the first decade of this century prompted a re-evaluation of the research agenda in support of the CFTEP (Pérez de León et al. 2010; Lohmeyer et al. 2011). Action was taken based on research needs in consultation with stakeholders to address the main concerns with acaricide resistance (Pérez de León et al. 2013), the role of native and exotic ungulates as cattle fever tick reservoirs (Pound et al. 2010), climate variability as a driver for the reintroduction of cattle fever ticks into the free zone (Giles et al. 2014), and a re-evaluation of financial losses associated with these concerns and events (Anderson et al. 2010).

Research in support of integrated cattle fever tick eradication provides a pathway to generate scientific evidence that could be used to adapt CFTEP operations that minimize the impact of global change (Pérez de León et al. 2012). Aspects related to the mechanism of action of organophosphate acaricides allowed charging the dipping vats at 0.3% coumaphos to mitigate concerns by the CFTEP with organophosphate-resistant cattle fever tick outbreak populations (Miller et al. 2005). The detection of pyrethroid resistance in cattle fever ticks infesting cattle and white-tailed deer, *Odocoileus virginianus* (Zimmermann), a wild ungulate species native to the Americas and a host of cattle fever ticks that is abundant in south Texas, limits treatments with permethrin by the CFTEP (Busch et al. 2014). Use of an injectable formulation of 1% doramectin was adapted by the CFTEP as an alternative eradication procedure (Davey et al. 2012). Macrocyclic lactone resistance among cattle fever tick outbreak populations has so far not been reported.

Further studies are required to determine if research can be translated into protocols involving the use by the CFTEP of safer acaricides to treat cattle and wild ungulates (Costa-Júnior et al. 2016; Gross et al. 2017).

A device using corn as bait to attract white-tailed deer for self-treatment was developed for use by the CFTEP because white-tailed deer cannot be gathered for treatment as it is done with cattle (Pound et al. 2012). The white-tailed deer consuming corn rub against acaricide-impregnated rollers placed on the device during the hunting season and are thus treated topically, whereas corn medicated with ivermectin acting systemically to control cattle fever ticks is used to bait white-tailed deer during the off-hunting season (Lohmeyer et al. 2013). However, complex white-tailed deer behaviours and social interactions to access the bait stations and other logistical aspects limit the use of this technology in the Permanent Quarantine Zone (Currie 2013).

Impediments for cattle fever tick eradication associated with the presence of nilgai (*Boselaphus tragocamelus* (Pallas)) in parts of south Texas, where they can coexist with cattle and white-tailed deer, further exemplify the challenges presented by the livestock-wildlife interface for area-wide tick management (Wang et al. 2016; Singh et al. 2017; Lohmeyer et al. 2018). Nilgai are introduced bovid hosts of cattle fever ticks and suspected reservoirs of *B. bovis* and *B. bigemina* with home ranges larger than white-tailed deer (Foley et al. 2017; Olafson et al. 2018). Research is underway to determine if nilgai can be attracted to sites where they would be treated against cattle fever tick infestation (Goolsby et al. 2017).

The high efficacy of the Bm86 antigen against *R. annulatus* prompted efforts to research the use of an anti-tick vaccine as part of integrated cattle fever tick eradication procedures (Miller et al. 2012). Research involved reverse vaccinology to pursue the discovery of antigens that could be formulated for use by the CFTEP with efficacy against *R. microplus* equivalent to that of Bm86-based vaccines against *R. annulatus* (Guerrero et al. 2014a). In the interim, a public-private partnership enabled the use of a Bm86-based vaccine by the CFTEP (Pérez de León et al. 2018). This was a significant event in the history of cattle fever tick eradication in the USA because federal and state statutes, more than a century old governing the CFTEP, were adapted to use the anti-tick vaccine technology. This Bm86-based vaccine was used in a research project for integrated *R. microplus* management in Puerto Rico (Wang et al. 2019).

Integrating vaccination of white-tailed deer against cattle fever ticks would complement the effects of the self-treatment bait stations described above (Carreón et al. 2012; Estrada-Peña et al. 2014). However, delivery systems remain to be refined to vaccinate free-ranging white-tailed deer against cattle fever ticks in the Permanent Quarantine Zone.

3.2. *Research Perspectives to Mitigate Tick-borne Disease Burden Focused on Integrated Tick Management*

Applying the concept of precision agriculture and making use of newly available technologies, provides the opportunity to establish exact and targeted interventions to realize substantial savings in inputs for area-wide tick management (Urdaz-Rodríguez et al. 2015; Pérez de León 2017).

Experiments with unmanned aerial vehicles or drones showed this technology can support surveillance by the CFTEP (Goolsby et al. 2016), but it could also be integrated with remote sensing using ground-truth data for strategic cattle fever tick suppression (Phillips et al. 2014; Leal et al. 2018). Robotic technology is being adapted for tick control as well, showing potential in reducing tick densities (Gaff et al. 2015).

Precision tick management could facilitate the adoption of safer control technologies for effective area-wide campaigns. These include commercially available alternatives to the conventional use of acaricides such as acaropathogenic fungi or nematodes, and botanical acaricides, although they require further testing for adoption by the CFTEP (Thomas et al. 2017; Goolsby et al. 2018; Singh et al. 2018). Additionally, big data strategies facilitate the translation of genomic information into knowledge that can be applied to develop technologies which specifically target cattle fever ticks (Munoz et al. 2017; Brock et al. 2019).

Tick-borne diseases threaten public health in the USA. Around twenty human diseases or clinical conditions are associated with tick bites (USHHS 2018). Current trends indicate that >75% of the vector-borne disease cases reported are tick-borne (Rosenberg et al. 2018). Among the ticks commonly found biting humans (Eisen et al. 2017), the black-legged tick *Ixodes scapularis* Say is known to transmit seven pathogens of human diseases (Eisen and Eisen 2018). Controlling tick populations, together with personal protection measures, reduce exposure of the public to infected ticks, which prevents tick-borne diseases (Stafford III et al. 2017; White and Gaff 2018).

A higher level of public acceptability is associated with area-wide interventions employing technologies that are safe for people, pets, and the environment (Aenishaenslin et al. 2016; Keesing and Ostfeld 2018). These include the integrated use of host-targeted devices delivering minimal acaricide quantities with broadcast application of acaropathogenic fungus, as well as white-tailed deer reduction to decrease the risk of human exposure to *I. scapularis* infected with *Borrelia burgdorferi* Johnson et al. (Telford 2017; Williams et al. 2018). Additionally, internet-based surveillance tools and citizen science participation may enhance area-wide integrated tick management practices (Pollett et al. 2017; Nieto et al. 2018; Jongejan et al. 2019).

The detection in 2017 of *Haemaphysalis longicornis* Neumann, commonly known as the Asian longhorned tick, and subsequent reports of infestations in humans, domestic animals, and wildlife in the USA is a reminder of the threat posed by invasive ticks to the health of humans and other animals (Rainey et al. 2018). *H. longicornis* is a known vector of pathogens affecting humans, domestic animals, and wildlife in its native range and previously invaded areas, but it remains to be determined if it is transmitting pathogens in the USA (Beard et al. 2018).

Habitat suitability analyses indicate that *H. longicornis* could become established also in other parts of North America (Magori 2018; Hutcheson et al. 2019; Rochlin 2019). Challenges managing the spread of this Asian longhorned tick in the USA present an opportunity to apply the One Health concept where governmental agencies, academic institutions, public organizations, and private industry representing the agricultural, public health, medical, and veterinary sectors operate under a national strategy to prevent cases of *H. longicornis*-borne diseases in humans and other animal species.

Implementation research is needed to accelerate advancements in area-wide tick management. Achieving this goal will facilitate the adaptation and adoption of those advancements to improve prevention across tick-borne diseases while contributing to vector control globally (WHO 2017; Theobald et al. 2018; Fouet and Kamdem 2019; Petersen et al. 2019).

4. CONCLUSIONS

Ticks and tick-borne diseases continue to present new and emerging threats to humans, domestic animals, and wildlife. Constraints faced by the CFTEP to continue maintaining the USA cattle fever tick-free, a successful area-wide programme that has been operating in the USA since its establishment in 1906, illustrate how global change impacts area-wide tick management efforts.

Current issues are complex and need to be addressed by veterinary and public health programmes dealing with ticks and tick-borne diseases. This grand challenge requires a reassessment of strategies to manage tick populations. The One Health approach provides a framework to mitigate the health burden of tick-borne diseases on humans, domestic animals, and wildlife.

Advances in transdisciplinary scientific research present opportunities to adapt the strategy for area-wide tick management. The integration of novel technologies can decrease the use of acaricides significantly. Pilot field studies help determine the utility of integrated tick management strategies under real-life conditions. Outcomes from those pilot field studies inform decisions on the extent of interventions to prevent tick-borne diseases through improved tick population management. Progressive tick control affords flexibility to fine-tune the integration of technologies through the exchange of scientific information between stakeholders engaged in the adaptation process and provides feedback to revise the research agenda.

Implementation research can accelerate the translation of earlier research efforts to area-wide tick management practice. It is important for scientists to also understand the socio-economic context of research. Grasping the expectations of end-users of technology is paramount to realize the common vision of improving the outcomes of tick control interventions. This process will enhance the quality of evidence delivered by scientific research. Such scientific evidence can be used to generate the support for resources to establish the capacities required for the effective management of ticks to mitigate the burden of tick-borne diseases.

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