International risk of secondary hantavirus clusters following MV Hondius outbreak

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Body

An outbreak of Andes virus (ANDV) infection aboard the MV Hondius cruise ship has become the focus of international public-health attention. As of May 17, 10 cases had been reported, including eight confirmed and three deaths. ANDV can cause hantavirus pulmonary syndrome, a severe disease with high case fatality, and, unlike other hantaviruses, ANDV has documented capacity for person-to-person transmission, with estimates of the basic reproduction ratio R_0 above one in previous outbreaks[1]. In response to the current outbreak, extensive tracing of contacts exposed before implementation of coordinated medical repatriation has been initiated, including passengers potentially exposed during international flights before confirmed cases were identified[2]. Isolation and follow-up practices currently differ across countries, ranging from hospital-based isolation to home monitoring alone. In parallel, uncertainty remains regarding the potential for pre-symptomatic transmission.

We adapted a stratified branching process model[3] to estimate the probability of secondary transmission clusters (≥3 infections). We considered 30 countries with documented links to known cases, MV Hondius crew or passengers, or their contacts[2],and parameterized national contact tracing and isolation capacity using the Global Health Security (GHS) Index[4,5] *Early Detection and Reporting* score and *Facilities Capacity* score, respectively. Assuming that 10% transmissions occur before symptom onset and a conservative R_0=1.5, the probability of secondary clusters ranged from 0.4% to 0.7%, depending on national contact tracing capacity, under fully effective isolation (Fig. 1A). Using higher R_0 estimates from previous outbreaks[1] increased this range to 0.8%-1.2% (Fig. 1B). When isolation was only 90% effective (Fig. 1C,D), probabilities rose to 1.5%-2.3% for lower R_0 and 2.9%-4.4% for higher R_0. Doubling the proportion of pre-symptomatic transmission further increased probabilities to as high as 3.1%-4.8% and 5.9%-9.6%, respectively. High effectiveness in isolation of symptomatic cases substantially reduced the probability of secondary cluster emergence. With no pre-symptomatic transmission, countries with isolation effectiveness of at least 80% kept the probability of secondary clusters below 4% in both R_0 scenarios, irrespective of contact tracing capacity (Fig. 1E). Assuming 10% pre-symptomatic transmission instead required isolation effectiveness of at least 90% (Fig. 1F).

Although the probability of sustained transmission remains low, secondary clusters may still emerge under heterogeneous isolation practices and uncertain pre-symptomatic transmission. Maintaining rapid case identification, coordinated contact tracing, and effective isolation across countries may therefore be critical to limiting further international spread.

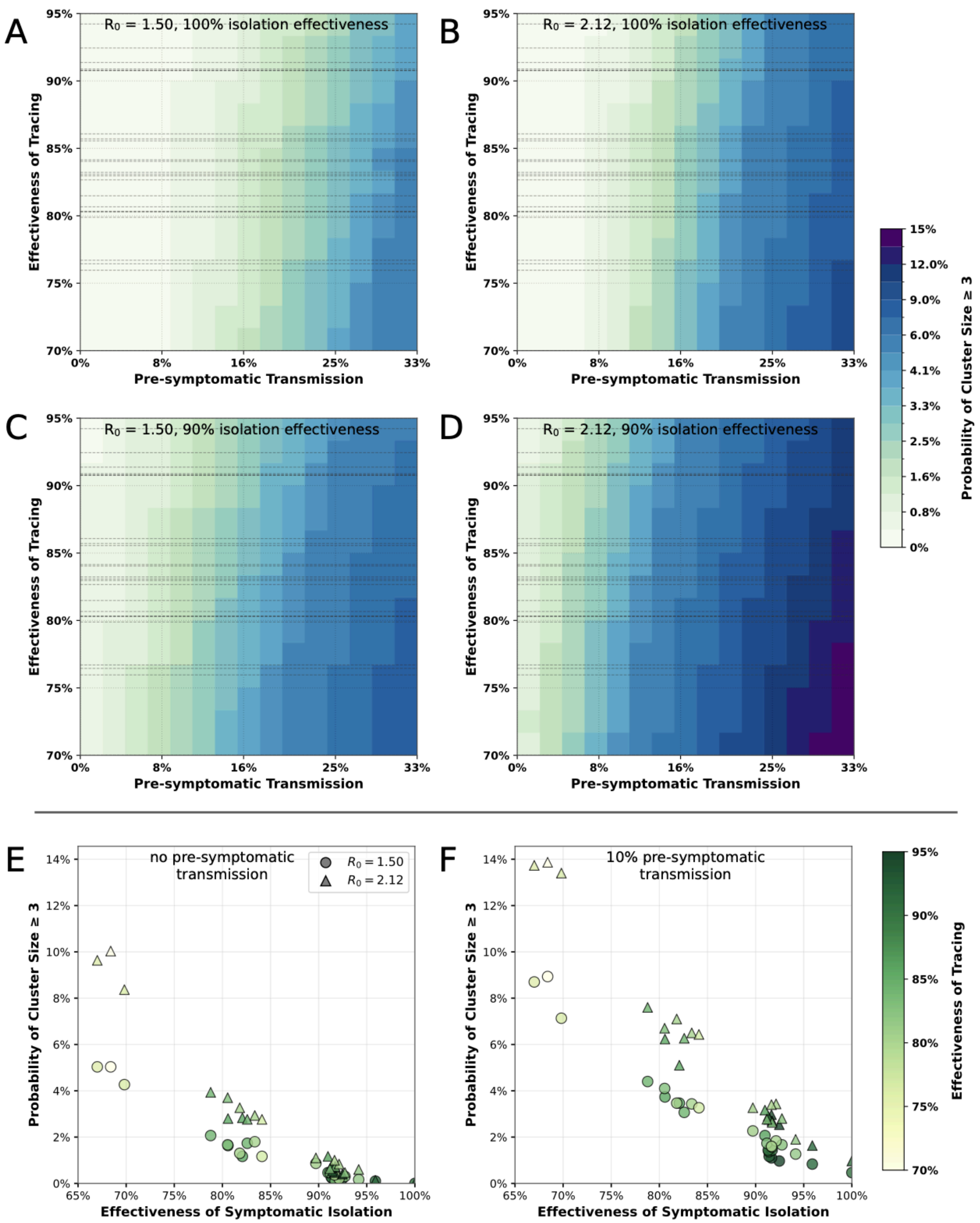

Figure 1: Risk of secondary clusters by pre-symptomatic transmission, tracing capacity and isolation effectiveness. A) Probability of cluster emergence as a function of the estimated pre-symptomatic transmission (fraction of transmission events occurring before symptom onset) and the effectiveness of tracing and isolation of contacts. 100% effectiveness means all contacts of a case are traced and isolated before they can infect. We used the Global Health Security (GHS) Index4 *Early Detection and Reporting* score as a proxy for each country's test-and-trace capacity (countries indicated as horizontal lines). We set R_0=1.5 and assumed

that isolation of symptomatic cases is 100% effective in stopping all transmission since the onset of symptoms. B) Same as A but with R_0=2.12 as estimated in Ref.[1]. C) Same as A but assuming that the isolation of symptomatic cases is 90% effective, i.e., prevents on average 9 in 10 transmission events occurring since the onset of symptoms. D) Same as B but assuming that the isolation of symptomatic cases is 90% effective. E) Probability of cluster emergence as a function of the effectiveness of isolation of symptomatic cases. We used The GHS index *Facilities Capacity* as a proxy for each country's isolation capacity. The effectiveness of test-and-trace is also explored (color bar). R_0=1.5 is shown in circles and R_0=2.12 in triangles. We assumed no pre-symptomatic transmission. F) Same as E but assuming 10% pre-symptomatic transmission. Methodological description as well as supplementary results (alternative assumptions) are provided in the Appendix.

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APPENDIX
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Contents

1 Materials and Methods

1.1 The transmission model

We model human-to-human transmission as a discrete-generation, stratified branching process. Strata are the combination of age classes ($[0,18), [18,40), [40,60), [60,80), [80,\infty)$) and the whether the contacts of a detected case are traced and isolated before they can transmit or not. The age-stratified contact matrix C was sourced from Ref. [1] through `socialcontactdata.org`, and normalized so that its spectral radius matched the target R_0. We tested $R_0 = 2.12$ following Ref. [2] a lower value of $R_0 = 1.5$. We seeded the initial infection in the $[60, 80)$ age class, compatible with the cases of the MV Hondius. The number of secondary infections in age class j of an infected individual in class ℓ that could occur in the absence of any control is sampled as follows:

$$X_{\ell j} \sim \text{NegBin}(\text{mean} = C_{\ell j}, \text{variance} = C_{\ell j}\,(1 + \omega C_{\ell j})). \tag{1}$$

We set $\omega = 0$ to model age-stratified community circulation. In Fig. 2 we tested a different value (see Sec. 2) Public-health control is represented as a thinning of this potential offspring distribution. Let ϕ be the probability that an infection is actually occurring, i.e., not prevented by control. This effectively models pre-symptomatic transmission, i.e., the probability that one infection is generated before symptom onset, in the case of prompt and effective isolation of symptomatic cases. It can also model infection after symptom onset but before effective isolation, i.e., isolation stopping all onward transmission. This gives

$$X_{\ell j}^{(\text{occurring})} \sim \text{Binomial}(X_{\ell j}, \phi). \tag{2}$$

The resulting infections are then split according to contact-tracing performance. There is a country-level parameter p that encodes *contact tracing capacity*, i.e., the probability that, for each source individual, its secondary cases are traced and isolated before they can transmit. If they are, they will not generate additional infections, under the assumption that they are placed in effective pre-emptive isolation. Otherwise, they will contribute to onward transmission as described before.

1.2 Parametrization of contact tracing and isolation capacity

We selected 30 countries that have relevant involvement with the occurring outbreak, either because their nationals were known to have been onboard the MV Hondius or been in contacts with cases or people who had been onboard the ship, or because visited by the ship, or because known to have had cases or contacts in their territories. They are Argentina, Australia, Belgium, Cabo Verde, Canada, Chile, France, Germany, Greece, Guatemala, India, Ireland, Italy, Japan, Montenegro, Netherlands, New Zealand, Philippines, Poland, Portugal, Russian Federation, South Africa, Spain, Switzerland, Taiwan, Turkey, Ukraine, United Kingdom, United States.

We used indicators from the Global Health Security (GHS) Index (`ghsindex.org`). We used the indicators *Early Detection and Reporting score* as a proxy for national capacity to trace contacts of cases and isolate them pre-emptively before they can transmit, to parametrize the parameter p.

We assumed a range p_{min} and p_{max} and then computed each country's p from its indicator value x through a linear interpolation:

$$p = p_{min} + \frac{p_{max} - p_{min}}{x_{max} - x_{min}}\left(x - x_{min}\right), \tag{3}$$

with x_{max}, x_{min} computed over the selected countries. We selected $p_{min} = 0.7$ and $p_{max} = 0.95$.

As a proxy for countries capacity to enforce effective isolation of symptomatic cases we used the indicator *Facilities capacity*. We then assumed that no pre-symptomatic transmission occurred and parametrized ϕ through the indicators as the fraction of infection events occurring before effective isolation is in place. We used the same approach as before:

$$\phi = \phi_{min} + \frac{\phi_{max} - \phi_{min}}{y_{min} - y_{max}}\left(y_{min} - y\right), \tag{4}$$

with y_{max}, y_{min} being this indicator computed over the selected countries. We selected $\phi_{min} = 0$ and $\phi_{max} = 0.33$.

2 Supplementary results

In Fig. 1 we report cluster emergence probabilities when setting a cutoff cluster size of 4 instead of 3. In Fig. 2 we test the effect of assuming the overdispersion reported in Ref. [2]. That value, however, however, was estimated in superspreading events and on age-unstratified data. In any case, the different choice had a minimal impact on the results.

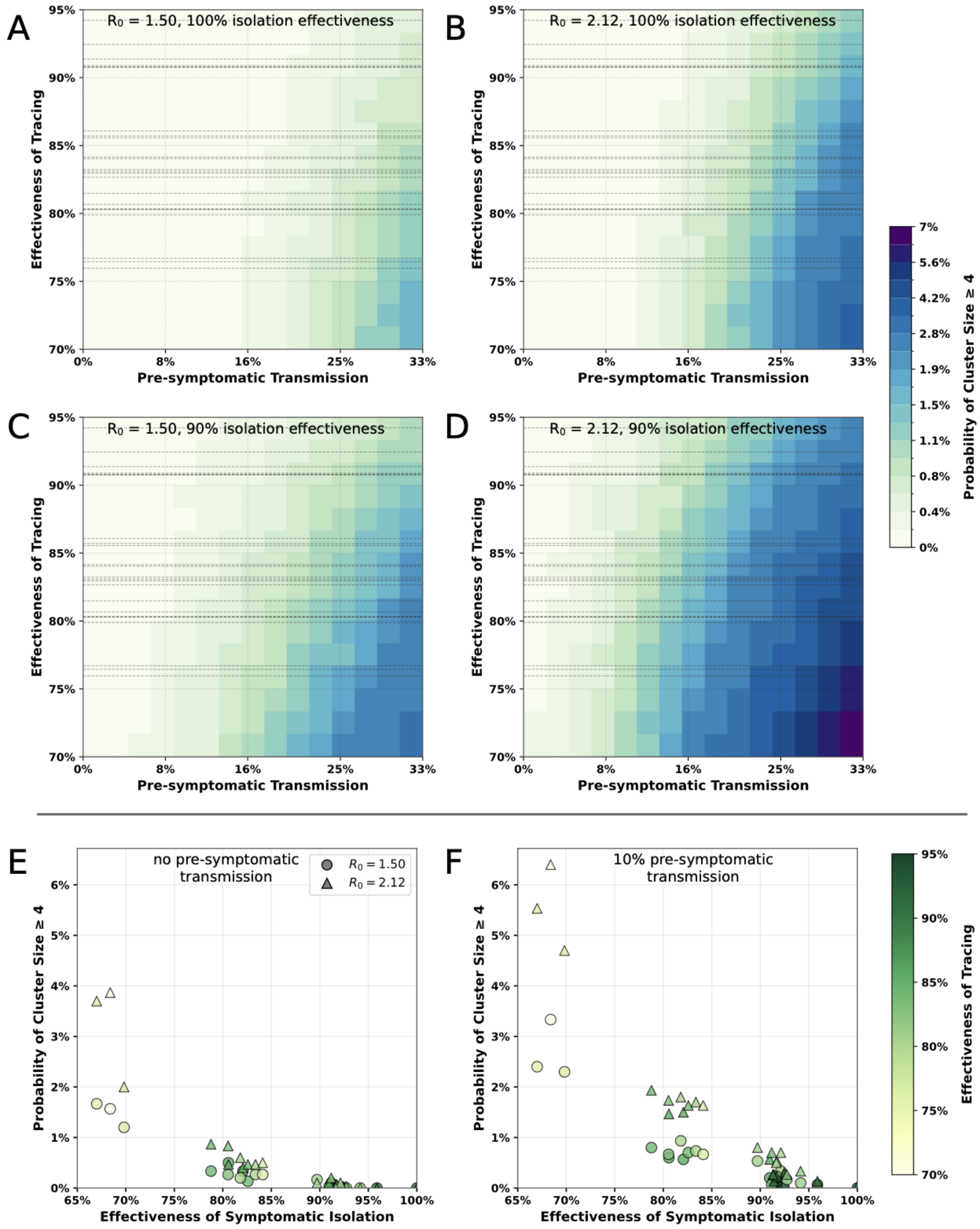

Figure 1: Same as the figure of the main text, but with cutoff cluster size set at ≥ 4.

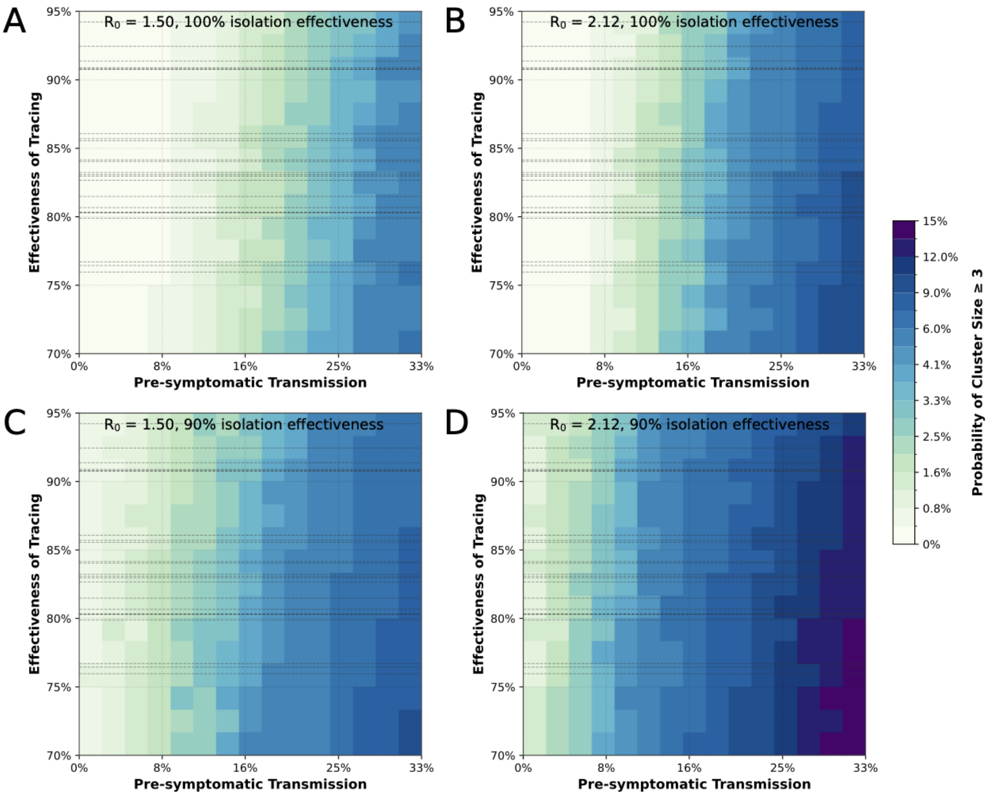

Figure 2: Same as the figure of the main text (panels A-D), but setting overdispersion parameter $\omega = 1.6$ (see Ref. [2]).

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