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Use of infectious disease surveillance reports to monitor the Zika virus epidemic in Latin America and the Caribbean from 2015 to 2017: strengths and deficiencies

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ABSTRACT

Objectives To summarise the occurrence of congenital Zika syndrome (CZS) in Latin America and the Caribbean from 2015 to 2017 using two outcome measures derived from infectious disease surveillance reports and to assess the completeness of these reports.

Design Surveillance study.

Setting Pan American Health Organization (PAHO)/WHO epidemiology reports on confirmed and suspected Zika virus infection and cases of CZS.

Participants Populations of 47 countries in the South and Central Americas, Mexico and the Caribbean.

Primary and secondary outcome measures The number of CZS cases per 1000 births (using 2016–2017 births as a denominator) and the number of CZS cases per 1000 births in women with Zika virus infection during pregnancy.

Results By 4 January 2018, 548623 suspected and 239063 confirmed Zika virus infections had been reported to PAHO/WHO from 47 countries. In 25 countries, over 80% of infections were reported as suspected. There were 3617 confirmed CZS cases in 25 countries; 2952 (82%) had occurred in Brazil. The number of CZS cases per 1000 births varied considerably with Brazil and several Caribbean island communities (Puerto Rico, St Martin, Martinique, Guadeloupe and Grenada) having the highest CZS prevalence above 0.5 per 1000 births. Analysing the number of CZS cases per 1000 births in women infected with Zika virus during their pregnancy highlighted the inaccuracies of the data, with Venezuela likely to have had severe under-reporting of CZS.

Conclusions Expressing data on CZS in relation to total births, rather than as absolute numbers, better illustrates the burden of disease, providing that under-reporting of CZS is not too severe. Data on infections in pregnant women enable potential under-reporting of CZS to be identified. Both measures are recommended for future PAHO/WHO publications. Evidence of severe under-reporting of Zika virus infections and CZS makes interpretation of the data and comparisons between countries challenging.

Strengths and limitations of this study

- A strength is that surveillance data from every country in Latin America and the Caribbean were analysed.
- A further strength is that the number of congenital Zika syndrome cases were population-weighted by the number of births, which is not regularly done in Pan American Health Organization/WHO reports, and which gives a better idea of the disease burden.
- A limitation is that the publicly available data do not include the numbers of people in a population who were tested (including the numbers of pregnant women), and the indication for testing, which would enhance the interpretation of the reported incidence of Zika virus.

INTRODUCTION

In 2015 in North East Brazil, a sudden increase in cases of microcephaly were reported after the introduction of Zika virus into Brazil.[1] Since then it has been established that Zika virus infection in the first trimester of pregnancy does increase the risk of the fetus having microcephaly.[2] Several studies have subsequently characterised additional brain abnormalities associated with Zika virus infection during pregnancy and the diagnosis of congenital Zika syndrome (CZS) has been defined.[3–5] There is uncertainty about the risk of CZS given a woman is infected with Zika virus in the first trimester with one study reporting the risks of CZS[3] and three studies reporting the risks of microcephaly.[6–8] Microcephaly is not always present in CZS and therefore the prevalence of microcephaly in women with first trimester Zika virus infections will be lower than the prevalence of CZS.[9] A study of women in America who were pregnant and had evidence of Zika virus infection during pregnancy (both symptomatic and asymptomatic) found that 60 per 1000 pregnancies were diagnosed with CZS.[3] A case-control study comparing neonates in

Recife Brazil with microcephaly with controls without estimated that the relative risk of microcephaly given Zika virus infection during pregnancy was 73.1.[6] If the prevalence of microcephaly in women without Zika virus infections is as estimated by Orioli *et al* at 0.44 per 1000,[10] a relative risk of 73.1 is equivalent to an absolute risk of around 32 per 1000 births to women with Zika virus infections.[3] Cauchemez *et al* retrospectively analysed the Zika virus outbreak in French Polynesia and estimated that the risk of microcephaly from infection in the first trimester was 9.5 per 1000 women infected in the first trimester.[7] Brady *et al* used data from Brazil to estimate that 4 per 1000 pregnancies infected with Zika virus in the first two trimesters would result in a case of microcephaly.[8] In summary, estimates of the risk of microcephaly or CZS given the mother was infected with Zika virus during pregnancy vary from 4 per 1000 (the lowest estimate for microcephaly) to up to 60 per 1000 births for CZS.

The aim of this study was to summarise the occurrence of CZS in Latin America and the Caribbean from 2015 to 2017 using the number of CZS cases per 1000 births and the number of CZS cases per 1000 births in women with Zika virus infection during pregnancy. These two measures can be derived from infectious disease surveillance reports and provide information about the burden of disease and the completeness of the surveillance reports.

METHODS

Since May 2015, Pan American Health Organization (PAHO)/WHO have reported data on the spread of the Zika virus in all countries in Latin America and the Caribbean.[11] The weekly reports include the cumulative numbers of reported Zika virus cases (suspected and confirmed), the incidence rates per 1000 people, the numbers of deaths among Zika infection cases and the numbers of confirmed CZS cases.

Data were taken from the PAHO/WHO publications of cumulative cases available on the website (http://www.paho.org/data/index.php/en/?option=com_content&view=article&id=524&Itemid=) up until January 2018 (accessed 8 October 2020).

A series of reports published on 25 September 2017 from all countries and territories with autochthonous transmission of Zika virus in the Americas provided additional information on the number of pregnant women with suspected and confirmed Zika virus infections up until week 35 in 2017. These data were downloaded from the website: https://www.paho.org/hq/index.php?option=com_content&view=article&id=11603:countries-and-territories-with-autochthonous-transmission-of-zika-virus-in-the-americas-reported-in-2015-2017&Itemid=41696&lang=en (accessed 3 January 2020). Several countries only reported pregnancies in 2016 and hence were likely to have excluded some infected pregnancies occurring in 2017.

Data from Canada, the USA and Bermuda were excluded—only countries in the South and Central Americas, Mexico and the Caribbean were analysed. Apart from in Brazil, no cases of CZS were reported in 2015—they were all reported in 2016 and 2017. Therefore, we calculated the CZS per 1000 births using the total number of births in 2016 and 2017. The numbers of live births occurring during 2016 and 2017 were obtained in each country from the United Nations Demographic Yearbook 2017.[12] In the following countries, the numbers of births were only available for earlier years and the numbers occurring in 2016–2017 were estimated to be twice that in the most recent year of data available: Honduras (2012), Haiti (2013), Grenada (2014), Trinidad and Tobago (2015), El Salvador (2015) and Guyana (2015).

The PAHO/WHO case definitions for suspected and confirmed Zika cases and CZS that were communicated to the member states and were used to report cases within the International Sanitary Regulations are given at http://www.paho.org/hq/index.php?option=com_content&view=article&id=11117&Itemid=41532&lang=en (accessed 22 May 2020).

Statistical analysis

The number of CZS cases per 1000 births was calculated to give a population-adjusted measure of the relative size of the CZS epidemic in each country, as well as a measure of the proportion of births affected relative to other perinatal problems.

Island communities have been reported to often experience much higher infection rates than larger mainland communities[13] and therefore it might be expected that the number of CZS cases per 1000 births would be higher on islands. To investigate this, a binomial regression model was fitted with each country as a random effect and island as a fixed effect.

Each country reported both suspected and confirmed Zika virus infections. Main analyses reported are based on both confirmed and suspected cases, but analyses including only confirmed cases were also performed and are compared where relevant.

The number of pregnant women who were infected with the Zika virus during their pregnancy was obtained from individual country reports on 25 September 2017 covering all reports up until week 35 of 2017. Some countries reported both suspected and confirmed cases separately, while other countries reported suspected and confirmed cases in total or either only suspected or confirmed cases. The total number of suspected and confirmed cases was analysed and if this was not available the number of cases reported was used regardless of whether they were suspected or confirmed. The number of CZS cases per 1000 women who were infected with the Zika virus during their pregnancy was calculated and will be referred to as CZS cases per infected pregnancies. This measure would be expected to be around 4–60 per 1000 pregnancies with differences highlighting possible reporting issues.

Linear associations between variables were quantified using Spearman's rho rank correlation coefficients.

RESULTS

Table 1 shows that by the 4 January 2018, 548623 suspected Zika virus infections and 239063 confirmed Zika virus infections had been reported to PAHO/WHO. There were 3617 confirmed CZS cases, of which the largest numbers of cases were reported in Brazil (2952 cases; 82%) and Colombia (248; 7%).

Figure 1 compares the number of CZS cases per 1000 births with the incidence rate of Zika virus infections (confirmed and suspected). The two measures are linearly related (spearman's rho=0.64, p=0.008) as is expected as a higher incidence of Zika virus would be expected to lead to a higher birth prevalence of CZS. However, there is much variation in the number of CZS cases per 1000 births not explained by the incidence of Zika virus in the population. The random effects model estimated that countries that are islands have 82% (95% CI 54% to 116%) higher rates of CZS per 1000 births than non-island communities. Haiti is the exception with only 1 CZS case reported out of over 3000 Zika virus infections, indicating under-reporting of CZS. French Guiana, Honduras, El Salvador, Nicaragua, Mexico and Argentina also have lower number of CZS cases per 1000 births than might be expected due to their reported incidence of Zika virus infections, also indicating under-reporting of CZS. The correlation between the birth prevalence and the incidence of Zika virus is weaker (spearman's rho=0.48, p=0.02) if only confirmed Zika virus infections are analysed (data not shown). This can be partly explained by several countries having over 90% of their cases suspected rather than confirmed and three countries having no confirmed cases (Martinique, Haiti and Venezuela) indicating that in these countries Zika virus infections although they are suspected are often not confirmed. Another explanation could be differential reporting of CZS, which we know occurred with Brazil being more likely to diagnose CZS than other countries. Table 1 shows that four countries had over 6000 Zika virus infections and yet reported no cases of CZS (Venezuela, Jamaica, Peru and Curacao) suggesting potential under-reporting of CZS in these countries.

Table 2 shows that 36025 pregnancies were reported to have been confirmed as having been infected with Zika virus, with 32% of these being in Brazil and 18% in Colombia. A total of 71230 pregnant women were reported as having confirmed or suspected Zika virus infections (assuming that the number of suspected or confirmed cases is equal to the number of confirmed cases in countries only reporting confirmed cases); 37% in Brazil and 28% in Colombia.

Figure 2 and table 2 present the number of CZS cases per 1000 women who were infected with Zika virus during their pregnancy for each country compared with the reported values from previous studies of between 4 and 60 CZS cases per 1000 pregnant women with Zika virus.[3 6–8] Many countries do have a prevalence close to these values. Slightly higher rates (such as in Brazil) may suggest more extensive reporting of CZS than of infected pregnancies, or the use of wider microcephaly definitions earlier in the epidemic. In Argentina, there were five cases of CZS reported and only five pregnant women were reported as being infected with Zika virus indicating that reporting only occurred when CZS was confirmed and therefore their rate of 1000 CZS per 1000 pregnancies is clearly incorrect (and not plotted in figure 2). Three other countries reported at least one case of CZS, but did not report any infected pregnancies (Guyana, Grenada and Suriname). Several countries such as French Guiana, Mexico and Nicaragua have much lower values indicating that cases of CZS were being under-reported. This can be explained for Nicaragua by the fact that they reported infected pregnancies only up until week 1 of 2017. Four countries in figure 2 reported >200 pregnant women having Zika virus infections (Venezuela (3463), Jamaica (712), Peru (279) and the Virgin Islands (USA) (286)) and yet reported no cases of CZS. The upper CI being around 1 suggests under-reporting of CZS in Venezuela, but the numbers of infected pregnancies are too small to be informative in the other countries. Haiti only reported infected pregnancies up until week 21 of 2016. Figure 2 indicated that Haiti might have under-reported CZS cases and therefore figure 2 indicates that they are also likely to have under-reported the number of infected pregnant women as the ratio of the two values is reasonable.

Figure 3 shows the number of pregnant women who were infected with Zika virus per 1000 births and compares this with the reported incidence of Zika virus in the population. The majority of countries were above the line of equality indicating that infections in pregnant women were more likely to be reported than infections in the rest of the population. This was likely to be due to pregnant women being more likely to be tested for Zika virus infection, since they are the high-risk segment of the population. The countries below the line of equality were perhaps under-reporting the numbers of pregnant women with Zika virus infection, particularly Haiti, Belize and Saint Vincent and the Grenadines who only reported infected pregnancies in 2016 not in 2017.

Zhang *et al*[14] used data from a study in Bahia in Brazil from October 2014 to February 2016[15] and data from a study of the 2013 Zika virus outbreak in French Polynesia[13] to develop a global stochastic epidemic model to analyse the spread of the Zika virus (ZIKV) in Latin America and the Caribbean. Table 3 compares their predictions with the reported figures. The agreement is reasonable for Brazil, Colombia and Puerto Rico, but much higher for Mexico, El Salvador, Honduras, Haiti and Venezuela. These later countries are all countries which our analysis has indicated have under-reporting of CZS cases. This provides further indication that the reporting to PAHO/WHO is not sufficiently accurate to validate prediction models in some countries.

Table 1 Zika virus infections and CZS cases reported to PAHO/WHO by countries in the South and Central Americas, Mexico and the Caribbean, 2016 – 2017* and the estimated number of CZS cases per 1000 births to pregnant women with Zika virus

	Zika virus infections†						CZS			
Country	Suspected	Confirmed (including imported)	% Suspected	Total suspected and confirmed	Incidence of Zika virus (suspected and confirmed) per 1000 people per year	Incidence of Zika virus (confirmed) per 1000 people per year	CZS cases	CZS per 1000 births (2016/17)	Population ('000) in 2016/17	Annual births in 2016/17‡
	A	***B***		*A+B*	*(A+B)/2D*	*B/2D*	***C***	*C/2E×1000*	***D***	***E***
Brazil*	205 997	155 820	56	361 817	0.86	0.372	2952	0.507	209 428	2 911 930
Colombia	100 255	9717	91	109 972	1.13	0.099	248	0.190	48 860	652 112
Guatemala	4003	1054	79	5057	0.15	0.031	140	0.181	16 793	386 023
Dominican Republic	5248	336	93	5584	0.26	0.015	85	0.296	10 708	143 822
Puerto Rico	–	36 871	0	36 871	10.02	10.016	47	0.892	1840	26 357
Mexico	–	11 791	0	11 791	0.05	0.045	20	0.004	128 897	2 263 873
Costa Rica	21	9949	0	9970	1.02	1.019	19	0.137	4881	69 410
Panama	4786	1059	81	5845	0.72	0.130	17	0.113	4044	75 008
Trinidad and Tobago	–	722	0	722	0.26	0.264	17	0.475	1367	17 883
Ecuador	3722	3011	55	6733	0.20	0.091	14	0.025	16 505	283 020
Bolivia	2216	816	73	3032	0.14	0.037	14	0.027	10 970	255 713
Honduras	31 378	266	99	31 644	1.81	0.015	8	0.022	8727	184 312
Martinique	37 997	–	100	37 997	48.65	0.000	5	0.674	390	3711
Guadeloupe	32 250	28	99	32 278	35.05	0.030	5	0.570	460	4389
Argentina	536	276	66	812	0.01	0.003	5	0.003	44 059	716 322
El Salvador	12 467	3	99	12 470	1.00	0.000	4	0.018	6262	109 617
Suriname	2816	733	79	3549	3.19	0.659	4	0.203	555	9847
Guyana	–	34	0	34	0.04	0.044	3	0.115	385	13 060
Nicaragua	751	614	55	1365	0.11	0.049	2	0.007	6184	137 772
Grenada	335	119	73	454	2.04	0.533	2	0.672	111	1487
Paraguay	106	14	88	120	0.01	0.001	2	0.008	6768	128 117
French Guiana	10 742	48	99	10 790	19.30	0.085	1	0.065	279	7663
Haiti	3077	–	100	3077	0.28	0.000	1	0.002	5424	247 025
Saint Martin	1580	200	88	1780	55.63	6.250	1	1.000	16	500
Barbados	672	137	83	809	1.39	0.234	1	0.196	291	2552
Venezuela	61 708	–	100	61 708	0.97	0.000	0	0	31 748	602 123
Jamaica	6958	186	97	7144	1.25	0.032	0	0	2846	35 164
Peru	5737	1293	81	7030	0.11	0.020	0	0	31 969	502 591
Curacao	4362	2020	68	6382	21.27	6.733	0	0	150	1668
Belize	1762	269	86	2031	2.74	0.362	0	0	371	7200
Cuba	1305	324	80	1629	0.07	0.014	0	0	11 439	115 921
Aruba	830	645	56	1475	6.44	2.816	0	0	114	1230
Dominica	1154	79	93	1233	8.33	0.533	0	0	74	721
Saint Vincent and the Grenadines	505	84	85	589	5.77	0.823	0	0	51	1634
Saint Kitts and Nevis	554	33	94	587	5.59	0.314	0	0	52	641
Antigua and Barbuda	537	25	95	562	2.97	0.132	0	0	94	1085
Bahamas	510	25	95	535	0.68	0.031	0	0	394	4055

Continued

Table 1 Continued

	Zika virus infections†						CZS			
Country	Suspected	Confirmed (including imported)	% Suspected	Total suspected and confirmed	Incidence of Zika virus (suspected and confirmed) per 1000 people per year	Incidence of Zika virus (confirmed) per 1000 people per year	CZS cases	CZS per 1000 births (2016/17)	Population ('000) in 2016/17	Annual births in 2016/17‡
Virgin Islands (USA)	400	56	87	456	4.43	0.543	0	0	51	1415
Sint Maarten	248	148	62	396	4.77	1.783	0	0	41	363
Saint Lucia	280	52	84	332	1.01	0.158	0	0	164	2103
Saint Barthelemy	270	61	81	331	36.78	6.777	0	0	4	72
Cayman Islands	229	30	88	259	2.25	0.260	0	0	57	642
Turks and Caicos Islands	197	25	88	222	2.13	0.240	0	0	52	518
Virgin Islands (UK)	74	53	58	127	1.84	0.768	0	0	34	266
Anguilla	30	23	56	53	1.56	0.676	0	0	17	155
Montserrat	18	5	78	23	2.30	0.500	0	0	5	46
Bonaire, St Eustatius and Saba	–	9	0	9	0.35	0.346	0	0	13	346
Total	548 623	239 063	70	787 686			3617			

1. Brazil Ministry of Health case definition for confirmed cases of congenital syndrome associated with Zika virus infection includes confirmed and probable cases per PAHO's case definition.
2. The number of confirmed congenital syndrome associated with Zika include two autochthonous cases and three imported cases.
3. The reported number of suspected cases of Zika virus infection are estimates. According to Santé publique France, the estimated number of suspected cases is the sum of the number of visits recorded by the Decentralised Centres of Prevention and Care and the estimated number of people who sought medical care from a general practitioner for this purpose. The estimate is based on data collected by the sentinel physician network.
4. The case reported by Santé publique France corresponds to a fetus with cerebral malformation of a mother infected with Zika.
5. In addition to the five reported cases of congenital syndrome, Santé publique France reported 16 fetuses with cerebral malformations of mothers infected with Zika.
6. Santé publique France reported 21 fetuses with cerebral malformations of mothers infected with Zika.
7. In addition to the one reported case of congenital syndrome, Santé publique France reported 18 fetuses with cerebral malformations of mothers infected with Zika.

*CZS cases in Brazil occurring in 2015 are included.

†PAHO/WHO case definitions for suspected and confirmed Zika virus infections is available at: http://www.paho.org/hq/index.php?option=com_content&view=article&id=11117&Itemid=41532&lang=en.

‡Total births were estimated as twice the most recent birth years if data were not available for 2016 and 2017: Honduras (2012), Haiti (2013), Grenada (2014), Trinidad and Tobago (2015), El Salvador (2015) and Guyana (2015).

§Confirmed congenital syndrome associated with Zika virus infection case definition: live newborn who meets the criteria for a suspected case of congenital syndrome associated with Zika virus and Zika virus infection was detected in specimens of the newborn, regardless of detection of other pathogens. Case definitions for congenital syndrome associated with Zika virus infection is available at: http://www.paho.org/hq/index.php?option=com_content&view=article&id=11117&Itemid=41532&lang=en.

CZS, congenital Zika syndrome; PAHO, Pan American Health Organization.

DISCUSSION

This study is the first comprehensive study in the Americas of the entire course of the Zika epidemic using the infectious disease surveillance reports together with the number of population births. The study demonstrates again that the vast majority of CZS cases occurred in Brazil. In Brazil, 2952 CZS cases were reported, compared with a baseline of about 380 cases of microcephaly expected over that 2-year period.[16] The study has shown in addition a high epidemic intensity in some of the Caribbean islands. The phenomenon of a very high proportion of individuals on an island being infected has been noted for both Zika virus and other infections. Kucharski *et al* studied the outbreak of ZIKV from 2013 to 2014 in French Polynesia and concluded that 94% of the population were infected during the outbreak.[13] The first reported epidemic of Zika virus in the island of Yap in 2007[17] reported over 70% of residents had been infected. Dengue shows a similar pattern of high infection rates on islands, and this also results in a more cyclical pattern of population infection every 12–15 years compared with the lower and more constant dengue virus infection rates in larger communities.[18]

Susceptibility to Zika virus infection varies hugely according to climatic, environmental and social factors. How, it would be expected that the risk of an infected

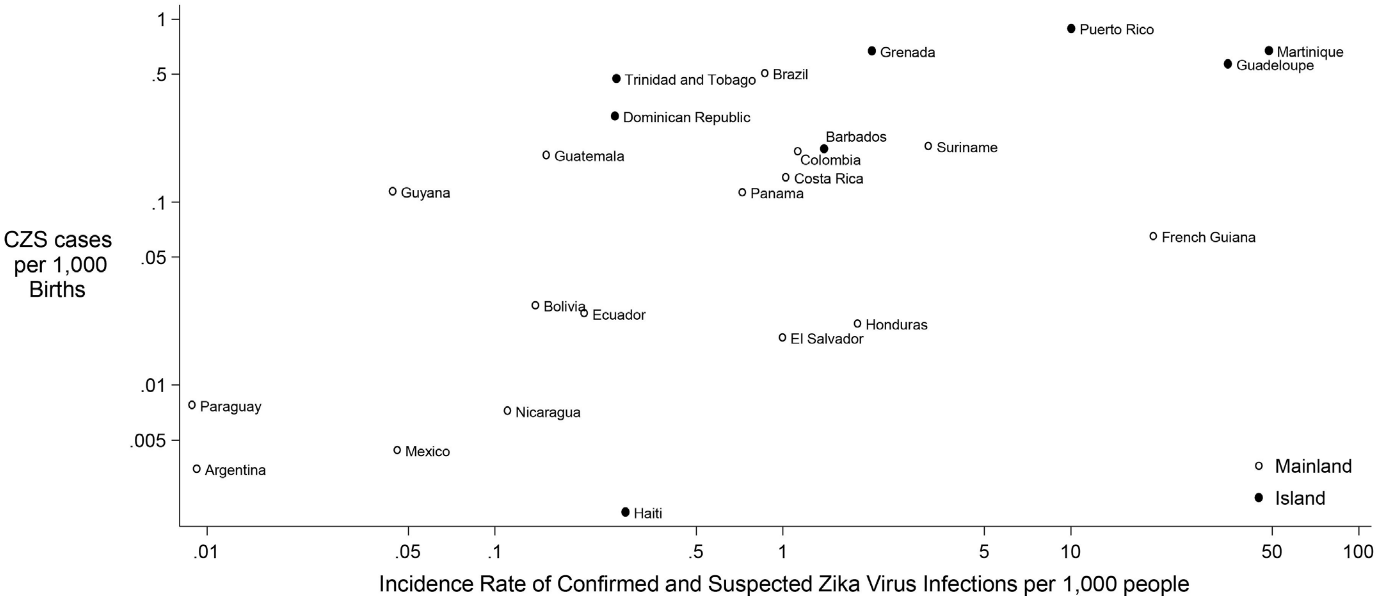

Figure 1 Congenital Zika syndrome (CZS) cases per 1000 births compared with the incidence of Zika virus infections.

pregnancy resulting in CZS is likely to have a much small variation. The occurrence of discordant twins for CZS shows that ZIKV infection during pregnancy is not deterministic for CZS phenotype and that other susceptibility factors might be involved.[19] Comparing the calculated number of CZS cases per 1000 infected pregnent woman with the expected 4–60 CZS case per 1000 infected pregnant women, reveals the huge variations in testing and reporting of Zika virus infections in Latin America. Interpretation of infectious disease reports should therefore be cautious. Although we found a clumping of countries around the expected 4–60 CZS per 1000 infected pregnant women, the infectious disease reports are clearly not suitable for such estimations which must come from properly designed epidemiological studies such as cohort studies. However, the potential imbalance due to susceptibility factors is likely to be of a much smaller order of magnitude than the occurrence of under-reporting indicated in this study.

A comparison between Brazil, Colombia and Puerto Rico is instructive to understand the complexity of comparing CZS figures between countries. The incidence of confirmed plus suspected Zika virus cases per 1000 people varied >10-fold from 0.86 in Colombia, 1.12 in Brazil to 10 in Puerto Rico, while in contrast the prevalence of CZS per 1000 births varied <5-fold from 0.19 in Colombia, to 0.51 in Brazil and 0.89 in Puerto Rico. In Colombia, termination of pregnancy was allowed in cases with CZS,[20] thereby potentially decreasing the birth prevalence of CZS in Colombia relative to the infection rate. Brazil used a lower threshold for diagnosing microcephaly and hence CZS at the beginning of the epidemic which may have inflated the earlier reports relative to other countries. All three countries were more likely to test and report Zika virus infections in pregnant women than in the general population. Calculating the number of CZS births per 1000 births to women infected with Zika virus (suspected or confirmed) results in values of 12 in Colombia, 113 in Brazil and 12 in Puerto Rico. In addition to Brazil using a lower threshold for diagnosing microcephaly, at the start of the epidemic in Brazil pregnant women were not tested for Zika virus infection, but only judged to have been infected once the child was diagnosed with CZS, both of which would cause the number of CZS cases per infected pregnant women to be much higher. However, there may also be some under-reporting of CZS in Colombia and Puerto Rico compared with Brazil.

There are many factors influencing the reporting of both Zika virus and CZS. For Zika virus, reporting depends on the true rate of infection in the population, the proportion of symptomatic people with access to healthcare presenting at health centres, the policy as to which suspected infections should have laboratory confirmation (eg, in Brazil testing was restricted mainly to pregnant women), the difficulties of retrospective confirmation of infection as it is difficult to distinguish Zika from other flaviviruses outside the viraemic phase, and the exhaustiveness of public health reporting mechanisms.

For CZS, reporting also depends on the proportion of affected babies/mothers with clinical signs of CZS tested for Zika virus, and the proportion of affected pregnancies who proceed to live birth. In addition to the above factors, and particularly the difficulty of confirming fetal Zika virus infection after birth, there are issues with the consistency of diagnoses of microcephaly, and with the reporting of terminations of pregnancy where they are legal. Inconsistencies in microcephaly diagnosis have been identified across European, US and South American congenital anomaly registries prior to the Zika epidemic.[10 21 22] In March 2016, WHO issued new guidance as to the diagnoses of microcephaly 'Neonates with a head circumference >2 SD below the mean are considered to have microcephaly. Neonates with a head

Table 2 Zika virus infections in pregnant women in countries in the South and Central Americas, Mexico and the Caribbean, 2015–2017 and the number of CZS cases per 1000 pregnant women with Zika virus and number of pregnant women with Zika virus per 1000 births

Country	CZS cases (table 1)	Reported number of pregnant women with Zika virus		Date pregnancies reported (week/year)	CZS cases per 1000 pregnant women with Zika virus suspected or confirmed*	Number of pregnant women with Zika virus suspected or confirmed per 1000 births*
		Zika virus suspected or confirmed	Zika virus confirmed			
	C	**G**	*H*		*C/G×1000*	*G/E (table 1)×1000*
Brazil	2952	26 066	11 546	22/2017	113.3	4.5
Colombia	248	19 993	6365	33/2017	12.4	15.3
Guatemala	140	1414	341	31/2017	99.0	1.8
Dominican Republic	85	966	271	30/2017	88.0	3.4
Puerto Rico	47	NR	4047	35/2017	11.6	76.8
Mexico	20	NR	5667	34/2017	3.5	1.3
Costa Rica	19	NR	210	33/2017	90.5	1.5
Panama	17	212	86	35/2017	80.2	1.4
Trinidad and Tobago	17	NR	463	**8/2017**†	36.7	12.9
Ecuador	14	NR	912	32/2017	15.4	1.6
Bolivia	14	NR	189	24/2017	74.1	0.4
Honduras	8	681	125	33/2017	11.7	1.8
Martinique	5	NR	830	30/2017	6.0	111.8
Guadeloupe	5	NR	815	30/2017	6.1	92.8
Argentina	5	NR	5	35/2017	1000.0	0.003
El Salvador	4	391	NR	33/2017	10.2	1.8
Suriname	4	NR	NR	35/2017		
Guyana	3	NR	NR	35/2017		
Nicaragua	2	NR	1117	**1/2017**†	1.8	4.1
Grenada	2	NR	NR	22/2017		
Paraguay	2	31	3	28/2017	64.5	0.1
French Guiana	1	NR	2211	36/2017	0.5	144.3
Haiti	1	22	NR	**21/2016**†	45.5	0.04
Saint Martin	1	NR	48	30/2017	20.8	48.0
Barbados	1	NR	32	32/2017	31.3	6.3
Venezuela	0	3463	NR	12/2017	0	2.9
Jamaica	0	712	78	12/2017	0	10.1
Peru	0	NR	279	33/2017	0	0.3
Curacao	0	NR	30	**44/2016**†	0	9.0
Belize	0	NR	1	**20/2016**†	0	0.1
Cuba	0	NR	NR	35/2017		
Aruba	0	NR	NR	35/2017		
Dominica	0	13	10	**38/2016**†	0	9.0
Saint Vincent and the Grenadines	0	3	1	**35/2016**†	0	0.9
Saint Kitts and Nevis	0	NR	NR	35/2017		
Antigua and Barbuda	0	16	6	27/2017	0	7.4
Bahamas	0	NR	NR	35/2017		
Virgin Islands (USA)	0	NR	286	34/2017	0	101.1

Continued

Table 2 Continued

Country	CZS cases (table 1)	Reported number of pregnant women with Zika virus: Zika virus suspected or confirmed	Reported number of pregnant women with Zika virus: Zika virus confirmed	Date pregnancies reported (week/year)	CZS cases per 1000 pregnant women with Zika virus suspected or confirmed*	Number of pregnant women with Zika virus suspected or confirmed per 1000 births*
Sint Maarten	0	10	1	35/2017	0	13.8
Saint Lucia	0	84	39	**41/2016**†	0	20.0
Saint Barthelemy	0	NR	11	30/2017	0	76.4
Cayman Islands	0	NR	NR	35/2017		
Turks and Caicos Islands	0	NR	NR	35/2017		
Virgin Islands (UK)	0	NR	NR	35/2017		
Anguilla	0	NR	NR	35/2017		
Montserrat	0	NR	NR	35/2017		
Bonaire, St Eustatius and Saba	0	NR	NR	35/2017		
Total	3617	54 077	36 025			

*Numbers of pregnancies suspected or confirmed used unless this is not reported. In this case, number of confirmed pregnancies is used.
†Potentially incomplete data on infected pregnancies due to early reporting dates.
NR, not reported.

circumference >3 SD below the mean should be considered to have severe microcephaly'. (Assessment of infants with microcephaly in the context of Zika virus Interim guidance 4 March 2016 'WHO/ZIKV/MOC/16.3 Rev.1' http:// www.who.int/csr/resources/publications/zika/assessment-infants/en/.) Many countries had been using

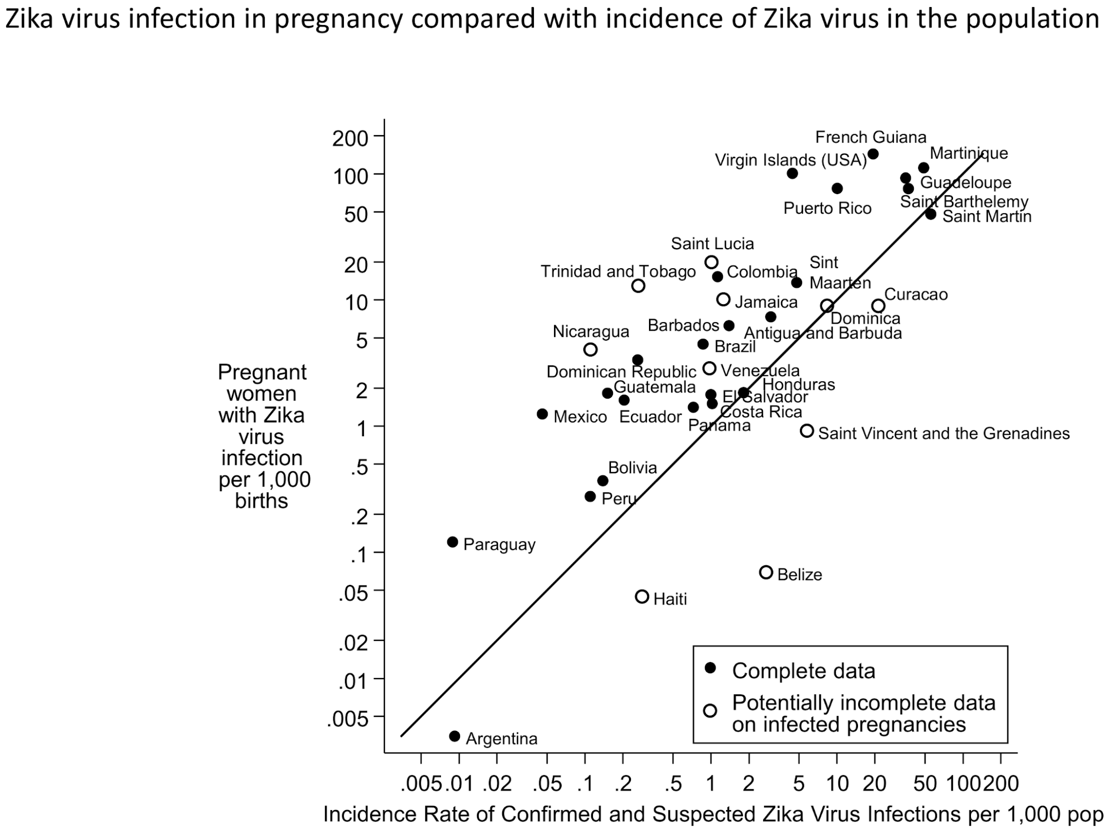

Figure 2 Number of congenital Zika syndrome (CZS) cases per 1000 infected pregnancies (95% CI).

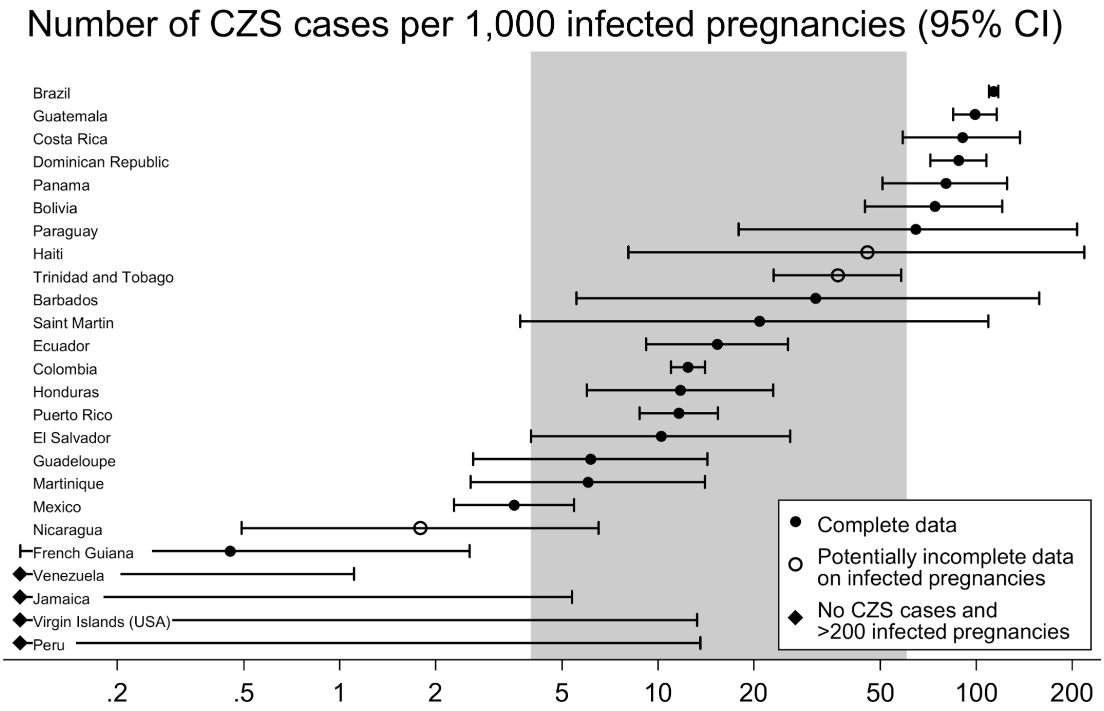

Figure 3 Zika virus infection in pregnancy compared with incidence of Zika virus in the population.

a definition of >3 SD below the mean for microcephaly. This change in definition was likely to have greatly increased the numbers of microcephaly diagnoses made. At the start of the CZS epidemic, many countries did not have the resources to diagnose cases as soon as they were born.[23]

Despite the evidence of under-reporting, other researchers have attempted to use these published figures to investigate the Zika virus epidemic. A study by Hay *et al*[24] used the publicly available data from Brazil and Colombia to attempt to determine the gestational age risk of ZIKV infection and microcephaly. They concluded that the currently available surveillance data were insufficient to use in estimating risks of microcephaly from ZIKV infection.

Our analyses of CZS per 1000 births and the number of CZS per 1000 births to pregnant women with Zika virus provides considerable added value for estimating the burden of disease, including highlighting areas of data inconsistency, and we suggest this should be added to routine PAHO output, and to WHO output in general in tracking future epidemics. This will also make it easier to assess the impact of preventive interventions (eg, to prevent infection among pregnant women during an epidemic). Countries also need to report centrally how they ascertain cases of both Zika virus and CZS in order

Table 3 Comparison of cumulative numbers of CZS reported to PAHO/WHO and those predicted by Zhang *et al* in spread of Zika virus in Latin America and the Caribbean[14]

	Predicted number by December 2017			Reported to PAHO/ WHO by January 2018
	First trimester risk (per 1000)			
	9.5	21.9	45.2	
Brazil	1297 (1190–1428)	2991 (2744–3291)	6173 (5664–6792)	2952
Colombia	219 (194–248)	504 (447–572)	1041 (922–1180)	248
Mexico	314 (226–367)	723 (522–845)	1493 (1077–1744)	20
Puerto Rico	19 (13–26)	43 (29–60)	86 (60–124)	47
El Salvador	39 (32–47)	91 (75–108)	187 (154–223)	4
Honduras	144 (124–163)	332 (286–376)	686 (590–775)	8
Haiti	316 (276–357)	728 (637–824)	1502 (1315–1700)	1
Venezuela	271 (237–308)	624 (546–711)	1288 (1127–1468)	0

CZS, congenital Zika syndrome; PAHO, Pan American Health Organization.

to help interpretation, as this information is currently not publicly available in a coordinated manner. These issues have recurred again in a different form in COVID-19 reporting, where WHO figures lack population denominators, and lack information about testing regimes in different countries, leading to potentially misleading interpretations of differences between countries.

CZS is likely to identify only those children severely affected and identifiable at birth. It is believed that many further thousands of children will suffer some effects despite appearing healthy at birth. These figures show the cost of the Zika virus epidemic across the South and Central Americas, Mexico and the Caribbean and highlight that many areas will need considerable resources to cope with the long-term effects in children.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

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