VOLUME 00 NO 00

Systematic Review

Interventions for the control of *Aedes aegypti* in Latin America and the Caribbean: systematic review and meta-analysis

Ariel Esteban Bardach[1,2], Herney Andrés García-Perdomo[3], Andrea Alcaraz[1], Elena Tapia López[1], Ruth Amanda Ruano Gándara[1], Silvina Ruvinsky[4] and Agustín Ciapponi[1,2]

1 *Instituto de Efectividad Clínica y Sanitaria, Centro de Investigación de Epidemiología y Salud Pública, Buenos Aires, Argentina*
2 *Consejo Nacional de Investigaciones Científicas y Técnicas and Centro Cochrane, Buenos Aires, Argentina*
3 *Universidad del Valle, Cali, Colombia*
4 *Hospital de Pediatría "Pedro Garrahan", Ciudad Autónoma de Buenos Aires, Buenos Aires, Argentina*

Abstract

OBJECTIVE To determine the effectiveness and degree of implementation of interventions for the control of *Aedes aegypti* in Latin America and the Caribbean (LAC) as reported in scientific literature.

METHODS We searched MEDLINE, EMBASE, CENTRAL, SOCINDEX, and LILACS, for experimental and observational studies, economic assessments and qualitative experiences carried out in LAC from 2000 to 2016. We assessed incidence and morbimortality of *Aedes aegypti*-related diseases and entomological indices: Breteau (containers), House, and Pupae per Person. We used GRADE methodology for assessing quality of evidence.

RESULTS Of 1826 records retrieved, 75 were included and 9 cluster randomised clinical trials could be meta-analysed. We did not identify any intervention supported by a high certainty of evidence. In consistency with qualitative evidence, health education and community engagement probably reduces the entomological indices, as do the use of insecticide-treated materials, indoor residual spraying and the management of containers. There is low certainty of evidence supporting the use of ovitraps or larvitraps, and the integrated epidemiological surveillance strategy to improve indices and reduce the incidence of dengue. The reported degree of implementation of these vector control interventions was variable and most did not extend to whole cities and were not sustained beyond 2 years.

CONCLUSIONS We found a general lack of evidence on effectiveness of vector control in the region, despite a few interventions that showed moderate to low certainty of evidence. It is important to engage and educate the community, apart from achieving the implementation of integrated actions between the health and other sectors at national and regional level.

keywords Latin America, *Aedes aegypti*, public health, systematic reviews, meta-analysis

Introduction

Aedes aegypti is the mosquito that causes the propagation of diseases such as zika, dengue, chikungunya and yellow fever. This mosquito is present both in urban and forest environments, in almost all countries of the American continent except for Canada and Chile [1]. The most important macro-determinants for the development of the diseases are population density increase, poor health conditions in the urban areas, deterioration of the public health systems and lack of effective vector control programs, together with environmental factors such as rainfall levels and average temperatures [2].

Currently, 61 countries and territories globally report the active transmission of these diseases [3, 4]. In the last years their burden and impact in the region have increased, including a reappearance of yellow fever in Brazil [5]. In 2015, the Zika virus was introduced in Brazil and it rapidly spread all over the Americas. Since then, there has been a confirmed increase in the rates of microcephaly, placental failure, growth delays and foetal death related to Zika virus infection during pregnancy and an increase in the cases of Guillain-Barre syndrome. Thus WHO declared, on February 1, 2016, a major international public health emergency related to the Zika virus infection, and recommended an increase in surveillance and research activities [6]. Meanwhile there are approximately 50–100 million new cases of dengue and about 2500 million people living in endemic areas worldwide [7]. Throughout the year, low-level transmission has been observed, but most countries exhibit an epidemic pattern [8]. Our group published a systematic review on Dengue epidemiology in Latin America and the Caribbean (LAC) [9], which analysed the incidence trends of both classic and hemorrhagic dengue, mortality and direct health costs attributed to it between 1995 and 2010.

In the past, different programs for vector control introduced in Latin America included different approaches, some vertical and others decentralised [10]. The world strategy for the prevention and control of dengue has five main components: vector control, based on the principles of vector integrated management; active disease surveillance based on a comprehensive health information system; emergency preparedness; capacity development and training; and vector control research. The Pan-American Health Organization (PAHO) managed in the last 15 years an intensive program called Communication for Behavioral Impact (COMBI) [11] with the objective of ensuring a flow of timely and accurate information to the public. Capacity building was considered the main tool in this program for developing social mobilisation and communication activities focused on behavioral change. The current PAHO strategy is known as EGI-Dengue. Although facing many obstacles, such as lack of continuity, lack of validated behaviour indicators or support from ministries, the program succeeded in achieving health education goals in many countries. Another potential public health strategy is vaccination for the prevention of dengue in high-demand areas, which is currently in the planning stage.

With regards to yellow fever, vaccination is recommended for areas at risk of active transmission within the different countries in the region [12], although the current epidemic of yellow fever in the Americas so far does not involve *Aedes aegypti*. There are no recommendations for chikungunya [13].

Although there are many ongoing programs with significant resource allocation, no systematic reviews have been done so far to comprehensively synthesise performance of strategies in the LAC region. The purpose of this study was hence to collect information on effectiveness, cost-effectiveness of the vector control strategies [14] and implementation experiences as reported in scientific literature. This work was part of a wider mixed qualitative [15, 16] and quantitative research.

Box 1 Assessed *Aedes aegypti* control strategies

- Insecticide treated materials
- Insecticide-treated bednets, curtains, net screens
  - Use of larvicides in breeding sites
- Use of larvicides and adulticides
  - Outdoor fogging
  - Indoor residual spraying
- Lethal Oviposition Trap-Based Mass Interventions
- Container management/reduction
- General population health education
- Behavioral change
- Community engagement
- Media campaigns
- Training of health teams
- Intersectoral coordination
- Advocacy (informed influence activities on policy-makers from civil society)
- Integrated surveillance
  - Epidemiological or entomological surveillance as part of a control program
- Biological control of mosquitoes (Biogents): Use of other living organisms (insects [e.g. RIDL], fish, etc.)
- Mosquito coils / repellents
- House inspection

Methods

The report of this systematic review and meta-analysis of observational studies follows the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) [17] and the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) [18] guidelines. Also, it was registered in the PROSPERO (CRD42016038067) database of systematic reviews. The protocol for this work was published in the PAHO journal [14].

We performed a systematic search in several databases, including MEDLINE, EMBASE, CENTRAL, SOCINDEX and LILACS from January 2000 to September 2016 (see Appendix S1 for details on the search strategy). We included grey literature through personal contact with the main authors, and by means of generic internet searches. Moreover, we searched the websites of WHO, several NGOs, Google and Google Scholar, specific sites of health ministries for arboviruses, scientific societies, vector congresses, the ISOPS VIII International Symposium on Phlebotomine Sandflies, the Annals of the International Society for Infectious Diseases international congresses, the Pan American Dengue Research Network meeting repositories, the site of the EGI Dengue Integrated Management Strategy and grey literature databases such as Teseo (Spanish theses), Opengray and Sigle.

Experimental, quasi-experimental and observational studies, economic assessments and qualitative studies related to control interventions on diseases transmitted by the *Aedes aegypti* mosquito, such as dengue, zika, chikungunya and yellow fever were considered. Studies conducted since 1995, assessing the control strategies described in Box 1 were included. We excluded mathematic model reports without direct observation, and entomological or epidemiological surveillance studies that were not part of a wider vector control program.

Study selection and data collection

The study selection was made by means of EROS® (Early Review Organizing Software, Institute for Clinical Effectiveness and Health Policy [IECS], Buenos Aires), a web platform designed to facilitate the execution of systematic reviews [19]. We included articles from any epidemiological design, from LAC countries, reporting about the effectiveness or degree of implementation of vector control interventions of any kind. Independent researchers, in pairs, reviewed all identified studies by title and abstract, and then analysed the full text of all selected articles that fulfilled the above-mentioned inclusion criteria. Disagreements were resolved by consensus within the review team. If the data of the included studies were considered to be unclear or insufficient, the authors were consulted.

We used a previously piloted web-based spreadsheet to compile the information. One reviewer extracted the data from the included studies, and another verified them. The following data were included: Continent and country; publication date; effectiveness related to vectoral indices; intervention implementation level and type; type of epidemiological design of the study; rural or urban environment; special population groups (pregnant women, workers) and type of sampling (probabilistic or not).

The outcomes under consideration were: incidence and morbimortality of *Aedes aegypti*-related diseases, larval indices for monitoring the effect of control strategies including Breteau, House index and Pupae per Person index, and degree of implementation or coverage levels by jurisdiction. These density indices are globally the most used in surveillance. We also assessed other vectoral indices such as recipient productivity, adult population estimation and ovitrap positivity rate. Finally, we considered general knowledge of the population on vector control, and the programmatic costs and cost-effectiveness data whenever available.

Risk of bias assessment

With regards to the risk of bias assessment of observational studies, we used a tool based upon the verification list STROBE [20], two methodological documents, Sanderson *et al.* [21] and Fowkes and Fulton [22]. This tool considered four major criteria (study participant selection methods, methods of exposure measuring and variable results, methods to control the confounding factors and comparability between the groups) and two minor criteria (statistical methods, excluding confounding and conflict of interest) (see Appendix S2). We used the Cochrane Handbook to assess the quality of the evidence from clinical trials, and quasi-experimental studies were assessed with the EPOC group tool of Cochrane [23]. In order to assess the quality of economic evaluations, we used the tool proposed by Drummond *et al.* [24] and for qualitative studies, the Mays *et al.* checklist [25]. Two independent reviewers assessed the methodological quality of all included studies. Discrepancies were resolved by consensus of the whole team. Finally, to assess the quality of evidence provided by each category of interventions, we used the GRADE methodology [26]. Briefly, the GRADE quality of evidence can be High, Moderate, Low and Very Low. High quality means that further research is very unlikely to change our confidence in the estimate of effect; moderate quality refers to further research likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality implies further research very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low quality means that we are very uncertain about the estimate.

Statistical analysis

We used simple descriptive statistics when it was not possible to calculate association measurements. Meta-analyses were carried out for analytic studies by using Odds Ratio (OR) and Relative Risks (RR), with their corresponding Confidence Intervals (CI). Additionally, we utilised the method of the inverse of the generic variance in order to combine different effect measurements. To perform these analyses, we used RevMan version 5.3. A DerSimonian-Laird random effect model was selected, taking into account potential differences in methods, result measurement tools and populations as possible sources of heterogeneity [19], assessed by means of the I^2 statistic. We planned publication bias analyses by means of funnel graphs, if the number of studies selected for meta-analysis was at least an arbitrary number of ten. Sub-group analyses considered *a priori* were: area of infestation by mosquitoes by aedic index; flavivirus disease incidence rate and classification of the country's income level according to the World Bank classification.

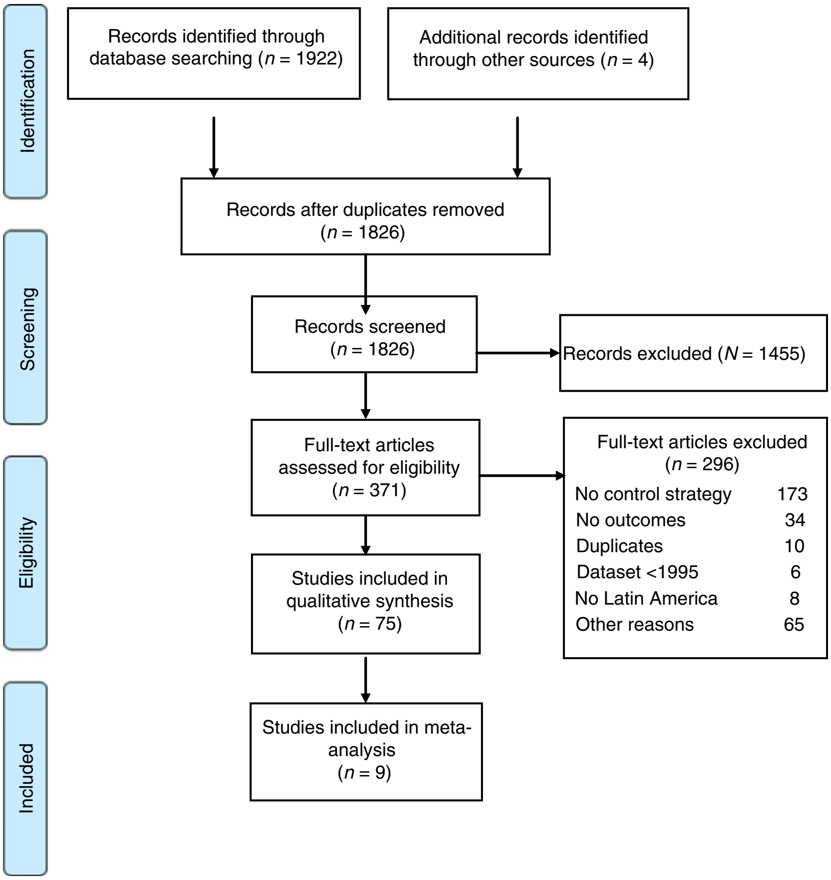


Figure 1 Study flow diagram.

Results

The search strategy yielded 1926 studies in the databases described. Figure 1 shows a flowchart of the selection process. Of the 75 studies included, which met the inclusion criteria for data synthesis, 51 were quantitative with varied epidemiological designs and 24 were of a qualitative-type. The most frequent reason for exclusion was the lack of sufficient description of the implemented control strategies. A total number of nine cluster randomised controlled trials (RCTs), of 15 relevant trials, could be meta-analysed. Most epidemiological studies were from Cuba (*N* = 11), Brazil (*N* = 10), Colombia (*N* = 6), Mexico (*N* = 4), Peru (*N* = 4) and multiple countries (*N* = 4) (Table 1). Other countries represented were Argentina, Costa Rica, Guatemala, Honduras and Puerto Rico. Main characteristics and results are shown in Table 1.

Regarding the methodological quality and bias risk, of the 51 quantitative studies included, 15 used a cluster RCT design; nine were non-randomised controlled field trials; four were interrupted time-series; 10 were before-after studies, six were descriptive or ecological observational studies, and seven were economic evaluations. In Appendix S3, a graphical report of the methodological quality of the studies identified can be found, according to their epidemiological design. RCTs are of moderate or low methodological quality in most domains explored, except for the domain related to blinding of evaluators, where the risk of bias was generally low. In non-randomised clinical trials, the risk of bias was generally high in most domains, except for incomplete or selective reporting of data and conflicts of interest. Interrupted time series showed a moderate risk of bias in most domains, except for how to address the effects of secular trends, where bias risk was high. Before/after studies lacked description of some domains, such as baseline measurements or of those characteristics of studies used as control and showed low risk of information bias but entailed relatively moderate detection bias. Qualitative studies showed a low-to-moderate risk of bias, except for the process of research and sampling, where a high risk of

Table 1 Characteristics of the studies identified in Latin America and the Caribbean about *Aedes aegypti* control strategies

Country	Year of publication	Reference	Study design	Type of intervention	Participants	Main outcomes
Argentina	2003	Masuh *et al.* (2003) [27]	Simple before-after	Use of insecticides (larvae and adults) in the field	Colonia Delicia, Misiones. 4750 inhabitants	Breteau Index, House Index
Argentina	2008	Orellano *et al.* (2008) [28]	Economic assessment	Cost-effectiveness of different interventions	Economic model (Decision tree, with hypothetical interventions)	Cost-effectiveness of adult mosquito control intervention using fumigation together with actions to control immature forms
Argentina	2009	Gurtler *et al.* (2009) [29]	Simple before-after	Larvicides, source reduction, home inspections	Clorinda, northeastern Argentina. 1808 participants	Breteau index, House index. Dengue incidence
Brazil	2008	Regis *et al.* (2008) [30]	Controlled before-after	Larvicides and adulticides in the field	Recife city. General population	Ovitrap index
Brazil	2008	Varjal de Melo Santos (2008) [31]	Simple before-after	Ovitraps	Moreno, Pernambuco. 56 650 inhabitants	Number of ovitraps
Brazil	2009	Silva *et al.* (2009) [32]	Non-randomised clinical trial	Trap-based mass interventions	Campo Grande, Rio de Janeiro state	Number of eggs or larvae found (in %, in traps)
Brazil	2009	Pessanha *et al.* (2009) [33]	Ecological study	National control plan (Information campaigns, epidemiological surveillance, vector reduction)	National	Number of municipalities with an incidence of dengue of more than 100/100 000 and number of municipalities with a post-intervention dengue fatality rate greater than 1%
Brazil	2011	Luz *et al.* (2011) [34]	Economic assessment	Adulticides and larvicides in the field	Economic model	Costs
Brazil	2013	Regis *et al.* (2013) [35]	Non-randomised clinical trial	Routine control measures (bimonthly application of temephos; the “Dengue Day” annual campaign; use of insecticides (adulticides)	Pernambuco	Number of larvae
Brazil	2014	Maciel-de-Freitas *et al.* (2014) [36]	Interrupted time series	Epidemiological surveillance as part of a control program	Boa Vista, Roraima. Nearly 285 000 inhabitants	Breteau index, House index
Brazil	2014	Macoris *et al.* (2014) [37]	Cross-sectional	Adulticides and larvicides in the field	Cities of Sao Paulo state (Barretos, Campinas, Marília, Ribeirao Preto, Santos and Sao Jose do Rio Preto)	Breteau index

Table 1 (*Continued*)

Country	Year of publication	Reference	Study design	Type of intervention	Participants	Main outcomes
Brazil	2014	Degener *et al.* (2014) [38]	Cluster RCTs	Biogents Sentinel traps (BGS)	City of Manaus. 12 clusters. 1487 houses	Reduction in the *Aedes aegypti* population density by questionnaire to inhabitants. Serological survey
Brazil	2015	Brazil (2015) [39]	Cross-sectional	Epidemiological surveillance as part of a control program	42 locations in the city of Gama	Number of eggs
Brazil, Colombia, Ecuador, Mexico, Uruguay	2016	Alfonso-Sierra *et al.* (2016) [40]	Economic assessment	Cost-effectiveness of different interventions	Fortaleza (Brazil), Girardot (Colombia), Machala (Ecuador), Acapulco (Mexico) and Salto (Uruguay).	Costs
Colombia	2002	Romero-Vivas *et al.* (2002) [41]	Record-Surveillance	Covers for soaked containers	Puerto Triunfo, Antioquia	Reduction of containers
Colombia	2010	Pacheco-del Coral *et al.* (2010) [42]	Cross-sectional	Epidemiological surveillance as part of a control program	La Dorada. 228 people, heads of household	Presence of the immature vector (rapid sweeping method), and adults (active collection)
Colombia	2010	Cáceres-Manrique *et al.* (2010) [43]	Non-randomised clinical trial	Community engagement	Bucaramanga four neighborhoods with high incidence of dengue.	Knowledge about the mode of transmission, warning signs, timely care and adequate management of patients and environmental management to prevent the spread of the disease to co-habitants
Colombia	2014	Alarcon (2014) [44]	Controlled before-after	Reduction of reservoirs in the field	Two neighbourhoods of the Municipality of Apartado and 2 of Carepa	Breteau index
Colombia	2014	Ocampo *et al.* (2014) [45]	Simple before-after	Adulticides and larvicides in the field	Guadalajara de Buga	Incidence of dengue
Colombia	2014	Quimbayo *et al.* (2014) [46]	Non-randomised clinical trial	Ovitraps	Medellin Colombia, Aranjuez neighbourhood	Number of larvae emerged from ovitraps
Costa Rica	2003	Perich *et al.* (2003) [47]	Cluster RCTs	Adulticides and larvicides in the field	Costarena city, two neighborhoods	Mortality of adult mosquitoes

Table 1 (*Continued*)

Country	Year of publication	Reference	Study design	Type of intervention	Participants	Main outcomes
Costa Rica	2009	Marín Rodríguez *et al.* (2009) [48]	Simple before-after	Management of reservoirs in the field	Huetar Atlantica Region, Province of Limón, which is divided into six counties: Pococí, Siquirres, Guácimo, Matina, Limón and Talamanca	Breteau index, House index and container index
Cuba	2007	Toledo *et al.* (2007) [49]	Controlled before-after	Community engagement	Santiago. 20 neighborhoods	In the experimental areas, the processes, findings and entomological outcomes were monitored. In the control areas, only the information about entomological indicators was collected
Cuba	2007	Baly *et al.* (2007) [50]	Economic assessment	Health education	Santiago de Cuba City. Economic assessment	Program costs. Process indicators
Cuba	2009	Vanlerberghe *et al.* (2009) [51]	Cluster RCTs	Community engagement	32 clusters consisting of 500 houses and 2000 inhabitants in Guantanamo	Breteau index
Cuba	2009	Sanchez *et al.* (2009) [52]	Non-randomised clinical trial	Epidemiological surveillance as part of a control program	Municipality of Playa, northwest of the city of Havana	Questionnaire to assess people's involvement in the decision-making, implementation and evaluation of dengue control activities Routine entomological surveillance data collected by the National Vector Control Program. Breteau Index
Cuba	2009	Baly *et al.* (2009) [53]	Economic assessment	Cost-effectiveness of different interventions	Guantanamo	Program costs.
Cuba	2011	Toledo *et al.* (2011) [54]	Cluster RCTs	Insecticide-treated bednets and curtains	Guantanamo. 12 clusters (500 homes approximately)	House index

Table 1 (*Continued*)

Country	Year of publication	Reference	Study design	Type of intervention	Participants	Main outcomes
Cuba	2011	Castro (2011) [55]	Cluster RCTs	Entomological surveillance as part of a Control Program	La Lisa, Havana. 16 intervention clusters (389 houses)	Breteau Index, engagement, knowledge, perception and behaviour
Cuba	2012	Sanchez *et al.* (2012) [56]	Non-randomised clinical trial	Health education	Municipality of Playa, northwest of the city of Havana	Container Index. Breteau Index.
Cuba	2012	Baly *et al.* (2012) [57]	Economic assessment	Health education	Guantanamo	Entomological indicators: Household index Production of the *Aedes* control program: houses inspected/treated. Health services: number of fever cases detected, laboratory tests carried out, hospitalised patients. Hospital indicators: number of admissions due to dengue, number of discharges, average length of stay, number of diagnostic tests performed
Cuba	2015	Toledo *et al.* (2015) [58]	Cluster RCTs	Insecticide-treated bednets and curtains	Guantanamo. 12 clusters of 500 houses each	House Index
Cuba	2015	Baly *et al.* (2015) [59]	Economic assessment	Insecticide-treated bednets and curtains	Guantanamo	Costs
Guatemala	2012	Rizzo *et al.* (2012) [60]	Cluster RCTs	Entomological surveillance as part of a Control Program	Poptun. 10 experimental clusters and 10 control clusters. 2357 houses	House index
Honduras	2004	Montes *et al.* (2004) [61]	Non-randomised clinical trial	Educational intervention in schools to promote healthy environments, with proper reservoir management	Comayaguela. Four schools, two experimental and two control	Breteau Index, House index, Reservoir index

Table I (*Continued*)

Country	Year of publication	Reference	Study design	Type of intervention	Participants	Main outcomes
Honduras	2012	Montes *et al.* (2012) [62]	Simple before-after study	Community education. 2-day training course for teachers and students.	Comayaguela. Teachers and students. 10 marginal communities. 6740 households and 36 800 inhabitants	Breteau index, House index, Reservoir index
Mexico	2002	Espinoza-Gomez *et al.* (2002) [63]	Cluster RCTs	Use of insecticides (larvae and adults) in the field	Colima. 187 houses grouped into 4 blocks	Number of positive containers per house
Mexico	2013	Lorono-Pino *et al.* (2013) [64]	Cluster RCTs	Curtains and tulle screens soaked in insecticide	Mérida. East, South sub-areas	Breteau Index, House Index, Reservoir Index
Mexico	2015	Che-Mendoza *et al.* (2014) [24]	Cluster RCTs	Curtains and tulle screens soaked in insecticide	City of Renacimiento, Acapulco	Infestation index
Mexico	2015	Manrique-Saide *et al.* (2015) [65]	Cluster RCTs	Community engagement	Acapulco. 20 clusters	Overdispersion index
Mexico and Venezuela	2006	Kroeger *et al.* (2006) [66]	Cluster RCTs	Insecticide-treated bednets and curtains	Veracruz and Trujillo	Breteau index, House index
Mexico, Nicaragua and Mexico	2015	Andersson *et al.* (2015) [67]	Cluster RCTs	Community Engagement – Reduction in reservoirs	60 clusters in Nicaragua and 90 in Mexico. In Mexico, the population is from Costa Grande, Acapulco and Costa Chica. In Nicaragua, the population is from Managua	Specific dengue infection rate (saliva samples) in children aged 3–9 years. House, Container, Breteau and Pupae per Person Indices
Peru	2002	Machaca *et al.* (2002) [68]	Record-Surveillance	Reduction in reservoirs in the field	City of Sechura	Breteau index
Peru	2012	Astete *et al.* (2012) [69]	Non-randomised clinical trial	Ovitraps	Iquitos. 2800 households	Breteau index
Peru	2012	Wesson *et al.* (2012) [70]	Non-randomised clinical trial	Lethal Ovitraps	Iquitos. Two comparable neighbourhoods with 2500 inhabitants each	Incidence of dengue
Peru	2016	Paredes-Esquivel *et al.* (2016) [71]	Interrupted time series	Residual indoor spraying	Iquitios. 36 households	Breteau index. House index Container index

Table 1 (*Continued*)

Country	Year of publication	Reference	Study design	Type of intervention	Participants	Main outcomes
Puerto Rico	2014	Barrera *et al.* (2014) [72]	Controlled before-after	AGO traps	La Margarita – Villodas. Two communities, one experimental (AGO trap) and one control	Breteau index
Venezuela	2003	Vivas *et al.* (2003) [73]	Non-randomised clinical trial	Health education	Girardot. Nine schools	Knowledge about dengue
Venezuela	2011	Vanlerberghe *et al.* (2011) [74]	Simple before-after	Insecticide-treated bednets, curtains and covers	Valera, Venezuela and one port city of Thailand	Collection and use of soaked tulle curtains and soaked tulle covers
Venezuela	2011	Vanlerberghe *et al.* (2011) [75]	Simple before-after	Insecticide-treated bednets and curtains and container covers	Trujillo. 10 clusters (five urban + five suburban neighbourhoods of 300–600 households)	Breteau index. Pupae index
Venezuela, Mexico, Peru, and other countries	2009	Tun-Lin *et al.* (2009) [76]	Cluster RCTs	Insecticides for indoor use, reduction in reservoirs, health team training	Venezuela, Mexico, Peru, Kenya, Thailand, Myanmar, Vietnam and Philippines	Breteau index. Pupae index.

bias was frequent. In health economic evaluations, the risk of bias was moderate, in general. Differential adjustment by time and characterisation of uncertainty of costs and health consequences were the domains with the worst performance; in general, the rest of the domains showed moderate-to-low risk of bias. Finally, in observational studies, the risk of bias was globally moderate, with a worse performance in the domain of control of confounders. Appendix S4 shows the characteristics and main findings for the remaining 24 qualitative research studies.

Effectiveness of interventions

Insecticide-treated materials. Five cluster RCTs that evaluated insecticide-treated materials (ITM) were identified [58, 60, 65, 66, 76, 77], two of them from the same experience in Cuba [65, 77]. Regarding treated bednets and/or curtains, a non-significant reduction in the Breteau Index was observed after the evaluation period (Risk Difference −5.00; CI 95%: −11.69 to 1.69; sub-studies = 2 (66)), similar to the House Index (Mean Difference, inverse variance, of −0.04; CI 95%: −0.14 to +0.06; studies = 1 (58)). As for treated water covers, Tun-Lin *et al.* [76] in Venezuela reported that the BI showed a non-significant reduction (Risk Difference 0.84; CI 95%: −8.94 to 10.62) and the Pupae per person index (PPI) showed an also non-significant OR of 0.98; CI 95%: 0.47–2.02. Considering both types of ITMs in combination, the PPI showed a non-significant reduction of 0.84 CI 95%: 0.61–1.16; studies = 3 [60, 76, 77]), although Che-Mendoza *et al.* [77]. found statistically significant evidence of reduction in the House Index (OR 0.44 CI 95%: 0.26–0.74).

Acceptance for interventions was high in Venezuela and Mexico, with more than 87–95% of respective households in the cities with interventions using treated curtains, and to a lesser extent, water jar covers. Similarly, a high coverage of the population was achieved in the Guatemala study by Rizzo *et al.* [60]. The effect of ITMs lasted at least 24 months in Mexico as reported by Che-Mendoza *et al.* [77], but dropped to 50% in the Venezuelan study by Tun Lin [76]. Two large quasi-experimental studies conducted in Venezuela [74, 75] reported similar results (Table 2 of non-randomised studies).

Table 2 Key findings of non-randomised studies

Country	Study	Design	Methods	Interventions	Results
1. Insecticide-treated bednets and curtains					
Venezuela and Thailand	Vanlerbergue *et al.* (2011)	Simple before-after	A baseline survey was carried out. A 6-month follow-up was done after the distribution of the tools with a household survey in a random sample of 782 houses. In 2009, 22 months later, these houses were revisited	Treated curtains and water jars	The use of insecticide-treated materials was 76.7% in Venezuela. In the second phase, the use decreased to 38.4% in Venezuela and 59.7% in Thailand. Short-term use was determined by the perceived effectiveness (OR Venezuela 13.0 95% CI 8.7–19.5; OR Thailand 4.9 95% CI 3.1–7.8)
Venezuela	Vanlerbergue *et al.* (2011)	Simple before-after	Insecticide-treated materials (PermaNet) were distributed to 10 groups (5 urban + 5 suburban neighbourhoods of 300 to 600 households, with medium to low socioeconomic status, with at least 50% of resident population). More than 4000 households in Trujillo, Venezuela were compared with untreated areas of both municipalities	Treated curtains and water jars	The percentage of > 1 soaked curtain in urban areas was 79% and in suburban areas, 75% but it decreased to 32% and 39%, respectively after 18 months. Before the intervention, BI was 8.5 in urban areas and 42 in suburban areas, and PPI was 0.2 and 0.9, respectively. BI decreased 55%, both in urban and suburban areas. Incidence Risk Ratio 0.98 95% CI 0.97 – 0.99. Covers reduced the infestation levels in at least 50%
2. Health education and community engagement					
Colombia	Cáceres Manrique *et al.* (2010)	Non-randomised clinical trial	Four high-incidence neighbourhoods were included: Two received intervention and two served as control. Home visits were made, research about knowledge, practice and appropriation or “empowerment” of control measures was carried out, breeding sites were identified, and education was provided.	Training of community leaders	Difference in knowledge about symptoms were as follows: bodily pain ($P = 0.000$), abdominal pain ($P = 0.024$), characteristics ($P = 0.008$) and reproduction cycle of the mosquito vector ($P = 0$); in pool washing practices ($P = 0.007$), spraying ($P = 0.008$), use of bednets ($P = 0$), consulting a physician ($P = 0.004$), participate in meetings ($P = 0$), prevention methods ($P = 0.013$), willingness to lead anti-mosquito campaigns ($P = 0.009$), and to get help for programs ($P = 0.016$). There was a decrease in larval rates from 20% to 15.9% in both groups. The difference in prevalence of dengue was 4.8% in the experimental group and 6.7% in control ($P = 0.065$).

Table 2 (*Continued*)

Country	Study	Design	Methods	Interventions	Results
Cuba	Toledo *et al.* (2007)	Controlled before-after	The intervention phase was conducted in 2 years. Two locations with high *Aedes* infestation levels were selected. 20 family doctors with their catchment neighbourhoods were randomly selected as experimental groups and, also, controls were identified	Community engagement	At household level, the containers identified decreased from 49% to 2.6% between 2000 and 2002. There was a decrease of 75% in the absolute number of positive containers and a decrease of 1.23% to 0.35 in the House Index
Cuba	Sánchez *et al.* (2012)	Non-randomised clinical trial	A longitudinal assessment was conducted in two dengue epidemics. The first stage focused on strengthening intersectoral coordination and was started in 2000. Later, in 2003, the community was empowered in the middle of the experimental area	Health education: mixed intervention: Educational, entomological surveillance and use of larvicides	Differences in the BI between intervention and control areas remained significant until December 2002, although for the next 2 years no differences were observed
Honduras	Montes *et al.* (2004)	Non-randomised clinical trial	Educational intervention was delivered in schools to promote healthy environments, with proper reservoir management. It involved four schools, two experimental and two controls	Community education	The House Index, 23.4 *vs.* 26.5, and the Breteau Index, 30.5 *vs.* 38.1, were lower in the experimental communities, although not statistically significant. In the experimental schools, a significant increase in the knowledge of students and teachers was observed
Honduras	Montes *et al.* (2012)	Simple before-after	Teachers and students in 10 marginal communities, including 6740 households and 36 800 inhabitants. A 2-day training course was conducted for teachers and students, which included water and solid waste management.	Community education	The House Index, 29.9 *vs.* 7.8, and the Breteau Index, 64.5 *vs.* 16.7, were lower before the intervention. The behavioural change and the reduction in larval indices improved in most of the schools
Venezuela	Vivas *et al.* (2003)	Non-randomised clinical trial	Nine schools were selected; three classrooms were set up, and the teachers randomly selected in which of the three classrooms would the game and the didactic material given to the teacher be used	Health education	Knowledge about dengue and the set of skills acquired measured before the scheduled program was implemented were lower than those obtained in the final test, and this reached statistical significance
3. Use of larvicides and adulticides					
Argentina	Masuh *et al.* (2003)	Simple before-after	Plastic cups covered with a mesh containing 10 adults, 100 mL of water and 10 third stage larvae were placed in three different locations in the houses. Insecticides (larvae and adults) were used in the field Fumigant canister (CIPEIN pF-	Use of insecticides (larvae and adults)	House Index and Breteau Index before the intervention were 51% and 106%, respectively, falling to 23% and 44% after the intervention

Table 2 (*Continued*)

Country	Study	Design	Methods	Interventions	Results
			7 (Bolate) containing 120 g of fumigant mixture and 6 g beta-cypermethrin.		
Argentina	Gurtler *et al.* (2009)	Simple before-after	As part of the citywide control program aimed at reducing the risk of occurrence of native dengue cases in Clorinda, diffusion in mass media and vector control strategies, which included focal treatment with larvicides for 4 months (14 cycles), were used	Use of larvicides	Breteau Indices declined significantly in nearly all focal points. Large water-storage containers were the most infested sites. The reported incidence of dengue cases declined from 10.4 per 10 000 to 0 (2001–2006), and then rose to 4.5 cases per 10 000 in 2007, whereas in neighbouring Paraguay, the reported incidence of dengue was 30.6 times higher than in Clorinda
Brazil	Regis *et al.* (2008)	Interrupted time series	At each selected site, 80–100 ovitraps were installed for geo-referencing. Additionally, information on environmental conditions was collected. Egg collection was carried out using 64 sentinel-ovitraps previously described for 24 months	Adulticides and larvicides in the field	The capacity for egg-collection was > 7000 eggs/trap and it was possible to detect variations in population sizes. Massive egg-collection carried out at one of the sites prevented an outbreak
Brazil	Regis *et al.* (2013)	Interrupted time series	From 2008 to 2011, a mosquito surveillance network was installed, based upon ovitraps and mosquito aspiration. From 2009 to 2011, integrated control measures were implemented. Routine control measures (bimonthly application of temephos; an annual campaign: the "Dengue Day"; application of organophosporous or piretroids (adulticides)). Geo-referenced sentinel equipment was used: Ovitraps with semi-automatic egg counting and GPS	Use of adulticides	Egg density decreased by 90% after 2 years. In Ipojuca, 1.1 million mosquito eggs were suppressed and a 77% reduction in egg density was achieved
Colombia	Ocampo *et al.* (2014)	Simple before-after	This was a 3-year study (2008–2010). It consisted of a baseline (phase 1 – entomological baseline) with the purpose of establishing baseline information on breeding sites, pupal productivity and development of vector control strategies. The second phase was used to assess entomological indices	Use of larvicides and adulticides	Reduction in the dengue incidence after the intervention was achieved ($P < 0.001$)

Table 2 (*Continued*)

Country	Study	Design	Methods	Interventions	Results
			after the intervention. Monthly application of pyriproxyfen was used		
Peru	Paredes-Esquivel *et al.* (2016)	Interrupted time series	36 houses were selected, 12 constructed with painted wood, 12 with unpainted wood and 12 with unpainted bricks. Additionally, three houses were used for each type of material as untreated controls and time-length follow-up was carried out	Use of larvicides and adulticides in the field	Adult indices fell 4 weeks after the intervention ($P < 0.05$). They remained low even for 16 weeks. HI decreased from 9 to 4 at 4 weeks. BI decreased from 15 to 4 in 4 weeks and the Container Index decreased from 4 to 2 in 4 weeks. On the other hand, mortality reached > 80% 8 weeks after application in all surfaces
4. Management of containers					
Costa Rica	Marin Rodriguez *et al.* (2009)	Simple before-after	It was carried out in Limon county, in 15 locations. Larvae samples were collected. The first survey was carried out without a vector control action, whereas the second survey was carried out 3 days after the implementation of anti-vectorial measures. The intervention consisted in the reduction in reservoirs in the field, using Non-conventional garbage collection, destruction of breeding sites, use of temephos or abate in the water storage containers, heat treatment for adult vectors inside the house with Swing fog equipment and deltamethrin plus as insecticide, on top of treatment	Reduction in containers	Overall, in 10 locations (66.6%) CI and BI values were reduced, in comparison to the first survey. A very significant difference was found between the first and the second entomological survey for CI, RI and BI ($P < 0.001$)
5. Lethal Oviposition Trap-Based Mass Interventions					
Brazil	Varjal de Melo Santos *et al.* (2008)	Simple before-after	Entomological surveillance study which intervention type was ovitraps based on BTI (ovitraps similar to the model described by Santos *et al.* (2003). The ovitraps contained 1 liter of tap water treated with 1.0 g of biolarvicide, and the control was monitoring ovitraps	Ovitraps with biolarvicide	Nossa Sra Fatima Pre-intervention 284 ovitraps Post-intervention 502 ovitraps; Nossa Sra das Gracas Pre 37 ovitraps Post 41 ovitraps; Massaranduba Pre 80 Post 66 ovitraps; CEN Pre NA Post 23 ovitraps; Casa Forte/ Parnamirim Pre 896 ovitraps Post 772 ovitraps; Engenho do Meio Pre 826 ovitraps Post 1350 ovitraps; Brasília Teimosa neighborhood Pre 891 ovitraps Post 2050

Table 2 (*Continued*)

Country	Study	Design	Methods	Interventions	Results
					ovitraps. The massive collection/destruction of eggs integrated to the larvicide treatment of the breeding places had a negative impact on the population of Aedes spp
Brazil	Silva *et al.* (2009)	Non-randomised clinical trial	The surveys were conducted in 2005 in Rio de Janeiro. 25 traps used for 13 weeks	Larvitraps and ovitraps	Larvitraps presented greater capacity for positive findings, thereby highlighting its importance as a monitoring tool for vector surveillance
Colombia	Quimbayo *et al.* (2014)	Non-randomised clinical trial	Six combinations of lethal ovitraps were assessed in 30 households randomly selected of the neighbourhood Aranjuez in Medellin. A lethal ovitrap and an ovitrap for control were placed in each house	Lethal ovitraps	The most efficient ovitrap combined deltamethrin, towel and 10% hay infusion
Peru	Wesson *et al.* (2012)	Non-randomised clinical trial	It assessed two cohorts of 2500 each, during 2011. The experimental cohort used ovitraps ALOT and fumigation was used in control.	Use of ovitraps (ALOT)	9 months after the trial, the dengue incidence, measured by fever surveillance, was 78% lower (0.3 *vs.* 1.34%) in the experimental area compared to control area ($P < 0.0001$). A difference in the adult mosquito indices of approximately 50% (for example, 65–30 female/100 houses) between the two areas was also observed
Peru	Astete *et al.* (2012)	Non-randomised clinical trial	Lethal ovitraps (Attractive lethal ovitrap, ALOT) for the reduction of the vector in Iquitos. 20 nets of approximately 7000 traps placed in approximately 2800 houses being assessed on a duplicate basis using two strains of *A. aegypti* were selected	ALOT ovitraps	Vector mortality varied from 72 to 100% in Iquitos. Net component of ALOT traps was maintained over an 8-month period under field conditions
Puerto Rico	Barrera *et al.* (2014)	Controlled before-after	An experiment was carried out to compare *Aedes aegypti* density between both areas before and after the intervention. Two communities were selected, one experimental (CDC Autocidal Gravid Ovitrap SAGO) and one for control (BG ovitrap)	SAGO ovitraps	There was a decrease in the capture of *Ae. aegypti* (53–70%) in the experimental area. The presence of three to four AGO traps per household prevented *Ae. aegypti*-related events expected during the rains in 81%
6. Epidemiological surveillance as part of a control program					
Brazil	Maciel de Freitas *et al.* (2014)	Interrupted time series	Surveillance with “Larval Index Rapid Assay for *Aedes aegypti*” (LIRAa). Random	Mechanical and chemical	Total House Index Pre-intervention: 1.7 and 1.37 post-intervention/Breteau

Table 2 (*Continued*)

Country	Study	Design	Methods	Interventions	Results
			sampling was used in blocks of houses and individual residences. Mechanical and chemical control measures: Mechanical control consisted of source reduction, whereas chemical control was based on the application of an insect growth regulator (diflubenzuron) and on pyrethroid deltamethrin spraying against adults	control measures	Index pre-intervention 1.79 and 1.51 post-intervention
Brazil	Pessanha *et al.* (2009)	Ecological	The National Dengue Control Plan (PNCD) implemented in 2002 included information campaigns, epidemiological surveillance and vector reduction strategies	Epidemiological surveillance as part of a control program	During 2001–2 and 2003–6, 66 and 49% of municipalities with an incidence greater than 100/100 000, respectively, as well as 32 and 23% of municipalities with a dengue fatality rate greater than 1% were observed
Cuba	Sánchez *et al.* (2009)	Non-randomised clinical trial	The community empowerment intervention targeted five participatory processes: training, community dengue surveillance, social communications, behavioural change and participation assessment. Routine dengue prevention activities consisting of vector control, surveillance and health education were conducted throughout the study period	Epidemiological surveillance as part of a control program	80% of households exhibited adequate behavioural patterns. The Breteau went down from 1.1 to less than 0.2

Insecticides in breeding sites. As for the use of larvicides in breeding sites, in Peru Tun Lin in 2009 [76] showed non-significant results (OR 1.44, CI 95%: 0.97–2.14) in the reduction of larval indices for active *vs.* non-active arms, after 5 months of follow up. In two of the non-randomised studies conducted in Brazil [30, 35], a multi-faceted intervention including control of breeding sites and the mass collection of eggs in one of the sites prevented the occurrence of a hypothetical *Aedes* population outbreak (Table 2). Another study in Colombia reported a reduction in the incidence of dengue cases (RR 0.19; CI 95%: 0.12–0.30, $P < 0.001$) [45].

Indoor residual spraying. Two cluster RCT assessed the use of indoor residual spraying [63, 76]. No statistically significant benefits were found in any of the assessed indices, OR of 0.84 [0.59, 1.19] for Espinoza-Gomez [35] in the House Index. No RCT was identified testing the effectiveness of outdoor fogging. The level of coverage of the population of western Colima by Espinoza-Gomez [35] was of 3% of households.

Two non-randomised studies conducted in Argentina and Peru were identified [27, 71]. These studies reported a reduction in larval indices with the use of insecticide spraying in houses. A cross-sectional study in Brazil [37] with multiple surveys assessed insecticide resistance for various agents in the state of Sao Paulo. The authors found evidence of resistance and suggested that management of resistance development needs to be adopted when insect populations show reduced susceptibility.

Lethal oviposition trap-based mass interventions. No randomised clinical trials were found. Three non-randomised trials and two before/after studies [31, 46, 69, 70, 72] carried out in Brazil, Colombia, Peru and Puerto Rico were identified, which reported a reduction in vector densities by means of the use of lethal oviposition trap-based mass interventions, for example ALOT ovitraps and CDC autocidal ovitraps. In one of these studies, it was suggested that the association with the use of deltamethrin was effective [46]. In Wesson's study, apart from reduction in indices, a reduction in the incidence of dengue was also found. Finally, the aforementioned studies of mixed interventions [30, 35] also used traps. (Table 2)

Management of containers. One single cluster RCT, Tun Lin 2009 – Mexico [76], evaluated the usefulness of reservoir reduction in mosquito control, reporting a statistically non-significant reduction in the Breteau index (−12.65; IC 95%: −28.77 to +3.47). A statistically significant reduction in the pupae per person index (−0.529; CI 95%: −1.034 to −0.024) was mentioned. A quasi-experimental study [48] performed in Costa Rica reported a sharp decline in larval indices with an adequate reservoir management (Table 2).

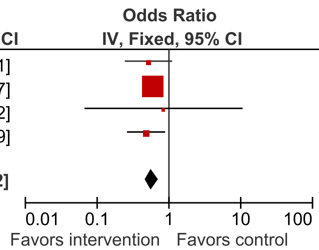
Health education and community engagement. Four cluster RCTs assessed the implementation of health education strategies and the incentive of community engagement [51, 55, 67, 76]. These studies demonstrated a significant reduction in the Breteau Index (pooled OR 0.58; CI 95%: 0.46–0.72; studies = 4, Figure 2), in the House Index (OR 0.53; CI 95%: 0.32–0.86; studies = 2) and in the Pupae Index (OR 0.38; CI 95%: 0.18–0.78; studies = 2).

High levels of coverage of interventions were achieved by the Camino Verde study in Nicaragua and Mexico [67], being community-based trials. Among six additional non-randomised studies [43, 49, 56, 61, 62, 73] carried out in Colombia, Venezuela and Cuba two found a reduction in the larval indices, one showed a reduction in the number of reservoirs and two studies that assessed knowledge and attitudes related to mosquito prevention reported a reduction in mosquitoes. Table 2 shows the main results of non-experimental studies.

Epidemiological surveillance as part of vector control programs. Under this topic we frame multifaceted studies using an integrated approach and part of a vector control program. We found a single non-randomised clinical trial performed in Cuba [52]. Their community empowerment intervention targeted five participatory processes: training, community dengue surveillance, social communications, behavioral change and participation assessment, and showed the achievement of adequate behavioral pattern with a reduction in BI. In Colombia, in the city of La Dorada, in 2010, Pacheco Coral *et al.* [42]. described a study that utilised cluster sampling in neighborhoods with the highest number of cases of *Aedes aegypti*-borne diseases and the highest density of mosquitoes reported in previous years, and where the Information, Education and Communication (IEC) strategy had been implemented needing surveillance. Within these neighbourhoods, 228 houses were randomly selected. Reservoirs were tested. There were also no larvae or pupae in homes where people had knowledge about dengue disease and its transmission. Almost 80% of the people in the target area were educated on the topic thanks to this strategy. Also in Colombia, in 2002, Romero Vivas *et al.* [41]. described a method to identify the most

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI	Risk of Bias A	B	C	D	E	F	G	H
Andersson 2015	-0.6561	0.388	8.6%	0.52 [0.24, 1.11]	+	+	?	+	?	?	?	+
Castro 2012	-0.5128	0.129	77.5%	0.60 [0.47, 0.77]	?	+	?	+	?	?	?	+
Tun-Lin 2009	-0.1744	1.2945	0.8%	0.84 [0.07, 10.62]	?	?	?	+	?	?	+	+
Vanlerberghe 2009	-0.734	0.3128	13.2%	0.48 [0.26, 0.89]	?	?	?	+	?	?	?	+
Total (95% CI)			**100.0%**	**0.58 [0.46, 0.72]**								

Heterogeneity: $\chi^2 = 0.59$, df = 3 ($P = 0.90$); $I^2 = 0\%$
Test for overall effect: $Z = 4.86$ ($P < 0.00001$)



Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Conflict of interest
(**H**) Other bias

Figure 2 MA pooled effectiveness of health education and community engagement, Breteau Index.

productive containers (surveillance), but also to avoid oviposition mechanically by using netted lids built with local materials. The intervention consisted of mechanical barriers (lids) fitted on the most productive breeding sites. Although no correlation was observed between temporal fluctuation of populations of larval *Aedes aegypti* and monthly rainfall, the barriers were effective.

Finally, in Peru, Machaca *et al.* [68] described in 2002 a surveillance study based on planned and periodic campaigns for the washing of water recipients for human and/or animal consumption (reservoirs, cylinders, buckets, clay pots, flowerpots, tires, etc.). The aedic index decreased from 46% to 3.3% in 20 days.

The remaining RCTs we found [38, 44, 47, 51, 54, 64] could not be included in pooled analyses due to lack of detail, data duplication, or lack of controlled comparisons. The summarised findings for other non-randomised studies, quasi-experimental designs and health economic evaluations are shown in Table 1.

The evidence found for other interventions, such as surveillance programs, school programs or training of community leaders is shown in Table 2. For some other interventions, such as advocacy, biogents, mosquito repellent or coils or media campaigns, we found no evidence on effectiveness in the LAC region.

We identified 25 qualitative studies regarding different topics related to *Aedes aegypti* control (see Appendix S4). In general, the risk of bias in those studies was low or moderate. Methodologies were varied, including surveys, structured interviews, and focus groups; mainly done in general population, although health professionals and decision makers were also interviewed in some of them. The main topics mentioned were: the need for community commitment; the partial knowledge about the real health risk that dengue disease entails and the relatively broad knowledge of the measures to control the vector, but with a lack of application. Contradictory results were found in relation to the perception of the usefulness of fumigation. The risk of vector multiplication in favourable environments for their dissemination, such as abandoned houses, vacant lots and streams, was better known than the perception of risk within the household. Some studies revealed the perception that actions carried out by the government were insufficient or uncoordinated. An important barrier to control was observed due to the need to store water in tanks without the possibility of keeping them free of larvae, as well as some resistance to the implementation of bednets and curtains impregnated with insecticides due to their maintenance and feeling of insecurity. Details are found in Appendix S4. The PRISMA Checklist is in Appendix S5.

Discussion

This study summarises the information identified in the LAC region regarding the interventions for the control of *Aedes aegypti* for over 15 years. A comprehensive literature review and an assessment of the methodological quality of the studies included was conducted.

Most of the available data were from Brazil, Argentina, Cuba, Mexico and Peru. The RCTs were of moderate or low methodological quality. The main findings were that in the LAC region, there is an important knowledge gap; that few types of interventions were supported by evidence on their effectiveness, and that many others showed low effectiveness. As previously mentioned, for most interventions listed in Chart 1, however, we found no (or very scarce) scientifically sound evidence on effectiveness.

ITMs may reduce the entomological indices, both in experimental and quasi-experimental studies, although trials' estimates did not reach statistical significance. For insecticides in breeding sites, although a few non-randomised studies showed some degree of effectiveness, RCTs showed non-significant results. No statistically significant benefits were found in any of the assessed indices for indoor residual spraying; yet some low-quality evidence showed reduction in larval indices. No RCT was identified which tested the performance of outdoor fogging. Regarding trap-based mass interventions, no RCTs were found. However, three non-randomised studies reported effectiveness. For the management of containers, we found only one RCT, with mixed results, and a quasi-experimental study showing a sharp reduction in indices with adequate reservoir management. Epidemiological surveillance as part of integrated control programs showed some degree of effectiveness coming from non-randomised studies. Vector control integrated strategies not always increase efficacy. The Integrative Vector Management strategy (IVM) has been pointed out as the ultimate action of governments and public health departments to mitigate disease transmission. Even a combined approach might have little impact if community engagement is not an integral part of IVM strategy. Regarding health education and community engagement, which assess knowledge and prevention-related attitudes, we found statistically significant and relevant public health outcomes in pooled estimates of effectiveness coming from four RCTs identified for these interventions, with better long-term results. After undertaking an overview of systematic reviews on dengue vector control from 2007 to 2016, Alvarado *et al.* [78] found that community mobilisation programs are an effective intervention to reduce indices, as observed in our work.

It is not known whether reductions in aedic indices are sufficient to affect dengue transmission, and the overall effect on clinical infections remains to be evaluated. Entomological endpoints are not always good predictors of relevant epidemiological outcomes, which are necessary to demonstrate efficacy of any intervention in protecting populations. It would be preferable, when possible, to inform the outcomes related to disease transmission rather than the measures of vector density.

The relevance of tools evaluated during inter-epidemic periods, to prove the performance during epidemic periods, is relatively unknown. Studies identified for assessing the efficacy of vector control interventions were often poorly conducted.

There are several systematic reviews, with or without meta-analysis, assessing vector control strategies worldwide with different levels of focus depth for LAC. Bowman *et al.* [79] conducted a systematic review with meta-analysis with worldwide focus, that suggests a lack of high-quality evidence about the effectiveness of any vector control method, similar to what we describe in our study. The author reported that on the basis of a meta-analysis, the screening of homes significantly reduced the risk of acquiring dengue (OR 0.22, CI 95%: 0.05–0.93; $P = 0.04$), as well as the combination of community-based environmental strategies and the reduction in water containers (OR 0.22, CI 95%: 0.15–0.32, $P < 0.001$). According to this study, indoor spraying did not have a significant impact on the risk of infection (OR 0.67; CI 95%: 0.22–2.11; $P = 0.50$). Cutaneous repellents, nets or traps treated with insecticides did not have a statistically significant effect either ($P >$ NS). Bouzid *et al.* [80] conducted an overview that included 13 systematic reviews that investigated the effect of control measures on the entomological parameters or disease incidence. Biological controls seem to achieve a better reduction in entomological indices than chemical controls [80], whereas education campaigns may reduce the breeding habitats. A cluster field study in Cayman Islands demonstrated that the release of sterile male mosquitoes reduced entomological indices in the experimental group *vs.* the control group [81]. Other studies that involve genetically modified mosquitoes or intracellular *Wolbachia* in field studies have demonstrated the reduction in vector population [82]. However, there is no evidence at present of the cost-effectiveness of the implementation of this type of strategies in LAC. The WHO Vector Control Advisory Group is currently reviewing new interventions of public health value to incorporate. WHO- [83]

The effectiveness of any control program depends on the zone configuration, type of intervention, available resources and study length, which may partly explain the variable degree of success across the studies. However, the quality of the evidence found was mostly low to very low due to the poor conducting and/or reporting of study design, observational methodologies, heterogeneity and indirect results, which makes evidence-based recommendation difficult. Fogging with chemical control agents commonly used do not seem to be associated to a sustainable reduction in mosquito populations. In fact, as they contribute to create a false sense of safety, chemical control agents might reduce the effectiveness of the educational interventions in order to eliminate the mosquito breeding sites.

On the other hand, contamination or spillover effects between different study arms due to the movement of vectors or human populations among clusters and short duration of follow-up periods, may also hamper validity [84]. For example, for entomological outcomes, follow-up periods need to be sufficiently long, and repeated measurements need to be taken to gain a picture of transmission in the area, for example in RCTs at least one or two transmission seasons are required. RCTs should also be adequately powered, which is not always the case.

Lima *et al.* [85] conducted a systematic review with meta-analysis to identify the most effective vector control strategies worldwide and the factors that contributed to the success or failure of each strategy. They included 26 studies from 15 countries: five with biological products, five with chemicals, three mechanical and 13 integrated strategies. The integrated interventions were the most effective method for the control of *Aedes aegypti*, always considering the influence of eco-bio-social determinants in the virus-vector-man epidemiological chain and community engagement.

Achee *et al.* [86] conducted a narrative review that highlights the growing consensus that no single intervention will be sufficient to control dengue disease. Even if there is an effective dengue vaccine available in the market, we will continue to rely on vector control because both strategies complement and enhance each other. Although the comprehensive intervention concept for dengue prevention is gaining increasingly wider acceptance, up to this date no consensus has been reached about the details regarding how and what combination of strategies may be implemented with greater effectiveness to control the disease. In order to fill this gap, the Partnership for Dengue Control (PDC) proposed a three-step process: (i) a critical assessment of current vector control tools and tools under development, (ii) set a research agenda to determine definitively the tools that work better, and (iii) determine how to combine the best vector control options.

Some of the strengths of our study include a thorough bibliographic search with the use of multiple databases and strict criteria for the assessment of the quality of the papers, and the contact with experts in charge of specific programs.

There are also some limitations in the present review. The observational nature of several of the studies selected and the different definitions of the exposure and the result caused different degrees of heterogeneity for most of the analyses. Nevertheless, in order to deal with this fact, the random effects model was used in the meta-analyses, as high levels of heterogeneity were predicted. The confidence intervals of the estimators are more valuable than the central value related to this.

In many cases, the interventions are carried out jointly, and the effectiveness of a particular intervention cannot be isolated from the effectiveness of a set of interventions. It is also difficult to compare the effectiveness of an intervention to the other, as the no-intervention arm in the comparative studies is heterogeneous. It is advisable to use a contemporaneous control group because longitudinal changes, such as rain-fall, may impact epidemiological outcomes and can exaggerate or mask an intervention effect [84]. As far as we know, there may be, of course, other health measures in the region that may have been implemented but have not been assessed and reported in scientific journals at present.

Most studies' effectiveness is measured through *Aedes* larval indices which correlate poorly with new or existing dengue cases or with adult mosquito abundance. Moreover, more carefully considered and more rigorously designed vector control studies are needed [84].

In conclusion, as far as we know, this is the first meta-analytical systematic review to establish the effectiveness of the different public health strategies for the control of *Aedes aegypti* in the LAC region. We found important evidence gaps, but also solid evidence supporting interventions such as community mobilisation and integrated actions as starting points to get evidence into practice.

Acknowledgements

The authors thank Daniel Comandé, librarian of the Institute for Clinical Effectiveness and Health Policy in Buenos Aires, for his significant help with the literature searches and Mrs. María Cecilia Olivera for English language revision.

References

1. Pan American Health Organization. Key messages for individuals and families regarding surveillance and control of *Aedes aegypti* : transmitter of dengue, chikungunya, Zika and other arbovirus diseases in the Americas. Regional office for the Americas, 2016.
2. Chang MS, Christophel EM, Gopinath D, Abdur RM. Challenges and future perspective for dengue vector control in the Western Pacific Region. *Western Pac Surveill Response J* 2011: **2**: e1–e.
3. Zika. *Strategic Response Plan*. World Health Organization: Geneva; 2016. (Available from: http://apps.who.int/iris/bitstream/10665/246091/1/WHO-ZIKV-SRF-16.3-eng.pdf?ua = 1&ua=1).
4. Petersen LR, Jamieson DJ, Powers AM, Honein MA. Zika virus. *New Engl J Med* 2016: **374**: 1552–1563.
5. Salud OMdl. Preparación y respuesta ante emergencias. (Available from: http://www.who.int/csr/don/27-January-2017-yellow-fever-brazil/es/).
6. Organization PAH. *Guía para la vigilancia de la enfermedad por el virus del Zika y sus complicaciones*. World Health Organization: Washington, 2016.
7. Wilder-Smith A, Chen LH, Massad E, Wilson ME. Threat of dengue to blood safety in dengue-endemic countries. *Emerg Infect Dis* 2009: **15**: 8–11.
8. WHO. PAHO WHO | Dengue [Internet]. Webpage, 2015. (Available from: http://www.paho.org/hq/index.php?option=com_topics&view=article&id = 1&Itemid = 40734) [04 May 2017]
9. Cafferata ML, Bardach A, Rey-Ares L *et al*. Dengue epidemiology and burden of disease in Latin America and the Caribbean: a systematic review of the literature and meta-analysis. *Value Health Reg Issues* 2013: **2**: 347–356.
10. San Martín JL, Brathwaite-Dick O. La Estrategia de Gestión Integrada para la Prevención y el Control del Dengue en la Región de las Américas. *Rev Panam Salud Pública* 2007: **21**: 55–63.
11. Organization PAH. Comunicación para impactar en conducta (COMBI), 2017. (Available from: http://www.paho.org/hq/index.php?option=com_content&view=article&id = 4504%3A2010-comunicacion-impactar-conducta-combi&catid = 901%3Adengue-content&Itemid = 41040&lang=es)
12. World Health Organization. Yellow fever vaccination requirements and recommendations; malaria situation; and other vaccination requirements, 2018. (Available from: https://www.who.int/ith/ITH_country_list.pdf)
13. Centers for Disease Control and Prevention. Yellow fever, 2018. (Available from: https://www.cdc.gov/yellowfever/index.html)
14. Bardach A, Ciapponi A, Alcaraz A *et al*. Intervenciones para el control de *Aedes aegypti* en América Latina y el Caribe: revision sistemática y estudio cualitativo. *Rev Panam Salud Publica* 2017: **41**: e17.
15. Ciapponi A, Bardach A, Alcaraz A *et al*. Taller de priorización de intervenciones para el control del mosquito *Aedes aegypti* en América Latina y el Caribe: diálogo de políticas (Policy dialogue). *Cadernos de Saudé Pública*; in press.

16. Tapia-López E, Bardach A, Ciapponi A *et al.* Experiencias, barreras y facilitadores en la implementación de intervenciones para el control de *Aedes aegypti* en América Latina y el Caribe: estudio cualitativo con entrevistas en profundidad. *Cadernos de Saudé Pública*; in press.
17. Stroup DF, Berlin JA, Morton SC *et al.* Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000: **283**: 2008–2012.
18. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009: **6**: e1000097.
19. Glujovsky D, Bardach A, Martí SG, Comandé D, Ciapponi A. PRM2 EROS: a new software for early stage of systematic reviews. *Value Health* 2011: **14**: A564.
20. von Elm E, Altman DG, Egger M *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med* 2007: **147**: 573–577.
21. Sanderson S, Tatt ID, Higgins JP. Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: a systematic review and annotated bibliography. *Int J Epidemiol* 2007: **36**: 666–676.
22. Fowkes FG, Fulton PM. Critical appraisal of published research: introductory guidelines. *BMJ* 1991: **302**: 1136–1140.
23. Epoc CEP, Organisation of Care G. The Data Collection Checklist Quality Criteria 2010 (Available from: http://epoc.cochrane.org/epoc-resources-review-authors).
24. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Gw T. Critical assessment of economic evaluation. In: Oxford University Press (eds). *Methods for the Economic Evaluation of Health Care Programmes*, 4th ed. Oxford Medical Publications: Oxford; 2015. p. 41–76.
25. Mays N, Pope C. Assessing quality in qualitative research. *BMJ* 2000: **320**: 50–52.
26. GDT. G-. 2018 (Available from: https://gradepro.org).
27. Masuh H, De Licastro SA, Lopez PA, Vega C, Zerba E. Field evaluation of a smoke-generating formulation containing beta-cypermethrin against the dengue vector in Argentina. *J Am Mosquito Control Assoc* 2003: **19**: 53–57.
28. Orellano PW, Pedroni E. Cost-benefit analysis of vector control in areas of potential dengue transmission. *Rev Panam Salud Publica* 2008: **24**: 113–119. 7p.
29. Gürtler RE, Garelli FM, Coto HD. Effects of a five-year citywide intervention program to control *Aedes aegypti* and prevent dengue outbreaks in Northern Argentina. *PLoS Negl Trop Dis* 2009: **3**: e427.
30. Regis L, Monteiro AM, Melo-Santos MA *et al.* Developing new approaches for detecting and preventing *Aedes aegypti* population outbreaks: basis for surveillance, alert and control system. *Mem Inst Oswaldo Cruz* 2008: **103**: 50–59.
31. Varjal de Melo Santos M. *Aedes aegypti* (DIPTERA:CULICIDAE): ESTUDOS POPULACIONAIS E ESTRATÉGIAS INTEGRADAS PARA CONTROLE VETORIAL EM MUNICÍPIOS DA REGIÃO METROPOLITANA DO RECIFE, NO PERÍODO DE 2001 A 2007, 2008. (Available from: http://wwwcpqamfiocruzbr/bibpdf/2008santos-mavmpdf) [Sept 2017].
32. Silva VC, Serra-Freire NM, Silva J dos S *et al.* [Comparative study between larvitraps and ovitraps for evaluating the presence of *Aedes aegypti* (Diptera: Culicidae) in Campo Grande, State of Rio de Janeiro]. *Rev Soc Bras Med Trop* 2009: **42**: 730–731.
33. Pessanha JE, Caiaffa WT, César CC, Proietti FA. [Evaluation of the Brazilian National Dengue Control Plan]. *Cad Saude Publica* 2009: **25**: 1678–4464.
34. Luz PM, Vanni T, Medlock J, Paltiel AD, Galvani AP, Galvani AP. Dengue vector control strategies in an urban setting: an economic modelling assessment. *Lancet* 2011: **377**: 1673–1680(1474-547X (Electronic)).
35. Regis LN, Acioli RV, Silveira JC Jr *et al.* Sustained reduction of the dengue vector population resulting from an integrated control strategy applied in two Brazilian cities. *PLoS ONE* 2013: **8**: e67682.
36. Maciel-de-Freitas R, Avendanho FC, Santos R *et al.* Undesirable consequences of insecticide resistance following *Aedes aegypti* control activities due to a dengue outbreak. *PLoS ONE* 2014: **9**: e92424.
37. Macoris Mde L, Andrighetti MT, Wanderley DM, Ribolla PE. Impact of insecticide resistance on the field control of *Aedes aegypti* in the State of Sao Paulo. *Rev Soc Bras Med Trop* 2014: **47**: 573–578.
38. Degener CM, Eiras AE, Azara TMF *et al.* Evaluation of the effectiveness of mass trapping with bg-sentinel traps for dengue vector control: a cluster randomized controlled trial in manaus, Brazil. *J Med Entomol* 2014: **51**: 408–420.
39. Brasil LM, Gomes M, Atilde MF *et al.* Web platform using digital image processing and geographic information system tools: a Brazilian case study on dengue. *BioMedical Eng OnLine* 2015: **14**: 69.
40. Alfonso-Sierra E, Basso C, Beltran-Ayala E *et al.* Innovative dengue vector control interventions in Latin America: what do they cost? *Pathog Glob Health* 2016: **110**: 14–24.
41. Romero-Vivas CM, Wheeler JG, Falconar AK. An inexpensive intervention for the control of larval *Aedes aegypti* assessed by an improved method of surveillance and analysis. *J Am Mosq Control Assoc* 2002: **18**: 40–46.
42. Pacheco-Coral Adel P, Quinones-Pinzon ML, Serrato-Pomar IM, Rivas-Munoz FA. Evaluating an Information, Education and Communication (IEC) strategy which was adopted for *Aedes aegypti* control in La Dorada, Colombia. *Rev Salud Publica (Bogota)* 2010: **12**: 380–390.
43. Cáceres-Manrique FDM, Angulo-Silva ML, Vesga G, Gómez C. Efficacy of the social mobilization and the social participation in dengue control measures. *Biomedica* 2010: **30**: 539–550.
44. Alarcon EP, Segura AM, Rua-Uribe G,Parra-Henao G. [Ovitraps evaluation for surveillance and control of *Aedes aegypti* in two urban settlements of Uraba, Antioquia]. *Biomedica* 2014: **34**: 409–424.

45. Ocampo CB, Mina NJ, Carabalí M, Alexander N, Osorio L. Reduction in dengue cases observed during mass control of Aedes (Stegomyia) in street catch basins in an endemic urban area in Colombia. *Acta Trop* 2014: **132**: 15–22.
46. Quimbayo M, Rúa-Uribe G, Parra-Henao G, Torres C. Evaluation of lethal ovitraps as a strategy for *Aedes aegypti* control. *Biomedica* 2014: **34**: 473–482.
47. Perich MJ, Rocha NO, Castro AL *et al.* Evaluation of the efficacy of lambda-cyhalothrin applied by three spray application methods for emergency control of *Aedes aegypti* in Costa Rica. *J Am Mosquito Control Assoc* 2003: **19**: 58–62.
48. Marín Rodríguez R, Marquetti Fernández MdC, Díaz Ríos M. Índices larvales de *Aedes aegypti* antes y después de intervenciones de control en Limón, Costa Rica. *Rev Cubana Med Trop* 2009: **61**.
49. Toledo ME, Vanlerberghe V, Baly A *et al.* Towards active community participation in dengue vector control: results from action research in Santiago de Cuba, Cuba. *Trans R Soc Trop Med Hyg* 2007: **101**: 56–63.
50. Baly A, Toledo ME, Boelaert M *et al.* Cost effectiveness of *Aedes aegypti* control programmes: participatory versus vertical. *Trans R Soc Trop Med Hyg* 2007: **101**: 578–586.
51. Vanlerberghe V, Toledo ME, Rodríguez M *et al.* Community involvement in dengue vector control: cluster randomised trial. *BMJ* 2009: **338**: b1959.
52. Sanchez L, Perez D, Cruz G *et al.* Intersectoral coordination, community empowerment and dengue prevention: six years of controlled interventions in Playa municipality, Havana, Cuba. *Tropical Med Int Health* 2009: **14**: 1356–1364. https://doi.org/10.1111/j.1365-3156.2009.02379.x.
53. Baly A, Toledo ME, Rodriguez K *et al.* The incremental economic cost of controlling dengue disease in Guant&Atilde. *Tropical Med Int Health* 2009: **14** (suppl 2): 168.
54. Toledo ME, Lambert I, Popa JC *et al.* Effectiveness of insecticide treated curtains in a setting with low *Aedes aegypti* infestation levels and an intensive routine vector control programme. *Tropical Med Int Health* 2011: **16**: 240.
55. Castro M, Sanchez L, Perez D, Carbonell N, Vanlerberghe V, Stuyft P. A community empowerment strategy embedded in a routine dengue vector control programme: a cluster randomized controlled trial. *Tropical Med Int Health* 2012: **106**: 242–243.
56. Sanchez L, Maringwa J, Shkedy Z, Castro M, Carbonell N, Van Der Stuyft P. Testing the effectiveness of community-based dengue vector control interventions using semiparametric mixed models. *Vector-Borne Zoonotic Dis* 2012: **12**: 609–615.
57. Baly A, Toledo ME, Rodriguez K *et al.* Costs of dengue prevention and incremental cost of dengue outbreak control in Guantanamo, Cuba. *Tropical Med Int Health* 2012: **17**: 123–132.
58. Toledo ME, Vanlerberghe V, Lambert I, Montada D, Baly A, Van Stuyft PD. No effect of insecticide treated curtain deployment on Aedes infestation in a cluster randomized trial in a setting of low dengue transmission in Guantanamo, Cuba. *PLoS ONE* 2015: **10**: e0119373.
59. Baly A, Toledo ME, Lambert I *et al.* The cost of intensive routine control and cost-effectiveness of insecticide treated curtain deployment in a setting with low *Aedes aegypti* infestation. *Tropical Med Int Health* 2015: **20** (suppl 1): 380.
60. Rizzo N, Gramajo R, Escobar MC *et al.* Dengue vector management using insecticide treated materials and targeted interventions on productive breeding-sites in Guatemala. *BMC Public Health* 2012: **12**: 931.
61. Avila Montes GA, Martinez M, Sherman C, Fernandez Cerna E. Evaluation of an educational module on dengue and *Aedes aegypti* for schoolchildren in Honduras. *Rev Panam Salud Publica* 2004: **16**: 84–94.
62. Montes GAÁ, Araujo R, Leontsini E, Herrera GO, Cerna EF. Un programa escolar para el control del dengue en Honduras: del conocimiento a la práctica. *Rev Panam Salud Pública* 2012: **31**: 518–522.
63. Espinoza-Gomez F. Educational campaign versus malathion spraying for the control of *Aedes aegypti* in Colima, Mexico. *J Epidemiol Community Health* 2002: **56**: 148–152.
64. Lorono-Pino MA, Garcia-Rejon JE, Machain-Williams C *et al.* Towards a Casa Segura: a consumer product study of the effect of insecticide-treated curtains on *Aedes aegypti* and dengue virus infections in the home. *Am J Trop Med Hyg* 2013: **89**: 385–397.
65. Manrique-Saide P, Che-Mendoza A, Barrera-Perez M *et al.* Use of insecticide-treated house screens to reduce infestations of dengue virus vectors, Mexico. *Emerg Infect Dis* 2015: **21**: 308–11. 4p
66. Kroeger A, Lenhart A, Ochoa M *et al.* Effective control of dengue vectors with curtains and water container covers treated with insecticide in Mexico and Venezuela: cluster randomised trials. *BMJ* 2006: **332**: 1247–1252.
67. Andersson N, Nava-Aguilera E, Arosteguí J *et al.* Evidence based community mobilization for dengue prevention in Nicaragua and Mexico (the Green Way): cluster randomized controlled trial. *Brit Med J* 2015: **351**: h3267.
68. Machaca J, Llontop F, Pasapera F *et al.* Eliminación mecánica de huevos del *Aedes aegypti* para la erradicación del Dengue urbano. Localidad de Sechura – Piura, abril – diciembre 2001. *Rev Peru Epidemiol (Online)* 2002: **10**: 1–5.
69. Astete H, Hudson TML, Paz-Soldan VA *et al.* Evaluation of long-lasting alpha-cypermethrin impregnated nets in attractive lethal ovitraps (ALOT) against *Aedes aegypti* for dengue control in Iquitos, Peru. *Am J Trop Med Hyg* 2012: **87**: 219–220. https://doi.org/10.4269/ajtmh.2012.87.150
70. Wesson DM, Morrison AC, Soldan VAP *et al.* Evaluation of an attractive lethal ovitrap (ALOT) against *Aedes aegypti* for dengue control in Iquitos, Peru. *Am J Trop Med Hyg* 2012: **87**: 419.
71. Paredes-Esquivel C, Lenhart A, del Río R *et al.* The impact of indoor residual spraying of deltamethrin on dengue vector populations in the Peruvian Amazon. *Acta Trop* 2016: **154**: 139–144. https://doi.org/10.1016/j.actatropica.2015.10.020
72. Barrera R, Amador M, Acevedo V, Caban B, Felix G, Mackay AJ. Use of the CDC autocidal gravid ovitrap to

control and prevent outbreaks of *Aedes aegypti* (Diptera: Culicidae). *J Med Entomol* 2014: **51**: 145–154.
73. Vivas E, De Sequeda MG. A game as an educational strategy for the control of *Aedes aegypti* in Venezuelan schoolchildren. *Rev Panam Salud Publica* 2003: **14**: 394–401.
74. Vanlerberghe V, Villegas E, Jirarojwatana S *et al.* Determinants of uptake, short-term and continued use of insecticide-treated curtains and jar covers for dengue control. *Tropical Med Int Health* 2011: **16**: 162–173 https://doi.org/10.1111/j.1365-3156.2010.02668.x.
75. Vanlerberghe V, Villegas E, Oviedo M *et al.* Evaluation of the effectiveness of insecticide treated materials for household level dengue vector control. *PLoS Negl Trop Dis* 2011: **5**: e994.
76. Tun-Lin W, Lenhart A, Nam VS *et al.* Reducing costs and operational constraints of dengue vector control by targeting productive breeding places: a multi-country non-inferiority cluster randomized trial. *Tropical Med Int Health* 2009; **14**: 1143–1153.
77. Che-Mendoza A, Guillermo-May G, Herrera-Bojorquez J *et al.* Long-lasting insecticide-treated house screens and targeted treatment of productive breeding-sites for dengue vector control in Acapulco, Mexico. *Trans R Soc Trop Med Hyg* 2015: **109**: 106–115.
78. Alvarado-Castro V, Paredes-Solis S, Nava-Aguilera E *et al.* Assessing the effects of interventions for *Aedes aegypti* control: systematic review and meta-analysis of cluster randomised controlled trials. *BMC Public Health* 2017: **17** (Suppl 1): 384.
79. Bowman LR, Donegan S, McCall PJ. Is dengue vector control deficient in effectiveness or evidence? Systematic review and meta-analysis. *PLoS Negl Trop Dis* 2016: **10**: e0004551.
80. Bouzid M, Brainard J, Hooper L, Hunter PR. Public health interventions for Aedes control in the time of Zikavirus–A meta-review on effectiveness of vector control strategies. *PLoS Negl Trop Dis* 2016: **10**: e0005176.
81. Harris AF, McKemey AR, Nimmo D *et al.* Successful suppression of a field mosquito population by sustained release of engineered male mosquitoes. *Nat Biotechnol* 2012: **30**: 828–830.
82. McGraw EA, O'Neill SL. Beyond insecticides: new thinking on an ancient problem. *Nat Rev Microbiol* 2013: **11**: 181–193.
83. WHO-Vector Control Advisory Group Periodically reviewed Level of evidence. (Available from: http://apps.who.int/iris/bitstream/handle/10665/274451/WHO-CDS-VCAG-2018.03-eng.pdf) [Jan 2019].
84. Wilson AL, Boelaert M, Kleinschmidt I *et al.* Evidence-based vector control? Improving the quality of vector control trials. *Trends Parasitol* 2015: **31**: 380–390.
85. Lima EP, Goulart MO, Rolim Neto ML. Meta-analysis of studies on chemical, physical and biological agents in the control of *Aedes aegypti*. *BMC Public Health* 2015: **15**: 858.
86. Achee NL, Gould F, Perkins TA *et al.* A critical assessment of vector control for dengue prevention. *PLoS Negl Trop Dis* 2015: **9**: e0003655.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1 Search strategy.

Appendix S2 Tool for assessing risk of bias in observational studies.

Appendix S3 Risk of bias of Included Studies.

Appendix S4 Qualitative studies identified.

Appendix S5 PRISMA checklist.

Corresponding Author Ariel Bardach, Instituto de Efectividad Clínica y Sanitaria, Centro de Investigación de Epidemiología y Salud Pública, Argentina. E-mail: abardach@iecs.org.ar