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Border closure for island nations? Analysis of pandemic and bioweapon-related threats suggests some scenarios warrant drastic action

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The risk to human populations from new and pandemic infectious agents has probably never been higher.[1,2] Synthetic bioweapons are an additional threat. Two recent publications have speculated on the possibility of island nation refuges closing their borders to protect a human population against a catastrophic pandemic that poses an existential risk to humanity.[3,4] The most recent paper described an index based on characteristics of an island nation's population, location, resources and society. The authors used this index to conclude that Australia and New Zealand are the island nations most likely to be able to be both isolated from the rest of humanity in a pandemic and to also have the resources to reboot a thriving technological society following a pandemic that devastated the rest of global society as we know it, thereby acting as 'island refuges'.[4] Previous analysis in this journal has argued the economic case for border closure by island nations in the face of extreme pandemics.[5] This work reported that 100 per cent border closure for six months by New Zealand, that results in the country avoiding any pandemic cases, could have a net present value of NZ$7.86 (US$5.29) billion for its "Scenario A" (involving half the mortality rate of the 1918 influenza pandemic) and NZ$144 (US$96.9) billion for preventing a pandemic with 10 times this mortality.

There is evidence for travel restrictions being successful in controlling the spread of influenza between countries, and small islands successfully used protective sequestration and maritime quarantine to avoid the 1918–1919 influenza pandemic (see this systematic review[6]). However, the 1918-19 pandemic still appeared to reach most of the world's islands. Drastic measures such as border closure have potentially large benefits (if successful) but also potentially major harmful consequences including economic harm. Some of these potential trade-offs are illustrated by the 2014 Ebola outbreak where the GDP of countries affected fell by 12% during the emergency even without successful complete border closures.[7]

According to the International Health Regulations (IHR),[8] countries that adopt measures that significantly interfere with international traffic (such as refusing international travellers' entry or exit for more than 24 hours) must provide the World Health Organization (WHO) with the public health rationale and scientific information for their actions. This wording of the IHR appears to logically permit border closure if the rationale for this intervention is compelling.

However, the question remains, which pandemics, if any, might ever plausibly justify partitioning a segment of the human population through border closure by island nations to reduce major burdens of morbidity and mortality? It is this question we address in the present commentary.

Persisting major pandemic threats

Some analysts consider biological error and/or biological terror to be among the greatest catastrophic risks of the 21st Century.[9] A meeting of UK experts on high impact bio-threats noted that as of November 2018, the world is 'grossly unprepared' to deal with high-consequence bioweapon threats.[10] The WHO Global Preparedness Monitoring Board Report 2019 repeatedly notes widespread lack of preparedness for a significant pandemic.[11] The world faces persisting threats from naturally occurring pandemics, biological weapons, biological mistakes, and as yet unknown biological threats.

Pandemic of existing known organism: There have been four influenza pandemics in the last 110 years (in 1918, 1957, 1968 and 2009), with that in 1918/19 being most severe.[12] Risks may be increasing with air travel, the emergence of more megacities and the intrusion of humans into ecosystems hosting zoonotic pathogens.[13]

Conventional biological weapon or biological terrorism: Some countries (and perhaps individual groups or actors) are likely to still have bioweapon development programs and could use these in conflict situations.[14] There is evidence of disregard for international bioweapon agreements historically and a massive level of deception.[15]

Biological error or laboratory breach: There is a persisting risk that bioweapon agents will escape from laboratories (where they are perhaps being legally studied for defensive purposes or illegally studied for offensive purposes). Existing pathogens could be accidentally modified increasing pandemic threat, by enhancing transmissibility, pathogenicity and antimicrobial resistance.

Emergence of a novel Disease X (or synthetic Disease X): WHO has adopted the placeholder name, "*Disease X*",[16] for any as yet unknown disease that may include emerging and re-emerging disease, or synthetic pathogens with moderate to high case-fatality and transmissibility. Advances in synthetic biology, and also the ease and availability of 'kitchen biology', raise concerns about the potential for production of novel synthetic pathogens which could be released as bioterrorist weapons or used as weapons of war.[13] An exploding number of new scientific publications explain how these manipulations are performed, constituting a risk that this information may be used nefariously.

Border closure options in pandemic plans

It is plausible that for small island nations, border closure could be a rational and effective response to the greatest of these threats. But only if implemented

completely and in time. The option of border closure in severe public health threats of international concern is detailed in planning documentation for some island nations, e.g. New Zealand,[17] the Cook Islands and Samoa, although it is usually not considered a first-line response (references available on request). Some larger islands may have a role in preventing transmission of pandemic diseases to smaller island states that may have limited resources to manage such public health threats, e.g. 'some Pacific countries may request flights from New Zealand be stopped'.[17]

Specifically for influenza, the 2017 New Zealand Influenza Pandemic Action Plan[18] distinguishes 'Keep It Out' and 'Stamp It Out' phases of pandemic response. The Plan states on p.118:

> *In a potential or actual global pandemic, New Zealand may be able to prevent the virus from entering the country or to delay its entry, allowing other response measures to be put in place (during the Keep It Out phase). Such an intervention may be feasible because of* ***New Zealand's geographical isolation, its limited number of entry points and its well-coordinated border management systems*** *… Elevated measures may include increasing information to arriving passengers, providing travel advisories,* ***closing the border to certain categories of arrival*** *or imposing mandatory quarantine for categories of arrivals* (emphasis added).

The plan also notes that any decision might require strong action to be taken initially until the global situation becomes clearer, as measures can always be relaxed, but the option to escalate may have passed.

The New Zealand Ministry of Health emphasises that border closure to keep a pandemic out of New Zealand is an unlikely scenario, and that "most public health threats can be effectively managed with less restrictive measures".[17 (p4)] We agree with this assessment, but it is also important to note that the relevant threats are broader, and potentially more serious, than the specific threat of naturally occurring pandemic influenza, also that some countries may not be able to 'effectively manage' public health emergencies with 'less restrictive measures'.

Which diseases could plausibly warrant border closure for islands?

In what follows we consider three categories of diseases: the 2018 WHO list of priority diseases;[16] a list of bioweapon-related diseases that could plausibly spread to island nations;[19] and a list of additional diseases based on those specifically listed in the *Decision Instrument* of the IHR 2005,[20] if not already covered in the previous two lists.

The diseases we considered were: Crimean-Congo haemorrhagic fever, Ebola and Marburg virus diseases, Lassa fever, Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) coronavirus infections, Nipah virus infection, Rift Valley Fever, Zika Virus infection, Emerging Disease X (e.g. zoonotic threat), Synthetic Disease X (e.g. weaponised biological agents, engineered pathogens), smallpox, pneumonic plague, anthrax, botulism, tularaemia, novel human influenza subtype infection, wild-type poliovirus infection, cholera, yellow fever and West Nile fever.

For each disease we considered the potential for human-to-human transmission in an island setting, the feasibility of control using effective and available interventions, and the potential for high case-fatality. The option of border closure was then considered in the context of these epidemiological characteristics and from considerations of cost-effectiveness and cost-benefit analyses, which unfortunately only exist for New Zealand.[5,21] For interested readers, Supplementary Table S1 summarises the selected diseases, their epidemiological characteristics and our border closure recommendations.

Based on the known epidemiological characteristics, most of these diseases would never appear to require border closure as a control option for island nations. However, the pros and cons of border closure should be considered for the following exceptional diseases if the risk of spread to the island nation is plausible: human influenza caused by a new subtype with high transmissibility and case fatality (approaching, or exceeding, the severity potential of the 1918 pandemic); smallpox; an unknown emerging *Disease X*, such as a newly emerging zoonotic disease with human-to-human respiratory spread; or a novel synthetic *Disease X*, such as a bioweapon (e.g. that enhanced a known organism such as the plague bacillus by making it resistant to available antibiotics). The reason that these four exceptional cases may warrant border closure is because the pandemic has the potential to exhibit relatively high transmissibility, high case-fatality and difficulties for containment (as described in Supplementary Table S1) when compared with other diseases (a number of which are considered in Supplementary Table S1).

Table 1 illustrates this conceptually indicating which pandemic diseases might ever plausibly warrant border closure for island nations. The largest threats are those listed in the right upper quadrant of the figure, which exhibit the combination of high transmissibility and high case fatality. We suggest that new modelling work be undertaken to define specific thresholds in terms of transmissibility and case fatality at which border closure becomes compelling for various islands, both from a public health perspective and a long-term economic perspective. For novel diseases, early outbreak epidemiological data would be essential to determine which quadrant the new threat lies in.

Supplementary Table S2 gives further details by outlining one scenario where border closure might be rational for the benefit of some islands, or where closing an island's borders might be rational to partition its population from the rest of the world's population in a situation where there is an existential threat to humanity.

Table 1: Conceptual approach to which pandemic diseases might ever plausibly warrant border closure for island nations, the largest threats are those with high transmissibility and high case fatality.

	Relatively low transmissibility	Relatively high transmissibility
Relatively high case fatality risk	Middle East Respiratory Syndrome (MERS) Ebola virus disease (EVD) Severe Acute Respiratory Syndrome (SARS) Avian Influenza A(H5N1)	Novel non-seasonal influenza (approaching the severity potential of the 1918 influenza pandemic) Smallpox An emerging *Disease X* (e.g. emerging zoonotic disease) A novel synthetic *Disease X* (e.g. a bioweapon)
Relatively low case fatality risk	Influenza A(H1N1) – 2009 pandemic Poliomyelitis	Chickenpox Measles

Discussion

The key conclusion of our analysis is that there is a small number of exceptional scenarios where border closure to prevent severe human morbidity and mortality locally, or a designated island refuge to preserve human civilisation, would be advantageous.

These scenarios are the 'right upper quadrant pathogens' from Table 1: severe novel non-seasonal pandemic influenza, smallpox and two forms of *Disease X* (i.e. natural as in an emerging zoonotic disease; and synthetic as per a bioweapon). For these scenarios, we recommend that health officials now focus on articulating measurable triggering thresholds for border closure (i.e. elaborating on Table S2).

At the final stage of writing, the zoonotic coronavirus causing COVID-19 began spreading around the world. On the basis of early information, this novel virus appears to have relatively high transmissibility (though some countries appear to have successfully contained it) and a case fatality risk of about one per cent. In terms of the need to "keep it out" of island nations such as New Zealand, the health burden impact has been supplemented with discussions around health equity, the risk to those with comorbid conditions and the need to protect Pacific countries and territories. Such considerations seem relevant to borderline decisions where the imperative to close the border is not clear-cut. While full border closure probably does not seem justified for COVID-19 from a societal view (considering both health and the economy), targeted travel restrictions directed at source countries might possibly be justified. That is if these expand preparation time in the initial weeks – but only if the country uses this time to actually prepare in a meaningful way (e.g. for widespread testing, case isolation, contact tracing and quarantine of contacts).

Our commentary has looked at a limited set of concerning diseases and could be expanded. The list of potential bioweapons is far from complete. Also, developments with gene editing technology could permit a wide array of bioengineered and synthetic bioweapons that could escape from laboratories or be released deliberately. The scenario described in Supplementary Table S2 is highly simplified and could benefit from more detailed development by experts in synthetic biology, disease surveillance, policy-making, ethics and law.

Government agencies could commission further work by national science bodies or universities with relevant expertise to determine how best to deal with such threats and to evaluate the costs and benefits from a societal perspective. An important consideration will be a risk assessment to identify the level of severity where healthcare provision will be overwhelmed with uncontrolled pandemic spread. This might tip the calculus in favour of border closure and will vary from island to island. Planning for generic mitigation strategies such as border closure (or indeed food and medicine stockpiling) may help ensure resilience and mitigate not just pandemics but a range of other catastrophic threats.

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Supporting Information

Additional supporting information may be found in the online version of this article:

Supplementary Table S1: Selected infectious diseases/intoxications and their relevance to potential border control being used by a developed country island nation.

Supplementary Table S2: Possible scenario and timelines for *Disease X*.

Supplementary Table S3: Vignettes of pandemic threats that could require rapid border closure.

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