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Vaccination coverage and preventable diseases in Peru: Reflections on the first diphtheria case in two decades during the midst of COVID-19 pandemic

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Dear Editor,

Peru has one of the most comprehensive immunization programs in the Latin-America, financed 100% by public resources under regulation of the Ministry of Health (MINSA) [1]. This free-of-charge schedule includes 17 vaccines that protect against around 26 diseases and reaches pregnant women and the elderly, although the primary target population is children under five-years-old [2–4].

In Peru, no diphtheria cases have been reported since 1999, consistent with the inclusion of the DPT-HepB-Hib vaccine (pentavalent) in the national scheme (Fig. 1). This vaccine (including Diphtheria, Pertussis, Tetanus, Hepatitis B, *Haemophilus influenzae* type b) is administered at 2, 4, and 6 months of age according to the national childhood vaccination schedule. Booster doses of the DPT are scheduled at 18 and 48 months of age [2–4].

On October 27, 2020, the MINSA reported the first case of diphtheria in 20 years in Lima (capital of Peru), in a 5-year-old girl who died due to associated-myocarditis on October 30, 2020. Diphtheria antitoxin was not yet available in Peru. MINSA professionals reported that the girl had an incomplete DPT schedule. This case caused significant social and media impact and led to declare a national epidemiological alert and to plan massive vaccination campaigns. In 2020, many people could not receive full doses as vaccination programs were affected by the government's lockdown due to the COVID-19 pandemic, that currently reached 1,007,657 cases (officially reported, December 28, 2020), and 37,368 related deaths [3,4].

We analyzed data from the 2010 to 2019 Demographic and Health Survey (DHS) in Peru (http://iinei.inei.gob.pe/microdatos/). We defined complete DPT-HepB-Hib coverage as having received the first three doses of this vaccine. We included children aged 13–59 months who had DPT-HepB-Hib vaccination data.

On the other hand, we performed purely spatial scan statistical analysis in Kulldorff's SaTScan™ version 9.6 to identify high-risk areas of low DPT-HepB-Hib vaccination coverage in 2015 and 2019, based on DHS data. SaTScan employs a circular scanning window that moves systematically around the study area to detect clusters using Bernoulli-based model. Children with incomplete DPT-HepB-Hib coverage were defined as cases and children with full coverage as controls. We used maximum cluster size of 5% of the population as an upper limit to identify small clusters. The most probable (primary) cluster was the highest log-likelihood ratio (LLR); the others were considered secondary clusters. To estimate each potential cluster's significance, an LLR test and p-value were calculated based on 999 Monte Carlo replications.

Nationwide, the DPT-HepB-Hib vaccine coverage was 84.65% (95% CI 83.78–85.49) in 2019; however, there was high variability between regions. The regions with the lowest coverage were Puno (78.94%), Ica (79.12%), and La Libertad (80.64%), while the regions with the highest coverage were Tumbes (94.21%), Tacna (92.71%), and Huanuco (92.14%). Additionally, Lima's coverage was 82.59% (Fig. 1). This high variability could be explained by social factors (e.g., anti-vaccine groups), limited access to health services, and vaccines' availability. Moreover, it has been described that there are geographical clusters of vulnerable areas of vaccine-preventable diseases [5]. For these reasons, spatial analysis could be crucial to estimate the geographical distribution of DPT-HepB-Hib vaccine coverage. Otherwise, the dropout rate between the first (DPT-HepB-Hib 1) and third (DPT-HepB-Hib 3) doses of the DPT-HepB-Hib vaccine in the last ten has remained above the 5% recommended by the PAHO (Fig. 1). Besides, although DHS does not provide data about booster doses, MINSA reported that coverage of the second booster dose was 59.9% in 2019 (https://www.minsa.gob.pe/reunis/).

The SaTScan spatial analysis identified ten statistically significant clusters of low DPT-HepB-Hib coverage in 2015 and eight in 2019 (Fig. 1). In 2015, the primary cluster was in the southern region of Peru (LLR = 26.44, $p < 0.0001$), whereas in 2019, it was situated in the northeast region (LLR = 37.80, $p < 0.0001$). Furthermore, in 2015, three secondary clusters were placed in the north, three in the center, two in the south, and one in the country's east. Meanwhile, in 2019, five secondary clusters were located in the center, one in the northeast, and one in the south. These areas are vulnerable and at high risk from an epidemic outbreak of diphtheria, tetanus, or pertussis, as well as of poliomyelitis or *Haemophilus influenzae* infection. Surprisingly, one of

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the clusters detected in 2019 was located in Lima (LLR = 12.8, p = 0.0077), where approximately a third of the Peruvian population lives. The recently reported diphtheria outbreak's location coincides with the geographic area of the high-risk cluster located in Lima in 2019.

Vaccines have significantly reduced the burden of many infectious diseases. However, multidisciplinary, and inter-institutional efforts are needed to reduce the pandemic's harmful effects on vaccination coverage. If this outbreak increases, there is a possibility of a syndemic. It is not enough to offer a comprehensive vaccination scheme; it is essential to administer it efficiently. There are regional differences and high-risk clusters for preventable diseases in Peru, which could explain the differences in these diseases' incidence. Lima was at risk even before the pandemic.

Besides, it is worth mentioning that other Latin American countries, such as Venezuela, have recently faced a significant diphtheria re-emergence (among other vaccine-preventable diseases). That has been

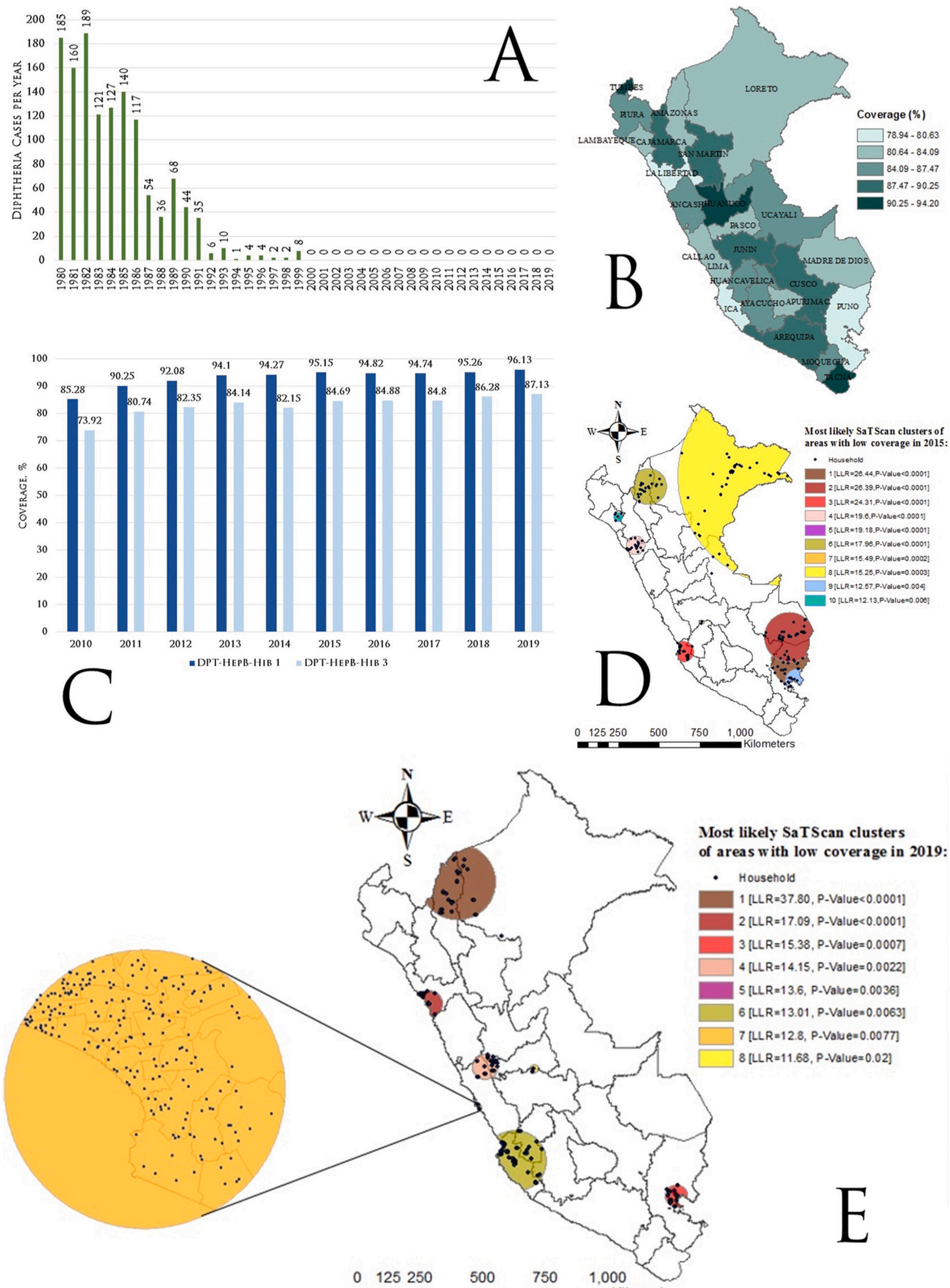


Fig. 1. Epidemiological scenario of the reemergence of diphtheria in Peru. **A.** Reported cases of diphtheria between 1980 and 2019 in Peru. **B.** DPT-HepB-Hib vaccine coverage by regions in Peru, 2019. **C.** DPT-HepB-Hib vaccine dropout rate between 2010 and 2019 in children aged 13–59 months in Peru. **D.** Spatial clustering of areas with low DPT-HepB-Hib vaccine coverage in Peru, 2015. **E.** Spatial clustering of areas with low DPT-HepB-Hib vaccine coverage in Peru, 2019. Maps were plotted with ArcGIS version 10.8 (ESRI, Redlands, CA, United States of America).

associated with a low coverage in the country, where vaccination campaigns have been abandoned due to the crisis and their multiple public health consequences for other nations [6].

Declaration of competing interest

None.

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