Conditional probability and ratio-based approaches for mapping the coverage of multi-dose vaccines

Introduction

Many vaccines are often administered in multiple doses to boost their effectiveness. In the case of childhood vaccines, the coverage maps of the doses and the differences between these often constitute an evidence base to guide investments in improving access to vaccination services and health system performance in low and middle-income countries. A major problem often encountered when mapping the coverage of multi-dose vaccines is the need to ensure that the coverage maps decrease monotonically with successive doses. That is, for doses for doses i and j, $i < j \Rightarrow p_i(\boldsymbol{s}) \geq p_j(\boldsymbol{s})$, where $p_i(\boldsymbol{s})$ is the coverage of dose i at spatial location $\boldsymbol{s}$. In this work, we explore conditional probability and ratio-based approaches for mapping $p_i(\boldsymbol{s})$, embedded within a geostatistical modelling framework, to address this problem.

The proposed methodology

Bayesian binomial geostatistical model

We begin by specifying the base model – a Bayesian binomial geostatistical model. We assumed that $Y(\boldsymbol{s})|p(\boldsymbol{s}) \sim \text{Binomial}\big(m(\boldsymbol{s}), p(\boldsymbol{s})\big)$, where $Y(\boldsymbol{s})$ and $m(\boldsymbol{s})$ are the numbers of children vaccinated and sampled at location $\boldsymbol{s}$,respectively, and $p(\boldsymbol{s})$ is the true vaccination coverage at the location. Further, we specify a logistic regression model for $p(\boldsymbol{s})$ such that

$$\text{logit}\big(p(\boldsymbol{s})\big) = \mathbf{x}(\boldsymbol{s})^T\boldsymbol{\beta} + \omega(\boldsymbol{s}) + \epsilon(\boldsymbol{s}) \qquad (1)$$

where $x(s)$ is a covariate vector, β are regression coefficients, $\omega(\boldsymbol{s})$ is a spatial random effect and $\epsilon(\boldsymbol{s})$ is an iid random effect. We now consider two approaches to enforce the monotonic constraint $p_1(\boldsymbol{s}) \geq p_2(\boldsymbol{s}) \geq p_3(\boldsymbol{s})$ in equation (1) for a three-dose vaccine.

Conditional probability (CP) approach

With this approach, we model the indicators $p_1(\boldsymbol{s}), p_{2|1}(\boldsymbol{s})$ and $p_{3|2}(\boldsymbol{s})$, where, for example, $p_{2|1}(\boldsymbol{s})$ is the probability of receiving the second dose given receipt of the first dose. We will then derive estimates of the remaining indicators by noting that $p_2(\boldsymbol{s}) = p_{2|1}(\boldsymbol{s}) \times p_1(\boldsymbol{s})$ and $p_3(\boldsymbol{s}) = p_{3|2}(\boldsymbol{s}) \times p_2(\boldsymbol{s})$. It can be shown that the monotonic constraint is preserved in this approach since $p_1(\boldsymbol{s}), p_{2|1}(\boldsymbol{s}), p_{3|2}(\boldsymbol{s}) \in [0,1]$. Cluster level sample sizes for the modelled indicators can be obtained easily and these can be expressed as $m(\boldsymbol{s}) \geq m_1(\boldsymbol{s}) \geq m_2(\boldsymbol{s})$.

Ratio-based (RB) approach

In this approach, the modelled indicators are constructed as ratios of successive doses. These are: $p_1(\boldsymbol{s})$, $p_{21}(\boldsymbol{s}) = p_2(\boldsymbol{s}) \times p_1^{-1}(\boldsymbol{s})$ and $p_{32}(\boldsymbol{s}) = p_3(\boldsymbol{s}) \times p_2^{-1}(\boldsymbol{s})$, with $p_1(\boldsymbol{s})$ being the reference indicator. Pseudo binomial counts can be obtained for these modelled indicators, but the cluster sample sizes remain the same for all. This helps solve the sample size problem with the CP approach.

Data

- Georeferenced cluster-level data on the coverage of each of the three doses of diphtheria-tetanus-pertussis vaccine (DTP1-3) were obtained from the 2018 Nigeria Demographic and Health Survey (DHS).
- We also obtained geospatial demographic and covariate data from the survey (through kriging interpolation) and from other sources.

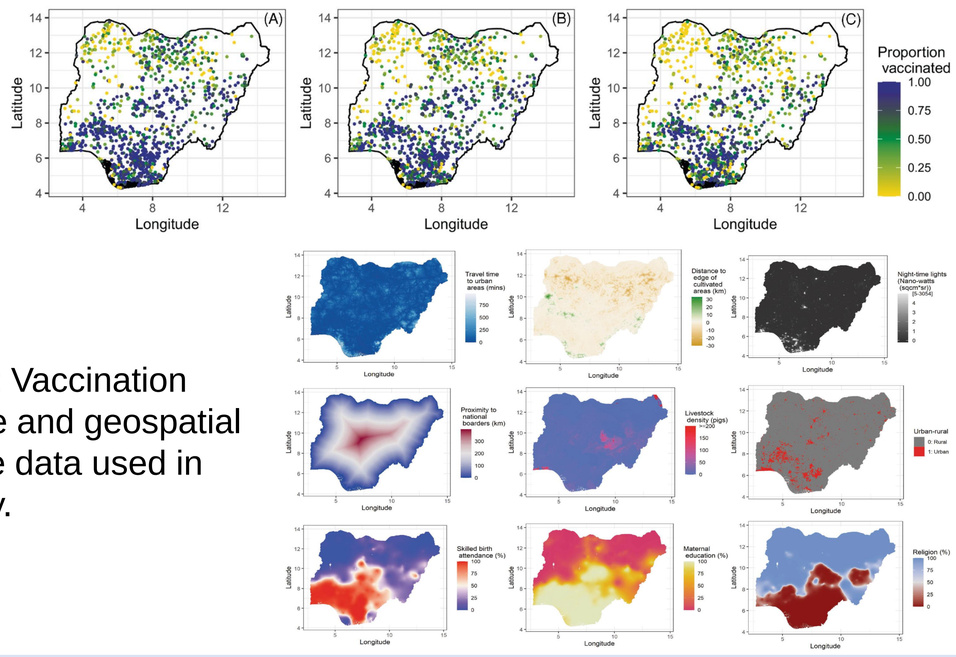


Figure 1: Vaccination coverage and geospatial covariate data used in the study.

Simulation study

We conducted a simulation study to evaluate the effect of varying point/cluster level samples sizes on the predictive performance of the CP and RB approaches. The sample size distribution considered were the discrete uniform distributions given by $U\{2,10\}, U\{2,20\}, U\{2,30\}, \ldots, U\{2,80\}$. Other parameters were held constant in the model. We used the correlation, root mean square error (RMSE), mean absolute error (MAE), average bias and the coverage of the 95% prediction intervals to evaluate predictive performance.

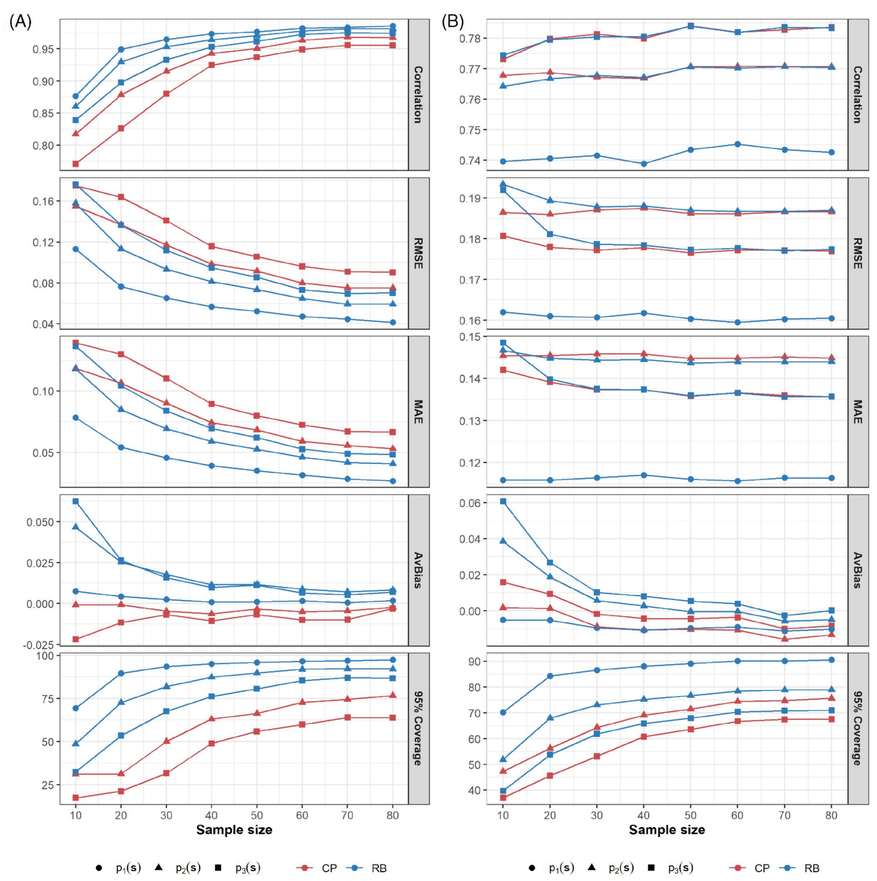
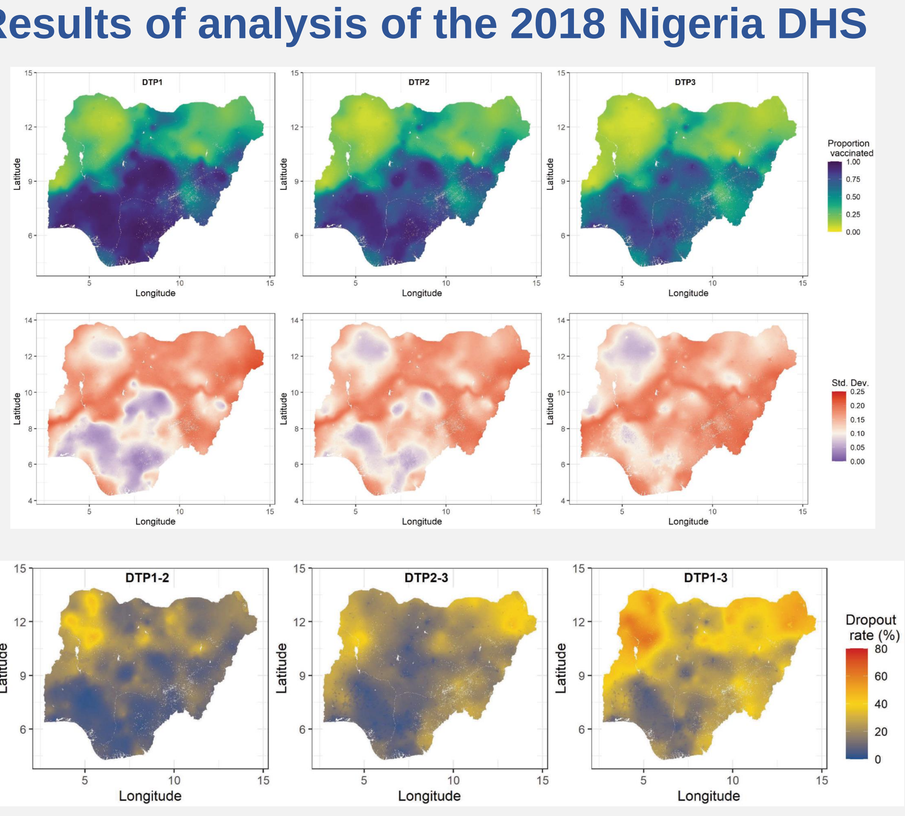


Figure 2: Predictive performance of the conditional probability (CP) and ratio-based (RB) approaches based on different sample size distributions for spatially correlated point level data (A) in-sample prediction of the target indicators (B) out-of-sample prediction of the target indicators over a 5x5 km grid.

Results of analysis of the 2018 Nigeria DHS



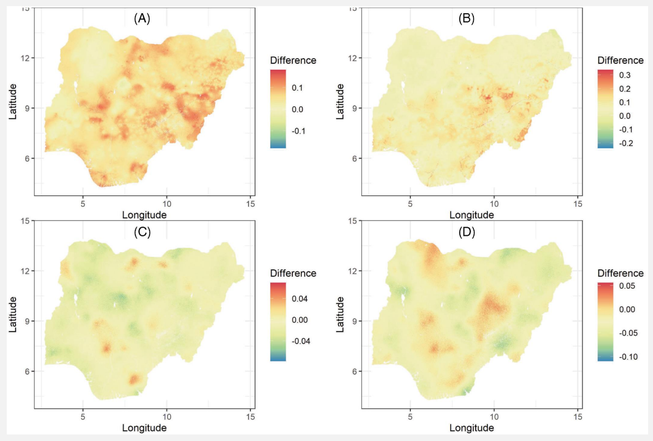


Figure 3: Predicted 1x1 km maps of DTP1-3 coverage using the CP approach; differences between 1x1 km predicted maps of DTP2 (A, C) and DTP3 (B, D) obtained through using the CP and RB approaches when covariates were included (A, B) and excluded (C, D) from the fitted models; and dropout rates between the doses.

Summary and conclusions

- Both proposed approaches are flexible in terms of using either the first or the last dose in the vaccination series as the reference indicator (this is usually more robustly estimated).
- The RB approach is not subject to cluster level sample size restrictions.
- Increasing point-level sample sizes had marked positive impact on in-sample prediction using both approaches; however, no approach was consistently the better approach for out-of-sample prediction. The increase in point-level sample sizes mainly led to decreases in bias and improvements in uncertainty estimation.
- Our work adds to the growing body of methodology for producing maps of vaccination coverage and can be easily applied to other multi-dose vaccines, e.g. PCV1-3.

Reference: Utazi CE, Aheto JMK, Chan HMT, Tatem AJ, Sahu SK. Conditional probability and ratio-based approaches for mapping the coverage of multi-dose vaccines. Statistics in Medicine. 2022; 41(29): 5662-5678. doi:10.1002/sim.9586.