Review

CellPress

Framework for rapid assessment and adoption of new vector control tools

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Evidence-informed health policy making is reliant on systematic access to, and appraisal of, the best available research evidence. This review suggests a strategy to improve the speed at which evidence is gathered on new vector control tools (VCTs) using a framework based on measurements of the vectorial capacity of an insect population to transmit disease. We explore links between indicators of VCT efficacy measurable in small-scale experiments that are relevant to entomological and epidemiological parameters measurable only in large-scale proof-of-concept randomised control trials (RCTs). We hypothesise that once RCTs establish links between entomological and epidemiological indicators then rapid evaluation of new products within the same product category may be conducted through smaller scale experiments without repetition of lengthy and expensive RCTs.

Faster market introduction of new vector control tools

The ultimate goal of the Innovative Vector Control Consortium (IVCC) is to reduce transmission of mosquito-borne pathogens around the home through improved control of adult household vectors with innovative tools [1]. The development of new vector control tools (VCTs) and their endorsement by the WHO requires sufficient high quality research data for evidence-informed health policy making. The long lasting insecticidal net (LLIN) took 25 years from first evaluations [2] to universal coverage [3]. Although the time between registration of the insecticide dichlorodiphenyltrichloroethane (DDT) in 1939 and ubiquitous application as an indoor residual spray (IRS) during the Global Malaria Eradication Programme (GMEP, 1955–1969) [4] was much shorter, the quality of data on the epidemiological impact of IRS falls short of modern standards [5]. Although epidemiological data on insecticidal nets were more robust [6], it took substantial time to be accrued. Historically, evidence was consolidated through *ad hoc* mechanisms, although recently the WHO has established a Vector Control Advisory Group (VCAG) on New Tools (http://www.who.int/neglected_diseases/vector_ecology/VCAG/en/index.html) to serve as an advisory body to the WHO Malaria Policy Advisory Committee (MPAC) (http://www.who.int/malaria/mpac/en/) on new forms of vector control for malaria and other vector-borne diseases. The VCAG will review and assess the public health value, 'proof of principle' (epidemiological impact) of new VCT approaches and technologies, and make recommendations on their use for vector control. It is hoped that this will improve the speed at which recommendations will be achieved through making unambiguous the minimum dossier of evidence required for approval. By minimising lag-time between product concept and market introduction, new VCTs will have maximum disease impact. Rapid collection of high-quality datasets needed for policy approval by the VCAG will allow maximum-patented product time in the marketplace, encouraging greater investment from industry innovators.

With this in mind, we have constructed a framework of evidence generation for new VCTs, to help manufacturers, researchers, policy makers, and other stakeholders identify the endpoints measured, and the type of evidence required at each stage of product evaluation. We propose that synthesis of multiple datasets with standard reported outcomes from many sites will allow individual researchers to contribute to the much larger picture in the research field

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Glossary

Active case detection (ACD): the detection of malaria infections at community and household level in population groups that are considered to be at high risk. It can be conducted as fever screening followed by parasitological examination of all febrile patients or as parasitological examination of the target population without prior fever screening.
Biopesticides: pesticides (chemicals used to kill unwanted organisms such as insects) that are derived from plants, microbes, or other natural materials.
Cluster randomised trial (CRT): a type of randomised controlled trial in which groups of subjects (as opposed to individual subjects) are randomised.
Entomological end points: outputs measured by entomological studies, for instance, mosquito density, feeding inhibition; they may be predictors of epidemiological impact.
Experimental huts: the main semi-field means of evaluating vector control tools used in indoor interventions against mosquitoes in the field. Experimental huts are standardised structures representative of local housing that have been modified to make the measurement of entomological endpoints more standardised.
Human-landing catches (HLCs): the gold standard method to monitor exposure of the human population to vector populations, which involves individuals sitting with their legs exposed and collecting vectors that come to feed on them.
Indoor residual spraying (IRS): when mosquitoes and other insects rest in houses it is possible to kill them by spraying the walls with a residual (long-lasting) insecticide. Mosquitoes resting on sprayed walls come into contact with insecticide through their feet and are killed. Some insecticides irritate mosquitoes and cause them to leave houses.
Long-lasting insecticidal nets (LLINs): mosquito nets made from strong fibres impregnated with a quick-acting pyrethroid insecticide, which irritates or kills mosquitoes on contact, preventing them from finding openings for a period of up to 3 years.
Minimum efficacy threshold: the minimum impact of a molecule, prototype, or strategy measured by entomological endpoints that is required for decision making as to whether further investment in development and testing of that molecule, prototype, or strategy is warranted.
Passive case detection (PCD): detection of malaria cases among patients who on their own initiative went to a health post for treatment, usually for febrile disease.
Phased testing pathway: a step-wise testing procedure, involving stop/go decisions, for the evaluation of vector control products.
Randomised control trial (RCT): a study in which a number of people are randomly assigned to two (or more) groups to evaluate a specific intervention, treatment, device, or strategy with one group (experimental) randomly assigned to the intervention and the other (control group) receiving an alternative intervention or placebo.
Sample size calculation: the number of individuals that need to be enrolled in a study to have sufficient statistical likelihood of detecting a specified association if it is real.
Semi-field: enclosed environments, ideally situated within the natural ecosystem of a target disease vector and exposed to ambient environmental conditions, in which all features necessary for its life cycle completion are present that reflect end-user conditions.
Stop–go criteria: predefined minimum efficacy threshold on which decisions are based in dual-choice decision patterns that define whether further investment in exploring that tool or strategy is warranted.
Target product profile (TPP): is a dynamic summary that defines the ideal end goals for a product and guides the development process. It is open to change as knowledge of the product increases. Usually, the TPP briefly summarises the specific studies (both planned and completed) that will supply the evidence for each conclusion about that product.
Vector control tool (VCT): intervention that reduces the ability of an insect vector to transmit disease.
Vectorial capacity: the daily rate at which future inoculations of a parasite arise from a currently infective case, provided that all female vectors biting that case become infected.

by collaborating towards the generation of solid, accurate, and timely information needed for evidence-based decision making.

Capitalising on recent achievements, and risk mitigation

The development of new tools to combat vector-borne diseases is urgently needed to take advantage of recent reductions in vector-borne disease morbidity [3] with the goal of control of all disease vectors, even those not responsive to conventional tools [7], including vectors of neglected and emerging vector-borne diseases in a rapidly changing global situation [8]. Although the GMEP demonstrated that no single strategy can be applicable everywhere [9], we still rely almost entirely on applications of insecticides targeting vectors that feed and rest indoors at night, that is, IRS and LLINs, with high reliance on pyrethroid insecticides that are threatened by insecticide resistance [10].

Work is underway to counteract this bottleneck through preservation and improvement of existing insecticide-based interventions by: (i) reformulation and new-use applications of existing agricultural insecticides [11] and (ii) development and commercialisation of new active ingredients including biopesticides (see Glossary) with new modes of action (MOA) [12]. Efforts to exploit vector ecologies [13] include new VCTs targeted at different life stages including outdoor feeding [14] and resting [15], sugar feeding [16], using lures that mimic hosts [17] or oviposition sites [18], or even modifying mating success [19] in order to lower vectorial capacity (defined as the daily rate at which future inoculations arise from a currently infective case, provided that all female flies biting that case become infected; Box 1). Because an individual VCT may have different efficacy against diverse species with varying ecologies, data collection for product evaluation should be guided by MOA, environmental, and biological considerations [20].

Validation of new vector control tools

The ability of new product categories to achieve one or more primary effects (Table 1) is most efficiently determined by evaluations in a phased testing pathway (Figure 1) from small-scale laboratory assays (Phase I), which increase in scale, cost, and how much they reflect the real world, to operational research where a tool is delivered and used operationally while its effect on disease and user acceptability is monitored (Phase IV). To provide insights of more immediate relevance to disease control, however, a paradigm shift is necessary with model systems playing a complimentary role to research focused on natural systems and conditions [21].

Initial tests are economical and allow for high-throughput screening of many molecules, prototypes, or strategies.

Box 1. Vectorial capacity

$$C = \frac{ma^2 b\, p^n}{-\log_e p}$$

C	New infections disseminated from a single infectious human
m	Number of vectors per person
a	The probability that a vector feeds on a host (host preference)
b	Vector competence
ma	The number of bites per person per day
p	Probability of a vector surviving 1 day
n	The incubation period of the parasite
p^n	Proportion of mosquitoes surviving the incubation period of the parasite
$-\log_e p$	Duration of the vector's life after surviving parasite incubation