Unravelling the dynamics of hepatitis-E infections in displaced populations: implications for reactive vaccination campaigns

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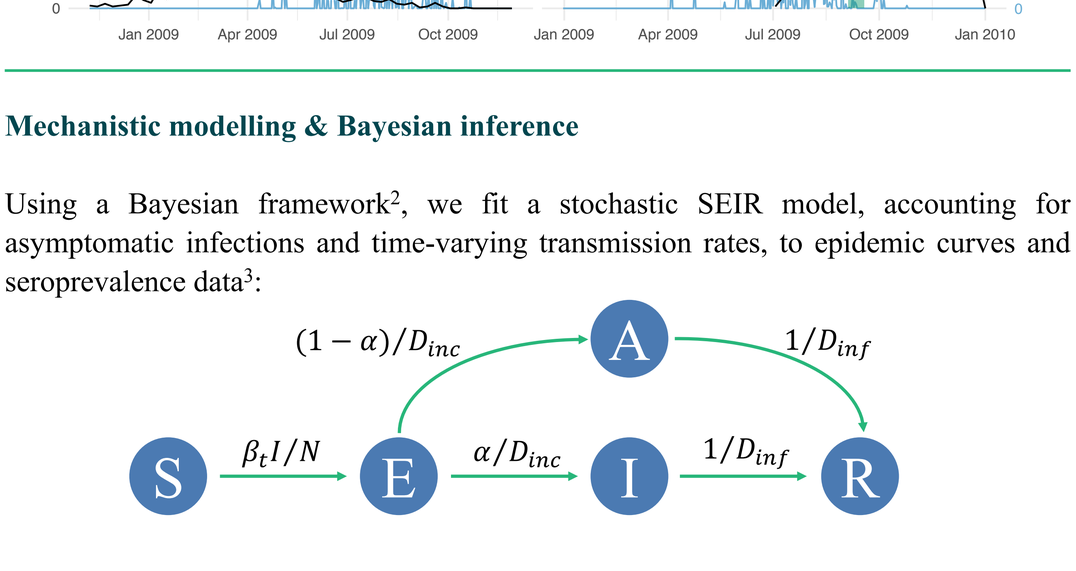
Public-health context

Hepatitis E virus has been responsible for massive protracted epidemics in Africa and Asia with case fatality in pregnant women up to 25%. With no effective treatment and little evidence that emergency water and sanitation improvements slow epidemics, public health practitioners have been paralysed in epidemic response. Recent development of an efficacious vaccine[1] has raised hopes for reactive vaccination in outbreaks. *However, with the three-dose immunization schedule, the poorly quantified natural history and complex epidemiology, the impact of reactive strategies remains unclear.* Here we investigate these issues by using a unique set of epidemiological, serological and environmental data from outbreaks that occurred in two camps of internally displaced populations.

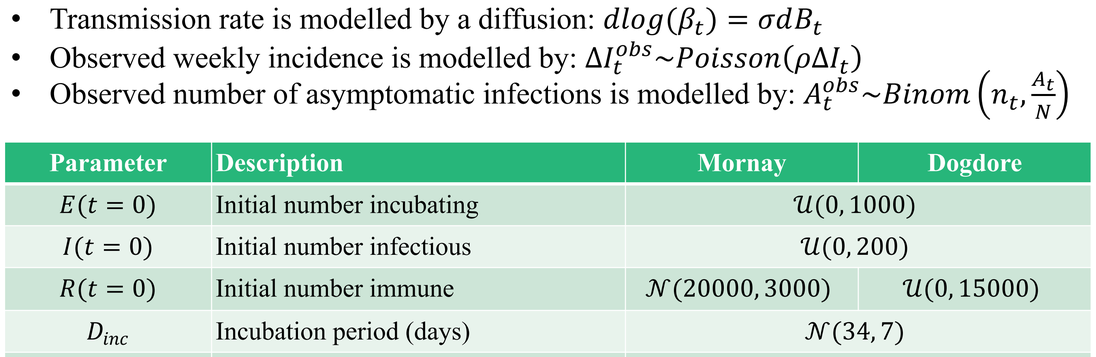
Epidemiological, serological & precipitation data

Despite similar symptomatic attack-rates, the epidemic dynamics were very different in the two camps, starting either during the dry (Dogdoré) or rainy (Mornay) seasons.



Dogdoré camp
Chad
Year: *2008/09*
Pop: *27,450*
Cases: *902*
Attack rate: *3.3%*

Mornay camp
Darfur (Sudan)
Year: *2004*
Pop: *78,000*
Cases: *2857*
Attack rate: *3.7%*



Mechanistic modelling & Bayesian inference

Using a Bayesian framework[2], we fit a stochastic SEIR model, accounting for asymptomatic infections and time-varying transmission rates, to epidemic curves and seroprevalence data[3]:

- Transmission rate is modelled by a diffusion: $dlog(\beta_t) = \sigma dB_t$
- Observed weekly incidence is modelled by: $\Delta I_t^{obs} \sim Poisson(\rho \Delta I_t)$
- Observed number of asymptomatic infections is modelled by: $A_t^{obs} \sim Binom\left(n_t, \frac{A_t}{N}\right)$

Parameter	Description	Mornay	Dogdore
$E(t=0)$	Initial number incubating	$\mathcal{U}(0, 1000)$	
$I(t=0)$	Initial number infectious	$\mathcal{U}(0, 200)$	
$R(t=0)$	Initial number immune	$\mathcal{N}(20000, 3000)$	$\mathcal{U}(0, 15000)$
D_{inc}	Incubation period (days)	$\mathcal{N}(34, 7)$	
D_{inf}	Infectious period (days)	$\mathcal{N}(21, 14)$	
α	Proportion of symptomatic infections	$\mathcal{U}(0, 1)$	$\mathcal{N}(0.057, 0.008)$
R_0	Basic reproduction number	$\mathcal{U}(0, 100)$	
σ	Volatility of transmission rate	$\mathcal{U}(0, 1)$	
ρ	Reporting rate	$\mathcal{U}(0, 1)$	

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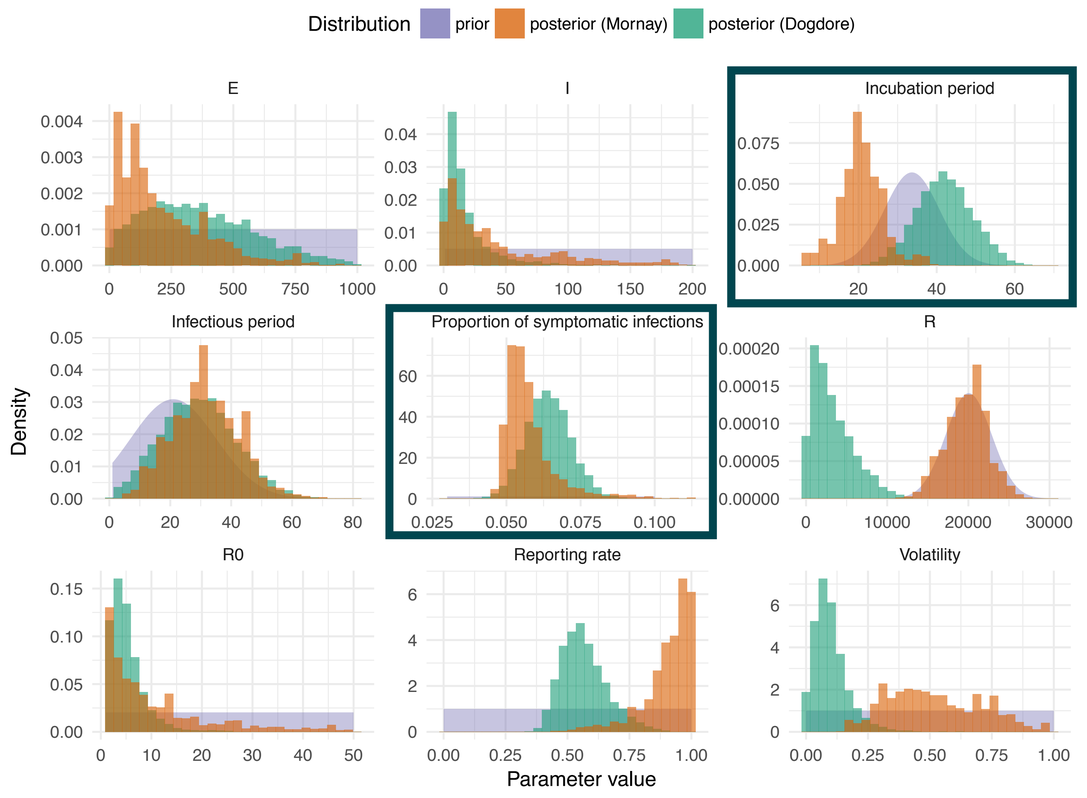
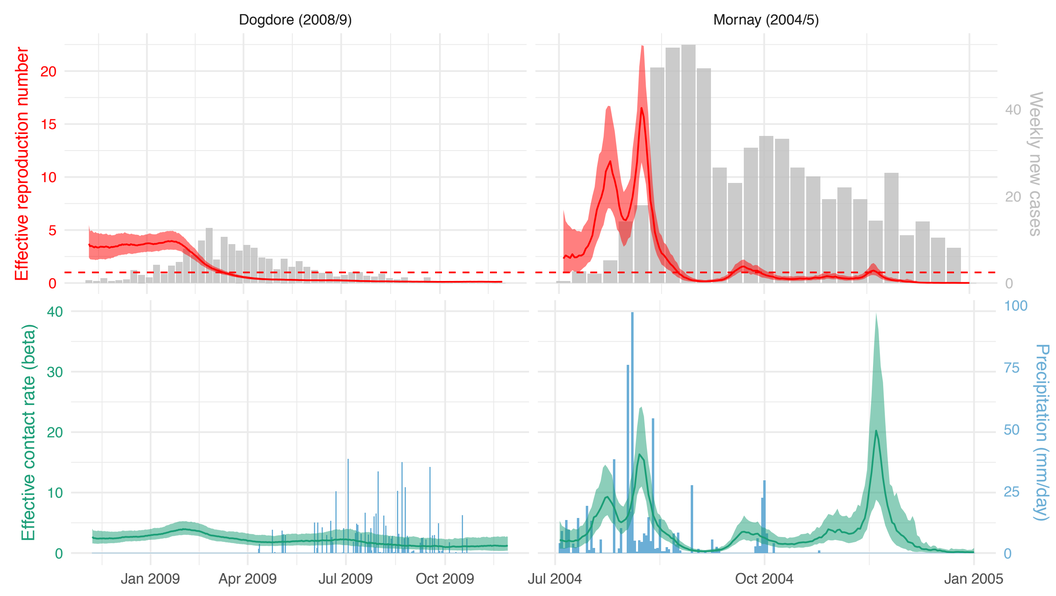
Posterior estimates identify key parameters

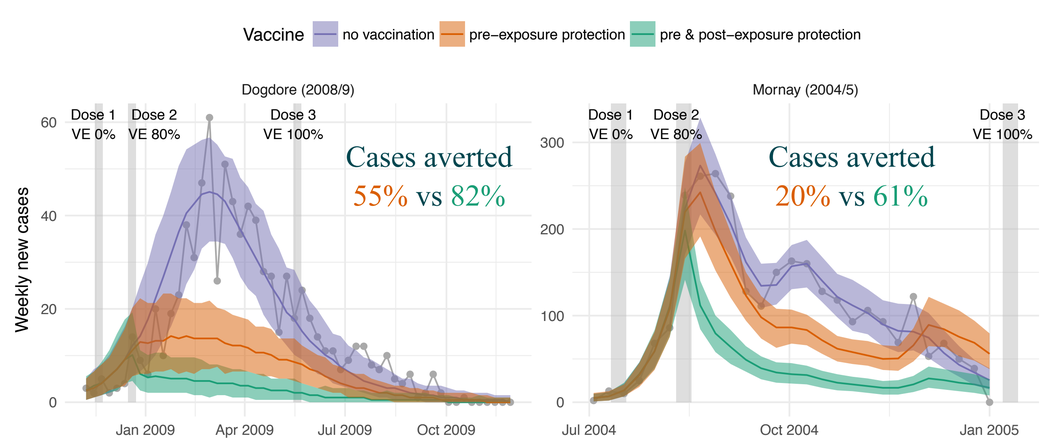


Time-varying transmission rates suggest different route of transmission

We found evidence that Mornay outbreak was likely catalysed by a large contamination event followed by low-levels of secondary transmission, while the epidemic in Dogdoré followed a person-to-person dynamics. *The apparent correlation between precipitation and transmission rate is suggestive of a threshold effect.*



Implications for reactive vaccination campaigns



While significant cases and deaths were averted in all simulations, the impact of vaccination varied across strategies and settings. In Mornay, the impact of vaccination campaigns was low compared to Dogdoré due to the large number of exposed and incubating individuals early in the outbreak. The vaccine has a larger impact if it provides protection during the incubation period and if one and two-doses prove to be efficacious.

Hepatitis E vaccines can play an important role in outbreak response, although the impact may be shaped by the modes of transmission and uncertain aspects of vaccine-protection.

1. Zhu F-C, Zhang J, Zhang X-F, *et al*. Lancet. 2010
2. Andrieu C, Doucet A & Holenstein R. J Roy Stat Soc B. 2010
3. Guthmann JP, Klovstad H, Boccia D, *et al.* Clinical Infectious Diseases. 2006.