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Zero-COVID-UK: What efforts to eliminate nine neglected tropical diseases can teach us about this disease target

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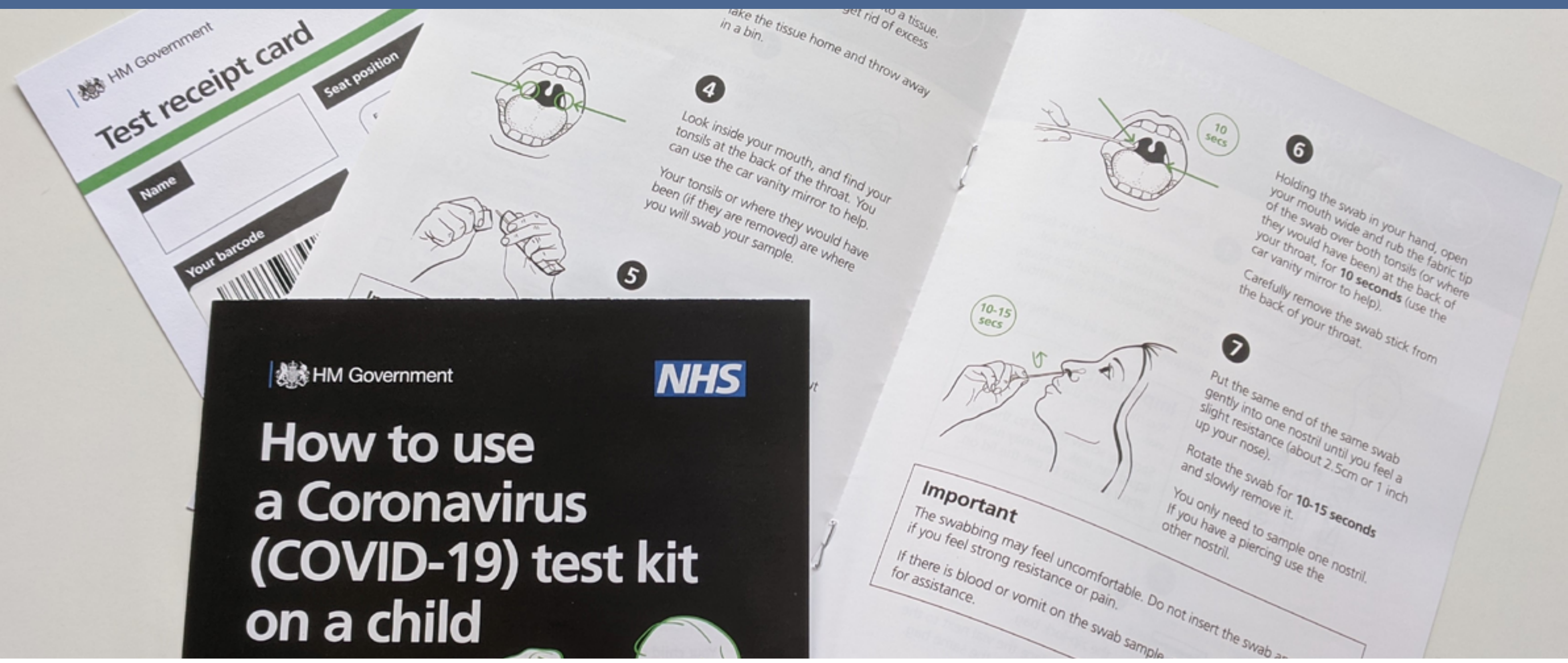

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Abstract

As the United Kingdom determines its next moves in responding to the COVID-19 pandemic, a growing number of voices are asking the Westminster Government to consider a disease elimination strategy for all four nations of the UK. This is in part due to New Zealand's example of favouring an elimination approach, but also a reflection of the relative success of Scotland and Northern Ireland in handling the pandemic (earlier in the year). Nevertheless, there is opposition to adopting such a goal within government, and vocal scepticism towards elimination as a disease target internationally. By reflecting on the experiences of nine neglected tropical diseases (NTDs) already marked out for elimination, this commentary hopes to inform the debate on Zero-COVID-UK. Firstly, by conveying a better sense of what elimination is (and is not); and secondly, by pointing to the additional value a disease elimination framework can provide for strategic planning. The experience of the NTDs demonstrates that elimination is a tailorable and temporary goal that can provide a template for action in the short-term, while also informing gap analyses. It also suggests that progress toward elimination centres as much on fidelity to proven public health measures and fostering local understanding, as it does on attaining technological advancements. In this light, one might reasonably describe COVID-19 elimination as a statement of intent, whereby a government adopts the position that the death toll and sequelae associated with COVID-19 transmission are unacceptable at any level.

Keywords: disease elimination; neglected tropical disease; Zero-COVID-UK; COVID-19; United Kingdom

During the 20th century, the African continent suffered three epidemics of the deadly parasitic disease human African trypanosomiasis (HAT). The last epidemic, which struck in the 1990s, peaked at 450,000 cases, but each outbreak has proved cataclysmic in terms of death toll and wider social and economic impact (Barrett 2006; Simarro et al. 2011).[1] Analogous to a spark that can set off a raging forest fire, it is the sinister capacity of HAT to lay dormant for decades before resurging at full strength that has proven to be its most frightening aspect. Yet, in 2018, there were just 977 cases of HAT identified across the African continent and, unlike in the past when it was widely accepted that HAT was routinely under-reported due to its non-specific presentation, today national programmes can have some confidence in their case reporting.[2] This is because HAT programmes are now guided by two disease elimination goals (focused on the *T. b. gambiense* strain). The first—set for 2020—aims to eliminate HAT as *a public health problem* in countries of focus using a combination of vertical and horizontal measures (defined as the reduction of *gambiense* HAT incidence to less than one new case per 10,000 population at risk in at least 90% of countries of focus, with fewer than 2000 cases reported globally). The second—set for 2030—aims to stop the global transmission of HAT entirely, with HAT diagnosis and treatment protocols fully integrated into national health systems to facilitate ongoing surveillance and response.

In August 2020, Togo became the first endemic country in Africa to formally eliminate HAT *as a public health problem.* The setting and pursuit of elimination goals for HAT has helped alter the trajectory of infection rates, stimulated product innovation for a disease of poverty, and informed the system-wide approaches needed to identify and respond to new and re-emerging cases in the future (Taylor and Smith 2020). As the world ponders how to live with COVID-19—another disease with the capacity to bounce back exponentially—it is worth exploring what lessons attempts to eliminate Neglected Tropical Diseases (NTDs) like HAT can teach us about elimination as a disease target.

In July 2020, the independent scientific advisory group to the UK government on COVID-19 published a report entitled *Zero-COVID-UK: Why Is England Not Pursuing an Elimination Strategy?* (Independent SAGE 2020). Citing the example of New Zealand, which from late March 2020 has operated on the basis of a COVID-19 elimination policy, the report seeks to persuade the UK government to rapidly move toward the objective of achieving ‘a Zero COVID UK, i.e. the elimination of the virus from the UK’ (2020, 1). This is defined as the ‘reduction to zero of new infections among people living in a country and the presence of the measures to prevent or deal with imported cases and associated spread from new arrivals’ (2020, 2). An elimination stance is slowly gaining traction in the UK, supported initially by the Scottish government’s decision to pursue regional elimination (Scottish Government 2020; Sridhar and Chen 2020) and more latterly by a cross-party committee of MPs in Westminster (Roach 2020).

Outside of this, the reaction to a proposed elimination goal for the UK as a whole has been less than supportive, with the Chief Medical Officer for England actively speaking out against disease elimination as a policy objective (Devlin 2020). Opposition within the media and on social media platforms goes further, ranging from pessimistic fatalism (‘impossible’) to out-and-out vitriol. Sceptics, like the US president, have been quick to jump on New Zealand’s seeming inability to sustain its elimination status in light of the recent COVID-19 outbreak in Auckland (Roy 2020). Yet such sceptics have likely misunderstood what is meant by the term ‘elimination’ in the first place (it does not denote a permanent status). They may also have failed to appreciate the time imperative attached to the Auckland response, which, guided by a defined elimination strategy, saw the city rapidly locked down. Having studied the changing fates of nine NTDs marked out for disease elimination, I’m now interested in identifying the specific areas of contention and controversy relating to the setting of a UK-wide elimination goal for COVID-19. The question is relevant for two reasons: firstly, because many of the measures required to reach elimination already align with what is needed to suppress the virus under the UK’s current approach (i.e., a functioning Find, Test, Trace, Isolate, Support (FTTIS) system and specific plans to contain and suppress local flare-ups); and secondly, because without the sudden introduction of a ‘silver bullet’ intervention, such as a vaccine, it is hard to envisage a better alternative to an elimination goal for the UK, which currently lacks a defined strategy for handling the next stages of the pandemic (Independent SAGE 2020).[3]

In the new millennium, the case was made that a number of tropical infections should be taken forward as a group by virtue of their ‘neglected’ status and shared geographic overlap, and because cost savings and synergies could be levied if the different disease programmes acted together (Molyneux et al. 2005; Smith and Taylor 2013). Of an initial 17 NTDs marked out for attention by the World Health Organization, nine were set global and regional elimination goals: Chagas disease, dog-mediated rabies, human African trypanosomiasis, leprosy, lymphatic filariasis, onchocerciasis, schistosomiasis, trachoma, and visceral leishmaniasis (WHO 2012). By drawing on the example of the NTDs, I hope to convey a better understanding of what elimination is (and isn’t) and to posit the added value of adopting a disease elimination framework in order to better inform the evolving debate on the prospect of a Zero-COVID UK.

Image 2: Microscopy retains a central role in NTD diagnosis (photo credit: DiaDev project, Edinburgh University).

A tailorable and temporary target

Given the 24-hour news cycle and the unprecedented pace of data production around COVID-19, it is hardly surprising that some of the language used to describe the outbreak is being deployed too casually. One common misstep is the use of the term disease 'eradication', which has been deployed erroneously by several parties. While the notion of eradicating COVID-19 aligns well with the military metaphors commonly used when discussing illness in the modern era, disease eradication actually has a very precise meaning, one that makes more sense if you recall that only one disease affecting humans has ever been eradicated (smallpox). At the current time, the correct word to describe most national approaches to COVID-19 would be 'control' (although 'mitigation' and 'suppression' are also used). Helpfully, the interrelated terms 'control', 'elimination', and 'eradication' as they relate to disease have been clearly defined (see Box 1).

Word	Definition
Control	The reduction of disease incidence, prevalence, morbidity, or mortality to a locally acceptable level as a result of deliberate efforts. Continued intervention measures are required to maintain the reduction.
Elimination	The reduction to zero of the incidence of a specified disease in a defined geographical area as a result of deliberate efforts. Continued intervention measures are required.
Eradication	The permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts. Intervention measures are no longer needed.

Box 1. Glossary of control, elimination, and eradication terminology (Molyneux et al. 2004).

These definitions help us distinguish between eradication and elimination by pointing out that it is the continued need for intervention measures that renders elimination the less ambitious goal. In addition, eradication is always a global goal, whereas elimination can be set globally or target a smaller geographical area. To expand, of the nine NTDs that have been marked out for disease elimination, four are targeted for global elimination (human African trypanosomiasis, leprosy, trachoma, and visceral leishmaniasis) and five for regional elimination (Chagas disease, dog-mediated rabies, lymphatic filariasis, onchocerciasis, schistosomiasis) (WHO 2012). Scrutinising the precise wording of disease targets therefore becomes important, and should alert us to the fact that an elimination goal is to some extent tailorable. Indeed, some critics have argued that elimination when set at anything less than zero transmission is little more than a control target—but it is one that sounds tantalisingly similar to eradication, with all the promise that holds (Stepan 2011).

Disease elimination should be understood as a temporary status that can be won and lost (and regained once more). Consider the example of measles: the UK was awarded elimination status for measles by the WHO in 2017 (defined as the absence of circulating measles), only to lose it again in 2019. By working to increase vaccine uptake, the country is now working toward regaining its elimination status. While the WHO has clear guidelines for attaining and certifying measles elimination status, it has been largely silent on the question of how and when COVID-19 might be eliminated. In the immediacy, therefore, it would be up to countries to determine their own strategic approaches for reaching COVID-19 elimination, as New Zealand has (Baker et al. 2020a).

To summarise, without a vaccine option or any evidence of natural herd immunity at this time, the eradication of COVID-19 is currently off the table. An elimination goal, on the other hand, could make sense in some focal countries given the imperative to stop person-to-person transmission in order to save lives, protect health systems, and curtail dangerous sequelae. To date, island settings are depicted as having an advantage in targeting COVID-19 elimination given their stronger control over borders (Graham-Harrison 2020), but the experience of Scotland is increasingly indicating that a single region can realistically aim for elimination even when sharing a border, providing it has autonomy over its health policy and funding (Sridhar and Chen 2020). Indeed, it was the relative success of Scotland, Northern Ireland, and the Republic of Ireland in suppressing COVID-19 compared to England earlier in the year that created the rationale for Independent SAGE (2020) to recommend a four-nations approach to COVID-19 elimination for the UK.

Elimination provides a template for action and guides gap analyses

A major advantage of pursuing an elimination goal is its capacity to provide a template for action. Here, again, lessons can be drawn from NTDs. While pharmaceutical solutions played an extremely important role in helping to get many of the NTDs, like schistosomiasis and onchocerciasis, under control, the move toward seeing nine of them eliminated has required a more nuanced approach which, while still reliant on treatment, has incorporated more preventative measures and (where applicable) the production and analysis of diagnostic data (Taylor 2020). Just as good-quality diagnostic data is seen as pivotal to the successful suppression of COVID-19 (for use in test and trace systems), real-time data from diagnosis is increasingly informing NTD programmatic decision-making, both at a local level and through international data platforms like Tropical Data (**https://www.tropicaldata.org/**) and ESPEN Collect (**https://espen.afro.who.int/tools-resources/espen-collect**). Diagnostic data in support of NTD elimination programmes is being used for different use cases: to map the geographical spread of NTDs; to determine whether disease programmes need to scale up or scale down interventions; to confirm decisions to stop interventions; and, once elimination targets are met, to help sustain success through surveillance measures (Taylor 2020). In this way, a disease elimination target can be seen as progressing a set of finite stages, which themselves can be used to inform policy in the immediate term, while also preparing programmes for a future exit strategy.

Planning for elimination can also help programmes identify the ways in which they might wish to deploy different diagnostic tools now and in the future (in a sequence, for example, or at the different tiers of the health system). Planning can also help those involved in programmes think about the ways they might come to digitise and transmit data so as to facilitate real-time decision making. Within this guiding framework, even when a diagnostic solution for a particular use case does not yet exist, an elimination target can help national programmes identify the kind of tools they still need so that they can then articulate this unmet need to developers. This gap analysis is of course applicable for other health products too, like vaccines and medicines. Target Product Profiles (TPPs) provide one mechanism through which disease programmes might articulate needs to developers. A TPP is a description of the ideal specifications needed for a given product, and is based on the needs of the patient and the main characteristics of the health system that serves them. The NTD community has played an active role in highlighting and articulating unmet needs for new tools to support NTD elimination programmes. This is because, as 'diseases of poverty', NTDs are not profitable avenues of research, meaning they struggle to stimulate investment in product development (MSF 2001; Taylor and Smith 2020). And although the profitability of COVID-19 products seems assured from an industry perspective ('Since the start of the COVID-19 crisis, more diagnostic tests have been developed for SARS-CoV-2 than for all 20 NTDs in the last 100 years' [de Souza et al. 2020, 4]), it will be of fundamental importance to ensure that access to COVID-19 products is equitable and that products are appropriately designed for the full range of patients and health settings that need them.

Criteria for success: fidelity to the basics and fostering local understanding

NTDs tend to proliferate in remote and impoverished areas underserved by formal healthcare structures. In this way, the study of the nine NTDs tells us that the decision to eliminate a disease doesn't necessitate high-performing health systems or a perfect product arsenal from the outset. Several of the NTDs, like HAT, were deemed 'tool deficient' when their original elimination targets were set (Médecins Sans Frontières 2001; Taylor and Smith 2020). Nevertheless, initial progress was achieved thanks to fidelity to a set of proven approaches delivered vertically and at scale (Simarro et al. 2011). Several of the NTD programmes targeting elimination, like Chagas disease and schistosomiasis, could still benefit from better tools, particularly around diagnosis (WHO 2020); nevertheless, national programmes have found workarounds to compensate for shortcomings while better approaches are sought (e.g., by conducting repeat testing or deploying tests in combinations and algorithms) (Taylor 2020).

Image 3: Materials for schistosomiasis field testing (photo credit: DiaDev project, Edinburgh University)

A feature of most elimination (and eradication) programmes is that great progress can be wrought in the early stages of a given campaign by transplanting a similar set of interventions *anywhere*. A number of NTD programmes—like onchocerciasis and lymphatic filariasis—have made notable progress toward elimination targets through the delivery of mass drug administration (the distribution of treatment to large numbers of people without need for diagnosis) (WHO 2020). The essential difficulty with elimination (and eradication) comes as you approach the endgame: when case numbers are down, community compliance begins to falter, and the costs attached to finding/preventing residual cases begins to escalate. Indeed, this is a key argument frequently used to discourage the setting of elimination and eradication targets in the first place: that after a certain point, the cost/benefit equation stops stacking up (BMJ 2020; Stepan 2011). However, NTD programmes have demonstrated that there are several ways to improve programme efficacy even as disease prevalence declines. The first is to improve the product arsenal. The elimination of HAT (meaning zero transmission) has become feasible thanks to the development of new tools that can be integrated into existing health structures (a safer oral treatment and rapid diagnostic tests) (Taylor and Smith 2020).

A second but equally important route to improving programme efficacy over time is to fine-tune interventions according to the particular needs of local settings. In support of NTD disease targets, initiatives like COUNTDOWN 2020 (**https://countdown.lstmed.ac.uk/**) and the Coalition for Operational Research on NTDs (**https://www.ntdsupport.org/cor-ntd**) have demonstrated how implementation and operational research, as well as the inclusion of social science disciplines in mixed-method approaches, can help make sense of factors that will increase/decrease the likelihood of success in a given setting over time (Parker et al. 2016). Involving local stakeholders in the co-production of this style of research drives up the likelihood that research findings will be appropriate and relevant. In short, as elimination looms, understanding the local settings in which disease programmes operate becomes an important determinant of elimination success. Appreciating the manner in which diagnostic data can also aid local understanding and programme adaptation is another key message to emerge from the NTD space (Taylor, 2020).

Image 4: Microscope station at the microbiology and molecular laboratory, Makerere University, Uganda (photo credit: DiaDev project, Edinburgh University).

It is pertinent therefore that much of New Zealand's success to date has been credited to its localised Find, Test, Trace, Isolate, Support (FTTIS) approach, which is managed through the country's 12 national health services (in addition to tight border control). New Zealand's elimination strategy has never hinged on major technological advancement, but rather on its fidelity to a number of proven public health measures delivered with local oversight. In this manner, one of the country's most important steps toward securing COVID-19 elimination was to urgently increase its workforce for contact tracing (Baker 2020b). In contrast, the poor performance of England's test and trace system has been blamed on a centralised approach that favoured private contractors over local public health teams (Mueller 2020).

Conclusion

Given the unprecedented nature of the threat, it is not surprising that the majority of countries have found themselves firefighting in the face of the COVID-19 pandemic. With a high proportion of countries also operating under pandemic plans better suited to an influenza outbreak, it made sense that early intervention measures favouring a mitigation or suppression approach were adopted to 'flatten the curve'. With influenza, there is no expectation of a pandemic being contained. Yet what the early experiences of China and New Zealand demonstrate is that, in light of its longer incubation period (median five to six days), there is an opportunity to contain COVID-19 (Baker et al. 2020a; WHO–China Joint Mission 2020). And, in some settings, particularly island states like the UK, this opportunity could lend itself to an elimination approach.

One of the main criticisms Independent SAGE levelled against the British government in July was that it had 'seen no evidence that the government has a considered strategy for the next stages of handling the pandemic in the UK' (2020, 3). This overview of how a disease elimination framework has worked for nine NTDs has attempted to show how the simple act of setting an elimination goal can create a template for action by helping countries move from a reactionary firefighting position to a proactive strategy of fire containment.[4] This is what the WHO, working in collaboration with other partners, has helped achieve for the deadly parasitic disease HAT. Given that HAT is an unprofitable 'disease of poverty' (a clear disincentive for industry to invest in product development and manufacturing), that the disease poses zero threat to global health (as a vector-borne disease, it is geographically contained in the tsetse fly belt of sub-Saharan Africa), and that the disease tends to proliferate in remote and rural areas underserved by formal health provision, one might reasonably proffer that the UK government is better positioned to contemplate the elimination of COVID-19 than many of the African governments that have embraced HAT elimination.

A disease elimination target doesn't require nation states to start from a particular position or to follow a set range of interventions. Rather, it is tailorable—interventions can be switched in and out depending on their impact in a given locale, and regional goals could feasibly become national goals over time. A disease elimination goal simply implies that countries plan with the end in mind by working through a set of logical stages. Subsequently, one might reasonably describe COVID-19 elimination as a statement of intent, whereby a government adopts the position that the death toll, sequelae, and possible years of social and economic dysfunction associated with COVID-19 transmission are unacceptable at any level (Alwan 2020; Independent SAGE 2020; McKee and Stuckler 2020). For the UK, which is in the midst of a second wave, a Zero-COVID-UK may seem like a far-fetched ideal for the time-being, but as our knowledge around the virus continues to grows and our approaches for dealing with it strengthen, I suspect an elimination target will come up for debate again.

Endnotes

1. Thirty-six African countries are endemic for human African trypanosomiasis.
2. See, for example, **https://www.who.int/news-room/fact-sheets/detail/trypanosomiasis-human-african-(sleeping-sickness)**
3. Decades of vaccine research have so far failed to produce a vaccine for HAT (La Greca and Magez 2011).
4. One of the advisors to the New Zealand government, Prof. Michael Baker (University of Otago, Wellington), used the analogy of a forest fire when describing the country's three-pronged elimination strategy. Component 1, 'Exclusion of cases', entails strict border control, and can be likened to a firebreak; Component 2, 'Case and outbreak management', involves test, trace, and isolate, and is akin to stamping out hotspots; and Component 3, 'Reducing transmission', uses measures like physical distancing and mask-wearing to douse out the main flames (Baker 2020b).

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