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Report

DOCUMENTING OUTPUTS, OUTCOMES AND LEARNING FROM ECOHEALTH PROJECTS: COMMUNICABLE DISEASES

Malaria
Ecohealth Project in Mexico

David J. Bradley

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1. Contextual Introduction

This report is one of three disease-specific reports addressing the projects that have been supported by IDRC in the field of Communicable Diseases within Latin America. It forms a contribution towards a study documenting outputs, outcomes and learning from Ecohealth projects. The study overall is intended to help present the case for integrated health and environment approaches to the prevention and control of communicable diseases before international scientific and donor communities, as well as to help IDRC to make informed decisions with respect to future support to programming in this area and associated strategies.

The overall study will focus on an IDRC portfolio of projects (past and on-going) on 3 important communicable diseases, namely Chagas' disease, malaria, and dengue. This report addresses the malaria Ecohealth project carried out in Mexico

2. Introduction and Methodology of Review

IDRC has supported a single, but very interesting and wide-ranging, as well as productive, malaria project in Southern Mexico where there are persistent foci of vivax malaria that act as sources of larger epidemics.

The PAD gives a detailed account of the genesis of the project and the substantial efforts put into the development of the protocol, as well as the DDT-ban context which has been addressed by others. The PAD and title firmly set the proposal in the context of the DDT controversy. The project itself comes at that issue obliquely, by analyzing a major residual malaria focus, exploring an alternative complex of approaches, and thereby making an alternative way forwards apparent. This is wholly creditable, since much of the DDT debate, certainly in Africa, has been sterile and misplaced due to confounding two questions, with the resulting discussion being emotional rather than rational. It is therefore attractive that the INSP has tackled the issues by a series of outflanking research activities.

The assessment of the project has been by a desk study of the researchers' technical project report, supplemented by several documents derived from it: a poster depicting the project results, an account of the project for a general readership, emphasizing the ways in which it provides an

alternative to use of DDT residual spraying, and the official internal document and a power point presentation. These all cover similar ground. Two full published papers have now appeared, a third has been seen in draft, and hopefully others will follow. Related publications have been consulted. There is limited contextual information, and the limitation that not only has the reviewer been unable to interview the research workers and other stakeholders, but he has not been to the field site (Mexico is one of the rather few countries unvisited by the reviewer at any time). The reviewer has first hand experience of malaria in West and Central Africa, in the Middle East , South Asia and South-East Asia, and in Colombia but not elsewhere in Latin America. This makes local comments difficult, although it is possible to comment with authority on the comparative aspects between countries and the extent to which conclusions from Mexico may be more broadly applicable. Three further reports, in Spanish, address the issues related to banning use of DDT in the region. This topic is not discussed at length.

The primary material was the final project report. This was, of course, written just at the end of the project when much further analysis remained to be done and only the early ethnographic results were available. The part summarized in Annex II has appeared as a very good published paper and shows the full potential of just one part of the project data. The Annex V material has just appeared as a paper also. The work in annexes III and VI deserve publication, though control aspects have been discussed in several papers of wider relevance. As comments are largely on the material in the report, now some years old, some suggestions for action may have already been implemented, and gaps outlined may already have been filled, and are probably already apparent to the research team. The comments are not intended as criticisms.

In this report, any Figures or Tables that I have made and appended to it are given reference letters of the alphabet (Figures A, B etc.). References to Roman numbered Annexes I through VI are to the annexes of the final project report. Since the Project was structured as a series of sub-projects the Annexes correspond to sections of the research.

The Report also raises various topics for more general discussion at IDRC. Other questions raised may have answers to which will be obvious to local people. These do not require detailed replies from local staff, and some discussions have taken place already. I use the limited data that I have to raise general issues with IDRC for discussion: they are not criticisms of the huge amount of work done with limited external funding. This report seeks to look at issues less covered in the Project Final Report and can be helpfully read in conjunction with it.

3. The Project on Malaria in Mexico

The Oaxaca malaria project is both multidisciplinary and multifaceted. To perceive its importance and value it has to be seen in the broader context of Mexican malaria and its National Malaria Control Programme, which is longstanding and effective, to the extent that most of Mexico is almost

malaria-free, and there is a series of persistent transmission foci that need controlling as they both cause local morbidity and also serve as the reservoir of infection at the root of occasional epidemics. These persistent foci vary in their characteristics: those in the North of Mexico are primarily due to limited access of control services to the areas; those in the extreme South East depend particularly on trans-border migration from more malarious countries. The major residual focus in Oaxaca State was less well characterized until this project was undertaken, but the key driving forces seemed unlikely to be the same as in the other areas mentioned. The overall malaria background of Mexico, prior to control, was that of highly unstable malaria, prone to epidemics, almost wholly due to vivax malaria (which is not often fatal, but is a serious disease) and with several mosquito vectors. Even the most important, *An. albimanus* and *An. pseudopunctipennis*, are relatively inefficient vectors (in global terms), as would be expected for unstable malaria. The task of malaria transmission control by measures aimed at the vectors is therefore relatively feasible, but the task of eliminating transmission is made more difficult by the relapsing pattern of vivax malaria, so that vector control needs to be balanced by measures directly against the parasite by chemotherapy. Fortunately, drug resistance is not a problem in Mexico.

4. Overall Assessment

The project as a whole is well conceived as a thorough investigation of the ecological and behavioural basis of persistent foci of malaria in Oaxaca State. In fact it tackles the classical epidemiological triad of time, place and person and brings nice insights and elegant analytical techniques to each component. The analyses of time, and especially place, are very well done and give a fine pictorial account of the processes of spatial recession prior to 1998. The scale on which the work is done, with a State population of 4 million and the study area of 20,000km^2 and 1 million people, is clearly not one at which the Ecohealth principles can be easily applied in the usual way, although both natural environmental and socio-economic variables were built into the spatial analysis of malaria distribution. The low malaria attack rates (<1/1,000 per annum for part of the time, and only reaching 15 per thousand in the post-hurricane epidemic year) make great statistical and analytical demands on the researchers in Latin America as compared to Africa, and this study takes this analysis to new heights. The work has had major policy impacts. It also has important lessons applicable at a global level.

5. The level of integration of IDRC's Ecohealth approach

Ecohealth involves both objectives and processes, and the nature of the problem tackled provides great opportunities for both aspects.

5.1 Environmental Management Objectives

So far as objectives are concerned, the situation in SW Mexico provides the best opportunity for environmental management for vector control that one could hope for, as shown by members of the current research team back in the early 1990's. *An. pseudopunctipennis*, in particular, breeds preferentially in riverine pools containing dense quantities of filamentous green algae, with an extraordinary linear correlation between algal coverage and mosquito productivity both in the natural situation, and also after interventions to remove the algae, with a very rapid response time to the latter. This has been implemented as a key control method. Other work has demonstrated its efficacy and it is reasonable to infer that it has contributed significantly to the fall in malaria incidence in Oaxaca State in recent years.

The work suggests that this is one component of a complex of interventions that need concurrent application to the problem, and the underlying transmission levels for vivax malaria in Mexico would suggest an inverse linear relation of this form of environmental management to malaria incidence in people.

5.2 Efficacy of Environmental Control of Breeding of A. pseudopunctipennis

From the report it appears that the key alternative intervention to the use of residual insecticides is the control of larval breeding of *A. pseudopunctipennis* by removal of filamentous algae from the surface waters. The central question then is whether or not this activity really does control the malaria, or in the absence of direct evidence, does it reduce one of the determinants of malaria transmission. This is not directly tackled in the project. Earlier (from 1990) members of the present team were involved in the work on the larval ecology of *A. pseudopunctipennis* in Southern Mexico which showed a highly significant correlation between larval abundance and the presence of filamentous algae in the breeding habitats. But, as is well known in public health, the correlation of two variables does not necessarily mean that manipulating the independent variable will necessarily produce the same effect in the dependent one.

However, a brief literature search revealed an outstandingly elegant study by an group of researchers including one of the present team (Bond et al. 2004) which showed that filamentous algae removal produces a marked reduction in *A. pseudopunctipennis* breeding (my Figures E and F). This study, with simultaneous controls, and arranged so that algal extraction was used for 3 km of river upstream from the control 3 km in 2001, and that the treatments were reversed in 2002, showed that algal extraction produced an immediate and massive fall in larval breeding which remained extremely low for 5-6 weeks. After that, larvae again appeared in increasing numbers until the onset of the rains a few weeks later stopped larval breeding in both the intervention and control sections of the study area. Adult mosquito numbers were much reduced, (though less completely than the larvae, whether this was assessed by biting catches or by light traps). Intervention and control densities of adult mosquitoes were significantly different for 6-7 weeks in both years and by both trapping methods. The overall reduction in the biting rate during the 6

weeks post-algal clearance appeared over fivefold (by inspection of the graphs). In all four cells of the study (by year and intervention) there was a remarkable linear correlation between larval mosquito density and % cover by filamentous algae per breeding site, with r^2 vales of 0.70, 0.98, 0.95, 0.82. This is striking, and makes *A. pseudopunctipennis* possibly the most obvious candidate anopheline for species sanitation in the world literature.

The seroprevalence study in Annex V is of great importance in extrapolating the effects of algal reduction from larval and adult mosquitoes to malaria transmission. What is striking, especially to a reviewer with primarily African experience, is the extremely slow rise in the age-prevalence curve, (annex V, Figure 2), with a mean of 2.5% in those aged 6-15 years. With African levels of endemicity one would see 100% by age 6 years, and in highly endemic African areas it would be 100% by 2 years (also at earlier ages, but those infant positives would have partly been due to passive immunity). The researchers are not certain for how long they would expect to continue to get a positive test in someone who became clearly positive as a result of a single infection but was not subsequently exposed to re-infection. Many would expect that infection's occurrence to remain detectable for many years. If so, the age-prevalence curve in Fig 2 of Annex A would reflect cumulative prevalence. If it did so strictly, the change of infection rate determined from the logarithmic age-uninfected-prevalence curve in its straightest part gives an incidence of infections which is well below 1% annually. It is, however, in marked contrast to that in some African situations with an entomological inoculation rate of over 1 per night and an observed incidence in visiting travelers (who are less exposed than local people) exceeding 2% per month. This comparison is highly relevant to attempts at extrapolation of these results.

Of the methodological pillars, all three are integrated into the project work, with an emphasis on involving many disciplines at all levels and on community involvement.

6. Methodological Pillars

6.1 Interdisciplinarity

The project is thoroughly multidisciplinary in conception and overall structure. Several of the subprojects are interdisciplinary over a few disciplines in a much tighter way, especially the spatiotemporal analysis, the case/control studies and the thinking underlying the surveillance change evaluation.

Research workers of several disciplines have collaborated closely in the work: physicians, geographical and spatial analysts, malariologists, entomologists, epidemiologists, anthropologists and ethnologists. This has given a powerful boost to the methodology of the various sub-projects. The most impressive has been the spatiotemporal analysis of transmission (Annex II) where the routine data collected by the malaria control programme have been handled in a sophisticated way to drive towards understanding the determinants of transmission. This has involved combining different measures of incidence and transforming locality-based information into unit area-related

data, these all being necessitated by the low incidence and the small but variable size of the towns. In the subsequent spatial analysis there was a nice combination of physical environment, meteorology, and human geographical factors in a well-controlled way.

The surveillance system modeling of annex III involves applying business system and process analysis to the logistical aspects of a key public health problem. It is original and interesting, and a method too rarely used in tropical health research. However, the way it is written up in the report (again, early on in thinking through the significance of the outputs) emphasizes the formal structure of the model used – helpfully for those without that background - so that the detailed discussions with MCP staff that inform the whole procedure are rather reduced to specified model component inputs. One hopes that in the subsequent fuller publication much more of the content of the discussion can set out more fully the assumptions and public health processes involved in the two ideal and perhaps also real approaches. The reader wonders how far the savings are due to the spread of diagnosis, how far passive search cost reduction has been offset by supervision of community workers, and variants on a mixed strategy. One would like to see more evidence, in the paper to be written, of the stakeholder (especially MCP staff) discussion of the findings of the cost analysis and the implications of the changes in sensitivity of the diagnostic test.

The sub-project on attitudes to malaria (Annex VI) was carried out by anthropologists and could be said to be mono-disciplinary, but where the study subjects were MCP staff this was perhaps interdisciplinary in a more profound way than anywhere else, as the entomologists and other public health workers were participating in a very active way with those of a social science discipline, probably for the first time. This section of the work is important and very well focused: if it was mainly done as a contract there will be a need to ensure that it is fully written up for journal publication.

The work on risk factors has just been published and is careful work. The case-control study of Annex V(B) involved social science questions but they were administered by MCP technicians. One wonders if this led to bias in the answers received. The work in annex I, IV and V(A) was primarily orthodox epidemiological and entomological work.

This has been set out at some length, because the question arises as to how far this was multi-disciplinary rather than interdisciplinary work. The division of a complex problem into a set of smaller and more soluble sub-projects is a sensible way to get the work done, but it may have tended to reduce interdisciplinary working, especially where the study villages differed between sub-projects. What are the costs and benefits of this approach? It may well weaken the Ecohealth holistic aspect but increase the number of problems solved. The degree of interdisciplinary interaction that underlay the planning of the whole project may which may have been greater than in the implementation as a result of the work being done in different locations.

The behavioural studies of the communities were rich in observations and interpretations which appeared to make an excellent framework for the design of interventions. They stop short of moving to a set of specific objectives for controlling malaria. The most obvious example of this

relates to the algal removal. At present this is undertaken by those who are remunerated for doing it. If the intention is to continue this way of working, which is straightforward and essentially competes in the market with other uses of the people's time, then one could query the need for the detailed behavioural study. If on the other hand, the aim is for a sustainable non-monetary activity, then this is a substantial and difficult transition, and, starting from this broad and useful background document, the next stage would be a highly focused study of how to achieve this in a way viable for the medium and long term.

6.2 Gender

Malaria is a less heavily gendered disease than are many others (except entomologically, where the male anopheline is usually ignored!). The research included women along with men in all the study samples for epidemiological work, in the case/control studies (where cases were matched with controls of the same gender), and in the behavioural focus groups of Annex VI, where there were appropriate focus groups for each sex, and considerable effort was put into ensuring that each sex was comparably represented.

In the results, the seroepidemiology was analyzed by gender, though rather limited attention was given to those results, which I have reanalyzed in my Figures C and D. The report discusses gender balance in seropositivity by village and rightly comments on variation between villages. Aggregating the basic data from all villages but analyzing by sex and age in Fig C, it appears that from mid-childhood to the end of the reproductive period there is a higher prevalence in women among cases. That is more evident in Figure D where the Female/Male ratio of rates is given by age in a bar chart. There is no obvious explanation for the raised prevalence in young girls, but the predominance by 33% in women of reproductive age perhaps merits comment since women are more often seriously ill from their falciparum malaria than men, and there have been some assertions from work elsewhere in the world that vivax malaria can affect pre-term mortality (though the evidence is weak). It is also quite possible that the sex ratio of cases may be influenced by gender differences in health seeking behaviour or other sources of bias that will be known locally.

Sadly, the final report does not give the extensive anthropological data that were so carefully collected, and it is to be hoped that they will be published or presented fully. Those results may well shed much further light on gender issues.

The other gender issue referred to in the documentation is that women play an important role in removing algae from dry-season pools in which breed *An. pseudopunctipennis*. Hopefully the full anthropological reports will discuss this fully, especially as this work is currently remunerated by the MCP and the household implications of the funds and their gendered distribution within the family will be important..

If the intention is to persist with algal removal for a long period, it seems a topic needing full attention of an Ecohealth type. Removing algae is not likely to persist as a sustainable activity

without remuneration unless some use can be found for the extracted algae that will be directly beneficial to the women. Can the algae be composted or used as green manure, or otherwise benefit agriculture? Are there food fish that might consume the algae? Does the aquatic nitrogen-fixing fern *Azolla* occur in the area? This proliferates in both China and Africa very rapidly, and once it reaches 90% coverage of the surface, anopheline breeding is prevented. However, as it can be invasive, its importation (even for research purposes) is not desirable if it is not already present.

6.3 Community Involvement

The issues of community involvement occur throughout the detailed investigations, most strongly in Annex VI, but of course play a greater role in the village-level and case/control studies than at landscape level. The involvement of malaria control staff is a particularly strong feature of this project so that there is continuity from the analytical work, through developing new patterns of intervention to their operational implementation. For the future there will be a need to systematize the collaborations and interactions between MCP and communities in such a way that they do not become merely formal activities but maintain the freshness of the work described in the Project.

7. Objectives and Outputs

The objectives of the project as formally stated were specific – to understand the determinants of and risk factors for a residual focus of malaria in Mexico. They have clearly been achieved. Because the study is firmly embedded in a whole series of antecedent entomological, ecological and parasitological investigations, concurrent intervention trials, and consequent policy changes, this review has looked at some broader issues as well as epidemiological detail.

The study also shows that, in a middle income country with developed institutions, work by a research organization and a disease control programme together can be very productive: not just additive but multiplicative, and that this facilitates the transition from research not merely to policy change but to implementation of that changed policy. The social science input was of a high quality but from an organization external to both. It will be interesting to see if the INSP internalizes that research capacity in the future.

8. Ecohealth Research Capacity Strengthening

It is reported that all those involved in the study have benefited from the Ecohealth approach and it has influenced the way they look at their work. I infer, as discussed elsewhere, that the MCP staff in particular may have gained insight from this Project and have a new realization of those whose

malaria they help to control. This is of special importance because of the much more interactive way in which the MCP is now aiming to work, and the new perceptions by the MCP workers will need regular reinforcement over the years if they are to change deeply their institutional culture.

It is clear that Dr. Rodriguez has been central, not only to the Project but also to the dissemination of the results and, with the MCP, turning them into policy and spreading Ecohealth ideas. He has now become the Director of INSP and this has two consequences. Firstly, he is now in a unique position to influence the institutional culture of an outstanding organization, and second, he must be hugely overworked and therefore will have difficulty making time to work fully through all the material to take forward all the various aspects together. However, his colleagues and staff seem to be moving the work ahead well.

There has clearly been marked internal capacity building for the team. My initial reaction over broader research capacity strengthening arising from the work was that the research was done by a research institute, a control programme and a consulting company, with no University involved, so that the work would be well integrated into policy and practice but less so into education of the next generation; but the Institute has substantial teaching activities. It would be good to know how far the work has penetrated regular graduate education in public health in Mexico. It would make a very nice case study and could be written up as a small book with that purpose in mind (if this has not already been done). I feel it is particularly valuable also as an example for teaching the importance of scale and scaling effects in public health analysis.

9. Lessons Applicable Globally

9.1 Preamble to discussing the lessons applicable globally: A Note on describing malaria transmission and the definition of 'hyperendemic' malaria

There is a problem of terminology in relation to the malaria endemicity in the area. It is important in discussions across countries and continents. The papers about this study refer to the area of most intense and persistent malaria transmission as a 'hyperendemic' area. The methodology used to study transmission patterns in the study was rigorous and well described in the reports. In what the authors call the 'hyper-endemic focus' the annual malaria incidence rate was between 22 and 125 cases per thousand of the population. In the climatic area of most intense perennial transmission the mean rate was 24.44 per thousand. Since from the context it appears that most cases were symptomatic and relatively promptly treated, this translates into a very low prevalence rate. The overall study area seroprevalence in the 6-15 year age group was approximately 2.5% (Annex V; Fig2), and since the seroprevalence approximates to cumulative incidence this is again low by global standards.

However, the formal World Health Organization definition of hyperendemicity is 'spleen rate [proportion of children with a palpably enlarged spleen] in children aged 2-9 years constantly over 50% and adult spleen rate also high'. There is some acceptance of an alternative definition: 'parasite rate in children 2-9 years constantly over 50%'. This is in the general population, not in those who are febrile or presenting as sick.

In other words the Mexican usage of hyperendemic as including an annual incidence of 2.4% (which if most cases are symptomatic and treated gives a point prevalence well below 1%) is completely different from the WHO agreed definition which sets a point prevalence exceeding 50% in children. The difference in transmission between these two situations is over a hundred-fold! This point is made at length because the Ecohealth programme includes both Latin America and Africa and great care is needed in transferring conclusions across continents. A persisting problem in the malaria literature is that many malariologists' experience is confined to either the Americas or Asia or Africa, and one tends to see the world through the spectacles of one's own experience. No doubt the present reviewer is similarly guilty.

The term 'residual foci' is a term not open to the confusion that may result from 'hyperendemic'.

9.2 Application to the Global Malaria Scene.

This study and the related work done in Mexico to deal with its residual malaria problems, have several lessons for other malarious parts of the world, both as examples of the strengths of an Ecohealth approach and as offering some observations for discussion of Ecohealth activities.

The world is seeing a swing of the pendulum regarding selective environmental management in malaria control. From the period in the first 3 decades of the 20th Century when the concept of species sanitation was formulated by the combined efforts of Swellengrebel and Watson and its abilities and limitations most thoroughly explored, particularly in SE Asia, the whole approach was eclipsed by the residual insecticides in the 1950-1970 period. Expertise was lost in relation to malaria (curiously, the last refuge of the malaria engineer was in the Tennessee Valley Authority of the USA). In the disorder that followed the collapse of malaria eradication as a global strategy, during the remainder of the 20th century, coherent approaches were slow to re-emerge, but in the last decade selective environmental management has begun to be re-explored as a method of malaria control, at first tentatively but more recently with somewhat uncritical enthusiasm in several quarters, either because of a narrow research focus not closely linked to sustainable upscaling, or by a rather inadequately contextualized reworking of the old data.

1. The Mexican situation provides a superb present-day example of the potential of species sanitation in ideal circumstances. The linear relation of algal coverage of small water bodies and *An. pseudopunctipennis* density is truly remarkable, as is the efficacy of algal removal, as demonstrated in work done in parallel with the IDRC project. It shows both the best that

can be attained by this approach and also the very high degree of ecological specificity needed for the approach to work. (Unfortunately, *An. gambiae* in Africa comes close to being at the other extreme of intractability in much of its range).

2. Secondly, the Mexican example, and the IDRC project in particular, is a fine example of the systematic analysis of a residual focus of transmission in a country of unstable malaria. There are many examples of such residual foci, often of the more lethal falciparum malaria, in tropical Asia and elsewhere. A clear example is the occurrence of malaria along the hilly forested elongated national borders of SE Asian States. All of those that have been studied have multiple facilitating factors for transmission, but these places are often either ignored or attacked in a simplistic way with standard tools. Yet complex social and economic causal factors are usually present. The Mexican project provides an encouraging example of how to tackle the analysis of a residual focus and can be an important methodological model for others.

3. A particularly important lesson from the Ecohealth project for failing control programmes elsewhere is the way in which socio-anthropological studies were undertaken not only with the affected populations but also with the control programme staff. In many parts of the world this has not been done (or even considered), yet it may be a key to control and even more to sustainability. Trainee malariologists are always taught that they should think like a mosquito, or even like a population of mosquitoes, and nowadays a few are being taught to think like the people who are enduring malaria transmission, but almost none are taught to understand control programme staff behaviour as a possible risk factor. This finding can helpfully be taken even to areas with a very different biological epidemiology of malaria.

10. More Detailed Comments on the Study Integration

10.1 Local Integration of Disciplines, and Ecohealth Detail for Large-Scale Control Problems

The several components of the Mexican project together form a comprehensive analysis of a persistent transmission focus and have moved forwards the necessary multifaceted approach to effective control. The practical exigencies of report writing and the scientific publishing conventions of short papers addressing specific questions have meant that the final report has a very general overview and then a series of annexes (each of which makes the basis for a separate scientific paper) which are more conventional in their subject matter, with an emphasis on a particular discipline. In the spatial analysis (annex II) paper which has now been published, the interdisciplinary aspects are very well developed.

Across the separate annexes it was quite difficult to link the localities in a way that allowed all the disciplinary work to be integrated to give a really full picture of the transmission process at local

level. The samples from different parts of the overall study do not always fit well together, or maybe they do but someone who is not from the Oaxaca region cannot readily sort out the relationships. To give two examples: it was hard to link the seroepidemiology of annex V with the spatial analysis of annex II. The former showed that Sierra villages had much the greatest seroprevalence of malaria, whereas annex II and the paper did not address this area at all as a separate zone, and rather concentrated on the foothills and coast as the high incidence places. I was left wondering why, and spending much time in trying to link them up (my Table A). If seroprevalence was so high, why were no entomological studies done in the Sierra. No doubt there are good explanations, perhaps very obvious to local researchers, but they are not given. Nor is there a detailed linkage between the 4 entomologically studied villages and their pattern of clinical cases over the period discussed in annex 2. Nor did the ethnologically studied villages of annex VI overlap with the entomology villages of annex I, although 2 overlapped with the seroepidemiology villages, and another ethnology village provided the most cases for the case-control study of annex V, but without appearing in the seroepidemiology. The four communities of the focus groups in Annex VI are said to be from the sample used to compare optimal with traditional diagnostic methods. But the Annex IV comparison was in a different state, Chiapas. In Annex V there is also mention of 30 towns where both methods were used. 2 of the 4 annex VI communities are found among the 23 in the seroprevalence studies. 2 are not; nor is it clear how the 23 seroprevalence villages relate to the 30+30 villages used in case finding. . It would, at a practical level, have saved much time for the reader to have a matrix list of all villages studied with indications of all the sub-studies in which each appears, and Table A attempts this for villages named in the text.

There is a richness of material, in the data from the studies that are interdisciplinary in the same villages, that appears to have not yet been tapped (though the documentation available to the reviewer may well have been too soon after the project for such work to have yet been attempted). While the relative scarcity of malaria in the study areas makes this detailed study of multidisciplinary sites less rewarding than in high prevalence areas, there may be much to be learned, possibly by adding other types of field-work to some of the villages which have yielded interesting or counter-intuitive results in one discipline. All this takes time and follow-up. Moreover, even epidemiologists are taught that analysis should be allocated at least as much tine as field data collection. These two observations suggest that, if the full benefits of interdisciplinary work are to be obtained, it will be beneficial to provide a low level of continuing support once a main project is completed, for several years, in order to ensure that the most Ecohealth benefits are gathered and true transdisciplinary analysis takes place.

Two things follow from this, and from various other attempts to relate results across studies. There is a need for a sort of index or overview paper, which will show in tables and maps exactly how the villages used in each study relate to each other. I specially wanted to see how the high seroprevalence Sierra villages relate to the 1997 map of Fig. 2 of Annex II. The key to differentiation in Annex V is altitude (coast, foothills, Sierra) but that in Annex II is climate. I do not doubt that these can all be fitted together, but it takes time for someone reading the project report and who does not know Oaxaca first-hand to sort out how all the parts of the jigsaw puzzle fit together.

Secondly, and more important, there is a need to link together the types of information given in the separate annexes for some key villages from which several types of data have been collected, where this is possible. The reader is keen to be able to link the behavioural data from the 4 villages in Annex VI to the appropriate entomological data from annex 1, to see precisely how they are located in the ecosystems of II and see their serology from Annex V, which is not wholly possible. It is, of course, true that the case data is hard to use in this way simply because the disease is too rare for risk factors to be calculated for the cases found in 4 villages. Moreover, the duration of the grant may well have meant that the studies had to be simultaneously executed and that it was not possible to use the data from one sub-study in the design of another.

The richness of the huge amount of work in this set of subprojects could perhaps be more fully exploited by bringing together those who have worked in the villages that received multiple protocols and to try to cross-relate the understandings gained, if it is not too long after the events. In my Table A all villages named in the report are listed and the studies they have supported are tabulated. Possible villages for such review are highlighted in yellow.

10.2 Project Implementation

The PAD lists institutions and key staff, naming four institutions and five staff as having made decisive contributions to formulating the Project and intending to implement it. Two of the organizations, and their staff, seem to have disappeared by the time of the final report, but it is clear that the INSP and MCP have worked very successfully to produce good work. A new organization has appeared, COMINCAP, and has particularly been responsible for Annex VI, the studies of knowledge and attitudes of villagers, traditional doctors, and staff of the MCP at all levels. The COMINCAP work appears very thorough, complements well that of the other two organizations and is commendably lucid and free of jargon. Sadly, the mass of detailed anthropological data was not available to me; I hope that it will be published more fully in the scientific literature.

11. Review in more detail of some of the Project Components

11.1 Vector Ecology (Annex 1)

The entomological work was sound and carried out by experienced workers. It forms one essential background component to the more original sections and in itself is orthodox in design and execution. The only unexpected aspect was that the four villages studied were in coastal and foothill areas of the state, whereas the Annex V seroepidemiology showed a higher prevalence of seropositivity in the Sierra Villages. In fact the all-ages seroprevalence in the four villages was 3.9%,

less than a quarter of that found in the most heavily infected village. Escobilla came closest to being an interdisciplinary study village, but there were no behavioural data for it.

11.2 Spatio-temporal Analysis (Annex 2)

The excellence of this sub-project has already been commended.

In the paper on spatio-temporal distribution of malaria in Oaxaca, the main lines of analysis are both clear and elegant. However, there are some difficulties for the careful reader. Tables II and III have identical titles but different data. I have inferred that table II is about towns and table III is about the identity of transmission per unit square after the Bayesian smoothing. The discussion of proximity to roads is rather unclear to me. Annex II asserts that risk in the high transmission intensity index villages is higher close to roads, but the paper states the reverse and table IV fits the latter view. In neither case is the difference in risk between those near to and those far from the road massive.

The sophisticated analysis of spatial distribution of malaria cases was very nice. I missed two sets of information. First was an unsophisticated presentation of the data as well, simply in terms of attack rates over the 10 year (1988-97) and 2-year (1998-99) periods in relation to population and altitude, climate, etc.; I imagine it was done prior to deciding on the more complex analysis, and it is always helpful to see the raw data as well (this is not to query what was done, but to see how far outcomes are methodologically dependent).

The second was a more complete discussion of the role of the two vector species over the spatial pattern. This seems relevant to the control procedures advocated: if algal removal is the key environmental intervention and is chiefly effective against *An. pseudopunctipennis*, then what is being done against *An. Albimanus* and can the focus be eliminated without specific action against it?

A non-trivial finding was in relation to distance from rivers and streams. The text rightly asserts that the relation between cases and being close to water bodies is highly significant in the multivariate analysis. What is surprising is that the relative risk ratio differs so little from 1 (RRR of 1.10 at most). If most cases occurred before the environmental control measures were thoroughly implemented I would have expected a much stronger association with proximity to water. I also have a query about the malaria transmission intensity index: within each of the three strata there is a strong relation of risk ratio to village size. Given other factors being equal, two of the factors used to construct the MTII, numbers 3 and 4 (both concerned with the numbers of years of transmission) will automatically tend to be greater with increasing village size. How is this allowed for in the calculations?

11.3 Influences on Control Policy and Assessing Impacts (Annexes III and IV)

In view of the very close link between *An. pseudopunctipennis* breeding and filamentous algae, and the related low transmission level of malaria (in global terms) in Oaxaca State, even its residual foci, which will make for a linear relation between mosquito density and malaria incidence, the benefits of environmental management are at their peak in this situation. It follows that this is a major opportunity for community-based mosquito control activities, as the project has demonstrated in practice.

The key issue then becomes how to maintain community activity in the medium term. The problem with effective preventive activities is how to sustain them in the absence of overt disease. There are many calls upon the time and energy of the local inhabitants, and as the memory of malaria epidemics fades it becomes harder to maintain enthusiasm for the task of algal removal. The general inquiry into perceptions of malaria by the local people of the residual focus has produced invaluable background information and also specific material on algal removal from streams (R annex VI, scripts for Zapotecan and Mestizo communities). Several helpful insights are provided, that could not have been inferred without the specific research on knowledge and attitudes. The study has also provided complementary information from interviews with personnel of the malaria control programme. It may well be that a more focused analysis of how to make the control activities sustainable, building on the work already done, may assist policy development. Hopefully the medium term should suffice for local eradication of the malaria parasites so that such activities for a further decade may be sufficient. The current approach appears to be dependent, directly or indirectly on funding from outside the community under some control by the MCP. This may need further exploration (which may have already occurred subsequent to the 2003 report).

I found it quite hard to assess the actual reductions in malaria due to the operational interventions by the community, for several reasons. One was the absence of basic tables of cases per year by subdivisions of the State of Oaxaca. The data are clearly available to the researchers, but the papers only present 'processed' data (entirely reasonably, because of word and space limitations) and I could not find the local data on the web. With unstable malaria, and all Mexican malaria is unstable in the malariological sense, there is great inter-year variation and it is not meaningful to take an epidemic peak year (1998; Hurricane Pauline) and simply compare lower subsequent years in order to point to successful control. More extreme variations are seen in e.g. Sri Lanka in the absence of adequate control (nor do the researchers directly claim such an intervention effect in their own writings). It would be easy for others, publicizing what is unquestionably a most impressive control strategy, to go beyond the evidence.

11.4 Risk Factors (annex V)

The findings on risk factors, particularly as presented in tables 2 and 3 of Annex V are really interesting, as both are described as case-control studies, although the methodology of the one, where cases were defined as those seropositive on survey, set out in table 2 is not described – it had 3129 people (822 cases, 2307 controls) and unclear if they were family data rather than individuals. What is striking is that the relative risks for the various postulated risk factors were low. Only three

were statistically significant (5% level) in logistic regression, and even for the strongest association, house type, the relative risk ratio was 1.44 (1.47 after adjustment). This contrasts markedly with Table 3 on the individual risk factors for actual current vivax infections, parasitologically demonstrated, where, in spite of a much smaller number of participants (119 cases and 238 controls), 14 risk factors were significant, and many were highly informative. While the difference between the two tables is in the expected direction, the difference in information content is very great. It suggests strongly that at these infection levels, the extra work involved in tracing cases rather than relying on serology is well worthwhile. I feel this is a useful and important finding and important methodologically.

Several specific case/control results on the infected people were interesting. It was not clear whether all the data were collected by questionnaire or by observation by the field worker during a house visit. In particular, the data on vegetation round the house, if completely reliable, is important as there is very little evidence globally that cutting vegetation around houses has any benefit for malaria control. These data show a huge increase (20-fold) in risk with much vegetation – it would be worth confirming with a specific study in which the vegetation would be recorded in detail and the meaning of vegetation standardized. The orthodox scientific view in Africa (with different vectors, of course) is that what is called here 'sanitation' round houses has no effect on malaria, which is in conflict with traditional public health messages, so good examples of this type are of particularly great practical importance as evidence.

11.5 Social and Behavioural Aspects (Annex VI)

The behavioural science studies were carried out in a meticulous and carefully planned way and could be a model of how to do such work. The systematic inquiry of communities and of those who control malaria, and how they interact, is an Ecohealth contribution (along with TDR Social Sciences in Malaria) that needs to be implanted into studies of malaria control worldwide. The dissection of the views of ethnic subgroups and their effects on social cohesion was helpful, and particularly the ay that people's perception was fragmented – this again has widely applicable messages – as well as the community perception of the MCP.

A central question will concern algal removal from ponded streams, funded by a government poverty relief programme at the time of the study. The anthropologists draw attention to the communal institution of Tequio, whereby algal clearing could perhaps be imported into the group of Tequio tasks. Perhaps this has already been undertaken. If not, experience elsewhere suggests that while such tasks may be initially undertaken, later they are hard to sustain, most especially if the disease the activity is intended to prevent has already become rare and recedes from people's experience. If there is to be a transition from funded to voluntary algal control, then it may require careful piloting and upscaling.

12. Challenges and Gaps

12.1 Formal Intervention Trials of Ecohealth type Interventions

The more general case for the Ecohealth approach is made by the project as a whole, but it may be helpful to also point to what seems a gap that could helpfully be filled, and which needs attention if the Ecohealth approach is to successfully mesh with the mainstream malaria work being heavily supported by other agencies. The Mexican study, as with some other IDRC Ecohealth studies, undertook a broad study of the perceptions, behaviour and socio-economic conditions of the affected population. This is surely the right place to start, because it can, and often does, light up issues that had not previously been considered and which may be essential to implementing control. But there may then be a jump from observed behaviour and expressed perceptions to an intervention that is applied. But we know from work with other interventions that one cannot reliably jump from observation to assuming that an intervention based on those behaviours will work. There is need for behavioural intervention trials of both efficacy and effectiveness, and thereafter sustainability has to be determined rather than assumed. The Mexican study illustrates how this was not done within the project for algal removal. This may well have been because the team were aware that another linked group had embarked upon that trial (nor was it among the objectives) so it is not put forward as a criticism, but the issue could be given more attention in the assessment of Ecohealth funding, as it will be the rigour of the evidence for the patterns of social and community-based interventions that will, in the end, determine the spread of the Ecohealth approach beyond IDRC.

A particular difficulty of disease control by a package of measures applied concurrently, as often has to happen in the real world, and is particularly encouraged by a holistic approach, is that every component of a control programme has a cost, and history has shown that ineffectual components of control (or case management) programme can be continued for prolonged periods, to the particular detriment of poor people. Now the Mexican situation is currently different in that control has been very effective, and at this stage efficacy in eliminating residual malaria is more pressing than economy of control measures. But, if the malaria were to persist, at some point the question will arise: is the environmental control adding anything to the 'find and treat early and thoroughly' component? This is where the orthodox and Ecohealth approaches tend to diverge somewhat, and careful judgement would be required to decide what is the preferable route.

12.2 Tradeoffs of Breadth and Focus

A feature of this and of some other Ecohealth studies is that, with a holistic goal in mind, a very large amount of material is collected across several disciplines. This is an admirable starting point and goal, as it contextualizes the work and brings up unexpected or counter-intuitive findings and uncovers issues that could have been missed but which turn out to be very important. The reviewer could give many examples, and strongly supports the approach. However, the reliability of individual

items from such a body of data, collected on a budget and in a short time, is inevitably limited. There needs to be reflection on the findings and then a much more focused study of the key issues. This has two implications: one is the need for some continuity of support and the other is a need to encourage a change of pace and rigour (I recall that simply to design a questionnaire for a leprosy study took two senior and experienced research workers all their time for 10 months).

The finding on vegetation in the case/control study is a possible case in point: it is important to know whether cutting vegetation and what is called in Mexico 'sanitation' will really affect malaria risk, because to remove a task from the household would be a great benefit, or to have data to insist on it would also be important – to design such a study with completely clear meanings for the variables would be a major undertaking; and of course the association of vegetation with malaria risk is not the same as saying that vegetation removal will reduce that risk. These are some of the issues relevant to discussion of tradeoffs.

Another related tradeoff is that if one is to minimize the large costs of gathering contextual field information, there is much to be said for concentrating studies in one area, yet locally over-concentrated field work could be misleading if applied to a million people, and uninformative at very low disease incidences.

12.3 Multi disciplinary versus Interdisciplinary in Large Scale Problems

In interpreting the report, questions arose as to whether this was more multi- than inter-disciplinary in that the separate sub-projects were not tightly integrated (indeed, Annex IV was carried out in another State) and although the community provided much information there were usually one or two disciplinary approaches that dominated each Annex. But this was not a village study; the population of the study area was of the order of one million people, and it is far from clear whether this would be best tackled by studying just a few villages in detail.

When a project has been tightly designed, as is usually the case in current research, there is often neither flexibility of time nor of funds to allow redesign in mid-study nor addition of promising and unexpected linkages, yet the nature of interdisciplinary work involves thinking together along the way. The rigidity is often more in the mind of the researcher than that of the funding agency, and it is good when that flexibility can be assured by the funder, as is often the habit of IDRC.

13. Conclusion

Having read the final report with care the reviewer is completely fascinated by this residual focus of malaria, impressed by what has been achieved, wanting to understand in more detail the geography of the core residual area, and feeling that someone should be tracking the residual cases in

individual detail, with a view to both understanding “the residual foci of this residual focus”(!), how the disease is maintained as numbers of cases fall, and hopefully to record the elimination of the focus as it happens.

The external acclaim for the work, of which this project is an important part, which has led to the reduction of malaria in Mexico is well known and documented in terms of influential lectures, use for teaching purposes to groups worldwide, and the award of the Jorge Rosenkranz Prize.

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Key Publications arising from the Project (up to 2007)

Danis-Lozano R, Rodriguez MH, Betanzos-Reyes AF, Hernandez-Avila JE, Gonzalez-Ceron L, Mendez-Galvan JF, Velazquez-Monroy OJ, Tapia-Conyer R. Individual risk factors for Plasmodium vivax infection in the residual malaria transmission focus of Oaxaca, Mexico. Salud Publica Mex. 2007 May-Jun;49(3):199-209.
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Hernandez-Avila JE, Rodriguez MH, Betanzos-Reyes AF, Danis-Lozano R, Mendez-Galvan JF, Velazquez-Monroy OJ, Tapia-Conyer R. Determinant factors for malaria transmission on the coast of Oaxaca State, the main residual transmission focus in Mexico. Salud Publica Mex. 2006 Sep-Oct;48(5):405-17.

Draft Paper: Factores asociados a la ocurrencia de casos secundarios atribuibles a recaídas por Plasmodium vivax ocurridos de 1994 al 2005 en el Estado de Oaxaca, México.

Other highlyRelevant Publications

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Rodriguez AD, Penilla RP, Henry-Rodriguez M, Hemingway J, Francisco Betanzos A, Hernandez-Avila JE. Knowledge and beliefs about malaria transmission and practices for vector control in southern Mexico. Salud Publica Mex. 2003 Mar-Apr;45(2):110-6.

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Figure A

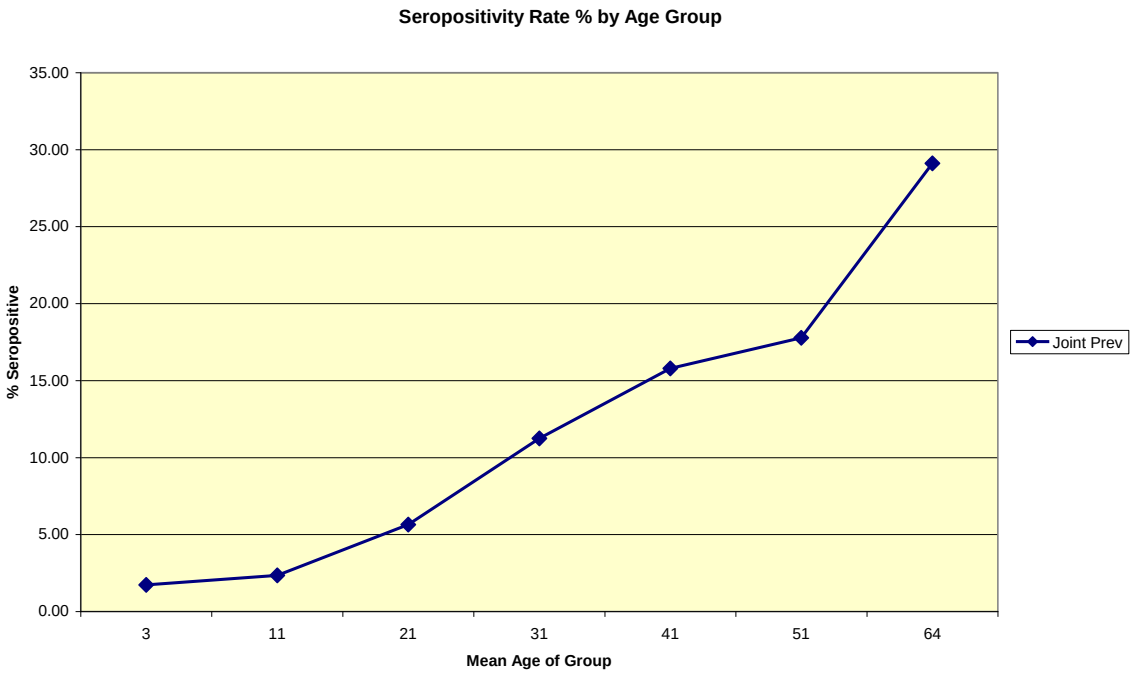

Figure B

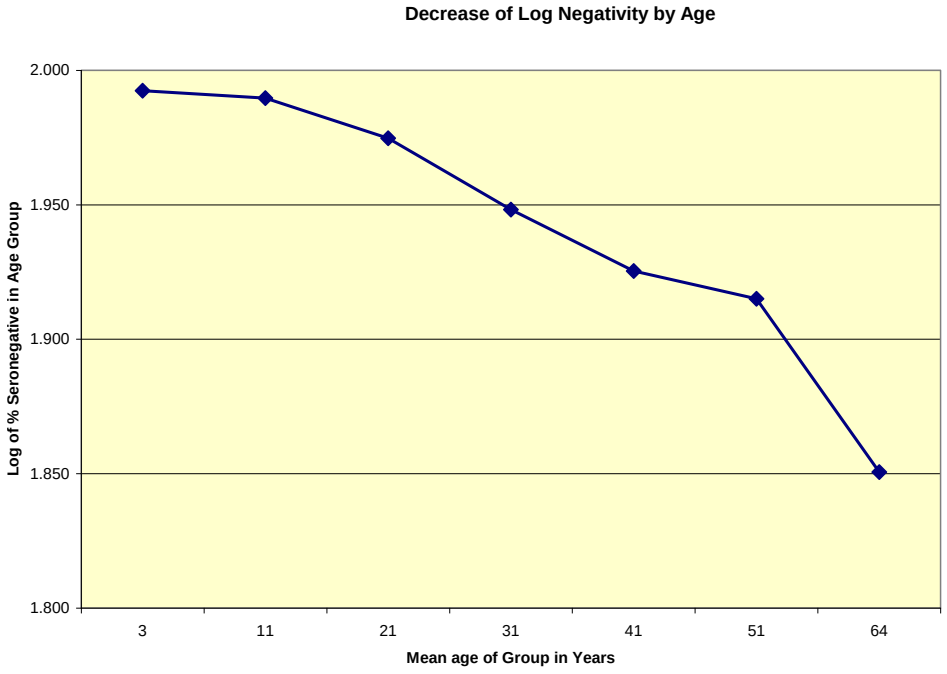

Figure C

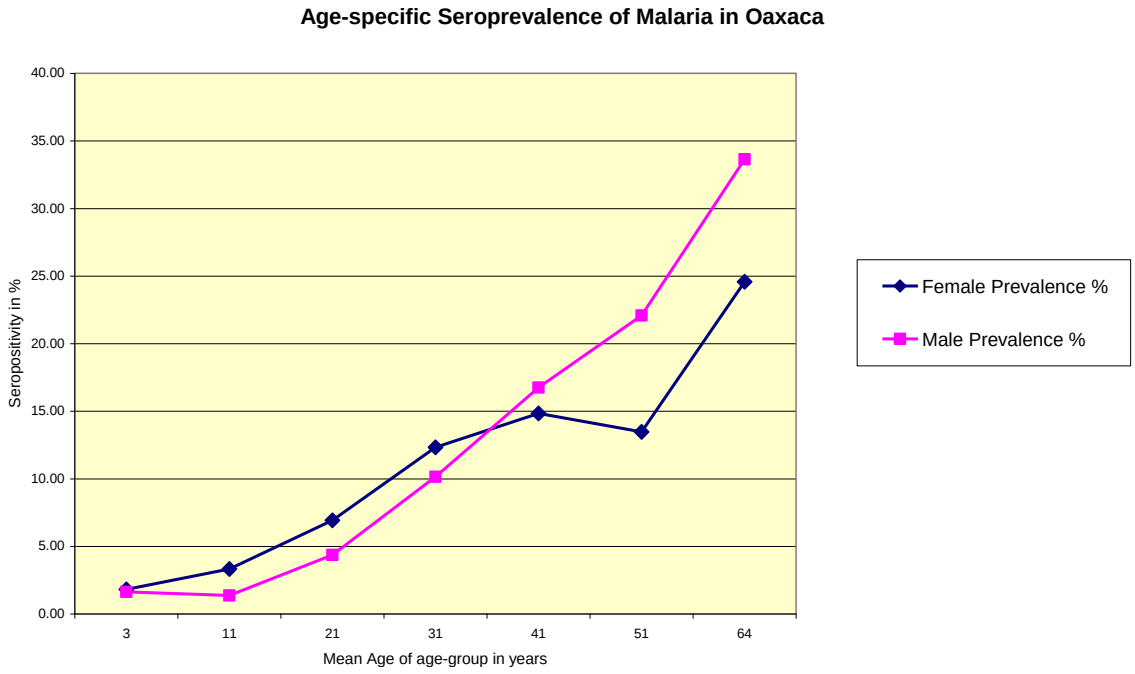

Figure D

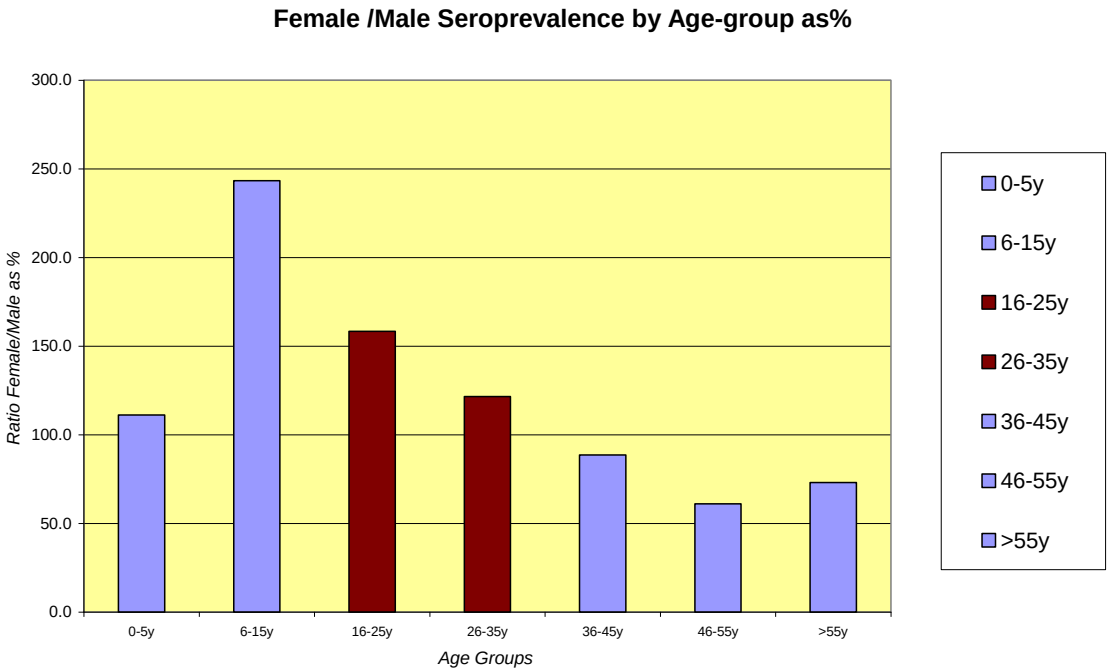

Figure E

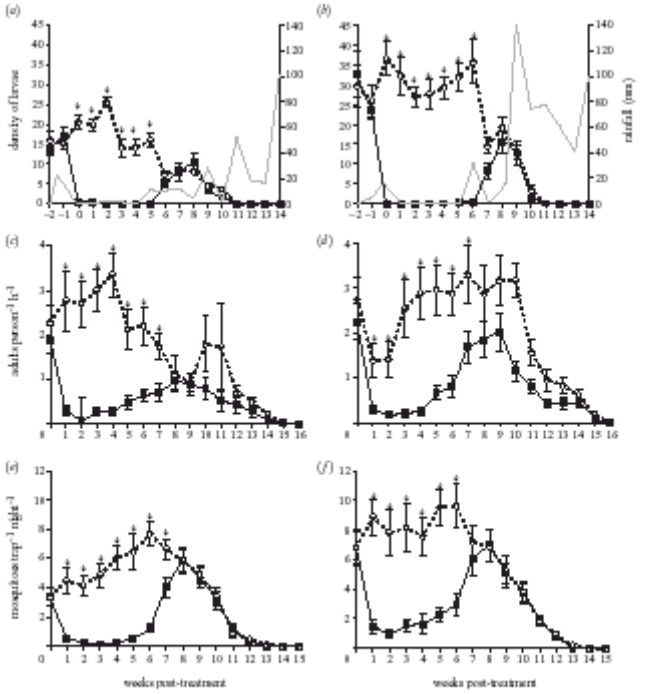

Figure 3. Effect of algal extraction from breeding sites of *An. pseudopunctipennis* on the density of larvae in the treated zone (black squares, solid line) and the control zone (open circles, dashed line) in the field experiment performed in (*a*) 2001 and (*b*) 2002. The moment of completion of algal extraction was taken as week zero. Weekly precipitation is shown by the grey line. Adult populations were monitored by human baits in (*c*) 2001 and (*d*) 2002, and by light trapping in (*e*) 2001 and (*f*) 2002. In all cases, the asterisks above the points indicate significant differences between values observed in the control and treated zones (repeated-measures ANOVA: $p \leqslant 0.05$).

Figure F

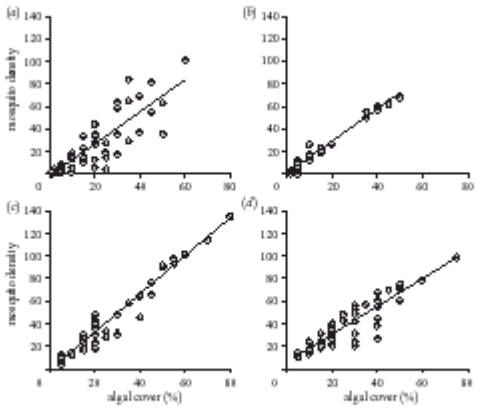

Figure 2. Linear regression of larval mosquito density (average number of larvae per dip) against the percentage cover of filamentous algae in breeding sites within the (*a*) control ($y = 1.43x - 2.35$, $r^2 = 0.70$) and (*b*) treated section ($y = 1.43x + 0.33$, $r^2 = 0.98$) of the River Coatán prior to algal extraction treatment in 2001, and (*c*) control ($y = 1.69x - 2.21$, $r^2 = 0.95$) and (*d*) treated section ($y = 1.23x + 5.45$, $r^2 = 0.82$) of the river in 2002.

Table A of Towns Named in Annexes

	Envt	Name	I Entomology Detail	Entomology ELISA	V Serology	V Cases++	VI Perceptions
1	C	Bajos de Coyula	**Y**	**Y**	**Y**		
2	C	Bajos del Arenal		**Y**	**Y**		
3	C	El Aguacate		Y			
4	C	Escobilla	**Y**	**Y**	**Y**	**Y**	
5	C	Valdeflores			Y		
6	C	San Fco Cozoaltepec			**Y**	**Y**	
7	C	Sto Dom de Morelos			**Y**	**Y**	
8	C	Bajos de Sto Domingo			Y		
9	C	El Pinal			Y		
1	SF	Pie de Montana			Y		
2	SF	Horcones			**Y**	**Y**	
3	SF	Cuajinicuil			Y		
4	SF	Azulillo			Y		
5	SF	Lagunalilla			Y		
6	SF	San Isidro Apango			Y		
7	SF	Herradura			Y		
8	SF	Arrollo Suchitl			**Y**		**Y**
9	SF	Llano Jicara			Y		
10	SF	San Miguel de Puerto			Y		
11	SF	Aguaje de Danta		Y			
12	SF	Cacahuatal		Y			
13	SF	Cofradia		Y			
14	SF	Colotepec		Y			
15	SF	Chepilme		Y			
16	SF	Junta Potrero		Y			
17	SF	La Galerita		Y			
18	SF	La Obscurana		Y			
19	SF	Las Carretas		Y			
20	SF	Paso Lagarto		Y			
21	SF	Rio Grande		Y			
22	SF	San Jose Chacalapa	**Y**	**Y**	**Y**		
23	SF	San Miguel Figueroa	**Y**	**Y**	**Y**		
24	SF	Tololote		Y			
1	S	Sirena Miramar			Y		
2	S	Piedra Virgen			Y		
3	S	Rio Santa Cruz			Y		
4	S	Quelove			**Y**		**Y**
1	?	Sta Maria Tepejipana				**Y**	**Y**
2	?	Comala				Y	
3	?	Laguna Seca					Y

Table B

Annual Data on Malaria Cases

	Mexico	***Oaxaca***	***Study Area***
1988		15,624	21969
1989			20422
1990	44513		7113
1991	26565		3925
1992	16170		2236
1993	15793		3997
1994	12864		3520
1995	7329		876
1996	6293		824
1997	4805	637	689
1998	25023	14,630	13568
1999	13450	4006	4002
2000	7362	673	
2001	4895	289	
2002	4624	266	
2003	3819		
2004			
2005			

Study area data derived from tables provided, but reviewer may have oversimplified inadvertently.

APPENDIX

Guiding questions, for the assessment, as provided by IDRC.

- What is the level of integration of IDRC's Ecohealth approach (and its methodological pillars) in the individual projects supported?

- What is the quality of outputs generated by individual projects (in terms of knowledge generation, social capital strengthening and knock-on or domino effects, capacity building for the team, publications, etc.), and their relevance to researchers and practitioners from the health and environment sectors?

- What are the intended outcomes of projects related to human health, environment and development? Have they been tracked? Are they being achieved and to what degree? How did projects contribute to their achievement?

- What are general gaps and challenges observed?

- How are the Ecohealth approaches utilized in the individual projects different from other approaches to CDs prevention and control. How are they the same? What is the added value? What is left out? What are the trade-offs?

- What lessons, insights, knowledge follow from the various sets of projects with respect to social and ecological determinants of disease transmission, prevention and control strategies, and coping capacity of communities *vis a vis* the diseases?

- Local relevance and utilization of research results: Who has and how have research results been utilized?

- What are examples of outstanding contributions of projects (eg. knowledge, strategies, policies, health outcomes) that can be documented to showcase the achievements and potential of ecohealth approaches?