



Disease X: Combating the next pandemic needs the nifty wastewater-based epidemiology tool

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Dear Editor,

The recent article [1] by Kate Bingham and Tim Hanes is a reminder and a warning that the next pandemic is inevitable, and it can potentially prove to be even more lethal than the last one. As noted by Kate Bingham and Tim Hanes, the flu pandemic in 1918–1919 caused an estimated 50 million deaths globally, and today one of the many viruses circulating have the potential to cause as much destruction internationally, this pathogen being Disease X.

Disease X is the name of a currently unknown pathogen that can cause a lethal epidemic globally by the WHO [2]. The list of pathogens that are currently under surveillance by the WHO for effective counter measures include COVID-19, Lassa fever, Middle East Respiratory Syndrome (MERS), Ebola virus, Zika Virus and Disease X.

The worry over Disease X arises as a consequence from an increasingly globalized and connected world [1,3]. The major concern being that with the rapid increase in population, large scale deforestation and presence of animal markets (such as the one in Wuhan, China, considered to be the origin of the COVID-19 pandemic) will result in the breakdown of barriers between animals which act as reservoirs of such diseases ultimately leading to the rise of a pathogen that potentially can be as infectious as SARS-CoV-2 combined with the fatality rate of illnesses such as Ebola leading to widespread catastrophe and death.

Whilst Kate Bingham focuses on the role of bolstering the production of vaccines to mitigate Disease X, it is equally imperative to monitor current vectors of infection of Disease X, one effective means being wastewater-based epidemiology (WBE) [4]. This methodology typically involved tracking a pathogen, such as SARS-CoV-2 RNA in wastewater and is a useful modality in supplementation to direct monitoring of diseases globally. It gained rapid prominence especially during the last 3 years as noted recently by Barcellos et al. in their review article and has been effectively used for monitoring not only disease pathogens but also illicit drug use and also pharmaceutical substances [4].

Hamouda et al. in their review article [5] talk in length of the lessons learnt whilst using WBE in tracking the spread of SARS-COV-2, and hence provide a framework that can be applicable for tracking Disease X. WBE can be effective in tracking infectious diseases in communities and can be helpful in low-and-middle income countries where limited

resources restrain direct testing of a large portion of the population along with the widespread presence of asymptomatic cases, such as in COVID-19. WBE has been effectively used for tracking viruses such as poliovirus, coxsackie virus and rotaviruses as noted by Hamouda et al.

However, a drawback of this WBE is that it can only provide pathogen concentrations in the water and not actual disease numbers. A recent paper by Lai et al. chose to address this challenge by incorporating time-series based machine learning (TSML) to boost the capacity of predicting COVID-19 cases using WBE [6]. They found that TSML enhanced the performance of WBE for tracking disease cases and was comparable, and in some instances even superior, to traditional disease monitoring using regression modeling alone. The use of AI to triage patients using COVID-19 as a disease model has also been noted by Charkoftaki et al. who utilized a machine-learning model of disease to triage patients having various clinical and metabolomic data and estimated patient hospitalization length, disease severity and need of transfer to the intensive care unit [7].

In light of this, the role of AI becomes significant in not only tracking the next pathogen, Disease X and can augment the role of WBE. The advent of Large Language models such as ChatGPT and Google Bard offer unique tools that can be of advantage and potentially prove revolutionary to the field of medicine [8]. With these tools at the helm, tracking the spread of Disease X using WBE can serve to ease global concerns about the warning raised by Kate Bingham and serve to provide another modality to be prepared for the next pandemic.

Leach et al. in their article discussed on how COVID-19 fundamentally changed the world, after it brought societies and economies to a stand-still [9]. It forced a reflection on how massively underprepared the world was. It also forced a shift in healthcare policy in monitoring disease outbreaks, with a new formed focus on epidemiological models driving underlying health policy decisions. Possas et al. [10] proposed a unique model based on the One Health paradigm and use of AI models to combat Disease X despite acknowledging the revolutionary change in vaccine development following the COVID-19 pandemic.

An approach that is grounded in tracking Disease X through WBE is the need of the hour, with Kate Bingham's clarion call to take action against Disease X once again bringing to the forefront the need to not only focus development on vaccines but also on disease monitoring and

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use of AI tools to augment current WBE traditional models to track and trace the next pandemic. Disease X is like a killer lurking in the shadows waiting for the right environmental and genomic milieu provided by the globalized world, and will strike without warning. WBE can serve as an effective tool to shed light on the next pandemic and make sure we are prepared before it can bring the world the devastation COVID-19 did.

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Author contribution

Ishrat Mohd and Namra Vinay Gohil: Conceptualization, Data curation. **ArunSundar MohanaSundaram:** Supervision, Writing-Original draft preparation. **Swathi Gurajala and Fabio Fuentes Gandara:** Validation, Writing- Reviewing and Editing. Investigation. **Md. Rabiul Islam:** Supervision, Writing- Reviewing and Editing.

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Consent

Not applicable.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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