*Original Article*

Journal of Evidence-Based Complementary & Alternative Medicine
2014, Vol. 19(3) 155-160

DOI: 10.1177/2156587214525402
cam.sagepub.com
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# A Reevaluation of the Effectiveness of Homoeoprophylaxis Against Leptospirosis in Cuba in 2007 and 2008

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## Abstract

*Objectives*: In 2007 and 2008, Cuban health officials conducted large homoeoprophylaxis interventions against rising rates of leptospirosis caused by extensive hurricane damage. Published results showed that the interventions were highly successful, but some questions regarding possible confounders were raised. The objective of this research was to assess the influence of potential confounders on initial results. *Design*: Weekly leptospirosis reporting data entries for 9 years were checked to ensure data consistency. Some errors in weekly reports for 2000-2008 were discovered, and corrected, and the changes incorporated in this analysis. The corrected data was reanalyzed to investigate the impact of potential confounders. *Results*: New analyses of the timing and extent of vaccination and chemoprophylaxis in 2007 and 2008 and changes in leptospirosis notifications were presented. *Conclusions*: The results support the previous conclusions that homoeoprophylaxis can be used to effectively immunize people against targeted infectious diseases such as leptospirosis.

## Keywords

leptospirosis, immunisation, homoeoprophylaxis

Received October 9, 2013. Revised December 21, 2013. Accepted for publication January 25, 2014.

## Introduction

In 2007, the Finlay Institute in Havana, Cuba[1] conducted a massive homeopathic immunization (homeoprophylaxis) intervention in 3 provinces to counter rapidly increasing cases of leptospirosis due to extensive hurricane damage. The intervention was repeated in 2008. Full details of the 2007 intervention were first released in December 2008[2] and first published in 2010.[3] Further information was released in other articles.[4-6]

The results from the 2007 and 2008 interventions were unambiguously successful in that the prevalence of leptospirosis was far lower than expected during the hurricane season in the 3 provinces where homeoprophylaxis was used (ie, in the intervened regions) compared with the remaining 12 provinces in Cuba (ie, rest of the country).

The aim of this report is to determine whether a further examination and analysis of official leptospirosis data and other potentially confounding variables such as rainfall, vaccination use, and chemoprophylaxis use provide any further validation of the effectiveness of the homeoprophylaxis interventions in 2007 and 2008

## Materials and Methods

Leptospirosis is a potentially serious disease caused by infection with pathogenic strains of Gram-negative bacterium *Leptospira* spp. In recent years, leptospirosis has emerged as one of the most important *zoonotic* (transmitted between humans and animals) diseases worldwide and a severe health problem in developing countries and the tropics. Human infection usually occurs through contact with water contaminated with the urine of domestic and wild animals, which are natural bacteria reservoirs. Infection enters through the mucosa or open skin lesions. Leptospirosis is endemic in Cuba, but peaks in the hurricane season from October through to December because of the increased levels of infrastructure damage and stagnant water caused by intense rainfall in affected areas of the country. Note that these months do not experience the highest quantity of rainfall, but do experience the most episodes of intense rainfall.

*vaxSpiral* is a 3-valent leptospirosis inactivated vaccine that was developed by and is being produced at the Finlay Institute in Havana, Cuba. It has been included on the national immunization program since 1998 for individuals older than 15 years in at-risk groups. Clinical trials conducted in Cuba suggested a 78.1% efficacy and good safety profile. The immunization schedule includes 2 intramuscular injections 6 to 8 weeks apart.

In 2007, scientists at the Finlay Institute developed *nosoLEP*, which was prepared from 4 strains of inactivated leptospiras ($10^6$ bacteria/mL),

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which were selected on basis of the frequency of isolation, viability, and virulence. Homeoprophylaxis treatment included a prime administration of 2 doses of *nosoLEP* 200C starting in week 46 in 2007, followed by a booster administration of 2 doses of *nosoLEP* 10MC in 2008. The 2 oral doses were given 7 to 9 days apart, and each dose consisted of 5 drops (250-300 μL) administered sublingually 10 minutes away from eating, smoking, or drinking. The application of *nosoLEP* was carried out by family doctors, nurses, social workers, and paramedical personnel previously trained in the administration procedure.

In the new analysis, 7020 weekly data reports covering each province for 9 years (2000-2008) were checked to ensure data consistency. The reports were prepared by the National Surveillance Program for zoonotic diseases under the Minister of Public Health of Cuba. Each report contained 20 variables, including suspected and confirmed cases of leptospirosis as well as deaths, demographic data, and use of vaccination and chemoprophylaxis. Simple data cross-checks were performed to ensure internal consistency of data. Some corrections were made (less than 0.1% of entries), and the changes incorporated in this analysis.

In addition, the extent to which the use of existing vaccination programs and/or existing chemoprophylaxis programs could have explained the changed rates of leptospirosis in the intervened regions compared with rest of the country following the homeoprophylaxis interventions in 2007 and 2008 was examined.

## Results

The effects of the October 2007 and the August/September 2008 homeoprophylaxis interventions on monthly confirmed leptospirosis cases are shown in Figure 1. The 2 homeoprophylaxis interventions are marked by arrows. Notifications in the intervened regions have historically been higher per head of population in intervened regions than in rest of the country because of severe hurricanes being most prevalent in the intervened regions.

Intervened region was damaged by hurricanes more severely than rest of the country in both 2007 and 2008, meaning that for both years leptospirosis notifications were expected to be much higher per head in intervened region than in rest of the country. Confirmed cases in the intervened region are seen to have fallen following the 2007 intervention, and have been kept to historical low levels in 2008.

Since 2000 there has only been 1 month in intervened region where December figures have been lower than November figures, and that was in 2007 following the leptospirosis homeoprophylaxis intervention, another indication of the impact of the intervention in that year.

Figure 2 reports the monthly average of leptospirosis cases from 2004 to 2008 and the monthly average rainfall per province from 2004 to 2008. The inverse relationship between cases and rainfall in November and December is apparent, demonstrating that the intensity of rainfall (such as caused by hurricanes) and not just total rainfall is a potential causative factor, given that leptospirosis is frequently carried through standing water.

Figure 3 and Table 1 show annual leptospirosis confirmed cases from 2000 to 2008 for the intervened region and the rest of the country. The average regional rainfall in meters is also shown for intervened region and rest of the country for the period 2004 to 2008.

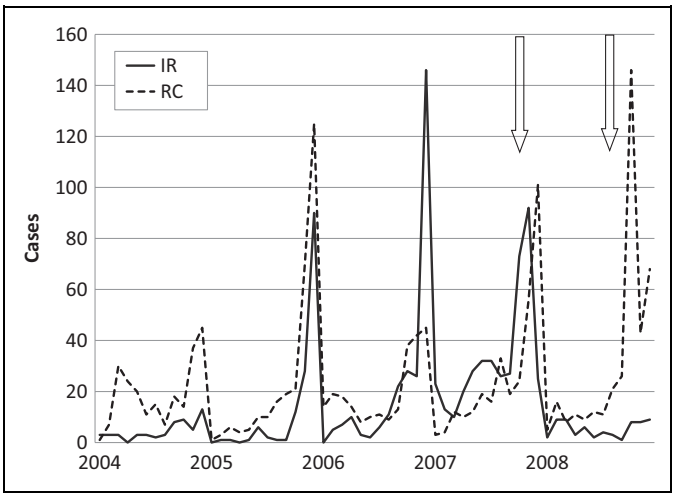


**Figure 1.** Confirmed leptospirosis cases per month in intervened region (IR) and rest of the country (RC) from 2004 to 2008.

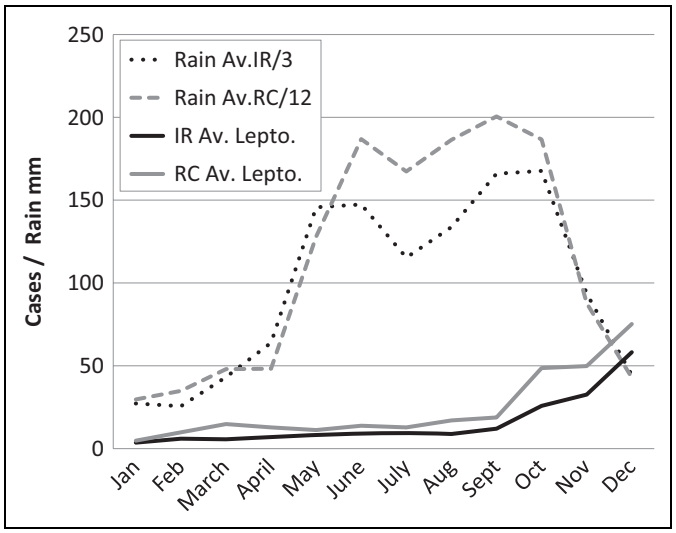


**Figure 2.** Monthly average of leptospirosis during 2004-2008 and average monthly rainfall (mm) per region 2004-2008. IR, intervened region; RC, rest of the country.

Figures 4 and 5 show the monthly data for vaccination and chemoprophylaxis against leptospirosis in the intervened region in 2007 and 2008, respectively. Both figures also show confirmed leptospirosis cases (×1000 for scaling purposes). Table 2 shows the annual data from 2000 to 2008. Note that Figure 4 does not fully show a chemoprophylaxis intervention involving 330 980 persons in Las Tunas province in week 47 of 2007 in order to make the other trends more easily seen. To be effective, the chemoprophylaxis intervention needs to be administered weekly, and this was not done (the chemoprophylaxis coverage in Las Tunas in the remaining weeks of 2007 was 0, there being 35 548 doses being given in the remaining 2 provinces over the last 5 weeks as shown in Table 3). There was a reduction in confirmed cases in Las Tunas in week 47; however, there was a slight increase in cases and 3 deaths in week

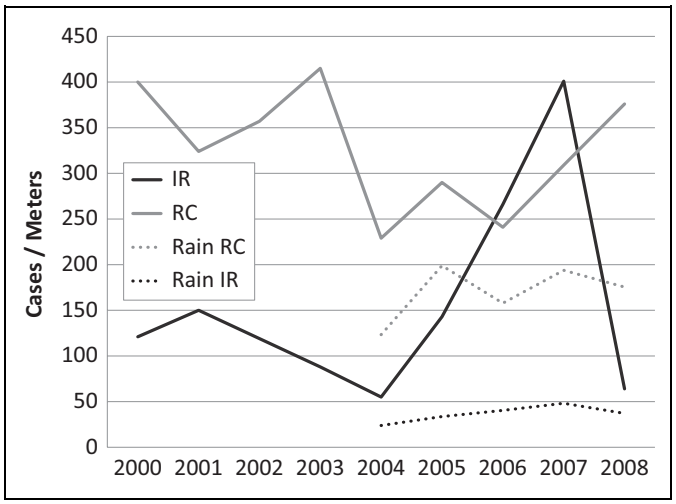


**Figure 3.** Confirmed leptospirosis cases per year during 2000-2008 and annual average rainfall (metres) per region 2004-2008. IR, intervened region; RC, rest of the country.

**Table 1.** Annual Confirmed Leptospirosis and Rainfall (Meters).

| | Leptospirosis | | Rainfall (Meters) | |
|---|---|---|---|---|
| | IR | RC | Rain RC | Rain IR |
| 2000 | 120 | 391 | | |
| 2001 | 150 | 304 | | |
| 2002 | 119 | 350 | | |
| 2003 | 88 | 411 | | |
| 2004 | 55 | 228 | 123 | 24 |
| 2005 | 143 | 287 | 199 | 34 |
| 2006 | 266 | 237 | 158 | 40 |
| 2007 | 401 | 319 | 194 | 48 |
| 2008 | 64 | 376 | 175 | 37 |

Abbreviations: IR, intervened region; RC, rest of the country.

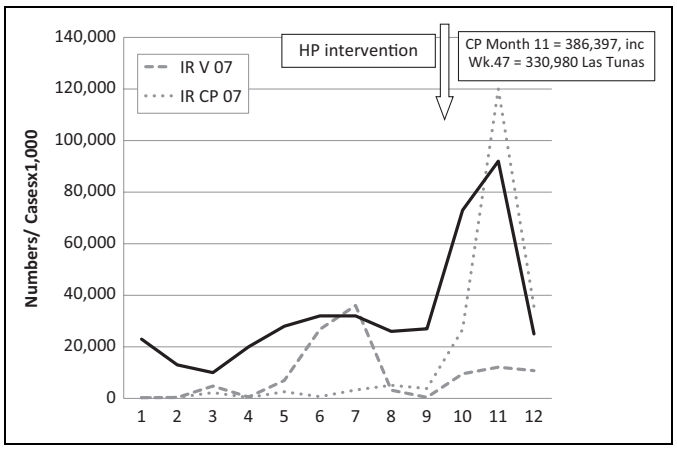


**Figure 4.** Vaccination (V) and chemoprophylaxis (CP) in 2007 in intervened region (IR); not showing full CP in week 47 in IR, plus leptospirosis cases (×1000). HP, homeoprophylaxis.

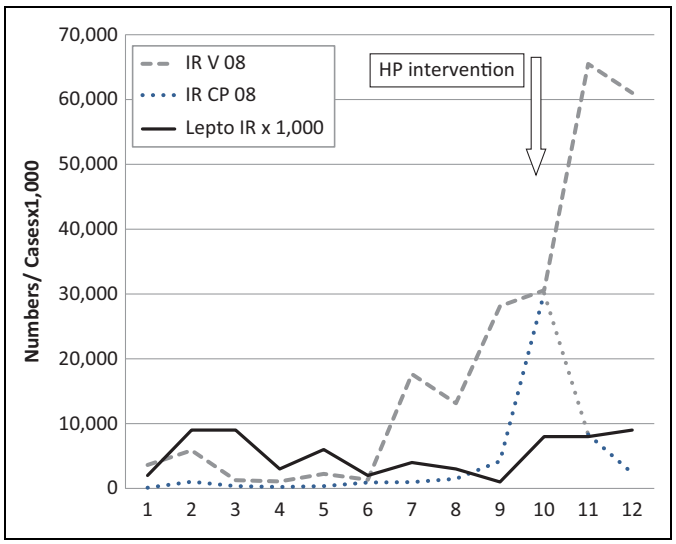


**Figure 5.** Vaccination and chemoprophylaxis in 2008 in intervened regions (IR), plus leptospirosis cases (×1000). CP, chemoprophylaxis; HP, homeoprophylaxis.

**Table 2.** Vaccination and Chemoprophylaxis in Cuba 2000-2008 by IR and RC.

| | IR | | RC | |
|---|---|---|---|---|
| | Vaccination | Chemoprophylaxis | Vaccination | Chemoprophylaxis |
| 2000 | 67 604 | 63 500 | 301 140 | 176 505 |
| 2001 | 145 427 | 66 784 | 386 930 | 98 880 |
| 2002 | 98 729 | 38 959 | 560 773 | 92 538 |
| 2003 | 135 136 | 12 720 | 274 445 | 66 781 |
| 2004 | 142 307 | 36 084 | 259 168 | 50 629 |
| 2005 | 35 266 | 79 909 | 255 060 | 42 925 |
| 2006 | 103 929 | 72 592 | 169 421 | 29 381 |
| 2007 | 111 889 | 467 537 | 194 843 | 94 738 |
| 2008 | 231 409 | 50 477 | 591 420 | 234 191 |

Abbreviations: IR, intervened region; RC, rest of the country.

**Table 3.** Chemoprophylaxis in the Intervened Region Provinces: Weeks 38 to 52, 2007.

| Week | Las Tunas | Holguin | Granma |
|---|---|---|---|
| 38 | 0 | 684 | 804 |
| 39 | 0 | 0 | 652 |
| 40 | 0 | 8000 | 0 |
| 41 | 6064 | 7863 | 1018 |
| 42 | 0 | 0 | 138 |
| 43 | 0 | 1897 | 1787 |
| 44 | 0 | 18 420 | 300 |
| 45 | 1910 | 16 305 | 465 |
| 46 | 0 | 17 301 | 716 |
| 47 | 330 226 | 0 | 754 |
| 48 | 0 | 32 093 | 1278 |
| 49 | 0 | 286 | 802 |
| 50 | 0 | 286 | 533 |
| 51 | 0 | 120 | 150 |
| 52 | 0 | 0 | 0 |
| | 338 200 | 103 255 | 9 397 |

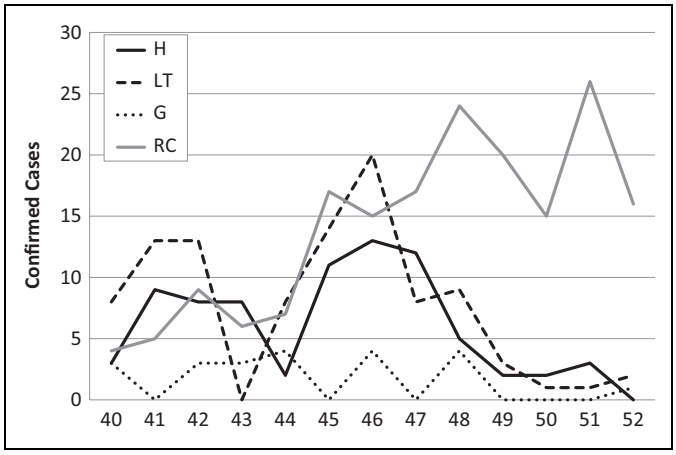


**Figure 6.** Leptospirosis in the 3 intervened region (IR) provinces and in rest of the country (RC): weeks 40 to 52, 2007. Province codes H, Holguin; LT, Las Tunas; G, Granma.

48, the week following the intervention (a very unexpected result, which is being further investigated to determine if there is a pattern or simply a coincidence). The incidence of the disease fell in Holguin and in Granma where there were minor chemoprophylaxis interventions only. The use of chemoprophylaxis fell in intervened region from 2007 to 2008 and rose in rest of the country (Table 2), yet leptospirosis cases rose in rest of the country and fell in the intervened region over that same period.

Figure 5 shows the increase in vaccinations from July to October, with a further increase in November and December. In 2007, over the whole of the intervened region there were 111 889 doses of *vaxSpiral* administered. Two doses are required to establish a reasonable level of immunity, so probably no more than 50 000 residents of the intervened region (2% of the intervened region) were fully covered. There was a doubling of vaccinations in the intervened region in the later months of 2008 meaning that around 100 000 (4%) residents of the intervened region were fully vaccinated.

Figure 6 shows the incidence of leptospirosis in the 3 provinces of the intervened region, and in rest of the country for weeks 40 to 52 of 2007, and Table 4 shows vaccination in the 3 provinces of the intervened region in weeks 38 to 52 of 2008. They show that vaccination was much higher in Las Tunas, which had the smallest population of the 3 yet that had the highest incidence of leptospirosis, and that in Holguin, with double the population of Las Tunas, there was very little vaccination yet there was less disease. Furthermore, 250 000 residents of rest of the country were fully vaccinated yet the incidence of the disease rose sharply in rest of the country in the later months of 2008. Furthermore, vaccination fully covered only 4.2% of the population of the intervened region whereas homeoprophylaxis covered 96% of the population (some people received both methods).

**Table 4.** Vaccination in the Intervened Region Provinces in Weeks 38 to 52, 2008.

| | Las Tunas | Granma | Holguin |
|---|---|---|---|
| Population | 534 018 | 835 381 | 1 035 388 |
| Leptospirosis weeks 38-52 | 14 | 6 | 5 |
| Week | | | |
| 38 | 3572 | 1744 | 18 638 |
| 39 | 920 | 0 | 0 |
| 40 | 269 | 1,771 | 320 |
| 41 | 630 | 913 | 9566 |
| 42 | 549 | 2285 | 0 |
| 43 | 11 988 | 2271 | 0 |
| 44 | 24 729 | 831 | 0 |
| 45 | 9964 | 7814 | 0 |
| 46 | 10 268 | 4888 | 0 |
| 47 | 5775 | 842 | 379 |
| 48 | 7954 | 2025 | 0 |
| 49 | 21 963 | 1774 | 0 |
| 50 | 5177 | 10 415 | 0 |
| 51 | 6362 | 1705 | 0 |
| 52 | 2477 | 1173 | 0 |
| Vaccination total | 112 597 | 40 451 | 28 903 |

## Discussion

Figures 1 to 3 and Table 1 all show the differences in confirmed leptospirosis cases in 2007 and 2008 between intervened region and rest of the country. The results in the intervened region suggest that the homeopathic interventions in 2007 and 2008 did provide significant immunization protection against the disease given that more cases were expected in the intervened region in both years because of more extensive hurricane damage in that region compared with rest of the country.

### *Vaccination Against Leptospirosis*

Given the lag times before immunity is established (roughly 2 weeks following the second dose of vaccine), and given the timing of the vaccines in 2007 (Figure 4), there appears to be no evidence that the vaccination programs in the intervened region in 2007 made any substantial difference to the dramatic fall in incidence following the homeoprophylaxis interventions. In fact, cases began to increase rapidly in September despite the increase in vaccination in June and July, and only fell following the homeoprophylaxis intervention in October.

There is no definitive evidence that the vaccination programs in 2008 (Figure 5) made a substantial difference to infections in the intervened region given that only 4% of the population of the intervened region were vaccinated compared with more than 95% receiving homeoprophylaxis. However, it is not possible to state that the increased vaccinations in the later months of 2008 made no difference at all to cases, given that the exposure to the disease would not have been identical in every part of the intervened region.

### *Chemoprophylaxis Against Leptospirosis*

There is no evidence arising from Figures 4 and 5 and Table 2 that the use of chemoprophylaxis influenced the leptospirosis

cases previously reported in 2007 and 2008. The single massive chemoprophylaxis intervention in Las Tunas in week 47 was not followed up as is needed to maintain immunity, and chemoprophylaxis in the remaining 2 provinces was insignificant as shown in Table 3.

### Other Possible Confounders

It was suggested that in 2008 rainfall in the intervened region fell from 2007 levels and leptospirosis cases simply returned to 2004 levels.[7] In fact, Table 1 shows that total rainfall in 2008 was 54% greater than in 2004, plus in 2008 there were 3 damaging hurricanes affecting the intervened region and rest of the country. In 2004, there was a brief hurricane which did little damage and was not centered over the intervened region. The data show clearly that 2004 and 2008 are not comparable years, and that a much higher incidence of leptospirosis was expected in the intervened region in 2008 compared with 2004, given the extent of hurricane damage in 2008. When compared with rest of the country (where rain totals also reduced but cases rose due to hurricane-damaged infrastructure), then the reduction in cases in the intervened region in 2008 can be seen clearly to be independent of a reduction in rainfall.

Another suggested confounder was possible increased awareness of natural methods of prevention (such as avoiding stagnant water) because of the homeoprophylaxis intervention in the intervened region. However, leptospirosis awareness programs were conducted in all parts of the country. As well, in 2008 the majority of cases were in rest of the country thus ensuring heightened public awareness of the disease within rest of the country.

Finally, the interventions were not randomized blinded trials with suitable control groups. The 2007 and 2008 interventions were an immediate practical response to an urgent public health problem caused by severe hurricane damage in the most at-risk parts of the country. A carefully controlled trial was simply not an option in such circumstances. It should be noted that there is a growing awareness in orthodox circles that randomized controlled trials are not essential to demonstrate a practically useful result, and in fact contain biases that often produce misleading results.[8] Rest of the country is not a perfect default control for the intervened region because the extent of hurricane damage was different in the 2 regions—it was much worse in the intervened region leading to an expectation of more leptospirosis cases. Given that the only other major factor of difference was the homeoprophylaxis intervention in the intervened region, the resulting reduction in cases in the intervened region is significant.

## Conclusions

The success of the homeoprophylaxis interventions in 2007 and 2008 is supported by the preceding analysis: The database has been rigorously cleansed, the possible impact of vaccination and chemoprophylaxis campaigns has been examined, and the possible impact of other confounders has been considered. No possible confounding factor appears to have exerted any appreciable influence on the positive impact of the homeopropylaxis interventions in 2007 and 2008, although the vaccination campaign in late 2008 in the intervened region targeting approximately 4% of the population may have prevented some cases.

The Cuban experience with homeoprophylaxis against leptospirosis has been and remains a very positive one. It has given rise to further government-directed immunization against hepatitis A, swine flu, pneumococcal disease, and dengue fever using homoeoprophylaxis. The Cuban health system in general demonstrates how orthodox and complementary medicine can be usefully integrated, and their willingness to use both vaccination and homoeoprophylaxis as evidence-based immunization options is an excellent example of this.

### Acknowledgments

The authors acknowledge the helpful comments made on an earlier draft of this article by Associate Professor Andrew Stranieri, School of Science, Information Technology and Engineering, Federation University, Ballarat, Australia.

### Author Contributions

IG worked with GB on data analysis in Cuba and Australia, and prepared preliminary drafts of the article. GB liaised with Cuban health authorities to obtain the weekly leptospirosis notification data used in the research, and worked with IG on data analysis in Cuba. GB was also the supervisor of the homoeoprophylaxis interventions undertaken by the Finlay Institute in 2007 and 2008.

### Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

### Ethical Approval

No ethics approvals were required for this research, which involved the collection and analysis of nationally available retrospective, de-identified, leptospirosis notification data, as well as national vaccination, chemoprophylaxis, and other data.

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