A systematic review and evaluation of Zika virus forecasting and prediction research during a public health emergency of international concern

Kobres P-Y[1], Chretien JP[2], Johansson MA[3], Morgan J[4], Whung P-Y[5], Mukundan H[6], Del Valle SY[6], Forshey BM[7], Quandelacy TM[3,8], Biggerstaff M[9], Viboud C[10], Pollett S[11,12,13*]

[1]School of Public Health, George Washington University, DC, USA

[2]Department of Defense, MD, USA

[3]Division of Vector-Borne Diseases, Centers for Disease Control & Prevention, Atlanta, GA, USA

[4]Joint Research and Development Inc, VA, USA

[5]Office of Research & Development, US Environmental Protection Agency, DC, USA

[6]Los Alamos National Laboratory, NM, USA

[7]Armed Forces Health Surveillance Branch, MD, USA

[8]Johns Hopkins School of Public Health, MD, USA

[9]Influenza Division, Centers for Disease Control & Prevention, Atlanta, GA, USA

[10]Fogarty International Center, National Institutes for Health, MD, USA

[11]Viral Diseases Branch, Walter Reed Army Institute of Research, MD, USA

[12]Department of Preventive Medicine & Biostatistics, USUHS, MD, USA

[13]Marie Bashir Institute, University of Sydney, NSW, Australia

Short title: Zika virus forecasting and prediction studies: a systematic review and evaluation

***Corresponding author:** simon.d.pollett.ctr@mail.mil

Abstract

INTRODUCTION: Epidemic forecasting and prediction tools have the potential to provide actionable information in the midst of emerging epidemics. While numerous predictive studies were published during the 2016-2017 Zika Virus (ZIKV) pandemic, it remains unknown how timely, reproducible and actionable the information produced by these studies was. **METHODS**: To improve the functional use of mathematical modeling in support of future infectious disease outbreaks, we conducted a systematic review of all ZIKV prediction studies published during the recent ZIKV pandemic using the PRISMA guidelines. Using MEDLINE, EMBASE and grey literature review, we identified studies that forecasted, predicted or simulated ecological or epidemiological phenomenon related to the Zika pandemic that were published as of March 01, 2017. Eligible studies underwent evaluation of objectives, data sources, methods, timeliness, reproducibility, accessibility and clarity by independent reviewers. **RESULTS**: 2034 studies were identified, of which n = 73 met eligibility criteria. Spatial spread, R_0 (basic reproductive number) and epidemic dynamics were most commonly predicted, with few studies predicting Guillain-Barré Syndrome burden (4%), sexual transmission risk (4%) and intervention impact (4%). Most studies specifically examined populations in the Americas (52%), with few African- specific studies (4%). Case count (67%), vector (41%) and demographic data (37%) were the most common data sources. Real-time internet data and pathogen genomic information were used in 7% and 0% of studies, respectively, and social science and behavioral data were typically absent

in modeling efforts. Deterministic models were favored over stochastic approaches. Forty percent of studies made model data entirely available, 29% provided all relevant model code, 43% presented uncertainty in all predictions and 54% provided sufficient methodological detail allowing complete reproducibility. Fifty-one percent of predictions were published after the epidemic peak in the Americas. While the use of preprints improved the accessibility of ZIKV predictions by a median 119 days sooner than journal publication dates, they were used in only 30% of studies. **CONCLUSIONS:** Many ZIKV predictions were published during the 2016-2017 pandemic. The accessibility, reproducibility, timeliness, and incorporation of uncertainty in these published predictions varied and indicates that there is substantial room for improvement. To enhance the utility of analytical tools for outbreak response, it is essential to improve the sharing of model data, code, and preprints for future outbreaks, epidemics and pandemics.

Author summary: Researchers published many studies which sought to predict and forecast important features of Zika virus (ZIKV) infections and their spread during the 2016-2017 ZIKV pandemic. We conducted a comprehensive review of such ZIKV prediction studies and evaluated their aims, the data sources they used, which methods were used, how timely they were published, and whether they provided sufficient information to be used or reproduced by others. Of the 73 studies evaluated, we found that the accessibility, reproducibility, timeliness, and incorporation of uncertainty in these published predictions varied and indicates that there is substantial room for improvement. We identified that the release of study findings before formal journal publication ('pre-prints') increased the timeliness of Zika prediction studies, but

note they were infrequently used during this public health emergency. Addressing these areas can improve our understanding of Zika and other outbreaks and ensure that forecasts can inform preparedness and response to future outbreaks, epidemics and pandemics.

Introduction:

Zika virus (ZIKV) is a positive sense RNA flavivirus primarily transmitted through the *Aedes aegypti* mosquito (1-3). While the majority of ZIKV infections are asymptomatic or present as a self-limiting febrile illness, strong evidence links ZIKV infection with microcephaly and a range of other birth defects including limb deformity and retinopathy (4, 5). ZIKV is also associated with Guillian-Barre syndrome, and a spectrum of other neurological disorders including meningoencephalitis and acute myelitis (6-9). ZIKV was discovered in Uganda in a febrile non-human primate in 1947 (10), and the first human case was detected in Nigeria in 1953 (11). ZIKV outbreaks were detected in South East Asia and the Pacific Islands in the early 21st century (12-16) followed by wide spread epidemics in the Americas from late 2014 onward with a cumulative count of 583,144 suspected and 223,336 laboratory-confirmed Zika cases reported across 49 countries and territories by the end of 2017 (17, 18).

The Director-General of the World Health Organization declared the ZIKV pandemic a public health emergency of international concern (PHEIC) on February 1, 2016 (19). The urgency for immediate, coordinated global response was further accelerated by the Olympic and Paralympic games set to take place in Rio De Janeiro, Brazil during August 2016 (20). As public

health and medical research efforts for Zika increased across the Americas, scientists developed mathematical models to anticipate further outbreak spread, evaluate possible control measures, and gain insight into outbreak dynamics. These models used a range of data sources including case counts, vector abundance and distribution, population age structure, human mobility, climate information, viral sequence and serological data, and internet 'big data' streams. A range of statistical and mathematical models predicted the spread and other epidemic dynamics of ZIKV, as well as the burden of its complications (21-26).

While the WHO PHEIC status was lifted in November 2016 and the neotropical Zika pandemic has waned, the forecasting activities during the pandemic have not been systematically examined, particularly whether the studies were published in a manner and time-frame that was actionable during the Zika pandemic (27). Such an exercise is critical, not only due to the ongoing risk of Zika globally (28), but also to inform modeling efforts for future major epidemics. We therefore undertook a systematic review to identify all published ZIKV prediction and forecasting studies during a time period which encompassed the PHEIC period and the peak and waning phase of the epidemic in the Americas. The first aim of this systematic review was to identify all published models that predicted, forecasted or simulated any ecological or epidemiological phenomenon about the Zika pandemic and describe the predicted phenomena, the range of data sources used and the modeling methods employed. This first aim sought to characterize the methods and data employed to answer key questions during the epidemic and to identify potentially underutilized data or methods. The second aim was to evaluate key scientific characteristics of these studies, including (i) accessibility and timeliness

of the publication, (ii) reproducibility of the methods and access to the statistical code and data, and (iii) clarity of the presentation of the prediction results, including uncertainty in prediction estimates. The third aim was to describe the funding structure and major contributing sectors, such as government, industry, non-governmental organizations, or academia, behind these publications.

Methods

The PRISMA and Cochrane systematic review guidelines were adopted (29). A panel of 12 investigators developed the systematic review protocol including the eligibility criteria and the data abstraction tool. No formal protocol was published for this systematic review.

Literature search strategy:

We conducted a literature review using EMBASE and MEDLINE (PubMed) to identify all potentially eligible studies, which predicted or forecasted phenomenon of the ZIKV pandemic. In MEDLINE we performed a highly sensitive search solely using the term “Zika”. A complementary search in EMBASE used a more specific ontology: “Zika AND (forecasting OR prediction OR model OR modeling OR modelling OR risk OR estimating OR dynamics) NOT mouse”. Both database searches were limited to articles published as of March 1, 2017, and the MEDLINE searching was restricted to those publications released between February 1, 2016 and March 1, 2017. We complemented these database search results with ‘grey literature’,

133 including hand-searching of bibliographies of major Zika epidemiological review articles (17, 30,
134 31) and contacting experts in the field of Zika modeling to identify any studies which we may
135 have been missed by the above search strategies.
136
137 *Screening and eligibility determination:*
138
139 Using a two-reviewer system (with consensus for disagreements and conferral with a 3rd party
140 adjudicator if a consensus was unable to be reached), all articles identified through the above
141 literature search were screened by reviewing the title and abstract to remove all articles that
142 clearly did not meet the eligibility criteria (below). The full text of the remaining articles was
143 reviewed by two reviewers, with a third reviewer if a consensus was not reached by the first
144 two reviewers. Eligibility was based on the following inclusion and exclusion criteria:
145
146 *Inclusion criteria*:
147 Forecasted, predicted or simulated any epidemiological or ecological phenomenon about the
148 Zika pandemic (including studies regarding previous outbreaks and epidemics, and regions
149 outside the Americas), including but not limited to spatial spread risk, host and ecological
150 range, disease and complication burden, economic impact transmission and other epidemic
151 dynamics. We didn't require studies to explicitly present a future phenomenon risk, and we
152 included time agnostic estimations of key epidemic parameters and other phenomena.
153
154 *Exclusion criteria:*

- Did not include original analyses (e.g. review articles, perspective pieces, editorials, recommendations, and guidelines)
- Duplicated studies
- Animal and mosquito in-vivo pre-clinical models (e.g mouse, non-human primates)
- *In vitro* studies
- Descriptive epidemiological publications (e.g. describing case positive proportions, total case numbers, descriptive mapping of incidence by geographic information systems)
- Models which only examined causality of ZIKV in Guillain-Barré Syndrome (GBS) or microcephaly (rather than estimating risk or burden, for example)
- Studies which only modeled non-ZIKV arboviruses, unless the central aim of the study was to explicitly forecast or predict ZIKV phenomenon based on the known dynamics of other arboviruses

Data abstraction, collation and analysis:

Data were abstracted from the full texts by 12 reviewers (single-reviewer abstraction) across the domains of (i) objectives and study population, (ii) methodology and reproducibility, (iii) accessibility, timeliness and other bibliometrics of eligible studies, and (iv) author affiliation and funding sources (Table S1). In addition, the availability of preprint manuscripts was assessed using the pre-print search webtool *search.bioPreprint* (32), a server which identifies preprints from arXiv, bioRxiv, F1000Research, PeerJ Preprints, and Wellcome Open Research.

Additionally, we manually searched arXiv and bioRxiv archives to confirm pre-print availability. These pre-print repositories are distinct from the advanced electronic publications made available by most journals after acceptance and peer review. Such 'grey literature' review extended beyond the cut-off date for the main literature database searches. A two-reviewer approach was used to ascertain whether eligible studies were made available as pre-print. From the abstracted data, descriptive analyses (medians, IQR, ranges and proportions) and limited hypothesis testing were performed using Stata version 13.0 (StataCorp, College Station, TX, USA).

Results:

Of 2034 studies identified, 73 articles published predominantly from 2016 to 2017 met the inclusion criteria (Fig 1) (20-26, 28, 33-97). The most commonly predicted phenomena were spatial spread (34%), followed by R_0 (basic reproductive number) or R_E (effective reproductive number) (29%), epidemic dynamics (peak size/timing, final size and trajectory) (28%), microcephaly burden (15%), and vector competence and ecology (12%) (Table 1). Most of the geographically resolved predictions were concentrated in the Americas (42%) and Asia-Pacific (21%), while few studies were from Africa (4%). Across 73 studies, the most commonly used data were infection case counts, vector data, and demographic data, followed by climate, meteorological, earth science and transport data (Table 2). Genomic data was not used in any of the studies and few studies used novel real-time internet data streams such as those harnessing open access social media and internet-search engine platforms.

199

200 Only 40% of studies made all relevant source data entirely accessible, while more than 20% of
201 the eligible studies did not make any source data available either directly (e.g. an associated
202 data repository) or indirectly (e.g. a citation or web-link) (Table 2). The visual display of model
203 output was at least partly clear and accurate in 95% of the studies. Over a third of the studies
204 did not present estimates of prediction uncertainty. Approximately half of the studies did not
205 entirely present methods with a level of detail to allow reproducibility. Over 60% of the studies
206 did not provide any computational code used for the analyses. We classified more models as
207 deterministic (76%) as opposed to stochastic. It should be emphasized we only ultimately
208 evaluated whether a model was deterministic versus stochastic.

209

210 The large majority of published manuscripts were freely accessible (e.g. without a paywall),
211 although 4% were published with paid access only (Table 3). Less than one third of manuscripts
212 were posted on rapid preprint servers (e.g. bioRxiv (98), prior to publication in a peer-reviewed
213 journal. The median time from journal submission to e-journal publication time was 93.5 days,
214 with the maximum time greater than 1 year. This included delays after manuscript acceptance,
215 25% of the studies had delays of more than 24 days between acceptance and publication (Table
216 3). Most of the prediction studies were published late in the epidemic, well after the peaks in
217 reported Zika cases (Fig 2, Fig 3). Submitting manuscripts to preprint servers made results
218 available earlier by a median of 119 days (maximum 331 days, IQR 30 – 177 days) (Table 3). This
219 shift led to more results being available close the time of the 2016 South America and Central
220 America epidemic peaks and prior to the epidemic peak in the Caribbean and the 2017 peak in

Central America (Fig 2, Fig 3). Comparing the impact factor of journals accepting studies which were posted as preprints (versus the impact factor of those journals accepting studies which were not posted as pre-prints), there was no significant difference (median impact factor 4.37 vs. 4.45 respectively; p = 0.84 by Mann-Whitney U test).

Over 90% of the studies included authors with academic affiliations (Table 4). Government affiliated authors participated in a minority of studies, although this may simply reflect "in-house" operational models not being published through journals. Among studies with identifiable funding sources, funding was divided among several sources, though the most common was the United States government, which funded or partially funded 50% of the studies (Table 4). However, many of those studies and other had a variety of funding sources, 85% had at least one non-U.S. government source. Non-governmental organizations were the second most common source, being included in 35% of the studies.

Discussion:

Public health agencies, policy-makers, and other stakeholders are carefully examining the response to Zika. Such 'lessons-learned' exercises have been fruitful for prior pandemics and outbreaks, including Ebola, SARS, MERS-CoV, pH1N1, and chikungunya viruses. These exercises have included introspection, analysis, and recommended action with respect to research, public health and policy agendas (99-104). To date, public health 'lessons-learned' activities related to the Zika PHEIC have focused on improved ethics preparedness for rapid research during public

243 health emergencies (105), identification of other high-epidemic-risk pathogens with relatively
244 inadequate countermeasure investment (106), expedited approaches to vaccine and other
245 medical countermeasure development (107), rapid data-sharing and material transfer (108-
246 110), and enhancing the role of media communication during epidemics (111).
247
248 In contrast to existing reviews on models developed during the ZIKV pandemic, which described
249 specific contributions of modeling (112) or validated analytical assessment of results (113), this
250 systematic review focused on capturing lessons that could improve the functional use of
251 mathematical modeling in support of future infectious disease outbreaks. Extending an
252 approach used by Chretien et al. in their evaluation of Ebola models, we focused on aspects of
253 the studies that likely are particularly relevant to their usefulness during an outbreak (103). This
254 included modeling methods and input data, timeliness and accessibility of the publications,
255 reproducibility (e.g. provision of data and code), and the communication of uncertainty.
256
257 Our systematic review identified a large number of Zika models that predicted a wide range of
258 epidemiological and ecological phenomena. The most commonly predicted phenomena were
259 spatial spread, R_0, epidemic dynamics, microcephaly burden, and vector competence. Notably
260 few of the studies modeled the impact or cost-effectiveness of interventions, sexual
261 transmission risk, or GBS burden. Not surprisingly, the majority of the studies were set in the
262 Americas where most of the cases were reported during the pandemic. Notably one of the
263 global gaps for understanding ZIKV dynamics is Africa, where ZIKV was discovered, is endemic,
264 and poses a risk of future epidemics (114-116).

The leading data types for the examined studies were conventional case counts, vector, demographic, climate and transport data. This finding reflects not only the availability but also the importance of such data. Case count data in particular are often hard to access but critical to many modeling approaches. Rapid sharing of case count data during international public health emergencies, as well as open, curated, rapidly accessible baseline demographic, human mobility, climate, and environmental datasets are essential to quickly leverage modeling and forecasting efforts (109). Our review also identified several relatively underused data streams. First, socioeconomic and behavioral data were conspicuously absent. The lack of behavioral components in these models is concerning given the importance of these factors on disease dynamics. Second, real-time internet-based data-streams, such social-media and internet search-engine data, were used in a minority of ZIKV prediction studies identified in this systematic review. The limited use of internet 'big data' in the models suggests that either these data are of lower value for epidemic forecasting or that methods have yet to be developed to efficiently extract important information from them. Such data streams may be more commonly used in forecasting in the future as their strengths and weakness become clearer (117).

Genomic data were absent from these published models. During the pandemic, sequencing platforms were employed to generate data critical to diagnostic and countermeasure development (118), but our systematic review revealed that these data were not incorporated into prediction frameworks during the first year of ZIKV pandemic. This may reflect that early

287 molecular epidemiology studies aimed to reconstruct the invasion and evolution of ZIKV rather
288 than forecasting future changes (119, 120). Some phylodynamic studies were published after
289 the time period of the systematic review, with interesting results highlighting the possibility for
290 phylogenetic data to provide unique insight into epidemic dynamics and possibly forecasting
291 (120-122). The relative delay of these studies (relative to other to those using other data
292 sources) echoes a similar time lag of phylogenetic studies during the 2015 Ebola epidemic (103).
293 The lack of phylogenomic studies captured by this review also suggests that substantial
294 bottlenecks still exist in using these data sources in epidemic response, despite advances in
295 mobile near "real-time" sequencing technologies (118). In the future, as new methods are
296 developed, and genomic data become more readily available, the use of these data will likely
297 become more common in prospective forecasting frameworks.
298
299 Our systematic review did not delve deeply into modeling approaches, but did identify a
300 preponderance of deterministic as opposed to stochastic models. Both categories of models
301 have pros and cons and their use is often informed by the specific question being addressed, in
302 addition to data availability (123). Deterministic models may generally be easier to produce, but
303 they do have limitations for intrinsically stochastic processes like epidemics, such as
304 underestimating uncertainty (124). Uncertainty is particularly important in this context where
305 uncertainties are generated by the epidemic itself, data collection, and analytical approaches.
306 Moreover, forecasts are ideally used to inform the mobilization of resources to save lives, a
307 context in which clearly characterizing uncertainties is paramount. This is also a clear area for
308 improvement in model output reporting; only 43% of studies completely reporting uncertainty.

Our review also provided a unique evaluation of the more functional aspects of published predictions and forecasts. We determined that the visual clarity of model output was high but indicate room for improvement in publishing datasets used for model fitting and validation, sharing computational code for others to potentially rapidly implement the model, presenting estimates of prediction uncertainty, and methodological detail to allow the study to be reproduced. The variable quality in sharing model code and methodological detail shown here does suggest that epidemic model reporting consensus guidelines, which establish a minimum standard for the reporting of epidemic modeling, may be valuable. A recent review of the modeling efforts for the Ebola epidemic also called for standardization of modeling practice (103). Many other fields of biomedical research have established reporting guidelines to improve research quality and implementation (125-128).While reporting guidelines have been proposed for population health model on a broader scale (129), none have been established for epidemics.

This review also indicated that a majority of studies (60%) did not completely disclose the data they used. To the extent permissible with ethical and privacy constraints, publishing the aggregated data used to fit and validate models is critical. Not only would sharing data support full reproducibility, but sharing would also enable other researchers to use data in their own complementary modeling efforts. Modelers could therefore help answer calls for increased data sharing during public health emergencies (103, 109, 130). Exploring how data can be

shared more openly and quickly during a public health emergency would be useful, as this remains a challenge.

Many studies identified in this review were published on a time-scale that was relevant to the Zika response. However, a large number of predictions were published well after the epidemic peaks, limiting their ability to inform the response. Nonetheless, those studies may well be used to inform other preparedness activities and contributed to the general knowledge of the biology, epidemiology and/or ecology of ZIKV. Further, results may have been informally shared with public health officials or other relevant decision makers prior to publication. Similar delays to publication have also been noted in an analysis of modeling efforts during the 2015 Ebola epidemic, which noted a median publication lag of around three months [103].

We identified two modifiable bottlenecks in the dissemination of results. First, delays from acceptance to journal publication were generally minimal (median 15 days), but a quarter of the evaluated studies had greater than 24 days delay from journal acceptance to publication. Immediate posting of accepted papers, as practiced by many journals, could cut this time down substantially. Second, we found that only 30% of studies were made available as preprints prior to peer review despite endorsements of preprints by major public agencies, funders, and journals. Those posted were available a median of 119 days prior to peer-reviewed publication. An analysis of preprints for all Zika publications over a similar time period found similar publication delays but much lower overall preprint use compared to the studies analyzed here (3.4% versus 30%) (131). This greater adoption may indicate a changing preprint culture which

352 was also reflected by our finding that preprint posting did not have a demonstrable effect on
353 the impact factor of the journal in which the study was published, and we suggest that pre-
354 prints be more frequently used in future public health emergencies, echoing other similar
355 recent arguments (131).
356
357 Our review also provided a unique analysis of the funding sources and author affiliations of the
358 published ZIKV prediction and forecast efforts across the ZIKV pandemic. These results
359 indicated a range of stakeholders. We note that while academia contributed to the greatest
360 volume of published studies, our search strategy would not have captured in-house models
361 developed by US federal agencies or other unpublished models which may have provided direct
362 operational support.
363
364 This systematic review has three important weaknesses. First, due to scale, a completely
365 independent two-reviewer system was not used for abstracting most of the data and for
366 evaluation of aspects such as reproducibility. Second, we did not formally search for preprint
367 manuscripts as part of the literature searching phase of the systematic review, only assessing
368 whether eligible manuscripts had corresponding preprints. We may have therefore missed
369 important research that had been posted but not yet peer-reviewed. Lastly, we had to restrict
370 the time frame for publications to consider in the review. This restriction again led to missing
371 studies, some of which may have already been published but not yet posted in EMBASE or
372 MEDLINE.
373

374 Overall, the review identified several areas of improvement such as providing data and code,
375 developing reporting standards, posting preprints, and communicating uncertainty. Addressing
376 these areas can improve our understanding of Zika and other outbreaks and ensure that
377 forecasts can inform preparedness and response to future outbreaks, epidemics and
378 pandemics.
379
380 **Acknowledgements:**
381
382 The authors wish to thank members of the Pandemic Prediction and Forecasting Science and
383 Technology Working Group for their helpful feedback. The authors also acknowledge the
384 valuable curated Zika case count data used with permission by the Andersen lab
385 (https://andersen-lab.com/).
386
387
388 **Disclaimer:**
389
390 The views expressed in this article are those of the authors and do not necessarily reflect the
391 official policy or position of the Department of the Army, Department of Defense, USUHS, nor
392 the U.S. Government. Several of the authors are US Government Employees. This work was
393 prepared as part of their official duties. Title 17 U.S.C. § 105 provides that 'Copyright protection
394 under this title is not available for any work of the United States Government.' Title 17 U.S.C.

§101 defines a U.S. Government work as a work prepared by a military service member or employee of the U.S. Government as part of that person's official duties.

The contents of this publication are the sole responsibility of the authors and do not necessarily reflect the views, assertions, opinions or policies of the Uniformed Services University, the Department of Defense, the Centers for Disease Control & Prevention, or US Environmental Protection Agency. Mention of trade names, commercial products, or organizations does not imply endorsement by the U.S. Government. More than one author is an employee of the U.S. Government and as such under the provisions of 17 U.S.C. 105, copyright protection is not available for this work

References:

1. Dick GW. Zika virus. II. Pathogenicity and physical properties. Trans R Soc Trop Med Hyg. 1952;46(5):521-34.

2. Lee VH, Moore DL. Vectors of the 1969 yellow fever epidemic on the Jos Plateau, Nigeria. Bulletin of the World Health Organization. 1972;46(5):669-73.

3. Marchette NJ, Garcia R, Rudnick A. Isolation of Zika virus from Aedes aegypti mosquitoes in Malaysia. Am J Trop Med Hyg. 1969;18(3):411-5.

4. Mlakar J, Korva M, Tul N, Popovic M, Poljsak-Prijatelj M, Mraz J, et al. Zika Virus Associated with Microcephaly. N Engl J Med. 2016;374(10):951-8.

5. Oliveira Melo AS, Malinger G, Ximenes R, Szejnfeld PO, Alves Sampaio S, Bispo de Filippis AM. Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: tip of the iceberg? Ultrasound Obstet Gynecol. 2016;47(1):6-7.

6. Carteaux G, Maquart M, Bedet A, Contou D, Brugieres P, Fourati S, et al. Zika Virus Associated with Meningoencephalitis. N Engl J Med. 2016;374(16):1595-6.

7. Mécharles S, Herrmann C, Poullain P, Tran TH, Deschamps N, Mathon G, et al. Acute myelitis due to Zika virus infection. Lancet. 2016;387(10026):1481.

8. Corrêa-Oliveira GE, do Amaral JL, da Fonseca BAL, Del-Ben CM. Zika virus infection followed by a first episode of psychosis: another flavivirus leading to pure psychiatric symptomatology. Rev Bras Psiquiatr. 2017;39(4):381-2.

9. World Health Organization. Zika Situation Report: Microcephaly and Guillian-Barre Syndrome March 17, 2016. 2016.

10. Dick GW, Kitchen SF, Haddow AJ. Zika virus. I. Isolations and serological specificity. Trans R Soc Trop Med Hyg. 1952;46(5):509-20.

11. Macnamara FN. Zika virus: a report on three cases of human infection during an epidemic of jaundice in Nigeria. Trans R Soc Trop Med Hyg. 1954;48(2):139-45.

12. Cao-Lormeau VM, Blake A, Mons S, Lastere S, Roche C, Vanhomwegen J, et al. Guillain-Barre Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. Lancet. 2016;387(10027):1531-9.

13. Duffy MR, Chen TH, Hancock WT, Powers AM, Kool JL, Lanciotti RS, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. N Engl J Med. 2009;360(24):2536-43.

14. Kwong JC, Druce JD, Leder K. Zika virus infection acquired during brief travel to Indonesia. Am J Trop Med Hyg. 2013;89(3):516-7.

15. Perkasa A, Yudhaputri F, Haryanto S, Hayati RF, Ma'roef CN, Antonjaya U, et al. Isolation of Zika Virus from Febrile Patient, Indonesia. Emerg Infect Dis. 2016;22(5):924-5.

16. Alera MT, Hermann L, Tac-An IA, Klungthong C, Rutvisuttinunt W, Manasatienkij W, et al. Zika virus infection, Philippines, 2012. Emerg Infect Dis. 2015;21(4):722-4.

17. Lessler J, Chaisson LH, Kucirka LM, Bi Q, Grantz K, Salje H, et al. Assessing the global threat from Zika virus. Science. 2016;353(6300):aaf8160.

18. Pan American Health Organization, World Health Organization. Zika Cumulative Cases. 2018.

19. WHO Director-General summarizes the outcome of the Emergency Committee regarding clusters of microcephaly and Guillain-Barré syndrome [press release]. 2016.

20. Lewnard JA, Gonsalves G, Ko AI. Low Risk of International Zika Virus Spread due to the 2016 Olympics in Brazil. Ann Intern Med. 2016;165(4):286-7.

21. McGough SF, Brownstein JS, Hawkins JB, Santillana M. Forecasting Zika Incidence in the 2016 Latin America Outbreak Combining Traditional Disease Surveillance with Search, Social Media, and News Report Data. PLoS Negl Trop Dis. 2017;11(1):e0005295.

22. Bogoch, II, Brady OJ, Kraemer MU, German M, Creatore MI, Brent S, et al. Potential for Zika virus introduction and transmission in resource-limited countries in Africa and the Asia-Pacific region: a modelling study. Lancet Infect Dis. 2016;16(11):1237-45.

457 23. Santos J, Meneses BM. An integrated approach for the assessment of the Aedes aegypti
458 and Aedes albopictus global spatial distribution, and determination of the zones susceptible to
459 the development of Zika virus. Acta Trop. 2017;168:80-90.
460 24. Ogden NH, Fazil A, Safronetz D, Drebot MA, Wallace J, Rees EE, et al. Risk of travel-
461 related cases of Zika virus infection is predicted by transmission intensity in outbreak-affected
462 countries. Parasit Vectors. 2017;10(1):41.
463 25. Craig AT, Butler MT, Pastore R, Paterson BJ, Durrheim DN. Acute flaccid paralysis
464 incidence and Zika virus surveillance, Pacific Islands. Bull World Health Organ. 2017;95(1):69-75.
465 26. Gardner LM, Chen N, Sarkar S. Global risk of Zika virus depends critically on vector status
466 of Aedes albopictus. Lancet Infect Dis. 2016;16(5):522-3.
467 27. Organization PAH, Organization WH. Zika Cumulative Cases. 2018.
468 28. Althouse BM, Vasilakis N, Sall AA, Diallo M, Weaver SC, Hanley KA. Potential for Zika
469 Virus to Establish a Sylvatic Transmission Cycle in the Americas. PLoS Negl Trop Dis.
470 2016;10(12):e0005055.
471 29. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for
472 systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol.
473 2009;62(10):1006-12.
474 30. Althaus CL, Low N. How Relevant Is Sexual Transmission of Zika Virus? PLoS Med.
475 2016;13(10):e1002157.
476 31. Diaz-Menendez M, Trigo E, de la Calle-Prieto F, Arsuaga M. Zika virus infection during
477 the Olympic Games in Rio: A fear or an actual risk? Rev Clin Esp. 2016.

478 32. Iwema CL, LaDue J, Zack A, Chattopadhyay A. search.bioPreprint: a discovery tool for
479 cutting edge, preprint biomedical research articles. F1000Res. 2016;5:1396.
480 33. Ahrens KA, Hutcheon JA, Gavin L, Moskosky S. Reducing Unintended Pregnancies as a
481 Strategy to Avert Zika-Related Microcephaly Births in the United States: A Simulation Study.
482 Matern Child Health J. 2017.
483 34. Alex Perkins T, Siraj AS, Ruktanonchai CW, Kraemer MU, Tatem AJ. Model-based
484 projections of Zika virus infections in childbearing women in the Americas. Nat Microbiol.
485 2016;1(9):16126.
486 35. Alfaro-Murillo JA, Parpia AS, Fitzpatrick MC, Tamagnan JA, Medlock J, Ndeffo-Mbah ML,
487 et al. A Cost-Effectiveness Tool for Informing Policies on Zika Virus Control. PLoS Negl Trop Dis.
488 2016;10(5):e0004743.
489 36. Althouse BM, Hanley KA, Diallo M, Sall AA, Ba Y, Faye O, et al. Impact of climate and
490 mosquito vector abundance on sylvatic arbovirus circulation dynamics in Senegal. Am J Trop
491 Med Hyg. 2015;92(1):88-97.
492 37. Andronico A, Dorleans F, Ferge JL, Salje H, Ghawche F, Signate A, et al. Real-Time
493 Assessment of Health-Care Requirements During the Zika Virus Epidemic in Martinique. Am J
494 Epidemiol. 2017:1-10.
495 38. Attaway DF, Waters NM, Geraghty EM, Jacobsen KH. Zika virus: Endemic and epidemic
496 ranges of Aedes mosquito transmission. J Infect Public Health. 2017;10(1):120-3.
497 39. Baca-Carrasco D, Velasco-Hernandez JX. Sex, Mosquitoes and Epidemics: An Evaluation
498 of Zika Disease Dynamics. Bull Math Biol. 2016;78(11):2228-42.

499 40. Bonyah E, Okosun KO. Mathematical Modeling of Zika Virus. Asian Pacific Journal of
500 Tropical Disease. 2016;6(9):673-9.
501 41. Burattini MN, Coutinho FA, Lopez LF, Ximenes R, Quam M, Wilder-Smith A, et al.
502 Potential exposure to Zika virus for foreign tourists during the 2016 Carnival and Olympic
503 Games in Rio de Janeiro, Brazil. Epidemiol Infect. 2016;144(9):1904-6.
504 42. Butt AM, Siddique S, Gardner LM, Sarkar S, Lancelot R, Qamar R. Zika virus in Pakistan:
505 the tip of the iceberg? Lancet Glob Health. 2016;4(12):e913-e4.
506 43. Caminade C, Turner J, Metelmann S, Hesson JC, Blagrove MS, Solomon T, et al. Global
507 risk model for vector-borne transmission of Zika virus reveals the role of El Nino 2015. Proc Natl
508 Acad Sci U S A. 2017;114(1):119-24.
509 44. Carlson CJ, Dougherty ER, Getz W. An Ecological Assessment of the Pandemic Threat of
510 Zika Virus. PLoS Negl Trop Dis. 2016;10(8):e0004968.
511 45. Cauchemez S, Besnard M, Bompard P, Dub T, Guillemette-Artur P, Eyrolle-Guignot D, et
512 al. Association between Zika virus and microcephaly in French Polynesia, 2013-15: a
513 retrospective study. Lancet. 2016;387(10033):2125-32.
514 46. Cetron M. Revision to CDC's Zika Travel Notices: Minimal Likelihood for Mosquito-Borne
515 Zika Virus Transmission at Elevations Above 2,000 Meters. MMWR Morb Mortal Wkly Rep.
516 2016;65(10):267-8.
517 47. Champagne C, Salthouse DG, Paul R, Cao-Lormeau VM, Roche B, Cazelles B. Structure in
518 the variability of the basic reproductive number (R0) for Zika epidemics in the Pacific islands.
519 Elife. 2016;5.

520 48. Chowell G, Hincapie-Palacio D, Ospina J, Pell B, Tariq A, Dahal S, et al. Using
521 Phenomenological Models to Characterize Transmissibility and Forecast Patterns and Final
522 Burden of Zika Epidemics. PLoS Curr. 2016;8.
523 49. Dinh L, Chowell G, Mizumoto K, Nishiura H. Estimating the subcritical transmissibility of
524 the Zika outbreak in the State of Florida, USA, 2016. Theor Biol Med Model. 2016;13(1):20.
525 50. Dirlikov E, Kniss K, Major C, Thomas D, Virgen CA, Mayshack M, et al. Guillain-Barre
526 Syndrome and Healthcare Needs during Zika Virus Transmission, Puerto Rico, 2016. Emerg
527 Infect Dis. 2017;23(1):134-6.
528 51. Ellington SR, Devine O, Bertolli J, Martinez Quinones A, Shapiro-Mendoza CK, Perez-
529 Padilla J, et al. Estimating the Number of Pregnant Women Infected With Zika Virus and
530 Expected Infants With Microcephaly Following the Zika Virus Outbreak in Puerto Rico, 2016.
531 JAMA Pediatr. 2016;170(10):940-5.
532 52. Evans MV, Dallas TA, Han BA, Murdock CC, Drake JM. Data-driven identification of
533 potential Zika virus vectors. Elife. 2017;6.
534 53. Ferguson NM, Cucunuba ZM, Dorigatti I, Nedjati-Gilani GL, Donnelly CA, Basanez MG, et
535 al. EPIDEMIOLOGY. Countering the Zika epidemic in Latin America. Science.
536 2016;353(6297):353-4.
537 54. Funk S, Kucharski AJ, Camacho A, Eggo RM, Yakob L, Murray LM, et al. Comparative
538 Analysis of Dengue and Zika Outbreaks Reveals Differences by Setting and Virus. PLoS Negl Trop
539 Dis. 2016;10(12):e0005173.

55. Gao D, Lou Y, He D, Porco TC, Kuang Y, Chowell G, et al. Prevention and Control of Zika as a Mosquito-Borne and Sexually Transmitted Disease: A Mathematical Modeling Analysis. Sci Rep. 2016;6:28070.

56. Gonzalez-Salazar C, Stephens CR, Sanchez-Cordero V. Predicting the Potential Role of Non-human Hosts in Zika Virus Maintenance. Ecohealth. 2017.

57. Grills A, Morrison S, Nelson B, Miniota J, Watts A, Cetron MS. Projected Zika Virus Importation and Subsequent Ongoing Transmission after Travel to the 2016 Olympic and Paralympic Games - Country-Specific Assessment, July 2016. MMWR Morb Mortal Wkly Rep. 2016;65(28):711-5.

58. Guzzetta G, Poletti P, Montarsi F, Baldacchino F, Capelli G, Rizzoli A, et al. Assessing the potential risk of Zika virus epidemics in temperate areas with established Aedes albopictus populations. Euro Surveill. 2016;21(15).

59. Huff A, Allen T, Whiting K, Breit N, Arnold B. FLIRT-ing with Zika: A Web Application to Predict the Movement of Infected Travelers Validated Against the Current Zika Virus Epidemic. PLoS Curr. 2016;8.

60. Jaenisch T, Rosenberger KD, Brito C, Brady O, Brasil P, Marques ET. Risk of microcephaly after Zika virus infection in Brazil, 2015 to 2016. Bull World Health Organ. 2017;95(3):191-8.

61. Johansson MA, Mier-y-Teran-Romero L, Reefhuis J, Gilboa SM, Hills SL. Zika and the Risk of Microcephaly. N Engl J Med. 2016;375(1):1-4.

62. Kucharski AJ, Funk S, Eggo RM, Mallet HP, Edmunds WJ, Nilles EJ. Transmission Dynamics of Zika Virus in Island Populations: A Modelling Analysis of the 2013-14 French Polynesia Outbreak. PLoS Negl Trop Dis. 2016;10(5):e0004726.

562 63. Lessler J, Ott CT, Carcelen AC, Konikoff JM, Williamson J, Bi Q, et al. Times to key events
563 in Zika virus infection and implications for blood donation: a systematic review. Bull World
564 Health Organ. 2016;94(11):841-9.
565 64. Li R, Simmons KB, Bertolli J, Rivera-Garcia B, Cox S, Romero L, et al. Cost-effectiveness of
566 Increasing Access to Contraception during the Zika Virus Outbreak, Puerto Rico, 2016. Emerg
567 Infect Dis. 2017;23(1):74-82.
568 65. Li X, Liu T, Lin L, Song T, Du X, Lin H, et al. Application of the analytic hierarchy approach
569 to the risk assessment of Zika virus disease transmission in Guangdong Province, China. BMC
570 Infect Dis. 2017;17(1):65.
571 66. Majumder MS, Santillana M, Mekaru SR, McGinnis DP, Khan K, Brownstein JS. Utilizing
572 Nontraditional Data Sources for Near Real-Time Estimation of Transmission Dynamics During
573 the 2015-2016 Colombian Zika Virus Disease Outbreak. JMIR Public Health Surveill.
574 2016;2(1):e30.
575 67. Manore CA, Ostfeld RS, Agusto FB, Gaff H, LaDeau SL. Defining the Risk of Zika and
576 Chikungunya Virus Transmission in Human Population Centers of the Eastern United States.
577 PLoS Negl Trop Dis. 2017;11(1):e0005255.
578 68. Martinez ME. Preventing Zika Virus Infection during Pregnancy Using a Seasonal
579 Window of Opportunity for Conception. PLoS Biol. 2016;14(7):e1002520.
580 69. Massad E, Tan SH, Khan K, Wilder-Smith A. Estimated Zika virus importations to Europe
581 by travellers from Brazil. Glob Health Action. 2016;9:31669.
582 70. Messina JP, Kraemer MU, Brady OJ, Pigott DM, Shearer FM, Weiss DJ, et al. Mapping
583 global environmental suitability for Zika virus. Elife. 2016;5.

584 71. Monaghan AJ, Morin CW, Steinhoff DF, Wilhelmi O, Hayden M, Quattrochi DA, et al. On
585 the Seasonal Occurrence and Abundance of the Zika Virus Vector Mosquito Aedes Aegypti in
586 the Contiguous United States. PLoS Curr. 2016;8.
587 72. Moreno VM, Espinoza B, Bichara D, Holechek SA, Castillo-Chavez C. Role of short-term
588 dispersal on the dynamics of Zika virus in an extreme idealized environment. Infect Dis Model.
589 2017;2(1):21-34.
590 73. Nah K, Mizumoto K, Miyamatsu Y, Yasuda Y, Kinoshita R, Nishiura H. Estimating risks of
591 importation and local transmission of Zika virus infection. PeerJ. 2016;4:e1904.
592 74. Ndeffo-Mbah ML, Parpia AS, Galvani AP. Mitigating Prenatal Zika Virus Infection in the
593 Americas. Ann Intern Med. 2016;165(8):551-9.
594 75. Nishiura H, Mizumoto K, Rock KS, Yasuda Y, Kinoshita R, Miyamatsu Y. A theoretical
595 estimate of the risk of microcephaly during pregnancy with Zika virus infection. Epidemics.
596 2016;15:66-70.
597 76. Nishiura H, Mizumoto K, Villamil-Gomez WE, Rodriguez-Morales AJ. Preliminary
598 estimation of the basic reproduction number of Zika virus infection during Colombia epidemic,
599 2015-2016. Travel Med Infect Dis. 2016;14(3):274-6.
600 77. Nishiura H, Kinoshita R, Mizumoto K, Yasuda Y, Nah K. Transmission potential of Zika
601 virus infection in the South Pacific. Int J Infect Dis. 2016;45:95-7.
602 78. Quam MB, Wilder-Smith A. Estimated global exportations of Zika virus infections via
603 travellers from Brazil from 2014 to 2015. J Travel Med. 2016;23(6).

604 79. Reefhuis J, Gilboa SM, Johansson MA, Valencia D, Simeone RM, Hills SL, et al. Projecting
605 Month of Birth for At-Risk Infants after Zika Virus Disease Outbreaks. Emerg Infect Dis.
606 2016;22(5):828-32.
607 80. Riou J, Poletto C, Boelle PY. A comparative analysis of Chikungunya and Zika
608 transmission. Epidemics. 2017.
609 81. Rocklov J, Quam MB, Sudre B, German M, Kraemer MU, Brady O, et al. Assessing
610 Seasonal Risks for the Introduction and Mosquito-borne Spread of Zika Virus in Europe.
611 EBioMedicine. 2016;9:250-6.
612 82. Rojas DP, Dean NE, Yang Y, Kenah E, Quintero J, Tomasi S, et al. The epidemiology and
613 transmissibility of Zika virus in Girardot and San Andres island, Colombia, September 2015 to
614 January 2016. Euro Surveill. 2016;21(28).
615 83. Saad-Roy CM, van den Driessche P, Ma J. Estimation of Zika virus prevalence by
616 appearance of microcephaly. BMC Infect Dis. 2016;16(1):754.
617 84. Samy AM, Thomas SM, Wahed AA, Cohoon KP, Peterson AT. Mapping the global
618 geographic potential of Zika virus spread. Mem Inst Oswaldo Cruz. 2016;111(9):559-60.
619 85. Scata M, Di Stefano A, Lio P, La Corte A. The Impact of Heterogeneity and Awareness in
620 Modeling Epidemic Spreading on Multiplex Networks. Sci Rep. 2016;6:37105.
621 86. Tang B, Xiao Y, Wu J. Implication of vaccination against dengue for Zika outbreak. Sci
622 Rep. 2016;6:35623.
623 87. Teng Y, Bi D, Xie G, Jin Y, Huang Y, Lin B, et al. Dynamic Forecasting of Zika Epidemics
624 Using Google Trends. PLoS One. 2017;12(1):e0165085.

88. Teng Y, Bi D, Xie G, Jin Y, Huang Y, Lin B, et al. Model-informed risk assessment for Zika virus outbreaks in the Asia-Pacific regions. J Infect. 2017.

89. Towers S, Brauer F, Castillo-Chavez C, Falconar AK, Mubayi A, Romero-Vivas CM. Estimate of the reproduction number of the 2015 Zika virus outbreak in Barranquilla, Colombia, and estimation of the relative role of sexual transmission. Epidemics. 2016;17:50-5.

90. Viennet E, Mincham G, Frentiu FD, Jansen CC, Montgomery BL, Harley D, et al. Epidemic Potential for Local Transmission of Zika Virus in 2015 and 2016 in Queensland, Australia. PLoS Curr. 2016;8.

91. Villela DA, Bastos LS, LM DEC, Cruz OG, Gomes MF, Durovni B, et al. Zika in Rio de Janeiro: Assessment of basic reproduction number and comparison with dengue outbreaks. Epidemiol Infect. 2017:1-9.

92. Wiwanitkit S, Wiwanitkit V. Predicted pattern of Zika virus infection distribution with reference to rainfall in Thailand. Asian Pac J Trop Med. 2016;9(7):719-20.

93. Yakob L, Kucharski A, Hue S, Edmunds WJ. Low risk of a sexually-transmitted Zika virus outbreak. Lancet Infect Dis. 2016;16(10):1100-2.

94. Zinszer K, Morrison K, Brownstein JS, Marinho F, Santos AF, Nsoesie EO. Reconstruction of Zika Virus Introduction in Brazil. Emerg Infect Dis. 2017;23(1):91-4.

95. Bogoch II, Brady OJ, Kraemer MUG, German M, Creatore MI, Kulkarni MA, et al. Anticipating the international spread of Zika virus from Brazil. Lancet. 2016;387(10016):335-6.

96. Castro LA, Fox SJ, Chen X, Liu K, Bellan SE, Dimitrov NB, et al. Assessing real-time Zika risk in the United States. BMC Infect Dis. 2017;17(1):284.

646 97. Rodriguez-Barraquer I, Salje H, Lessler J, Cummings DA. Predicting intensities of Zika
647 infection and microcephaly using transmission intensities of other arboviruses. bioRxiv. 2016.
648 98. bioRxiv: The Preprint Server for Biology: Cold Spring Harbor Laboratory; [cited 2018
649 June 21]. Available from: https://www.biorxiv.org.
650 99. Chowell G, Viboud C, Simonsen L, Merler S, Vespignani A. Perspectives on model
651 forecasts of the 2014-2015 Ebola epidemic in West Africa: lessons and the way forward. BMC
652 Med. 2017;15(1):42.
653 100. Cheng VC, Chan JF, To KK, Yuen KY. Clinical management and infection control of SARS:
654 lessons learned. Antiviral Res. 2013;100(2):407-19.
655 101. Johansson MA, Powers AM, Pesik N, Cohen NJ, Staples JE. Nowcasting the spread of
656 chikungunya virus in the Americas. PLoS One. 2014;9(8):e104915.
657 102. Zumla A, Alagaili AN, Cotten M, Azhar EI. Infectious diseases epidemic threats and mass
658 gatherings: refocusing global attention on the continuing spread of the Middle East Respiratory
659 syndrome coronavirus (MERS-CoV). BMC Med. 14. England2016. p. 132.
660 103. Chretien JP, Riley S, George DB. Mathematical modeling of the West Africa Ebola
661 epidemic. Elife. 2015;4.
662 104. World Health Organization. Preparing for the second wave: lessons from current
663 outbreaks. Geneva: 2009 August 28, 2009. Report No.: Contract No.: Briefing Note 9.
664 105. Saenz C. Zika virus: ethics preparedness for old and new challenges. Lancet Glob Health.
665 2016;4(10):e686.
666 106. World Health Organization. Methodology for Prioritizing Severe Emerging Diseases for
667 Research and Development. Geneva: 2017 February. Report No.

668 107. Malone RW, Homan J, Callahan MV, Glasspool-Malone J, Damodaran L, Schneider Ade B,
669 et al. Zika Virus: Medical Countermeasure Development Challenges. PLoS Negl Trop Dis.
670 2016;10(3):e0004530.
671 108. Wellcome Trust. Statement on data sharing in public health emergencies 2016 [cited
672 2017 November 30]. Available from: https://wellcome.ac.uk/what-we-do/our-work/statement-
673 data-sharing-public-health-emergencies.
674 109. Chretien JP, Rivers CM, Johansson MA. Make Data Sharing Routine to Prepare for Public
675 Health Emergencies. PLoS Med. 2016;13(8):e1002109.
676 110. Yozwiak NL, Schaffner SF, Sabeti PC. Data sharing: Make outbreak research open access.
677 Nature. 2015;518(7540):477-9.
678 111. United Nations Educational S, and Cultural Organization,. Inform, engage, investigate:
679 Lessons learned from Zika outbreak2016 November 30, 2017. Available from:
680 http://www.unesco.org/new/en/media-services/single-
681 view/news/inform_engage_investigate_lessons_learned_from_zika_outbr/.
682 112. Keegan LT, Lessler J, Johansson MA. Quantifying Zika: Advancing the Epidemiology of
683 Zika With Quantitative Models. J Infect Dis. 2017;216(suppl_10):S884-S90.
684 113. Carlson CJ, Dougherty E, Boots M, Getz W, Ryan SJ. Consensus and conflict among
685 ecological forecasts of Zika virus outbreaks in the United States. Sci Rep. 2018;8(1):4921.
686 114. Pollett S, Melendrez MC, Maljkovic Berry I, Duchêne S, Salje H, Cummings DAT, et al.
687 Understanding dengue virus evolution to support epidemic surveillance and counter-measure
688 development. Infect Genet Evol. 2018;62:279-95.

689 115. Lourenço J, de Lourdes Monteiro M, Valdez T, Monteiro Rodrigues J, Pybus O, Rodrigues
690 Faria N. Epidemiology of the Zika Virus Outbreak in the Cabo Verde Islands, West Africa. PLoS
691 Curr. 2018;10.
692 116. Kraemer MUG, Brady OJ, Watts A, German M, Hay SI, Khan K, et al. Zika virus
693 transmission in Angola and the potential for further spread to other African settings. Trans R
694 Soc Trop Med Hyg. 2017;111(11):527-9.
695 117. Pollett S, Althouse BM, Forshey B, Rutherford GW, Jarman RG. Internet-based
696 biosurveillance methods for vector-borne diseases: Are they novel public health tools or just
697 novelties? PLoS Negl Trop Dis. 2017;11(11):e0005871.
698 118. Faria NR, Sabino EC, Nunes MR, Alcantara LC, Loman NJ, Pybus OG. Mobile real-time
699 surveillance of Zika virus in Brazil. Genome Med. 2016;8(1):97.
700 119. Faria NR, Azevedo Rdo S, Kraemer MU, Souza R, Cunha MS, Hill SC, et al. Zika virus in the
701 Americas: Early epidemiological and genetic findings. Science. 2016;352(6283):345-9.
702 120. Faria NR, Quick J, Claro IM, Thézé J, de Jesus JG, Giovanetti M, et al. Establishment and
703 cryptic transmission of Zika virus in Brazil and the Americas. Nature. 2017;546(7658):406-10.
704 121. Grubaugh ND, Ladner JT, Kraemer MUG, Dudas G, Tan AL, Gangavarapu K, et al.
705 Genomic epidemiology reveals multiple introductions of Zika virus into the United States.
706 Nature. 2017;546(7658):401-5.
707 122. Thézé J, Li T, du Plessis L, Bouquet J, Kraemer MUG, Somasekar S, et al. Genomic
708 Epidemiology Reconstructs the Introduction and Spread of Zika Virus in Central America and
709 Mexico. Cell Host Microbe. 2018;23(6):855-64.e7.

123. Del Valle SY, McMahon BH, Asher J, Hatchett R, Lega JC, Brown HE, et al. Summary results of the 2014-2015 DARPA Chikungunya challenge. BMC Infectious Diseases. 2018;18(1):245.

124. King AA, Domenech de Cellès M, Magpantay FM, Rohani P. Avoidable errors in the modelling of outbreaks of emerging pathogens, with special reference to Ebola. Proc Biol Sci. 2015;282(1806):20150347.

125. Cohen JF, Korevaar DA, Altman DG, Bruns DE, Gatsonis CA, Hooft L, et al. STARD 2015 guidelines for reporting diagnostic accuracy studies: explanation and elaboration. BMJ Open. 2016;6(11):e012799.

126. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. Int J Surg. 2011;9(8):672-7.

127. White RG, Hakim AJ, Salganik MJ, Spiller MW, Johnston LG, Kerr L, et al. Strengthening the Reporting of Observational Studies in Epidemiology for respondent-driven sampling studies: "STROBE-RDS" statement. J Clin Epidemiol. 2015;68(12):1463-71.

128. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4:1.

129. Bennett C, Manuel DG. Reporting guidelines for modelling studies. BMC Med Res Methodol. 2012;12:168.

130. Littler K, Boon WM, Carson G, Depoortere E, Mathewson S, Mietchen D, et al. Progress in promoting data sharing in public health emergencies. Bull World Health Organ. 2017;95(4):243.

131. Johansson MA, Reich NG, Meyers LA, Lipsitch M. Preprints: An underutilized mechanism to accelerate outbreak science. PLoS Med. 2018;15(4):e1002549.

Supporting Information Legends:

Table S1. Data abstraction and study evaluation tool used by reviewers

Tables:

Table 1. Objectives and study population of eligible studies

	n	%[a]
Total number of studies	73	100
Zika-related phenomenon forecasted or predicted[b]		
Predicted microcephaly burdens	11	15
Gullain-Barre syndrome burden	3	4
Epidemic peak size	4	5
Epidemic peak timing	4	5
Epidemic curve trajectory	8	11
Epidemic final size	5	7
Spatial spread	25	34

742

Force of infection	7	10
Cost-effectiveness	2	3
Intervention impact	3	4
Case fatality ratio	0	0
R_o or R_{eff}	21	29
Sexual transmission risk	3	4
Vector competence / ecology	9	12
Other[c]	2	3
Geographic region in which predictions made[d]		
Africa	3	4
Americas (excluding Continental USA)	31	42
Asia – Pacific	15	21
Continental USA	7	10
Europe	4	5
Global	18	24

[a]Denominator excludes those studies where unable or no basis to judge

[b]Some studies predicted more than one phenomenon

[c]Ecological determinants of vector minimum abundance rate (n=1); epidemic size and number of infectious at time of first microcephaly case detected (n=1)

[d]Some studies included >1 geographic category

743

Table 2. Data sources, methodology and reproducibility of eligible studies

	N	%[a]
Data types used[b]		
Case count	49	67
Demographic	27	37
Genomic sequence data	0	0
Climate, meteorological and earth science	21	29
Transport	14	19
Economic	7	10
Vector	30	41
Internet search engine, social media or news-wire scraping data	5	7
Other[c]	9	12
Relevant data made available		
Entirely	29	40
Partially	27	37
Not at all	16	22
Model type(s) used in analysis[d]		
Stochastic	21	29
Deterministic	56	76
Availability of statistical modeling computational code (e.g. R script provided)		
Entirely	21	29
Partly	7	10
Not at all	45	62
Clear and accurate visual display of the model output		
Entirely	49	67
Partly	20	27

Not at all	4	5
Estimates of prediction uncertainty provided (e.g. confidence intervals) provided		
Entirely	31	43
Partly	13	18
Not at all	28	39
Methods presented with a level of detail that allowed the study to be reproduced		
Entirely	37	54
Partially	28	41
Not at all	4	6

[a]Denominator excludes those studies where unable or no basis to judge

[b]Some studies used multiple data types

[c]Viremia duration and dynamics (n=3); sexual contact network (n=2); semen viral persistence (n=2), non-human primate demographics (n=1), mammalian diversity (n=1)

[d]Some studies used both stochastic and deterministic models

744

745

746

747

Table 3. Accessibility, timeliness and other bibliometrics of eligible studies

	n	%[d]
Open access[a]	68	96
Pre-print access[b]	22	30
	median	IQR (range)
Journal impact factor	4.37	2.65 - 7.62 (1.48 – 79.26)
Submission to acceptance time, days	83	44 - 112 (0 - 256)
Acceptance to publication time, days[c]	15	7 - 24 (-255 - 279)[e]
Submission to publication time, days	93.5	47 - 141 (1 - 389)

[a]Includes non-journal open access websites. Open access defined as able to be viewed without any payment or institutional journal license

[b]Biorxiv n = 19, ResearchGate n=1, *Bull WHO* rapid journal pre-acceptance pre-print n = 2

[c]Negative values exist as *Bull WHO* articles published upon receipt (within 24 hrs) and then accepted later

[d]Denominator may vary in cases where these metrics were unable to be determined

[e]Publication time based on electronic journal version where available

Table 4. Author affiliation and funding source of eligible studies

Affiliation of authors[a]	n	%
Academia	68	93
Govt (US)	14	19
Govt (non-US)	19	26
Industry[b]	4	5
NGO	14	19
Other type of organization[c]	4	5
Funding source[d]	**n**	**%[e]**
USG		
CDC	1	2
DHS	2	4
DoD	3	6
LANL	1	2
NASA	1	2
NIH	21	39
NSA	2	4
NSF	12	22
USAID	1	2
USDA	3	6
Other USG[f]	1	2
Any USG	27	50
Any Non-US Govt	46	85
Any Industry	3	6

Any NGO	19	35
Any international normative body	6	11
Other[g]	6	11

[a]Multiple affiliations associated with some studies

[b]Scientific contracting/consulting (n = 3), spatial epidemiology software (n =1)

[c]World Health Organization (n=2), European Centers for Disease Control (n=1), HealthMap (n=1)

[d]Multiple funding streams associated with some studies

[e]Unable to be determined or unfunded in a number studies, denominator = 54

[f]State Dept of Health (TX)

[g]Academic intramural funding (n = 5)

Figure 1. PRISMA flow-chart indicating the number of studies identified, screened and confirmed for eligibility into this systematic review

Figure 2. Comparative trends of reported Zika cases in Latin American and publication times of Zika prediction studies. Zika case counts were obtained from https://andersen-lab.com/ with permission

762 **Figure 3.** Comparative trends in publication times of ZIKV prediction studies with and without

763 the use of preprints.

764

765

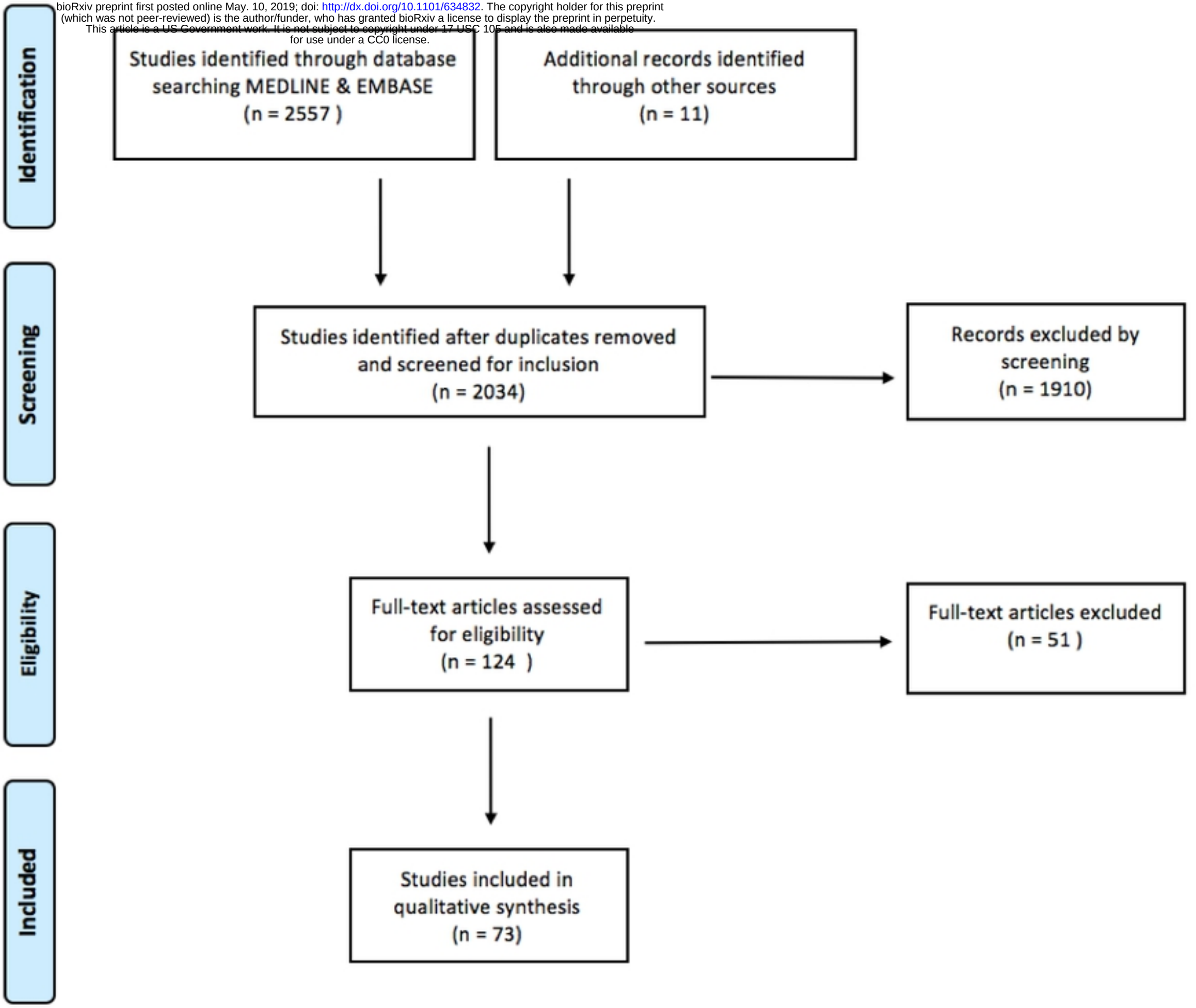

Figure 1

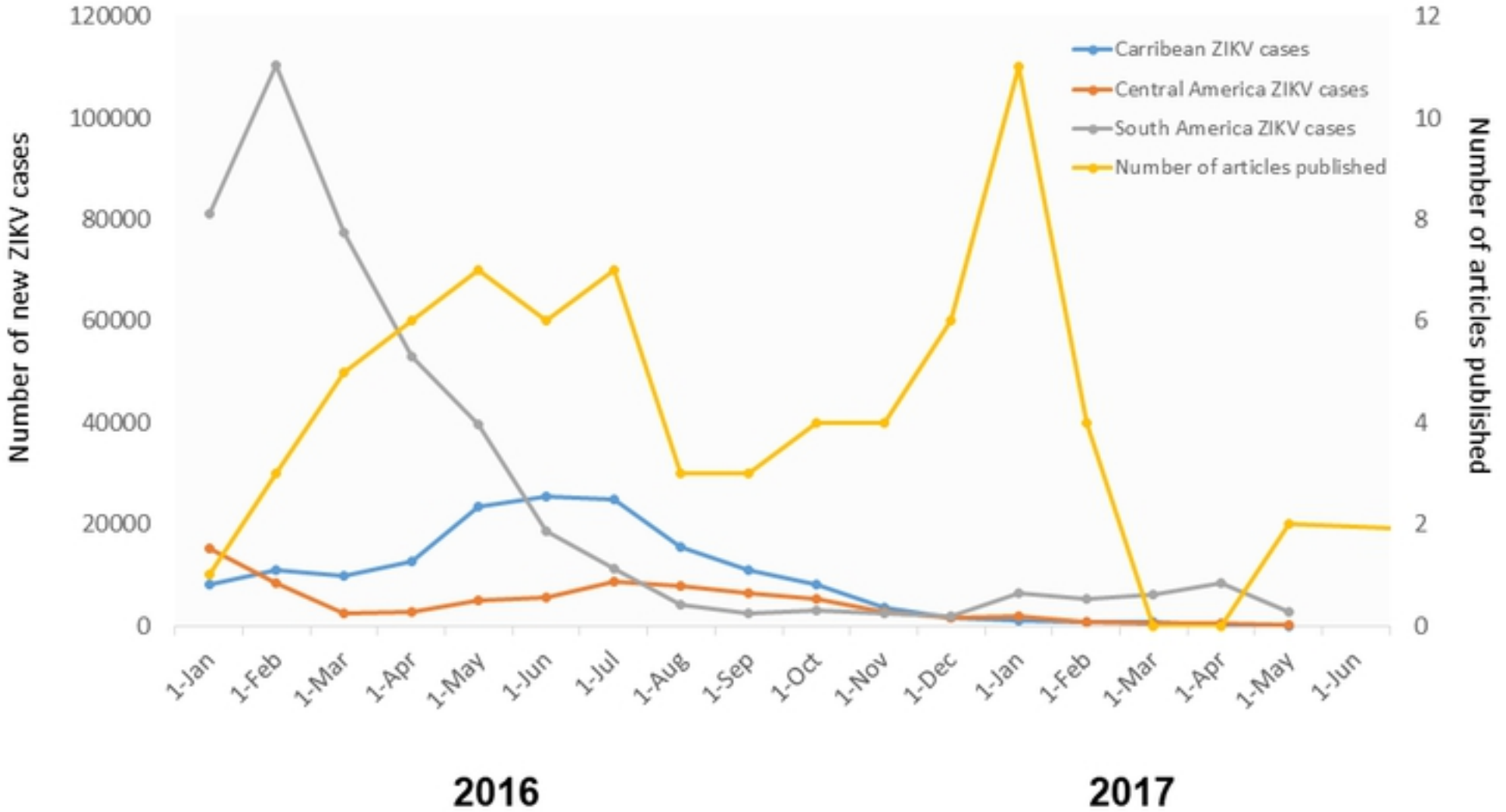
Number of new ZIKV cases
Number of articles published
120000
100000
80000
60000
40000
20000
0
12
10
8
6
4
2
0
Carribean ZIKV cases
Central America ZIKV cases
South America ZIKV cases
Number of articles published
1-Jan
1-Feb
1-Mar
1-Apr
1-May
1-Jun
1-Jul
1-Aug
1-Sep
1-Oct
1-Nov
1-Dec
1-Jan
1-Feb
1-Mar
1-Apr
1-May
1-Jun
2016
2017

Figure 2

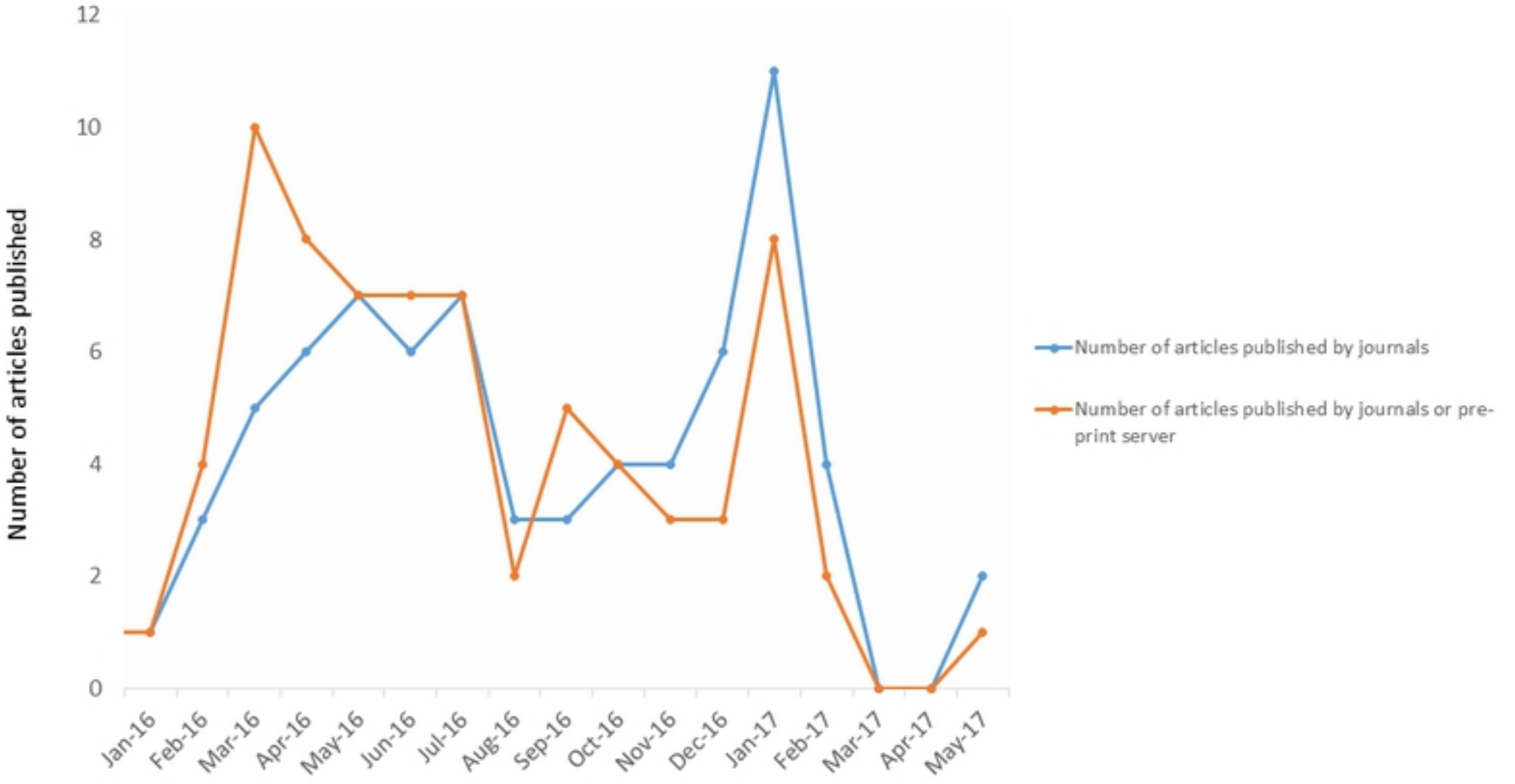
Number of articles published
12
10
8
6
4
2
0
Jan-16
Feb-16
Mar-16
Apr-16
May-16
Jun-16
Jul-16
Aug-16
Sep-16
Oct-16
Nov-16
Dec-16
Jan-17
Feb-17
Mar-17
Apr-17
May-17
Number of articles published by journals
Number of articles published by journals or pre-print server

Figure 3