Pandemic visits a doctor

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APPENDICES

SUMMARY

The COVID-19 pandemic exposed the global vulnerability to infectious diseases, despite clear historical precedents such as the Spanish Flu. It is not feasible yet to successfully achieve full Pandemic Prevention, but it is necessary to aim for Pandemic Preparedness. This can be structured around three pillars:

1. Limiting the speed of the spread of infection
2. Optimizing healthcare resource allocation during a pandemic
3. Ensuring effective and safe vaccination campaigns

This thesis focusses on these three pillars in pandemic prevention, i.e., speed of spread, planning of healthcare resources, and vaccination, and is divided in two parts.

Part 1: Surveillance of infectious disease using population derived data during the start of a newly emerging pandemic and the application of these data.

Chapter 2 presents the development and validation of the **COVID RADAR app**, which enabled large-scale reporting of symptoms and risk behavior by citizens. With the app we could show that self-reported data correlated well with national case numbers, demonstrating potential as an early warning tool during pandemics.

Chapter 3 shows how these symptom and behavior data can predict COVID-19 related **primary care demand** during the COVID-19 pandemic. This predictive capacity is particularly valuable at the onset of a pandemic when healthcare systems are under strain and diagnostics are scarce.

Chapter 4 presents data on community-dwelling COVID RADAR app users, revealing that 5%–10% experienced post-acute COVID symptoms 100 days after a positive test result. These symptoms clustered into distinct entities with varying incidences, patient characteristics, and vaccination effects, suggestive of multiple mechanisms behind the development of post-acute COVID symptoms.

Part 2: Coagulation and venous thrombotic events as adverse events following SARS CoV-2 vaccination and infection.

Chapter 5 explores the relationship between the pre-existing coagulation potential and COVID-19 severity. In older adults with comorbidities, a higher than average tendency to clot did not increase the risk of infection but could be associated with more severe outcomes. Concentrations of several proteins related to the inflammation and coagulation system were also linked with infection and COVID19 severity. These results could aid further exploration of intrinsic risk factors for severe courses of an infectious disease.

In **chapter 6** presents a secondary analysis of a trial comparing fractional intradermal (ID) and full intramuscular (IM) doses of the SARS-CoV-2 vaccine. Both administration methods resulted in transient increases in inflammatory and coagulation markers, with the effects being more pronounced following IM vaccination. A correlation was observed between the inflammatory response and changes in coagulation parameters.

Chapter 7 it is reported that SARS-CoV-2 vaccines are associated with venous thromboembolism (VTE), with variation in the incidence based on vaccine type, sex, and age. On a population level in the Netherlands in 2021, it was estimated that the benefits of vaccination resulted in a net reduction in VTE events, due to the reduction in COVID-19 incidence.

Based on the experiences with the COVID RADAR app several recommendations were made **in chapter 8** for syndromic surveillance tools. Challenges such as selection bias and variability in user engagement were encountered. Despite these limitations, the data demonstrated strong validity for symptom and behavior patterns. Nevertheless, this data collection method, being simple and inexpensive, could enhance pandemic preparedness by monitoring pandemic progression potentially leading to limiting pathogen spread and optimizing healthcare resource allocation (first two pillars of pandemic preparedness).

Chapter 8 proceeds discussing various methods for monitoring adverse events associated with vaccines during a pandemic. This chapter includes various methods for monitoring adverse events associated with vaccines during a pandemic. Commonly used methods, such as the Observed vs. Expected design, the self-controlled case series, and cohort designs, are effective at detecting signals but fail to provide unbiased relative risk estimates in a pandemic context. Challenges include selective underreporting of events, violations of methodological assumptions, and difficulties in establishing appropriate control groups. Although not free from bias, the case-control design appears to be superior in addressing these challenges, and offers a more robust approach to evaluate vaccine safety under pandemic conditions.

During the COVID-19 pandemic, vaccines were developed in record-breaking time, marking a significant achievement in medical science. However, achieving sufficient vaccination coverage depends on public willingness to be vaccinated—a challenge compounded by growing vaccine hesitancy. To address this, public communication must improve, emphasizing not only the risks but, more importantly, the substantial benefits of vaccination. This may require a shift in mindset, encouraging individuals to consider the collective impact of vaccination. The narrative should transition from “What’s in it for me?” to “What’s in it for us?” fostering a sense of shared responsibility and communal benefit. This need for collective thinking extends beyond infectious diseases to other health challenges and future threats, such as an aging population and planetary health.