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TOWARDS THE PREDICTION OF INFLUENZA-LIKE ILLNESS CASES IN BELGIUM

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Keywords: Influenza, ILI Prediction, Confidence Region.

The influenza epidemics is a main public health concern worldwide. Its easy airborne transmission and the fact that there are different types of viruses make that annually there are 3 to 5 million severe cases and 250,000 to 500,000 deaths [1, 2]. The seasonality of influenza epidemics is typically observed in countries with a temperate climate. Children, elderly people and pregnant women are among the highest risk groups [3, 4]. This requires the management of public health policies, which include alerts for hospitals, the implementation of health protocols and provision of the necessary infrastructure [5]. Therefore, monitoring the incidence of influenza among the population is an important step for the characterization of the epidemic. In Belgium, there is a network of Sentinel General Practitioners (SGPs) for the early detection of an influenza epidemic. This network reports the number of influenza-like illness (ILI) cases per week and can be used to monitor influenza incidence. There is much data variability regarding the onset, the peak and the duration across different epidemic seasons. In addition to this intrinsic variability, human population dynamics and the different virus types make it difficult to predict the onset of the epidemic. Here we propose an approach for the real-time prediction of the number of ILI cases. The first step of the proposed method is the construction of a confidence region, which takes into account the data of the previous epidemic seasons and incorporates the variability for what concerns the number of ILI cases as well as their time of occurrence. We make use of the SIR compartmental model for the prediction of the number of ILI cases. In the second step, an optimization procedure is used in order to obtain the parameter set that leads to the best agreement between the simulated and the observed number of ILI cases. We used the Belgian SGP data corresponding to the epidemic seasons 2010-2011 to 2015-2016 for the evaluation of the proposed approach. The results show that the use of the historical record of seasonal influenza epidemics can improve the prediction of the number of ILI cases. At the same time, as ILI data for increasingly more seasons will become available, the representativeness of the confidence region will grow. The proposed approach can be used as a decision-supporting tool, as it can be used to predict the number of ILI cases for an ongoing epidemic season.

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ASSESSING INTERVENTION RESPONSES AGAINST H5N1 AVIAN INFLUENZA OUTBREAKS IN BANGLADESH

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Keywords: Epidemiology, Avian influenza, H5N1, Control, Mathematical modelling.

Highly pathogenic avian influenza H5N1 remains a persistent public health threat, capable of causing infection in humans with a high mortality rate while simultaneously negatively impacting the poultry production sector. One of several countries in South and Southeast Asia gravely affected is Bangladesh, whose high population density, intensifying farming system and substantial poultry population make it a prime candidate for being the source of newly emerging influenza strains with pandemic causing potential.

In anticipation of further outbreaks, it is therefore crucial to utilise knowledge on the regionspecific transmission-dynamic mechanisms and risk factors driving previous epidemics to predict the effectiveness of proposed control measures in limiting spread between poultry premises and curbing zoonotic transmission risk.

We evaluated the predicted impact of a variety of culling, vaccination and active surveillance intervention actions applied within the Dhaka division of Bangladesh, demonstrating how the effectiveness of a given intervention strategy depends upon: (1) transmission being predominately premises-to-premises, versus a scenario also considering external factors, (2) resource availability, and (3) the control objective being optimised. These were assessed via simulations of H5N1 influenza transmission models, previously fitted to historical H5N1 epidemic data from the Dhaka division, incorporating both poultry-to-poultry and zoonotic transmission [1].

Our results indicate that the impact of reactive culling and vaccination control policies are dependent upon epidemiological characteristics as well as control objectives and capacities. However, proactive surveillance schemes appear to significantly outperform reactive surveillance procedures irrespective of these conditions. Furthermore, in situations where

between-premises transmission is weak, the enforcement of control measures not directly applied to poultry flocks themselves (e.g. public awareness campaigns) can dramatically cut the risk of spillover transmission, reducing H5N1 human case occurrence. Our findings may advise the type of control measure, plus its severity, that would be most appropriate in combating re-emergent H5N1 outbreaks amongst poultry in Bangladesh.

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SHOULD WE EXPECT ATTACK RATES FOR INFECTIOUS DISEASE TO VARY ACROSS SMALL SPATIAL SCALES?

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Keywords: Epidemics, Influenza, Hetereogeneity, Spatial, High-resolution.

High-resolution demographic data is becoming increasingly available. We also have evidence for variation in human immune response to different strains of influenza within a large urban area. Our work originates in attempting to understand this variation via mechanistic modeling of influenza transmission.

Initial results show that subtle differences in the construction of a force of infection term lead to notably different patterns in attack rate across space. In particular, when mobility is dependent on infection status, we observe correlations with population density and gradient thereof. These correlations can be reversed by weighting the spatial kernel by population density or distance.

The availability of high-resolution, age-stratified data for the UK allows us to evaluate the effect of non-trivial age distributions on attack rates under different mobility assumptions. We also show the importance of accounting for duration of contacts between each age-group, and the effect of age-dependent mobility.

Next, we incorporate multi-annual dynamics in order to study the burden of seasonal influenza. This is initially achieved via recursive final-size calculations, where we show that a single lineage respects the spatial trends in attack rate observed in the pandemic case. Moreover, these trends are robust to perturbation. The time series of seasonal attack rates shows similar qualitative behaviour to standard SIRS models in which successive incidence peaks are recorded. Any small-scale variation in attack rate is therefore a result of changing demography on a seasonal timescale.

Finally, we develop our model to account for multiple circulating subtypes such that crossimmunity exists only within each season, and subtype-specific immunity is subject to longerterm waning. The model is initially evaluated against country-specific ILI incidence and serological data before including heterogeneity in age and space. Results for the fully heterogeneous model are still pending, though we hope to conclude whether heterogeneity in demography, together with multiple circulating lineages, is sufficient to drive the highresolution heterogeneity in attack rate that would give rise to the observed spatial variation in immune response.

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OPTIMAL CONTROL OF A FRACTIONAL EPIDEMIC MODEL WITH APPLICATION TO HRSV DISEASE

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Keywords: Human Respiratory Syncytial Virus (HRSV), Compartmental Mathematical Models, Fractional Optimal Control.

A state wide HRSV surveillance system was implemented in Florida in 1999 to support clinical decision-making for prophylaxis of premature infants. A periodic SEIRS mathematical model was used in [1] to fit real data collected by that system. In this work, this model is modified to a fractional SEIRS and a fractional optimal control problem is formulated and solved with treatment as control variable. The cost-effectiveness analysis of the fractional model is carried out.

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