Sleeper Protocols for Pathogen X: Surveillance, Risk Stratification and the Uptake, Effectiveness and Safety of Vaccinations and Pharmacological Interventions

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Introduction

We need to learn from recent pandemics, so we are better prepared for the next. The World Health Organization (WHO) has highlighted the need for integrated responses both within and between member states.[1] For any future epidemic or pandemic caused by Pathogen-X, there are core considerations for which it is vital we are better prepared. These include improved surveillance capabilities, dynamic risk stratification, and the ability to assess uptake and the effectiveness and safety of vaccines and other pharmacological interventions in near real-time. Building on the work we have undertaken during recent pandemics in developing and deploying the Royal College of General Practitioners Research and Surveillance Centre (RSC) in England[2] and the Early Pandemic Evaluation and Enhanced Surveillance of COVID-19 (EAVE II) in Scotland,[3] we were commissioned by the UK Health Security Agency (UKHSA) to develop sleeper protocols that could be urgently activated following the emergence of Pathogen X with epidemic or pandemic potential.

Near-real time access to national data infrastructures is a foundational consideration:

Both the RSC and EAVE II offer national surveillance capabilities that are run in conjunction with national public health agencies. Their key strengths include national coverage (33% and 99%, respectively), near real-time access to high quality primary care data and unique individual identifiers that enable linkage to a range of other datasets. Additionally, as primary care is a registration base-system, and nearly all care is delivered by National Health Services (NHS), comprehensive, population level personal health profiles, exposure and outcome data are available. Both the RSC and EAVE II were extensively deployed during the influenza A H1N1 (swine flu)[4,5] and coronavirus 2019 disease (COVID-19) pandemics.[6,7] Key lessons learned from our own and international experiences are that rapid access to curated, linked data is essential to enable timely responses, which in turn are crucially dependant on an agreed roadmap for urgently (within hours) obtaining ethical approval and related permissions to respond to infectious disease crises. Our work has also highlighted the need rapidly to create new clinical codes (e.g., for thrombosis with thrombocytopenia syndrome (TTS) and long-COVID)[2] as delays hamper the ability to mount data-enabled responses.

Sleeper protocols

Sleeper protocols aim to provide a playbook that can be then adapted, as needed, depending on the particular characteristics of Pathogen X. There is a need to extend capabilities beyond maintaining hibernating data infrastructures proposed following H1N1,[8] to datasets that are routinely deployed and can be urgently pivoted if needed to undertake pre-determined analyses specified in sleeper protocols. Our protocols can be accessed from xxxx[a] and are summarised in Figure 1 and below.

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Our first protocol provides a framework for moving from ongoing background infectious disease surveillance to enhanced and then surge testing capability as guided by the UKHSA's incident response management team. In addition to providing indicators to guide decisions to increase surveillance capabilities, we also underscore the need to activate corollary considerations such as personal protective equipment (PPE) supplies and increasing testing and analysis of specimens. There should be sufficient capacity to, for example, support UKHSA's requirement for nationally representative microbiological sampling early in any emergency.

Our second protocol highlights the need for dynamic risk stratification. This is needed because there can be enormous differences in natural immunity, for example older people in the 2009 H1N1

[a] UKHSA. A Public Health Response Framework for Pathogen X: Safeguarding Communities through Sleeper Protocols for Emerging Epidemics and Pandemics. URL: XXXX

pandemic,[9] and in the transmissibility and clinical impact of different variants, as demonstrated in the COVID-19 pandemic.[10] For such assessments, we underscore the need for linkages of pathogen sequencing, health processes (including vaccine exposure) and outcomes.

The third protocol concerns monitoring the uptake, safety and effectiveness of vaccines and other pharmacological interventions. These may primarily be vaccines, but also treatments such as anti-virals, monoclonals and long-acting antibodies. We consider the range of study designs that could be considered depending on data availability. As of routine, assessments of their acceptability to patients and public should be part of this process, as promoted in the UK National Data Guardian 2022 report.

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Conclusion

In alignment with WHO's guidance, we seek to make the sleeper protocols we have developed internationally available and are now keen to collaborate with partners in further developing and stress-testing these. The hibernated data infrastructures proposed following the H1N1 pandemic were of undoubted help in enabling science-based responses to COVID-19, but were insufficient.[5] Learning from this, we have sought to build on our experiences and enhanced data capabilities to develop sleeper protocols that can be urgently activated and dynamically adapted. We hope these sleeper protocols will contribute to even greater protection against future – inevitable – epidemics and pandemics.

750/750 Words

Contributorship:[b] Conceptualisation: AS, TS, UA, CR, TF and SdeL, in response to a UKHSA commissioned report to provide A Public Health Response Framework for Pathogen X: Safeguarding Communities through Sleeper Protocols for Emerging Epidemics and Pandemics. Through a series of workshops, in addition to th above the following contributed: XG, BM-T, SA, JO-M, EB NA, DT, JB-L and RB, TS lead a writing group including UA, XG, BM-T, and JO-M with expert input and reviews and final edits from CR, AS and SdeL. SdeL AS and TS drafted this commentary.

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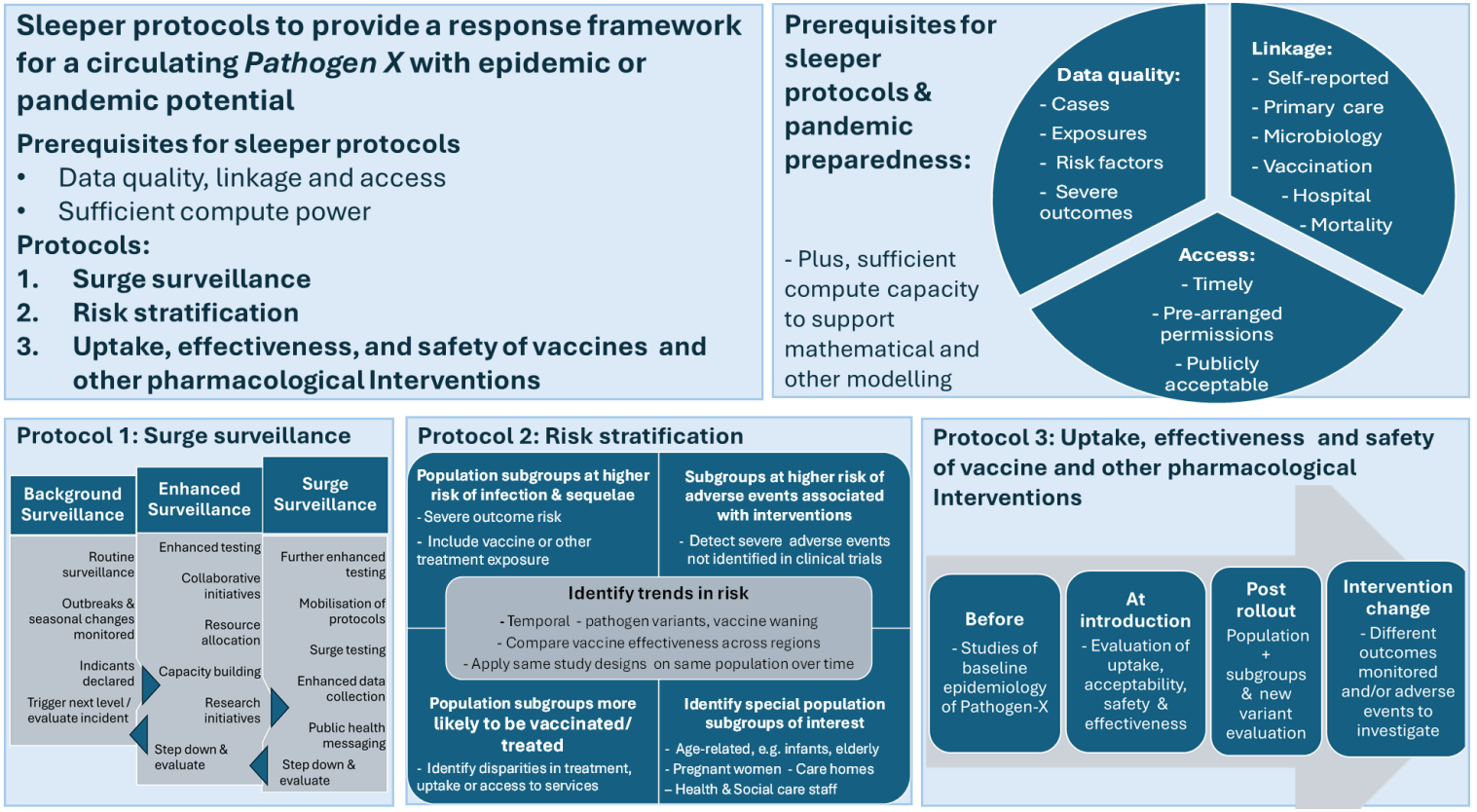
Conflict of interests: AS has served on a number of government COVID-19 advisory groups and is PI of EAVE II. SdeL is Directors of the RSC. He has received research funding through is University for vaccine related research from: AstraZeneca, GSK, Moderna, MSD, Pfizer, Sanofi, and Seqirus; he has been members of advisory boards for AstraZeneca, GSK, Sanofi and Seqirus, with any funding paid to his university.

[b] AS=Aziz Sheikh, TS=Ting Shi, UA=Utkarsh Agrawal, XG=Xinchun Gu, BM-T=Bernardo Meza-Torres, SA=Sneha Anand, JO-M-A=Jose Ordonez-Mena, CR=Chris Robertson, TF=Tom Fowler, EB=Edward Blandford, NA=Nick Andrews, RP=Richard Pebody, DT=Dan Todkill, JL-B=Jamie Lopez-Bernal, SdeL=Simon de Lusignan

Figure 1:Infographic summarising the report.



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Protocols 3 has first letters capitalised

Not sure what where change means in protocol 3

Look at use of capitalisation in first box

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