**Life of a 'Fact': Understanding Infectious Disease Transmission**

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A simulated 'fact' uncovers indirect effects of vaccinations such as the reduction of bacterial circulation in a population and the optimal vaccination coverage to reach herd immunity threshold. An agent-based simulation model is capable of revealing indirect, population level, effects on transmission: effects from the type of vaccine used, the schedule followed, contact patterns and demographical details. All these factors affect the disease transmission in a population. But how do these models capture the finesses of disease transmission? In more general terms, the main focus of this study is to explore the ways in which our understanding of the key questions in infectious disease studies evolved over time and across disciplines. This will provide a way to reflect in a broader sense how 'facts' travel across time and how useful the vehicle of mathematization is in that process.

Our story will show that transmission of disease is not covered by a single, solid account of the process in which a susceptible person encounters a carrier and falls ill. There are various, pathogen, population structure, age-specific and immunity related factors that need to be taken into account. On the other hand, historical studies reveal how the understanding of transmission dynamics developed into the current forms, which are oftentimes summarised in a generalised, pathogen-specific transmission pattern that can be depicted in computational algorithms. Interestingly, the generalised 'facts' of transmission were to be *tailored* into a simulation model to produce *sharpened facts* of, for example, precise transmission rates. The focus in this study is limited to the life of the transmission 'fact' and its capability to become adopted and adjusted in the mathematical forms presented through modelling. The life history offers us a way to ask: Why do we know what we know of disease transmission in epidemiology?

By examining the ways in which our understanding of disease transmission has developed through the course of historical and current studies in epidemiology, we notice certain unsolved puzzles. Transmission as a concept is itself related to a set of variables. These *general 'facts'* of transmission have developed over time as our understanding has increased, but still, to examine the phenomena in a detailed level, requires specification. Furthermore, we may ask whether we are able to identify *protofacts* of transmission i.e. ideas that proceed the scientific facts and might even be hazy or superfluous (e.g. Fleck 1979).

This study builds up a *life history* of the facts of disease transmission (cf. Daston 1999), which enables us to understand the underlying currents of its birth, maturation, reaching of reproductive age and passing away. This metaphor offers tools to depict the gradual, cyclic development and refinement of 'facts', instead of relying on the constructionist metaphors of scientists as carpenters in the business of 'fact' production. The analysis is based on historical resources on mathematical epidemiology, recent textbooks and publications on mathematical modelling and its applications in infectious disease studies, and ethnographic observations on modelling practices that led to the published Hib simulation model. The analysis combines micro-sociological and micro-historical approaches in a narrative of a life of a 'fact'.

This study presents a life-history of disease transmission in the case of *Haemophilus influenzae type* b bacteria, which is capable of causing severe diseases, such as *bacterial meningitis* in children. More precisely, this story traces back the ways in which our understanding of disease transmission gradually developed into the formulations captured in mathematical models used in current infectious disease studies. In order to follow the general evolvement and refinement of the disease transmission on a population level, the narrative will explore three distinct phases in the epidemiological research, all of which refined and reiterated the concept of disease transmission in a population leading to the key formulations used in current simulation models as *force of infection* or $R_0$ (the basic reproductive rate).

The first phase will focus on the early development of mathematical epidemiology in the turn of the 19th Century. Formulation of the germ theory of disease created a new framework to identify singular causal factors behind infectious diseases. Koch's postulates formed the generalised principles for the conditions upon which an organism can be accepted as a cause of a particular disease. However, the challenge remained how to address the disease transmission in a population. For mathematical epidemiologists, the quest was to search for explanations for the "global patterns of disease in time, space and population" (Fine 1979). This search resulted in understanding the cyclic patterns of infections (e.g. Hamer 1906), refining the mathematical theory of epidemics that presented the problem of which factors govern the "spread of contagious epidemics" (Kermack and McKendrick 1927), and in a misfortunate conception of *infectiousness* (by Brownlee in Fine 1979).

The second phase will follow the refinement of these theoretical and experimental observations of disease transmission and explore how they become simplified and sharpened into probabilistic infectious disease models. A special focus is on the disease patterns which classify individuals into susceptible, infected and recovered groups (or different variants of these). These patterns are usually expressed as SIS, SIR or SEIR (susceptible, infectious, infected, and recovered) depending on the bacterial agent in question. In our story the pattern is SIS since Hib does not convert to permanent immunity. Interestingly though, these patterns form a generalised body of knowledge that facilitates the parameterisation of infectious disease models. However, in the early phases of epidemiological modelling, this classification led to deterministic compartmental models of disease transmission. These models are insensitive to the impact of chance in small populations and oftentimes ignore agent-based dynamics. So, the second phase of the exploration will clarify the difference between deterministic and probabilistic models and discuss the ways of understanding disease transmission in a population.

The third phase ends our story with a structured simulation model, which is capable of capturing agent-based dynamics, addressing mixing patterns and including vaccination effects on the circulation and transmission of Hib. This fine-grained, population simulation model is hence capable of telling us the full notion of Hib transmission, immunity and disease (Auranen et. al. 2004). Our story will take a detailed look at the transmission dynamics captured by the model and discuss the ways in which transmission is represented, simplified and quantified in the model assumptions and parameters.

Through these three phases that form the backbone of our narrative, we will learn how the understanding of disease transmission evolved from the discovery of germs as singular cause of disease into the sophisticated ways of simulating disease transmission in population. The main findings discuss what kinds of translations 'facts', originating in epidemiological studies, face in order to be simplified, refined and 'mathematized' into models.

References:

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