Assessing the characteristics of un- and under-vaccinated children in low- and middle-income countries: A multi-level cross-sectional study

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(and other colleagues)

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WorldPop

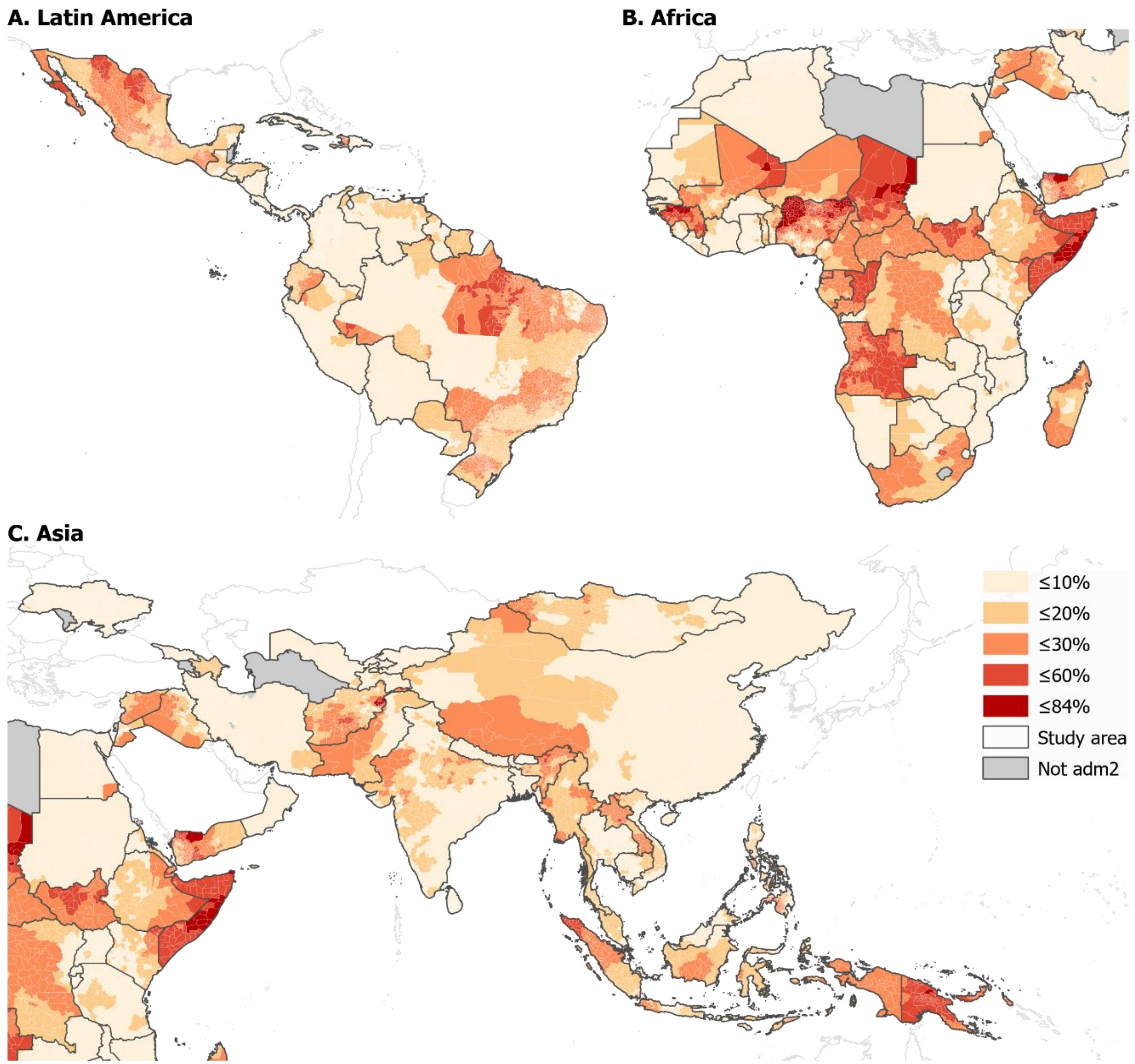
University of Southampton

Gavi
The Vaccine Alliance

Bill & Melinda Gates foundation

Introduction

- Immunization is a public health success story, but increasing the coverage of routine immunization to reach the last 20% of children in LMICs has been a challenge
- Persistence of geographical (and other forms of) inequities in coverage undermines disease control, elimination and eradication efforts
- There is currently a high level of interest in the development of strategies and interventions that target populations at risk of non-vaccination (zero dose) and under-vaccination
- Efforts geared towards achieving the SDGs, WHO's Immunization Agenda 2030 and Gavi Strategy 5.0



Proportion of under 1s estimated to have not received the first dose of the DTP vaccine in 2019 at ADM2 (Wigley et al, 2022)

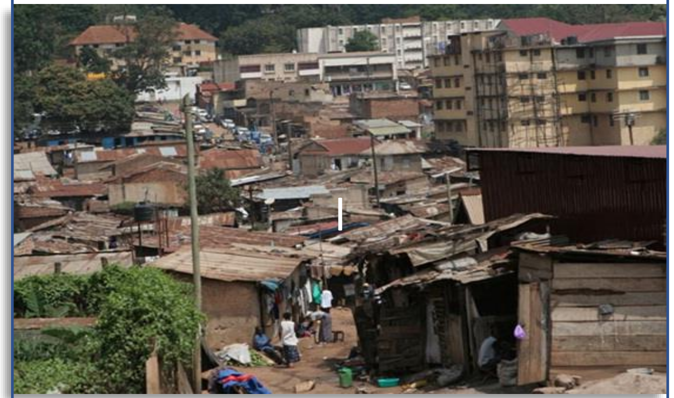
Introduction

- Communities at risk of non- and under-vaccination are often characterized by poverty, lack of access to health care and other basic services, civil/political unrest, poor sanitation practices, overcrowding, etc

- In 2017, the Equity Reference Group (ERG) for immunization identified these to be remote-rural, urban slums and conflict-affected areas

Remote-rural

Urban slums



Conflict areas

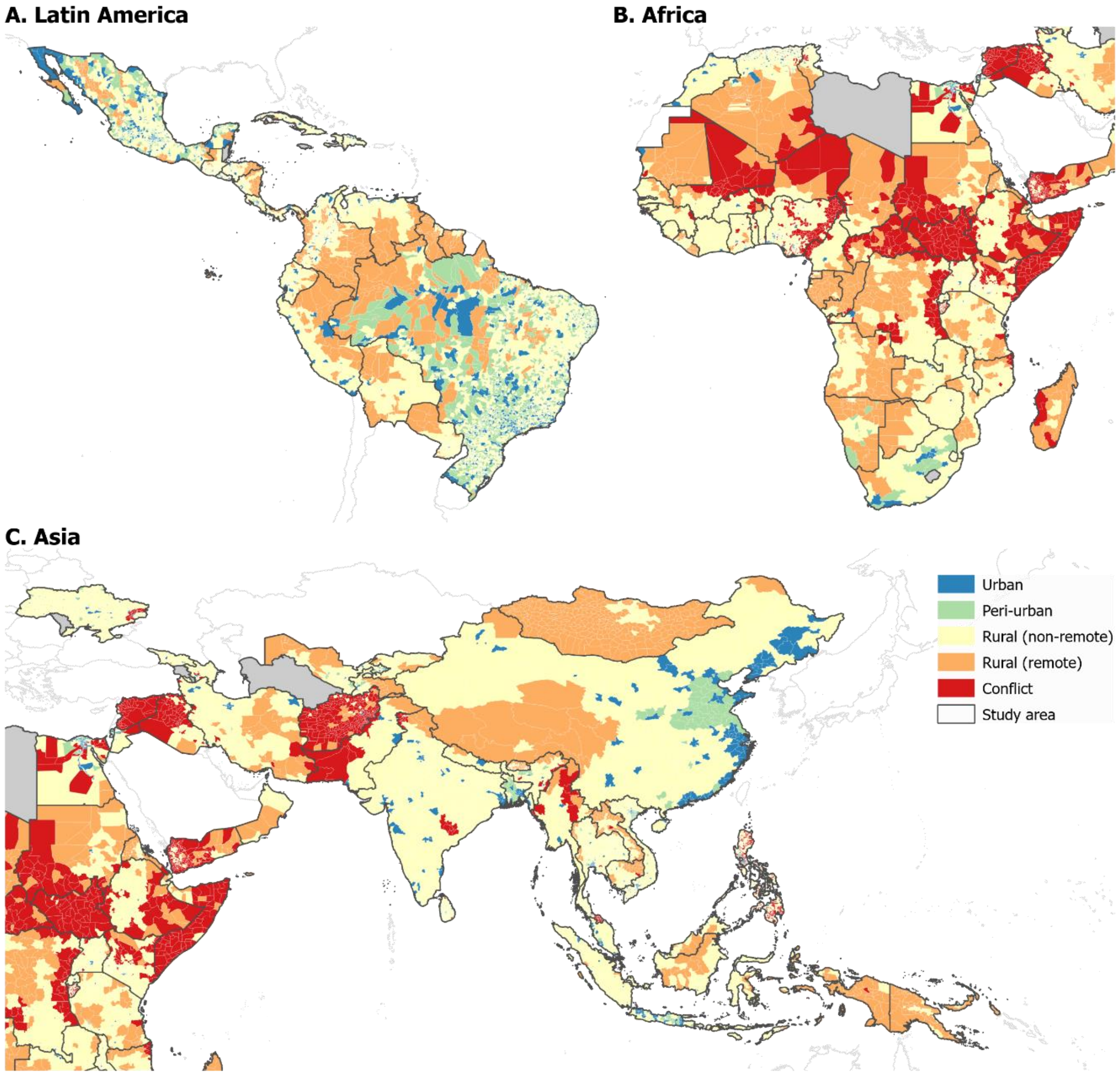
Introduction

- To target these at risk groups effectively, robust and current evidence on their population sizes, geographic distribution, immunisation levels, and other characteristics is needed

- A global scale work undertaken by WorldPop seeks to address this need

- Goal of current analysis:

"to investigate and quantify the relationships between non- and under-vaccination and key community variables–remoteness, conflict and urban slum—both when and when not controlling for other factors in nine LMICs"



Geographical setting with the most unvaccinated under 1s in 2019 at ADM2

Outcome variables for non- and under-vaccination

DTP1 Receipt of the first dose of diphtheria-tetanus-pertussis vaccine, determined through a vaccination card or caregiver recall

DTP3 Receipt of the third dose of diphtheria-tetanus-pertussis vaccine, determined through a vaccination card or caregiver recall

MCV1 Receipt of the first dose of measles-containing vaccine, determined through a vaccination card or caregiver recall

Age group: children aged 12 – 23 months

Study countries: Cambodia, DRC, Ethiopia, India, Madagascar, Mozambique, Nigeria, Pakistan, Zambia

Covariates

Non- and under-vaccination – Non-receipt of DTP1/MCV1/DTP3

Individual

Demographic
- Sex of child
- Birth quarter
- Birth order

Health
- Skilled birth attendance (SBA)
- Mother's tetanus toxoid (TT) vaccination status
- Antenatal care attendance (ANC)
- Post-natal baby care (PNC)

Household

Demographic
- Sex of head of household
- Maternal age
- Maternal marital status
- Household size
- Religion
- Ethnicity

Health
- Problem seeking medical advice/treatment
- Household owned a mosquito bednet or mother had knowledge of malaria
- Mother had health insurance

Socioeconomic
- Maternal education
- Maternal employment status or occupation
- Household wealth index
- Mother owned land
- Mother owned a bank account

Communication
- Media exposure (radio/TV/newspaper)
- Use of mobile phone and/or internet

Geographic
- Length of stay in place of residence

Cluster/Community

Geographic
- Region
- Urban/rural residence

- Travel time
- Conflict
- Urban slum

Key community variables

- Others covariates excluded due to missing data – women's participation in decision-making, birth interval and malnutrition (stunting, wasting and underweight)

Data sources

Outcome variables and covariates

Country	DHS year
Cambodia	2014
DRC	2013-14
Ethiopia	2016
India	2015-16
Madagascar	2008-09
Mozambique	2011
Nigeria	2018
Pakistan	2017-18
Zambia	2018

Key community variables

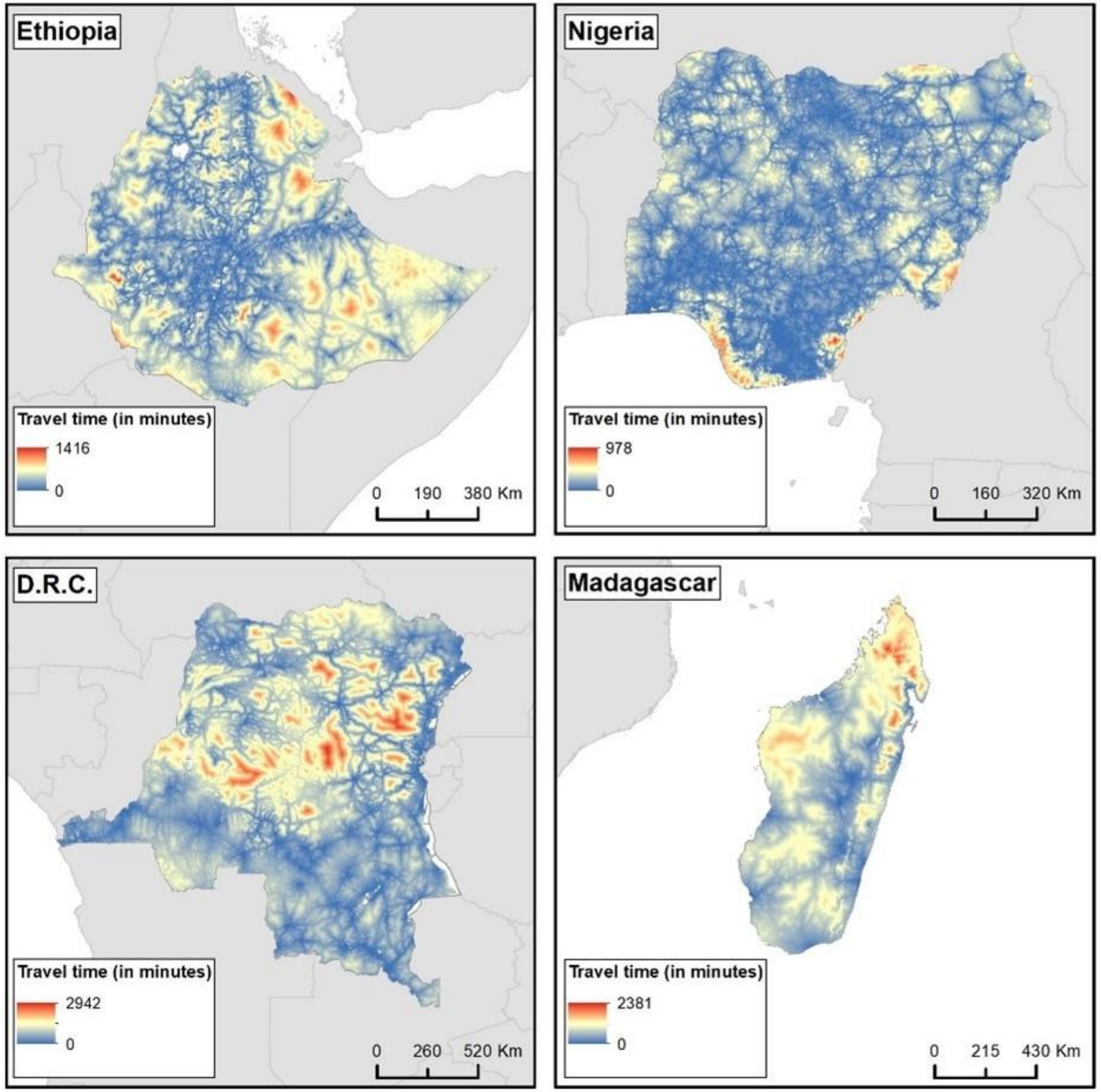
- Conflict: Geospatial data on conflict sourced from ACLED https://acleddata.com/
- Remoteness: Geospatial data on travel time sourced from MAP https://malariaatlas.org/research-project/accessibility_to_cities/
- Urban slums: Created using information from DHS data

Data – Remoteness

- Data on travel time to populated areas with at least 50, 000 people were obtained at 1x1 km resolution

- Data were processed for each DHS cluster location using standard approaches[1]

- Extracted data classified into three classes (lower, medium and higher) for each country based on the tertiles of their distributions



[1]Utazi et al (2018). High resolution age-structured mapping of childhood vaccination coverage in low and middle income countries. Vaccine 36(12):1583-1591.

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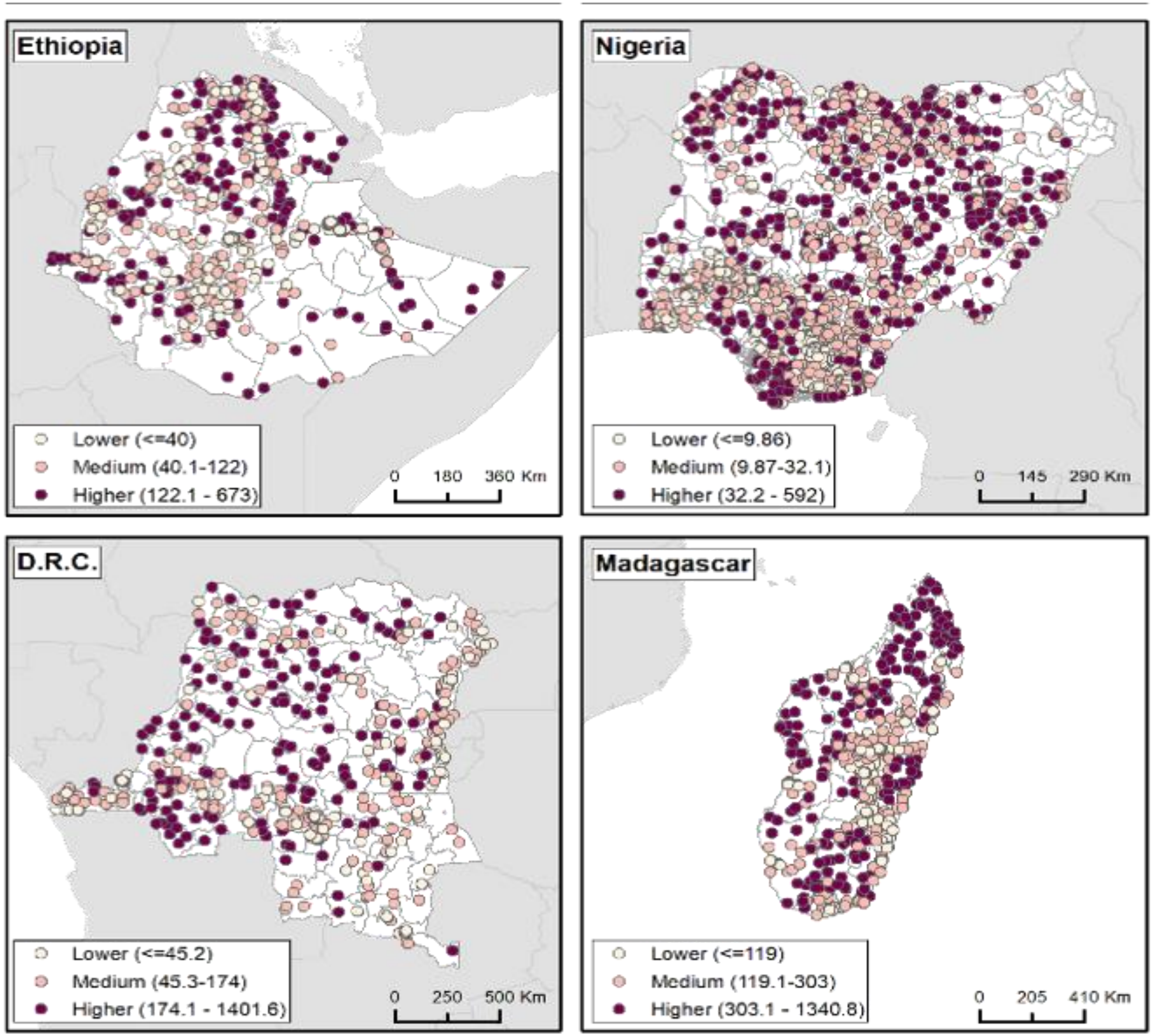

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Data – Conflict areas and urban slums

Defining conflict-affected areas

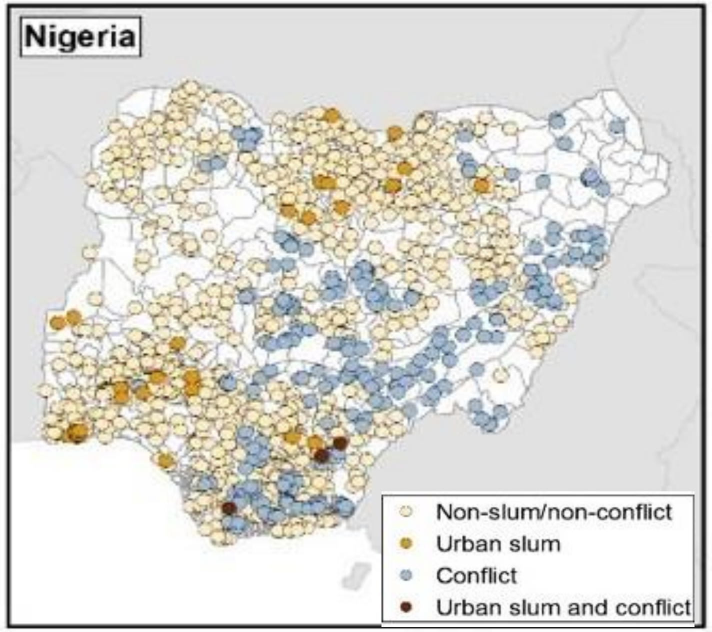
- Conflicts resulting in violent deaths (battles, explosions/remote violence, and violence against citizens) within the 2 years prior to the year of each DHS were considered

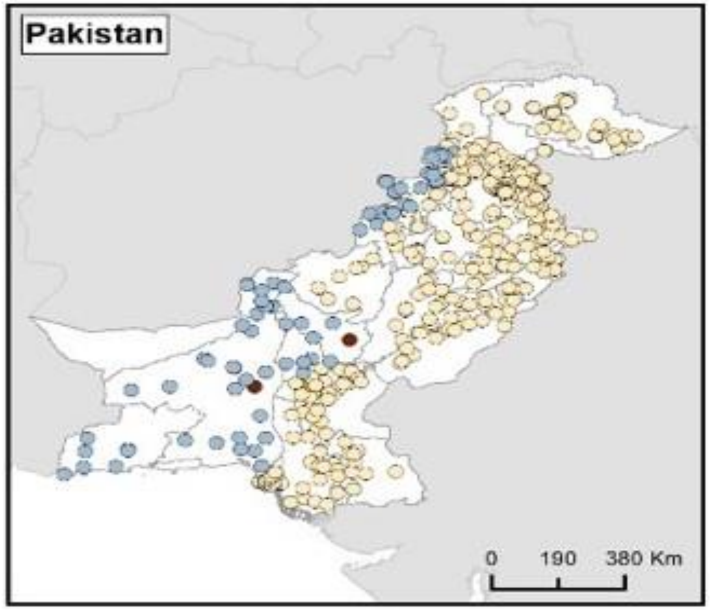
- Conflict data were aggregated to the 2nd admin level in each country

- Conflict areas were identified as areas that had ≥ 30 deaths per 1 million pop.[1] due to conflict

- Clusters falling within the admin areas were classified accordingly

[1]A narrower definition used in sensitivity analysis considered 300 deaths per 1 mil. Pop.





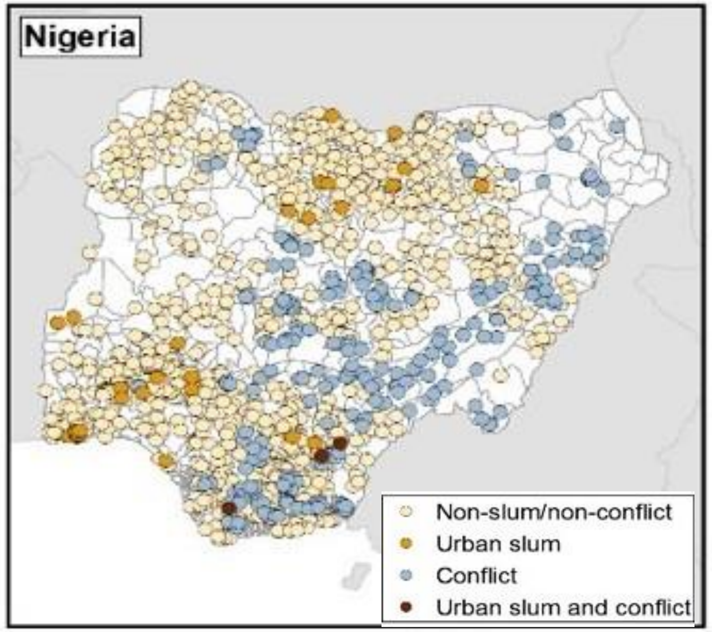
Data – Conflict areas and urban slums

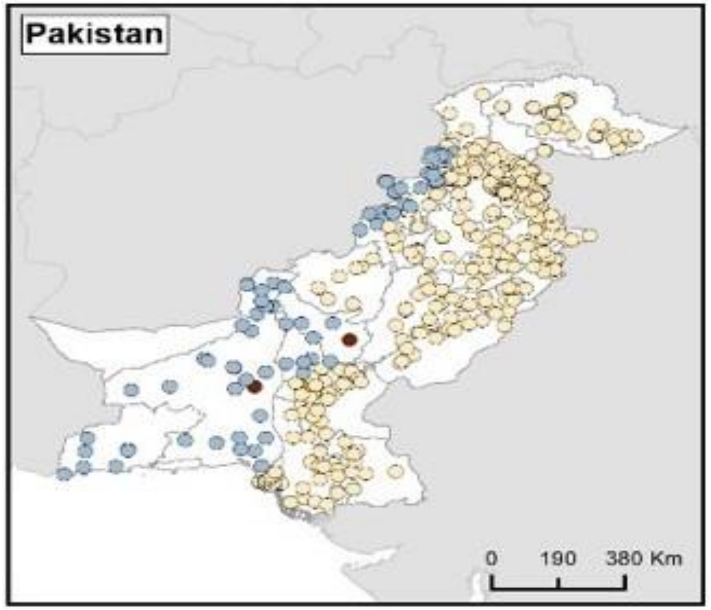
Defining urban slums

- DHS clusters were classified as urban slum areas using the UN-Habitat definition

- Households within the clusters were first classified as slum dwellings if they had any two of lack of access to clean water, improved sanitation and durability of housing, and overcrowding

- Urban clusters were classified as slums if ≥ 75% of their households were slum dwellings





Data – Coding of outcome and categorical variables

Outcome	Type	Original coding	Recoded values
(Received) DTP1	Binary	no don’t know reported by mother vaccination date on card vaccination marked on card	no/don’t know - 0 reported by mother - 1 vaccination date on card - 1 vaccination marked on card - 1
DTP3	Binary	no don’t know reported by mother vaccination date on card vaccination marked on card	no/don’t know - 0 reported by mother - 1 vaccination date on card - 1 vaccination marked on card - 1
MCV1	Binary	no don’t know reported by mother vaccination date on card vaccination marked on card	no/don’t know - 0 reported by mother - 1 vaccination date on card - 1 vaccination marked on card - 1

Data – Coding of outcome and categorical variables

- For the covariates, wherever possible, reference categories were mostly the categories with the least likelihood of vaccination

Example: Individual level covariates (coding)

- Sex of child (male – 0, female – 1)
- Birth order (ref. 1-2, 3-5, >5)
- Skilled birth attendance (SBA) (none - 0, yes - 1)
- Mother's antenatal care (ANC) visits during pregnancy (none/don't know – 0, 1 - 3 – 1, 4 or more – 2)
- Birth quarter (Jan – Mar – 0, Apr – June – 1, July – Sep – 2, Oct – Dec – 3)
- Mother's receipt of Tetanus Toxoid (TT) vaccination before birth (none/don't know – 0, 1 – 2 – 1, 3 – 4 – 2, 5 or more – 3)
- Post-natal check (PNC) of baby within 2 months after birth (no/don't know – 0, yes - 1)

Demographic; Health-related

Pre-modelling steps and variable inclusion/exclusion criteria

I. Data extraction, coding and recoding

II. Calculation of frequencies and percentages

III. Calculation of the proportion of missing data in each covariate and exclusion of covariates with >5% missing data

IV. Frequentist bivariate and multivariate analysis to identify and resolve (multi)collinearity (i.e. change in direction of estimated relationship or high generalized variance inflation factor)

V. Repeat steps I – IV where necessary, e.g. when original reference group has a very small frequency

Modelling framework – bivariate analysis

- Run independently for each country and vaccine-dose combination

- **Simple binary logistic regression model**
  - y_i - binary response (vaccinated or not) for the ith child
  - p_i - true probability of vaccination for the ith child
  - n - sample size
  - x_i - covariate value for the ith child

$$\boxed{\begin{aligned} y_i &\sim \text{Binomial}(1, p_i), i = 1, \dots, n \\ \log\left(\frac{p_i}{1-p_i}\right) &= \beta_0 + \beta_1 x_i \end{aligned}}$$

- Model fitted in a frequentist framework

- Crude odds ratio and 95% CI calculated

Modelling framework – multivariate analysis

- Run independently for each country and vaccine-dose combination

- **Bayesian multi-level logistic regression model**
  - y_{ijkl} - binary response (vaccinated or not) for the ith child, household j, cluster/community k and stratum l
  - p_{ijkl} - the corresponding true probability of vaccination

$$y_{ijkl} \sim \text{Binomial}(1, p_{ijkl}), i = 1, \ldots, n_{jkl}, j = 1, \ldots, n_{kl}, k = 1, \ldots, n_l, l = 1, \ldots, L,$$

$$\log\left(\frac{p_{ijkl}}{1-p_{ijkl}}\right) = \beta_0 + \sum_{p=1}^{r_1} \beta_p^{child} x_{pijkl} + \sum_{p=1}^{r_2} \beta_p^{house} x_{pjkl} + \sum_{p=1}^{r_3} \beta_p^{com} x_{pkl} + \delta_{jkl}^{house} + \delta_{kl}^{com} + \delta_l^{strat},$$

$$\delta_{jkl}^{house} \sim N(0, \sigma_{house}^2), \quad \delta_{kl}^{com} \sim N(0, \sigma_{com}^2), \quad \delta_l^{strat} \sim N(0, \sigma_{strat}^2).$$

- Non-informative $N(0, 10^{-3})$ prior on the fixed effects and informative $\text{Gamma}(0.1,0.1)$ prior on the precisions of random effects

Modelling framework – multivariate analysis

- Why Bayesian?
  - Flexibility in accounting for sampling design (could use sampling weights or the design variables)
  - More robust estimation of parameters of the random effects through the use of appropriate prior distributions

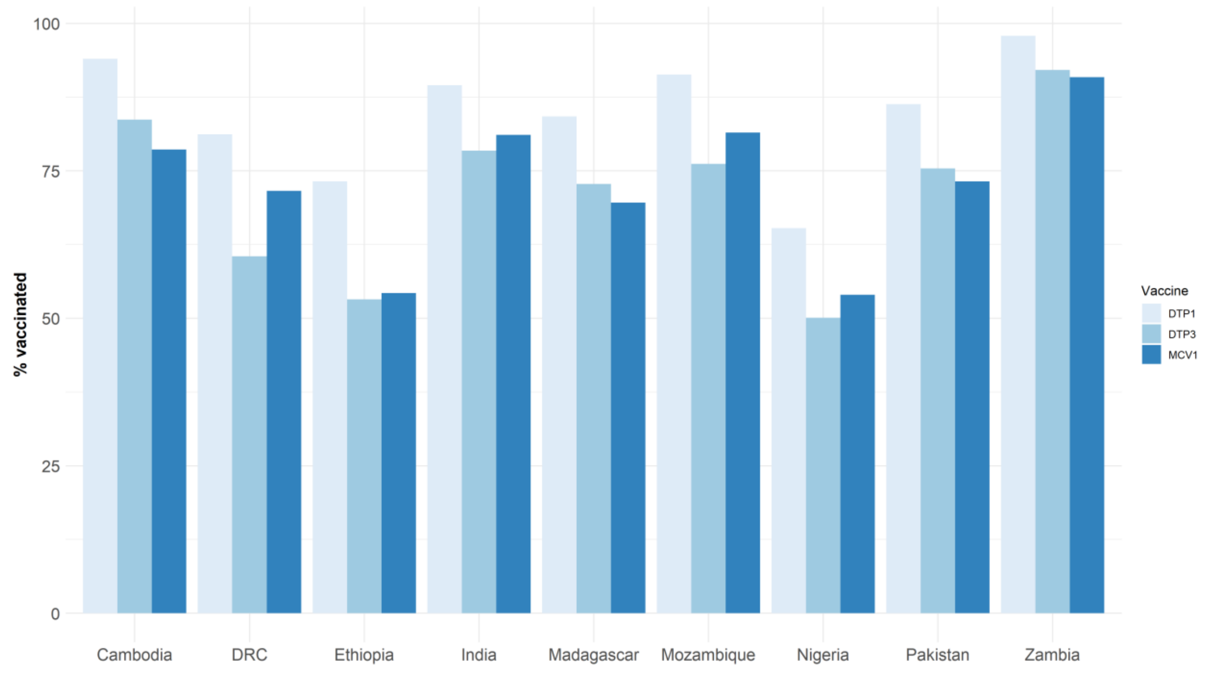
- Model fitted using R-INLA and adjusted odds ratios and 95% CI calculated

- Model validation
  - *Percentage change in total residual variation* (PCV) used to assess contribution of zero-dose/community variables
  - *Variance partition coefficient* (VPC) used to evaluate proportion of variation accounted for by various hierarchies in the model
  - Model discriminatory ability evaluated using the *area under the curve* (AUC) scores

Results – Sample characteristics

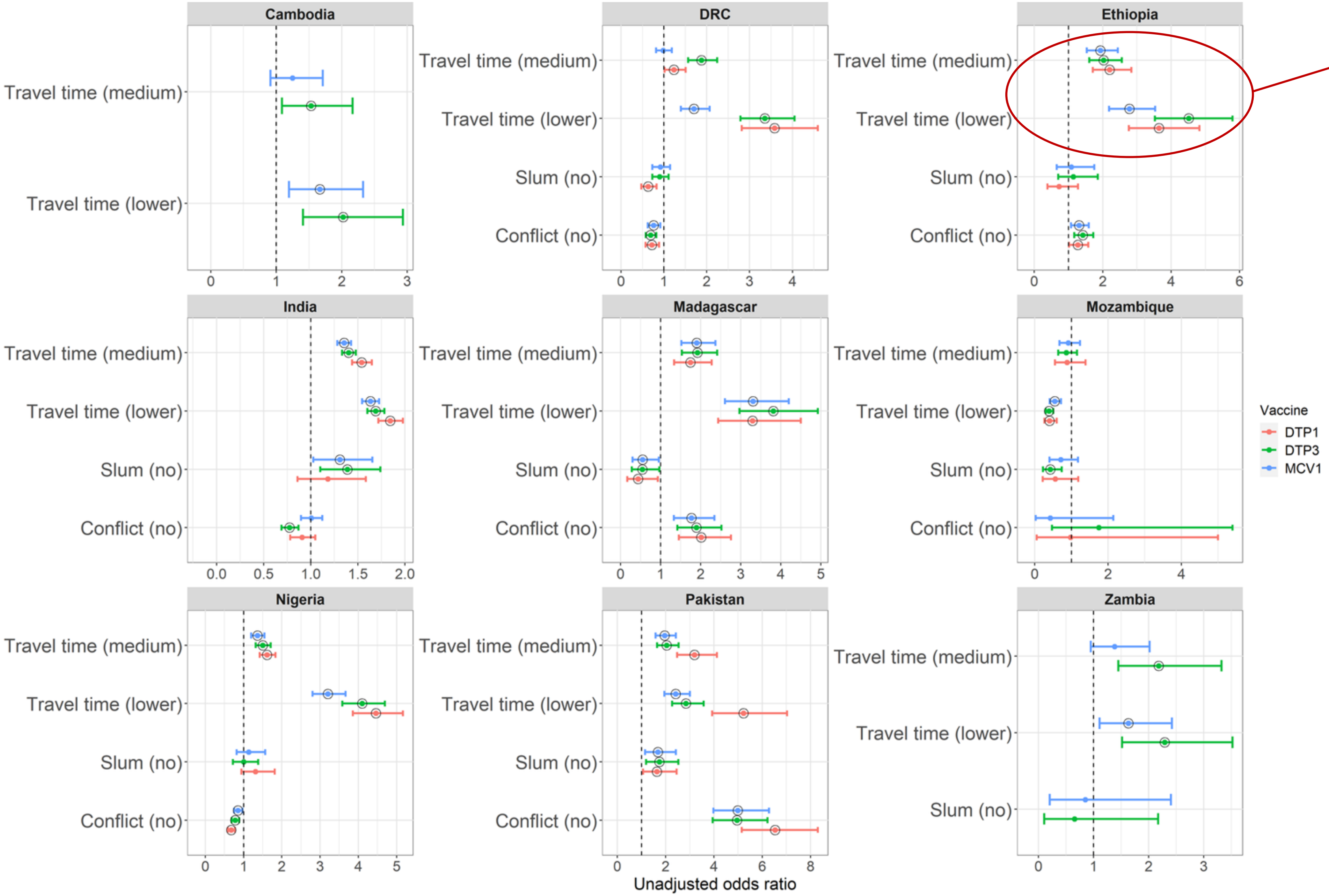
Country	Sample size 12-23 m (unweighted)	No of complete cases	No of DHS variables analyzed
Nigeria	6036	5704	24*
Zambia	1897	1818	23
DRC	3182	2948	24
Ethiopia	1868	1757	22
Cambodia	1441	1377	21
India	49056	46130	20
Pakistan	2312	2035	21
Mozambique	2221	2110	20
Madagascar	2145	2039	20

Distribution of coverage by country and vaccine**



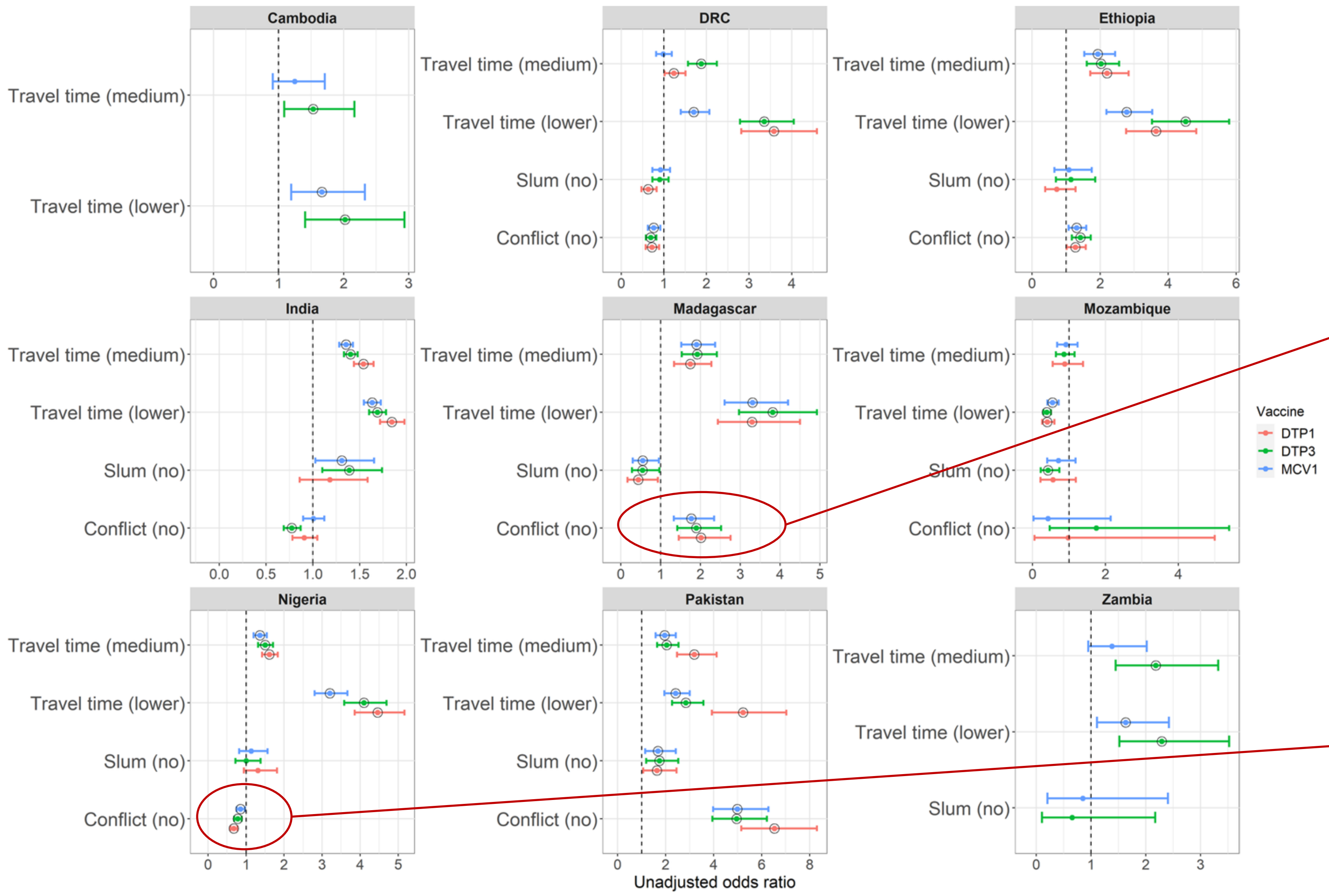
*Varies between countries due to missing data or variation in the questionnaires used in the DHS surveys.
**DTP1 not considered in the analysis for Cambodia and Zambia due to sample size limitations.

Results – Bivariate analysis



Remoteness significantly increased the odds of non- and under-vaccination in all the countries, except Mozambique

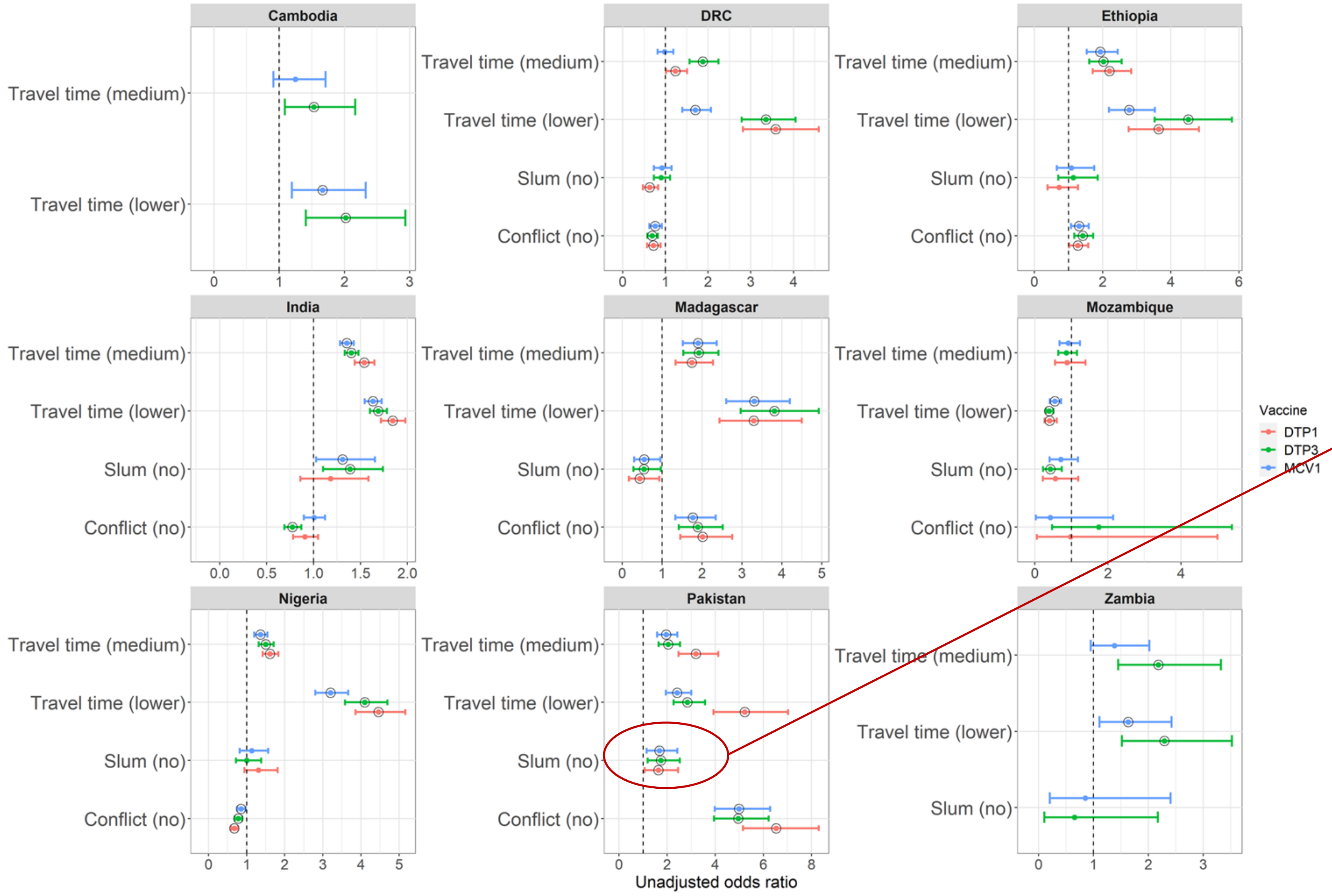
Results – Bivariate analysis



Living in a conflict-affected area significantly increased the odds of non- and under-vaccination in Ethiopia, Madagascar, Pakistan and India (DTP3)

In contrast to this result, “narrow” conflict definition revealed that conflict increased the odds of non- and under-vaccination in Nigeria.

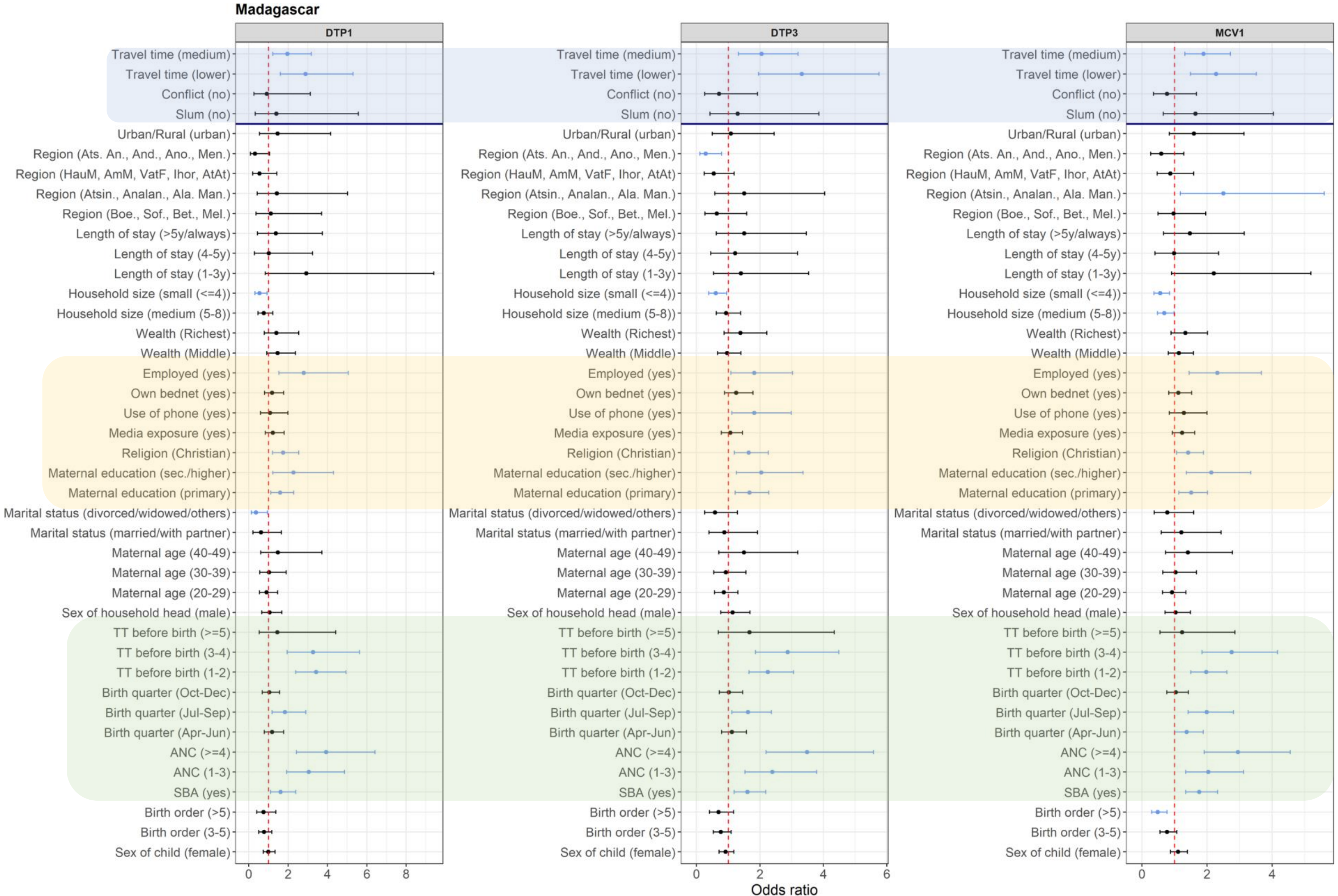
Results – Bivariate analysis



Living in an urban slum significantly increased the odds of non- and under-vaccination in Pakistan and India (DTP3) *only**

*Sensitivity analysis however showed that living in a slum area, compared to a formal urban area, increased the odds of non- and under-vaccination in many cases.

Results – Multivariate analysis



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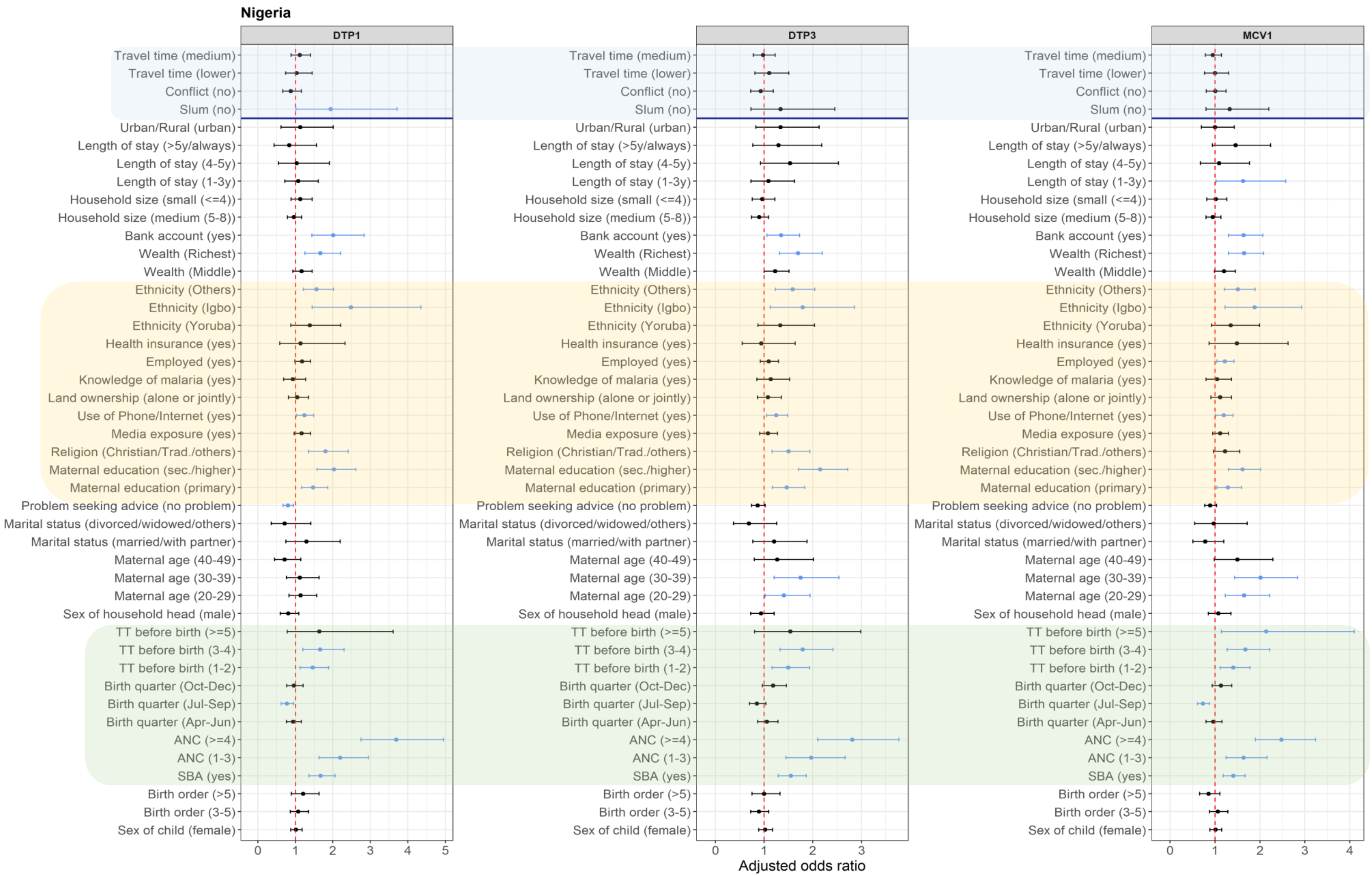

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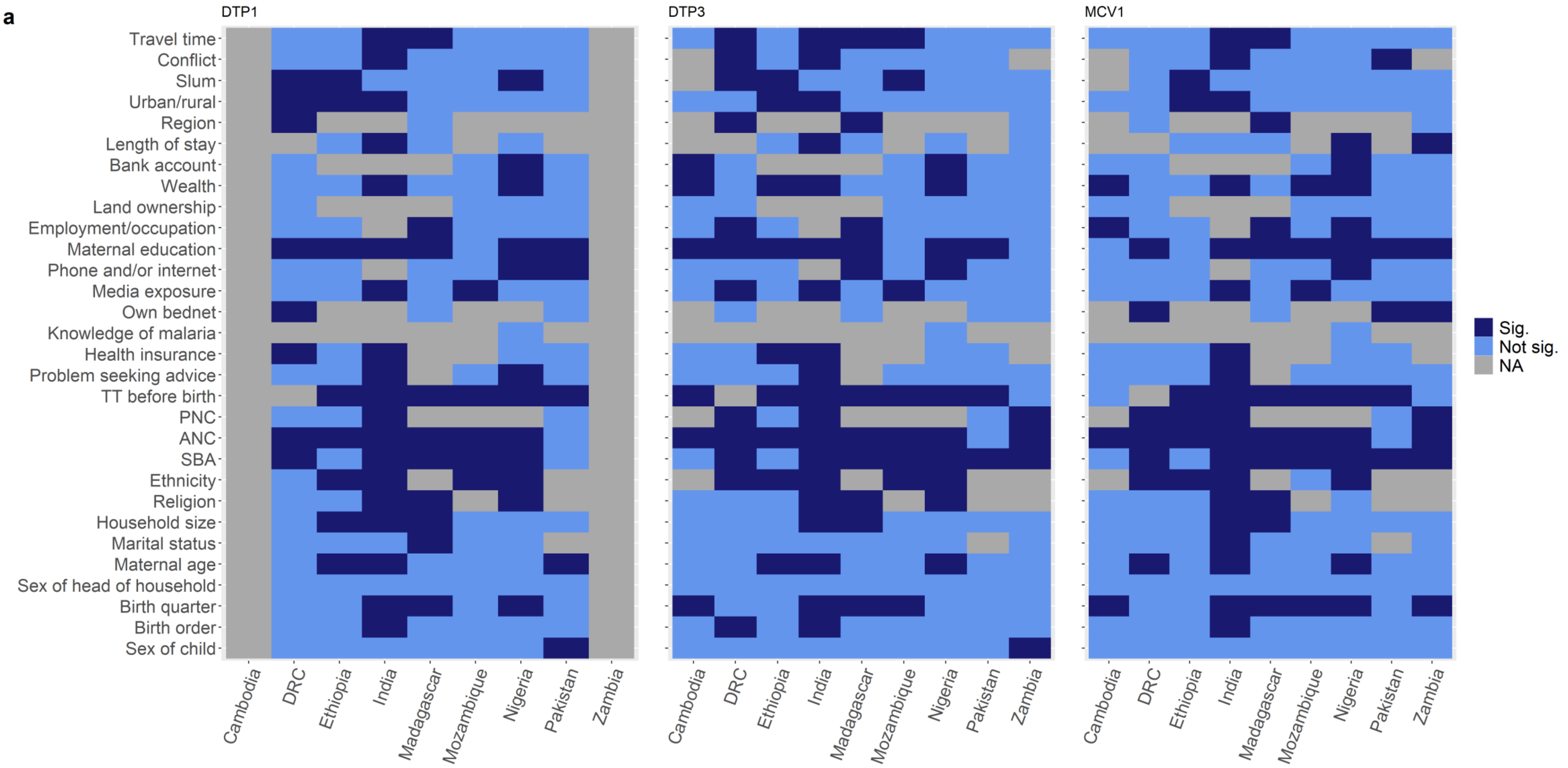

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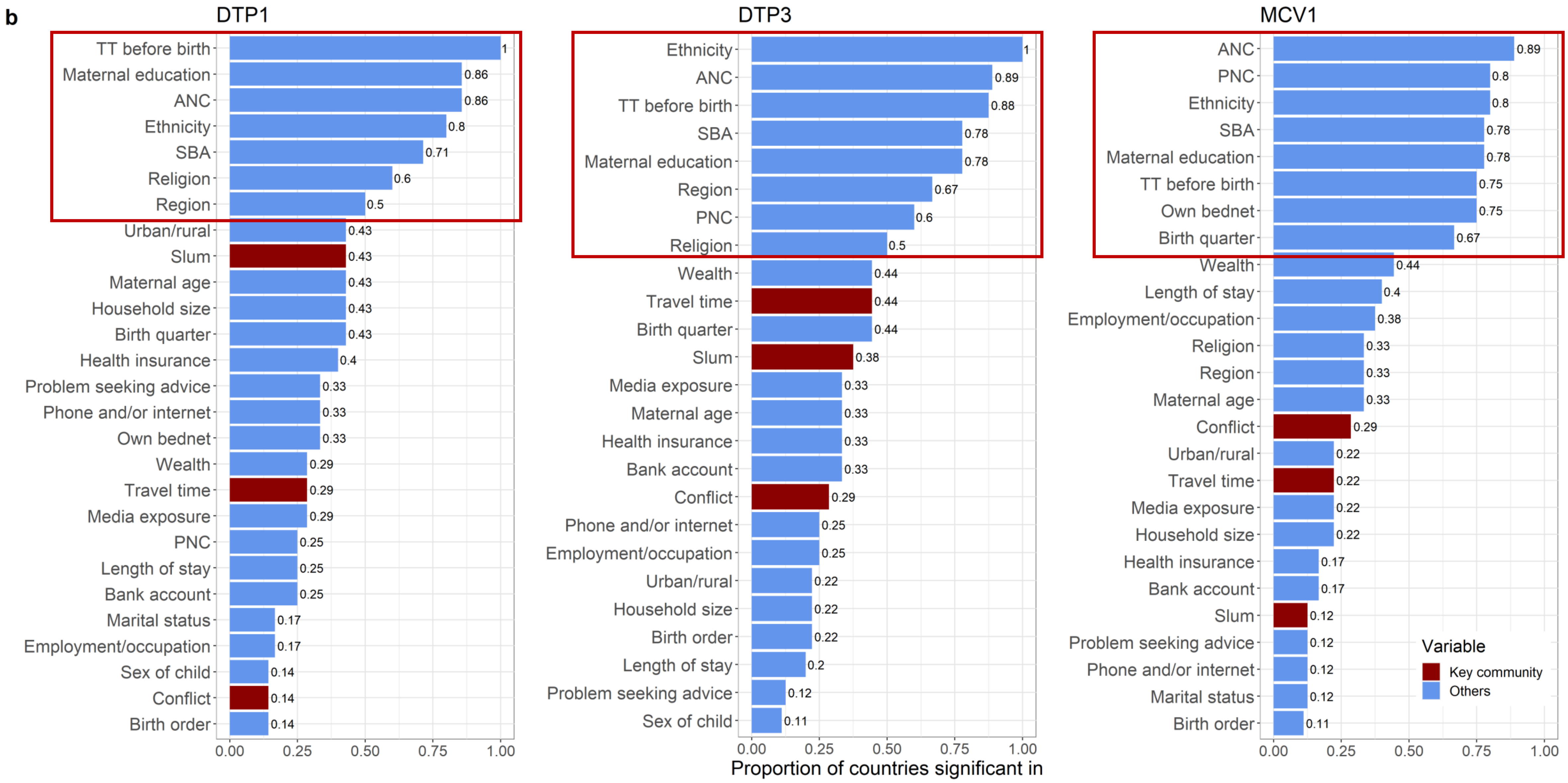

Summary and conclusions

- We found evidence that remoteness and living in urban slums and conflict-affected areas increased the odds of non- and under-vaccination in bivariate analysis. This evidence was strongest for remoteness.

- In multivariate analysis, these key community variables were sometimes associated with non- and under-vaccination, but they were not frequently predictors of these outcomes as expected.

- Several gender-related factors, including maternal utilization of health services, maternal education and ethnicity were more common predictors of non- and under-vaccination

- Country-specific strategies and integrated delivery approaches are needed to address barriers to immunization

- Study limitations include: potential underrepresentation of urban slums and conflict-affected areas in DHS surveys and difficulty in defining conflict-affected areas

Further information

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RESEARCH ARTICLE

Assessing the characteristics of un- and under-vaccinated children in low- and middle-income countries: A multi-level cross-sectional study

C. Edson Utazi, Oliver Pannell, Justice M. K. Aheto, Adelle Wigley, Natalia Tejedor-Garavito, Josh Wunderlich, Brittany Hagedorn, Dan Hogan, Andrew J. Tatem

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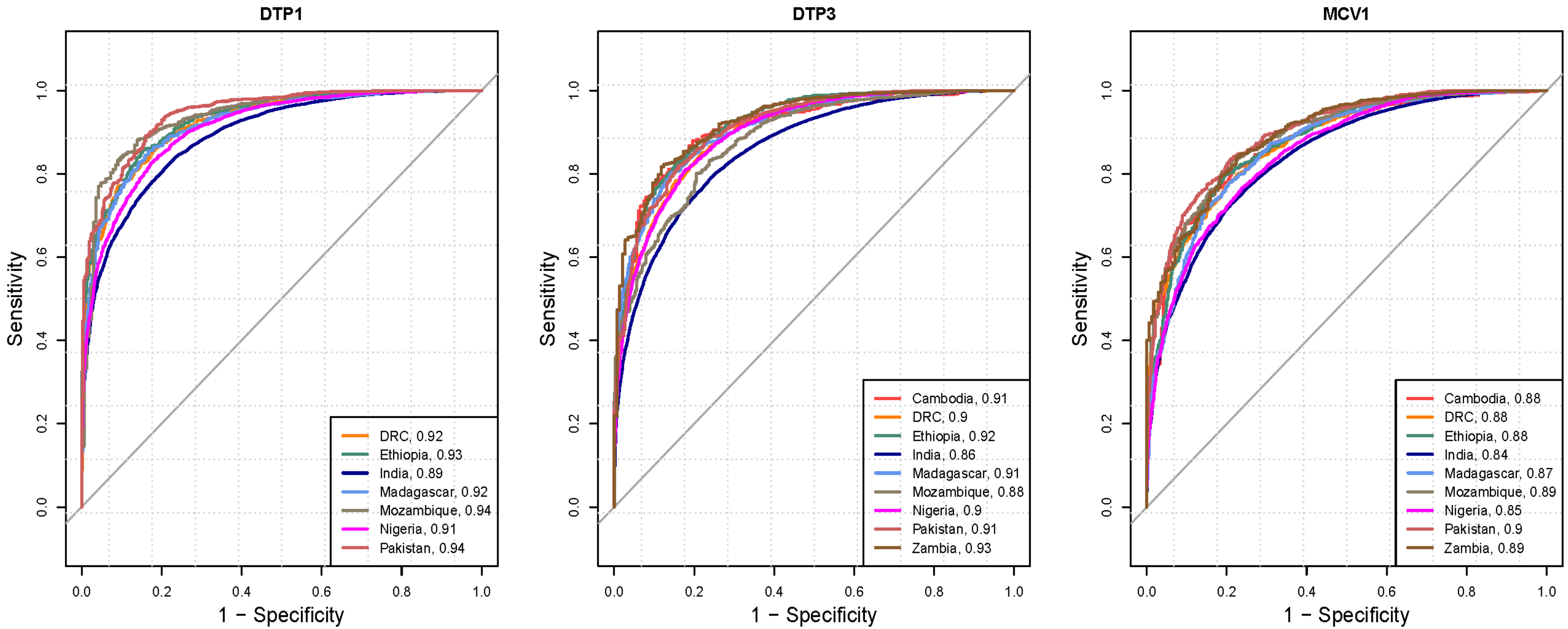
Additional results – model validation



AUC scores range between 0.84 and 0.94 for all the country-vaccine combinations, showing that all the fitted models had good discriminatory power.