Seroprevalence, Geospatial Distribution and Risk factors associated with Hepatitis E infection in Nepal

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Background

- Hepatitis E virus (HEV) is known to cause acute jaundice syndrome
- often considered a neglected disease: majority of HEV infections remain undetected due to poor surveillance and suboptimal access to diagnostics
- global burden estimates are highly variable
- approximately 939 million people with 100 million have recent or ongoing infection
- HEV is endemic in Nepal
- Five major HEV endemics: starting in 1982
- First outbreak outside Kathmandu in Biratnagar, in 2014: affected 7000 people, due to contaminated municipal water
- nationally representative disease burden data on HEV are lacking

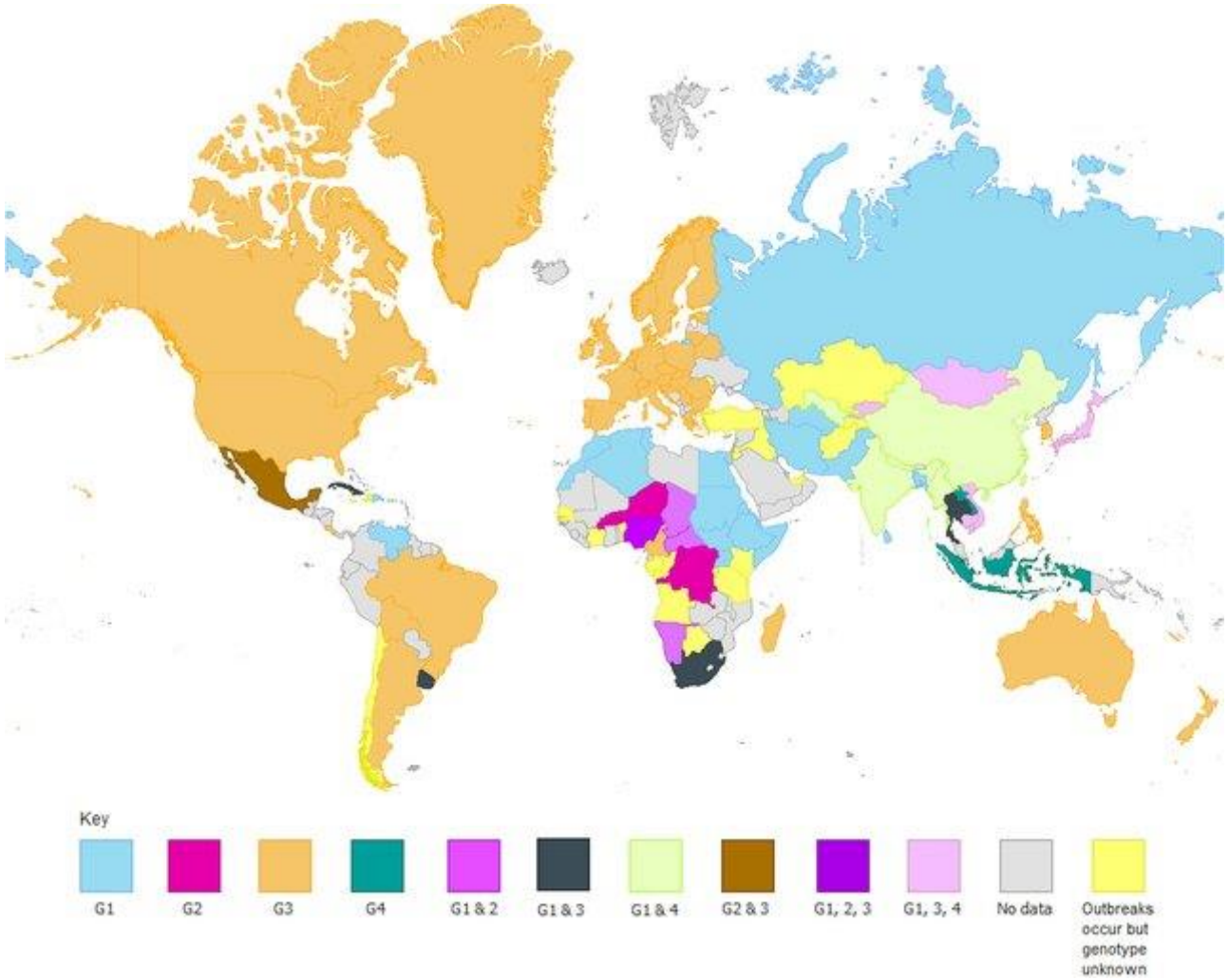

Figure 1: Geographical distribution of HEV (Source: Treagus et al, 2021)

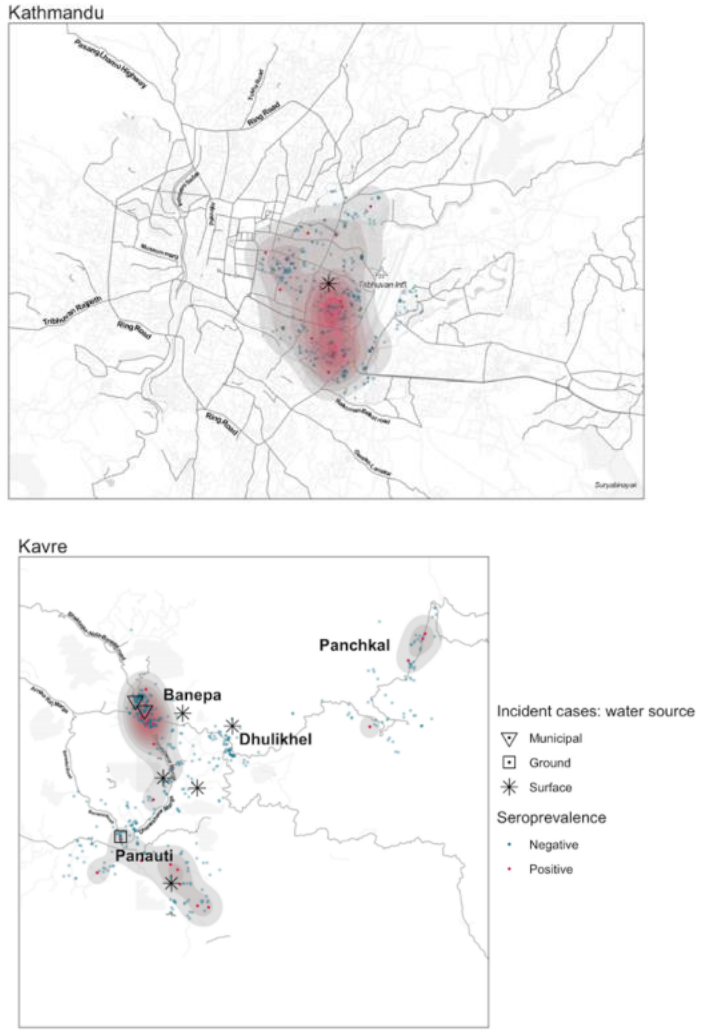

Figure 2: Longitudinal Study around Kathmandu Valley (Source: Katuwal et al, 2023)

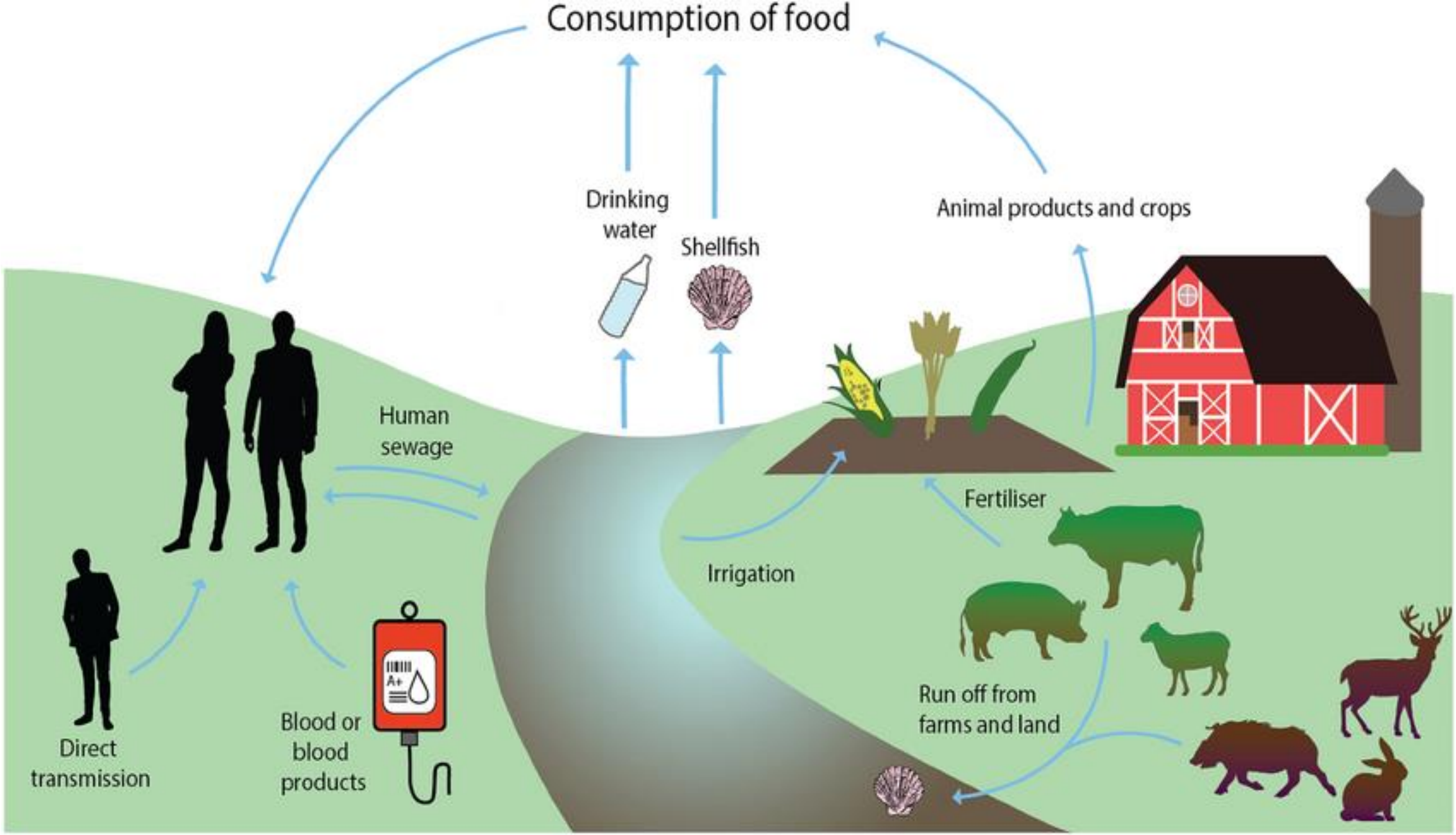

Figure 3: HEV Transmission Routes (Source: Treagus et al, 2021)

Objectives

- To estimate representative HEV seroprevalence in Nepal
- To describe the geospatial distribution and factors associated with HEV seropositivity

Methodology

- **Study Design:**
  - nationally representative CS sero-survey; Nov'21-Jan'22; 3707 samples
  - Ad-hoc to Sero-Survey of Cholera Study (NHRC: 166/2021)
  - 65 wards: stratified by ecological region and municipality type
  - 15 households per ward
  - aged ≥ 2 years
  - questionaries: household level and individual level
  - Ethical Approval: 235/2022 (NHRC) and 2020-016 (IVI)

- **Laboratory Analysis:**
  - Wantai HEV IgG ELISA Kit
  - OD ≥ 1.0 is positive; OD < 1.0 is negative
  - borderline samples retested

Methodology

- **Variables:**
  - urban and rural municipalities delineated into wards
  - Sources of water and household toilets categorized into improved and unimproved as per WHO's classification.

- **Statistical Analysis:**
  - Seroprevalence and 95%CI based on HEV IgG seropositivity
  - Mixed effects logistics regression for factors associated
  - Univariate analysis and Multivariate analysis
  - HEV seroprevalence across Nepal: hierarchical logistic spatial regression model

Results

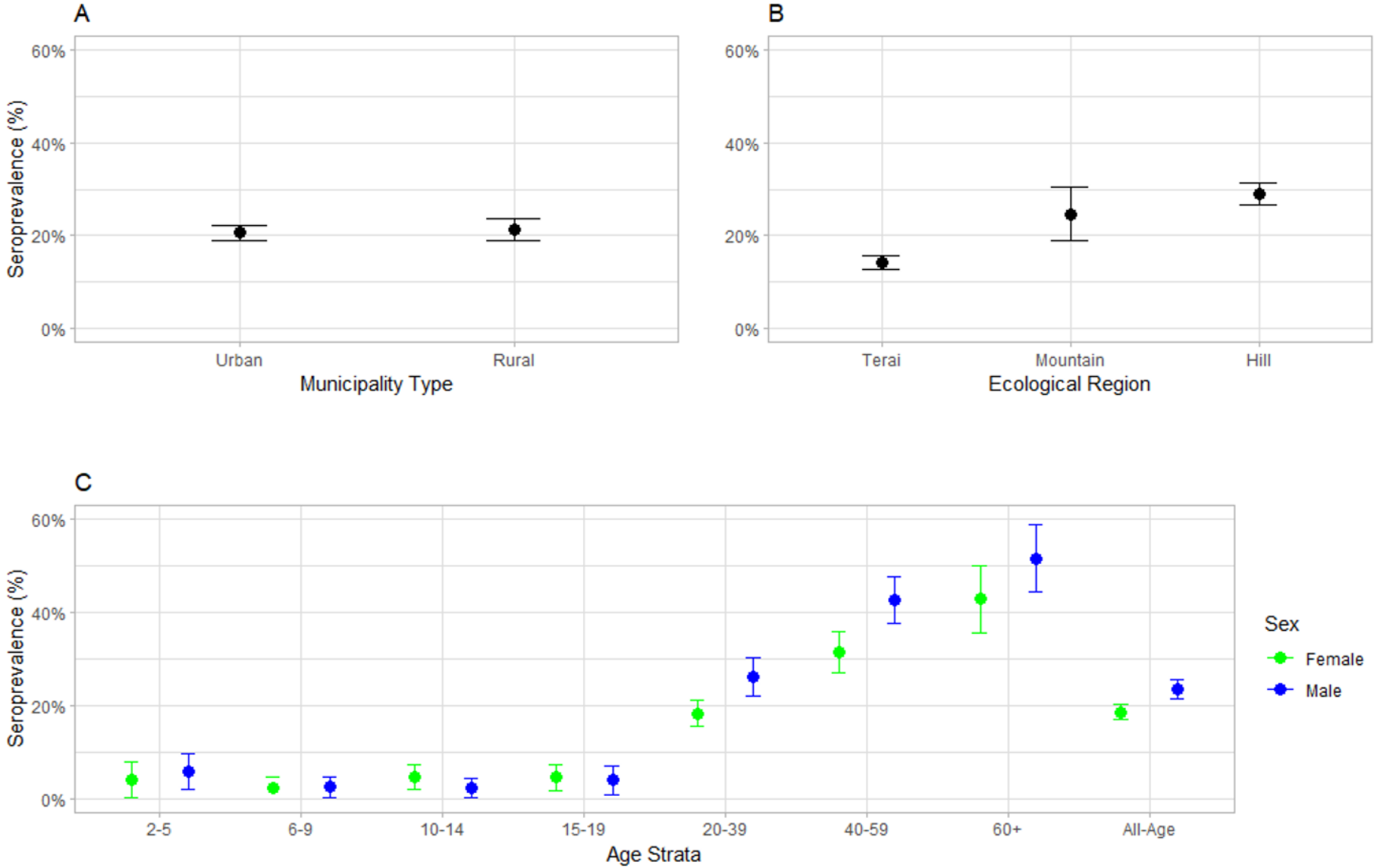

Figure 4: HEV Seroprevalence by Municipality, Ecological Region and Age

Factor	Frequency	Univariate Model		Full Model	
	N = 3,703[1]	Crude OR	95% CI	Adjusted OR	95% CI
Age, y					
2-5	5.0% (12/240)	—	—	—	—
6-9	2.3% (7/302)	0.43	0.16, 1.11	0.43	0.16, 1.14
10-14	3.4% (15/438)	0.62	0.28, 1.37	0.63	0.28, 1.43
15-19	4.3% (16/371)	0.76	0.35, 1.69	0.83	0.37, 1.88
20-39	21.3% (248/1,164)	6.15	3.30, 11.5	7.01	3.69, 13.3
40-59	36.7% (304/829)	15.0	7.96, 28.2	16.5	8.56, 31.7
60+	47.4% (170/359)	26.9	13.9, 52.2	29.2	14.7, 58.0
Sex					
Female	18.6% (374/2,010)	—	—	—	—
Male	23.5% (398/1,693)	1.39	1.17, 1.65	1.65	1.36, 2.01
Wealth quintile					
Highest	25.0% (219/876)	—	—	—	—
Lowest	26.7% (117/438)	1.11	0.75, 1.64	1.31	0.82, 2.11
Second	20.0% (89/446)	0.74	0.51, 1.08	0.95	0.61, 1.50
Middle	16.8% (126/750)	0.81	0.58, 1.12	0.89	0.61, 1.31
Fourth	18.5% (221/1,193)	0.78	0.60, 1.03	0.79	0.57, 1.09

Main drink water					
Improved	20.8% (763/3,673)	—	—	—	—
Unimproved	30.0% (9/30)	0.77	0.31, 1.89	1.29	0.39, 4.27
Alternative drink water					
Improved	20.7% (706/3,403)	—	—	—	—
Unimproved	22.0% (66/300)	0.76	0.52, 1.10	0.71	0.46, 1.11
Main other water					
Improved	20.6% (752/3,652)	—	—	—	—
Unimproved	39.2% (20/51)	0.88	0.43, 1.81	0.94	0.37, 2.38
Toilet facility					
Improved	20.7% (664/3,203)	—	—	—	—
Unimproved	21.6% (108/500)	0.98	0.75, 1.27	1.14	0.82, 1.57
Province					
Karnali	26.9% (59/219)	—	—	—	—
Province 1	13.6% (100/738)	0.41	0.19, 0.88	0.42	0.15, 1.18
Madesh	9.2% (62/673)	0.26	0.11, 0.57	0.38	0.12, 1.22
Bagmati	37.4% (280/748)	1.77	0.84, 3.73	1.40	0.54, 3.62
Gandaki	15.8% (52/330)	0.46	0.20, 1.09	0.30	0.10, 0.89
Lumbini	20.1% (138/685)	0.64	0.29, 1.39	0.83	0.28, 2.47
Sudurpashchim	26.1% (81/310)	0.94	0.39, 2.29	1.30	0.40, 4.21
Municipality					
Urban	20.6% (512/2,484)	—	—	—	—
Rural	21.3% (260/1,219)	1.05	0.64, 1.73	1.10	0.67, 1.79
Ecological region					
Terai	14.2% (281/1,974)	—	—	—	—
Mountain	24.6% (52/211)	2.32	0.98, 5.48	1.31	0.45, 3.84
Hill	28.9% (439/1,518)	2.80	1.84, 4.27	1.89	1.02, 3.52
Overall	20.8% (772/3,703)				

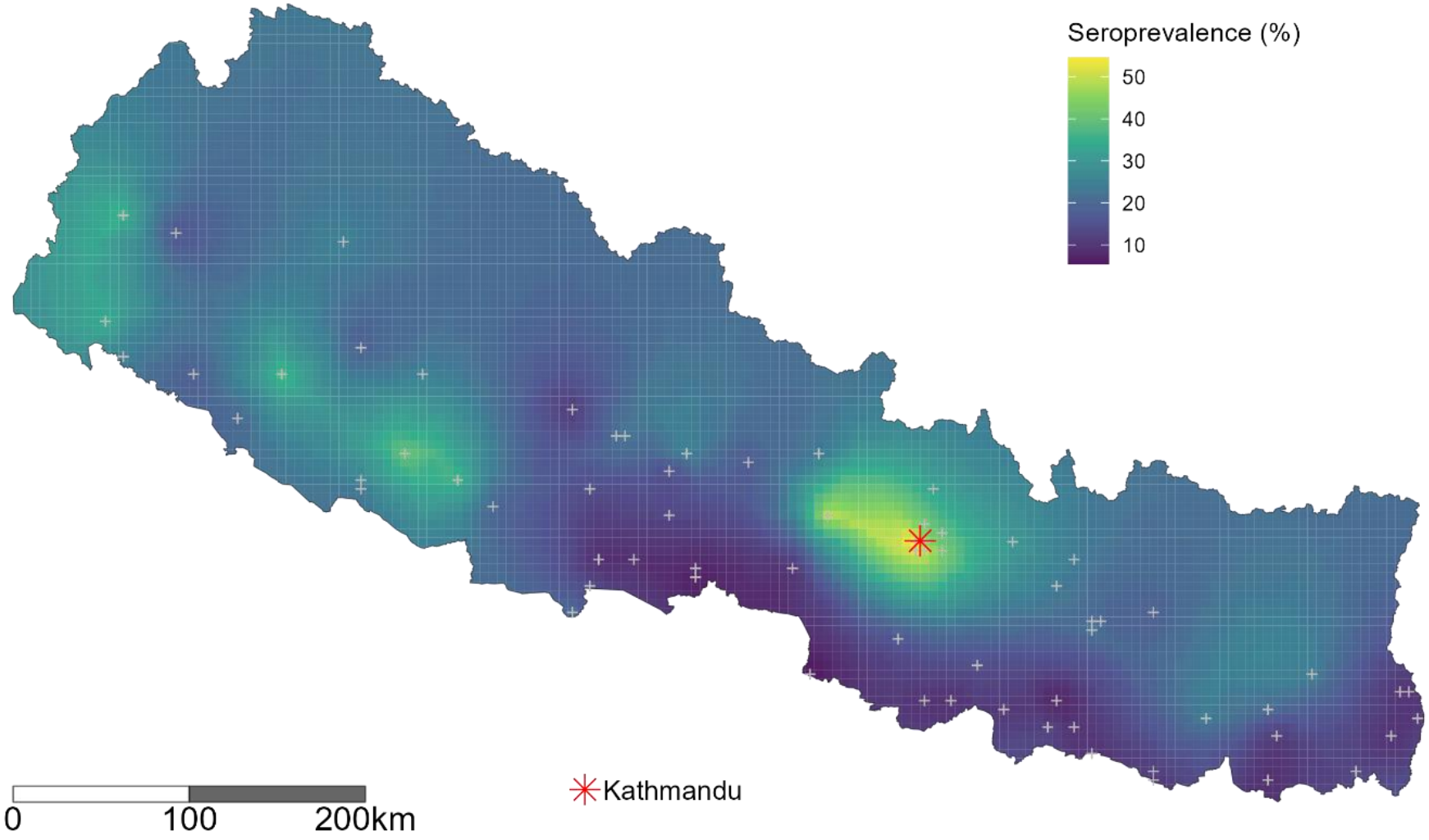

Figure 5: Predicted seroprevalence of HEV across Nepal (sampled locations: grey)

Conclusion

- 20.8% seroprevalence (prior HEV infection)
  - no significant difference between urban and rural settings
  - higher in hilly and mountain regions: lack of access to clean water
  - highest risk of infection within Kathmandu valley (50%)
  - steep rise in seropositivity after age of 20 years
- IgG as marker for infection
- residual sample investigation: cost effective, national representative for additional studies of public health concern (e.g: COVID)
- water, sanitation, and hygiene interventions along with HEV vaccine: for high-risk groups or during an acute outbreak.
- study in younger population to identify the incidence of infection and the role they play in transmission

Acknowledgements