

Roll Back Malaria Vector Control Working Group (RBM VCWG)
12th Annual Meeting, 8-10th February 2017
Moevenpick Hotel, Rue de Pre Bois 20, 1215 Geneva

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2nd IRS IRM Priorities Work Stream meeting
08:30-11:30, Thursday 9th February 2017
Co-leaders: Mark Hoppé & Dereje Dengela

Welcome and introduction – Mark Hoppé, Syngenta

Mark Hoppé opened the meeting and passed on apologies for absence from Dereje Dengela.

Spatiotemporal patterns of Insecticide Resistance – Mike Coleman, Liverpool School of Tropical Medicine and Malaria Atlas Project

The aim of MAP-IR is to produce regional risk maps of insecticide resistance; investigate drivers of selection and generate estimates of variation in resistance. Key findings of this exercise included that observation that clusters of resistance may correlate better to clusters of entomologists rather than where resistance is occurring. Publication bias was also evident, with large reporting on KDR a few years ago, but very little today despite the fact that KDR is still present in mosquito populations. Previous resistance data was stratified by species, however it was suggested that different categories such as behavioural profiles be used instead. Further work is planned to attempt to make data available and usable, and also to generate more data for *Aedes aegypti*.

Discussion

- It was asked whether country offices could be approached to see if some of the missing data does already exist. Some country office data have already been used, although there is some resistance to data sharing.
- It was asked whether the standard IR tests using 3-5 day old mosquitoes is appropriate, given these are unable to transmit malaria. Resistance testing protocols have continually changed (which has made the modelling quite complicated), but this project is not aiming to drive programme change.
- A comment was made that all data should be submitted to the WHO offices, even if it is being collected primarily for research. This enables data to be collated. It was remarked that MAP-IR has received data from offices, and has cleaned and geo-referenced it before feeding back.

Update on the Worldwide Insecticide resistance Network – Florence Fouque, WHO The Special Programme for Research and Training in Tropical Diseases

Worldwide Insecticide Resistance Network (WIN) was set up in 2015 to (1) identify areas where resistance challenges vector control and where resistance is under-reported, (2) fill knowledge gaps on insecticide resistance in arbovirus vectors through commissioned reviews, and participate to the discussion on research priorities, and (3) assist national authorities in decision-making for insecticide resistance management and deployment of alternative control tools. A workshop was held in Brazil

in December 2016 attracting 160 participants from 30 countries, and also recorded 73,000 live web viewings. The first commissioned review on the “contemporary status of insecticide resistance in the major *Aedes* vectors of arboviruses infecting humans” is planned to be published in June 2017. Other reviews are planned on (1) global trends in the use of public health and agriculture pesticides and impact on insecticide resistance in mosquito vectors, (2) insecticide resistance management strategies applicable to mosquito vectors, (3) alternative methods for the control of mosquito vectors, and (4) defining the global framework for the development of an international consortium for monitoring and management of insecticide resistance in mosquito vectors.

Discussion

- It was asked how can WHO engage the private pest control sector, as this sector carry out a lot of *Aedes* control. Although it is not a TDR task to engage with the private sector, WIN has already successfully reached out to these groups as evidenced by the workshop in Brazil. It was remarked that WIN has not yet engaged with the agricultural sector.

Implications of insecticide resistance for malaria vector control: outcomes from a WHO-coordinated multi-country evaluation – Tessa Knox, GMP, WHO

There is a lack of evidence of a link between insecticide resistance and any reduction in the effectiveness of malaria interventions (ITNs and IRS). Studies examining this question were completed in Africa, and are ongoing in India. More information on the methods is available at Kleinschmidt et al. *Malaria Journal*. 2015; 14:282. The findings suggest those using nets had a reduced malaria prevalence and clinical incidence of malaria, but there was no evidence of a relationship with insecticide resistance. In Sudan, there was no observed benefit to sleeping under a LLIN, but a switch from pyrethroid IRS to a non-pyrethroid spray was associated with a halving of the risk of malaria. Limitations of the work include the standard resistance indicator (WHO tubes); a lack of information on species composition and behaviour; and typical rather than worst-case background resistance levels. The implications of this research are that universal coverage with LLINs is essential; but even with high coverage transmission is likely to continue and new tools and strategies are required. Countries are urged to develop IR management plans. Further information is available from full presentations from 65th ASTMH in Atlanta: videos on MESA knowledge hub.

Discussion

- It was stressed that there is no room for complacency, nets still appear to work here, but none of the sites had really high levels of resistance, and we have no data about what would happen in this setting.

Exploring the epidemiological impact of insecticide resistance – Matt Thomas, Penn State University

A series of experiments was presented exploring the effect of normal exposure to a LLIN on resistant mosquitoes. Free flight tests were carried out with a person under a LLIN, which showed very high (80-90%) mortality from a 1 hour exposure, despite cone tests on these strains giving very low levels of mortality. It was also found that sub-lethal insecticide exposure reduced feeding by up to half, and also reduced response to the host for at least an hour. Field studies with strains showing 1700x resistance, found increased exit, mortality and a reduction in blood-feeding compared to untreated nets. When these findings are incorporated into a plot of mortality vs. feeding across different levels of ITN coverage, it suggests that with 80% coverage, and only 40% mortality, a reduction in malaria transmission is still possible, with feeding impairment, 20% mortality can still result in control. This may explain why insecticide resistance has not transferred directly into a detectable change in malaria transmission. It should be noted that the impact of resistance is very sensitive to coverage,

and as resistance increases, these findings suggest control failure will accelerate, possibly reach a tipping point, particularly in areas of low LLIN coverage.

Evidence based IRM – John Vontas, Agricultural University of Athens & Institute Molecular Biology Biotechnology/FORTH

A number of parallels between insecticide resistance in agricultural and public health were highlighted. Resistance molecular assays are sophisticated and a full suite can be very expensive (\$15-20 per mosquito), however they provide potentially valuable information. So although there is a temptation to rely solely on bioassays, molecular tools can be highly useful if used in conjunction with the bioassays. Molecular diagnostics can detect underlying mechanisms: an important evidence for IRM. The choice between carrying out molecular assays on individuals or pooled samples was addressed and it was reported that quantitative assays on pooled mosquitoes can give operationally relevant data.

The impact of IRS on malaria control in India – RS Sharma, former Scientist/Additional Director at HOD, Centre for Medical Entomology & Vector management, India

A history of IRS India was given, starting in 1953. It became a responsive programme following spike in malaria 1976. IRS is largely carried out in rural areas only (66 million people), which does not target the urban vector *An. stephensi*. Activities also include insecticide resistance status monitoring for many species for three classes of insecticides. This is used to inform the IRS microplan, to rotate insecticides to areas of susceptibility. Malaria is declining in all districts from 2006 to 2013.

Discussion

- It was reported that many African IRS projects have made progress using GIS (e.g. MSPRAY). It was reported that India is also following this, with for example, volunteer health workers giving mobile updates on malaria cases.

NgenIRS project update – David McGuire, IVCC

The NgenIRS project aims to increase uptake of third generation IRS, by increasing demand through short term co-payment (2/3 cost); improving market forecast and decreasing market volatility. It is a global partnership between the manufacturers (at present Syngenta only, but at least two more expected) and 12 African countries. The number of countries taking part tripled between 2016 and 2017. \$5.8 million spent in co-payment, allowing an extra 2 million people to be protected by 3GIRS. In some countries, the co-payment allowed conversion from carbamates to 3GIRS, and others it resulted in expansion of IRS. All targets were met or exceeded. Challenges: 3GIRS is much more expensive, and there is a concern of resistance especially where Actellic has been used for 5+ years. Only currently 1 product and 1 partner, timing of expansion is uncertain. At present there is a larger demand for the project than can be afforded with insufficient funds for co-payment. In 2017, an additional 6.5 million people will be protected compared to 2016 which requires \$11.3 million in co-payments.

IRM MOOC – proposal for the creation of an IRM training course – Mark Hoppé, Syngenta

There have been repeated calls for more training on IRM, right from the top down to practitioners. GPIRM is the main resource at present. However, IRM is an applied science and there is need to translate theory into practice. The target audience would be very large and geographically disperse, from net distributors through to decision makers, logisticians, financiers, monitors and students taking these roles in the future. An online approach would be suitable. MOOCs (Massive Open Online Courses) aim to deliver education to an unlimited audience and provide educational opportunity to those without formal education. Last year 58 million people attended over 7000 MOOCs. The proposal is to set up an IRM MOOC, open and delivered free, lasting 10-12 hours, 3-4 weeks,

delivered in an engaging multi-media approach, with facility for interaction between participants in a moderated forum. Learning outcomes would be an understanding on IRM theory and practice. It is hoped that leading experts will be involved and the course will be endorsed by the wider vector control community (although no endorsement by industry or one academic organisation). The FutureLearn platform is likely to be used. Once produced, the material can be used probably for 3-4 years before a major revision is used. The next steps will be to first identify a core team, then a steering committee to ensure the scientific integrity of the course. Resources will also need to be identified, including funding. A syllabus will need to be generated, probably using GPIRM as a basis. Then a producer will need to be appointed, the course produced, approved and delivered. Mark Hoppé requested confirmation from the work stream on the willingness of key institutes to endorse and promote the MOOC (particularly to key target audience), availability of funding; and any potential legal or intellectual property issues to be flagged.

Discussion

- It was noted that the LSTM serious game has many overlaps with this, and it may be possible to tie in, maybe by encouraging students to play at the beginning and end of the MOOC.
- It was asked if certification and testing was part of the platform. The FutureLearn platform does allow certification, but students might have to pay for this. Although it is hoped that the target audience would be provided with a certificate of course completion free of charge.
- It was asked what might be available in French, Spanish or Portuguese, and noted that Coursera offer different language courses. Coursera were investigated as a potential platform, but were rejected as they have a much more commercial attitude and students would have to pay for the MOOC.
- Janet Hemmingway offered help and also suggested refinement through a small group first before large scale release.

Open Discussion/idea generation, “how can we practically implement the GPIRM?” - All

- Idea of an IRS newsletter was put forward, where presentations, publications could be highlighted to the rest of the work stream.
- A query was made about the impact of aged nets on insecticide resistance. That has not been explored formally yet, but it is possible that you would move more quickly to control failure, so epidemiological consequences might increase with aging. So it is possible that a more frequent switch may be required. It was suggested that wash resistance data may be an interesting addition to the model.
- It was asked whether Matt Thomas’s results could be extrapolated to IRS. For example, in monitoring programmes, a switch is made at a 90% threshold, should that be reduced? It was acknowledged that this is a very important discussion to have, but at present we don’t have a full understanding of what the best strategy might be. With IRS, the main difference is that there is a blood feed followed by exposure, rather than exposure followed by a blood feed. So you would expect much less effect on feeding inhibition from IRS, therefore IRS is likely to be more sensitive to resistance.
- It was remarked that resistance management should start before resistance occurs, the 1000 genomes project, which has now sequenced ca. 3000 Anopheles, shows that resistance mechanisms may already be present in *An. gambiae* populations. So the strategy should be to get multiple modes of action out at once, rather than in sequence.

Feedback from the work stream meeting and discussions

Mark Hoppe gave apologies for absence from Dereje Dengela, and presented a summary of key points and actions. Presentations were given on: spatio-temporal risk mapping of IR; an update on WIN, a multi-country evaluation of IR and disease burden; the operational impact of IR; evidenced based IRM; IRS in India; and the NgenIRS project.

The work plan was presented with the main focus on a Massive Open Online Course (MOOC) on IRM. This is an attempt to turn the GPIRM into a more understandable and accessible resource for anyone with an interest in applied IRM. The target audience will be those who currently or in the future deliver IRM programmes. The course should be 10-12 hours over 3-4 weeks. The delivery date is expected for early 2018. In addition an IRS newsletter will be produced with space for IRS news, links to presentations and short practical information.

Discussion

- It was commented that the scope of GPIRM needs to be broadened with examples that capture lessons from agricultural IR management. This will be recommended for the MOOC's consideration.
- There was consensus that more varied vector data should be collected (including excito-repellency and feeding inhibition etc.) to help in the design of better programmes.
- It was commented that with the current tools, IRM is rather limited and the MOOC might be limited in practical information. There are more tools coming, and the MOOC will help prepare programme managers and practitioners for the arrival of these tools.