Infectious disease epidemics and pandemics will continue to happen and will probably accelerate in frequency. Mathematical reconstructions of the pandemic played a crucial part to inform policy and contributed to critical decisions when data were sparse. One goal of this chair grant is to develop these models further to prepare for future crisis. Statistically fitting a model to data is a well-studied task with many useful solutions, but the most useful models tend to be those that capture the mechanism of infection. During the pandemic a class of models based on a mathematical area called renewal theory emerged as one of the most common approaches to model a complex epidemic. The use of this theory in epidemics has a firm epidemiological motivation but the core mathematics have not been proved. Without understanding these mathematical foundations, our understanding will always be partial. In three recent publications, we have undertaken this highly technical task and have mathematically proved a series of relevant results. First, we have uncovered the core mechanisms and thereby identified the broad class of mathematical models from which renewal theory derives. In uncovering this core mechanism, we find the approaches in the literature are a limited, and special case of a broader class of models. Using our refined theory, we can use these broader models to understand an epidemic much better. For example, it is common to collect data routinely from individuals being infected from testing centres as well as a more structured randomised surveys/trials. Our framework naturally models both these data and can therefore help inform us how many cases we are missing, or what the population level infection count is. Next, we looked at the question of uncertainty – a crucial component in any risk analysis. The challenge is that we only ever observe one epidemic, and we can "rerun" an epidemic again from the start. However, our new framework enables us (with some assumptions) to do exactly this. We derived one of the most sophisticated and yet analytically tractable frameworks to date and were able to uncover new dynamics in what drives the variability in epidemics. We showed how easy it is to underestimate uncertainty without careful considerations and highlighted just how profoundly uncertainty grows in an epidemic – even without factors such as superspreading.

Aside from studying the theory of epidemic models, we have also applied these rich models with big data to answer question from the pandemic. We have studied the complex epidemic in Brazil where the Gamma variant led to substantial infection and mortality. Using patient records we built a Bayesian mathematical model to study in-hospital fatality rates and found, remarkably, that approximately half of the COVID-19 deaths in hospitals in the 14 cities could have been avoided without pre-pandemic geographic inequities and without pandemic healthcare pressure. These results underscored the need to consistently invest in investments healthcare resources, optimization, and preparedness. We contributed in part to two studies of the fatality rate of the Omicron variant in 2022 in both the UK and Denmark and found a milder infection – research that directly informed policy.

Moving forwards we are now considering the other key component of our program – using genetic data to inform epidemic dynamics. In keeping without desire to develop the state-of-the-art we are in the process of creating new techniques to perform phylogenetics. We will be applying these new approaches as well as those we have already developed to attempt to create a complete picture of the infection process in Denmark over the pandemic. This project will happen in collaboration with The Statens Serum Institute and Statistics Denmark.