Evidence based community mobilization for dengue prevention in Nicaragua and Mexico (*Camino Verde,* the Green Way): cluster randomized controlled trial

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ABSTRACT

OBJECTIVE
To test whether community mobilization adds effectiveness to conventional dengue control.

DESIGN
Pragmatic open label parallel group cluster randomized controlled trial. Those assessing the outcomes and analyzing the data were blinded to group assignment. Centralized computerized randomization after the baseline study allocated half the sites to intervention, stratified by country, evidence of recent dengue virus infection in children aged 3-9, and vector indices.

SETTING
Random sample of communities in Managua, capital of Nicaragua, and three coastal regions in Guerrero State in the south of Mexico.

PARTICIPANTS
Residents in a random sample of census enumeration areas across both countries: 75 intervention and 75 control clusters (about 140 households each) were randomized and analyzed (60 clusters in Nicaragua and 90 in Mexico), including 85 182 residents in 18 838 households.

INTERVENTIONS
A community mobilization protocol began with community discussion of baseline results. Each intervention cluster adapted the basic intervention—chemical-free prevention of mosquito reproduction—to its own circumstances. All clusters continued the government run dengue control program.

MAIN OUTCOME MEASURES
Primary outcomes per protocol were self reported cases of dengue, serological evidence of recent dengue virus infection, and conventional entomological indices (house index: households with larvae or pupae/households examined; container index: containers with larvae or pupae/containers examined; Breteau index: containers with larvae or pupae/households examined; and pupae per person: pupae found/number of residents). Per protocol secondary analysis examined the effect of *Camino Verde* in the context of temephos use.

RESULTS
With cluster as the unit of analysis, serological evidence from intervention sites showed a lower risk of infection with dengue virus in children (relative risk reduction 29.5%, 95% confidence interval 3.8% to 55.3%), fewer reports of dengue illness (24.7%, 1.8% to 51.2%), fewer houses with larvae or pupae among houses visited (house index) (44.1%, 13.6% to 74.7%), fewer containers with larvae or pupae among containers examined (container index) (36.7%, 24.5% to 44.8%), fewer containers with larvae or pupae among houses visited (Breteau index) (35.1%, 16.7% to 55.5%), and fewer pupae per person (51.7%, 36.2% to 76.1%). The numbers needed to treat were 30 (95% confidence interval 20 to 59) for a lower risk of infection in children, 71 (48 to 143) for fewer reports of dengue illness, 17 (14 to 20) for the house index, 37 (35 to 67) for the container index, 10 (6 to 29) for the Breteau index, and 12 (7 to 31) for fewer pupae per person. Secondary per protocol analysis showed no serological evidence of a protective effect of temephos.

CONCLUSIONS
Evidence based community mobilization can add effectiveness to dengue vector control. Each site implementing the intervention in its own way has the advantage of local customization and strong community engagement.

TRIAL REGISTRATION
ISRCTN27581154

WHAT IS ALREADY KNOWN ON THIS TOPIC

Current dengue control rests heavily on using the organophosphate pesticide temephos (Abate) in household water storage containers

The dengue pandemic has continued to grow despite widespread use of temephos, and resistance to this pesticide is well documented. Space spraying with other pesticides is common but of little proved value

Though several studies have shown an impact of community interventions on vector control, none has shown an impact on dengue illness or serological evidence of infection

WHAT THIS STUDY ADDS

The Camino Verde (Green Way) is pesticide-free evidence based community mobilization, each community choosing and implementing its own mix of dengue prevention actions based on local vector reservoirs and community resources

The project had a positive impact on serological evidence of dengue virus infection in children, reported illness at all ages, and all dengue vector control indices

This is the first report of serological evidence of impact of community interventions

Serological evidence could not confirm any protective effect of temephos against infection with dengue virus—overall or in any subgroups

Introduction

Dengue is a major international health problem, with some 100 million cases and 400 million infections a year globally.[1,2] In most countries, contemporary dengue control depends on placing an organophosphate larvacide—temephos (Abate)—in water storage containers that are potential breeding sites for the main vector *Aedes aegypti*.[3] This has not curbed dengue epidemics. Space spraying with other pesticides is common, although of little proved value in dengue control.[4] Multiple serotypes of dengue virus continue to spread worldwide, while *A aegypti* resistance to temephos increases.[5-8]

Failure of vertically managed pesticide distribution has increased interest in primary healthcare approaches, with community engagement to reduce mosquito breeding sites. A 2007 systematic review reported weak evidence that this might control dengue;[9] none of the studies reviewed used clustered designs, however, despite recognition that mosquitoes fly between households and community mobilization is a group phenomenon. Subsequently, cluster randomized trials in Cuba and India showed impact of community mobilization on vector indices,[10 11] as did community volunteers in Thailand.[12] A 2011 review of 22 studies of education for community dengue control confirmed effectiveness in reducing entomological indices, though no study measured infection with dengue virus.[13] A recent review of 14 studies of *Bacillus thuringiensis israelensis* reported evidence of impact on the number of *Aedes* but again little evidence of impact on risk of dengue.[14] The literature suggests that non-pesticide measures should prevent dengue, but there is little direct evidence to confirm health benefits.

A four year feasibility study in Managua developed a non-randomized pesticide-free intervention (10 intervention and 20 control clusters, 132 houses/clusters, and 3300 children aged 3-9). Community volunteers used serological and entomological evidence to engage residents in interventions: household visits, demonstration of mosquito eggs and larvae/pupae, and simple tools for elimination of breeding sites. All 5596 households allowed examination of vector reservoirs around the home; all but 21 answered questions about recent illness. Intervention communities showed a lower risk of dengue.[15] Nicaragua's history of community mobilization, however, raised issues of relevance to other settings.

This cluster randomized controlled trial assessed the added value of evidence based community engagement in dengue prevention—in Managua by scaling up already tested strategies, in southern Mexico by implementing these strategies in environments less hospitable to them, and in both places in a random sample of census enumeration areas (fig 1).

Methods

The hypothesis was that informed community mobilization adds effectiveness to government run dengue control programs in Managua, Nicaragua, and the coastal regions of Mexico's Guerrero state.[16] Specific objectives were to determine cluster level entomological and serological status; translate these results into action against dengue through dialogue with participating communities; and identify cluster level real life impact of informed community mobilization.

After a baseline study in a random sample of census enumeration areas in Nicaragua and Mexico, we randomly allocated one half to receive the intervention. These clusters followed a protocol to engage communities in dengue prevention alongside the usual government dengue prevention activities for one year. We measured the impact during a second study at the end of the following dengue season.

Patient involvement

Patients who had previously had dengue and their families were not involved in setting the research question or the outcome measures, but they were they intimately involved in design and implementation of the intervention. Patients and their families were also central to dissemination of the baseline information, which helped to motivate community involvement during and beyond the study.

Participants

Participants were all residents in a stratified last stage random sample of enumeration areas[17] (the geographic area canvassed by one census representative) from the latest censuses, with 60 clusters in Nicaragua and 90 in Mexico. We included all children aged 3-9 whose parents consented to them providing a saliva sample. The Guerrero sample covered three coastal regions (Costa Grande, Acapulco, and Costa Chica), stratified for population size and dengue prevention programs. The Nicaraguan sample came from the capital city of Managua, where a quarter of the national population lives. This sampling frame excluded 17 wealthy enumeration areas, where residents typically make private security arrangements and do not participate in public health initiatives for the popular neighborhoods. Table A in appendix 1 shows baseline demographic, infrastructural, and socioeconomic factors that could influence dengue transmission.

Before the baseline surveys, we received permission from the mayoral office and community leaders. Individual consent was also read to every respondent, all of whom were told that they were free to decline to answer any question they opted not to answer. Parents gave individual consent for each child who contributed saliva samples. The interventions started with requesting permission from community leaders.

Interventions

Before randomization, interviewers returned entomology results to all households and individual serology results to parents of the children who had provided saliva samples for serological testing. All clusters continued the official government dengue control programs (monthly deposits of temephos sachets in water storage of all households and space spraying), and all participated in a baseline and follow-up trial survey.

Interventions covered self identified neighborhoods and were not confined to the 140 household impact assessment clusters within them. All intervention communities followed the same intervention protocol, initiating the community engagement through three protocol steps:

- The researchers asked permission from community leaders and engaged them in discussion of baseline evidence

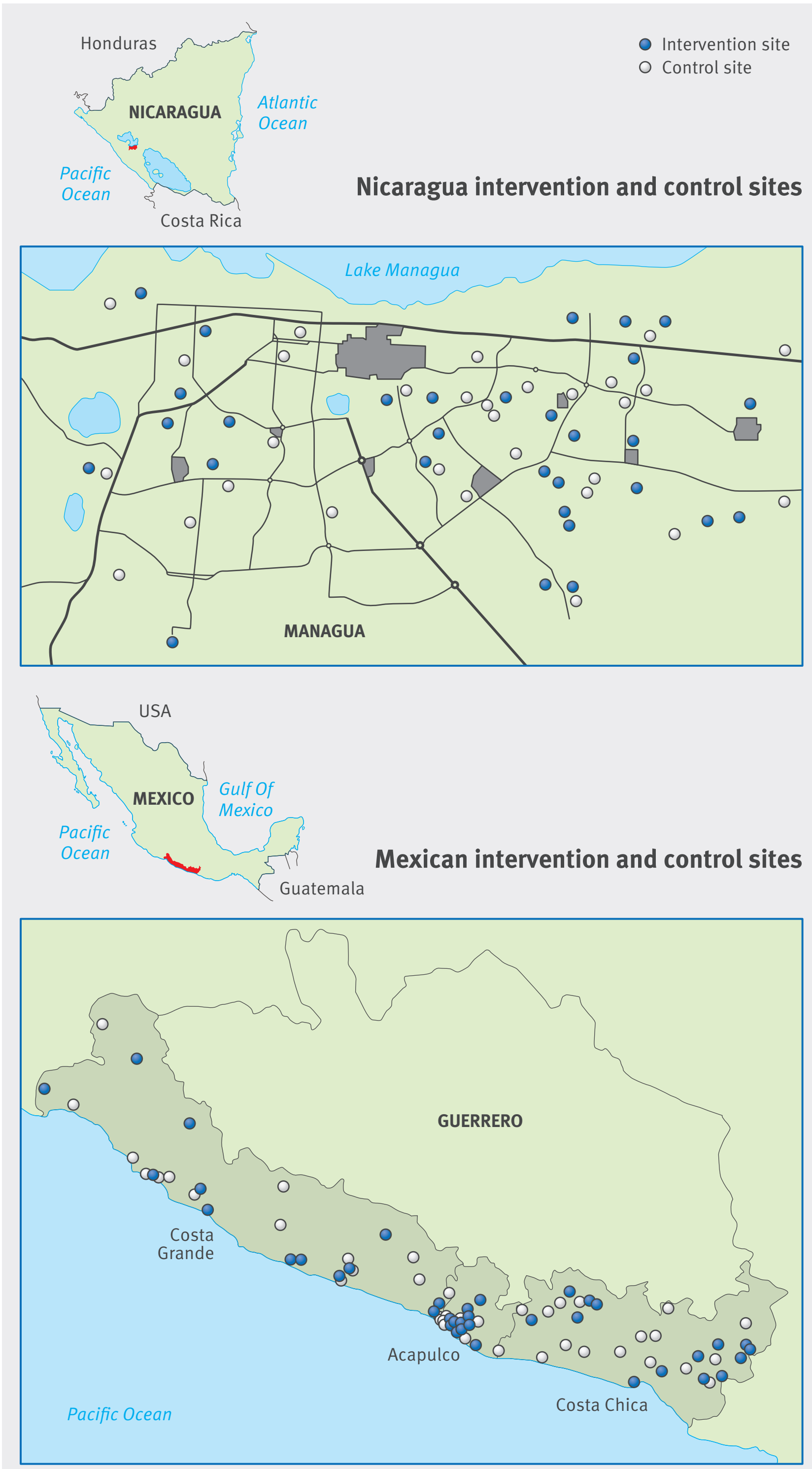

Fig 1 | **Areas covered by study of evidence based community mobilization for dengue prevention in Nicaragua and Mexico**

- Facilitators convened and ran intervention design groups—8-10 people, usually separately for men and women—to discuss survey results, cost implications, and specific prevention strategies in each community. The exact process for convening the groups varied from place to place, with some participants suggested by community leaders, some being key figures like school teachers, and some identified by door to door invitation. In Managua, facilitators were former volunteers from the feasibility study; in Mexico, they were recent university graduates in social sciences. Communities opted for a range of activities to share basic information on the mosquito life cycle and how to interrupt it (emptying, brushing/scrubbing the interior walls of, or covering receptacles hosting mosquito eggs or larvae); community events to raise awareness, like puppet shows and basketball tournaments; clean up campaigns focused on unoccupied and public premises; introduction of fish into water storage containers (Mexico only); and other activities listed in appendix 2
- Through local community leaders in Nicaragua and directly in Mexico, the research team invited volunteers (brigadistas) from participating communities to receive training as organizers and educators. In all intervention communities, brigadistas visited households and schools to show evidence of larval/pupal infestation in water receptacles, to inform households and schools of the mosquito's life cycle, and to counsel on ways to interrupt the cycle. Brigadistas also added interventions as their community work advanced (see appendix 2). In Nicaragua, brigadistas received no remuneration; in Mexico, they received allowances for travel, lunch, and child care on the days they worked.

Exchanges between countries informed by the Nicaraguan feasibility study sought commonality of function by assuring the same protocol to generate community led interventions rather than uniformity of the specific actions.[18] Mid-stream peer evaluation assessed fidelity to the intervention and dynamics of engagement and encouraged interaction among neighborhoods.

The baseline survey included an entomological survey in the dry season, paired saliva samples before and after the dengue epidemic, and one questionnaire related to dengue and one related to social capital/costs. The baseline survey took place between August 2010 and January 2011. The follow-up impact assessment likewise included an entomological survey in the wet and dry season, paired saliva samples before and after the dengue season, and one questionnaire related to dengue and one related to social capital/costs. In Nicaragua, this was from August 2012 to January 2013 and in Mexico from August to November 2012.

Sequence of steps—The baseline surveys and results from the paired saliva samples preceded, and provided stratifying data for, the randomization. Randomization was followed by the intervention, followed by the impact assessment. The baseline and impact assessments were each made up of two surveys to allow for collection of the paired saliva samples. Serological status from saliva samples was based on differences between the first and second sample. This also enabled vector assessments in the wet and dry season; we report only the dry season entomology assessment.

Timelines—Figure 2 summarizes the timings of the study.

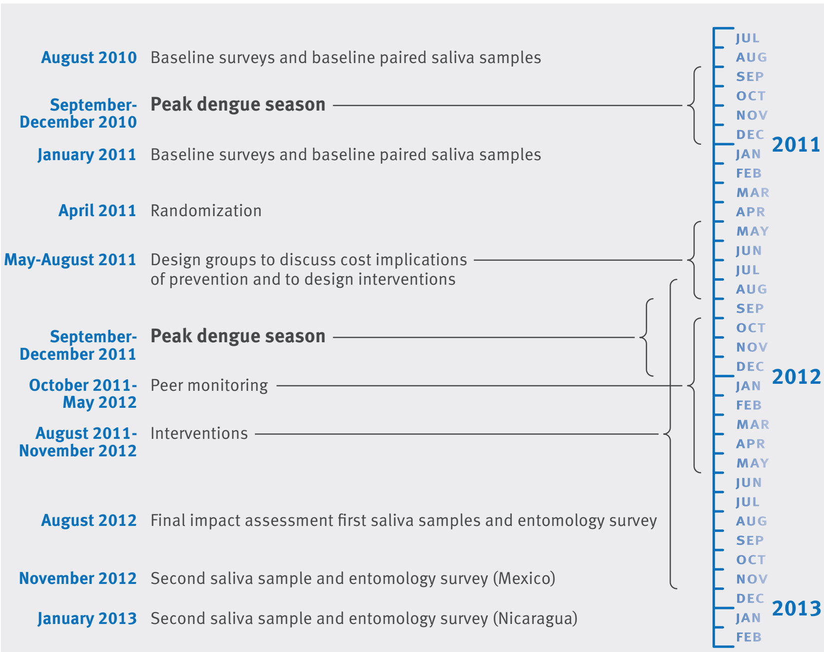

Fig 2 | **Timeline of study of evidence based community mobilization for dengue prevention in Nicaragua and Mexico**

Outcomes

The primary outcomes were cluster specific rates of dengue virus infection in paired saliva samples (before and after the 2012 dengue season) from children aged 3-9; reported cases of dengue (any age) in the past year; and entomological indices of *A aegypti* breeding sites. For recent dengue virus infection, during household visits the interviewer asked children to spit 0.5-2 mL of saliva into a plastic receptacle. Reference laboratories in Acapulco and Managua divided this sample into aliquots and stored them at −80°C until they could process paired samples side by side in an IgG capture enzyme linked immunosorbent assay (ELISA). Paired saliva samples collected before and after the dengue epidemic in 2010-11 were processed side by side in the laboratory. We shared these baseline results with the parents and used them to stratify clusters for the randomization. In the final impact assessment, another set of paired saliva samples was collected before and after the dengue epidemic in 2012-13 and processed side by side to determine the final outcome. In this trial, we used a 2× cut off for increase in dengue virus specific IgG units in saliva samples collected before and after the dengue season, based on a previous study.[19]

We analyzed evidence of infection as households with positive serology results, not individual infections. Quality control included procedures for duplicates and repeating discrepancies.[20] We limited serological status to young children because, as a large proportion in this age group has never had a dengue virus infection, we could detect new infections using our assay, which can get saturated by high titres before and after secondary infection. Previous serological studies by our co-authors in Managua showed that over 90% of children aged 10-12 have been exposed to one or more dengue virus serotypes.[21] In older age groups, still more people have immunity to one or more serotypes, and it is harder to detect incident secondary infections with our assay. The assay relied on non-invasive saliva samples to estimate incidence of infection in large numbers of participants (low refusal rate). We used self reported dengue as an outcome indicator because, notwithstanding its imperfect reliability, this does include all age groups. The funds and scope of the trial did not permit active surveillance to capture all cases of dengue confirmed by laboratory.

Dengue illness—Self reported cases of dengue were recorded from responses to a direct question about each household member in turn "Did this person suffer from dengue in the last year?"

Vector assessment—Entomology evaluators inspected indoor and outdoor containers, tires, flower vases, water barrels, wash basins, tarpaulins, and discarded containers. The impact assessment focused on household breeding sites; interventions also dealt with breeding sites in open lots and public spaces. Fieldworkers who were not part of the intervention used nets to collect all larvae and pupae from each container. Supervisors transported samples in labeled plastic bags to the respective entomology laboratories for identification. Entomological indices included *A aegypti* house index (households with larvae or pupae/households examined), container index (containers with larvae or pupae/containers examined), Breteau index (containers with larvae or pupae/households examined), and pupae per person (pupae found/number of residents). There was onebaseline collection in the dry season, and a final assessment in the wet and the dry season. We report here the final assessment in the dry season.

Per protocol secondary outcomes focused on information from face-to-face interviews regarding conscious knowledge about dengue and its prevention and control; attitudes (respondents who agreed to a direct question that temephos and fumigation are the best way to avoid mosquitoes/households interviewed); subjective norms (what neighbors do) and positive deviations from a negative norm; intention to change behavior in the future and to implement preventive action; agency (collective and individual self efficacy)—respondents who said communities can themselves control dengue/households interviewed; discussion—talk with neighbors about how to avoid mosquitoes or prevent dengue; action (interventions, practices)—households that purchased pesticides in the past month; and health literacy, resilience and social capital (see table 3). A separate study, now in progress, will report on the economic costs and implications for sustainability.

Randomization

Sequence generation—Each cluster was a census enumeration area. Computer generated random numbers allocated interventions in each stratum; strata comprised all eligible clusters in each country divided into region and, from the baseline survey, categories of risk of dengue virus infection in children aged 3-9 and vector indices.

Allocation concealment—Intervention status was disclosed once interventions began in both countries.

Implementation—A sampling statistician not engaged in the study conducted random selection from the population census and central random allocation of clusters to intervention.

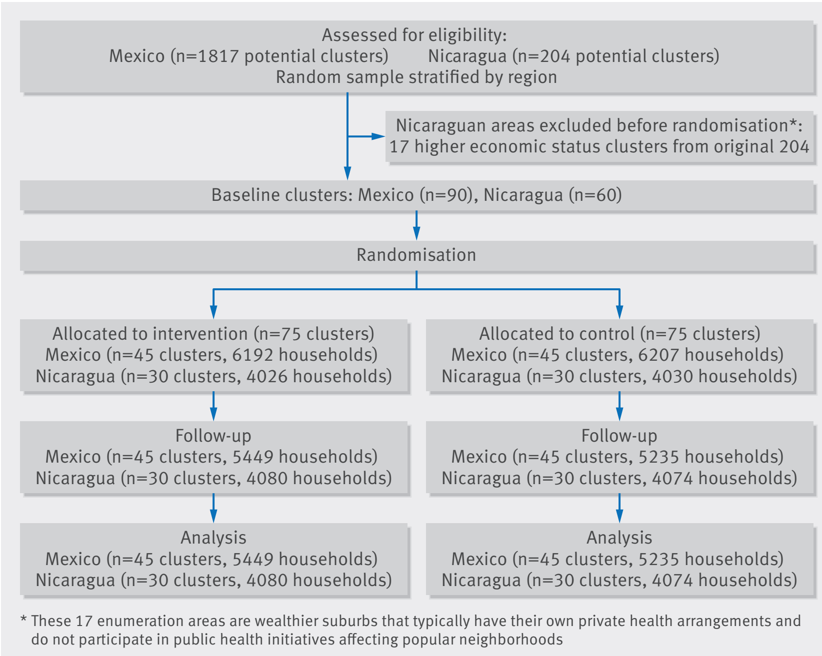

Fig 3 | **Identification and flow of clusters and households in study of community mobilization in Nicaragua and Mexico for dengue prevention**

Masking—Intervention efforts were obvious to residents in intervention sites, and some outcomes (like collective self efficacy) could be influenced by this knowledge. The main outcomes (serological evidence of recent risk of infection and entomological indices) are less susceptible to this bias. As far as possible, interviewers and entomological assessors in the follow-up survey were unaware of intervention status. Data operators were unaware of intervention status.

Estimates of sample size

The 2004-08 Managua feasibility study facilitated estimation of required sample size. Control communities showed serological evidence of recent dengue virus infection in children: 1.5% to 7.4% across 20 non-intervention clusters (intraclass correlation=0.18, estimated by dividing variance between clusters by total variance in the control group). Serology of 40 children in each of 150 clusters (75 clusters per arm) would detect a 33.3% reduction in risk of infection (4.5% to 3%) with 80% power at a significance level of 5%. These calculations assumed equal cluster size, homogeneous treatment effect, and a two sided test with cluster as unit of primary analysis in unmatched parallel groups. Calculations used the approach of Taylor and Bosch for parallel group cluster trials.[22]

Statistical methods

Data entry and security—Data operators ignorant of intervention status entered household responses twice, with verification of discordant entries from the original questionnaires. A data manager checked digitized data for logical errors.

Principal analysis—We used a *t* test in an intention to treat analysis of cluster specific rates.[23] We included in the analyses the two Nicaraguan intervention sites that declined to participate. Continuous variables in each site were proportions of children showing a more than twofold increase in IgG units between two samples from the same child before and after the dengue season, households with a reported dengue case, and thresholds of conventional entomological indices (above 0). We also used cluster as the unit analysis for our secondary outcomes—household responses to an administered questionnaire. We estimated relative risk reduction (RRR) as 1−relative risk, using variance of the relative risk (Delta method) to estimate confidence intervals. We estimated the number needed to treat (NNT) as the inverse of risk difference (RD) and intraclass correlation (ICC) by dividing the variance between clusters by the variance between and within clusters across the control series.[24]

Secondary analysis—Per protocol bivariate and then multivariate analysis evaluated impact (evidence of recent dengue virus infection in the household) of living in intervention sites in the context of other factors that might influence infection, mostly household responses to an administered questionnaire. These included temephos exposure (sachets found in water storage containers), household pesticide purchase, household water supply ("How often does your household receive water?"), baseline level of dengue virus infection, and sex of the respondent. We included all those significant at the 5% level (adjusted for cluster) in a generalized linear mixed model (GLMM) with country and cluster as random effects. We report the odds ratio and adjusted odds ratio. Planned subgroup analysis focused on geographic variations of the protective effect, especially population density (urban/rural) and the particular choices of intervention.

Missing data—The follow-up survey included new arrivals in both groups but did not follow those leaving. People who decline to respond might be less involved with dengue control, thus reducing the measured effect. We used Amelia II[25] to impute values for missing data with an expectation-maximization algorithm for the primary outcome household report of dengue illness. Estimates reconciled data from 10 imputed datasets with Rubin's approach[26] in the R package Zelig[27].

Software—CIETmap[28] is open source software with a Windows-like interface for the open source statistical programing language R.

Results

Participant flow

Figure 3 describes the numbers of clusters and participants completing the study protocol and analyzed for primary outcomes. There were no deviations from protocol.

Baseline data

Table 1 lists 2010-11 baseline results for individuals and clusters in intervention and control groups, showing similar risks of dengue virus infection in households with children aged 3-9 (around 9% in Mexico and twice that rate in Nicaragua), household reports of dengue in the past year (6% in Mexico and 9% in Nicaragua), and proportion of households positive for *A aegypti* larvae/pupae (16% in Mexico and 20% in Nicaragua).

Table 1 | Group and individual baseline data at random assignment to intervention and control in study of community mobilization (intervention) in Nicaragua and Mexico for dengue prevention. Figures are numbers (percentage)

	Mexico		Nicaragua	
	Intervention	Control	Intervention	Control
Individual and household rates at baseline				
Serology: households with evidence of recent dengue virus infection in children aged 3-9/ No of households contributing paired samples (%)	317/3331 (9.5)	259/3051 (8.5)	316/1747 (18)	300/1765 (17)
Self reported dengue illness: households with dengue/households surveyed (%)	400/6191 (6.5)	389/6207 (6.3)	330/4023 (8.2)	349/ 4024 (8.7)
House index: No of households with larvae or pupae/households surveyed (%)	1020/6192 (16.5)	1014/6207 (16.3)	798/4026 (20)	750 /4030 (19)
Collective self efficacy: respondents who believe community can prevent dengue on its own/households surveyed (%)	4716/6103 (77.3)	4650/6126 (75.9)	1991/3940 (51)	2131/3967 (54)
Purchased pesticide: households that purchased pesticide in past month/households surveyed (%)	2631/6155 (42.7)	2767/6170 (44.8)	2092/3931 (53)	2095/3955 (53)
Cluster factors at baseline*				
No of clusters	45	45	30	30
Risk of recent dengue virus infection: No of clusters with higher than country rate at baseline	15 (33)	17 (38)	13 (43)	14 (47)
Self reported dengue cases in past year: No of clusters with higher than country rate at baseline	18 (40)	19 (42)	14 (47)	13 (43)
House index: No of clusters with higher than country rate at baseline	18 (40)	22 (49)	12 (40)	10 (33)
Collective self efficacy: No of clusters with higher than country rate at baseline	23 (51)	26 (58)	12 (40)	15 (50)
Purchased pesticide: No of clusters with higher than country rate at baseline	21 (47)	22 (49)	14 (47)	16 (53)

*Average country baseline rate for each factor defined as in upper half of table (for example, 9% of children in Mexico showed serological evidence of dengue virus infection). Lower half of table is proportion of clusters in intervention and control groups where average was higher than respective country baseline rate.

Numbers analyzed

The study included 85 182 residents in 18 838 households in 150 clusters (1414 (7%) declined). Some 9499 children in 6698 households contributed saliva samples for the impact estimation (37 (0.4%) declined), and evaluators examined 70 388 vector breeding sites (table 2).

Outcomes and estimation

Table 3 and appendix 3 show primary outcomes and confidence intervals for each group with cluster as the unit of analysis. Intervention clusters had significantly lower rates of all primary outcomes— risk of dengue virus infection in children aged 3-9 old (relative risk reduction 29.5%, 95% confidence interval 3.8% to 55.3%; number needed to treat 30, 95% confidence interval 20 to 59). Applied to our study population, this implies 33 young children per 1000 were spared increased levels of IgG across paired samples (absolute rate 11.3% in intervention children and 14.6% in control children, table 3). Intervention clusters also reported fewer dengue cases in the past year (24.7%, 1.8% to 51.2%; number needed to treat 71, 48 to 143). Applied to our study population, this implies 14 households per 1000 were spared having a case of dengue (absolute rates of 5.7% in intervention households and 7.1% in control households).

There were also significant reductions in *A aegypti* larvae and pupae in the intervention group, again with cluster as the unit of analysis. The relative risk reductions were 44.1% (95% confidence interval 13.6% to 74.7%) for a lower house index, 36.7% (24.5% to 44.8%) for the container index, 35.1% (16.7% to 55.5%) for the Breteau index, and 51.7% (36.2% to 76.1%) for fewer pupae per person. The numbers needed to treat were 17 (14 to 20) for the house index, 37 (35 to 67) for the container index, 10 (6 to 29) for the Breteau index, and 12 (7 to 31) for fewer pupae per person.

Table 3 shows these parameters in a cluster analysis, the effect size (absolute difference and relative risk reduction estimated as 1−relative risk), precision

Table 2 | Numbers of individuals and households available for follow-up in study of community mobilization (intervention) in Nicaragua and Mexico for dengue prevention

	Mexico		Nicaragua		
	Intervention	Control	Intervention	Control	Total
Clusters	45	45	30	30	150
Households interviewed	5449	5235	4080	4074	18 838
Mean (range) No of households per cluster	121 (72-155)	116 (61-163)	136 (126-152)	136 (132-140)	126 (61-163)
Residents involved	23 039	21 781	19 992	20 370	85 182
Mean (range) No of residents per household	4.3 (1-25)	4.2 (1-16)	4.9 (1-21)	5.0 (1-21)	4.5 (1-25)
Children aged 3-9 contributing saliva samples	2626	2230	2320	2323	9499
Households with saliva samples of children	1803	1563	1657	1675	6698
Mean (range) No of children providing samples per household	0.47 (0-5)	0.42 (0-5)	0.56 (0-7)	0.56 (0-7)	0.50 (0-7)
Mean (range) No of children providing samples per cluster	40 (12-94)	35 (11-72)	55 (38-75)	56 (29-73)	45 (11-94)
Vector breeding sites examined	21 988	21 088	13 545	13 767	70 388
Mean (range) No of breeding sites per household	0.15 (0-10)	0.24 (0-10)	0.22 (0-24)	0.33 (0-24)	0.23 (0-24)
Missing data:					
Households declined to participate	570	596	122	126	1414
Children declined to provide saliva sample	7	20	6	4	37
Children lost to follow-up second sample	269	325	142	141	877

(95% confidence interval), P value and degrees of freedom, and intraclass correlation coefficient. Table B in appendix 1 shows the cluster-specific rates used to compute these values. Table C in appendix 1 provides a mixed effects household level analysis with the intervention as the fixed effect and cluster as random effect.

Secondary outcomes

In a cluster analysis, residents in intervention clusters were more likely than those in control clusters to believe that communities can control dengue on their own and less likely to believe pesticides are the best way to deal with mosquitoes. Households in intervention clusters were also less likely to buy pesticide (table 3).

Per protocol secondary analysis with household as the unit of analysis investigated serological evidence of risk of dengue virus infection in children aged 3-9. Bivariate analysis identified several associations (table 4). In a multivariate analysis of these variables, with country and cluster as random effects, living in an intervention site (adjusted odds ratio 0.74, 95% confidence interval 0.59 to 0.93) and temephos in water containers (1.44, 1.20 to 1.72) remained in the final model (unadjusted odds ratio 1.49, 1.22 to 1.83; table 4). Temephos in household water containers was associated with higher levels of serological evidence of infection. Unadjusted data show 16.8% (238/1418) of households with temephos and 11.9% (613/5156) without temephos during the entomological assessment had at least one child with serological evidence of infection. To test if this might be explained by vector control authorities applying temephos disproportionately in households reporting dengue cases, we repeated the analysis of serological evidence in households reporting no known cases in the past year. This produced similar results (adjusted odds ratio 1.44, 1.19 to 1.73). A cluster adjusted household level analysis of control sites showed that, in households where the entomological assessment found temephos in water containers, people were significantly less likely to say they had participated in community activities to control dengue: 501/2222 households with temephos and 1870/6696 households without said they had participated (cluster adjusted odds ratio 0.75, 95% confidence interval 0.58 to 0.97).

Ancillary analysis

Per protocol subgroup analysis focused on regional differences, especially in rural communities. When we repeated the primary analysis for rural coastal communities (Costa Grande and Costa Chica regions of Guerrero, Mexico) across all intervention communities, 5.4% (72/1332) of households had a child showing serological evidence of

Table 3 | Cluster analysis for primary and secondary outcomes and intention to treat, with cluster as unit of analysis (risk difference (RD) across clusters, relative risk reduction (RRR), and intraclass correlation coefficient (ICC))*

	Mean in intervention clusters (n=75)	Mean in control clusters (n=75)	RD (95% CI)	RRR† (95% CI)	P value (df) for cluster *t* test	ICC‡
Primary outcomes						
Serology§: household evidence of recent dengue virus infection, children aged 3-9, ≥2× increase of IgG across paired samples	11.3%	14.6%	−3.3 (−4.9 to −1.7)	29.5 (3.8 to 55.3)	0.038 (148)	0.031
Self reported dengue illness: households reporting in past year/responding households	5.7%	7.1%	−1.4 (−2.1 to −0.7)	24.7 (1.8 to 51.2)	0.039 (148)	0.021
House index: houses infested with larvae or pupae/houses inspected	13.6%	19.6%	−6.0 (−7.1 to −5.0)	44.1 (13.6 to 74.7)	0.001 (148)	0.075
Container index: containers with larvae or pupae/containers inspected	5.3%	8.0%	−2.7 (−3.9 to −1.5)	36.7 (24.5 to 44.8)	0.001 (148)	0.078
Breteau index: containers with larvae or pupae/houses inspected	19.7%	30.2%	−10.5 (−17.6 to −3.4)	35.1 (16.7 to 55.5)	0.001 (148)	0.061
Pupae per person index: No of pupae/residential population ×100	9.2%	17.5%	−8.3 (−13.4 to −3.2)	51.7 (36.2 to 76.1)	0.001 (148)	0.068
Secondary outcomes (household responses to administered questionnaire)						
Conscious knowledge: recognize sample of larva and know its relevance (Mexico only)	98.4%	97.5%	0.9 (0.1 to 1.8)	1 (0.1 to 1.8)	0.059 (88)	0.097
Opinion of pesticides: agree (direct question) that temephos and fumigation are best way to avoid mosquitoes/households interviewed	80%	82%	−3.2 (−3.8 to −1.5)	−3.4 (−6.5 to −0.2)	0.018 (148)	0.029
Subjective norm: your neighbors believe it worthwhile to put time and energy into eliminating breeding sites in their homes (Mexico only)	70.6%	68.8%	1.8 (−0.1 to 3.8)	2.6 (−4.0 to 9.1)	0.43 (88)	0.066
Intention to change: do you plan to dedicate time and money each week to eliminate breeding sites (Mexico)?	81%	78.4%	2.6 (−1.0 to 6.3)	3.2 (−1.2 to 7.7)	0.158 (88)	0.071
Collective self efficacy: agree communities can themselves control dengue/households interviewed	48%	44%	4.7 (3.2 to 6.1)	9.6 (3.4 to 15.8)	0.002 (148)	0.030
Socialization/discussion: talk with neighbors about how to avoid mosquitoes	42%	39%	3.2 (−1.7 to 81)	7.5 (−3.5 to 18.6)	0.341 (148)	0.087
Purchased pesticide: households that purchased in past month/households interviewed	51%	55%	−4.0 (−5.9 to −3.0)	−8.8 (−15.4 to −1.2)	0.011 (148)	0.032
Social capital: neighbours in this street help one another out	63.2%	62.4%	0. 9 (−0.5 to 2.2)	1.3 (−4.4 to 7.1)	0.51 (148)	0.048

*Full cluster specific results for primary outcomes are provided in appendix 1 table B.
†RRR=1−RR.
‡ICC estimated for control group.
§Proportion of households with positive case, not total positive cases

Table 4 | Dengue virus infection and potential risk factors (increased IgG units across paired samples) in bivariate models adjusted for cluster*

	No (%) with evidence of infection	No (%) with no evidence of infection	OR (95% CI)
Intervention status of cluster:			
Yes	391 (11.3)	3069 (88.7)	0.74 (0.59 to 0.93)
No	474 (14.6)	2764 (85.4)	
Temephos found in household water storage during entomological assessment:			
Yes	238 (16.8)	1180 (83.2)	1.49 (1.22 to 1.83)
No	613 (11.9)	4543 (88.1)	
Purchase of insecticide:			
Yes	473 (13.2)	3119 (86.8)	1.06 (0.91 to 1.22)
No	387 (12.6)	2696 (87.4)	
Problems with water supply in response to question: "How often do you receive water":			
Yes	340 (12.7)	2331 (87.3)	0.97 (0.83 to 1.12)
No	524 (13.1)	3474 (86.9)	
Sex of informant:			
Male	119 (12.2)	860 (14.8)	0.92 (0.73 to 1.13)
Female	745 (13.1)	4960 (85.2)	
Prior levels of dengue virus infection (baseline serology, 2×increase in IgG units across paired samples):			
Low	474 (14.0)	2903 (86.0)	0.82 (0.65 to 1.03)
High	391 (11.8)	2930 (88.2)	
Region:			
Urban	668 (15.9)	3533 (84.1)	2.21 (1.87 to 2.64)
Rural	197 (7.9)	2300 (92.1)	
Country:			
Mexico	340 (10.1)	3026 (89.9)	0.60 (0.52 to 0.70)
Nicaragua	525 (15.8)	2807 (84.2)	

*In multivariate models (generalized linear mixed model) adjusted odds ratios (95% CI) were 0.74 (0.59 to 0.93) for living in an intervention site and 1.44 (1.20 to 1.72) for temephos found in water containers during entomological assessment.

infection compared with 10.7% (125/1165) in control communities (cluster *t* test=–2.949, 58 df, P=0.005).

Multiple imputation of non-respondents to question about recent dengue cases reconciled 10 datasets (1000 iterations each) to generate almost identical data to those from the original dataset (difference –0.012, 95% confidence interval –0.020 to –0.004).

Discussion

Principal findings

Informed community mobilization adds effectiveness to government run dengue control. The Camino Verde project reduced *A aegypti* larvae and pupae and protected against dengue virus infection. To the best of our knowledge, this is the first trial that used serological evidence of recent childhood infection and self reported dengue cases to show an impact of community mobilization on infection with dengue virus.

Our finding that temephos was a risk factor for infection with dengue virus in a prespecified supplementary analysis merits further comment. Reporting bias is unlikely as serological evidence of recent infection was invisible to respondents and health services alike. Consistency of the findings in households reporting no case of dengue in the previous year makes it difficult to explain by vector control programs placing the temephos in response to reported cases. Possibly the increased risk of infection results from a false sense of security engendered by knowledge of pesticide in water storage containers; this could demotivate temephos users from taking physical measures to deal with mosquitoes.

Strengths and limitations of the study

The serological methods using saliva samples were based on our previous community based study[19] that compared several serological assays and sample types to determine the best approach to detect incidence of dengue virus infection in paired saliva samples.

A large scale intervention could have a greater impact than we measured, as we returned serology and entomology results to all households before randomization; this probably mobilized intervention and control communities alike. If entomological evaluators knew the intervention status of communities and felt a vested interest, this could bias their assessment. An intensive government anti-dengue campaign in Managua during the impact assessment almost certainly reduced the contrast between intervention and control, as did inclusion of two non-participating clusters assigned to the intervention group. The public security situation in Mexico restricted access to intervention communities and limited community engagement. Exclusion of wealthy Nicaraguan communities precludes conclusions about this social segment.

Comparison with other studies

Our results are comparable with those in published randomized controlled trials of community participation and entomological indices.[10 11 29-32]

Conclusions and policy implications

The strong Nicaraguan history of community engagement facilitated success there, but the trial was also successful in Mexico, with quite different community dynamics. In both countries, CIET's strong background in community engagement likely favored success. Nevertheless, the Camino Verde approach might have wider relevance in a range of geographic, cultural, and security settings. We believe the next step is for governments in dengue-endemic countries to implement a similar approach.

We do not, however, expect community participation in dengue control to be easy or easily sustainable. The intervention protocol that engages leadership and community members in discussing evidence and defining local strategies is a promising starting point for a wide range of settings. Each site implementing the intervention in its own way has the advantage of local customization and strong community engagement.

Because of this, a leading question for future research is how best to integrate dengue control within primary healthcare. In contrast with current largely vertical programs distributing temephos or fumigating, this implies dengue control should be rebuilt with fuller community engagement, collaboration with schools, and operational integration with local/municipal services like water supply and garbage disposal.

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Transparency declaration: NA (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Data sharing: No additional data available.

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Appendix 1: Supplementary tables A-C

Appendix 2: Details of the Camino Verde intervention

Appendix 3: Primary outcomes and confidence intervals for each group with cluster as unit of analysis