

Review

Integrated Mosquito Management: Is Precision Control a Luxury or Necessity?

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The versatility of mosquito species that spread emerging arthropod-borne viruses such as Zika has highlighted the urgent need to re-evaluate mosquito-control standards. The prospect of using precise knowledge of the geographic distribution and vector status of local populations to guide targeted interventions has gained renewed attention, but the feasibility and utility of such an approach remain to be investigated. Using the example of mosquito management in the USA, we present ideas for designing, monitoring, and assessing precision vector control tailored to different environmental and epidemiological settings. We emphasize the technical adjustments that could be implemented in mosquito-control districts to enable targeted control while strengthening traditional management.

The Challenge of Vector Heterogeneity in Mosquito Control

Diverse mosquito-control programs have recently been deployed in response to the rise in cases of several diseases spread to humans through the bite of infected mosquitoes [1–6]. These efforts have had significant impacts on transmission, but have also considerably affected the biology and distribution of mosquito populations and the pathogens they carry. Therefore, effective mosquito-borne disease control now requires more specific approaches, with actions informed by locally relevant evidence and targeted to specific contexts.

Recent years have witnessed an increased availability of **Geographic Information Systems (GIS)** (see [Glossary](#)) and powerful sequencing and computing platforms enabling fine-scale analyses of environmental and molecular data. In particular, developing and applying novel technologies, especially electronic-based tools, is a growing trend in **vector-borne disease management** ([Box 1](#)). These technological advances are renewing enthusiasm for approaches to control that would be guided by knowledge of the environmental and of entomological and epidemiological characteristics of the target area [7–10]. However, an appraisal of the feasibility and benefits of specific interventions in well defined operational settings is still lacking. Traditional **integrated mosquito control (IMC)**, as implemented in the USA for the surveillance of several mosquito-borne illnesses, provides opportunities to re-evaluate **vector control** measures in light of recent technological advances. Here we re-examine the current protocols for mosquito-borne disease surveillance in the continental USA with the aim of addressing the feasibility and utility of precision mosquito management.

Mosquito Control in the Continental USA

A recent report has indicated an alarming rise in the burden of vector-borne diseases in the USA over the past 15 years [11]. Lyme-carrying vectors – ticks – are a constant public health concern, but the incidence of several diseases spread by mosquitoes is the most significant. Lack of vaccines for most mosquito-borne diseases therefore puts effective diagnosis, clinical

Highlights

New strategies to tackle emerging arthropod-borne diseases are urgently needed; this will require not only new products and technologies but also more precise and flexible management approaches.

The proliferation of advanced technologies in vector control lays the foundation for designing and monitoring specific mosquito-surveillance programs that best suit the needs, the resources, and the environmental and epidemiological characteristics of a target region.

Critical knowledge gaps, and the limited resources of mosquito-control organizations, impede widespread application of precision management, but the feasibility of targeted measures is increasing, as is the number of contexts where specific control is needed.

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Box 1. Developing Technologies and Resources for Mosquito Control

Applying technologies to improve mosquito management at the individual, household, or community level is a long-standing endeavor of vector control. Prospective mosquito-control technologies now represent a multimillion dollar market featuring some of the largest companies in the world such as Google and Microsoft. The main trends include the following:

- Smart traps: 'smart traps' that can allow for rapid sorting and identification of mosquitoes, or even sex-specific collections, are being designed to circumvent some of the limitations of conventional traps such as the CDC light trap or ovitraps used for mosquito surveillance. The market of lethal traps that use CO₂, octenol, heat, or light – or a combination of those – to lure mosquitoes in, then trap them in containers where they die, is also growing exponentially.
- Aircraft and drones: sophisticated aircraft have been used for decades for aerial adulticide and larvicide spraying around the world. Drones are being designed for a variety of mosquito-control activities, including seeking hard-to-find pockets of water, accessing difficult-to-reach areas, and achieving fast and efficient release of laboratory-reared mosquitoes in the wild.
- GIS-based equipment: remote sensing from satellite images and super-sensitive radars can be used to map standing water and to detect the presence of adult mosquitoes at a fine scale, but the low resolution and the waiting time for data acquisition still limit the operational impact of these resources. A greater hope is placed upon the new generation of GIS tools, consisting of user-friendly devices that are portable or incorporated in motorized equipment such as trucks.
- Genetic tools: evidence from recent outbreaks suggests that the future of arboviral disease surveillance relies increasingly on hand-held DNA sequencing devices. Portable and affordable DNA sequencers are also expected to facilitate rapid and efficient diagnostics of population structure and pesticide resistance testing in mosquitoes.
- Other technologies: other emerging tools such as portable acoustic devices used for killing mosquito larvae in water in the wild, cell phones used for mapping mosquito distribution, or robots enabling rapid and efficient sorting and sexing of laboratory-reared adults for sterile male release programs may become key players in mosquito management in the near future.
- Citizen science and data science: community engagement and accessible resources providing detailed information on local vector populations are a key component of mosquito management. Very encouraging examples of citizen science and data science programs for mosquito control include NASA's GLOBE Mosquito Habitat Mapper, The Global Mosquito Alert Consortium, VectorBase's Population Biology (PopBio) resource², and several success stories on public engagement in mosquito-borne disease management reported in Europe and in the USA [28,64].

management, and vector-control methods at the forefront of management strategies for these diseases. Mosquito-borne diseases such as malaria and yellow fever have posed major challenges to public health over the past centuries in the continental USA, particularly in the humid subtropical zone [12]. Since 1930, significant public interventions have been implemented to reduce exposure to mosquito vectors that occur in the USA. Despite great strides, such as malaria eradication in the 1950s, the arrival of West Nile virus in 1999 coupled with the recent geographic expansion of invasive *Aedes* mosquito species has dramatically increased the risk of several mosquito-borne illnesses across the USA [13–15]. Local and federal authorities have recently stepped up mosquito-control efforts in response to this epidemiological challenge.

More than 1900 vector-control organizations are responsible for designing and implementing early-warning systems for several mosquito-borne diseases as well as integrated mosquito control within delimited geographic areas across the USA [16]. Mosquito-control professionals perform year-round surveillance and deploy intervention measures when needed. Common methods used in IMC include public information and education, source reduction and habitat management, chemical control, biological control, and microbial control [10]. Larval control is done by removing standing water or by using biological or chemical **larvicides** to eliminate mosquito larvae. Community education programs consist of using several media platforms to provide information to the public on how to avoid mosquito bites and mosquito-borne illnesses. When surveillance activities show that adult mosquito populations are on the rise, or that there is an increase in the spread of mosquito-borne viruses, professionals may decide to apply

Glossary

Adulticide: a type of pesticide that may be used by a mosquito-control program, a licensed pest-control professional, or as a do-it-yourself application to kill adult mosquitoes.

Citizen science: projects creating collaborations between professional scientists and the general public in order to expand opportunities for scientific data collection while raising awareness for research questions that affect people's lives.

Data science: an interdisciplinary field which combines several types of expertise at the intersection of the fields of statistics, information and computer science, to design and manage large databases.

Geographic Information Systems

(GIS): a set of tools that enable the acquisition, analysis, and display of geographically referenced information in the form of maps.

Integrated mosquito control

(IMC): a term used to describe the comprehensive approach of managing mosquito populations that utilizes various techniques in order to reduce mosquito numbers and protect public health while minimizing the adverse environmental effects.

Larvicide: a pesticide designed for killing the immature forms of an insect, such as mosquito larvae and pupae.

Mark-release-recapture

experiments: a method used to estimate population size, which involves capturing, marking, and releasing a sample of individuals in nature. Another sample of marked individuals is then recaptured and the individuals are counted to estimate parameters such as life expectancy, flight distance, and dispersal, and to infer population size.

Mosquito control district (MCD):

an independent special district charged with managing mosquito populations at levels that reduce the risk of mosquito-borne disease transmissions to humans and other vertebrates within a designated geographic area.

Polygenic adaptation: a process in which a population adapts through small changes in allele frequencies at a large number of loci.

Spatial analysis: a set of analytical techniques employed to determine the spatial distribution of a variable,

adulticides using backpack sprayers, trucks, or airplanes [10]. To manage major mosquito-borne disease outbreaks (e.g., the 2016 arrival of Zika in Florida), local health departments and **mosquito control districts (MCDs)** partner with various agencies – including the Centers for Disease Control and Prevention (CDC) – to implement more intense interventions such as massive insecticide spraying in addition to traditional IMC [17].

On the one hand, reduced financial resources deeply limit the competencies of mosquito-control districts as shown by a recent nation-wide survey [16]. Yet on the other hand, a significant number of novel technologies designed to improve vector control are reaching the market (Box 1). It is clear that controlling versatile mosquito species that spread emerging arthropod-borne viruses (arboviruses) in unexpected places does require more flexible interventions capable of determining, predicting, and accounting for variability within and between pest populations. Therefore, examining how the technology can empower such interventions should be a key component in decision-making regarding the acquisition of novel technologies in MCDs.

Definition of Precision Mosquito Control

Implementing spatially targeted interventions is a long-standing idea in vector-borne disease control [18]. For instance, the prospect of using entomological indicators such as indoor resting densities to perform targeted malaria control has been around for two decades [19,20]. Targeted interventions may be more conceivable now than they were two decades ago due to considerable progress in our understanding of mosquito ecology and genetics. However, questions remain about the feasibility and the capacity of such interventions to be efficiently embedded in integrated mosquito management. In this study, we have defined ‘precision mosquito control’ in light of two related concepts: ‘precision medicine’ and ‘precision public health’, which aim to promote intervention strategies that use technologies (e.g., genomics, spatial analysis, big data, etc.) to take individual- or population-level variations into account [21,22]. In the next sections, we have assessed the potential benefits of precision control by addressing the different competencies of integrated mosquito management whose outcomes can be improved with novel technologies (Table 1 and Figure 1). We have also emphasized some of the technical adjustments needed to make MCDs competent in implementing precise surveillance.

Accounting for Geographic and Temporal Heterogeneity

An important element of mosquito control consists of finding the vector populations and assessing the risk they represent to public health. Key components of alert systems that trigger interventions and guide the spatial prioritization of vector control during mosquito season in the USA include detecting geographic clusters of mosquito abundance or mosquito-borne disease cases in humans, and testing the prevalence of arboviruses in animal reservoirs or in vector populations. Analyzing spatial and temporal patterns of entomological and epidemiological indicators is therefore a cornerstone of risk assessment for arboviral disease control [10].

A central goal of research fields such as geospatial health or spatial epidemiology consists of using a GIS framework to model the relationships between the spatial distribution of human pathogens, their vectors, the prevalence of vector-borne diseases, and some environmental predictors. Although interest in these research fields has continued to grow in vector biology [7,23–27], the use of spatial distribution models in day-to-day vector control activities remains limited. Several obstacles, including seasonal distribution and rapid range shifts, make it difficult

the relationship between the spatial distribution of variables, and the association of the variables of an area using geographic information systems.

Vector-borne diseases: infections caused by pathogens transmitted by the bite of infected arthropod species – collectively called ‘vectors’ – such as mosquitoes, ticks, triatomine bugs, sandflies, and blackflies.

Vector control: a series of measures and methods used to reduce exposure to vector populations or to mitigate their ability to transmit pathogens.

Vectorial capacity: a measurement of the efficiency of vector-borne disease transmission, which depends on multiple factors such as the incubation period of the pathogen, the survival rate of the vector, and other behavioral, environmental, and ecological features.

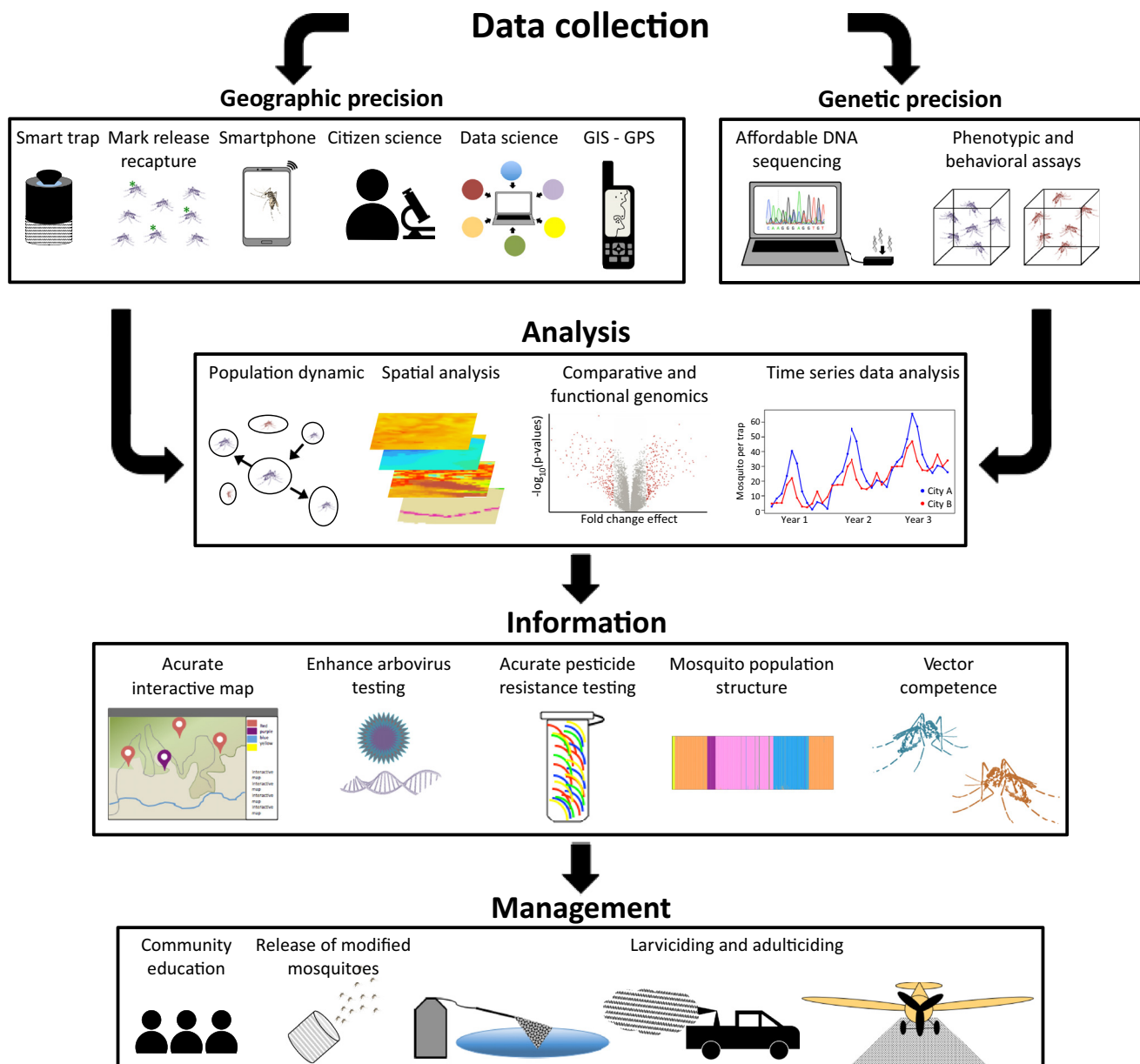
Table 1. Core and Supplemental Competencies of Traditional Integrated Mosquito Management and Some Precision Control Methodologies That Could Be Foreseeable in Relatively Well-equipped Mosquito Control Districts. Other precision competencies that are not yet feasible due to knowledge gaps or technical difficulties are also suggested as future improvements, which will require long-term actions

	Core competencies				
Traditional integrated mosquito management ^a	(i) Routine mosquito surveillance through standardized trapping and species identification	(ii) Treatment decisions using surveillance data	(iii) Larviciding, adulticiding or both	(iv) Routine vector control activities	(v) Pesticide resistance testing
Precision mosquito control	• Smart traps • Interactive GIS maps • Time-series data collection • Spatial analysis • Citizen science • Data science • Mark-release recapture	• Advanced pesticide resistance testing • Mosquito population size • Advanced arbovirus detection • Mosquito population structure	• Targeting clusters of mosquito densities • Use of drones • Efficient chemical application • Resistance monitoring • Monitoring the impacts	• Geographic precision • Targeted control • Accurate surveillance data	• Unbiased phenotypic tests • Advanced molecular detection
Future improvements	• Population dynamics	• Mosquito fitness • Vector competence • Mosquito microbiome		• Evaluation of precision control capabilities	• Insecticide resistance and mosquito fitness • Insecticide resistance and vector competence • Field trials
	Supplemental competencies				
Traditional integrated mosquito management ^a	(vi) Licenced pesticide application	(vii) Vector control activities other than chemical control	(viii) Community outreach and education campaigns regarding mosquito-borne diseases	(ix) Regular communication with local health departments regarding surveillance and epidemiology	(x) Outreach with nearby vector control programs
Precision mosquito control	• Flexible regulation	• Geographic precision	• Citizen science • Interactive GIS maps • Web development	• Data science • Interactive GIS maps • Web development	• Data science • Citizen science • Flexible regulation

^aAs defined by the National Association of County and City Health Officials (NACCHO) [16] using the CDC framework for vector control competency as guidance [65,66].

to reliably model the habitats and epidemiological significance of mosquito vectors that occur in the USA. In particular, the spatial distribution and disease risk associated with invasive *Aedes* species that spread or disappear rapidly in different places are notoriously difficult to predict with a spatiotemporal resolution that would be relevant to MCDs. These limitations, coupled with the significant level of skill required, contribute to undermine the interest of mosquito-control professionals in spatial distribution models, as shown by recent surveys [16].

However, a new wave of GIS-based applications designed by MCDs, academic partners, and private companies is rapidly emerging (Box 1). Some of these tools are particularly suited for field operations and for engaging the public at the scale of an MCD. Notable examples include a series of user-friendly and accessible tools such as interactive maps used by mosquito-control professionals to locate vector distribution and to inform the public in MCDs. GIS-equipped trucks are also enhancing the capacity to track larval habitats and to apply larvicides and adulticides exactly where needed. Finally, several **citizen science** projects that have been precious in identifying mosquito vectors and assessing vector-borne disease risk in some



Trends in Parasitology

Figure 1. Summary of Some of the Main Features of Precision Mosquito Control That Could Be Implemented at the Level of a Mosquito Control District. Capacity strengthening in various aspects of geographic and genetic precision could empower mosquito-control professionals to acquire fine-scale data on vector distribution and disease transmission. Several analytical procedures may be utilized to decipher the determinants of mosquito abundance, vectorial capacity, and disease transmission within a designated geographic area. This information could then be used to inform targeted area-wide mosquito-control measures.

regions would not have been possible without the help of GIS tools enabling accurate geographic positioning and data management [28] (Box 1). In the long run, in addition to their critical role in field operations and outreach activities, novel GIS-based tools may empower MCDs to routinely collect fine-scale data that best reflect the fitness and epidemiological significance of local populations. Therefore, developing and applying tools enabling geographic

precision within MCDs should be an integral part of mosquito-borne disease surveillance and would likely improve both standard management and the prospects of targeted control (see Outstanding Questions and [Figure 1](#)).

Precision Genomics in Mosquito Control

High-quality genomic data on insect pests, human pathogens and microbiomes of disease vectors are rapidly accumulating^{i-iv}. In addition, the increased availability of affordable or hand-held devices (e.g., Illumina MiSeq[®] and MinION[®]) allowing for point-of-need DNA sequencing makes us think that genomic expertise may be within the reach of some MCDs. However, despite a plethora of scientific publications in mosquito genomics, many conditions remain to be fulfilled to convert genomic knowledge into operationally viable tools for vector control. Genomic information can be helpful for at least three aspects relevant to mosquito-borne disease surveillance at the level of MCDs: pesticide resistance testing, arbovirus surveillance, and improving the understanding of the factors underlying the **vectorial capacity** of mosquito populations in a given region ([Figure 1](#) and [Table 1](#)).

Pesticide Resistance Testing

Assessing the sensitivity of local populations is critical to predict the efficacy of chemical pesticides used in mosquito control and to understand and mitigate the epidemiological and operational implications of pesticide resistance [6,29]. For example, analysis revealed that aerial and truck sprays of several classes of insecticides had no or little effect on adult *Aedes aegypti* mosquito counts during the Zika outbreak in July, 2016 in Miami-Dade County, Florida [17]. Such observations highlight the need to better understand the factors that are crucial to the success of chemical control. Pesticide resistance tests performed in MCDs consist of laboratory-based standard bioassays [16,30,31]. These phenotypic tests aim to determine the proportion of individuals that can survive exposure to a standard dose of pesticide for a given period of time. In a few well equipped MCDs, a PCR-based detection of mutations of the voltage-gate sodium channel gene associated with increased resistance is occasionally performed in addition to bioassays ([Table 1](#)).

The mechanisms and consequences of insecticide resistance in insects are incredibly complex, and we may never have a complete understanding of the processes underlying the rapid adaptation of mosquito populations to chemical insecticides [32–35]. Pesticide exposure triggers a variety of adaptive changes, reflecting complex **polygenic adaptation** that would be best addressed with a combination of genomic tools, phenotypic and behavioral tests, and field trials. One of the main challenges of insecticide resistance monitoring is developing molecular assays that may simultaneously screen favorable mutations at a large number of genetic loci associated with resistance. Recent genome-scale studies have pinpointed a significant number of genes involved in insecticide resistance that can be harnessed to develop multiplex polygenic tests in mosquitoes [36,37]. Such tests could be implemented using PCR or affordable next-generation sequencing platforms accessible to MCDs, and could be crucial to better characterize insecticide resistance and its operational and epidemiological consequences.

Enhancing Arbovirus Surveillance

Arbovirus surveillance requires special infrastructure and trained personnel, and only a few accredited laboratories have the capacity to perform arbovirus testing across the USA [38]. Traditionally, the presence of a list of known arboviruses is detected in animal reservoirs, humans hosts, or mosquitoes using immunoglobulin tests, PCR, or virus-isolation tests [39]. Prior to arbovirus testing in mosquitoes, specimens have to be sorted and identified, which can be labor intensive and time consuming. Novel diagnostic tools for arbovirus detection in

mosquitoes – based on digital health systems and nanotechnology, honey-baited nucleic acid preservation cards or sugar bait stations, or high-throughput DNA sequencing – are being developed to mitigate some of the limitations of current protocols [39–43].

Importantly, the rapid evolution of arboviruses, as well as the emergence/re-emergence of new species, highlights the need for advanced testing procedures that may provide a fine-scale description of genetic variation within the virus genome. Indeed, our understanding of the conditions that favor the emergence of new viral lineages responsible for outbreaks, as well as the drivers of their fitness and virulence, remains limited [44–48]. Laboratory protocols are being developed to sequence RNA viruses directly from clinical samples in a way that is cheap, accurate, and scalable under resource-limited conditions [49,50]. Interestingly, these protocols can be used with hand-held DNA sequencers and provide a potentially effective diagnostic tool for examining the genetic diversity of viral isolates in MCD/State laboratories. These advanced molecular tests will likely lay the foundation for a more precise detection of local viral lineages and improve our understanding of the epidemiological relevance of genetic variation in arboviruses.

Deciphering the Vectorial Capacity of Local Mosquito Populations

Within a mosquito vector species, vector competence for a given pathogen is limited to a fraction of individuals that ultimately contribute to disease transmission [51–53]. Identifying this fraction of the population, as well as the environmental and genetic factors that increase its fitness in a given region, would provide vital information for mosquito-borne disease surveillance and for designing targeted control. Unfortunately, despite significant research, the phenotypes and genes associated with mosquito fitness and the ability of vectors to transmit pathogens remain poorly understood. In theory, observational and experimental approaches based on comparative and functional genomics may help to uncover some of the fitness traits and extrinsic factors that shape vectorial capacity of local populations [54–56]. However, the genetic architecture of vectorial capacity is extremely complex, and it remains unclear whether state-of-the-art genomic studies can yield insights into what makes mosquito species efficient or prolific in terms of reproductive success of the vector populations in a given area. In addition, efficient genomic studies in mosquitoes are costly, require high levels of skills, and would be complicated to implement even in the best-equipped MCDs. Nevertheless, genomic techniques such as reduced representation sequencing [57] are cost-effective and are transferable to MCD/State laboratories close to operational settings. Those may provide effective ways to address population subdivisions within a geographic region. Even though the underlying traits remain elusive, knowledge of local population structure is crucial to better understand the patterns of colonization and the putative origin of invasive mosquito species.

In summary, genomic precision in mosquito control has an unfulfilled potential that should be neither underestimated nor overstated. Most variables that are vital for targeted control are underpinned by complex traits that are difficult to study even with powerful genomic analyses. Capacity-building in genomics in MCDs could prioritize aspects that will be both helpful and feasible in MCD facilities in the near future – such as rapid and efficient insecticide-resistance testing, analysis of mosquito population structure, and arbovirus testing (Table 1).

Monitoring the Impacts of Mosquito Control

Ideally, monitoring the effects of human interventions on mosquito physiology, ecology, and vectorial capacity requires in-depth analyses of wild populations with multidisciplinary approaches (Table 1). Advanced molecular and geographic surveys may become increasingly feasible in well-equipped MCDs if capacity-building leverages the widespread availability of

precision technologies. One aspect that necessitates further scrutiny is the dynamic of vector populations. Variations in mosquito population size are challenging to quantify, and the effects of human interventions are difficult to disentangle from other natural drivers that modulate the presence and abundance of a species in a given environment.

Mosquito population size can be estimated via direct counts using traps, **mark-release-recapture experiments** or genetic tests. Combining improved trapping methods such as the use of smart traps, time-series data collections, **spatial analysis**, and effective citizen science and **data science** programs will likely contribute to more reliable evaluations of mosquito densities (Box 1). In principle, all of these technical adjustments are accessible to normally equipped MCDs and would be particularly helpful in addressing the dynamics of invasive species with erratic natural cycles. Mark-release-recapture experiments are labor intensive, but have been effectively used to estimate *Aedes* population size in small areas and may provide a valid alternative approach in some contexts [58]. Genetic tests aim to detect acute changes in population size due to variations in the number of individuals whose genetic material is passed on to the next generation. However, genome-scale studies have shown that the demographic changes possibly associated with vector-control efforts are either too weak or undetectable at the genetic level in large mosquito populations, even with powerful sequencing technologies [36,59]. Therefore, it is unclear whether genetic analyses of population size, which are technically challenging, would be of any utility in MCDs. In the short term, robust estimates of mosquito densities may effectively guide decision-making and responses to alert protocols. Nonetheless, there is a crucial need to design other indicators that can be used in MCDs to monitor the long-term effects of area-wide control strategies on mosquito populations and disease risk.

The Release of Modified Mosquitoes

One of the strategies currently being developed to control mosquito-borne diseases consists of releasing modified mosquitoes that are equipped to reduce the fertility of wild populations, with whom they mate, or to lower their ability to transmit pathogens [4,5,60–63]. Reducing mosquito populations or their epidemiological significance in a geographic area can be achieved via the release of males sterilized with radiation, males or females infected with a bacterium (*Wolbachia*), or genetically modified individuals.

A *Wolbachia*-based method is being tested in Fresno, California and Miami, Florida, to control *A. aegypti* populations. *Wolbachia* is not naturally present in wild *A. aegypti*, and females lay eggs that do not hatch when they mate with males that have been artificially infected with the bacterium and released in nature. This mosquito-control strategy is therefore sustained by recurrent releases of millions of *Wolbachia*-infected adult males, whose flight range is typically 30–100 m, with the hope of reducing fertility and suppressing the naturally occurring populations within the precisely delimited geographical area. As a result, fine-scale analysis of geographic clusters of mosquito abundance in localized areas would be crucial to the effective deployment and monitoring of this method. Empowering MCDs to effectively perform spatial analyses would be vital to gain a precise idea about the optimal spatial extent, resolution, and spacing needed for the releases. Rectangular grids designed using GIS can be utilized to split the target area into regular cells in which mosquitoes are released, sampled, and monitored.

Concluding Remarks

The greatest successes achieved so far in controlling important vector-borne illnesses worldwide – including the recent global reduction of malaria cases – have been based on uniform deployment of conventional methods such as insecticide application or the distribution of bed

Outstanding Questions

If current surveillance protocols need to be upgraded to better handle the epidemiological complexity of emerging arboviral diseases, are spatially targeted interventions among the top priorities?

In contexts where targeted interventions are justified and feasible, how many ecological, behavioral, and genetic variables should be taken into account to characterize local populations and to implement effective precision mosquito management at the scale of a control district?

Can emerging technologies be effectively applied to design and monitor precision mosquito control? How far will knowledge gaps and the paucity of resources in mosquito control districts impact the feasibility of precision management? Are current methodological approaches robust enough for precision management, or do we absolutely need to develop new interdisciplinary conceptual frameworks?

Are mosquito control districts plagued by financial difficulties ready to embrace alternative management strategies that may come with additional costs?

nets. A central question is to know if, given the complex challenge of emerging arthropod-borne diseases, surveillance programs can be effective and sustainable without a progressive incorporation of tools enabling precision management (see Outstanding Questions).

Integrated mosquito management programs are increasingly challenged to reduce costs, duration, and environmental impacts, to engage the public, and to comply with multiple corporate and public regulations. These requirements have increased the urgency to develop and apply novel technologies that may optimize surveillance and control (Box 1). Nonetheless, while applying technologies is gaining momentum – especially in wealthy MCDs – the capacity to form a decision support system that corresponds to inter- and intrapopulation variability remains weak. The potential benefits of new technologies in mosquito management are obvious, but their optimal application relies on capacity-building in MCDs. Precision management, in particular, is hampered by our limited knowledge of components of vectorial capacity that could be used to target local populations as well as the significant cost, time, and skills needed to implement complex analytical approaches. However, in addition to reinforcing the financial and technical capacity of MCDs, novel methodological frameworks and technologies should be incorporated in integrated vector-management protocols to meet the ever-growing challenges due to emerging/re-emerging vector-borne illnesses. The technical capacity and the human and financial resources vary tremendously from one MCD to another. Therefore, it is difficult to tell precisely what technical adjustments could be feasible, or should be prioritized, to reinforce the competencies of MCD/State facilities. With this caveat in mind, we have indicated precision control methodologies whose implementation in relatively well-equipped MCDs could be foreseeable now or in the near future (Table 1). If some of the hurdles that undermine targeted control can be overcome, precision management may provide efficient tools to achieve effective vector-borne disease surveillance in contexts where higher standards of intervention are needed.

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Resources

- ⁱwww.cdc.gov/amd/index.html
- ⁱⁱwww.predictconsortium.eu/
- ⁱⁱⁱ<http://mcbridelab.princeton.edu/875-2/>
- ^{iv}www.malariagen.net/projects/ag1000g
- ^vwww.vectorbase.org/

References

1. Gubler, D.J. (2002) The global emergence/resurgence of arboviral diseases as public health problems. *Arch. Med. Res.* 33, 330–342
2. Mayer, S.V. *et al.* (2017) The emergence of arthropod-borne viral diseases: a global prospective on dengue, chikungunya and Zika fevers. *Acta Trop.* 166, 155–163
3. Gould, E. *et al.* (2017) Emerging arboviruses: why today? *One Health* 4, 1–13
4. Flores, H.A. and O'Neill, S.L. (2018) Controlling vector-borne diseases by releasing modified mosquitoes. *Nat. Rev. Microbiol.* 16, 508–518
5. Alphey, L. (2014) Genetic control of mosquitoes. *Annu. Rev. Entomol.* 59, 205–224
6. Hemingway, J. (2017) The way forward for vector control. *Science* 358, 998–999
7. Clements, A.C.A. *et al.* (2013) Further shrinking the malaria map: how can geospatial science help to achieve malaria elimination? *Lancet Infect. Dis.* 13, 709–718
8. Rinker, D.C. *et al.* (2016) Disease vectors in the era of next generation sequencing. *Genome Biol.* 17, 1–11
9. Wesolowski, A. *et al.* (2018) Mapping malaria by combining parasite genomic and epidemiologic data. *BMC Med.* 16, 190
10. American Mosquito Control Association (2017) *Best Practices for Integrated Mosquito Management: A Focused Update*, AMCA
11. Rosenberg, R. *et al.* (2018) Trends in reported vectorborne disease cases – United States and Territories, 2004–2016. *Morb. Mortal. Wkly. Rep.* 67, 496–501
12. Moreno-Madrinán, M.J. and Turell, M. (2018) History of mosquito-borne diseases in the United States and implications for new pathogens. *Emerg. Infect. Dis.* 24, 821–826
13. Miller, J.R. (2001) The control of mosquito-borne diseases in New York City. *J. Urban Health* 78, 359–366

14. Williams, L.L. (1963) Malaria eradication in the United States. *Am. J. Public Health Nations Health* 53, 17–21
15. Powell, J.R. and Tabachnick, W.J. (2013) History of domestication and spread of *Aedes aegypti* – a review. *Mem. Inst. Oswaldo Cruz* 108, 11–17
16. National Association of County and City Health Officials (2017) *Mosquito Control Capabilities in the U.S.*, NACCHO
17. Stoddard, P.K. (2018) Managing *Aedes aegypti* populations in the first Zika transmission zones in the continental United States. *Acta Trop.* 187, 108–118
18. Carter, R. *et al.* (2000) Spatial targeting of interventions against malaria. *Bull. World Health Organ.* 78, 1401–1411
19. Protopopoff, N. *et al.* (2008) Spatial targeted vector control is able to reduce malaria prevalence in the highlands of Burundi. *Am. J. Trop. Med. Hyg.* 79, 12–18
20. Kamdem, C. *et al.* (2012) Spatially explicit analyses of anopheline mosquitoes indoor resting density: implications for malaria control. *PLoS One* 7, e31843
21. Weeramanthri, T.S. *et al.* (2018) Editorial: Precision public health. *Front. Public Health* 6, 3–5
22. Khoury, M.J. *et al.* (2018) From public health genomics to precision public health: a 20-year journey. *Genet. Med.* 20, 574–582
23. Focks, D.A. *et al.* (1999) The use of spatial analysis in the control and risk assessment of vector-borne diseases. *Am. Entomol.* 45, 173–183
24. Palaniyandi, M. (2012) The role of remote sensing and GIS for spatial prediction of vector-borne diseases transmission: a systematic review. *J. Vector Borne Dis.* 49, 197–204
25. Eisen, L. and Lozano-Fuentes, S. (2009) Use of mapping and spatial and space-time modeling approaches in operational control of *Aedes aegypti* and dengue. *PLoS Negl. Trop. Dis.* 3, 1–7
26. Eisen, L. and Eisen, R.J. (2011) Using geographic information systems and decision support systems for the prediction, prevention, and control of vector-borne diseases. *Annu. Rev. Entomol.* 56, 41–61
27. Tjaden, N.B. *et al.* (2018) Mosquito-borne diseases: advances in modelling climate-change impacts. *Trends Parasitol.* 34, 227–245
28. Jordan, R.C. *et al.* (2017) Citizen science as a tool for mosquito control. *J. Am. Mosq. Control Assoc.* 33, 241–245
29. WHO (2012) *Global Plan for Insecticide Resistance Management in Malaria Vectors*, World Health Organization
30. Centers for Disease Control and Prevention (2012) *Guideline for Evaluating Insecticide Resistance in Vectors Using the CDC Bottle Bioassay*, CDC
31. Centers for Disease Control and Prevention (2016) *Guideline for Aedes aegypti and Aedes albopictus Surveillance and Insecticide Resistance Testing in the United States*, CDC
32. Liu, N. (2015) Insecticide resistance in mosquitoes: impact, mechanisms, and research directions. *Annu. Rev. Entomol.* 60, 537–559
33. Hemingway, J. and Ranson, H. (2000) Insecticide resistance in insect vectors of human disease. *Annu. Rev. Entomol.* 45, 371–391
34. French-Constant, R.H. (2013) The molecular genetics of insecticide resistance. *Genetics* 194, 807–815
35. Gattton, M.L. *et al.* (2013) The importance of mosquito behavioural adaptations to malaria control in Africa. *Evolution* 67, 1218–1230
36. Miles, A. *et al.* (2017) Genetic diversity of the African malaria vector *Anopheles gambiae*. *Nature* 552, 96–100
37. Faucon, F. *et al.* (2015) Unravelling genomic changes associated with insecticide resistance in the dengue mosquito *Aedes aegypti* by deep targeted sequencing. *Genome Res.* 25, 1347–1359
38. Hadler, J.L. *et al.* (2015) Assessment of arbovirus surveillance 13 years after introduction of West Nile virus, United States. *Emerg. Infect. Dis.* 21, 1159–1166
39. Ramirez, A.L. *et al.* (2018) Searching for the proverbial needle in a haystack: advances in mosquito-borne arbovirus surveillance. *Parasit. Vectors* 11, 1–12
40. Batovska, J. *et al.* (2018) Effective mosquito and arbovirus surveillance using metabarcoding. *Mol. Ecol. Resour.* 18, 32–40
41. Batovska, J. *et al.* (2017) Metagenomic arbovirus detection using MiniON nanopore sequencing. *J. Virol. Methods* 249, 79–84
42. Coffey, L.L. *et al.* (2014) Enhanced arbovirus surveillance with deep sequencing: identification of novel rhabdoviruses and bunyaviruses in Australian mosquitoes. *Virology* 448, 146–158
43. Russell, J.A. *et al.* (2018) Unbiased strain-typing of arbovirus directly from mosquitoes using nanopore sequencing: a field-forward biosurveillance protocol. *Sci. Rep.* 8, 1–12
44. Grubaugh, N.D. *et al.* (2016) Genetic drift during systemic arbovirus infection of mosquito vectors leads to decreased relative fitness during host switching. *Cell Host Microbe* 19, 481–492
45. Grubaugh, N.D. *et al.* (2017) Mosquitoes transmit unique West Nile Virus populations during each feeding episode. *Cell Rep.* 19, 709–718
46. Ebel, G.D. (2017) Promiscuous viruses – how do viruses survive multiple unrelated hosts? *Curr. Opin. Virol.* 23, 125–129
47. Weger-Lucarelli, J. *et al.* (2018) Using barcoded Zika virus to assess virus population structure *in vitro* and in *Aedes aegypti* mosquitoes. *Virology* 521, 138–148
48. Forrester, N.L. *et al.* (2014) Arboviral bottlenecks and challenges to maintaining diversity and fitness during mosquito transmission. *Viruses* 6, 3991–4004
49. Grubaugh, N.D. *et al.* (2018) An amplicon-based sequencing framework for accurately measuring intrahost virus diversity using PrimalSeq and iVar. *bioRxiv* Published online August 5, 2018. <http://dx.doi.org/10.1101/383513>
50. Quick, J. *et al.* (2017) Multiplex PCR method for MiniON and Illumina sequencing of Zika and other virus genomes directly from clinical samples. *Nat. Protoc.* 12, 1261–1276
51. Kramer, L.D. and Ciota, A.T. (2015) Dissecting vectorial capacity for mosquito-borne viruses. *Curr. Opin. Virol.* 15, 112–118
52. Gonçalves, C.M. *et al.* (2014) Distinct variation in vector competence among nine field populations of *Aedes aegypti* from a Brazilian dengue-endemic risk city. *Parasit. Vectors* 7, 1–8
53. Main, B.J. *et al.* (2018) Vector competence of *Aedes aegypti*, *Culex tarsalis*, and *Culex quinquefasciatus* from California for Zika virus. *PLoS Negl. Trop. Dis.* 12, e0006524
54. Shin, D. *et al.* (2014) Transcriptomics of differential vector competence: West Nile virus infection in two populations of *Culex pipiens quinquefasciatus* linked to ovary development. *BMC Genomics* 15, 1–11
55. Severson, D.W. and Behura, S.K. (2016) Genome investigations of vector competence in *Aedes aegypti* to inform novel arbovirus disease. *Insects* 7, 58
56. Lambrechts, L. (2011) Quantitative genetics of *Aedes aegypti* vector competence for dengue viruses: towards a new paradigm? *Trends Parasitol.* 27, 111–114
57. Baird, N.A. *et al.* (2008) Rapid SNP discovery and genetic mapping using sequenced RAD markers. *PLoS One* 3, e3376
58. Cianci, D. *et al.* (2013) Estimating mosquito population size from mark-release-recapture data. *J. Med. Entomol.* 50, 533–542
59. Fouet, C. *et al.* (2018) Human interventions: driving forces of mosquito evolution. *Trends Parasitol.* 34, 127–139
60. Ritchie, S.A. and Johnson, B.J. (2017) Advances in vector control science: rear-and-release strategies show promise... but don't forget the basics. *J. Infect. Dis.* 215, S103–S108
61. Dorigatti, I. *et al.* (2018) Using *Wolbachia* for dengue control: insights from modelling. *Trends Parasitol.* 34, 102–113
62. Ritchie, S.A. *et al.* (2018) Mission accomplished? We need a guide to the 'post release' world of *Wolbachia* for *Aedes*-borne disease control. *Trends Parasitol.* 34, 217–226

63. Hammond, A. *et al.* (2016) A CRISPR-Cas9 gene drive system targeting female reproduction in the malaria mosquito vector *Anopheles gambiae*. *Nat. Biotechnol.* 34, 78–83
64. Palmer, J.R.B. *et al.* (2017) Citizen science provides a reliable and scalable tool to track disease-carrying mosquitoes. *Nat. Commun.* 8, 1–12
65. Centers for Disease Control and Prevention (2013) *West Nile Virus in the United States: Guidelines for Surveillance, Prevention, and Control*, CDC
66. Centers for Disease Control and Prevention (2017) *Integrated Mosquito Management for Aedes aegypti and Aedes albopictus Mosquitoes*, CDC