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The rising global economic costs of invasive *Aedes* mosquitoes and *Aedes*-borne diseases

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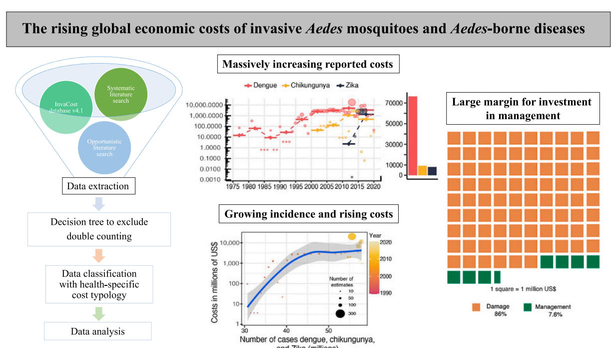
HIGHLIGHTS

- Dengue, Zika and chikungunya are transmitted by *Aedes aegypti* and *Aedes albopictus*.
- These invasive species carry a significant but not well-characterized economic cost.
- Our study reports costs from 166 countries and territories, spanning 45 years.
- The cumulative reported cost amounted to at least US$ 94.7 billion.
- Costs are increasing and only a modest proportion (1/10) is invested in prevention.

GRAPHICAL ABSTRACT



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ABSTRACT

Invasive *Aedes aegypti and Aedes albopictus* mosquitoes transmit viruses such as dengue, chikungunya and Zika, posing a huge public health burden as well as having a less well understood economic impact. We present a comprehensive, global-scale synthesis of studies reporting these economic costs, spanning 166 countries and territories over 45 years. The minimum cumulative reported cost estimate expressed in 2022 US$ was 94.7 billion, although this figure reflects considerable underreporting and underestimation. The analysis suggests a 14-fold increase in costs, with an average annual expenditure of US$ 3.1 billion, and a maximum of US$ 20.3 billion in 2013. Damage and losses were an order of magnitude higher than investment in management, with

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Chikungunya
Invasive mosquitoes

only a modest portion allocated to prevention. Effective control measures are urgently needed to safeguard global health and well-being, and to reduce the economic burden on human societies. This study fills a critical gap by addressing the increasing economic costs of *Aedes* and *Aedes*-borne diseases and offers insights to inform evidence-based policy.

1. Introduction

The spread of the invasive arbovirus vectors *Aedes aegypti* and *Aedes albopictus* is a paradigmatic case of the impact of human globalization (trade and travel, climate change), further exacerbated by unplanned urbanization and inefficient water storage and waste disposal systems (Kraemer et al., 2019; Gubler, 2011; Juliano and Lounibos, 2005). *Ae. aegypti*, the yellow fever mosquito, is an African species that was brought to the Americas aboard slave ships during the 16th and 17th centuries, and later reached Europe, Asia, Australia and the Pacific regions (Lounibos and Kramer, 2016; Powell et al., 2018; Brady and Hay, 2020). Since the 1970s, the Asian tiger mosquito, *Ae. albopictus,* has spread from Asia to all continents, including tropical and temperate areas (Paupy et al., 2009; Lambrechts et al., 2010). *Ae. aegypti* is considered the principal vector of dengue and Zika, and although *Ae. albopictus* is a less efficient epidemic vector for both these diseases, it has developed a greater ability to transmit some strains of chikungunya (Lounibos and Kramer, 2016; Brady and Hay, 2020; Paupy et al., 2009; Lambrechts et al., 2010; Tsetsarkin et al., 2007; Weaver and Vasilakis, 2009). Yellow fever caused a significant health burden from the 16th to the early 20th century, and although well-implemented vertical vector control and immunization campaigns to deliver an efficacious vaccine were successful in controlling this disease, there is still local sylvatic transmission remains (Powell et al., 2018; Brady and Hay, 2020). Nonetheless, the past 50 years have witnessed the emergence and massive spread of dengue, chikungunya and Zika, with the potential to affect the majority of the world's population (Kraemer et al., 2019).

Besides the obvious threats to public health, the emergence and subsequent circulation of *Aedes*-borne arboviruses entail significant economic costs in both the short and the long term. This economic burden needs to be appropriately quantified if the efforts of policymakers and stakeholders are to be facilitated, and management decisions and actions strengthened (Diagne et al., 2021).

The recent InvaCost initiative (Diagne et al., 2020) generated a comprehensive public database of the reported economic costs of biological invasions worldwide. This database is a robust, standardized, global-scale compilation and description of the cost estimates associated with invasive alien species (Bradshaw et al., 2016; Diagne et al., 2020b). Initial analysis of this dataset revealed *Ae. aegypti* and *Ae. albopictus* as the costliest invasive species worldwide (Diagne et al., 2021). However, health costs were not explicitly targeted nor was a health-specific cost typology considered. Our aim is therefore to update and refine these initial estimates by developing a cost typology that focuses specifically on the reported health costs of these mosquito species and the diseases they transmit, which will allow us to assess how cost types are linked to different stakeholders. Furthermore, as the initial analysis encompassed several duplicates of cost estimates, we developed a methodology to systematically deal with double counting to avoid temporal or spatial duplications of cost estimates. These data can be used to inform evidence-based policy and provide decision-makers with relevant insights into the nature and distribution of *Aedes*-borne costs.

2. Material and methods

2.1. Literature search

First, we compiled a dataset comprising all the entries in the InvaCost database (version 4.1) referring to *Ae. aegypti* and *Ae. albopictus,* a total of 108 references (Diagne et al., 2020; Diagne et al., 2022; Angulo et al., 2021). We supplemented this dataset with data obtained from a systematic search of the published scientific literature on the economic impacts of these *Aedes* species and the human disease-causing viruses they transmit up to December 31, 2021. To minimize the risk of omitting relevant materials, we conducted this search in two online sources: the Web of Science (WoS) platform (https://webofknowledge.com/) and the PubMed repositories (https://www.ncbi.nlm.nih.gov/pubmed/). We carefully composed appropriate search strings, and consensually retained those we considered the most efficient, based on a handful of references provided by the authors (Diagne et al., 2020). The final search string for Pubmed was as follows: (search string: *cost-effectiveness [Title/Abstract] OR cost effectiveness[Title/Abstract] OR monetary[Title/Abstract] OR dollars[Title/Abstract] OR euros[Title/Abstract] OR sterling [Title/Abstract] OR DALY[Title/Abstract] OR expenditur*[Title/Abstract] OR economi*[Title/Abstract] OR cost of illness[Title/Abstract] OR cost-of-illness[Title/Abstract]*) AND (zika[Title/Abstract] OR chikungunya [Title/Abstract] OR dengue[Title/Abstract] OR yellow fever[Title/Abstract] OR albopictus[Title/Abstract] OR aegypti[Title/Abstract]): and for WoS (search string: ("cost effectiveness" OR "cost-effectiveness" OR monetary OR dollars OR euros OR sterling OR DALY OR expenditur* OR economi* OR "cost of illness" OR "cost-of-illness")) AND (TS = (zika OR chikungunya OR dengue OR "yellow fever" OR albopictus OR aegypti)).

2.1.1. PRISMA methodology

We combined into a single file the potentially relevant materials obtained from the systematic search and screened for duplicates. The documents retrieved were individually assessed at three levels in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statements (Moher et al., 2009): titles, then abstracts, and finally full text (Fig. S1). In the final step, we selected only relevant materials containing records of economic costs associated with *Ae. aegypti* and *Ae. albopictus*.

2.1.2. Opportunistic search

To address specific information gaps revealed during the systematic search we retrieved additional materials through an opportunistic search using two different strategies. In one, we included cost records that had been identified from other source materials when establishing the methodology for the project (e.g., when testing different search string combinations in the initial stages of the work), but were missed in the systematic search. In the other, we conducted direct searches of the grey literature of specific subjects we had identified as underrepresented (e.g., tourism costs) (Fig. S1). We used the Google Scholar search engine for this, and a search string with the following general structure: "economic cost" followed by the specific cost to be searched and the disease (either dengue, Zika or chikungunya), and screened the results from the first ten search pages. Note that this material was not subjected to PRISMA guidelines.

2.2. Exclusion/inclusion criteria

The materials included for data extraction were required to meet the following *inclusion criteria:* (i) peer-reviewed article, book chapter or report by an official body; (ii) articles written in English, French, Italian, Portuguese or Spanish; (iii) mention of at least one cost record for a particular geographic area (municipality, region, country, continent) and a given period; (iv) costs exclusively associated with *Ae. aegypti or Ae. albopictus* or with the diseases caused by the viruses they transmit (i.e., dengue, chikungunya, Zika or yellow fever); (v) costs expressible in monetary terms, relating to medical services, management, and market losses. *Exclusion criteria* were: (i) the material contained records of only the cost per inhabitant (several papers estimated the medical costs per inhabitant, mostly for dengue) or the cost per patient (these records did not provide additional information that would the costs for the affected population within a particular geographic area and period to be accurately estimated); (ii) records of costs per disability-adjusted life years (DALY), as they did not allow us to estimate the economic costs for a particular geographical area and period; (iii) future projections for vector control or vaccination methods (as these are potential costs); (iv) experimental field trials of vector control (as they cannot be transposed into operational actions for public health purposes at this stage). Each document was double checked independently by two researchers to ensure transparency and consistency. The exclusion criteria for the retrieved grey literature were the same as previously detailed, with the additional restriction that only peer-reviewed or official sources (graduate dissertations, government or institutional reports) or sources citing official data (e.g., press releases) were included. Finally, we checked all entries in the database to ensure there were no duplicated records (i.e., multiple documents referring to identical cost records) or mistakes. Our procedures ensure that the database is, as far as possible, a comprehensive, up-to-date list of references.

2.3. Extraction, description and standardization of cost records

We compiled all the relevant materials (i.e., all the "*Aedes*" related references from InvaCost v4.1, our results from the systematic search processed with PRISMA guidelines, and the additional cost records identified from opportunistic searches of other sources) and scrutinized the material for data on economic costs (Fig. S1). We conducted the final stage of inclusion/exclusion during this data extraction phase.

To contribute to the InvaCost database effort, we extracted data using the same structure and data descriptors as the InvaCost database version 4.1 (Diagne et al., 2022). However, in line with our specific aims of investigating the distribution of *Aedes*-borne costs, we added three additional columns to the current database format: (i) a column listing the disease that the costs were associated with; (ii) a column detailing any further processing needed to estimate the costs where applicable; (iii) a column indicating who bore the burden of the cost. Full definitions and details of the descriptions of each column in our dataset are given in Data S1. We extracted the raw cost data as reported in the original sources and assessed the primary sources of the data, where available, to better characterize the reported cost (the 'Previous materials' column in Data S1). If several cost values were provided for a single situation (e.g., different cost records according to different management scenarios for the same invasive population) we calculated median values following previously established methodology (Diagne et al., 2020; Diagne et al., 2021). If a range of estimated costs was reported, we also extracted the minimum and maximum estimates. Any further processing carried out to obtain cost records is reported in the 'Additional processing' column.

After extracting the costs in the reported currencies, we standardized the raw cost data as cost records per year ('Annualized cost estimate' column) following the same methodology as that used for the InvaCost database (Diagne et al., 2020). The total and the annualized cost data were then standardized to a common currency (2017 US$) and adjusted for inflation using the Consumer Price Index to make them comparable across space and over time, following the methodology originally proposed in Diagne et al., 2020. We further transformed these costs into 2022 US$ values by multiplying them by an inflation factor of 1.193, based on the World Bank's Consumer Price Index (https://data.worldbank.org). In addition, each cost record was characterized by a number of descriptors (Data S1), including the scale and time at which the cost was reported. Each of the *Aedes* costs incurred in a particular country in a particular year was related to one or both *Aedes* species, based on historical data on *Aedes* colonization in each country or region when unspecified in the original document (Data S2). As some countries have non-contiguous overseas territories, each cost was also related to the country or territory in which it was reported. For instance, costs associated with invasive species in La Réunion (a French island in the Indian Ocean) were attributed to Africa as 'Geographic region' and to 'La Réunion' as 'Country or territory' although its administrative country is France on the European continent. In some instances, costs in the original sources were estimated for two or more diseases together (e.g., dengue and chikungunya; dengue and Zika; dengue, Zika and chikungunya). These were entered into the database as reported in the original source and are referred to throughout the paper as DEN-CHIK-ZIKA. The typology of each disease cost was further broken down into sub-typologies (Table 1), as explained in the next section (The nature of costs). We evaluated the reliability of the authors' methodologies for obtaining cost records (Bradshaw et al., 2016; Diagne et al., 2020; Diagne et al., 2021). Once all the data had been collated, we double-checked the final dataset for errors.

The nature of the information retrieved and the choices made to characterize each cost are summarized in Data S1.

2.4. The nature of costs

We developed a specific cost typology to classify the economic costs of invasive *Aedes* species and *Aedes*-borne diseases, for which we considered previous frameworks on the economic costs of invasive species (Diagne et al., 2021; Vaissière et al., 2022), but took into account the particular characteristics of the study species. Hence, the typology presented in this work constitutes an original framework (Table S1) that focuses on monetary costs and makes a major distinction between damage/losses and management costs.

We defined damage/loss costs as those incurred through losses or in repairing the damage caused by *Aedes* and the diseases they transmit. Damage costs include several cost subcategories, extensively described within the health economics literature. These are: direct medical costs, defined as the expenses incurred relating to diagnosis, hospital admission, hospitalization, ambulatory cases, patient care, and treatment of the illness, whether they are paid for by the patients or the health providers; direct non-medical costs, which relate to other expenses involved in the state of illness besides treatment, such as transportation, and food and accommodation for patients; and indirect costs, which are those associated with lost productivity due to illness, morbidity or premature death. Losses are defined as the monetary value lost from products/services traded on the market, which in this case covers tourism, trade, and economic growth; these are borne by communities, and, in some cases, individuals. Some non-market values, defined as those that are not traded on markets, such as loss of quality of life, can be captured by ad hoc economic evaluation methods (Vaissière et al., 2022). However, as

Table 1
Total and average annual costs by disease. Total raw costs and average annual costs (in US$ 2022) for dengue, Zika and chikungunya. Total costs include damage/losses and management costs. The mixed category (DEN-CHIK-ZIKA) refers to cost records calculated jointly for more than one disease (dengue, chikungunya and/or Zika). The nuisance category refers to contexts where no disease cost has been estimated and there is no endemic arboviral circulation in the country. Estimated costs of long-term disease sequelae, which are potential costs, are shown separately in Table S2. b = billion, m = million.

Disease	Total raw costs (US$)	Average annual costs (US $)	Period	Maximum annual cost (US$)	Year of maximum
Dengue	76.5 b	1.7 b	1975–2020	17.5 b	2013
Zika	8.1b	1.7 b	2013–2017	2.8 b	2017
Chikungunya	9.3 b	514.2 m	2003–2020	2.8 b	2013
Nuisance	59.8 m	2.5 m	1995–2018	19.6	2008
DEN-CHIK-ZIKA	908.12	53.4	2003–2019	243.5	2016
Total	94.7 b	2.1 b	1975–2020	20.3	2013

few of the studies we examined were found to use non-market valuation methods, we restricted our data analysis to monetary costs derived from market values.

We defined management costs as those assigned to managing invasive *Aedes* vectors and *Aedes*-borne diseases. These include the costs of (entomological and epidemiological) surveillance, vector control and other (entomological and epidemiological) preventive actions, including vaccination, screening the blood-supply system, implementing communication campaigns and personal protection measures, and research and innovation.

Within each of these categories, we looked at how the costs are distributed among the various stakeholders (as proposed by Castro et al., 2017): health providers, the individual (or household), and the community. Health providers include public and private health providers, as well as other administrative/private bodies, such as ministries of agriculture, education or tourism, NGOs or UN agencies, according to the type of intersectoral collaboration for *Aedes*-borne disease control (Roiz et al., 2018).

Community refers to the administrative unit of analysis (e.g., neighborhood, village, municipality, province, state, country) bearing large-scale costs associated with *Aedes* invasion and *Aedes*-borne disease infections in the area (Castro et al., 2017), but may also refer to costs that represent a transfer in purchasing power from general taxpayers to individual citizens (e.g., disability and welfare payments). At the individual or the household level, the costs incurred are out-of-pocket payments made by those affected by the illness or by their family members/caregivers.

2.5. Data analysis

After extracting the cost data, we used the 'invacost' package to carry out the analysis (Leroy et al., 2022), updating it for our particular needs. We filtered out unreliable costs by selecting only for high reliability data (*Method_reliability = 'High')*, observed costs (*Implementation = 'observed'*), and costs based on direct observations or estimations (*Acquisition_method = 'Report/Estimation' and 'Extrapolation')*. We also excluded potential costs (i.e., not incurred but expected cost under specific scenarios), e.g., the costs of a disease becoming endemic in a place where there are currently only sporadic outbreaks, or the costs related to lost productivity due to premature mortality. The long-term costs of possible disease sequelae were treated as a type of indirect costs, but because of their estimation methods they were not integrated into the cumulative costs (Note S1), but were instead provided separately as supplementary results due to their particular nature. Besides these criteria, and to avoid data duplication in cost estimation, we took several steps to address the potential issue of double-counting. The methodology was standardized using a decision tree (Fig. S2) to determine which cost would be retained where the same disease, species, cost type, geographical area or/and time frame was involved. Estimates of global-level economic burdens were excluded at this stage and were instead used to make comparisons with our results. Country-level cost records were selected over site-level costs when they overlapped in space and time. For example, if two studies estimated the costs of disease in Colombia in 2010, but one concerned a hospital in the city of Medellin in that country, and the other the entire country, the latter was retained. If two country-level records overlapped in time, we used complementary criteria to evaluate the reliability and completeness of the cost records (Diagne et al., 2020); if reliability was the same, the study that provided more detailed information on costs (clearly defined cost typologies, a longer time span) was retained. Note that, although we made great efforts to avoid double counting, we are aware that "hidden" sources of double-counting could have been missed, particularly at the cost estimation level in the original sources. For example, if authors counted doctor's salary as a separate cost and also included it in the total medical care cost.

We conducted temporal and geographical analyses of the data to determine the distribution and trends of the costs of invasive *Aedes* mosquitoes and the three major *Aedes*-borne diseases (dengue, chikungunya and Zika).

For the temporal analyses of the costs, we standardized the temporal variable 'Impact_year' which refers to the year in which the costs were incurred. For one-year costs, the year of the cost was the same as the year under study. When the cost referred to a period of several years, the mean yearly cost was extended to cover all the years of the study period by applying the 'expandYearlyCosts' function of the 'invacost' package (Leroy et al., 2022). There is a temporal bias that should be acknowledged: we can expect a delay between the economic impact of an invasive *Aedes* species and the estimation and publication of the value of the impact in a report or a journal. Hence, any analysis covering recent years will be based on incomplete data and is therefore highly likely to underestimate the actual costs, thus we estimated the publication lag. We also calculated the observed cumulative and average costs over a 5-year period using the 'summarizeCosts' function of the 'invacost' package (Leroy et al., 2022). This was done for total costs, for damage costs, for management costs, for the *Aedes* species of interest costs, and for specific disease costs (either for dengue, chikungunya or Zika, but not for DEN-CHIK-ZIKA, as we were unable to separate the contribution of each disease). To describe the general patterns of the extracted costs, we used the subset of the data with high reliability over the entire period (1975–2020), filtered according to the criteria described at the beginning of this section However, we used the period with the highest data completeness (1995–2014) (Table S4), to make robust comparisons of costs between periods and for the estimation of mean annual costs.

To assess the behavior of temporal trends in damage and management costs, we used the 'modelCosts' function of the 'invacost' package (Leroy et al., 2022), which fits multiple models to cost data as a function of time. We used different modeling approaches (Supplementary text) to describe the temporal relationship for the accumulation of damage and management costs, choosing 1995 to 2017 as the most appropriate period for because of the sensitivity of the models to the time lag in cost reporting and the discontinuity of data before 1995 (Supplementary text). We used the Global Burden of Disease 2019 (GBD) dataset to compare the trends in the global incidence of dengue and Zika with the evolution of the economic costs of these diseases based on our data synthesis. The GBD is available for over 360 disease and is widely considered as the most up-to-date and systematic assessment of data on disease incidence (Yang et al., 2021). However, because chikungunya incidence is not included in this database, we conducted an additional search based on the outbreaks listed in Data S3 to collate the number of cases associated with these outbreaks. For data on chikungunya in the Americas, we consulted the Pan American Health Organization (PAHO), which has systematically reported on the number of cases since 2013. For other regions, we consulted data reported by official sources (e.g., government or health organizations data) after conducting a directed search based on the list in Data S3. The complete list of data sources is given in Data S3. Total disease incidence was obtained by adding the estimated number of cases of each disease per year. Note that due to gaps in data availability, the number of cases was estimated from 1990 onwards.

3. Results

3.1. Results of the systematic search

The systematic search identified 3242 articles (1972 in WoS and 1270 in PubMed, respectively), and after removing duplicates ($n = 993$), 2249 articles remained (Fig. S1). From the final full-text screening (Fig. S1), we retained 214 references and extracted 1156 cost records covering 166 countries and overseas territories (Data S1). The cost records were distributed across each disease as follows: 760 cost records for dengue, 72 for chikungunya, 270 for Zika, 20 for dengue, chikungunya and/or Zika jointly (DEN-CHIK-ZIKA), and only 2 for yellow fever, while 32 were classified as nuisance costs (not linked to diseases, mostly in European countries where the viruses have not yet been reported). Most (76.6 %) of the reported costs were related to damage (886), followed (22 %) by management (255) and lastly (1.3 %) mixed management and damage costs (15).

From this dataset, we obtained a subset of cost records by applying the criteria described in the Data Analysis section to determine and exclude unreliable cost records and avoid double counting (based on S2; see Appendix 1 for the categories of data that were retained and Table S1 for cost type classification). This subset, which we used of data for all subsequent cost estimations, comprised data from 857 unique cost records covering 157 countries and territories obtained from 148 references (out of 214) that met the criteria. The estimated median delay between impact and publication was 3 years (25 % quartile: 2 years; 75 % quartile: 7 years) (Fig. S3).

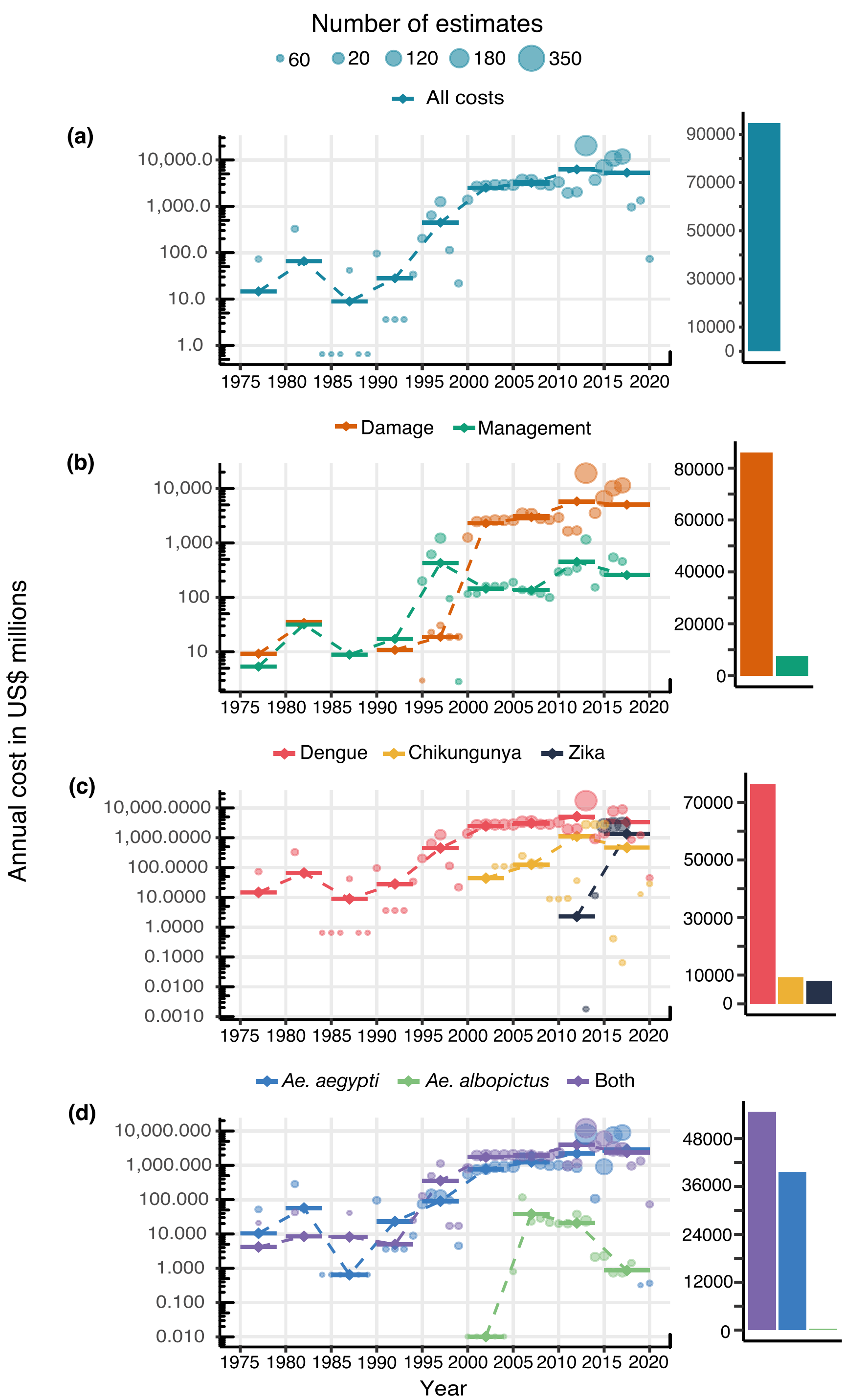

Fig. 1. Temporal trends. Temporal trends (line charts – note the $\log_{10}$ scales) and total cumulative global costs (bar graphs) in 2022 US$ millions between 1975 and 2020. From top to bottom: (a) all costs incurred; (b) damage and management costs; (c) costs of chikungunya, dengue and Zika; (d) estimated costs of *Ae. aegypti* and *Ae. albopictus* separately and together. Solid horizontal bars in the line charts represent 5-year averages, while points show annual totals scaled to the number of final cost estimates included in the conservative version of the dataset for each year. Note that total accumulated costs and damage and management plots include all costs detailed in Table 1, while the disease plot only includes the costs of the individual diseases, and the species plot includes the costs of the diseases associated with the two *Aedes* species, separately and together.

3.2. Cumulated costs

The reported costs to human societies of *Aedes* and the diseases caused by the arboviruses they transmit came to an aggregated value of 2022 US$ 94.7 billion, accumulated over the period 1975–2020 (Fig. 1a-c, Table 1). The estimated average annual cost, calculated over a period of two decades with high data completeness (1995 to 2014) was US$ 3.29 billion with a maximum of US$ 20.3 billion in 2013 (Table S3). The largest costs (79 %) were due to dengue: US$ 76.5 billion between 1975 and 2020, with a maximum of US$ 17.5 billion in 2013. Reported costs of chikungunya (10.7 %) amounted to US$ 9.3 billion during the period 2003–2020, with a maximum of US$ 2.8 billion in 2013. Zika cost US$ 8.1 billion during the period 2013–2017 (9.3 %), with a maximum of US $ 2.8 billion in 2017. However, if we consider the potential costs of the sequelae of chikungunya (rheumatism and cognitive delay) and Zika (microcephaly and Guillain-Barré syndrome) the total costs were considerably higher for both diseases (Table S2; Supplementary text). The total costs of chikungunya sequelae were estimated at US$ 219.3 billion for the period 2013–2015, with an annual average of US$ 73.1 billion. Total Zika costs were estimated at US$ 4.2 billion for the period 2015–2017, with an annual average of US$ 1.4 billion. Therefore, the total estimated cost of the sequelae of these diseases comes to an estimate of US$ 223.5 billion for the period 2013–2017 (Table S2). If we add the cost of the sequelae to the conservative estimate of reported costs, we arrive at an estimated grand accumulated total of US$ 318 billion.

In terms of impacts by species, in areas where *Ae. aegypti* and *Ae. albopictus* occur together, they incurred a minimum reported cost of US$ 54.7 billion during the period 1975–2020, with a maximum of US$ 12.1 billion in 2013 (Fig. 1d, Table 2). An additional cost of US$ 39.7 billion in areas where only *Ae. aegypti* is present and transmits diseases was reported, with an annual maximum of US$ 9.0 billion in 2017. Costs in areas where only *Ae. albopictus* is a concern, records of which were available for the period 2000–2020, amounted to US$ 299.6 million, with an annual maximum of US$ 116.6 million in 2006 (Table 2), which related in particular to the chikungunya epidemic on Réunion Island (Tsetsarkin et al., 2007).

3.3. Management costs vs damage and losses

Reported costs associated with *Aedes* invasion and disease transmission have increased over the last three decades (Fig. 1a), with damage costs being consistently higher than management costs (Fig. 1b). Indeed, accumulated management costs, which amounted to US$ 7.6 billion with a maximum of 1.2 billion in 1997, are approximately an order of magnitude less than damage costs, which have risen to US$ 86.0 billion with a yearly maximum of US$ 19.1 billion in 2013. Average annual reported costs of damage are estimated at US$ 1.9 billion, and average annual management costs US$ 166.3 million, equating to a more than ten-fold difference in terms of annual average reported costs between damages and management.

Table 2
Total and average annual costs *Aedes* species. Total raw costs and average annual costs (in US$ 2022) for *Aedes aegypti* and *Aedes albopictus*. b = billion, m = million.

Aedes species	Total raw costs (US$)	Average annual costs (US $)	Period	Maximum annual cost (US$)	Year of maximum
Aedes aegypti	39.7 b	862.4 m	1975–2020	9.0 b	2017
Aedes albopictus	299.5 m	14.3 m	2000–2020	116.6 m	2006
Aedes aegypti and Aedes albopictus	54.7 b	1.2 b	1975–2020	12.1 b	2013

Costs increased by an estimated 14-fold over the period following Zika and chikungunya emergence (2010–2014) to US$ 31.3 billion compared with US$ 2.2 billion for the period 1995–1999 (Table S3). The average annual cost over the recent period 2010–2014 was US$ 6.2 billion, with a maximum of US$ 20.3 billion in 2013 caused by a huge burden of dengue together with chikungunya (Table S4).

Temporal assessment of accumulated reported costs generally indicates that reported costs of damages have continued to increase since 1995, whereas management costs have only slightly increased staying within the same magnitude, although the period of estimated growth differs between models (Fig. 2a, Supplementary text). The increasing trend in the cumulated costs of dengue, chikungunya and Zika corresponds with the growing incidence of these diseases (Fig. 2 b, c).

3.4. Geographical distribution

The Americas and Asia are the regions with the highest cumulated reported costs at US$ 44.9 billion and US$ 47.8 billion, respectively, between 1975 and 2020, respectively (Fig. 3a). Current reports of economic costs are inconsistent across regions, several of which lack studies (such as Africa and the European Mediterranean region) (Fig. 3a). There is also considerable disparity among countries: for some, few of the costs are reported while certain countries and geographic regions provide more comprehensive reports (Fig. 3b).

3.5. Distribution by type of costs

In terms of cost distribution, we found the reported costs to be primarily direct medical expenditure for dengue transmitted by *Ae. aegypti,* followed by indirect costs and losses (Fig. 4a). The reported cumulative medical care costs (including direct medical and direct non-medical costs) rose to an accumulated US$ 46.3 billion over the period 1975–2020, with a maximum of 5.0 billion in 2016. In the same period, indirect costs accounted for US$ 20.7 billion, with a maximum of 4.6 billion in 2013, while losses amounted to US$ 9.4 billion, with a maximum of 2.5 billion in 2016. Different stakeholders incurred or paid the various costs, but health providers absorbed most of the medical costs associated with dengue, chikungunya, and Zika (Fig. 4a). The burden of the direct medical costs of dengue and chikungunya was also shouldered by individuals (out-of-pocket costs), in addition to health providers. Losses were estimated to be larger for Zika and dengue, with the community bearing most of these costs (Fig. 4a, b). Indirect costs were largely absorbed by individuals or the community.

4. Discussion

4.1. Massively increasing reported global costs

Our study is a pioneer in terms of integrating cost reports to produce a synthetic estimate of the different types of economic cost related to dengue, Zika, and chikungunya associated with *Ae. aegypti* and *Ae. albopictus*. While our cost-synthesis is based on reported evidence obtained from high-reliability records and does not represent an incidence-based assessment of economic burden, it provides much-needed insights into the broader economic implications of *Aedes*-transmitted diseases. The results confirm *Ae. aegypti* and *Ae. albopictus* as the invasive species with the highest costs (Cuthbert et al., 2022a,Cuthbert et al., 2022b), sustained mostly in areas where both species occur together (55.5 %), rather than in areas where only *Ae. aegypti* (44.0 %) or only *Ae. albopictus* (0.3 %) occur.

Our results - a total cumulative cost of US$ 94.7 billion, a mean annual cost of 3.29 billion, and a maximum of US$ 20.9 billion - are within the same order of magnitude as other large-scale global estimates. Shepard et al. (2016) estimated the cost of dengue at US$ 8.9

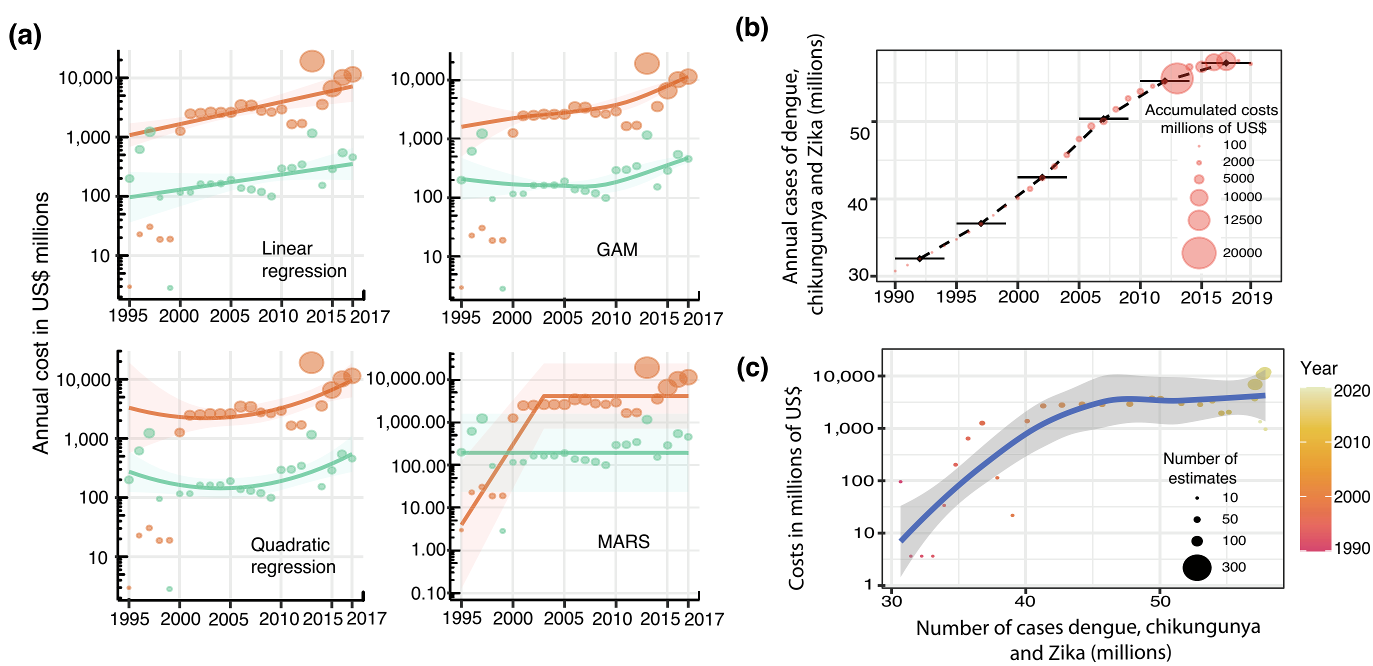

Fig. 2. Temporal trends in damage and management costs and their relation to disease incidence. (a) Temporal trends in damage and managent costs based on mean annual costs for 5-year intervals and modelled predictions for 1995–2017 assessed with 4 different statistical models: robust linear regression, robust quadratic regression, generalized additive model (GAM), and multivariate adaptive regression splines (MARS). Note that only in the case of the MARS model, the shaded areas do not represent 95 % confidence intervals but rather prediction intervals. (b) Accumulated annual number of cases of dengue, Zika and chikungunya from 1990 to 2019 (see Supplementary Note 3 for details on how the number of cases was estimated). Solid horizontal bars represent 5-year averages, while points represent annual totals, scaled to the number of accumulated cost estimates (in 2022 US$ millions) for a particular year, as estimated from the conservative data subset. (c) Relationship between annual costs and number of cases of dengue, Zika and chikungunya. The blue line represents the average trend fitted with locally estimated scatterplot smoothing. The shaded area represents the 95 % confidence interval.

billion in 2013, a little under half our figure of US$ 17.5 billion for that same year (Table S4). Based on several assumptions (Shepard et al., 2016) and extrapolated potential costs, Selck et al. (2014) arrived at an estimated US$ 39 billion for 2011. A study conducted by the World Bank estimated the global cost of Zika at US$ 3.5 billion in 2017 (World Bank, 2018), and our estimate for the same year was comparable to this at US$ 2.8 billion. We should make it clear that our results are based on reported costs, and do not include hypothetical potential costs, such as those that may be associated with future loss of productivity due to premature mortality, a likely source of the differences with estimates from other studies. Furthermore, our stringent criteria for excluding double-counting allowed us to refine previous estimates (Diagne et al., 2021). Our methodology therefore constitutes an enhanced approach to synthesizing the reported global costs of *Aedes*-borne diseases.

Comparing our estimate of the global economic burden of *Aedes*-borne diseases with the incidence of these diseases, we can see that the dramatic increasing trends in the cumulative costs of dengue, chikungunya and Zika correspond with the growing incidences of these diseases (Fig. 2b, c). According to a report based on data from the Global Burden of Disease (GBD) 2019 study, dengue has increased by 85.5 % over the past 30 years (Yang et al., 2021), with 2019 seeing the worst dengue outbreaks recorded in the Americas (PAHO, 2020). The economic impact of *Aedes* and *Aedes*-borne diseases is likely to continue in future decades in conjunction with the increase in their drivers (climate change, global change, urbanization, tourism, trade), putting most of the world's population at risk (Kraemer et al., 2019; Messina et al., 2019; Ryan et al., 2019).

4.2. Is prevention better than cure?

The reported global economic costs of damage and losses are ten times higher than investment in management, equating to a more than ten-fold difference in terms of average annual and total reported costs of damages vs. management. Temporal assessment of the reported cumulated costs indicates that the costs of damage have continued to rise since 1995, while management costs have remained within the same magnitude, and consistently below damage costs, with an estimated 1–2 orders-of- magnitude of difference (Fig. 2a; Supplementary text).

This reflects the uneven and limited investment in mosquito control, where increases in reported management costs correspond with the emergence of chikungunya, Zika and epidemic dengue. Spending on effective actions to control *Aedes* and the diseases they transmit could lower the public health burden and reduce economic damages and losses in the longer term (Fitzpatrick et al., 2017; Ahmed et al., 2022). The damages and losses thus avoided represent the potential benefits of these management actions.

We note, however, that although we conducted a grey literature search on management costs, these are likely to be underestimated due to a lack of information accessibility, or to inaccessibility or unavailability of government expenditure reports. Nonetheless, our results might suggest that, despite the probable underreporting of these costs, there is a large margin for investment in management. The chronic underfunding of vector control has been highlighted as an increasingly exacerbating factor where *Aedes*-borne diseases are concerned (Wilson et al., 2020). While greater financial efforts in terms of investment in control strategies is needed, these are not always effective, and notable deficiencies in control programs are reported worldwide, including ineffective implementation, inadequate application coverage, and insecticide resistance, among others (Roiz et al., 2018; Wilson et al., 2020). Therefore, this would require case-by-case cost-effectiveness studies of strategies aimed at reducing potential cases of arboviral diseases, including through a reduction in *Aedes* densities. To date, there is limited evidence for and understanding of the effectiveness of vector control strategies and their economic costs (Vazquez-Prokopec et al., 2010; Roiz et al., 2018; Cuthbert et al., 2022a,Cuthbert et al., 2022b). It has been suggested that early action with proactive (preventive)

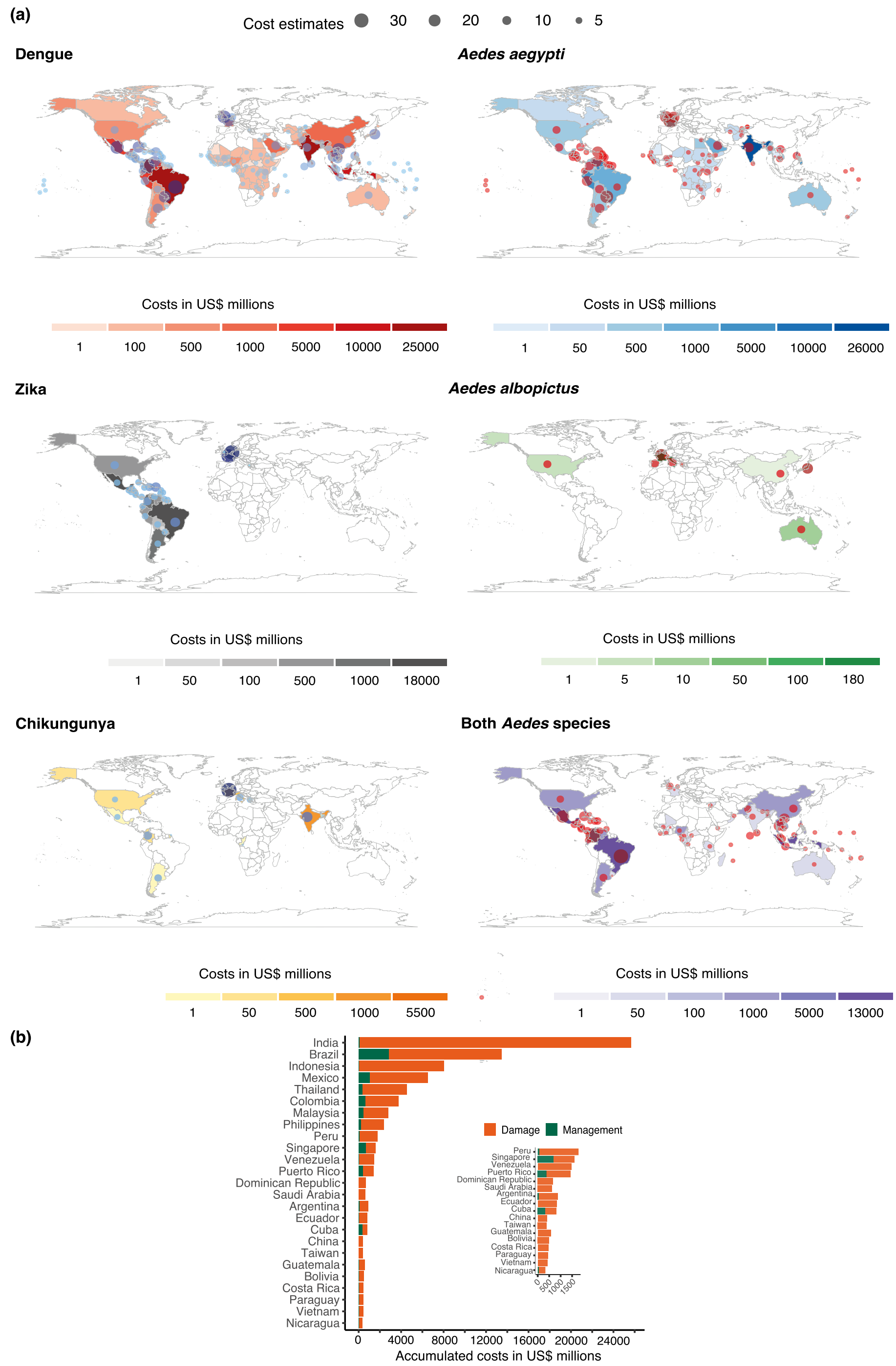

Fig. 3. Geographical patterns. (a) Cumulative costs by country for dengue, Zika, and chikungunya, and for *Ae. aegypti* and *Ae. albopictus* separately and together, calculated for the period 1975–2020 and expressed in 2022 US$ millions. The relative numbers of cost estimates available for each country is indicated by the size of the circles (blue for diseases and in red for *Aedes* species). Note that costs for overseas territories are included in the estimate for the associated country (e.g., La Réunion island is included in the total estimate for France). (b) Accumulated costs in 2022 US$ millions by type of cost (damage, management, and mixed) for the 25 countries with the highest estimated total costs for the period 1975–2020. Note that costs for overseas territories are added with those of their corresponding countries.

strategies rather than reactive (emergency) responses or even inaction will be more cost-effective (Vazquez-Prokopec et al., 2010; Fitzpatrick et al., 2017; Roiz et al., 2018; Ahmed et al., 2022). Cost-effectiveness studies of management strategies with statistically significant positive findings favorable to the intervention under study are also more likely to be published, creating a potential publication bias (Bell et al., 2006). There is still work to be done to provide pertinent, robust cost-effectiveness guidance for evidence-based management strategies, as little research has so far been published (Tschampl et al., 2020; Brady et al., 2020). The ultimate aims are the efficient, sustainable and integrated management of these invasive mosquitoes and their associated arboviruses. The benefits are not only economic, they also concern public health, such as the prevention of millions of cases of disease and thousands of deaths, and include indirect benefits to society and human well-being.

4.3. Costs are largely underestimated

Our consolidated dataset is the most up-to-date, comprehensive, standardized, robust, global-scale compilation of the reported monetary costs of *Ae. aegypti/albopictus* and arboviruses they transmit (dengue, chikungunya and Zika) for the period 1975 to 2020. However, our figures undoubtedly represent an underestimation of the economic costs of *Aedes* and *Aedes*-borne diseases, for reasons similar to those in other global investigations of the economic costs of invasive species (Diagne et al., 2021; Hulme et al., 2024).

First, we focused on the most reliable, observed costs in line with the general approach of Invacost (Diagne et al., 2021). An example of other

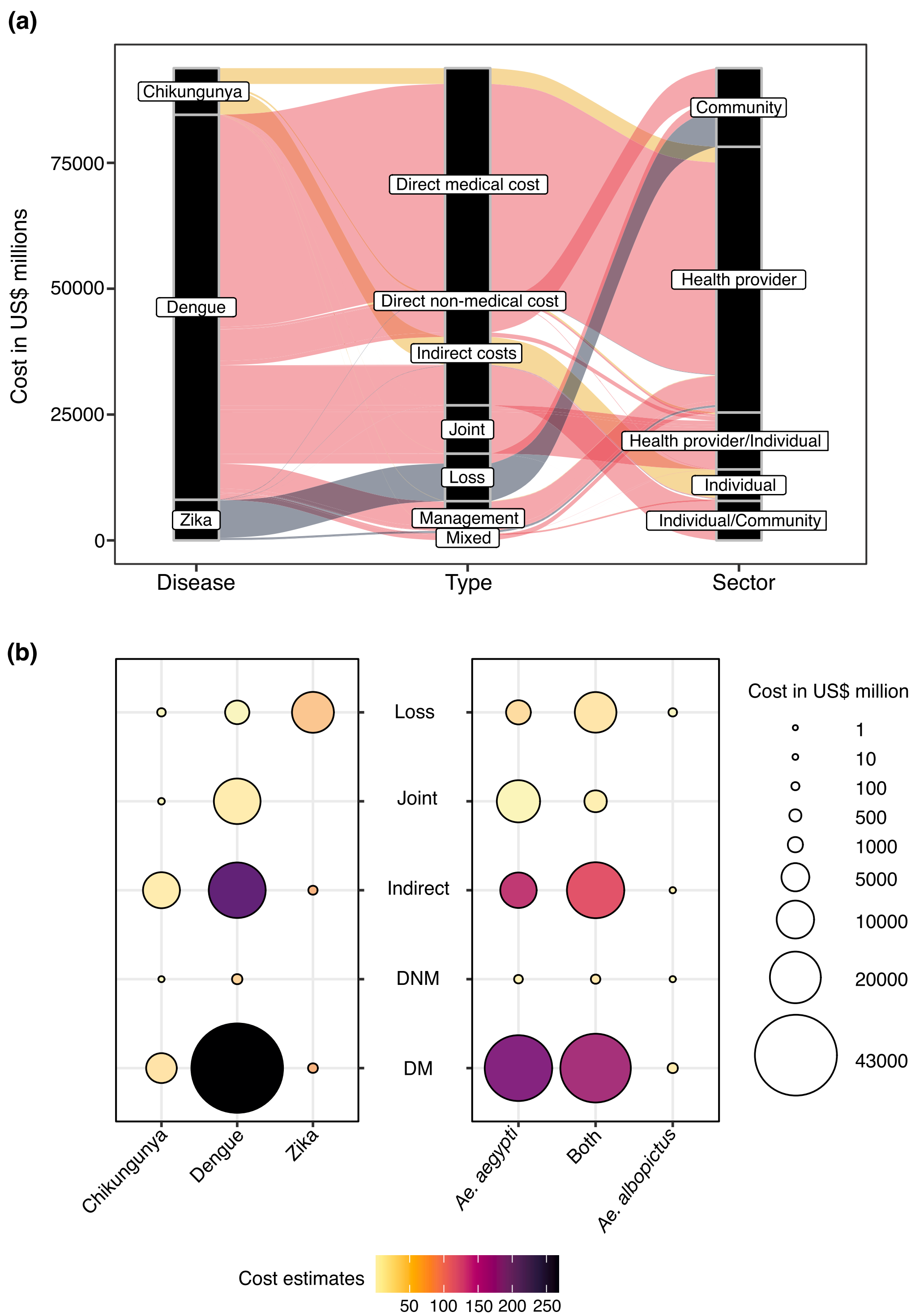

Fig. 4. Cost distribution. (a) Distribution flow of types of costs by disease and cost-bearers in 2022 US$ millions. Damage categories are further subdivided into direct medical, direct non-medical, indirect and joint costs, and losses. Management costs are not subdivided. Mixed costs refer to data entries where damage and management costs were given in the same estimate and could not be separated. Health providers carry the highest burden of reported costs. (b) Total costs for each subcategory of damage (in 2022 US$ millions) by disease and *Aedes* species. Cost subcategories are comprehensively defined in the main text (The nature of costs section). The joint cost subcategory comprises combined estimates for two or more damage subcategories that could not be separated (e.g. losses + direct medical costs). DM = Direct medical costs, DNM = Direct non-medical costs. These estimates do not include the costs of sequelae.

costs that could be provided separately to refine our estimates are those relative to the possible long-term sequelae of Zika and chikungunya, which would increase the total accumulated cost to US$ 318 billion (estimated from information available for the period 2013–2017) (Table S2). A more systematic follow-up of the incidence and costs of sequelae would improve current estimates (Supplementary text). In addition, other cost estimates currently excluded, such as scenario-based extrapolations, could be used as input for estimating the economic impact of *Aedes*-borne diseases as a result of both the observed disease burden and potential scenarios. However, the general InvaCost approach was not designed to extrapolate data into the future (i.e., the period after the database is used) due to the lack of certainty surrounding future cost trends (Diagne et al., 2021).

Second, it is likely that costs are either not measured, are underreported or are difficult to access. There is a huge disparity among countries, and a lack of high-quality data in low- and middle-income countries (Chilakam et al., 2023). Although our results show the Americas and Asia to be the regions with the highest reported cumulated costs, reports of economic costs are inconsistent across regions, with several (such as Africa and the Eastern Mediterranean region), lacking studies, and having been particularly neglected they have an unknown burden (Fig. 3a). The disparity of costs across different countries (Fig. 3b) needs to be viewed in the light of multiple factors, including research efforts, economic capacity, medical care costs dependent on the healthcare system, and the entomo-epidemiological context, to mention a few. The information presented is, therefore, inevitably fragmented and incomplete. A recent analysis found cost records to be often imprecise (Hulme et al., 2024). Furthermore, comparisons among areas should be treated with caution and context taken into account. For example, there are limited data on the economic impacts in high-income countries of temperate/Mediterranean Europe, where *Ae. albopictus* has spread and sporadic arboviral transmission is becoming an increasing concern. Comparison with tropical areas with endemic transmission might not be apposite.

Different stakeholders incur or pay the various costs, with health providers absorbing most of them (48.9 %; US$ 42.7 billion), specifically the direct medical costs, which are typically easy to identify and quantify, and are mainly due to dengue (Fig. 4b). Much more difficult to quantify, and hence potentially underreported, are the indirect medical costs, that are largely absorbed by individuals or the community and which may be not only hidden but also very high and burdensome in the long term (Supplementary text). There are few cost records concerning losses (such as in tourism, trade or economic growth), which were estimated to be larger for Zika and dengue, the costs of which were mostly borne by the community (Fig. 4a). Non-market losses are also common, particularly at the individual level, such as the loss of well-being due to illness or loss of education opportunities. However, they are underestimated since they have not been widely studied, and they were not included in the search strings we used (Diagne et al., 2020). Finally, the burden of out-of-pocket costs, largely due to indirect and direct non-medical costs absorbed by the individual, are not commonly covered by health providers in endemic areas (Fig. 4 a, b). These costs represent a disproportionate and underreported burden among impoverished populations without access to public health services, which further reinforces the poverty trap (Vanlerberghe and Verdonck, 2013).

Developing a framework for cost estimation will improve our ability to make a more comprehensive and accurate evaluation of the economic costs of *Aedes* and *Aedes*-borne diseases. We have several suggestions for limiting the uncertainty and underreporting of future cost compilations (Table S5). For instance, we recommend including information on whether the extracted costs are related to endemic or epidemic years, and analyzing in greater depth the distribution of healthcare costs among different countries to more accurately assess who bears the costs (Shepard et al., 2014). A greater degree of standardization in estimating and reporting of economic costs would ensure that the data were comparable across different countries, diseases, vector species, and types of costs. Although our specific cost typology framework was developed for *Aedes* and *Aedes*-borne diseases with specific adaptations, it could, with specific adaptations, be extended to other infectious diseases.

5. Concluding remarks

Our work provides key information on the reported economic cost estimation of *Aedes* and *Aedes*-borne diseases on a global scale, and on the distribution of costs over the impacted sectors. It fills a gap in our still limited understanding of the costs caused by these species, and will help decision-makers and stakeholders by providing them with robust benchmark estimates to make informed decisions, setting priorities, allocate resources, and or select control strategies (Fitzpatrick et al., 2017). In parallel, systematic societal changes and highly committed international collaboration will be essential to implementing prevention actions aimed at limiting the dispersal of invasive *Aedes* and the diseases they transmit worldwide. Such commitments represent an opportunity to take action toward preserving global health and reducing health inequalities. More broadly, we similarly advocate expanding efforts to manage the risks associated with other invasive alien species (Zhang et al., 2022) and with other emerging diseases (Bernstein et al., 2022).

CRediT authorship contribution statement

David Roiz: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Paulina A. Pontifes:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Christophe Diagne:** Writing – review & editing, Validation, Methodology, Conceptualization. **Boris Leroy:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation. **Anne-Charlotte Vaissière:** Conceptualization, Methodology, Writing – review & editing. **María José Tolsá-García:** Investigation, Validation, Writing – review & editing. **Jean-Michel Salles:** Writing – review & editing, Validation, Methodology, Conceptualization. **Fréderic Simard:** Writing – review & editing, Validation, Funding acquisition, Conceptualization. **Franck Courchamp:** Writing – review & editing, Validation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The database of the economic costs, including the database descriptors and the full list of references (Data S1), the database of *Aedes* invasions (Data S2), data sources for *Aedes*-borne disease incidence estimates (Data S3), and the Code for the analysis and graphs in R (Data S4) can be downloaded from the following Dryad repository (https://datadryad.org/stash/share/AJJnBnPHBWuRNBdCyKi2U1txf2YLUGHXU2daAXC1G9Q).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2024.173054.

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