13. Global Vector Control Response – supporting the pillars

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From the chapters in this volume it is evident that, in spite of remarkable progress in the control of vector-borne diseases (VBDs), these diseases continue to place a huge burden on human societies across many geographic regions. Although VBDs are transmitted by a large and diverse group of arthropod species (Mullen and Durden 2018), mosquitoes are without doubt the group that receives most attention because of the huge impact mosquito-borne diseases poses on many different aspects of societies.

With the realisation that interruption of pathogen transmission would be the most effective way of VBD control (Anderson and May 1992, MacDonald 1957), the introduction of insecticides in the 20th century created expectations that VBDs could be effectively controlled and even eliminated. More than 50 years later, it is realised that this expectation was too optimistic. Recurring developments of insecticide resistance and financial and logistical constraints for efficient roll-out of control programmes have led to a growing awareness that different strategies are required. This was made more explicit by the simultaneous emergence of *Plasmodium* drug resistance (Menard and Dondorp 2017), leaving the world without effective tools with which to combat malaria. To date, only two of these mosquito-borne diseases can be prevented by vaccination: yellow fever and Japanese encephalitis. As with insecticides, however, financial and logistical constraints sometimes lead to situations where the vaccines arrive too late to prevent an epidemic (Sérié *et al.* 1968). It is remarkable that both vaccines were developed and introduced already in the nineteen thirties, but that since then no other vaccines for mosquito-borne diseases became available. In recent years, though, significant progress has been made in the development of vaccines for a number of mosquito-borne diseases. For example, in 2016 for the first time a vaccine for dengue became available, but its use is restricted to people who have had dengue once and in non-immunes the vaccine may even increase the risk of severe dengue (Macias *et al.* 2020). The recent phase III trial of a malaria vaccine in three African countries is a breakthrough, but efficacy- and health concerns still remain (https://www.bmj.com/content/368/bmj.l6920.full). Vaccines for chikungunya and Zika are under various phases of development, but it is not clear when these may become available (Schrauf *et al.* 2020). Until vaccines for these diseases are effective, safe and widely available, vector control is the only effective tool for arboviral disease prevention.

The 2015-2016 Zika outbreak in South America triggered a radical switch in classical VBD control. With strong support from the Director General, the World Health Organization assembled an international group of experts with the task to develop a comprehensive approach for the control of VBDs: the Global Vector Control Response (GVCR) which includes incorporation of novel and innovative tools. This response, based on four pillars, makes a convincing plea for a radically different approach to VBD control: intersectoral collaboration, community engagement, monitoring, surveillance and evaluation, and integration of tools and approaches, supported by novel and innovative research, are the principle drivers that should lead to a reduction of the VBD disease burden (WHO 2017).

It is noteworthy that the GVCR was unanimously adopted by the World Health Assembly in its 70th session in May 2017. Since then, WHO has engaged on a programme to roll out the GVCR in all regions, with the specific mandate to strengthen intersectoral collaboration and community engagement. These aspects of the GVCR were in full development at the time of the first GVCR conference in 2019. The state-of the art of the various aspects of the GVCR were presented and discussed during the conference. Section 1 of this book covered scaling up and integration of tools and approaches based on the current and future use of insecticides (Chapters 2, 3, 4 and 5). Section 2 presented examples of innovative strategies, with a strong emphasis on integrated vector management (IVM). Section 3 discussed examples of intersectoral collaboration and community engagement.

Insecticides

Insecticides continue to play a large role in the prevention and control of malaria. The global distribution of insecticide-treated bed nets in 2000 as the main pillar of malaria prevention and control, has indeed led to a large and significant decrease in malaria morbidity and mortality (Cibulskis *et al.* 2016). The unwanted side effect of this global programme, however, has caused the very high levels of insecticide resistance that render the LLINs less effective (Okumu and Finda, Chapter 3). One could argue that this appears as a repeat of the 1955-1969 malaria eradication effort, where increased levels of resistance to DDT were among the factors that led to abandonment of the programme (Gabaldon 1969, Nájera *et al.* 2011). There is, however, a major difference with the previous campaign. The 1950s global campaign ran aground in the mid 1970s not only because of insecticide resistance, but also for lack of funds and logistical difficulties when it was rolled out in least developed countries. There, was also the lack of staff trained in the many different aspects of malaria control.

Today, the situation is radically different: international donors are committed to support the programme for the foreseeable future, and a large number of young people have received training in VBD control at all levels. Most malaria-endemic countries have a national malaria control strategy, with a national team of experts who can provide direction and leadership. Indeed, monitoring and evaluation has shown high levels of insecticide resistance (WHO 2019). Innovative research is expected to produce new classes of insecticides, while at the same time the concept of integrated control with less reliance on insecticides, is being introduced (Wilson *et al.* 2020). Okumu and Finda (Chapter 3) make a plea to conduct epidemiological trials with untreated bed nets, suggesting that modern nets of strong quality can provide sufficient physical protection against mosquito bites, leading to significantly less malaria. This approach, combined with other, innovative tools may open the way to insecticide-free malaria control which would be revolutionary after more than 100 years of reliance on these compounds (Wilson *et al.* 2020) and possibly prevent derailment of the malaria eradication campaign, as suggested by Hemingway *et al.* (2016).

Innovative strategies in integrated vector management

In contrast with malaria control, which continues to rely heavily on insecticide-based tools (see above), the control of arboviral disease focuses currently on highly innovative strategies and tools. Historically, insecticides played a major role in the control of the main vector *Aedes aegypti* and led indeed to the temporary disappearance of this vector in South America (Chapter 4) and Gubler (1989). Besides insecticide resistance, environmental and logistical reasons have led to less reliance on insecticides for the control of *Ae. aegypti* in favour of highly innovative and advanced technologies. The discovery that *Wolbachia*-transfected *Ae. aegypti* are refractory to dengue virus (Flores and O'Neill 2018, Moreira *et al.* 2009), as well as a population suppression approach with a self-limiting gene provide alternative, more sustainable interventions for dengue control programmes (Alphey *et al.* 2013, Patil *et al.* 2018, Qsim *et al.* 2017). The potential success of these technologies provides hope that in the not-too-distant future *Aedes*-borne arboviral diseases can be controlled more effectively than at present.

Until recently most mosquito-borne disease control programmes focused on the control of indoor-biting and resting vector populations. In spite of some highly successful control methods and decline in vector densities, disease incidence and prevalence, however, were not declining sufficiently, suggesting ongoing transmission elsewhere. These residual transmission foci were largely found to occur in the peri-domestic space and caused by various factors: intensive and longtime exposure to insecticides had led to selection for mosquitoes that preferentially fed outdoors (Moiroux *et al.* 2012, Russell *et al.* 2011, Sougoufara *et al.* 2014). Also, it was found that fractions of mosquitoes were naturally feeding outdoors, but had been overlooked or 'missed' in the historical monitoring and surveillance programmes which focused primarily on indoor biting and resting mosquitoes (Killeen 2014, Monroe *et al.* 2020, Riehle *et al.* 2011). To tackle outdoor populations, push-pull systems as well as toxic sugar baits are under development (Chapter 6). Another tool, with already proven epidemiological effectiveness, is the use of odour-baited traps that intercept and kill mosquitoes outdoors before they have had a chance to bite (Chapter 7). It has furthermore been realised that killing the vectors in their breeding sites may be more effective than focusing on adult vectors, as this prevents the building up of adult populations. For malaria, recent larval control methods have proven to be effective (Chapter 8). Many dengue control programmes include larval control, but it is unclear if these have led to significant epidemiological outcomes and hence, it is recommended to include adult control (Chapter 4).

From these encouraging developments it can be concluded that novel and effective vector-control tools are in an advanced stage of development, to be added to the toolbox of integrated vector management, with a lower dependence on insecticides and leading to higher sustainability.

Genetic tools for vector-borne disease control have in the last decade received much attention as they may lead to ways in vector control that do not require insecticides, with gene drive systems being among the most promising technologies for future vector control (Hammond *et al.* 2016, Wang *et al.* 2017). As these tools need to pass ethical and regulatory approval before they can be tested in the field (James *et al.* 2018), they have not been included in this volume.

Intersectoral collaboration and community engagement

The heavy burden on human health caused by vector-borne diseases has historically been well recognised and in efforts to lower this burden, disease-endemic countries, often with assistance from WHO, numerous international organisations and NGOs, run government-led control programmes with the aim to reduce the burden of disease caused by VBDs. In most countries the Ministry of Health (MoH) has a central role in initiation, decision making and execution of these programmes. This approach often leads to a vertical programme with little or no involvement of other government ministries, national and international organisations or the private sector (Herdiana *et al.* 2018). Allocation of funds independently to the partners for implementing vector control further augments the success of intersector collaboration. To improve the effectiveness of VBD prevention and control, collaboration between the health and non-health sectors is strongly encouraged (Chapters 9, 10 and 11). For example, in urban centres, water management cannot be arranged without interaction with the Ministry of Public Works or Housing. In rural areas, farming systems can, unwittingly, contribute to high VBD risk (Jaleta *et al.* 2013, Mutero *et al.* 2004), and farmers, (water)engineers and plant production experts need to be involved in redesigning farming systems to reduce this risk. Deforestation and/or reforestation can also affect populations of arthropod vectors (Lima *et al.* 2017, Nava *et al.* 2017), and collaboration between the MoH and the Ministry of the Environment can lead to different approaches for risk reduction. With the growing awareness of the importance of community engagement (see below), organisations and departments that engage in the social aspects of public health are increasingly involved in the rolling out of VBD control. A clear example of this involvement is the use of insecticide-treated bed nets for malaria control: the success of this programme depends strongly on social workers or village health workers who engage with community members and householders to explain the importance of bed net use (Bashar *et al.* 2012, Ingabire *et al.* 2015). For these reasons, the GVCR has placed intersectoral collaboration as the first pillar supporting the response (WHO 2017). More and intensified collaboration between the various sectors associated with VBD risk and mosquito production is required for more effective prevention and control of VBDs (Chapter 10).

As communities are the primary stakeholders in a VBD control programme, members of the community should be involved in the design of an intervention whether with classic, well-known methods as well as when novel tools will be used. In this way acceptance for and compliance with the measures being taken can be assured. Whereas clinical care, drug treatment and vaccination are done by well-trained and expert staff and which are primary health care interventions, where community members cannot be actively involved, this is different when vector control activities are required. Vector control requires action in the field: mosquito surveillance, house improvement, bed net distribution, *Bti* treatment of water bodies and setting up mosquito traps are among the activities where members of the local community should be involved (Chapters 9 and 11).

Chapter 8 demonstrated that, besides innovations in new vector control tools, also novel approaches for involving communities in vector control (e.g. the Farmer Field School, Open Space, and citizen science) have been developed and evaluated recently. A toolbox of community-engagement strategies thus exists and can be used to effectively integrate new tools into ongoing vector control programmes (Wilson *et al.* 2019). Which approach works best will of course be context and culture dependent, and this will require extensive collaborations across multiple sectors.

Research and development are expected to contribute to more sustainable, effective VBD control tools (GVCR2017). Novel tools should be tested solidly and having passed the appropriate regulatory procedures before they can be applied in a disease control programme (James *et al.* 2018). When innovative approaches involving genetic modification, gene drive or transfection are proposed, these can meet with strong resistance from the community and even prevent the application of these technologies. Resistance by communities often results from a lack of understanding of the mechanisms of the proposed intervention, such that communities perceive that the interventions lead to increased health risks (Ernst *et al.* 2015, WHO 2020, Wilke *et al.* 2018). Early involvement of target communities is therefore essential to ensure support and prevent long delays in the approval of such tools (Chapter 12).

Conference workshop

The conference not only discussed the various GVCR topics with experts, but also participated actively in an interactive workshop to provide new ideas and suggestions how the GVCR could be further strengthened and become a widely accepted strategy for integrated vector control. The workshop was divided in eight themes, and each group considered the Goals, Current Challenges, Potential solutions and Value for stakeholders for the theme they had been assigned. The outcome of the workshop is presented in the Appendix to this book.

Conclusions

The various chapters in this volume of ECDV provide state-of-the-art, in-depth information to advance the actions laid out in the Global Vector Control Response. In this book mosquito-borne diseases and their vectors are dominant, with focus on malaria and dengue. It is realised that a large number of other VBDs are vectored by arthropods such as flies, fleas, gnats, lice, assassin bugs and ticks. We hope that the strategies for VBD control as described in this book will be used for integration across multiple diseases as outlined by Golding *et al.* (2015). As vector-borne diseases will not disappear on their own, the GVCR provides a novel and practical pathway towards reduction of the heavy burden these diseases inflict on human societies.

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