Rev. Sci. Tech. Off. Int. Epiz., 2015, **34** (1), 265-275

Disease prevention and anti-vector campaigns: insects

J. Esterhuizen

Vector Biology Department, Liverpool School of Tropical Medicine, Pembroke Place, L3 5QA, Liverpool, United Kingdom
E-mail: johan.esterhuizen@liv.ac.uk

Summary
Control of insect vector populations is an integral part of disease management but has many challenges. Area-wide campaigns, mainly based on insecticide administration, are most effective for control of insect populations, whereas disease prevention is more localised and protects a smaller number of animals against insect vector contact. Various control and prevention techniques are available for use against most insect vectors and are illustrated here by focusing on two important insect groups: biting midges and tsetse flies.
Biting midges (*Culicoides*) present a major threat and challenge to disease and vector control because of limited large-scale control options and the huge population sizes and wide distribution of these insects. Localised disease prevention forms the basis for control, and there is a need for better understanding of the ecology and biology of these insects in order to develop large-scale control techniques.
The necessary techniques to effectively control tsetse flies (*Glossina*) and trypanosomosis exist for both localised and area-wide control. The development of a new, cost-efficient device has had a significant impact in the control of both human and animal trypanosomosis. This is especially relevant in Uganda, where the movement of livestock for trading purposes is implicated in disease distribution and poses an immediate health threat where the two forms of the disease overlap.
Although many successes have been achieved, continued research and development is needed to keep abreast of the multitude of challenges in insect vector control.

Keyword
Biting midge – Control – *Culicoides* – *Glossina* – Insect vector – Prevention – Trypanosomosis – Tsetse fly.

Introduction

Control and preventative measures against blood-feeding insects originated with primitive man, when humans picked fleas and swatted mosquitoes. With the development of agriculture and animal domestication, vector control comprised manual control, such as hand-removal of ticks from animals, together with preventative measures, such as the avoidance of high-risk areas, such as tsetse-fly belts, by livestock keepers. The use of smoking fires to disperse and deter blood-feeding insects in village corrals and housing compounds is an age-old, worldwide preventative measure that is still common in many rural areas today (1).

Since the 1960s the scale and potential of vector control has increased enormously, following the refinement of insecticide formulations and safe methods of application, as well as the use of nuclear irradiation methods. The current advancement in medical technologies, pharmaceuticals and vector control techniques is predicted to be sufficient to achieve a 'global convergence in health' by 2035, which would have a significant impact on major health and development issues (2). Nevertheless, irrespective of how sophisticated a technique or a country may be, the threat of insect invasion and disease dispersal is ever present and increasing. A good example of this is the rapid and unpredictable spread of biting midges (*Culicoides*) into Europe, including the United Kingdom (UK), between 2006 and 2008 (3).

Current and classic vectors

The *Culicoides* biting midges are currently among the most threatening vectors in the management of animal disease, particularly in Europe. Populations of these small flies are expanding on a global scale and are of high concern as vectors of bluetongue virus, African horse sickness virus and Schmallenberg virus (3, 4, 5).

A 'classic' vector that remains important is the tsetse fly (*Glossina*), which is the vector of animal African trypanosomosis (*nagana*) and human African trypanosomosis (sleeping sickness). Despite a long record of research and control activities, the presence of tsetse flies in 36 African countries remains a major restraint to development, agriculture and health (6).

These two examples form the basis for the present discussion of the issues, challenges and options in disease prevention and anti-vector campaigns, from the small, individual livestock-keeper level to large area-wide control operations. Although this paper focuses on just two insect groups, the technology is adaptable and applicable to other insect vectors because of the inherent similarities in their biology, behaviour and ecology, such as blood feeding, the use of visual or olfactory host-seeking cues, and specific breeding or resting habitats.

Vector control challenges

Natural and human factors

Advances in the control of insect vectors are continually challenged by the resilience of insects and their ability to spread almost unhindered. The environmental persistence and adaptability of pathogens, as well as the distribution and sizes of insect populations and their hosts, complicate epidemiological understanding. During disease outbreaks and epidemics, the size of insect vector populations and the geographical scale of their presence are often so immense that this excludes the possibility of large-scale interventions.

For example, controlling an outbreak of biting midges is near impossible, considering that population sizes are of such magnitude that a single monitoring trap can catch between 1,500 and 500,000 midges per night (7). The multitude of variable environmental conditions can further add unseen and often unpredictable constraints and challenges.

Moreover, the human factor is often instrumental in success or failure of vector control campaigns. For example, the disruption of control operations because of civil unrest or conflict can quickly negate area-wide successes, and inadequate political and financial commitment from governments and institutions can often lead to failure of control. On a smaller scale, community perceptions, spending capability and the market availability of products further add to the challenges. In addition, the movement of people into new habitats, such as the opening of fields for agriculture or mining, can result in exposure to disease and also introduce new disease into these areas (6, 8, 9, 10).

Understanding the insect and disease cycles

Effective control and rapid reaction to insect vector outbreaks and the diseases they spread are reliant on fundamental knowledge of the biological and ecological systems that influence both disease and insect life cycles. A holistic, integrated approach is needed for effective use of multiple opportunities, even tackling more than one disease at a time; for example, combining indoor residual spraying strategies to control the vectors of both malaria and Chagas disease (11, 12, 13).

Numerous mathematical and computer-based models have been developed to support and optimise vector control strategies and to enable decision-makers and scientists to be more pro-active. These models can help to implement intervention strategies in advance by predicting disease spread and can evaluate vector–host interactions, foresee control outcomes, assess risk and estimate costs (14, 15, 16, 17, 18, 19, 20, 21). The benefits of modelling are that possible scenarios and solutions can be evaluated prior to implementation, thus increasing cost-efficiency.

Insecticide resistance

Targeting the insect populations responsible for disease spread remains one of the mainstays of effective disease management, especially over large areas. The most efficient, versatile and adaptable techniques continue to be insecticide-based, and have a strong history in successful vector control campaigns that have resulted in major improvements in health and development conditions; for example, the localised control of mosquitoes, tsetse flies and various other agricultural pests. Nevertheless, insecticide resistance is increasing and consequently limiting the effectiveness of this approach, particularly for the mosquito-transmitted diseases (22, 23, 24).

Several alternatives to insecticide application are available for vector control, including environmental modifications to reduce insect development; for example, draining marshes to eliminate breeding sites, or removing habitat to limit sheltering sites. On a smaller and perhaps more environmentally acceptable level, laboratory-based research has investigated various approaches, such as the use of microbial pathogens to infect and kill target insects (e.g. *Bacillus thuringiensis* subspecies *israelensis* to control blackflies) and genetic manipulation of either the vectors, their symbiotic bacteria or the disease-causing parasite to reduce vector competence (25, 26, 27). Many of these techniques, however, lack large-scale practical and cost-efficient application and must overcome the regulatory challenges of releasing genetically modified organisms as a control measure.

Issues of scale and cost

The measure of a good technique for insect vector control lies in its adaptability and cost-efficiency in achieving rapid disease intervention with long-term sustainability. In large-scale campaigns, the cost-efficiency of any technique requires careful consideration because of the inherently long time-frame involved and the increased costs implied. Not surprisingly, the more complex a technique becomes, the higher the associated costs and risks to sustainability. An example of a complex control measure is the sterile insect technique, which involves the breeding, atomic radiation and mass release of sterile male insects of the target species, to compete with natural populations and disrupt viable breeding. This approach has worked extremely well in controlling the New World screwworm fly and some fruit fly species, but is too complex, too costly (see Table I) and impractical for sensible and cost-efficient use in, for example, large-scale tsetse fly control, owing to differences in the biology and ecology of the target species (15, 28, 29).

As anti-vector campaigns expand, the cost and bureaucratic restrictions increase. Campaigns are often unsuccessful because of soaring budgets and the massive practical inputs required for achieving successful large-scale and sustainable, long-term vector control. Consequently, there has been an increase in local or community and individual-driven campaigns, which focus more on localised prevention and/or control.

Control or prevention?

By definition, vector control campaigns aim to reduce or eliminate target insect populations in a specific geographical area or context. The aim is to either completely eliminate the local vector populations or reduce them to such low levels that transmission and circulation of the disease agent (e.g. parasite) is interrupted and stopped.

Eradication is the complete worldwide removal of the disease or its vector so that it no longer poses any threat. This is very difficult to accomplish and, thus far, has been achieved for only two diseases: smallpox in humans and rinderpest in livestock.

In contrast, in localised preventative measures against insect vectors there is an inherent acceptance of the continued presence of vector populations in the environment. Such measures do not aim to kill the insects but rather to prevent them from physically interacting with the animal host or, if contact is achieved, to reduce the contact time and prevent biting. For logistical reasons, preventative measures are mostly used on a smaller scale but have the general advantage of being applicable against several insect disease vectors.

Prevention: biting midges

Limited vector control options

Intervention measures against biting midges and the diseases they carry are mainly based on trying to prevent, or at least minimise, contact between individual insects and animal hosts. This is supported by targeting the pathogen through mass vaccination of livestock. Use of this approach enabled the 2007 outbreak of bluetongue virus, spread by biting midges in Europe (including the UK), to be controlled through mass vaccination and mass culling of animals; an extreme approach, but a highly effective example of preventing insect–host contact and disease spread.

Such extreme measures are clear indications of the lack of large-scale control methods against biting midges. In

Table I
Estimated costs of large-scale control techniques against tsetse flies

Technique	Annual cost*/km^2	Reference
Sterile insect technique	$850	29, 30
Aerial spraying	$500	29, 30
Ground spraying	$350	29, 30
Conventional cloth traps + targets	$300	29, 30
Insecticide-treated cattle	$30	29, 30, 31
New tiny target	$70	M.J. Lehane 2014, personal communication

*United States dollars

Europe there is no immediate prospect for any insecticide-based campaigns against biting midges, because the cost and benefits of implementing area-wide control have to be measured against the potential environmental and health risks in the long term (32, 33). The development of insecticide resistance in several *Culicoides* species also militates against insecticide use. Consequently, very few control trials with insecticide have taken place and none of them has been successful on any large scale (32).

Progress in understanding and controlling midge biology, ecology and disease epidemiology is further confounded by the limited knowledge of their breeding sites and the difficulty of rearing colonies of these insects for controlled studies (5, 34, 35, 36). Although recent advances with entomopathogenic fungi have shown promising results in killing biting-midge adults and in reducing feeding behaviour, the large-scale implementation and practicalities require further investigation (37).

Animal protection against biting midges

Current control practices against biting midges largely rely on individual farmers and are both pro-active and preventative. These practices are based on three approaches (32, 33, 35):

i) Protective netting or screens over stable entrances and windows, or as an enclosure around cattle or pig-pens and paddocks (Fig. 1). This forms a physical barrier that prevents or minimises contact between vector insects and animals. Long-lasting, deltamethrin-impregnated materials are commercially available for this purpose and can achieve effective protection against biting midges, tsetse flies, stable flies and other nuisance flies. Remarkably, the netting does not have to be much higher than 1.5 m (38, 39, 40, 41). However, such small-scale control can only provide protection for a limited number of animals and cannot achieve and sustain area-wide control of insect vectors. With regard to biting midges, the degree of protection that netting can provide depends on the proper sealing of openings and on the feeding behaviour of the *Culicoides* species (42). For example, *C. imicola*, the main vector of bluetongue virus and African horse sickness virus in South Africa, feeds significantly more often outdoors and therefore protective screening of stables will have limited success (43).

ii) Good husbandry practices aimed at the control of midge breeding sites; for example, removing wet manure from stables and paddocks, covering dung heaps with tarpaulins and draining moist or marshy areas. However, these control measures have limited local success and are logistically demanding, and large-scale implementation is further restricted by the need for cooperation with neighbouring farms/districts because of the size and unpredictability of insect vector populations and their spread (44).

iii) Localised application of insecticides as topical treatment on animals and local midge breeding sites. This approach can provide temporary vector control, but insecticide resistance, reduced insecticidal efficacy and the need for continuous usage are of practical concern.

Fig. 1
Protective netting around a livestock enclosure to minimise insect–host contact
Source: Food and Agriculture Organization of the United Nations (www.fao.org/news/story/en/item/173224/icode/)

Large-scale anti-vector campaigns: tsetse flies

In contrast to biting midges, an armament of area-wide control techniques is available for tsetse flies. This follows more than a century of active large-scale control campaigns, covering hundreds of thousands of square kilometres in several parts of sub-Saharan Africa, with varying levels of success. Tsetse flies are notorious for re-invading and re-establishing themselves in previously controlled areas, and consequently the focus is still on large-scale campaigns that cover enormous tracts of land (8, 45, 46, 47). With increased development and availability of control techniques and technologies, the focus has now shifted to improving cost-efficiency and applicability for area-wide control.

Tsetse control methods

The most applicable and practicable tsetse control methods, suitable for large-scale implementation, are based on the use of insecticide (predominantly deltamethrin). Tsetse flies are extremely susceptible to these synthetic pyrethroids and have shown very few signs of developing insecticide resistance. For tsetse control, insecticide can be used in several ways:

– Aerial spraying in ultra-low volumes from aeroplanes onto tsetse habitat. The application is executed over vast areas and achieves tsetse control within a relatively short period of time. This has been very successful and has a negligible impact on the environment. The benefits of a short intervention period, however, need to be weighed against the cost of this technique (Table I).

– Ground spraying onto tsetse habitat. This can be targeted to preferred tsetse resting and breeding sites. However, it is logistically demanding, rather costly (Table I), and is often environmentally unacceptable in conservation areas because of the elimination of non-target insects.

– Topical treatment of cattle. This requires the restricted application of insecticide to the legs and belly of the animals, where tsetse flies have a high feeding preference. This technique is very effective, with the cattle acting as live, mobile bait, and can achieve tsetse control over large areas (31, 48, 49). If this approach is well organised in large campaigns and is supported by neighbouring farmers who treat their animals and participate in the wider programme, it can be highly cost efficient (Table I). However, the technique is limited by cattle distribution and the need for a minimum density of grazing cattle in the tsetse habitat. This makes large parts of tropical Africa, which have low cattle densities but a high tsetse presence, unsuitable for this technique.

– Treatment of stationary cloth traps and targets or screens (Fig. 2) distributed throughout the tsetse area. This is very effective in controlling tsetse fly populations in diverse habitats (8, 50, 51, 52, 53, 54). The cost of this approach (Table I) depends on the biology and ecology of the target tsetse species. For example, in comparison with savannah flies, both riverine and forest tsetse species have low daily dispersal rates and their habitats are typically more dense, thus an increase in trap and target densities is required, as well as an increase in logistical costs (29, 30).

New development: cost-efficient tsetse target

Intensive research into modifications of the size, design and shape of tsetse targets has shown very promising results for several tsetse species responsible for the transmission of both human and animal trypanosomosis (55, 56, 57). This has led to the development of a new 'tiny target' (Fig. 2, far right) which uses between 8 and 20 times less material and insecticide yet still maintains the same killing efficiency as larger, conventional targets and traps (55, 58, 59).

Large, district-wide field trials in Uganda showed a more than 90% reduction of the tsetse fly population within three to five months of target deployment. In addition, the tsetse reduction also had a profound impact on trypanosome infection rates in local cattle, with trypanosome prevalence in cattle showing a decline of over 70%. In field trials of tiny targets on islands in Lake Victoria, complete elimination of local tsetse populations was achieved (60).

The cost-efficiency of these new targets lies in the savings in both material and logistics (e.g. manufacture, transport, storage) and in their ease of use in the field (e.g. deployment in dense vegetation, transport over long distances), compared with cumbersome conventional traps and targets. These factors reduce the estimated annual cost of large-scale use to about US$70/km^2 (Table I), making them very affordable.

Fig. 2
Insecticide-treated cloth targets and traps for tsetse fly control
From left to right: large insecticide-treated target, pyramidal trap, biconical trap next to new 'tiny target' and field assistant
Source: J. Esterhuizen

In time to avert disaster?

Uganda is the only country where animal trypanosomosis (*nagana*) and both forms of human trypanosomosis circulate in animal and human populations.

The south-eastern parts of the country have large herds of cattle that suffer from *nagana* and the human populations are at risk of the acute (Rhodesiense) form of the disease, which can kill within three months if treatment is not received. In the north-western part of Uganda the human population suffers from the chronic (Gambiense) form of the disease, which may be present for up to six years before causing death, in the absence of treatment. Here, *nagana* is a smaller problem because livestock densities are low. In recent years, however, owing to an increase in the trading and movement of livestock from the south-east into the north-west of the country, the geographical boundaries of the two forms of disease have begun encroaching on each other (61, 62). The same tsetse species, *Glossina fuscipes fuscipes*, is responsible for disease transmission between animals and humans in both areas.

Veterinary and entomological surveillance and control in Uganda is often insufficient because facilities are understaffed and under-equipped. The result is an imminent threat that the two disease forms will overlap in northern parts of the country. This will place the human population in the north at severe risk of infection with acute trypanosomosis and will leave local medical facilities ill equipped for diagnosis and rapid treatment of this form of the disease (47).

In this urgent context, the development of the new tiny targets comes at a critical time and consequently the Co-ordinating Office for Control of Trypanosomiasis in Uganda (COCTU) has adopted the technique in its intervention programme for regions within the Gambiense disease belt. Combined use of tiny targets and medical screening and treatment of the human population can achieve major successes in the control of trypanosomosis.

Conclusion

Responsibility for vector control and disease prevention increasingly lies in the hands of individual livestock owners and several techniques are now available for localised use. Choices between control or prevention methods are a balance between the economics of disease burden and the cost/benefit of intervention.

Understanding the ecology and role of insects in disease epidemiology and how to control their impact on humans and animals is concurrently becoming ever more relevant and challenging. More rapid and focused evaluation and testing mechanisms are required to develop and distribute new, highly effective vector control tools (63). Optimisation of vector control technologies, specifically in terms of cost-efficiency, applicability and sustainability, is crucial for effective long-term, sustainable intervention and disease control (30, 33, 64, 65).

Effective control relies on improved prevention and control strategies and the development of contingency plans to deal with insect vector outbreaks or threats at local, regional and international levels. Insecticide resistance and environmental considerations force the scientific and development community to continue investigating new approaches and, as ever, the funding for this research remains crucial. Implementation of the cost-efficient tiny targets for tsetse control has proven that even in classic cases, continuing research and development is essential.

■

Prévention des maladies et campagnes de lutte antivectorielle : les insectes

J. Esterhuizen

Résumé

La lutte contre les populations d'insectes vecteurs fait partie intégrante de la gestion sanitaire, tout en présentant des difficultés particulières. Les campagnes de grande envergure, principalement basées sur l'administration d'insecticides sur de vastes territoires, sont celles qui réussissent le mieux à contrôler les populations d'insectes, tandis que les méthodes spécifiques de prévention des maladies ont une dimension plus localisée et protègent un plus petit nombre d'animaux contre l'exposition aux insectes vecteurs. Il existe plusieurs techniques de lutte et de prévention contre la plupart des insectes vecteurs. L'auteur décrit ces techniques en donnant l'exemple de deux grands groupes d'insectes, les moucherons piqueurs et les glossines.

Les moucherons piqueurs (*Culicoides*) constituent une menace et un défi dans le domaine de la lutte contre les vecteurs et les maladies à transmission vectorielle, en raison de la rareté des méthodes de grande envergure disponibles et de la distribution et la taille considérables des populations de ces insectes. La prévention ciblée des maladies transmises par les moucherons piqueurs est donc aujourd'hui la base des stratégies de lutte, et seule une amélioration de nos connaissances sur l'écologie et la biologie de ces insectes permettra de mettre en place des techniques de contrôle à grande échelle.

En ce qui concerne les glossines et la trypanosomose, des méthodes de lutte existent, tant pour le contrôle ciblé que pour les campagnes de grande envergure. La mise au point d'un dispositif innovant et peu onéreux a fortement amélioré les capacités de lutte contre les trypanosomoses tant animales qu'humaines. C'est particulièrement pertinent en Ouganda où les déplacements du bétail aux fins de commerce contribuent à la propagation de la maladie et font peser une menace sanitaire immédiate lorsque les deux formes de la maladie sont présentes simultanément.

Au-delà des succès enregistrés, qui sont nombreux, il convient de poursuivre les activités de recherche et développement afin de rester à la pointe des multiples défis liés à la lutte contre les insectes vecteurs.

Mots-clés

Contrôle – *Culicoides* – Glossine – Insecte vecteur – Moucheron piqueur – Prévention – Trypanosomose.

■

Prevención de enfermedades y campañas de lucha antivectorial: insectos

J. Esterhuizen

Resumen

El control de las poblaciones de insectos que actúan como vectores forma parte integral de la gestión de ciertas enfermedades, pero presenta muchos problemas. Las campañas de gran alcance, basadas principalmente en la administración de insecticidas, resultan muy eficaces para controlar las poblaciones de insectos, mientras que la prevención de enfermedades reviste un carácter más circunscrito y protege del contacto con el insecto vector a un menor número de animales. Existen diversas técnicas de control y prevención que pueden utilizarse contra la mayoría de los insectos vectores, técnicas que el autor ilustra centrándose en dos importantes grupos de insectos: los jejenes y las moscas tsetsé.

Los jejenes (*Culicoides*) constituyen una importante amenaza y plantean grandes problemas a la hora de combatir tanto las enfermedades como al propio vector, debido a la escasez de métodos para luchar a gran escala y al gran tamaño y la amplia distribución de las poblaciones de estos insectos. La base de la lucha reside en la prevención localizada de enfermedades. Para dar con técnicas de control a gran escala es preciso entender mejor la ecología y la biología de los jejenes.

Para luchar eficazmente contra las moscas tsetsé (*Glossina*) y la tripanosomosis, ya sea de forma circunscrita o a mayor escala, ya existen las técnicas necesarias. La obtención de un nuevo y rentable dispositivo ha tenido efectos importantes en el control de la tripanosomosis tanto humana como animal, hecho que reviste especial importancia en Uganda, donde los movimientos de ganado con fines comerciales constituyen un factor ligado a la distribución de la enfermedad y entrañan una amenaza sanitaria inmediata allí donde se solapan las dos formas de la enfermedad.

Aunque ha habido numerosos éxitos, se requiere una labor permanente de investigación y desarrollo para seguir muy de cerca la multitud de problemas que van surgiendo en la lucha contra los insectos vectores.

Palabras clave

Control – *Culicoides* – *Glossina* – Insectos vectores – Jején – Mosca tsetsé – Prevención – Tripanosomosis.

■

References

1. Torr S.J., Mangwiro T.N.C. & Hall D.R. (2011). – Shoo fly, don't bother me! Efficacy of traditional methods of protecting cattle from tsetse. *Med. Vet. Entomol.*, **25** (2), 192–201.

2. Jamieson D.T., Summers L.H., Alleyne G., Arrow K.J., Berkley S., Binagwaho A., Bustreo F., Evans D., Feachem R.G.A., Frenk J., Ghosh G., Goldie S.J., Guo Y., Gupta S., Horton R., Kruk M.E., Mahmoud A., Mohohlo L.K., Ncube M., Pabloz-Mendez A., Reddy K.S., Saxenian H., Soucat A., Ulltveit-Moe K.H. & Yamey G. (2013). – Global health 2035: a world converging within a generation. *Lancet*, **382** (9908), 1898–1955.

3. Carpenter S., Wilson A. & Mellor P.S. (2009). – *Culicoides* and the emergence of bluetongue in northern Europe. *Trends Microbiol.*, **17** (4), 172–178.

4. Mellor P.S., Boorman J. & Baylis M. (2000). – *Culicoides* biting midges: their role as arbovirus vectors. *Annu. Rev. Energy*, **45**, 307–340.

5. Veronesi E., Henstock M., Gubbins S., Batten C., Manley R., Barber J., Hoffman B., Beer M., Attoui H., Mertens P.P.C. & Carpenter S. (2013). – Implicating *Culicoides* biting midges as vectors of Schmallenberg virus using semi-quantitative RT-PCR. *PLoS ONE*, **8** (3), e57747. doi:10.1371/journal.pone.0057747.

6. Aksoy S. (2011). – Sleeping sickness elimination in sight: time to celebrate and reflect, but not relax. *PLoS Negl. Trop. Dis.*, **5** (2), e1008. doi:10.1371/journal.pntd.0001008.

7. Van Ark H. & Meiswinkel R. (1992). – Subsampling of large light-trap catches of *Culicoides* (Diptera: Ceratopogonidae). *Onderstepoort J. Vet. Res.*, **59** (3), 183–189.

8. Torr S.J., Hargrove J.W. & Vale G.A. (2005). – Towards a rational policy for dealing with tsetse. *Trends Parasitol.*, **21** (11), 537–541. doi:10.1016/j.pt.2005.08.021.

9. Kilpatrick A.M. & Randolph S.E. (2012). – Drivers, dynamics, and control of emerging vector-borne zoonotic diseases. *Lancet*, **380** (9857), 1946–1955.

10. Bardosh K., Waiswa C. & Welburn S.C. (2013). – Conflict of interest: use of pyrethroids and amidines against tsetse and ticks in zoonotic sleeping sickness endemic areas of Uganda. *Parasit. Vectors*, **6**, 204.

11. Luckhart S., Lindsay S.W., James A.A. & Scott T.W. (2010). – Reframing critical needs in vector biology and management of vector-borne disease. *PLoS Negl. Trop. Dis.*, **4** (2), e566. doi:10.1371/journal.pntd.0000566.

12. Karesh W.B., Dobson A., Lloyd-Smith J.O., Lubroth J., Dixon M.A., Bennett M., Aldrich S., Harrington T., Formenty P., Loh E.H., Machalaba C.C., Thomas M.J. & Heymann D.L. (2012). – Ecology of zoonoses: natural and unnatural histories. *Lancet*, **380** (9857), 1936–1945.

13. Kelly-Hope L.A., Molyneux D.H. & Bockarie M.J. (2013). – Can malaria vector control accelerate the interruption of lymphatic filariasis transmission in Africa; capturing a window of opportunity? *Parasit. Vectors*, **6**, 39–43.

14. Barclay H.J. & Hargrove J.W. (2005). – Probability models to facilitate a declaration of pest-free status, with special reference to tsetse (Diptera: Glossinidae). *Bull. Entomol. Res.*, **95** (1), 1–11.

15. Vale G.A. & Torr S.J. (2005). – User-friendly models of the costs and efficacy of tsetse control: application to sterilizing and insecticidal techniques. *Med. Vet. Entomol.*, **19** (3), 293–305.

16. Luz P.M., Struchiner C.J. & Galvani A.P. (2010). – Modeling transmission dynamics and control of vector-borne neglected tropical diseases. *PLoS Negl. Trop. Dis.*, **4** (10), e761. doi:10.1371/journal.pntd.0000761.

17. Luz P.M., Vanni T., Medlock J., Paltiel A.D. & Galvani A.P. (2011). – Dengue vector control strategies in an urban setting: an economic modelling assessment. *Lancet*, **377** (9778), 1673–1680.

18. Torr S.J. & Vale G.A. (2011). – Is the even distribution of insecticide-treated cattle essential for tsetse control? Modelling the impact of baits in heterogeneous environments. *PLoS Negl. Trop. Dis.*, **5** (10), e1360. doi:10.1371/journal.pntd.0001360.

19. Alphey N., Alphey L. & Bonsall M.B. (2011). – A model framework to estimate impact and cost of genetics-based sterile insect methods for dengue vector control. *PLoS ONE*, **6** (10), e25384. doi:10.1371/journal.pone.0025384.

20. Eagles D., Walker P.J., Zaluckib M.P. & Durra P.A. (2013). – Modelling spatio-temporal patterns of long-distance *Culicoides* dispersal into northern Australia. *Prev. Vet. Med.*, **110** (3–4), 312–322.

21. Vale G.A., Hargrove J.W., Solano P., Courtin F., Rayaisse J.-B., Lehane M.J., Esterhuizen J., Tirados I. & Torr S.J. (2014). – Explaining the host-finding behavior of blood-sucking insects: computerized simulation of the effects of habitat geometry on tsetse fly movement. *PLoS Negl. Trop. Dis.*, **8** (6), e2901. doi:10.1371/journal.pntd.0002901.

22. World Health Organization (WHO) (1998). – Test procedures for insecticide resistance monitoring in malaria vectors; bio-efficacy and persistence of insecticides on treated surfaces. WHO/CDS/CPC/MAL/9812. WHO, Geneva.

23. Read A.F., Lynch P.A. & Thomas M.B. (2009). – How to make evolution-proof insecticides for malaria control. *PLoS Biol.*, **7** (4), e1000058. doi:10.1371/journal pbio.1000058.

24. Rivero A., Vézilier J., Weill M., Read A.F. & Gandon S. (2010). – Insecticide control of vector-borne diseases: when is insecticide resistance a problem? *PLoS Pathog.*, **6** (8), e1001000. doi:10.1371/journal.ppat.1001000.

25. Aksoy S., Maudlin I., Dale C., Robinson A.S. & O'Neill S.L. (2001). – Prospects for control of African trypanosomiasis by tsetse vector manipulation. *Trends Parasitol.*, **17** (1), 29–35.

26. Gooding R.H. & Krafsur E.S. (2005). – Tsetse genetics: contributions to biology, systematics and control of tsetse flies. *Annu. Rev. Entomol.*, **50**, 101–123.

27. Haines L.R., Lehane S.M., Pearson T.W. & Lehane M.J. (2010). – Tsetse EP protein protects the fly midgut from trypanosome establishment. *PLoS Pathog.*, **6** (3), e1000793. doi:10.1371/journal.ppat.1000793.

28. Enserink M. (2007). – Welcome to Ethiopia's fly factory. *Science*, **317** (5836), 310–313.

29. Shaw A.P.M., Torr S.J., Waiswa C., Cecchi G., Wint G.R., Mattiolo R.C. & Robinson T.P. (2013). – Estimating the costs of tsetse control options: an example for Uganda. *Prev. Vet. Med.*, **110** (3–4), 290–303.

30. Shaw A.P.M., Cattand P., Coleman P.G. & John M. (2008). – A basis for financial decision-making on strategies for the control of human African trypanosomiasis. TropIKA.net (Tropical Disease Research to Foster Innovation and Knowledge Application). Available at: www.tropika.net/svc/review/African_Tryps_Financial_decision_making (accessed on 10 June 2014).

31. Torr S.J., Maudlin I. & Vale G.A. (2007). – Less is more: restricted application of insecticide to cattle to improve the cost and efficacy of tsetse control. *Med. Vet. Entomol.*, **21** (1), 53–64.

32. Carpenter S., Mellor P.S. & Torr S.J. (2008). – Control techniques for *Culicoides* biting midges and their application in the UK and northwestern Palaearctic. *Med. Vet. Entomol.*, **22** (3), 175–187.

33. MacLachlan N.J. & Mayo C.E. (2013). – Potential strategies for control of bluetongue, a globally emerging, *Culicoides*-transmitted viral disease of ruminant livestock and wildlife. *Antiviral Res.*, **99** (2), 79–90.

34. Veronesi E., Venter G.J., Labuschagne K., Mellor P.S. & Carpenter S. (2009). – Life history parameters of *Culicoides* (*Avaritia*) *imicola* Kieffer in the laboratory at different rearing temperatures. *Vet. Parasitol.*, **163** (4), 370–373.

35. Carpenter S., Groschup M.H., Garros C., Felippe-Bauer M.L. & Purse B.V. (2013). – *Culicoides* biting midges, arboviruses and public health in Europe. *Antiviral Res.,* **100** (1), 102–113.

36. Mayo C.E., Osborne C.J., Mullens B.A., Gerry A.C., Gardner I.A., Reisen W.K., Barker C.M. & MacLachlan N.J. (2014). – Seasonal variation and impact of waste-water lagoons as larval habitat on the population dynamics of *Culicoides sonorensis* (Diptera: Ceratopogonidae) at two dairy farms in northern California. *PLoS ONE,* **9** (2), e89633. doi:10.1371/journal.pone.0089633.

37. Ansari M.A., Pope E.C., Carpenter S., Scholte E.-J. & Butt T.M. (2011). – Entomopathogenic fungus as a biological control for an important vector of livestock disease: the *Culicoides* biting midge. *PLoS ONE*, **6** (1), e16108. doi:0.1371/journal.pone.0016108.

38. Esterhuizen J. & Van den Bossche P. (2006). – Protective netting, an additional method for the integrated control of livestock trypanosomosis in KwaZulu-Natal Province, South Africa. *Onderstepoort J. Vet. Res.*, **73** (4), 319–321.

39. Maia M.F., Clausen P.-H., Mehlitz D., Garms R. & Bauer B. (2010). – Protection of confined cattle against biting and nuisance flies (Muscidae: Diptera) with insecticide-treated nets in the Ghanaian forest zone at Kumasi. *Parasitol. Res.,* **106** (6), 1307–1313.

40. Maia M.F., Abonuusum A., Lorenz L.M., Clausen P.-H., Bauer B., Garms R. & Kruppa T. (2012). – The effect of deltamethrin-treated net fencing around cattle enclosures on outdoor-biting mosquitoes in Kumasi, Ghana. *PLoS ONE*, **7** (9), e45794. doi:10.1371/journal.pone.0045794.

41. Bauer B., Holzgrefe B., Mahama C.I., Baumann M.P., Mehlitz D. & Clausen P.-H. (2011). – Managing tsetse transmitted trypanosomosis by insecticide treated nets: an affordable and sustainable method for resource poor pig farmers in Ghana. *PLoS. Negl. Trop. Dis.,* **5** (10), e1343. doi:10.1371/journal.pntd.0001343.

42. Viennet E., Garros C., Rakotoarivony I., Allene X., Gardes L., Lhoir J., Fuentes I., Venail R., Crochet D., Lancelot R., Riou M., Moulia C., Baldet T. & Balenghien T. (2012). – Host-seeking activity of bluetongue virus vectors: endo/exophagy and circadium rhythm of *Culicoides* in Western Europe. *PLoS ONE*, **7** (10), e48120. doi:10.1371/journal.pone.0048120.

43. Meiswinkel R., Baylis M. & Labuschagne K. (2000). – Stabling and the protection of horses from *Culicoides bolitinos* (Diptera: Ceratopogonidae), a recently identified vector of African horse sickness. *Bull. Entomol. Res.*, **90** (6), 509–515.

44. Harrup L.E., Gubbins S., Barber J., Denison E., Mellor P.S., Purse B.V. & Carpenter S. (2014). – Does covering of farm-associated *Culicoides* larval habitat reduce adult populations in the United Kingdom? *Vet. Parasitol.*, **201** (1–2), 137–145.

45. Hargrove J.W. (2000). – A theoretical study of the invasion of cleared areas by tsetse flies (Diptera: Glossinidae). *Bull. Entomol. Res.,* **90** (3), 201–209.

46. Hargrove J.W. (2005). – Extinction probabilities and times to extinction for populations of tsetse flies *Glossina* spp. (Diptera: Glossinidae) subjected to various control measures. *Bull. Entomol. Res.*, **95** (1), 13–21.

47. Hackett F., Berrang Ford L., Fèvre E. & Simarro P. (2014). – Incorporating scale dependence in disease burden estimates: the case of human African trypanosomiasis in Uganda. *PLoS Negl. Trop. Dis.*, **8** (2), e2704. doi:10.1371/journal.pntd.0002704.

48. Bourn D., Grant I., Shaw A. & Torr S.J. (2005). – Cheap and safe tsetse control for livestock production and mixed farming in Africa. *Asp. Appl. Biol.*, **75**, 1–12.

49. Welburn S.C., Coleman P.G., Maudlin I., Fèvre E., Odiit M. & Eisler M.C. (2006). – Crisis, what crisis? Control of Rhodesian sleeping sickness. *Trends Parasitol.*, **22** (3), 123–128.

50. Mérot P., Politzar H., Tamboura I. & Cuisance D. (1984). – Résultats d'une campagne de lutte contre les glossines riveraines au Burkina par l'emploi d'écrans imprégnés de Deltamethrin. *Rev. Elev. Méd. Vét. Pays Trop.*, **37**, 175–184.

51. Vale G.A., Lovemore D.F., Flint S. & Cockbill G.F. (1988). – Odour-baited targets to control tsetse flies, *Glossina* spp. (Diptera: Glossinidae), in Zimbabwe. *Bull. Entomol. Res.*, **78** (1), 31–49.

52. Van den Bossche P. (1997). – The control of *Glossina morsitans morsitans* in Zambia with targets. *Onderstepoort J. Vet. Res.*, **64** (4), 251–257.

53. Allsopp R. (2001). – Options for vector control against trypanosomiasis in Africa. *Trends Parasitol*., **17** (1), 15–19.

54. Esterhuizen J., Kappmeier Green K., Nevill E.M. & Van den Bossche P. (2006). – Selective use of odour-baited, insecticide-treated targets to control tsetse flies, *Glossina austeni* and *G. brevipalpis*, in South Africa. *Med. Vet. Entomol.*, **20** (4), 464–469 (4).

55. Esterhuizen J., Rayaisse J.-B., Tirados I., Mpiana S., Solano P., Vale G.A., Lehane M.J. & Torr S.J. (2011). – Improving the cost-effectiveness of visual devices for the control of riverine tsetse flies, the major vectors of human African trypanosomiasis. *PLoS Negl. Trop. Dis.*, **5** (8), e1257. doi:10.1371/journal.pntd.0001257.

56. Rayaisse J.-B., Esterhuizen J., Tirados I., Kaba D., Salou E., Diarrassouba A., Vale G.A., Lehane M.J., Torr S.J. & Solano P. (2011). – Towards an optimal design of target for tsetse control: comparisons of novel targets for the control of *Palpalis*-group tsetse in West Africa. *PLoS Negl. Trop. Dis.*, **5** (9), e1332. doi:10.1371/journal.pntd.0001332.

57. Tirados I., Esterhuizen J., Rayaisse J.-B., Diarrassouba A., Kaba D., Mpiana S., Vale G.A., Solano P., Lehane M.J. & Torr S.J. (2011). – How do tsetse recognise their hosts? The role of shape in the responses of tsetse (*Glossina fuscipes* and *G. palpalis*) to artificial hosts. *PLoS Negl. Trop. Dis.*, **5** (8), e1226. doi:10.1371/journal.pntd.0001226.

58. Lindh J.M., Torr S.J., Vale G.A. & Lehane M.J. (2009). – Improving the cost-effectiveness of artificial visual baits for controlling the tsetse fly *Glossina fuscipes fuscipes*. *PLoS Negl. Trop. Dis.*, **3** (7), e474. doi:10.1371/journal.pntd.0000474.

59. Esterhuizen J., Njiru B., Vale G.A., Lehane M.J. & Torr S.J. (2011). – Vegetation and the importance of insecticide-treated target siting for control of *Glossina fuscipes fuscipes*. *PLoS Negl. Trop. Dis.*, **5** (9), e1336. doi:10.1371/journal.pntd.0001336.

60. Tirados I., Esterhuizen J., Kovacic V., Mangwiro C., Hastings I., Solano P., Lehane M. & Torr S.J. (2014). – Tsetse control and Gambian sleeping sickness: implications for control strategy. *PLoS Negl. Trop. Dis.* (in press).

61. Picozzi K., Fèvre E.M., Odiit M., Carrington M., Eisler M.C., Maudlin I. & Welburn S.C. (2008). – Sleeping sickness in Uganda: a thin line between two fatal diseases. *BMJ*, **331** (7527), 1238–1241. doi:10.1136/bmj.331.7527.1238.

62. Wardrop N.A., Fèvre E.M., Atkinson P.M. & Welburn S.C. (2013). – The dispersal ecology of Rhodesian sleeping sickness following its introduction to a new area. *PLoS Negl. Trop. Dis.*, **7** (10), e2485. doi:10.1371/journal.pntd.0002485.

63. Vontas J., Moore S., Kleinschmidt I., Ranson H., Lindsay S., Lengeler C., Hamon N., McLean T. & Hemingway J. (2014). – Framework for rapid assessment and adoption of new vector control tools. *Trends Parasitol.*, **30** (4), 191–204.

64. Hendrickx G., de La Rocque S. & Mattioli R.C. (2004). – Long-term tsetse and trypanosomiasis management option in West Africa. PAAT Technical and Scientific Series No. 6. Food and Agriculture Organization of the United Nations, Rome.

65. Kovacic V., Tirados I., Esterhuizen J., Mangwiro C.T.N., Torr S.J., Lehane M.J. & Smith H. (2013). – Community acceptance of tsetse control baits: a qualitative study in Arua District, North West Uganda. *PLoS Negl. Trop. Dis.*, **7** (12), e2579. doi:10.1371/journal.pntd.0002579.