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Interactions between immuno-epidemiology and individual decision-making for nonpharmaceutical interventions

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There is an urgent need to disentangle interactions between infectious disease dynamics, immunity, and individual decision-making for adherence to nonpharmaceutical interventions (e.g., mask wearing or social distancing). Here, we outline the significant advancements that this will require, which include theoretical modeling, longitudinal data collection, and iteratively interfacing models with data.

Emergent need to integrate immunology, epidemiology, and human behavior

The coronavirus disease 2019 (COVID-19) pandemic has starkly underlined the importance of understanding individual decision-making for intervention adherence. Such an understanding is key to disentangling how decision-making is intertwined with population-level infectious disease dynamics and individual-level characteristics of immunity (i.e., immuno-epidemiology). This also involves exploring how these cross-scale interactions are shaped by perceived or actual host immunity. While there is a growing body of theoretical socio-epidemiological models (e.g., with cultural evolution [1], vaccination [2], social distancing [3], collective behavior [4], adherence to a nonpharmaceutical intervention (NPI) [5], and choice between two NPIs [6]; see [7] for a review), we still lack a broad synthesis that combines immuno-epidemiology with behavioral decision theory. The catalysis of such a blend between these fields could follow how new interdisciplinary frontiers in related areas were conceived. For instance, over the last few decades, a revolution that melds network science and epidemiology has led to 'network epidemiology' [8,9]. We argue here that an analogous undertaking is urgently needed to understand individual decision-making during infectious disease outbreaks, with the socio-immuno-epidemiology of adherence to NPIs particularly important for emerging pathogens. This major gap emerges because we do not yet have a sufficient understanding of the key drivers of individual decision-making for NPI adherence and how they relate to immunological and epidemiological characteristics of individuals. To resolve this, we outline theoretical developments and behavioral-immuno-epidemiological data that will be required.

Cross-scale feedbacks between immuno-epidemiology and human behavior

There are many complexities that make the intersection of immuno-epidemiology and human behavior an exciting and important area for future research. First, individual decision-making and epidemic dynamics have many cross-scale feedbacks (Figure 1, panel A). At a local scale, local information, such as peer behavior or infection levels, can shape decision-making. However, as highlighted during the COVID-19 pandemic, behavioral decisions can also be affected by external information about infection levels or adherence to NPIs (e.g., social media may be an important source of external information). In parallel, external infection levels can also drive local peer behavior. Therefore, a key question in behavioral-epidemiology is whether local or external information dominates (Figure 1, panel B). If the information that individuals use for decision-making is purely local, NPI adherence will likely reflect (perceived) local infection levels. However, if external information dominates, NPI adherence and local levels of infection may be decoupled (especially if local and global transmissions are not synchronized). The decision to either adhere to an NPI or become vaccinated can then directly affect (local) epidemiological dynamics. For example, vaccination or NPI adherence can reduce transmission, which can then affect infection levels and peer behavior (via lower risk perception). Vaccination can also directly change individual immunity and/or decrease the severity of infections, and both could influence local peer behavior.

While vaccination and recovery from infection can impart immunity and prevent infection (or decrease susceptibility to reinfection), individual immune waning and pathogen evolution lead to dynamic changes in immunity. Additionally, uncertainties in the strength and duration of host immune responses following recovery can complicate epidemiological projections, from local to global scales [10]. Empirical studies on the strength and duration of immune responses (which likely guide behavioral perception) generally focus on neutralizing antibodies, but other host responses could also decrease transmission or severity. Individuals may, therefore, not accurately perceive their immunity, and this mismatch could have important behavioral-epidemiological consequences. For example, an individual that erroneously believes they are immune may forgo NPI adherence and subsequently becomes infected (and transmits the pathogen forward). On the other hand, an individual that underestimates their immunity may adhere (due to higher risk perception) and therefore further decrease their risk of infection. Such misalignments can also manifest themselves at population levels, for example,

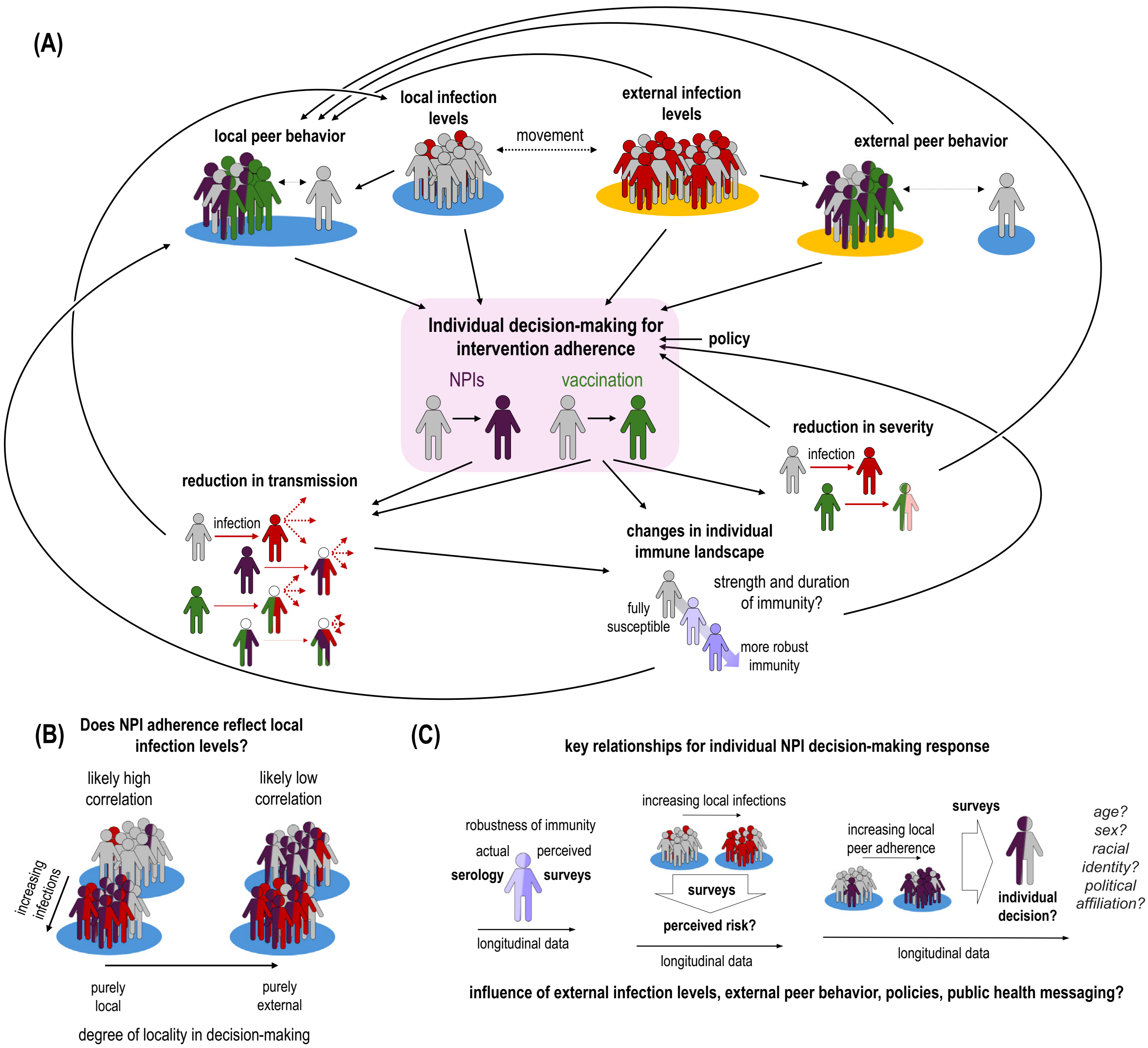

Figure 1. Cross-scale interactions between individual decision-making, epidemiological dynamics, and immunity. (A) Illustrative schematic of how local and external information can affect individual decision-making, and how, in turn, such decision-making can affect immuno-epidemiological dynamics (and therefore perception). Individual decision-making depends on many factors, including peer behavior (local and external), infection levels (local and external), policy, robustness of immunity, and risk of severe disease from infection. In turn, choosing to adhere to an NPI can reduce transmission, which can change the immunity of an individual. Obtaining a vaccination can change immunity directly, can also reduce transmission, and can reduce disease severity. Then, these effects can influence drivers of decision-making, resulting in important feedbacks. (B) Illustrative schematic for the role of locality in individual decision-making. (C) Key data that should be collected in future cohort studies, including both perceived/actual immunity and the effects of local infection levels or peer behavior on perceived risk. In particular, longitudinal data are crucial. NPI: nonpharmaceutical intervention.

when individuals estimate the degree to which a community is immune (e.g., via prior case counts or vaccination data) to evaluate their personal risk, especially in the context of seasonal diseases. A recent national study across Canada on trust in institutions by the Coronavirus Variants Rapid Response Network (CoVaRR-Net) revealed that trust in government and scientists rested on several factors: consistency of information, willingness to communicate uncertainty, and perceptions of conflict of interest in the motivation of scientists in vaccine development [11]. Thus, the interactions between socio-epidemiology and key characteristics of immunity can complicate cross-scale epidemiological dynamics. To untangle these interactions, it will be crucial to understand the relationship between perceived and actual individual immunity, and how perceived immunity affects individual decision-making.

Finally, recent work has revealed that contrary to assumptions about immune privilege [12], the brain has regions that exhibit immune responsivity through cytokines [13]. Prefrontal cortex neurons require interferon-γ and its receptor to induce social behavior in mice, with a gene expression signature conserved in fish and flies. Deficiencies result in social withdrawal, while overactivation of the interferon-induced transcription factor, Signal transducer and activator of transcription 1 (STAT1), is associated with hyperactivity [14]. These findings allude to a complex evolutionary link between sociability and immune protection at both the individual and community level.

Resolving these multiple feedbacks within individuals and populations will require complex models that bridge scales from individuals to populations and combine immune dynamics, epidemiology, and behavior. These should be built sequentially: starting from existing conceptual models to ones that progressively include more detail. Key building blocks for these novel models will be initial conceptual models designed to capture specific feedbacks between behavior and immuno-epidemiology. In tandem, these advancements in conceptual modeling could reveal any surprising effects that emerge from interactions between immunity, epidemiology, and decision-making (such as the independence of transmission on infection levels at partial adherence [5]). Crucially, these developments should be achieved in conjunction with the collection of key behavioral-immuno-epidemiological data. Initial models can inform data needs, and (subsequently) collected data can be used to parameterize more complex models that consider the confluence of individual behavior, immunity, and epidemiology. In an iterative process, these more complex models would then suggest additional data collection and subsequently enable greater model refinement. Our suggested coevolution between models and data therefore mirrors that which has occurred in many other fields, including network epidemiology (see [9] for an overview of this field).

In Figure 1 (panel C), we outline existing gaps in our understanding of factors that shape NPI decision-making response, and we highlight how they could be addressed through survey designs and data collection. Here, the unifying theme is the urgent need for longitudinal data on behavioral perception at multiple scales, in concert with the collection of immunological and epidemiological data. At an individual level, serology, in combination with surveys of perceived immunity, could determine the relationship between actual and perceived immunity and could inform how this relationship changes with time (especially during a seasonal or pandemic outbreak). At a community (local) level, longitudinal surveys could quantify how risk perception changes with the level of circulating infections. Furthermore, these surveys could be broadened to also address the impact of local peer adherence on decision-making and the influence of external (global) information, including policies, public health messaging, media, social media, misinformation, and disinformation. The inclusion of social components is, therefore, integral in future large-scale epidemiological and immunological monitoring, for example, in a Global Immunological Observatory [15].

A myriad of heterogeneities likely complicates individual decision-making for NPI adherence, and these may also interact with immuno-epidemiology. For example, younger adults may be less susceptible to infection following vaccination or recovery but may also overestimate the robustness of their immune responses and underestimate the severity of an infection. On the other hand, the perception of elderly individuals may be skewed differently. Furthermore, differences in transmission dynamics between and among age groups may also be important.

Beyond biological heterogeneities, different peer groups—and thus conflicting peer forces—could also have important socio-epidemiological effects. Individuals may wish to imitate their peers. However, if a population is stratified into groups (e.g., by political affiliation), individuals in one group may also avoid behaviors adopted in another (i.e., out-group aversion). This can have compounding effects: for example, if individuals in one group perceive risk based on certain characteristics (e.g., perceived immunity or circulating infections), they may choose to adhere to an NPI. At the same time, due to out-group aversion, individuals in another group in that same community may choose to not adhere. In turn, in the same community, the transmission dynamics in both groups would be rather different. Therefore, understanding how social learning and out-group aversion shape decision-making—and how it hinges on characteristics such as age, sex, racial identity, and political affiliation—should also be studied further. Relevant survey data to quantify these effects should be collected, and future cross-scale modeling endeavors should include these social phenomena.

Conclusions

A synthesis of socio-epidemiology, and understanding its confluence with immunity, is necessary to resolve key questions in infectious disease dynamics. In tandem, such advances could shape the rational deployment of future mitigation strategies, both for local epidemics and for future pandemics, and would greatly improve outbreak predictability. As we face recurrent outbreaks of many viruses and continued threats of pandemics, the need to untangle the interactions between individual decision-making responses for NPI adherence and epidemic dynamics is clear.

Declaration of interests

The authors declare no competing interests.

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