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ESTIMATING THE IMPACT OF NON-PHARMACEUTICAL INTERVENTIONS IN HETEROGENEOUS POPULATIONS DURING AN EMERGING INFECTIOUS DISEASE EPIDEMIC

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ABSTRACT

Non-pharmaceutical interventions (NPIs) such as quarantining or school closures are immediate measures to contain the diffusion of an emerging infectious disease in a susceptible population in absence of therapeutics or vaccinations. However, the effectiveness of containment measures strongly depends on regionally heterogeneous demographic structures (imagine school closures that yield limited contributions to disease containment in areas with little to no school-age population). In my work, I present a pathogen-generic agent-based simulation approach to produce regional estimations for the effectiveness of NPIs. The thesis consists of three blocks. First, an approach to generate realistic synthetic populations based on publicly available census data. Second, a modular agent-based model architecture to enable simulations of various pathogens, populations, and NPIs. Third, a case study demonstrating the evaluation of regional NPI effectiveness in the context of the German COVID-19 epidemic. I suggest that my work will support the development of more sophisticated intervention strategies during emerging epidemics.

1 INTRODUCTION

The ongoing SARS-Cov-2 pandemic has demonstrated the substantial value of infectious disease modeling to public health decision-making. Ordinary differential equation models are very useful to estimate general features such as the basic reproduction number or case numbers on a national scale. However, these models lack to represent regional or demographic heterogeneity as they rely on a compartmental structure that assumes the same characteristics for all members of such compartments. Hence, these models are not suited to estimate the regional impact of non-pharmaceutical interventions (NPIs) (such as school closures) as they do not take demographic heterogeneity into account (e.g. the fraction of households with school children). Agent-based models are generally capable of modeling such heterogenous structures. In my PhD thesis, I develop a comprehensive population model of Germany and a modular agent-based simulation framework to evaluate the (regional) impact of selected NPIs.

In my thesis, I rely on the well-established Design Science (DS) (Hevner et al. 2004) approach as the guiding methodological principle. In contrast to explanatory research, DS is a form of constructive research and focuses on the development of IT artifacts (such as epidemiological models) with a distinct emphasis on problem relevance, design evaluation, research rigor, and communication of research.

2 GENERATING SYNTHETIC POPULATIONS

In order to simulate and evaluate the effectiveness of NPIs during an emerging epidemic in a population, an accurate synthetic population model is required. For most population-based simulations, census data is used to model demographic structures. However, the census does not provide singular records for individuals but rather aggregated statistics. Thus, the first block of my thesis addresses the issue of generating representative synthetic populations from aggregated statistics. The problem is met by combining synthetic reconstruction and combinatorial optimization to generate baseline populations for German municipalities. Our current approach yields an average accuracy over all features (i.e. age distributions and household structures) of around 98%. The results are being published at this year's Winter Simulation Conference (submission ID: con254s1).

3 BUILDING A MODULAR SIMULATION FRAMEWORK

The second block concerns the development of a modular agent-based model architecture to execute simulations in various German municipalities. It comprises (1) a geographic layer: spatial data (i.e. about schools and businesses) obtained from open data sources such as Open Street Map, (2) a population layer: representative synthetic population, obtained from the first block of my thesis, (3) an activity layer: providing general assumptions about movement behavior, such as school children going to school, and (4) a disease layer: providing data on the natural history of the disease (e.g. incubation durations, etc…) obtained from epidemiological parameter studies. The resulting artifact will be evaluated according to the Principles of Good Practice for Decision Analytic Modeling in Health-Care Evaluation (Weinstein et al. 2003) regarding its internal validity (testing), calibration (consistency with available data), face validity (external verification through peers), and cross-validation (benchmarking against existing models, if available). Parts of this will be done in the subsequent third block.

4 APPLYING THE MODEL IN THE CONTEXT OF THE GERMAN COVID-19 EPIDEMIC

Having developed a realistic synthetic population and a modular model architecture, the third block focuses on the framework's application in the context of the German COVID-19 epidemic. In March 2020, the German COVID-19 epidemic was initiated by a superspreading event in the western German municipality of Gangelt during a carnival event (Streeck et al. 2020). While reliable tests were generally scarce, the epidemic circulated mostly undetected for two weeks until school closures and closures of non-essential businesses were implemented. In order to estimate the number of undetected cases, a research team based at the University of Bonn, conducted a representative antibody study in this very municipality and concluded that 15% of the population had antibodies six weeks after the outbreak, indicating prior infection. In my work, I plan to retrace the *Gangelt-outbreak* and assess the effectiveness of introduced interventions. In a subsequent step, I will run the simulation in other (German) municipalities to study the correlation of demographic features (e.g. age distributions or household compositions) and the effectiveness of NPIs. This shall provide evidence to answer the question: would the same set of interventions have had the same impact in a different demographic?

From a simulation-perspective, this is a very interesting use case for several reasons. First, there is a clear observation period from the carnival event to the first day of the study. Second, as this marked the first outbreak in Germany, there is almost no so-called background activity, which are cases that are not directly related to the event making it hard to evaluate a simulation model. And third, the timing and scope of the introduced interventions are well-reported and can be implemented in the model.

The results of this quantitative analysis shall provide insights into the interrelation of regional demographics and the expected impact of NPIs supporting the development of more sophisticated containment strategies.

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