Developing an analysis to determine the Value of Time when delaying the WHO's seasonal influenza vaccine strain selection recommendation

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INTRODUCTION

- **Seasonal influenza** is associated with a substantial clinical and economic burden globally:
  - Causes 3-5 million severe cases and 290,000-650,000 annual deaths globally.[1]
  - Incurs an annual economic burden of approximately $11.2 billion in the U.S..[2]
- One of the most effective approaches for preventing influenza is through use of **seasonal vaccines**.
- The **World Health Organization (WHO)** conducts annual consultations to determine the vaccine strain composition six to eight months prior to the start of the flu season.[3]
  - Antigenic drift during this period can lead to mismatches between vaccine and circulating strains, potentially impacting vaccine effectiveness (VE).[4]
  - The **impact of delaying WHO's recommendations** nearer to the time of vaccine distribution on VE is not well understood.

OBJECTIVE

- The objective of this study was to:
  - Conduct a **review** of the available data sources to inform a novel analytics approach designed to simulate the WHO's vaccine virus strain recommendations.
  - **Assess the benefit** of delaying the WHO's influenza vaccine strain selection process through a value of time (VoT) analysis.

METHODS

- A targeted literature review (TLR) was conducted to assess the criteria used by the WHO in their decision-making process to determine their influenza vaccine strain recommendations for the upcoming flu season.
- The TLR consisted of iterative keyword searches in PubMed (including influenza terminology, the selection criteria), government websites, key national health agencies websites (e.g., Centers for Disease Control and Prevention [CDC], WHO), and free text searches to identify data sources reporting on the strain selection process.
- For each identified criteria, publicly available data sourced from WHO vaccine strain selection reports and national databases found via grey literature searches, were compiled and reviewed to assess the feasibility of replicating the WHO's decision-making process for vaccine virus strain selection using publicly available data.
- Based on the data available, a method was developed that could potentially be used to replicate the WHO's vaccine strain selection process.

RESULTS

Literature review

- Seven strain selection criteria are considered in the WHO's vaccine strain selection: epidemiological, genetic, antigenic, serological, and vaccine effectiveness data, along with viral fitness forecasting and candidate vaccine virus information (Table 1).
- The weighting imposed to each criteria by the WHO during the selection process is unclear.

VoT analysis

- Based on the available epidemiological, genetic, and antigenic data, a metric was developed to determine the degree of coverage that each candidate vaccine virus strain may cover across the circulating influenza subtypes (i.e., how well each prevalent strain within the total population is covered by each candidate vaccine virus).
- A ranking system was created for each criteria to determine the most appropriate vaccine virus selection for the upcoming season.
- The WHO recommendations for 2022-2023 and 2023-2024 northern hemisphere were compared to the ranking of coverage from the vaccine virus strains to validate the methodology by the new method for influenza A H1N1 and influenza B Victoria.
- This method could be used to explore the impact of delaying the vaccine strain selection by generating predications for an "optimized strain" – the strains that would have been selected if WHO recommendations occurred nearer the start of the influenza season.

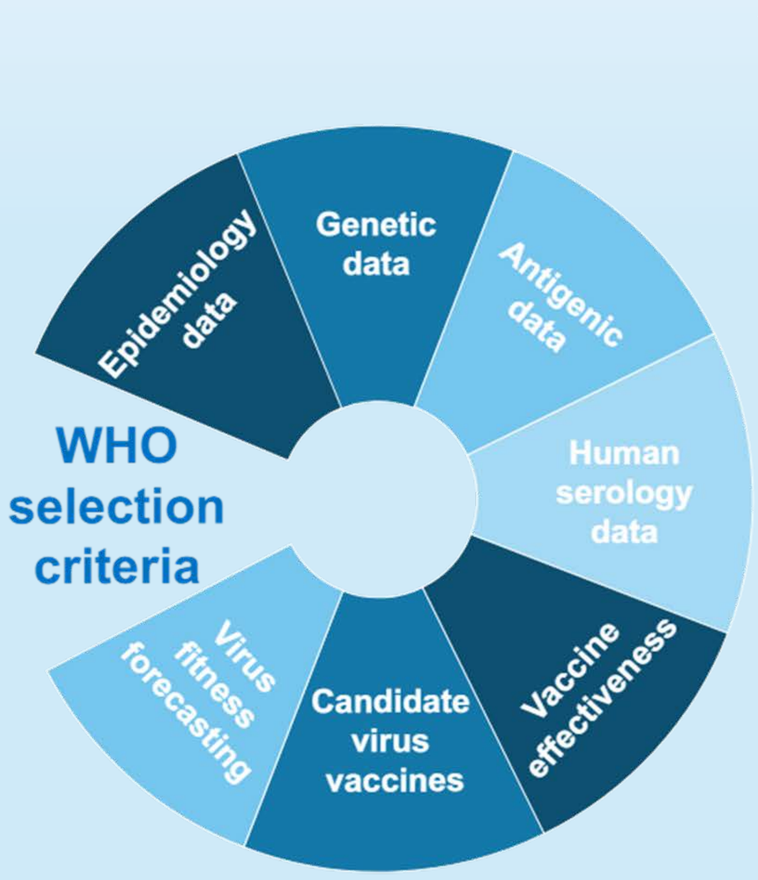
CONCLUSIONS

- The VoT analysis provides a data dependent methodology that could replicate the vaccine strain selection process.
  - Accuracy is dependent on the amount of data available.
  - Further research into the data and methods used by the WHO, and the involvement of clinical experts would allow for a more accurate reflection of the WHO's vaccine virus strain selection process.
- Estimating the relative vaccine effectiveness of the optimized vaccine versus chosen strain (while recognizing the assumptions and limitations) could inform an economic model to estimate the impact of time delay on clinical and economic outcomes of seasonal influenza.

References

1. World Health Organisation. Influenza (seasonal). Published 2018. Accessed August 2023.
2. Putri WCWS, Muscatello DJ, Stockwell MS, Newall AT. Economic burden of seasonal influenza in the United States. Vaccine. 2018;36(27):3960-3966.
3. Centers for Disease control and Prevention. CDC Seasonal Flu Vaccine Effectiveness Studies. 2022.
4. Centers for Disease Control and Prevention. Key Facts About Seasonal Flu Vaccine. 2022.
5. World Health Organisation. Global Influenza Programme: FluNet. 2023.
6. Nextstrain. Seasonal Flu: Real-time tracking of influenza evolution. 2023.
7. Centers for Disease Control and Prevention. Antigenic Characterization. 2023.
8. Centers for Disease Control and Prevention. Human Serology & Flu. 2023
9. World Health Organization. Candidate vaccine viruses and potency testing reagents. 2023
10. Centers for Disease Control and Prevention. CDC Seasonal Flu Vaccine Effectiveness Studies. 2023

Table 1. Description of criteria used in the World Health Organization strain selection process



Epidemiological data	The WHO conducts continuous surveillance of global influenza on the regional prevalence of circulating influenza virus subtypes and lineages (influenza A H1N1, influenza A H3N2, influenza B Victoria and influenza B Yamagata). FluNet provides weekly surveillance data.[5]
Genetic characterization data	Genetic characterization assesses the similarity of genes of currently circulating influenza viruses with the genes of older influenza viruses. Nextstrain provides information for the prevalence of specific clades and subclades of the different influenza strains.[6]
Antigenic characterization data	Antigenic characterization data were used to measure the antigenic similarity between vaccine strains and circulating viral strains and how well circulating strains are covered.[7] Data were extrapolated from hemagglutination inhibition assays from the WHO.
Human serology data	Human serology data allows the measurement of how well the antibodies elicited from influenza vaccination in humans can recognize and neutralize the influenza viruses in circulation.[8]
Candidate vaccine viruses (CVV)	Candidate vaccine viruses are virus strains prepared for use in the vaccine manufacturing process and were available from the WHO.[9]
Vaccine effectiveness	VE studies are conducted each year to assess how well previous season influenza vaccines are working to protect against circulating influenza viruses in real-world conditions.[10]
Virus fitness forecasting data	Viral fitness forecasting data are used to anticipate which influenza viruses are most likely to circulate during the upcoming flu season using modelling and expert insight by the WHO and were not publicly available.

Disclosures

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