Using a multi-species epidemiological model to assess optimal FMD vaccine allocations across India

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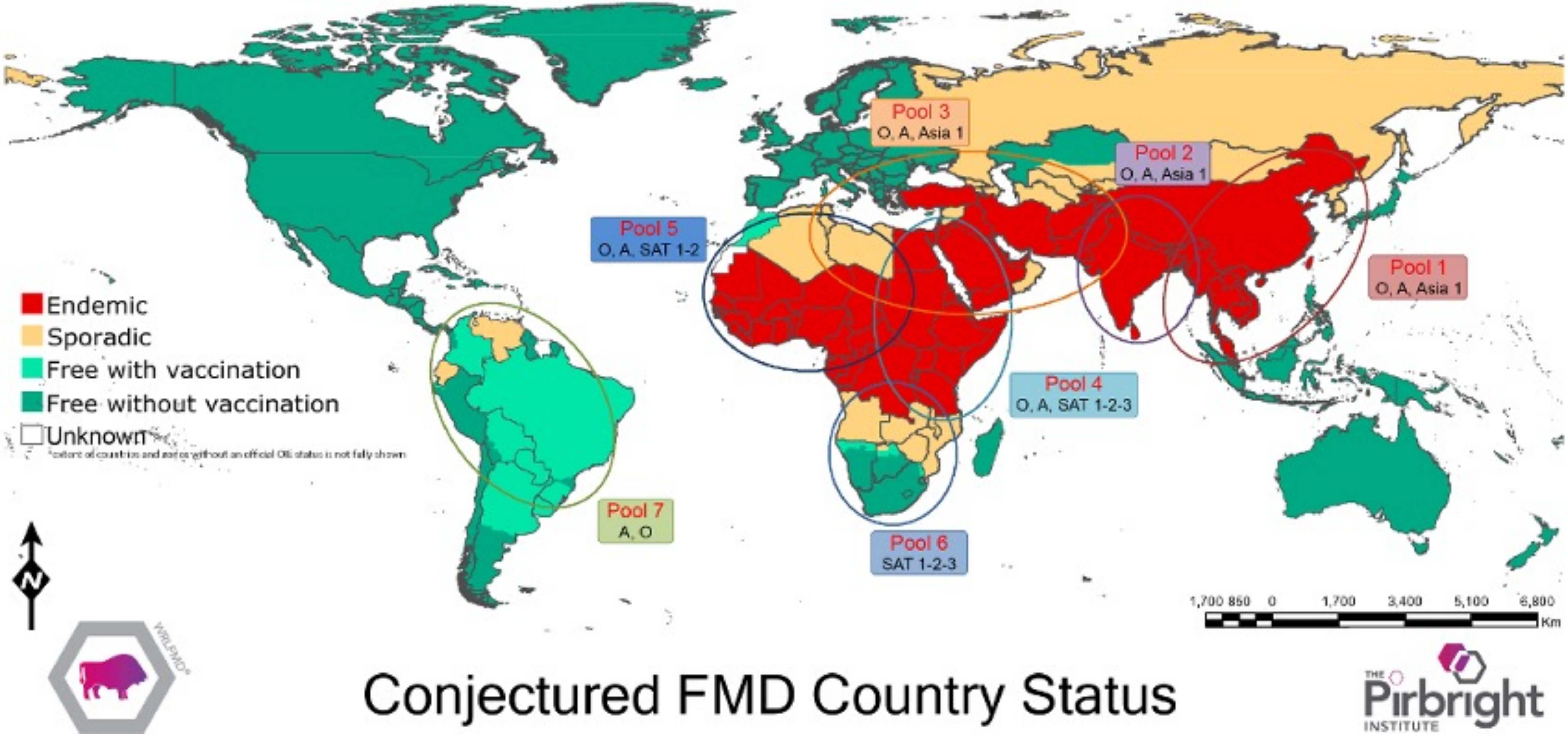
FMD and India

Foot-and-Mouth Disease

- Infectious viral disease of livestock
- Primarily affects cloven-hoofed animals
  - Cattle, buffalo, pigs, sheep, etc.
- Primary symptoms
  - Lesions around mouth and feet
  - Fever
  - Lameness
  - Milk drop
- Low mortality
  - But higher mortality in younger animals
  - Morbidity varies by species



Conjectured FMD Country Status

Source: www.wrlfmd.org

STAGE 0

FMD risk not controlled. No reliable information

STAGE 1

Identify risk and control options

STAGE 2

Implement risk-based control

STAGE 3

Implement control strategy to eliminate circulation

STAGE 4

Maintain zero circulation & incursions

STAGE 5

Maintain zero circulation & incursions; withdraw vaccination

Free without vaccination

FROM 0 to 1
Comprehensive study of FMD epidemiology planned

FROM 1 to 2
Risk-based FMD control plan

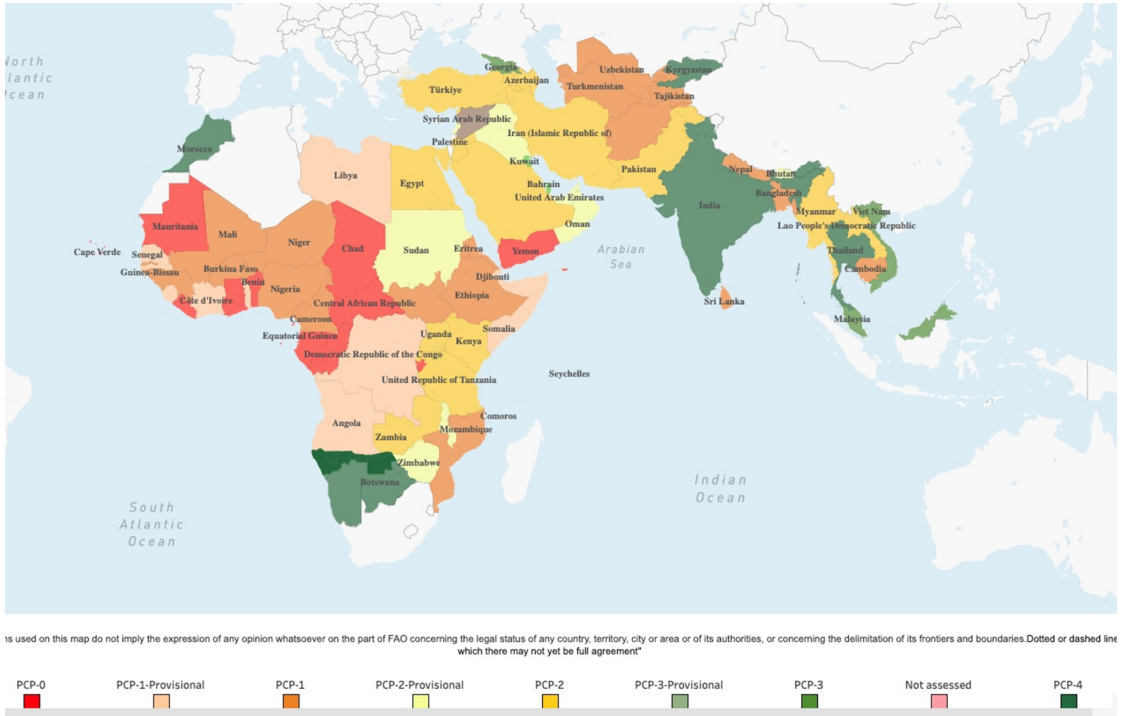
FROM 2 to 3
Develop aggressive strategy to eliminate FMD

FROM 3 to 4
No endemic FMD in domestic livestock

FROM 4 to 5
Apply for official status (OIE): 'free WITH vaccination'

Apply for official status (OIE): 'free WITHOUT vaccination'

MOVING UPWARDS REQUIRES EVIDENCE IN THE FORM OF PLANS TO UNDERTAKE ACTIONS PLUS EVIDENCE THESE HAVE COMMENCED



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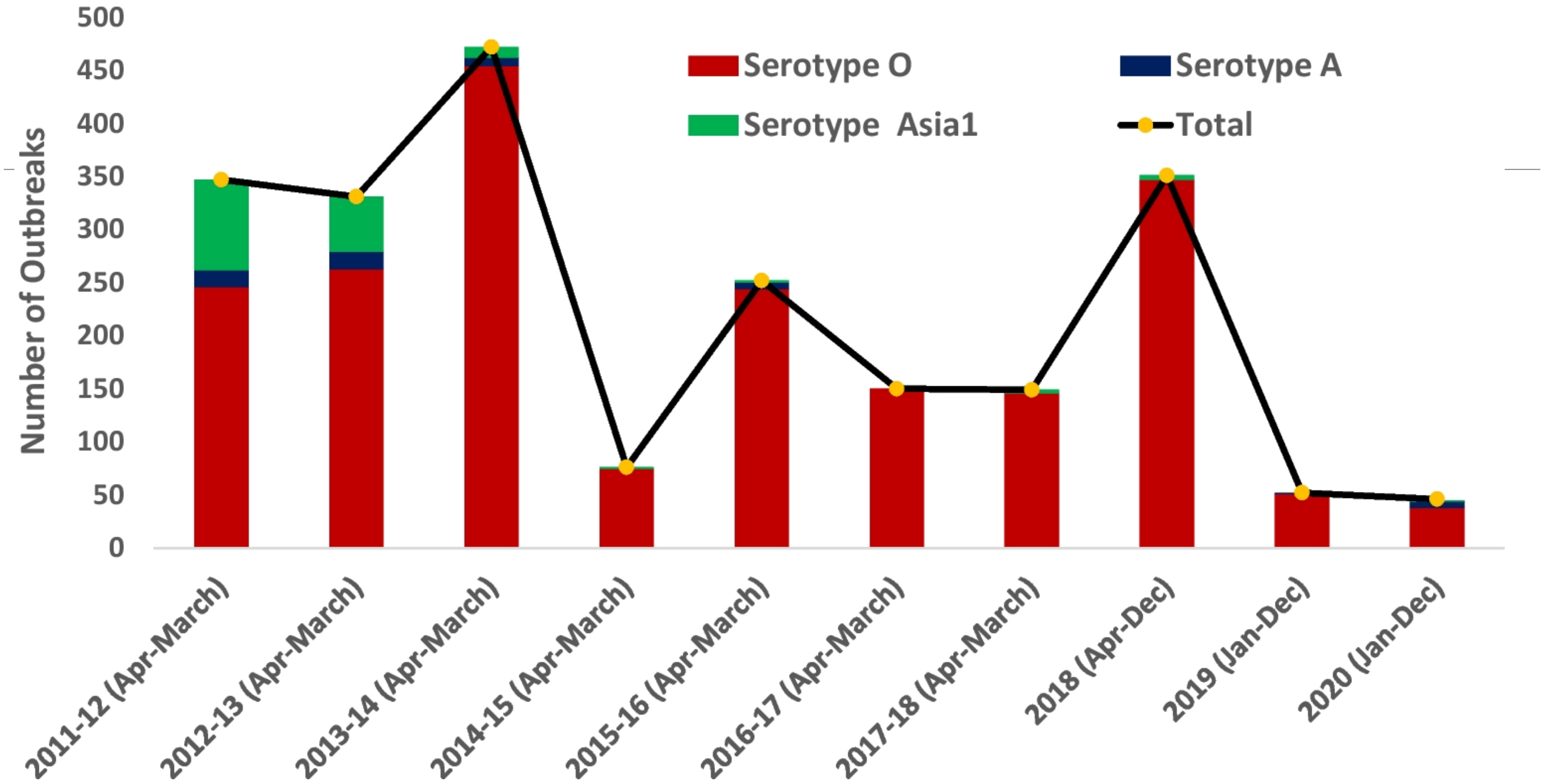
which there may not yet be full agreement"



Source: Subramaniam, S., Mohapatra, J.K., Sahoo, N.R. et al. Foot-and-mouth disease status in India during the second decade of the twenty-first century (2011–2020). Vet Res Commun 46, 1011–1022 (2022). https://doi.org/10.1007/s11259-022-10010-z

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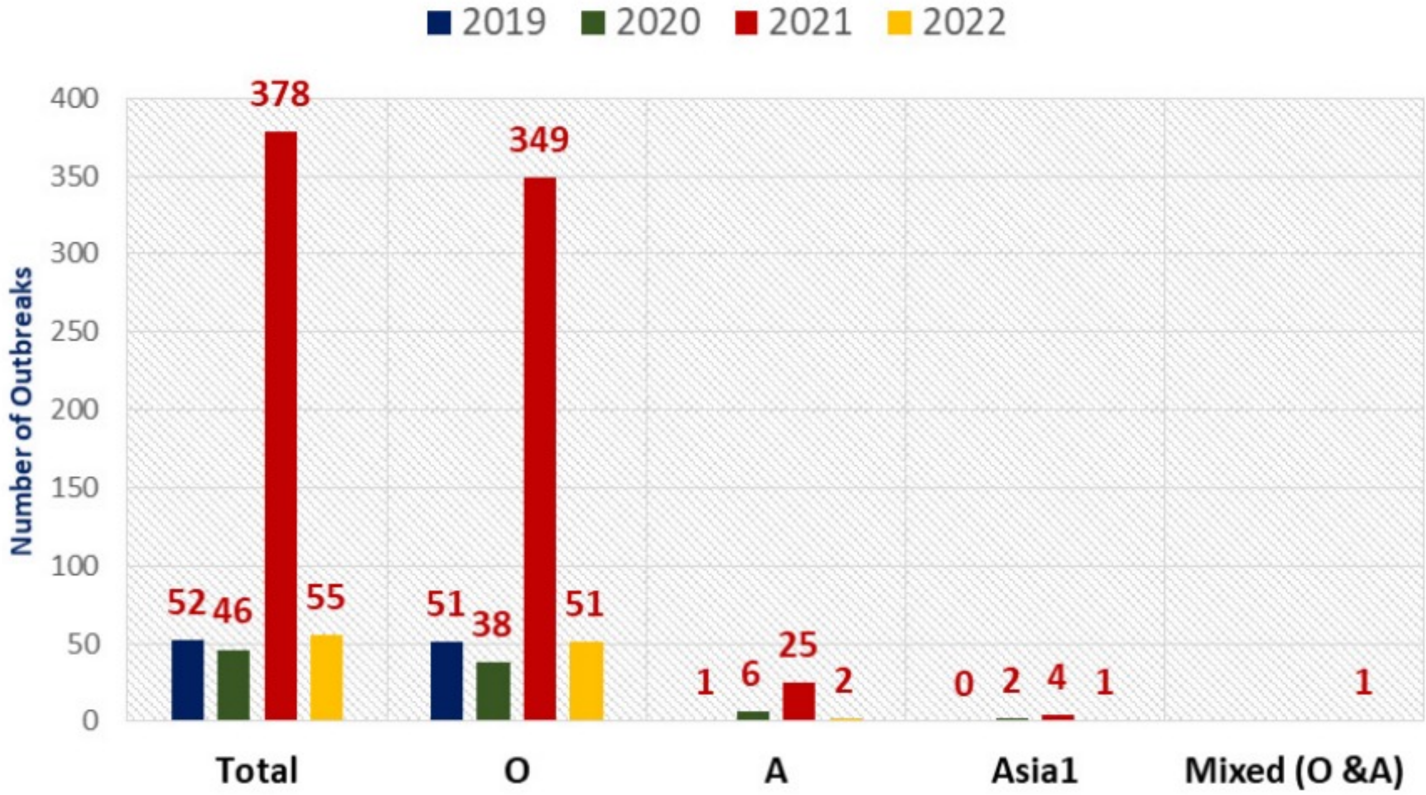
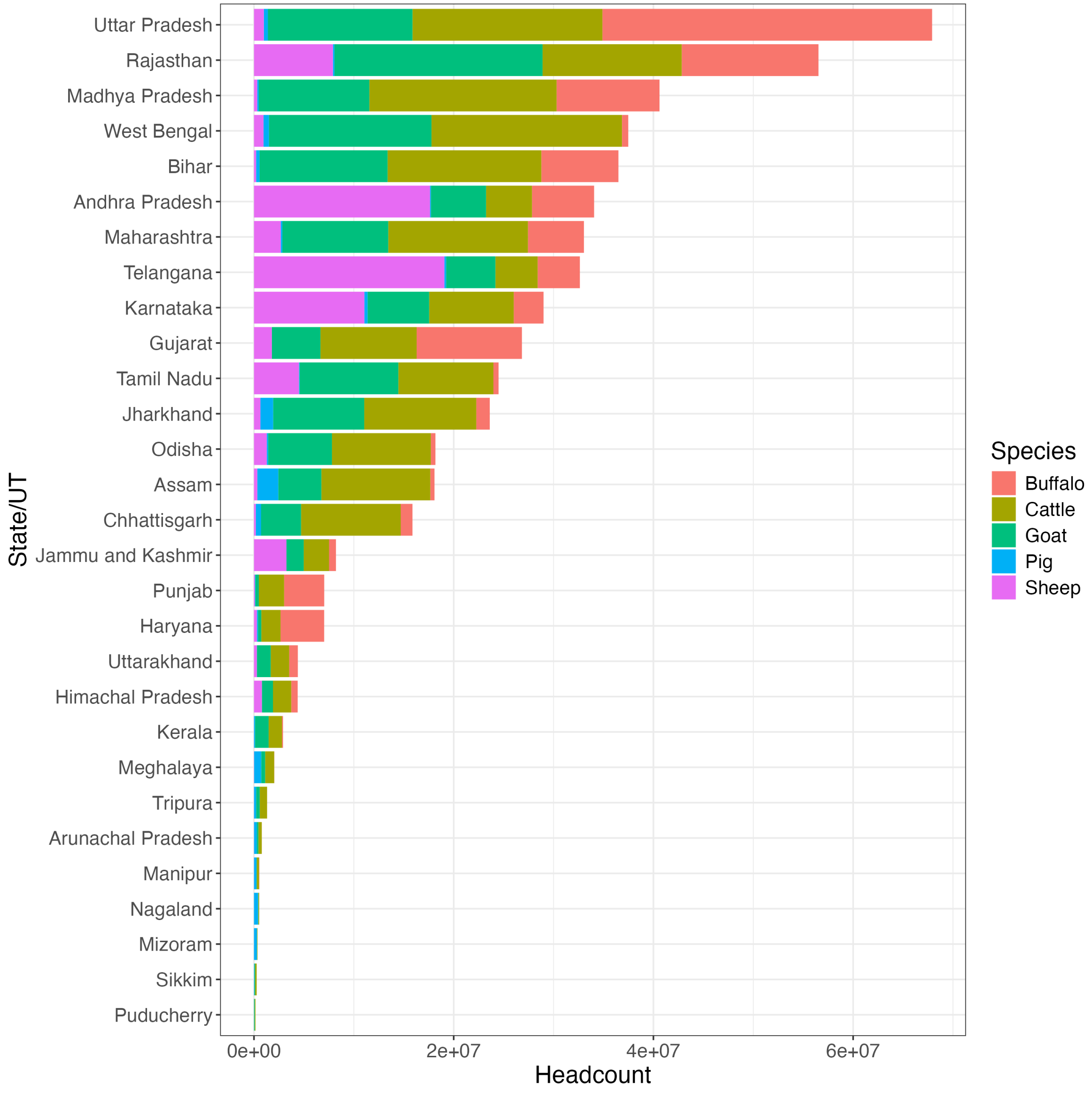


Fig 3: Year wise outbreaks/incidences of FMD and virus serotypes involved during last four years.

Model

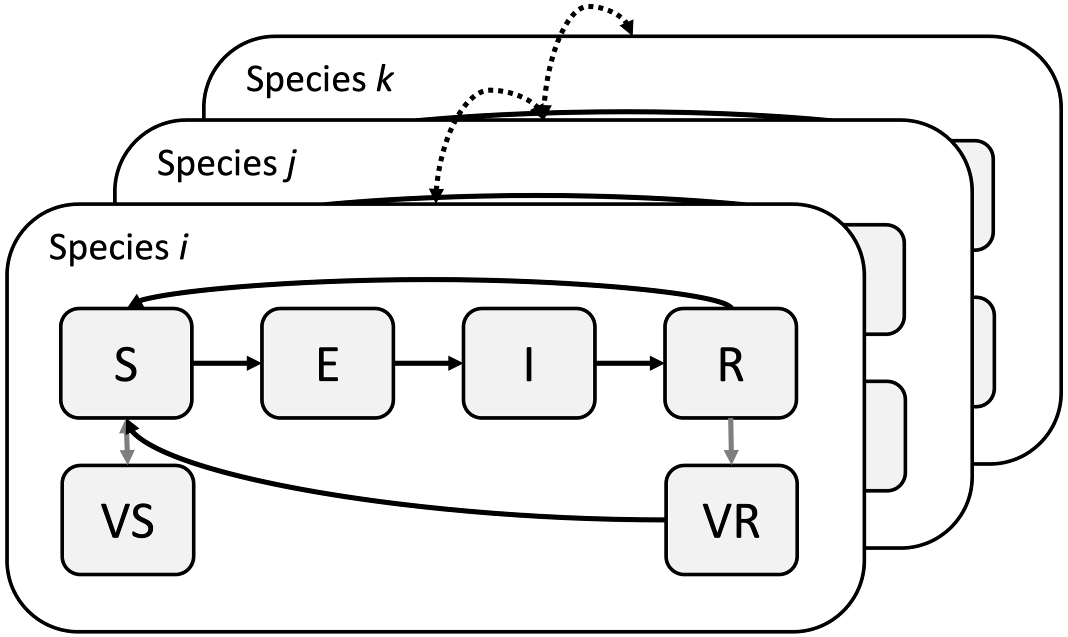
Data

- 2019 Agricultural census – livestock headcounts by village
  - Buffalo, cattle, goats, pigs, sheep
  - Large variation in dispersion of species
- State-wise DIVA data
- State-wise vaccination coverage



Multiple species ODE

- Deterministic Ordinary Differential Equations
- We focus on 5 species in our data: buffalo, cattle, goats, pigs, sheep.
- Cross-species transmission is possible, and occurs at different rates between different species (e.g. infected pigs can infect cows more easily than they can become infected by infectious cows)[1]



Infection moves within and between species

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[1] Fukai K, Nishi T, Morioka K, Yamada M, Yoshida K, Yamakawa M. Horizontal transmission of foot-and-mouth disease virus O/JPN/2010 among different animal species by direct contact. *Transbound Emerg Dis*. 2020; 67: 223–233. https://doi-org.ezaccess.libraries.psu.edu/10.1111/tbed.13344

Transmission

- Transmission between species varies by species – pigs are harder to infect but are much more infectious conditional on infection. Sheep and goats are typically not very infectious (but R0 slightly above 1).
- Transmission between species *i* from species *j*

$$\beta_{i,j} = C_{i,j} \cdot T_{i,j}$$

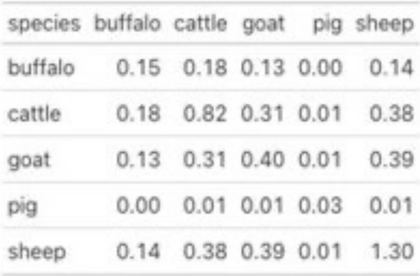
- Transmission matrix T is calculated taking the outer product of species susceptibility vector *s*, transmissibility vector *t*, and a scalar *a*

$$T = a\,(s \bigotimes t)$$

Contacts

- In addition to transmission, the number of contacts between different species can vary in different regions of India, depending on total animal population in a given village, as well as demographic makeup of the animals in the village (e.g., among all buffalo, cattle, goats, pigs, sheep in a village, the proportion that are goats)

- To calculate the baseline contact matrix for each state, we assumed the following:
- 1. Contact between animals occurs at the village level
- 2. More animals in a village == more contacts between animals



species	buffalo	cattle	goat	pig	sheep
buffalo	0.15	0.18	0.13	0.00	0.14
cattle	0.18	0.82	0.31	0.01	0.38
goat	0.13	0.31	0.40	0.01	0.39
pig	0.00	0.01	0.01	0.03	0.01
sheep	0.14	0.38	0.39	0.01	1.30

Example species contact matrix

Contacts

- We construct state-wise (s) contact matrices from the village-level (w) headcount data (h_w)
  - Calculate village level contact matrix

$$C_w = \frac{h_w \otimes h_w}{N_w}$$

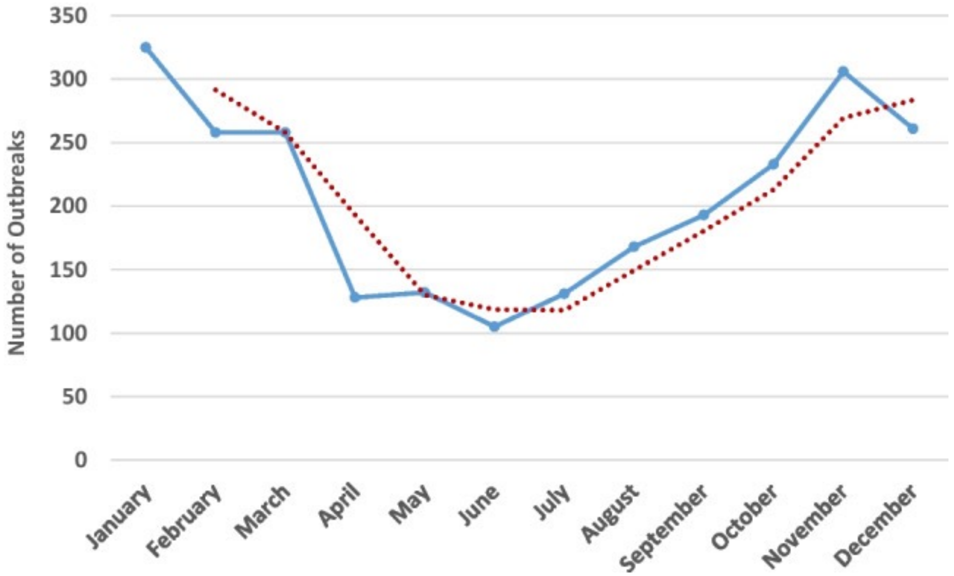
  - Take the state-wise average and multiply by scalar η

$$C_s = \frac{\eta}{|W|} \sum_{w=1}^{|W_s|} C_w$$

  - η is the same for all states to retain the ability to compare between them. We use the maximum species contact rate calculated using the entirety of India.

Seasonality & Pulsed Vaccination

- Seasonality cosine curve taken from literature
- India carry out mass-vaccination campaigns twice-yearly – in October and March
- Pulsed vaccination delta function – twice yearly



Seasonality curve

$$F(t) = 0.39\cos\left(\frac{2\pi t}{365}\right) + 1$$

Subramaniam S, Mohapatra JK, Sahoo NR, et al. Foot-and-mouth disease status in India during the second decade of the twenty-first century (2011-2020). *Vet Res Commun*. 2022;46(4):1011-1022. doi:10.1007/s11259-022-10010-z

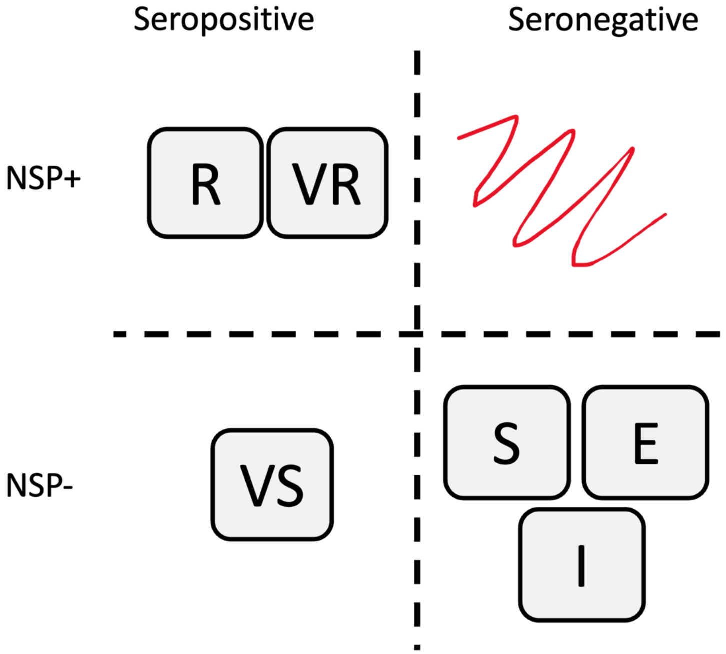
Model ODEs

$$
\begin{aligned}
\frac{dS_i}{dt} &= \nu_i N_i + \alpha_i R_i^5 + \alpha_{v,i}(VS_i^5 + VR_i^5) - \sum_{j=1}^{n} F(t)\beta_{i,j}\frac{S_i I_j}{N} - \mu_i S_i - \rho_i S_i \delta(t, T_v) \\
\frac{dE_i}{dt} &= \sum_{j=1}^{n} F(t)\beta_{i,j}\frac{S_i I_j}{N} - \sigma_i E_i - \mu_i E_i \\
\frac{dI_i}{dt} &= \sigma_i E_i - \gamma_i I_i - \mu_i I_i \\
\frac{dR_i^1}{dt} &= \gamma_i I_i - n\alpha R_i^1 - \mu_i R_i^1 - \rho_i R_i^1 \delta(t, T_v) \\
\frac{dR_i^m}{dt} &= n\alpha R_i^{m-1} - n\alpha R_i^m - \mu R_i^m - \rho_i R_i^m \delta(t, T_v) \qquad (\forall m = 2, \ldots, n) \\
\frac{dVS_i^1}{dt} &= \rho_i \delta(t, T_v) S_i - n\alpha_{v,i} VS_i^1 - \mu_i VS_i^1 \\
\frac{dVS_i^m}{dt} &= n\alpha_v VS_i^{m-1} - n\alpha_v VS_i^m - \mu_i VS_i^m \qquad (\forall m = 2, \ldots, n) \\
\frac{dVR_i^1}{dt} &= \rho_i \delta(t, T_v) \sum_{m=1}^{n} R_i^m - n\alpha_{v,i} VR_i^1 - \mu_i VR_i^1 \\
\frac{dVR_i^m}{dt} &= n\alpha_v VR_i^{m-1} - n\alpha_v VR_i^m - \mu_i VR_i^m \qquad (\forall m = 2, \ldots, n)
\end{aligned}
$$

Results

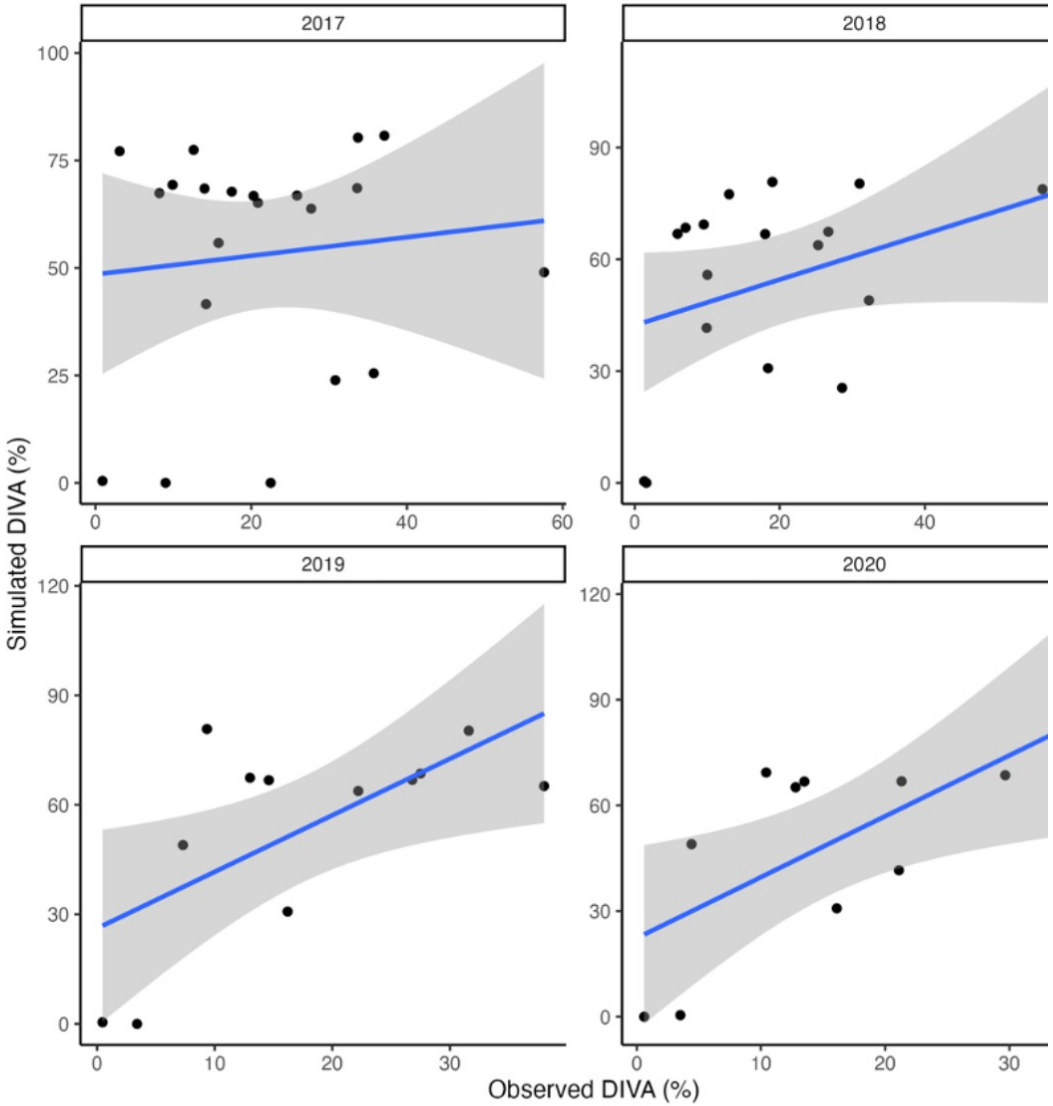
Parameterisation & Initial Validation

- Parameters sourced from the literature
- Model structure allows estimation of survey endpoints
  - DIVA, we can take (R + VR) / N
  - Seropositivity, we can do the same but take ((R + VR + VS) / N) instead.



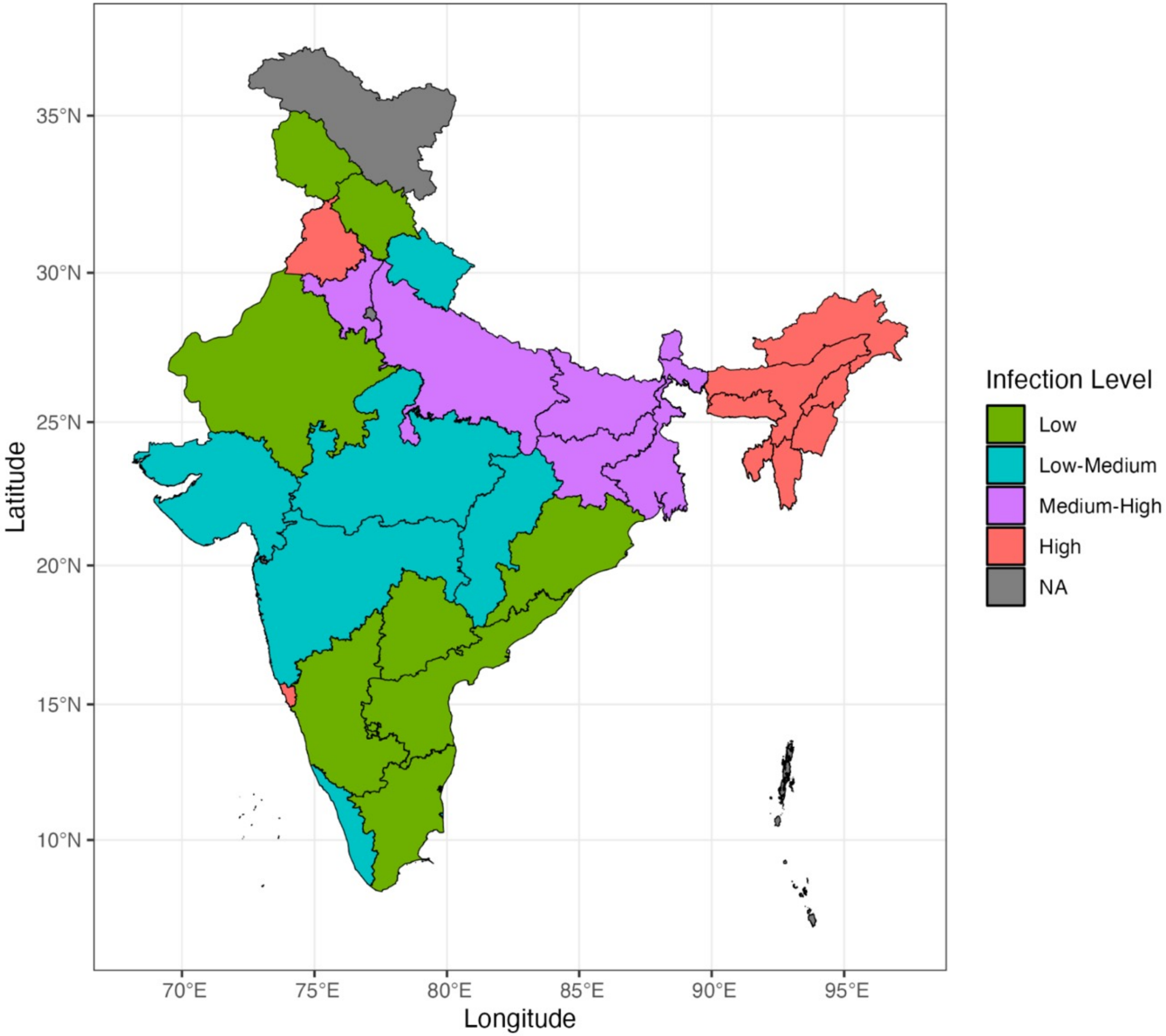
Model vs Observed DIVA

- Reasonable correlation with state-wise DIVA
  - 0.33 overall
  - 0.13 (2017), 0.33 (2018), 0.45 (2019), 0.50 (2020)



Predicted state-wise prevalence

- Run for 5 years for each state to assess long-term equilibrium prevalence
- The average simulated prevalence was 1.7%, ranging from essentially 0 (0.0000000964, Telangana) to 3.73% (Mizoram)
- Clear regionality of transmission – correlates with proportion of high-risk livestock (cattle, buffalo, pigs)



Optimal species-wise vaccine allocation

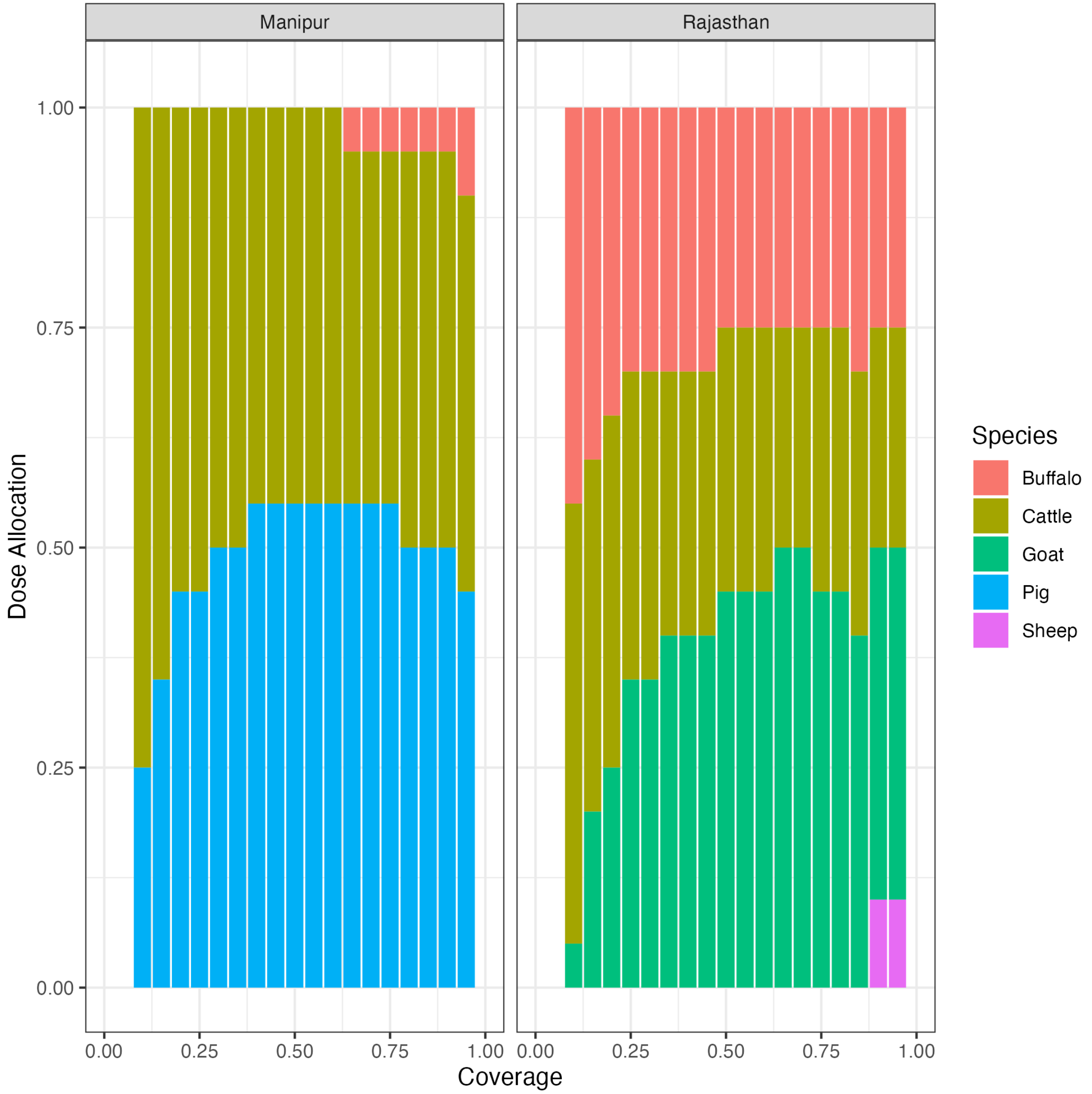
- At project-commencement only cattle and buffalo were routinely vaccinated in India
- 2019 – Prime Minister announced 100% coverage for all 5 species
- Current numbers of annual doses (~700 million) does not allow for the vaccination of all livestock animals in India (~535 million) twice a year.
  - ~65% coverage of all species possible, if equally allocated*

Optimal species-wise vaccine allocation

- Different allocations of available vaccines may be optimal in different states, at different times and numbers of available doses.
- We can explore the space of possible allocations
  - Generate all combinations of allocation of X doses across 5 species, at resolution of 5% (10,626 combinations!)
  - Simulate each state with each combination, at vaccine coverage levels of 10-95%.
  - Judge ‘optimal’ as minimising number of annual infections

‘Optimal’ state-wise allocations

- Heterogenous allocations by state



‘Optimal’ state-wise allocations

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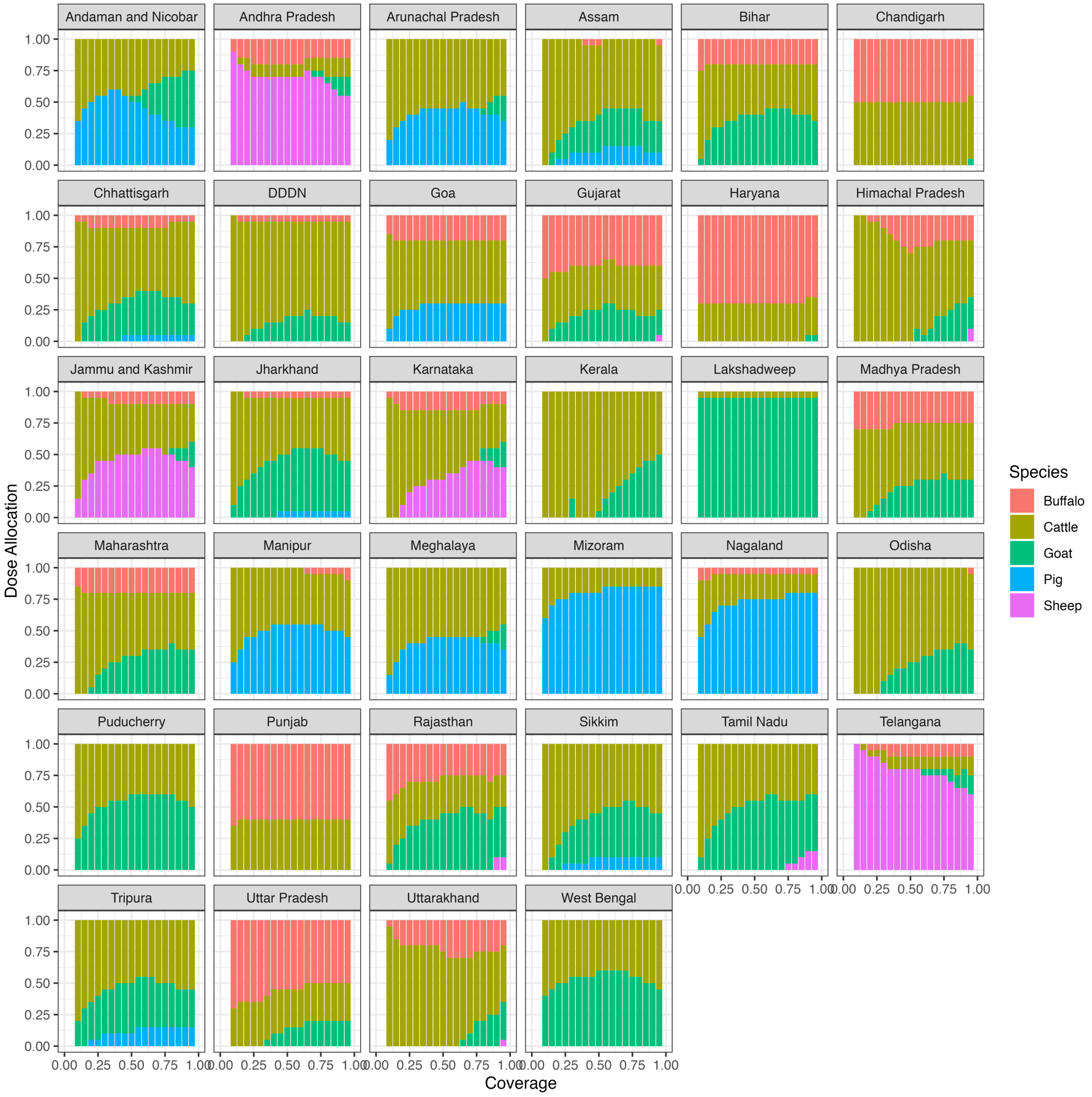
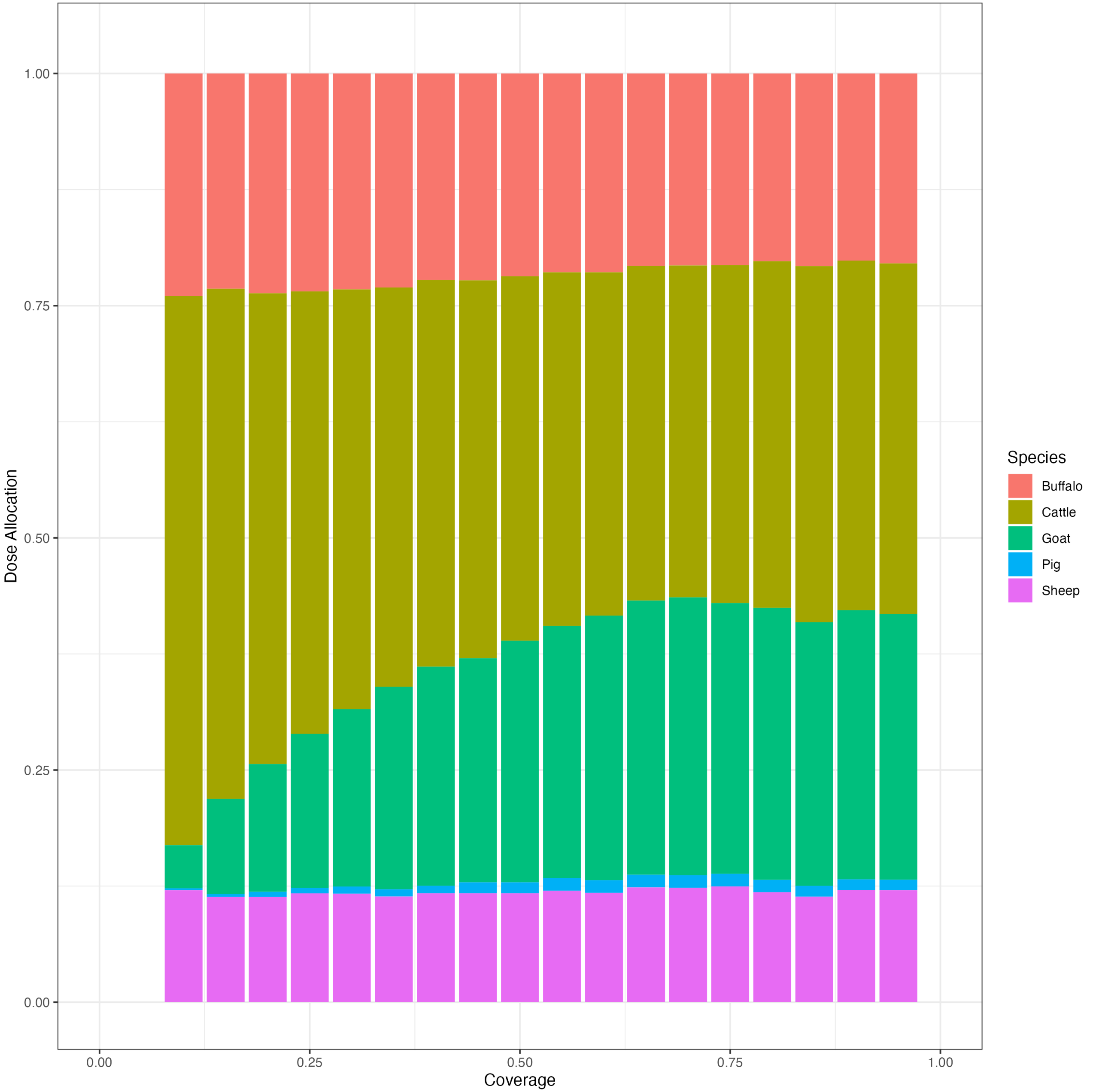


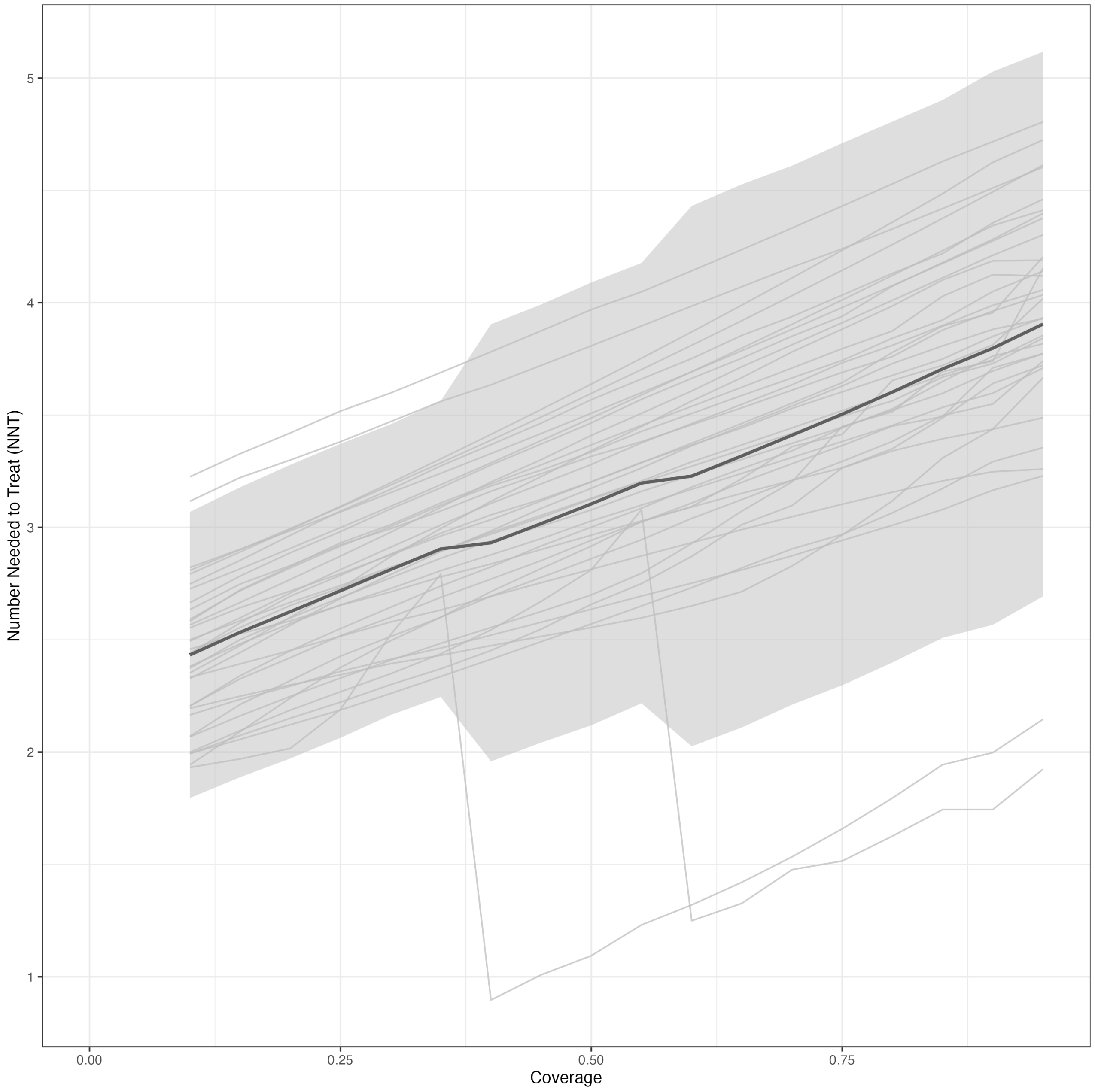
‘Optimal’ India-wide allocations

- This heterogeneity is masked looking at an India-wide perspective
- Only buffalo and cattle not optimal at any level of coverage



Number Needed to Treat (NNT)

- Number of vaccines needed to avert 1 infection
- Average 2.5-3.9
  - State-specific range ~1-4.5
- Varying state-specific livestock demographics means some states are easier to avert infections in



Conclusions

- Caveat: Single model, not ideal data, every animal valued the same
- Potential exists for more efficient vaccination
- If minimizing infections, vaccination of non-bovine livestock is necessary
  - Pigs are an easy win, given lower numbers and high transmission
- State-wise livestock heterogeneity should be taken into account

Acknowledgements

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Thanks for listening