Impregnated Nets Cannot Fully Substitute for DDT: The Field Effectiveness of Alternative Methods of Malaria Prevention in Solomon Islands, 1993-99

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Abstract

The incidence of malaria in Solomon Islands has been declining since 1992, but there is large geographical variation between areas in the incidence level and the rate of decline. A mix of control interventions has been used, including DDT residual house spraying and insecticide treated mosquito nets. Data on monthly incidence and control activities performed during the period January 1993 to August 1999 were gathered for 41 out of the 110 malaria zones in the country. Monthly reports on the number of fevers seen at outpatient health clinics in the same zones over the same time period were also extracted from the clinical health information system. Multivariate random effects regression including calendar month as an instrumental variable was used to investigate the relationship between the number of malaria or fever cases and the control measures applied by month and zone, while adjusting for rainfall and proximity to water. The results showed that DDT house spraying, insecticide treatment of nets, and education about malaria were all independently associated with reduction in incident cases of malaria or fever, while larviciding with temephos was not. This was true for confirmed malaria cases even when a variable representing the passage of time was included in the models. The results indicate how much each method used was contributing to malaria control in Solomon Islands and can be used to design the most cost-effective package of interventions. The evidence suggests that impregnated bednets cannot easily replace DDT spraying without substantial increase in incidence, but impregnated nets do permit a substantial reduction in the amount of DDT spraying.

Key words: malaria, mosquito control, insecticides, DDT, mosquito nets, Solomon Islands, Melanesia, multivariate regression analysis.

1. Introduction

Malaria prevention and control efforts consume a large proportion of health budgets in many endemic countries. A package of measures is often applied, with little evaluation of their effectiveness. Faced with limited health budgets, many countries face difficult choices about which are the most important intervention methods.

Malaria incidence in Solomon Islands declined by 67 percent between 1992 and 1999 (*1*). The major question we wished to answer was whether this decline could be attributed to the activities of the control program, or whether it was only the result of external environmental factors unrelated to the interventions. If the control program can be demonstrated to be effective, the next task is to evaluate the relative effectiveness of the different methods used.

Standard epidemiological approaches to the evaluation of health interventions call for randomized, placebo-controlled, prospective studies of prevention or control methods tested individually or comparatively. While this represents the ideal, it may not be possible once certain interventions or mixtures of interventions have become standard practice within the control program. An alternative approach is to use statistical methods to analyze retrospective data. This has the advantage that the interventions were carried out under operational conditions rather than in an artificial trial situation, and that costs can be associated with each of the activities performed. We have applied this approach to examine the effectiveness of malaria prevention and control methods used from 1993 to 1999 in Solomon Islands.

Malaria in Solomon Islands before 1992

Solomon Islands (Figure 1) is an island nation located northeast of Australia with a total population of 409,000 at a census in November 1999. The country is divided into 10 administrative units (9 provinces and Honiara City). One province, Rennell and Bellona, is free of malaria. Malaria is transmitted by mosquitoes of the *Anopheles punctulatus* group. The entomological inoculation rate (number of potentially infectious bites per person per night or year) varies widely over quite small areas. For example in North Guadalcanal, the inoculation rate was estimated to range from 0.03 to 2.8 infective bites per night (11 to 1022 infective bites per year) between six villages located within a radius of 18 km (*2*).

In the 1960s a malaria eradication plan was drawn up (*3*) and the country divided into “zones” with approximately 1500 to 5000 people in each (except small zones on remote islands). Residual house spraying was planned for each zone every six months. By the end of 1969, a total of 12-14 cycles of spraying had been successfully carried out in three pilot areas, and it was decided to proceed to a full malaria eradication program during 1970 to 1975 (*4*). With small changes, the zones remain in existence today as operational units for the control program.

DDT spraying had a large and immediate impact on mosquito numbers and parasite prevalence (*5*). The malaria eradication program set up a huge network of spray operators, and a comprehensive system of surveillance using both clinic–based and population-based methods for finding and treating cases. The legacy of this system is still evident in the wide-reaching microscopy network and the consistency of reporting of slide-confirmed cases from the microscopists stationed in rural health facilities to the national headquarters of the Vector-Borne Disease Control Program (VBDCP). Eradication was almost achieved by the mid-1970s (Figure 2), but there were certain areas such as North Guadalcanal where the campaign had negligible impact. At this time spraying refusal rates also began to rise (*6*).

In the late 1980s and early 1990s, several prospective trials in the southwest Pacific region demonstrated the effectiveness of mosquito nets impregnated with pyrethroid insecticides for significantly reducing transmission rates and malaria morbidity in children (*2, 7-8*). This method was adopted as part of national policy by the Solomon Islands in 1992, together with other elements of the WHO revised global strategy for malaria control (*9*). The policy remained in effect from 1992 until the malaria control program became the vector-borne disease control program in March 2001 and a revised policy was approved by Parliament .

Malaria Prevention and Control Since 1992

The incidence rates of both *P.falciparum* and *P.vivax* declined steadily from 1992 to 1997, although *P.falciparum* began to increase again in some provinces in 1998 (Figure 3). There is large variation in incidence within and between provinces, and each runs a decentralized control program using several different methods at varying intensity. These interventions include distribution, replacement and retreatment of insecticide-impregnated mosquito nets using permethrin, house spraying using DDT, larviciding with temephos (Abate) and other agents, health talks and information campaigns, and population surveys to identify and treat cases. The goal is to provide impregnated nets to all families at subsidized prices, with free net retreatment done on a yearly cycle. DDT house spraying and larviciding are done on a selective basis, with each province being responsible for selecting priority areas for these methods based on epidemiological indicators.

The choice of control methods applied is planned in advance on an annual basis according to provincial needs and preferences, and projected budgets. However, budgetary shortfalls and supply difficulties meant that plans were not consistently carried out or schedules slipped behind. Plans called for rapid response to local increases in incidence, but this was often impossible due to lack of resources for fuel or personnel.

Several health education methods were used by the program, and apart from interpersonal contact some notable ones are:

- *Radio thorns.* This program is unique to Solomon Islands. It started in 1993 and involves live discussions about malaria on the radio by a team of experts from the VBDCP. The public can ask any questions to this team through the telephone (hotline) and the answers are immediately given to them. In 1994 this program went on the air continuously for two days while in 1995-96 it was restricted to two hours per month for the whole year.
- *Radio spots, songs and jingles.* Several radio spots, jingles and songs have been developed by the Solomon Islands Broadcasting corporation (SIBC). These are occasionally played over the radio and their effectiveness is yet to be assessed.
- *Newspaper.* Though the circulation of the papers is limited to approximately 5000, articles on malaria frequently appear in this print medium. A recent sponsored column “Dear Doctor“ also addresses queries on malaria treatment, diagnosis and control.

Estimating the Effectiveness of Control Methods

The effects of different interventions on malaria incidence can be estimated because of the great variation in incidence over space and time, combined with the variable timing and intensity of the various interventions that have been applied. Using monthly data collected from 41 malaria zones in five different provinces for the years 1993 to 1999, we applied multivariate regression methods to assess the relative impact of permethrin impregnated mosquito nets, DDT residual house spraying, larval control, and health education on malaria incidence, while adjusting for rainfall and proportion of population residing near water.

Three of the control methods used in Solomon Islands (house spraying, mosquito net impregnation, and larval control) rely on the effects of insecticides (DDT, permethrin and temephos respectively) on the mosquito vector populations. Both DDT and permethrin affect the adult mosquitoes, although they act by a combination of repellency and direct knock down. Estimating the effect of insecticidal control methods in this study required us to make some assumptions about the persistence of these insecticides. Traditionally, the recommended interval between DDT house spraying cycles is six months, although this does not seem to be based on extensive entomological evidence. In fact, Metselaar (*10*) found that the mortality rate of *An.punctulatus* in huts sprayed with 2 g DDT /m^2 only declined from 89 to 67 percent after 6 months. Experiments conducted by Slooff (*11*) also demonstrated very little decline in the mortality rates of either *An.koliensis* or *An.farauti* over a nine-month period in huts sprayed with 2g DDT/m^2. When huts were sprayed with 1g/m^2, overall mortality rates were lower initially (40-50 percent for blood-fed *An.punctulatus* and *An.koliensis*), and declined to about two-fifths of the original level after six months. Permethrin-impregnated nets also seem to remain effective for longer than six months. Bioassay studies in Solomon Islands (*12*) found 100 percent mortality in samples of *An.punctulatus* exposed to a net up to 50 weeks after impregnation. As a conservative estimate, to simulate decay in insecticide effectiveness we chose to depreciate the amounts of DDT and permethrin applied by 20 percent per month. This means that the amount applied is estimated to have decayed to one third of its original value by six months and to 10 percent of the original amount by 12 months after application.

The larvicide tempehos (Abate) is applied monthly. A mixture of liquid and granule forms was used in Solomon Islands. No studies on temephos persistence have been done in Melanesia, but bioassay studies against *Aedes aegypti* showed that effectiveness declined from 100 percent to an average of 33 percent after 3-5 weeks (*13*). Therefore we chose to depreciate the amount of temephos applied by 67 percent per month.

Untangling the effects of control methods on incidence presents a challenge because of potential endogeneity in the data (*14*). Endogeneity describes a situation in which one or more of the supposedly independent variables (e.g. DDT spraying, permethrin impregnation) is determined, in part, by the dependent variable (malaria incidence). This would occur, for instance, if DDT house spraying were done in response to a high incidence of malaria, rather than as a preventive measure in advance of an anticipated peak malaria season. Failure to correct for endogeneity would lead to a biased estimate of the effectiveness of DDT, or even to the conclusion that DDT causes incidence to increase.

The method of correcting for such endogeneity in the data is to apply a technique known as “two-stage least squares“ or as “instrumental variable estimation“ (15). In this technique the potentially endogenous variable is first regressed on the exogenous variables and on a variable known as an “instrumental variable”. Such an instrumental variable should be correlated with the independent variable, but not with the disturbance term. Correcting for endogeneity in this way is frequently done in economic studies, but has not been widely applied in epidemiology.

The results of the current study, which uses a new approach for the analysis of retrospective data, will add significantly to the body of knowledge on effectiveness of interventions against malaria in Solomon Islands and elsewhere.

2. Methods and Data Collection

Number of Cases and Incidence of Malaria

The 8 malaria-endemic provinces are currently divided into 24 regions comprising 110 zones, with Honiara City treated as a separate unit occupying one of these zones. In this study we use two measures of malaria incidence, slide confirmed cases and clinical malaria cases:

Slide-confirmed malaria cases. Data on slide-confirmed malaria cases in each zone are almost complete for all zones for the ten-year period 1990-99. The monthly figures are reported to the headquarters of the Vector-Borne Disease Control Program (VBDCP), which produces summaries for annual reports and monitoring purposes. Data on number of slides examined, numbers of cases of *P.falciparum*, *P.vivax* and mixed infections, and total cases by month and zone were extracted from VBDCP written records, entered into EpiInfo Version 6.04c, checked, cleaned and exported to STATA version 6. Incidences of *P.falciparum, P.vivax,* and the two combined were calculated using population figures by zone from the VBDCP, adjusted by month for the average population growth rate.

Clinical malaria cases reported through the clinic-based health information system. All health clinics complete a monthly report of outpatient cases, which is forwarded to provincial health offices and subsequently to the Ministry of Health headquarters in Honiara where the data are entered into the outpatient Health Information System in Microsoft Access. Numbers of fever cases are recorded by sex and age-group (under 1 year, 1-4 years and >=5 years). Starting in mid-1995, the clinic monthly report form was modified to also include a section for malaria cases. These malaria cases include both slide-confirmed and presumptively treated fever cases (for clinics without microscopists), and should be a subset of total fever cases. Because this category was introduced partway through our study period and there was variation by clinic in whether this category was completed correctly or at all, we used the maximum value of either “malaria“ or “fever“ as our measure of fever cases by clinic and month.

There were a total of 105 clinics in our 41 study zones, ranging from provincial hospitals to small aid-posts. Because clinic catchment areas are not contiguous with malaria zones, each clinic was mapped to a zone using the national census data in MapInfo. All except 4 of the 41 zones had at least one clinic in them; the maximum number of clinics in a zone was 6. Data on monthly clinical malaria cases during the years of this study were extracted from the Access HIS database, exported to STATA version 6 and merged with data on slide-confirmed cases and control activities performed for the zones and months under study.

Prevention and Control Activities

Data on control activities were not routinely included in monthly and annual reports to VBDCP headquarters, and are not complete for all zones. Records were located in the provincial VBDCP offices for 41 of the 110 zones over the period Jan 1993 through August 1999. Data were extracted from the written records in each provincial or regional center, entered into EpiInfo 6.04c, checked, cleaned and exported to STATA version 6.0.

The 41 zones were in the following provinces: Central (4 zones, population 21,475 in 1999), Isabel (9 zones, population 20,396), Makira-Ulawa (12 zones, population 32,471), Malaita (25 zones in total, but data only available from 10 zones in Central and Eastern regions, population 61,502), and Temotu (6 zones, population 18,879). Thus we have data from five of the nine malaria-endemic areas in the country, representing approximately 31 percent of the total population (or 36 percent excluding the residents of Honiara city).

The amount of permethrin used per month was used to summarize the effects of provision of new treated nets and retreatment of previously owned nets. Where only the number of nets issued or retreated per month had been recorded, the average amount of permethrin used per net was derived by simple linear regression from locations that recorded both number of nets and amount of permethrin. DDT house spraying was quantified by the amount of insecticide used in charges (each charge was 0.534 kg of 75 percent DDT wettable powder). Where only the number of houses sprayed per month and zone had been recorded, the amount used per house was estimated from zones recording complete data by the regression method as described above for permethrin. Abate (temephos, a chemical larvicide applied to breeding sites for anopheline mosquitoes) was quantified as the number of liters used per zone and month. Other antilarval agents such as *Bacillus thuringiensis israelensis (Bti)* were used in only a few areas and are not included in this analysis.

Because the effects of these chemicals decay over time, the amount of DDT and permethrin used was depreciated by 20 percent each month, and the amount of temephos used by 67 percent per month, as discussed in the Introduction. The amount present in each month in a zone was estimated by cumulatively adding the new amount applied each month to the depreciated amounts present from previous months.

Health education activities were usually provided on a group basis and were quantified as the number of villages visited in a given zone and month. The educational activities comprised talks using flip charts, drama shows and/or communal source reduction activities. These were sometimes, but not always, done in conjunction with net treatment rounds, mass blood surveys, or larviciding activities. The content of the educational activities included advice to always sleep under a mosquito net and obtain prompt treatment for fever, as well as basic information on mosquito life cycle and breeding habits in order to encourage community participation in larval control.

Another activity performed in some villages was mass blood surveys followed by treatment of all positive cases. This tended to occur in response to a large number of cases occurring at health facilities, sometimes in conjunction with malaria education.

However the number of cases treated in this fashion was small compared to the number of cases treated at health facilities, and we have not included data on this mass treatment in our analysis.

Geographical Variables

Rainfall data by month for Jan 1993 to August 1999 was obtained from the Meterological Office for stations located in the provinces of Choiseul (Taro station), Makira-Ulawa (KiraKira station), Malaita (Auki station), Western (Munda station), and Temotu (Lata station) and from two stations in Guadalcanal Province (Honiara City and Henderson Airport). Since Isabel province had no official rainfall station, the mean rainfall from Taro and Munda stations was used for west Isabel zones, while for zones in east Isabel, we used mean rainfall from Auki and Honiara stations. For Central province zones we used rainfall data from the nearby Henderson airport station on Guadalcanal.

Since the larval development time of anopheline mosquitoes is 1-2 weeks, adult mosquito lifespan up to about 2 weeks, and the incubation period of malaria is a minimum 1 week, the rainfall data was lagged against the dependent variable by minus 1 month in some regression models.

Proximity to water, estimated as the proportion of the zone population residing within 0.5 km of water, was obtained from the Village Resources Survey database conducted by the Department of Development Planning. Because of the particular terrain in Solomon Islands (steep volcanic hills), this variable is a surrogate both for altitude and for proximity to the coast as well as representing proximity to fresh water.

3. Analysis

Data on malaria and fever cases and on malaria control activities was merged by matching on a unique zone/month variable, resulting in 2952 observations from 41 zones over 80 possible months of observation (Jan 1993 to August 1999).

Ordinary least squares, instrumental variable regression and cross-sectional time series regression analysis was performed using the *reg, ivreg, xtreg* and *xtivreg* procedures in STATA 7.0. Squared terms were introduced for the permethrin, education and rainfall variables to account for non-linearity in the relationships. To account for the different sizes of zones, the zone population in the mid-year of the analysis (1996) was introduced as an independent variable. In addition to current rainfall, a one month lag of rainfall was included to account for larval development time and parasite incubation period. The DDT spraying variable (cumulated depreciated DDT in kg) was instrumented by introducing a set of eleven dummy variables to capture the month of the year. The sequential month number was also used in some models to represent the passage of time. Both fixed and random effects models were tested.

4. Results

Descriptive Statistics

The annual incidence rates of slide-confirmed malaria per 1000 persons for *P.falciparum*, *P.vivax* and the total for the Solomon Islands as a whole over the years 1991 to 2000 are shown in Figure 3A. The rates for each province in the study are shown in Figure 3B to 3F. In the mid year of the analysis (1996) the average malaria incidence by province ranged from 59.9 to 171.8 cases per 1000 persons per year (Table 1). The proportion of cases represented by *P.falciparum* varied from 38.4 percent in Isabel Province to 65.7 percent in Malaita Province.

The monthly incidence rates of fever (suspected malaria) and confirmed malaria are shown in Figure 4. The ratio between fever and confirmed malaria cases varied greatly by province, from 3.1 to 1 in Temotu to 10.8 to 1 in Isabel. Overall the ratio was 4.9 to 1. Some factors possibly accounting for the different ratios are variability in the coverage of diagnostic facilities and in level of suspicion of malaria by clinical staff. Although the ratio between fever and malaria varied by province, there is clearly a common pattern of incidence observed over time.

Examples of the location of zones and major health clinics are shown in Figure 5, which illustrates Makira-Ulawa province.

Information on the amounts of control measures applied by zone for the whole study area during 1993-1999 are given in Table 2. The values given are for the non-depreciated amounts of chemicals added by zone and month.

Regression Analysis

Two different dependent variables were used. The main regression analysis was performed with the total number of confirmed malaria cases by zone and month as the dependent variable. Variability in zone population size was accounted for by inclusion of the variable “popmidz” (zone population in the midyear of the analysis) as an independent variable. We also explored the effect of using the number of fever cases per month in a zone as the dependent variable.

There were two categories of independent variables. The first category was those related to interventions against malaria:

> DDT, permethrin, temephos and education (all as cumulated depreciated amounts), as well as permethrin^2 and education^2.

The second category comprised those variables unrelated to control activities:

rainfall, rainfall^2, lagged rainfall (1 month), lagged rainfall^2, zone population, and percent of population living within 0.5km of water. In addition we included a variable "seq" (sequential month number) to represent a time trend.

Regression results are shown in Tables 3 and 4. The first column in Table 3 (model 1) demonstrates the results obtained when only zone fixed effects, rainfall and time trend are included (no intervention variables). Together these variables explain 58 percent of the variation in confirmed malaria cases. The coefficient for rain is positive while that for rainfall squared is negative, indicating that more rain increases malaria incidence up to a certain level, above which it decreases incidence. This is consistent with the observation that light to moderate rain increases the number of larval breeding sites, while heavy downpours wash away stagnant pools, open sandbars and increase river flow rates, reducing available breeding sites. Lagged rainfall significantly increased malaria cases in all but the last two of the models tested.

Adding the intervention variables to the regression (model 2 in Table 3) shows that they contribute substantially to explaining the pattern of changes in incidence. It can be seen that the regression coefficients are negative for the variables permethrin, temephos and education, indicating that, as expected, use of these methods is associated with decrease in malaria incidence. For the DDT spraying variable, the regression coefficient is positive and highly significantly associated with an increase in incidence. This indicates either that spraying makes malaria worse (unlikely based on all previous data on spraying) or that spraying is endogenous (spraying occurs in response to higher incidence of malaria).

In order to investigate further the apparently perverse relationship between spraying and incidence, we used a set of dummy variables representing the calendar month as instrumental variables. The required characteristics of an instrumental variable are that it affects whether the intervention occurs, but it is not directly related to the disturbance term in the regression. *(14,15)* Since the outcome is directly affected by the disturbance term, this means that the instrumental variable cannot be affected by the outcome. It may appear at first sight that calendar month would be directly related to the outcome, because incidence clearly varies by season. However, this seasonal variation is predominantly due to rainfall variation. Once rainfall is controlled for, there is no reason to suppose that calendar month directly affects incidence. Spraying, on the other hand, is related to calendar month due to the constraints of the budget cycle and to vacation schedules of personnel.

Results of the regression with instrumental variables are shown in model 3, Table 3. This analysis yields a more plausible estimate of the impact of spraying, which now has a negative coefficient. Permethrin and education remain significantly associated with reduction in incidence, while larval control with temephos does not. The F-statistic testing the hypothesis that the coefficients of all six variables characterizing the interventions are zero is 48.11 with 6 numerator and 2,559 denominator degrees of freedom, allowing rejection of the hypothesis that interventions have no effect at better than a significance level of 10^{-4}.

The final column (model 4) of Table 3 indicates the results of using a random effects model rather than the fixed effects model 3. The random effects model allows the introduction of the two variables, population and proximity to water, which in this data are constant within zone, due to lack of information on their changes over the time period. Neither here nor for the rest of the models to be discussed does the Hausman test reject the hypothesis that the zone-specific effects can be treated as random *(15.)* Including the population variable in the models 4 through 7 improves the interpretability of the results by adjusting the estimated effects for the number of people in a zone.

The association of malaria incidence with permethrin is smaller than in the fixed effects model 3, but remains statistically significant. The last lines of Tables 3 and 4 report the joint test that both permethrin coefficients are zero. In all but one of the seven models, we reject the hypothesis that bednets have no effect at the significance levels of .01 or below.

The models shown in Table 4 explore the effects of a) using fever instead of confirmed malaria as dependent variable, b) removing the time trend variable. For ease of comparison, we repeat in the first column of Table 4 the results of the random-effects instrumented model 4 from the last column of Table 3. Compare this with model 5 in Table 4, which shows the results when the dependent variable is fever rather than confirmed malaria. The results are similar but the effect of education is no longer statistically significant when the outcome "fever" is used, and larviciding now appears to have a positive association with fever. On the other hand, in this model and also in model 7, proximity to water is a statistically significant predictor of fever. It is possible that this variable predicts fever cases better than confirmed malaria cases, because proximity to water is associated with multiple causes of fever, not just with malaria.

In the last two columns of Table 4, we demonstrate the effects of removing the time trend variable from the model, with confirmed malaria (model 6) or fever (column 7) as outcome. Presumably because spraying, permethrin use and education have all been correlated with time, removing the time trend uncovers a stronger impact of all three of these interventions, with coefficients substantially larger than in the other models with the same dependent variable. For the simulations reported below we use model 6.

Figure 6a illustrates the effect predicted by model 6 of rainfall and lagged rainfall on malaria cases per zone per month, with a 95 percent confidence interval. Figure 6b shows the predicted effect on malaria cases per zone and month, with 95 percent confidence intervals, of each intervention method. Similar graphs could be drawn for the outcome “fever“ rather than confirmed malaria. However the lack of precision in the fever variable made it less suitable for this analysis than the number of confirmed malaria cases.

During this study, the monthly average number of confirmed malaria cases per zone was 33.6 (corresponding to an incidence rate of 11.0/1000 persons per month) and the average number of fever cases per month was 171.2 (representing monthly fever incidence of 56.2 cases / 1000 persons). According to models 4 and 6, the effect of each kg of DDT or liter of permethrin on confirmed malaria cases appears about equal, since the regression coefficients are similar. According to model 6, each kg of DDT was associated with a reduction of 2.5 malaria cases, while each liter of permethrin was associated with reduction of at most 2.9 malaria cases. (For permethrin, this is an approximation due to the non-linear association)

We also need to take into account the population covered by each unit of insecticide. The data on numbers of houses sprayed and their population show that the average household size in sprayed villages is 5.0 (standard deviation 3.1). The mean number of houses sprayed per zone was 111. Therefore spraying, when done in a zone, covered an average of 555 people (18 percent of the average zone population of 3045). The average kg of DDT used in a zone was 6.4 kg (Table 1), so 1 kg of DDT covered on average 87 people. For permethrin, the data show that mean amount of insecticide used per net was 11ml (0.011 liters). With 5 people per household, we can estimate 2 nets per household or 0.022 liters permethrin per 5 people. It follows that 1 liter of permethrin would cover 227 people, or 2.6 times as many people as I kg of DDT protects. Thus weight for weight of chemical, the results suggest that DDT exerts its effect on reduction in cases more efficiently than permethrin. At present, we do not have sufficient data to estimate the number of people affected by each liter of temephos or each village education program conducted.

The number of confirmed malaria cases observed is of course an underestimate of the actual number occurring, since many do not reach health facilities. For this reason we also used fever cases as an outcome in regression model 7, but fever case numbers are obviously an overestimate of malaria cases, since they included many other non-vector-borne and vector-borne diseases. Because of the measurement error it introduces into the outcome, using the fever data is not suitable for drawing detailed causal inferences, but the coefficients in model 7 may be regarded as an upper bound of the potential effects of the interventions on malaria. In model 7 the coefficients for DDT (-6.622), permethrin (-4.741), education (-5.41) and rainfall (0.245) are all larger than in model 6.

The parameter estimates of Model 6 can be used to answer the question, “By how much would it be necessary to provide impregnated bednets in order to achieve the same low number of malaria cases that could be achieved with DDT spraying, education and larvacide alone?“ Figure 7 graphs the tradeoff between spraying and bednest on the assumption that the other variables in Model 6 are held constant at their means. According to Model 6, raising the mean level of accumulated DDT from its average of 40 kilograms per zone to an average of 60 kilograms, for mean values of the other variables, would reduce the average number of cases to zero in the absence of any permethrin. By following the top curved line in Figure 7, one can see that the same zero number of cases could also be achieved at current levels of spraying, provided that average accumulated permethrin is raised from its current mean of 3.6 liters to approximately 22 liters. However, the gains from adding permethrin are estimated to decline with more intensive application (as captured by the statistically significant quadratic term on the variable *permethrin* in Model 6). Thus, according to these estimates no amount of permethrin would enable the program to attain a zero average number of cases while forgoing DDT spraying. Indeed, according to the bottom line of Figure 7, the lowest average number of cases that could be achieved without spraying while holding the other variables at their means, would be 100 confirmed cases per month, three times higher than the current mean. And this would only be achieved if accumulated permethrin were increased by seven- or eight-fold to about 25 or 30 liters per zone per month.

5. Discussion

This paper attempted to address the following question: in situations where malaria prevention and control seems to be working (e.g. Solomon Islands), why is it working? This is not immediately obvious when a set of different interventions has been used. The Solomon Islands Vector-Borne Disease Control Program has an unusually high quality and quantity of data on control measures compared to other published studies. There is also large variation in intensity and frequency of control measures by zone. This presented an opportunity to try to disentangle the effects of different interventions using multivariate regression methods. As far as we are aware, this is the first attempt to estimate effectiveness of control measures from retrospective data where a mixture of interventions has been used. It is also the first paper to apply multivariate random-effects regression with instrumental variables to this kind of data.

The results show that DDT spraying, permethrin impregration of mosquito nets, and educational activities were all independently associated with reduction in malaria cases, while larval control using temephos was not. The associations held even after adjusting for the other variables such as rainfall and proximity to water. The control methods significantly reduced malaria cases even when a time trend variable (representing unquantified environmental variables operating during the study period) was included in the model.

There may be other independent variables associated with incidence which we were unable to evaluate and control for in this study due to lack of information, including but not limited to:

- Geographical factors (e.g. average altitude of the zone, proximity to a town);
- Social factors (e.g. educational levels, access to cash for transport to clinic);
- Health system factors (time to a health facility; availability of roads);
- Control program factors (relative allocation of funds and staff between zones; timing of resource delivery).

Previous research in Solomon Islands has compared DDT house spraying with impregnated nets in an attempt to determine which method is better, on the assumption that only one method would be chosen (*2*, *16*, *17*). The results from the current study suggest that both methods, together with and educational activities, have been contributing significantly to the slow decline in malaria incidence in Solomon Islands, and that the decline would have been even slower if only one method had been used. Residual house spraying remains an effective option for malaria control, despite the fact that it has been claimed to have lost its effectiveness in Solomon Islands due to evolution of behavioral resistance in the main vector species *An. farauti* (*18*). Estimates of the synergy between spraying and permethrin (not reported here) suggest that the benefit of either is somewhat reduced in the presence of the other, but the interaction effect is not statistically significant.

Malaria exerts a large toll on the health of Solomon Islanders, with detrimental consequences on the ability to work or attend school (*19*). Previous studies in the country on cost-effectiveness of bednets versus spraying (*20*) were used to guide national policy towards the introduction of insecticide-impregnated mosquito nets on a large scale in 1992. The current study will provide improved data on comparative effectiveness of these methods, which can be combined with unit cost estimates to determine how much it costs to prevent a malaria case by each method, and thus to revise policy towards the most cost-effective mix of interventions. This analysis will need to include the cost of nets as well as the permethrin used to impregnate them. Such data are badly needed, as there are few data on the cost-effectiveness of malaria interventions, particularly packages of interventions (*21*). A recent comparison in South Africa estimated that nets impregnated with the pyrethroid deltamethrin were more effective but much less cost-effective than house-spraying with the same insecticide (*22*). A similar comparison in Solomon Islands in which the same quantity of insecticide was used in the two methods would be of great interest. In the present study, different insecticides were used for house-spraying and net impregnation.

A recent review comparing worldwide trials of impregnated bednets and house-spraying for malaria control suggested that pyrethroid treated nets were as effective as house spraying with DDT, malathion or a pyrethroid (*23*). However, recent insecticide-treated net trials appeared to be less effective than spraying programs conducted in the same areas over 30 years ago with non-pyrethroid insecticides including DDT, malathion and dieldrin.

The evidence from the current study and all other previous studies in Melanesia (*2, 7,8, 10-12, 16, 17*) suggest that impregnated bednets cannot easily replace DDT spraying without substantial increases in malaria incidence. Rather the role of bednets and other interventions is to permit a substantial reduction of DDT spraying for any given target incidence level. A full economic analysis would have to include not only the program costs of all alternative interventions, but also the environmental benefits of reducing DDT use in order to arrive at the socially optimal combination of malaria control interventions.

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Table 1: Slide positivity rates and annual incidence of malaria and fever for the zones studied, by province, in the mid-year of the analysis (1996)

Province	Population studied	No. of zones	Slide positivity rate, %	Annual incidence of slide-confirmed malaria / 1000 persons			Annual fever incidence /1000
				P. falciparum	*P. vivax*	Total	
Central	20,399	4	13.9	47.5	31.6	79.1	629.3
Isabel	15,499	9	8.9	22.4	35.8	58.2	616.0
Makira-Ulawa	30,770	12	17.8	34.3	46.0	80.3	325.2
Malaita	45,328	10	23.1	89.5	47.1	136.6	642.4
Temotu	14,855	6	28.8	104.8	67.2	171.8	500.7
TOTAL	126,852	41	19.3	63.0	45.3	108.2	543.5

Table 2: Descriptive statistics for the independent variables, by zone and month

Variable	Number of observations	Mean	SD	Min	Max
Permethrin (liters)	2460	0.97	3.39	0	44.4
DDT (kg)	2461	6.4	32.5	0	644.0
Temephos (liters)	2461	0.33	1.15	0	15.04
Education visits (no. of villages)	2277	0.61	3.65	0	65
Rainfall (mm) (from 7 stations)	536	242.2	159.1	4.6	930.9
Zone population in 1996	41	3045	2507.2	60	9869
% pop living <=0.5 km from water	41	38.7	26.4	0	82.9

Table 3: Regression results for the outcome “confirmed malaria cases“ using fixed and random effects models, with and without instrumental variable

Model no:	1	2	3	4
Outcome variable:	**Confirmed malaria cases**	**Confirmed malaria cases**	**Confirmed malaria cases**	**Confirmed malaria cases**
Type of model:	**Fixed effects, no interventions**	**Fixed effects**	**Fixed effects, instrumented**	**Random effects, instrumented**
DDT		0.42 (11.34)**	-1.589 (3.64)**	-1.62 (3.58)**
Permethrin		-2.108 (5.96)**	-1.637 (3.10)**	-1.12 (2.05)*
Permethrin^2		0.031 (2.90)*	0.014 (0.86)	0.004 (0.27)
Temephos		-4.221 (5.11)**	-0.21 (0.14)	-0.124 (0.09)
Education		-1.333 (4.38)**	-1.785 (3.91)**	-1.697 (3.67)**
Education^2		0.019 (3.36)**	0.026 (3.05)*	0.025 (2.87)**
Proximity to water				0.142 (0.85)
Zone population				0.022 (8.95)**
Rainfall	0.054 (3.63)**	0.06 (4.28)**	0.051 (2.48)*	0.046 (2.15)*
Rainfall^2	$-4.9\text{x}10^{-5}$ (2.54)*	$-5.4\text{x}10^{-5}$ (2.90)**	$-5.2\text{x}10^{-5}$ (1.9)	$-4.5\text{x}10^{-5}$ (1.62)
Lagged rainfall	0.019 (1.28)	0.024 (1.68)	0.018 (0.87)	0.013 (0.61)
Lagged rainfall^2	$-7.9\text{x}10^{-9}$ (0)	$-4.5\text{x}10^{-6}$ (0.24)	$-2.2\text{x}10^{-6}$ (0.08)	$-7.7\text{x}10^{-6}$ (0.27)
Seq. month	-0.496 (12.85)**	-0.19 (4.58)**	-0.729 (5.56)**	-0.762 (5.60)**
Constant	40.6 (11.95)**	18.595 (4.97)**	122.323 (0)	53.191 (2.68)**
N observations	2610	2610	2610	2610
Permethrin: X^2 (p)		28.1 ($p<0.0001$)[a]	23.8 ($p<0.0001$)	14.4 ($p=0.0007$)

Absolute value of t-statistics in parentheses.
*significant at 5% level; ** significant at 1% level, [a] In Model 2 only joint tests are F-tests.

Table 4: Results for the outcomes “confirmed malaria cases” or “fever cases“ using random effects models, with and without time trend variable

Model no:	4	5	6	7
Outcome variable:	Confirmed malaria cases	Fever/suspected malaria cases	Confirmed malaria cases	Fever/suspected malaria cases
Type of model:	Random effects, instrumented, with time trend	Random effects, instrumented, with time trend	Random effects, instrumented, without time trend	Random effects, instrumented, without time trend
DDT	-1.62	-5.028	-2.544	-6.622
	(3.58)**	(3.96)**	(3.29)**	(3.44)**
Permethrin	-1.12	1.693	-2.918	-4.751
	(2.05)*	(1.07)	(4.22)**	(2.63)*
Permethrin^2	0.004	-0.066	0.043	0.067
	(0.27)	(1.4)	(2.06)*	(1.28)
Temephos	-0.124	8.614	0.421	7.302
	(0.09)	(2.30)*	(0.23)	(1.65)
Education	-1.697	-1.74	-3.085	-5.41
	(3.67)**	(1.33)	(4.34)**	(3.06)**
Education^2	0.025	0.006	0.05	0.066
	(2.87)**	(0.26)	(3.75)**	(2.12)
Proximity to water	0.142	1.482	0.19	1.55
	(0.85)	(2.71)**	(1.07)	(2.62)**
Zone population	0.022	0.071	0.026	0.08
	(8.95)**	(10.54)**	(7.22)**	(9.04)**
Rainfall	0.046	0.145	0.075	0.24
	(2.15)*	(2.30)*	(2.67)**	(3.14)**
Rainfall^2	-4.5×10^{-5}	-1.4×10^{-4}	-1.1×10^{-4}	-3.4×10^{-4}
	(1.62)	(1.68)	(2.84)**	(3.27)**
Lagged rainfall	0.013	0.012	0.045	0.108
	(0.61)	(0.19)	(1.58)	(1.42)
Lagged rainfall^2	-7.7×10^{-6}	1.0×10^{-4}	-5.5×10^{-5}	-9.8×10^{-5}
	(0.27)	(1.26)	(1.42)	(0.99)
Seq. month	-0.762	-2.841		
	(5.60)**	(6.53)**		
Constant	53.191	162.351	43.16	84.837
	(2.68)**	(2.52)*	(1.92)	(1.26)
N observations	2610	2338	2610	2338
Permethrin: X^2(p)	14.4 (p=0.0007)	2.1 (p=0.35)	25.9 (p<0.0001)	10.2 (p=0.01)

Absolute value of t-statistics in parentheses.
* significant at 5% level; ** significant at 1% level.

Figure 1: Map of Solomon Islands showing provinces and location of the capital Honiara

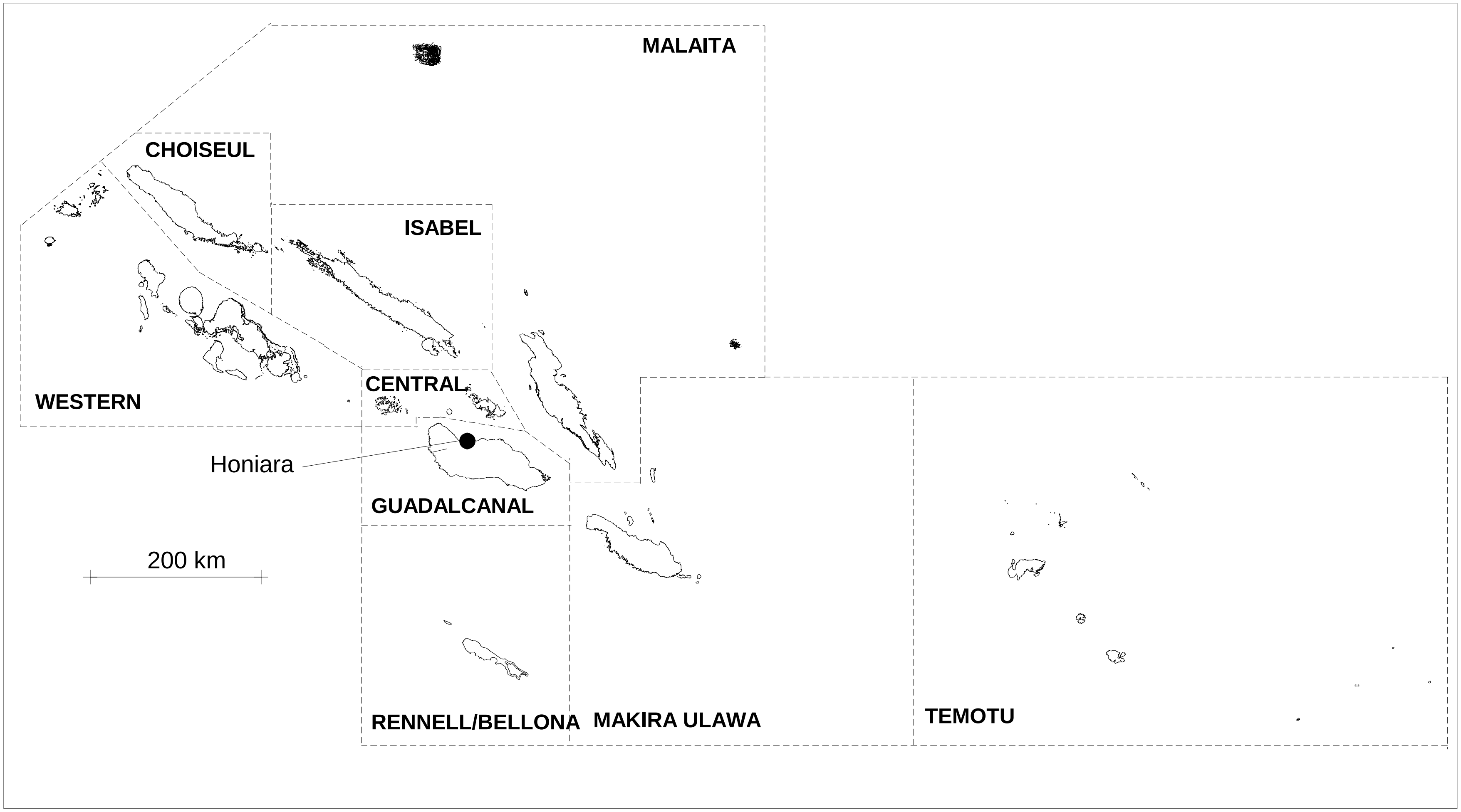

Figure 2: Annual incidence of slide-confirmed malaria per thousand persons in Solomon Islands, 1969 to 1999

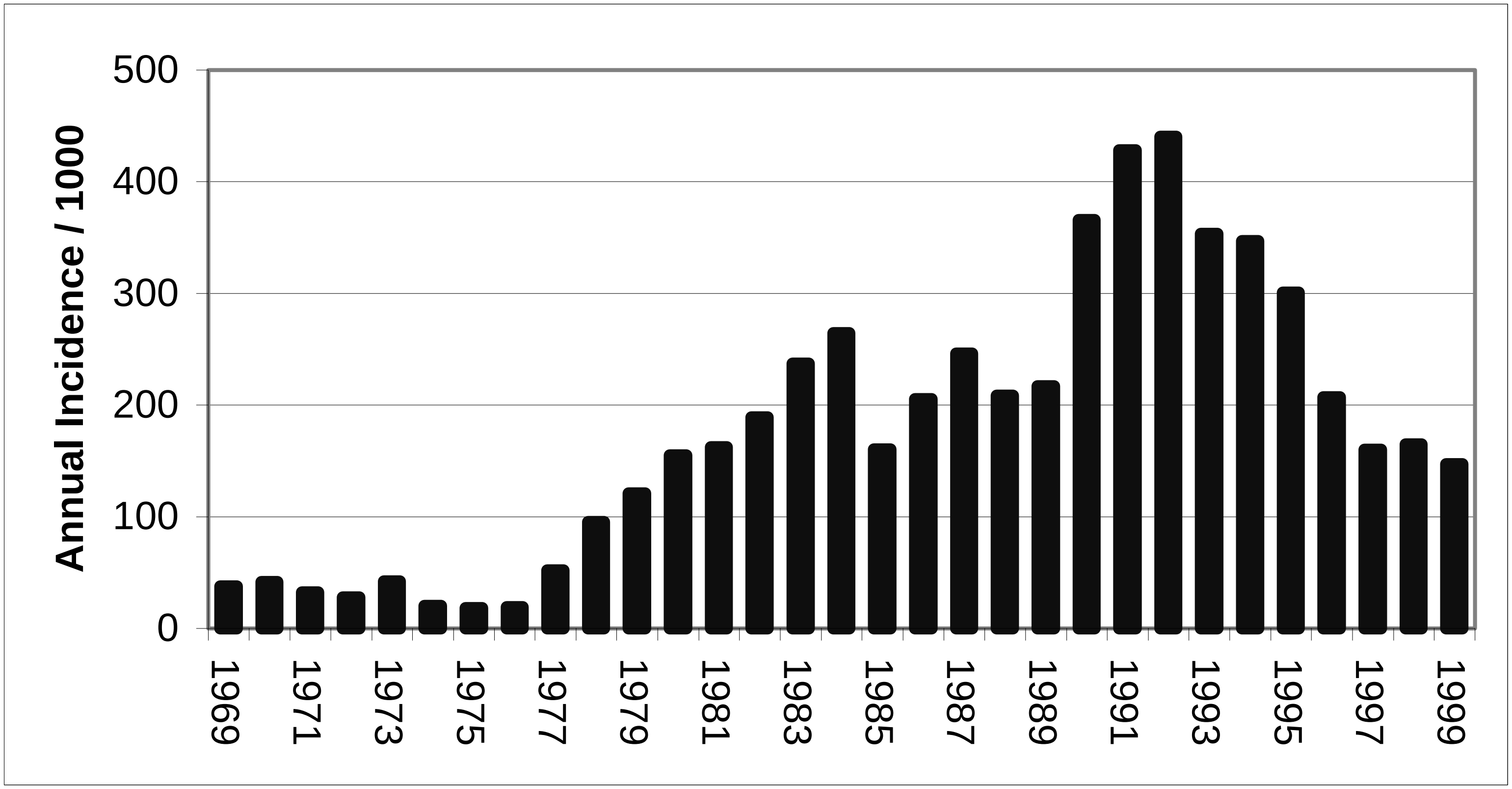

Figure 3: Annual incidence of *Plasmodium falciparum*, *P.vivax* and total cases of slide-confirmed malaria per 1000 persons in Solomon Islands and in selected provinces included in this study, 1991 to 2000. A: Solomon Islands; B: Central Province; C: Isabel Province; D: Makira Ulawa Province; E: Malaita Province (Central and Eastern regions); F: Temotu Province

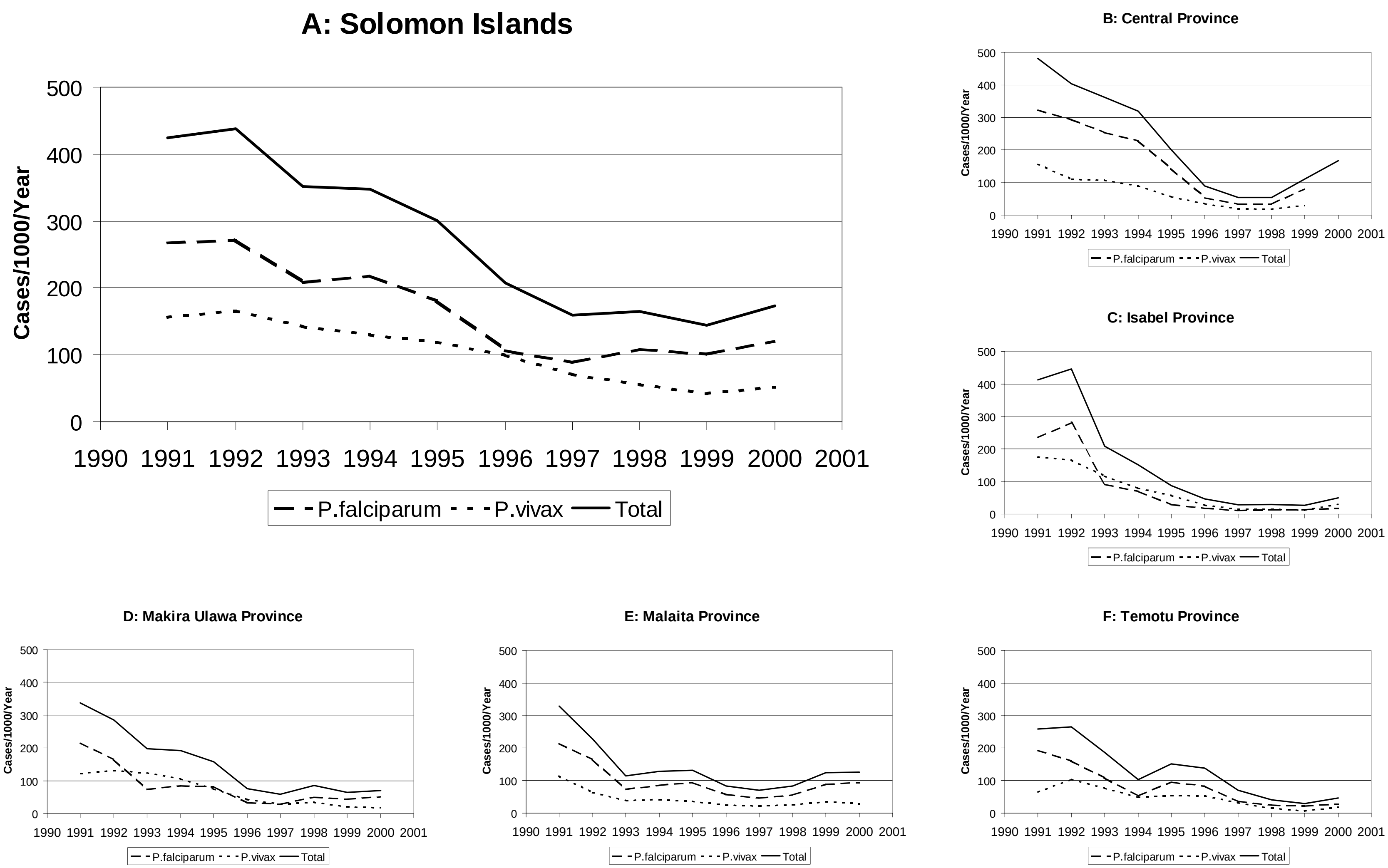

Figure 4: Monthly incidence of fever (suspected malaria) and slide-confirmed malaria per 1000 persons in Solomon Islands and in selected provinces included in this study, 1993 to 1999. A: Total for five provinces in the study; B: Central Province; C: Isabel Province; D: Makira Ulawa Province; E: Malaita Province (Central and Eastern regions); F: Temotu Province

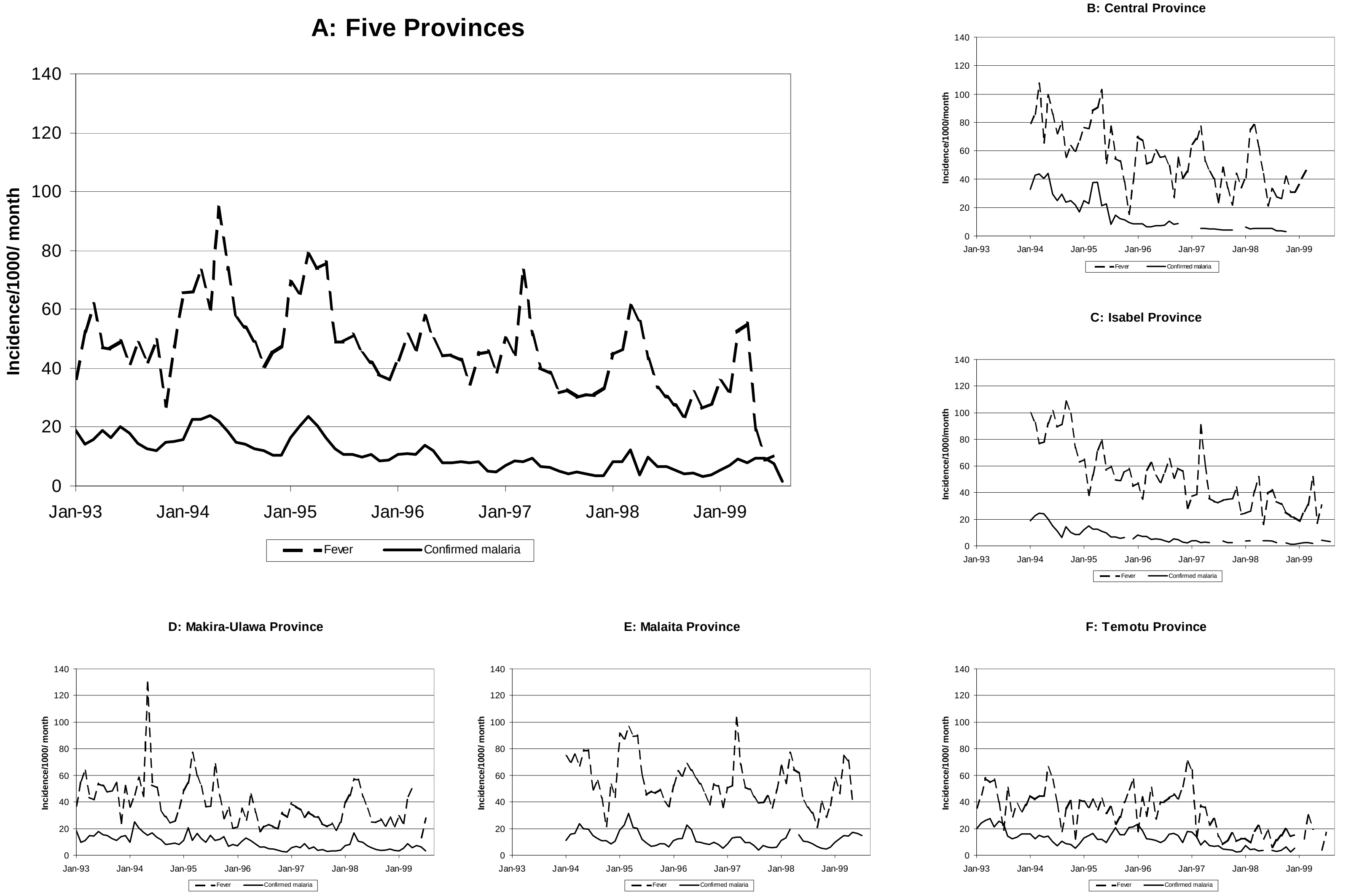

Figure 5: Map of Makira Ulawa Province showing location and numbers of malaria zones, major health clinics and the road. The provincial hospital and rainfall station are located at the capital Kira Kira

Figure 6: Predicted effects of rainfall (A) and interventions on malaria cases (B), using regression model 6 (time trend excluded)

6A: Rainfall

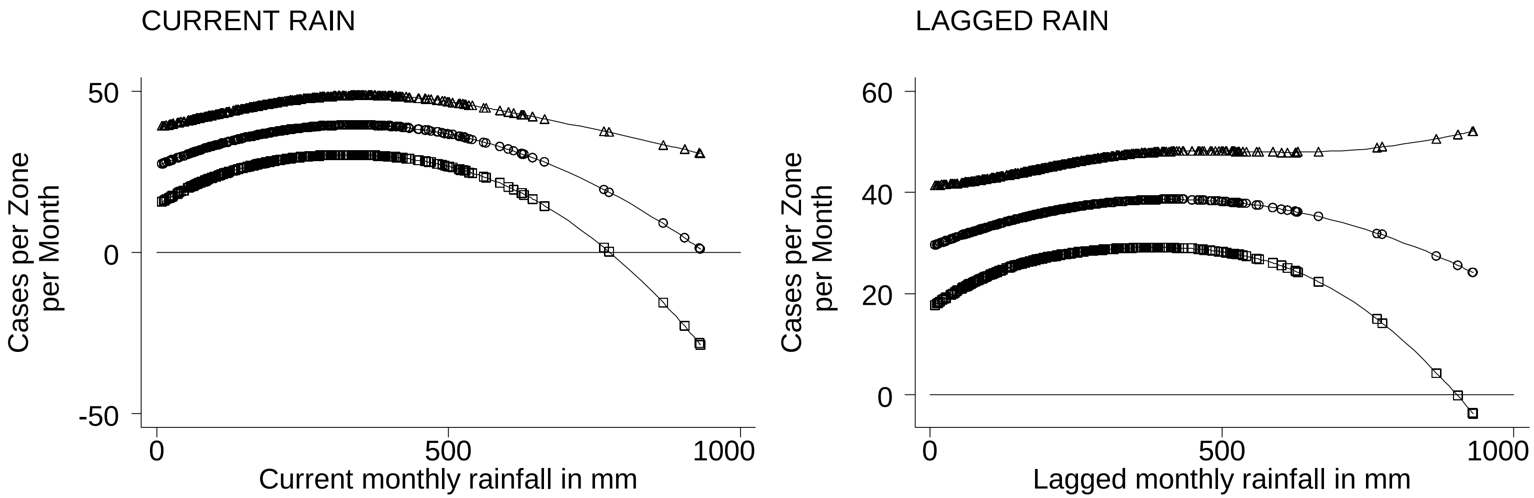

Figure 6B: Interventions

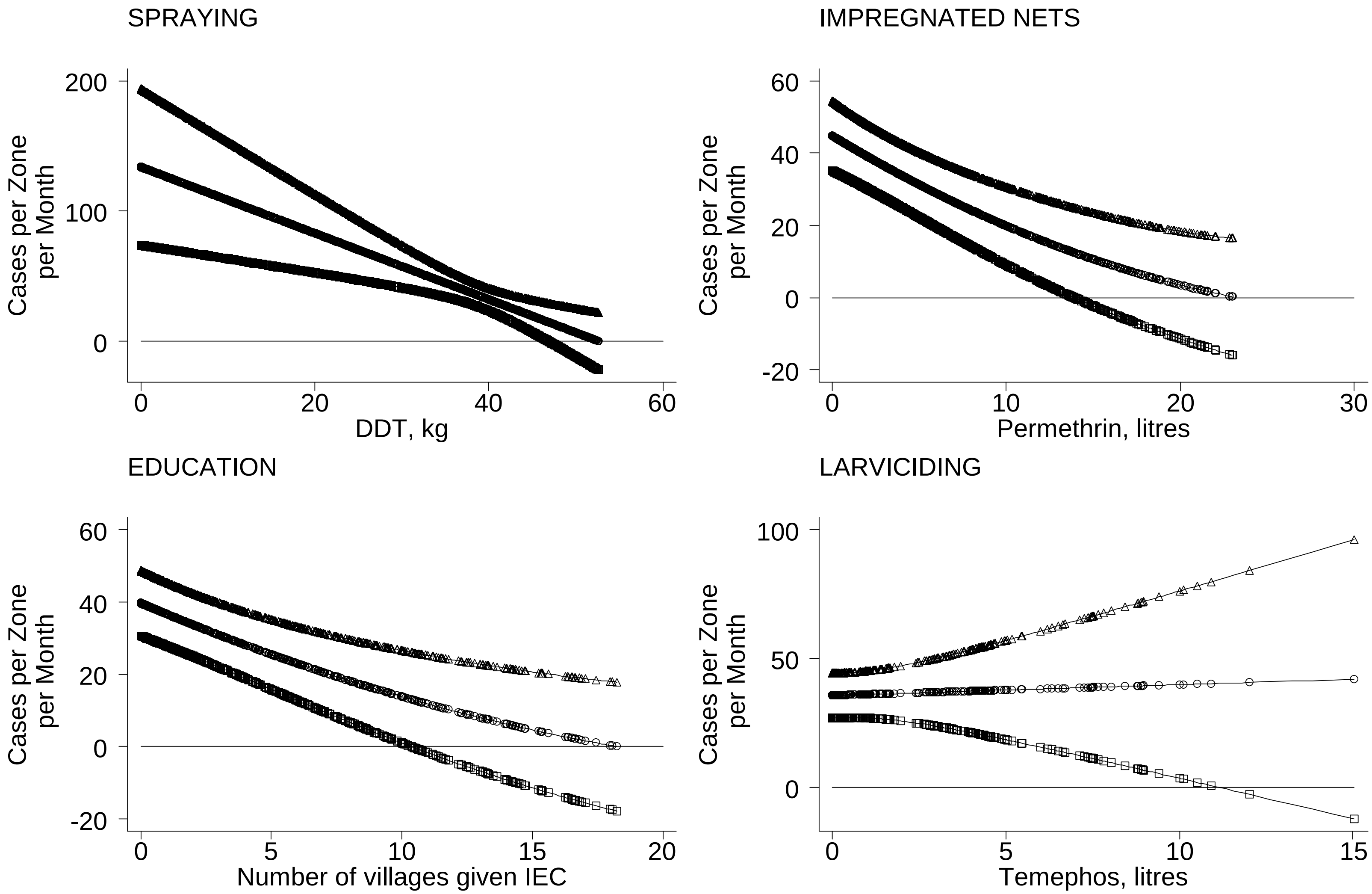

Figure 7: Combinations of accumulated sprayed DDT and accumulated applied permethrin, which lower malaria incidence to three specific levels given that other variables are held at their mean levels
(Computed from model 6 of Table 4)