Author's response to reviews

Title: Integrating vector control across diseases

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Version: 3
Date: 4 June 2015

Author's response to reviews: see over
Covering letter for the revised article: “Integrating vector control across diseases”

15th May 2015

Dear Mr Recchioni,

Many thanks for your email of the 14th May 2015 and your invitation to revise our manuscript.

We found the comments from both referees to be helpful and have made a number of revisions in the accompanying document. We provide below a point-by-point response to the editorial and reviewer comments.

We feel that the revised manuscript is significantly improved and represents a balanced and evidence-based argument which would be well suited as an Opinion piece in BMC Medicine.

We look forward to hearing from you soon.

Yours sincerely,

Nick Golding

on behalf of all the authors
Editorial comments

“please provide a paragraph with the abbreviations used in the manuscript.”

This has been added.

“We thought this article would be better suited as an Opinion piece, rather than a Debate. If you agree with this, we can change the article type on your behalf.”

We agree, and have changed the article type to an Opinion during resubmission.

Referee 1

“Overall, this is an outstanding, invaluable and delightfully brief little piece that I recommend highly for publication.”

Thank you!

“Some minor suggestions for discretionary revisions:
1. It would be useful if it is possible to provide even an approximate estimate of the proportion of disease burden accounted for by VBDs in the abstract.”

This is slightly complicated as the Global Burden of Disease project does not break numbers down by VBDs or by communicable diseases as distinct groups. The closest approximation to this is the burden of 10 named VBDs, divided by the burden of all communicable, maternal and nutritional disorders, which gives a proportion of 0.11. Since this represents a lower bound on the true proportion, we have amended the abstract to read as follows:

“Vector-borne diseases cause a significant proportion of the overall burden of disease across the globe, accounting for over 10% of the burden of infectious disease.”

2. While the conclusion that half the world’s population is exposed to at least two VBDs is powerful and merits a place in the abstract, a more relevant and useful indicator that should also be included in the abstract is the proportion exposed to two or more VBDs for which at least one common intervention might be appropriate.”

We have calculated this statistic and added it to the main text, 90% of those living in areas of disease overlap also live in areas where an intervention is shared across pairs of diseases. Whilst this is a useful number to provide in the manuscript, we feel that it is important to appropriately caveat this figure, since it might be misinterpreted as the fraction of cases for which integrated control would be effective. We therefore feel that it would be unwise to include this figure in the abstract, since the necessary caveats would be out of place there.

The relevant part of the Summary section is now followed by a caveat on this figure and reads:

“Of the 3.9 billion people living in areas at risk from at least two of the seven VBDs considered here, 3.5 billion (90%) inhabit regions where two or more of these diseases are likely to be susceptible to the same intervention. These global maps indicate where diseases are likely to overlap in their distributions, but diseases may not overlap at finer scales if their vectors have distinct environmental requirements.”

We have also added text to the abstract and main text reporting the proportion of the global population at risk of at least one vector-borne disease since we expect that this will be of interest to readers.
In the abstract:

“Such an analysis shows that over 80% of the global population live in regions of the world at risk from one vector-borne disease, and more than half the world’s population live in areas where at least two different vector-borne diseases pose a threat to health.”

and in the Background section:

“Nearly 82% of the global population live in areas at risk from one vector-borne disease with over half living in areas at risk of two or more of the major vector-borne diseases (see SI).”

“3. The point about integrated disease control including vaccines and drugs is great but seems to miss the opportunity to mention the example of the commonplace practice of bed net, or bed net subsidy voucher distribution through routine ANC and EPI contacts with pregnant women and young children, respectively.”

We have added the following sentence and appropriate references in the main text, after discussion of EPI (citation given below):

“Indeed these vaccine distribution networks and other public health programmes have already been used as a cost-effective and equitable method for distributing LLIN [16, 17].”

“4. An additional reference that might be useful has been published since this was submitted: PLoS Neglected Tropical Diseases 9:e0003597 (DOI: 10.1371/journal.pntd.0003597).”

Thank you for the recommendation. This article by Picado and colleagues details the frustrating lack of rigour in many trials of vector control interventions against leishmaniasis. This mirrors our feelings regarding much of the research for vector control interventions (with the arguable exception of malaria), and is the focus of another recently published article by some of the authors of this manuscript ([3] below, cited as 19 in the main text). We have therefore cited both of these articles after a sentence already in the manuscript:

“Robust experimental studies of the effectiveness of vector control methods are unfortunately scarce for most diseases other than malaria [18, 19].”

Referee 2

“Although the question posed by Golding et al (“Integrating vector control across diseases”) is not new, it is newly defined in this succinct and well illustrated, terse manuscript. The main point is that many of the major vector borne diseases overlap so much in geographic distribution that common methods could and should be applied to both. This is an interesting idea but carries important caveats that the authors need to consider carefully and incorporate into their ideas, and this manuscript. Figures are excellent and good maps based on rigorous quantitative analyses (vs hand drawn conjecture) are always useful. The authors need to consider at least four matters that can rightly be assigned to the category of major compulsory revisions. These might best be thought of as caveats to their central thesis.”

Thank you for your positive and constructive comments. We agree with the main caveats raised and have increased our emphasis on them by re-wording and adding text where appropriate. We address each of these points below.

“First, there are already are common methods but these are not based on single applications for multiple purposes but rather multiple applications for multiple purposes. It is rote insecticide application to habitats where adult or transmitting stages of the arthropods of insects dwell, typically in close proximity to where humans live, e.g. houses. By integrating, the authors mean
that a single application of a method or approach could have multiple outcomes. That is not quite the same as integrating further upstream at the industry level, where a single insecticide formulation is developed for multiple uses.”

The term ‘integration’ has been used to refer to a wide range of different aspects of vector control (see for example Figure 1 in [4]) including integration of vector control programmes with other sectors (such as industry) and the use of multiple interventions. Whilst each of these components is important, and an approach which includes all of them is advisable, for clarity this manuscript deals exclusively with the integration of vector control programmes to simultaneously target multiple diseases. We discuss the Integrated Vector Management framework at the end of the Background section before outlining the subject of this paper in the Discussion:

“Simultaneous deployment of multiple vector control methods can reduce disease transmission to far lower levels than those achieved using a single intervention and help slow the development of insecticide resistance thereby providing cost-effective and sustainable reductions in disease burden [11]. The simultaneous use of multiple methods is now the preferred vector control strategy and forms a cornerstone of integrated vector management - a best-practice framework for sustainable and cost effective vector control [12].”

We feel that it would be inappropriate and distracting to the reader to elaborate further on the integration of control programmes with industry or of the use of multiple interventions.

We do however agree that formulation of insecticides and insecticide-treated products which are effective for multiple species (and multiple application types) would enhance the joined-up vector control programmes we advocate. We have therefore added the following sentence to the section on larval control:

“The development of larval control products that are effective against multiple vectors could enhance these cost savings.”

“2. Improving housing and reducing poverty simultaneously could go a long way towards resolving all of these problems but they are only mentioned in a cursory and non-integrated way here. Poverty appears to be one of the key independent variables that informs the maps and indeed poverty likely explains the overlap of the various disease systems under discussion here, along with the habitat requirements and vector distributions. When we improve housing, we have in effect reduced poverty because an accepted measure of poverty is the quality and standard of housing. Improved housing necessarily includes insect proofing, ventilation, and the like. I am fairly certain that this is recognized as integrated, even beyond vector borne diseases to other matters in which housing is important to human health and well being.”

As above, we are wary of distracting readers by discussing integration of vector control with other sectors in this manuscript, such as the integration of vector control with other development activities as suggested here. However, we agree with the reviewer that house improvement is an important aspect of reducing many vector borne diseases and should therefore be referred to explicitly.

Whilst there is strong, published evidence for the effectiveness of house improvement, the varying definitions of ‘improvement’ (e.g. repairing walls for Chagas control vs. screening windows and roof spaces for malaria control) mean that we were unable to consider house improvement as a single intervention in our analysis. Instead we focussed on specific, standardised interventions such as the use of insecticide-treated screens and curtains.

We have however added brief discussion of the potential to carry out these various effective improvements simultaneously through broader programme integration, with the following text in the Discussion:

“For many vector-borne diseases, improving the quality of housing can be an effective method of disease control [39, 40]. Whilst house improvement can mean different things in different epidemiological situations (such as screening roof spaces for malaria control [41, 42] versus repairing plaster for Chagas disease [43, 44]).
integrated programmes that carry out multiple improvements could be an effective approach for jointly controlling multiple diseases.”

“3. The authors show convincingly that there is broad geographic overlap amongst many vector borne diseases, and thus the integrated control approach seems reasonable. But is it universally true at the microgeographic or local level? That is less likely. For example, dengue is typically an urban problem of congested human living conditions, whereas malaria is typically a rural problem, although admittedly there will be some overlap in some places. Thus, a map at the global scale as shown here might suggest broad overlap but locally it is not true. Further, day active dengue vectors are not going to come into contact with insecticide when humans (the natural attractant of such lethal baited night traps) are not sleeping under them during the day. Thus there are both spatial and temporal issues with the concept of integration, at least for these two disease systems (which appear to be of major concern in the article).”

We agree with the important point made by the reviewer regarding spatial scales: diseases may overlap to a lesser extent at local scales, and these local differences will hinder the cross-disease effectiveness of specific control methods. We had already provided some text to caveat this text in the summary:

“We agree with the important point made by the reviewer regarding spatial scales: diseases may overlap to a lesser extent at local scales, and these local differences will hinder the cross-disease effectiveness of specific control methods. We had already provided some text to caveat this text in the summary:

“Large-scale cross-disease vector control programmes would need to be adapted to local variation in disease epidemiology in order to best target the specific combination of diseases present.”

We have now edited the text to greater emphasise this key issue, and the evidence needed to overcome in a practical implementation of cross-disease vector control. The relevant section now reads (with additions in boldface):

“These global maps indicate where diseases are likely to overlap in their distributions, but diseases may not overlap at finer scales if their vectors have distinct environmental requirements. Large-scale cross-disease vector control programmes would need to be adapted to local-scale variation in order to best target the specific combination of diseases present in at-risk communities. Planning a large-scale programme of integrated vector control will therefore require more detailed knowledge of the spatial distribution of each disease, as well as their susceptibility to available vector control methods. The operational effectiveness of multi-disease vector control programmes must then be evaluated in the field.

Whilst these hurdles mean that cross-disease integration of vector control may not be feasible in all of these areas, the scale of the potential public health gains is sufficiently large to warrant serious attention and future research.”

In addition, we have modified the text at the start of the discussion to emphasise this caveat, and to shift the emphasis of the article towards integration at other levels of vector control programmes, changing:

“…targeting multiple diseases using the same interventions and infrastructure…”

to:

“…targeting multiple diseases using the same vector control programme infrastructure and possibly the same interventions …”

With specific reference to the efficacy of nets and screens against the *Aedes* vectors of dengue; whilst the differences in behaviour between these species and the *Anopheles* vectors of malaria imply that these interventions would likely be ineffective against the former, we have cited a number of published studies indicating that they can in fact have a controlling effect (see [2] for a systematic review covering this topic and [5–8] specifically). The reason for this may be the fact that endophilic *Aedes aegypti* will rest on these insecticide-treated surfaces during the day even without human ‘bait’, reducing vector populations.

More generally, our assessment of the effectiveness of all the considered interventions against each of these diseases (presented in Figure 2) was based entirely on published, peer-reviewed evidence which is detailed in the SI as well as in the specific examples cited in the main text.
“4. Fourth and lastly, attacks against the immature stages cannot be typically viewed as common in context. One could easily imagine, for example, a setting where leishmaniasis, dengue, Bancroftian filariasis borne by Culex, and malaria are all co-endemic yet the larval habitats of the sand flies or mosquitoes associated with these habitats are very different and non-overlapping, and further the insecticides, formulations, and cultural approaches to habitat (source) reduction, would all require separate and independent actions. Even some of the insecticidal formulations would have to be different (example: highly organically polluted Culex larval habitats require different types of insecticides and formulations than do cleaner and perhaps even potable water of Aedes aegypti larval habitats).”

We already dedicate a paragraph to the fact that integrating larval control across diseases will likely not be trivial, but that many operational costs may be shared by operatives targeting multiple habitat types on their rounds:

“Whilst insecticide treatment of nets, screens and walls are implemented at the household level, larval source management must be targeted at the breeding sites of the specific vector species of interest, necessitating different procedures for different vectors. For example, application of larvicides is appropriate for controlling Anopheles [32] whereas polystyrene beads may be more effective for the urban Culex vectors of lymphatic filariasis [33] and the removal or larvicidal treatment of water containers is more useful for the Aedes vectors of dengue and yellow fever [34, 36]. Nevertheless, there are many situations where Anopheles and Culex mosquitoes share the same habitat [37, 38], and control operatives could reasonably be tasked to treat or remove the distinct larval habitats of several key species in a single programme, sharing many of the costs of control. The development of larval control products that are effective against multiple vectors could enhance these cost savings. Evaluating the practical feasibility and quantifying the cost-effectiveness of such cross-disease integration of larval source management should be considered in detail in future studies.

“I have a fear that an article like this will mislead physicians and others in authority in public health, such as funders and policy makers, that the solutions to the vector borne disease problems are simpler than they really are. Unfortunately they are complex and often because of the local conditions which are not reflected in the broad-scale maps here. One could make the equally strong but less economically appealing argument that customized and highly focused interventions, developed for each case and even each local condition, are what are required instead. It is here that the analogy with the integrated vaccine strategy falls apart. Nevertheless I found this article appealing, enjoyed reading it, and viewing the interesting maps.”

The arguments that we present in this manuscript, backed up by published evidence, are intended to stimulate further debate and operational research into the integration of vector control programmes to target multiple diseases. Throughout the manuscript we have highlighted potential pitfalls and areas where evidence is lacking and call for further operational research in this area. We have added to these caveats and further improved the manuscript in response to the comments from both authors.

We therefore feel that the manuscript is a fair and balanced representation of the arguments in favour of further cross-disease integration of vector control and would therefore be appropriate as an Opinion article in BMC medicine.

References


