Anticipating the international spread of Zika virus from Brazil

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In May, 2015, locally acquired cases of Zika virus—an arbovirus found in Africa and Asia-Pacific and transmitted via *Aedes* mosquitoes—were confirmed in Brazil. The presence of *Aedes* mosquitoes across Latin America, coupled with suitable climatic conditions, have triggered a Zika virus epidemic in Brazil, currently estimated at 440 000–1 300 000 cases.[1] Viraemic travellers have now introduced Zika virus into at least 13 additional countries, where susceptible *Aedes* mosquitoes have become infected and perpetuated local transmission cycles. In Brazil, a precipitous surge in infants born with microcephaly and the detection of Zika virus RNA in the amniotic fluid of affected newborns has been reported.[1] We sought to identify high-risk international pathways for the dispersion of Zika virus and global geographies conducive to autochthonous transmission.

We created a global Zika virus spread model by adapting a seasonal model for dengue that integrates global ecological niche data for *Aedes aegypti* and *albopictus* and worldwide temperature profiles.[2,3] In Brazil, we identified airports within 50 km of areas conducive to year-round Zika virus transmission. We mapped the final destinations of international travellers departing from these airports from September, 2014, to August, 2015, using worldwide flight itinerary data from the International Air Transport Association. We used LandScan, a gridded global population dataset, to estimate numbers of people living in geographies at risk for autochthonous Zika virus transmission.

9·9 million travellers departed from the aforementioned Brazilian airports for international destinations, with 65% to the Americas (figure), 27% to Europe, and 5% to Asia. Traveller volumes were greatest to the USA (2 767 337), Argentina (1 314 694), Chile (614 687), Italy (419 955), Portugal (411 407), and France (404 525). China and Angola received the highest volume of travellers in Asia (84 332) and Africa (82 838), respectively. Argentina, Italy, and the USA have more than 60% of their populations residing in areas conducive to seasonal Zika

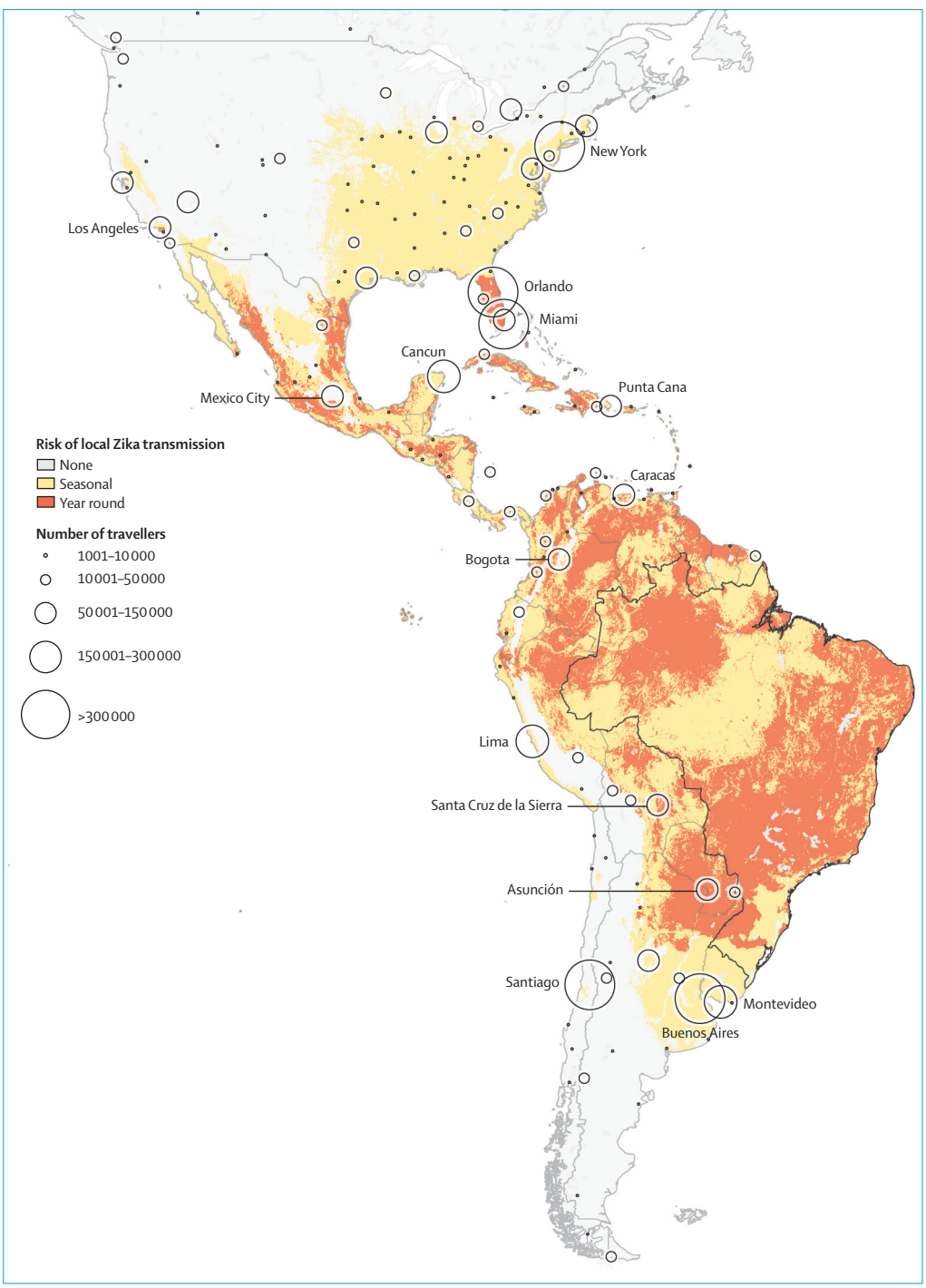

Figure: **Final destinations of travellers departing Brazil by potential for autochthonous Zika transmission**

virus transmission, whereas Mexico, Colombia, and the USA have an estimated 30·5, 23·2, and 22·7 million people, respectively, living in areas conducive to year-round transmission.

In parallel to the recent experience with chikungunya,[4] Zika virus has the potential to rapidly spread across Latin America and the Caribbean. With no vaccine or antiviral therapy available, possible interventions include: personal protection (ie, repellent use) and daytime avoidance of mosquito bites (especially pregnant women until more is known about the association between Zika virus infection and microcephaly); daytime avoidance of mosquito bites among Zika virus-infected individuals to disrupt human to mosquito to human transmission cycles (80% of infected individuals are asymptomatic and the remainder have clinical syndromes overlapping with dengue and chikungunya);[5] and community-level mosquito surveillance and control measures. The summer Olympic Games in Brazil in August, 2016, heighten the need for awareness of this emerging virus.

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Eltrombopag for chronic immune thrombocytopenia

The PETIT2 trial (Oct 24, p 1649)[1] reported outcomes that were different from those registered before trial commencement.[2] Of 22 prespecified secondary outcomes, 14 were reported in the Article, and eight were not reported anywhere in the paper. Additionally, the Article reported a new outcome ("concomitant drugs for immune thrombocytopenia") that was not prespecified, without flagging it as such. For clarity, we considered tables 2–4 in the Article to represent the main trial results, with secondary outcome measures split between them.

We declare no competing interests.

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1 Grainger JD, Locatelli F, Chotsampancharoen T, et al. Eltrombopag for children with chronic immune thrombocytopenia (PETIT2): a randomised, multicentre, placebo-controlled trial. *Lancet* 2015; **386:** 1649–58.
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Authors' reply

We thank Ioan Milosevic and colleagues for their inquiry regarding the PETIT2 trial.[1] We agree that the CONSORT statement for reporting of randomised trials is an important guide for communicating trial results, and we used these guidelines when drafting our report. Because of word limits, we presented only the key findings that would be of particular interest to clinicians who treat children with immune thrombocytopenia. Additionally, results are publicly available on ClinicalTrials.gov (number NCT01520909) and the GlaxoSmithKline clinical study registry (number 115450).

We wish to clarify that the study endpoints in the protocol were not different from those reported in our Article.[1] All the primary and secondary endpoints in the Article were the same as those in the protocol, including "reduction or discontinuation of concomitant drugs for immune thrombocytopenia", which was a secondary endpoint. Vital signs and clinical laboratory values were part of the safety assessment. Clinical laboratory values related to liver function adverse events were reported in the text and were also provided in the Article[1] appendix (table S2). The results of the ophthalmic examination were reported in the text.

We did not report the five pharmacokinetic endpoints in our Article[1] but will include them in a separate publication, in which these data will be combined with similar data from the phase 2 PETIT study.

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