VIEWPOINT: COVID-19

The engines of SARS-CoV-2 spread

Fighting SARS-CoV-2 requires a clear framework for understanding epidemic spread

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly across the globe, causing epidemics that range from quickly controlled local outbreaks (such as New Zealand) to large ongoing epidemics infecting millions (such as the United States). A tremendous volume of scientific literature has followed, as has vigorous debate about poorly understood facets of the disease, including the relative importance of various routes of transmission, the roles of asymptomatic and presymptomatic infections, and the susceptibility and transmissibility of specific age groups. This discussion may create the impression that our understanding of transmission is frequently overturned. Although our knowledge of SARS-CoV-2 transmission is constantly deepening in important ways, the fundamental engines that drive the pandemic are well established and provide a framework for interpreting this new information.

The majority of SARS-CoV-2 infections likely occur within households and other residential settings (such as nursing homes). This is because most individuals live with other people, and household contacts include many forms of close, high-intensity, and long-duration interaction. Both early contact tracing studies and a large study of more than 59,000 case contacts in South Korea found household contacts to be greater than six times more likely to be infected with SARS-CoV-2 than other close contacts (*1*, *2*). Household contacts accounted for 57% of identified secondary infections in the South Korean study, despite exhaustive tracking of community contacts. Globally, the proportion of cases attributable to household transmission will vary because of multiple factors, including household size. Contact studies suggest that 17 to 38% of contacts occur in households, implying that 46 to 66% of transmission is household-based (using the standard formula for attributable fraction) (*3*). This is consistent with household contact being a key driver of transmission for other respiratory viruses.

Even among close contacts within households, there are considerable heterogeneities in transmission risk. Spouses of index cases are more than twice as likely to be infected as other adult household members, and symptomatic index cases may be more likely to transmit the virus (*4*). Moreover, older age is associated with increased susceptibility to infection, increased transmissibility, and severe disease (*4*). Older members may face extra risk in multigenerational households if younger members have unavoidable work or school obligations, although young children may be less susceptible to infection and transmit the virus less readily (*4*).

Just as in households, those who live in congregate residences such as prisons, worker dormitories, and long-term care facilities have intense, long-duration, close contact. There are more potential contacts in these settings, which are often among older age groups. The confluence of these factors can lead to high infection rates in outbreaks (attack rate); for example, 66% of residents were infected in a homeless shelter, 62% in a nursing home, and 80% in a prison dormitory (*5*, *6*). Even when residents rarely leave, these facilities are highly connected to communities through workers and guests.

Although transmission may be easiest and most frequent in households and congregate residences, community transmission connects these settings and is, therefore, essential to sustain the epidemic, even if it directly causes fewer cases. Inevitably, "community contacts" include a heterogeneous mix of interactions. The probability that any of these interactions results in transmission stems from a complex interplay of pathogen attributes, host characteristics, timing, and setting. Hence, the properties of community transmission are difficult to measure, and this is where much of the remaining debate around SARS-CoV-2 transmission occurs.

A crucial factor in community transmission is that infected individuals not experiencing symptoms can transmit SARS-CoV-2. Infectiousness may peak before symptom onset (*7*). Viral loads appear to be similar between asymptomatic and symptomatic patients (*8*), although the implications for infectiousness are unclear. People experiencing symptoms may self-isolate or seek medical care, but those with no or mild symptoms may continue to circulate in the community. Because of this, those without severe symptoms have the potential to be "superspreaders" and may have an outsized influence on maintaining the epidemic.

Superspreading events, in which one person infects many, are often as much the result of setting as host characteristics. Apparent superspreading events of SARS-CoV-2 have occurred during choir practice (*9*), in department stores, at church events, and in health care settings (*5*). These are all settings where one individual can have many close contacts over a short period of time. Transmission can also be amplified if multiple subsequent infections occur in rapid succession, and outbreaks with high attack rates have occurred in close-contact settings such as schools (14%), meat processing plants (36%), and churches (38%) (*5*, *10*).

Both superspreading events and transmission-amplifying settings are part of a more general phenomenon: overdispersion in transmission. Overdispersion means that there is more variation than expected if cases exhibit homogeneity in transmissibility and number of contacts; hence, a small number of individuals are responsible for the majority of infections. This phenomenon has been described for diseases as diverse as measles, influenza, and pneumonic plague (*11*). For SARS-CoV-2, studies suggest that ~10% of cases cause 80% of infections (*1*). Overdispersion is characterized by a large number of people who infect no one, and most people who do transmit infect a low-to-moderate number of individuals. Large superspreading events (such as those infecting 10 or more people) are likely quite rare, although they are far more likely to be detected and reported.

Such events have driven much of the debate around the relative importance of different modes of transmission. In household settings, contacts are so long and intense that it matters little whether large droplets, fomites (contaminated surfaces), or aerosolized particles are driving spread; all have ample opportunity. In community settings, where there is greater variety in the nature of infectious contacts, these distinctions become more important, particularly because they affect policy. Aerosolization of fecal matter caused one of the largest superspreading events of the 2003 SARS-CoV

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epidemic (*12*), and aerosolizing medical procedures facilitate the spread of coronaviruses (*12*, *13*). Several SARS-CoV-2 transmission events suggest that aerosolized viral particles may play a role in transmission in everyday settings. Although the frequency of aerosolized transmission is uncertain, extended close contact and sharing of spaces poses the greatest risk. It is also difficult to generalize the importance of different modes of transmission across settings because their relative contributions can be modified by environmental conditions. For example, low–absolute humidity environments are associated with influenza virus transmission in temperate regions, probably because these conditions facilitate small droplet spread, yet influenza outbreaks are still common in tropical regions, with fomites potentially playing a larger role (*14*).

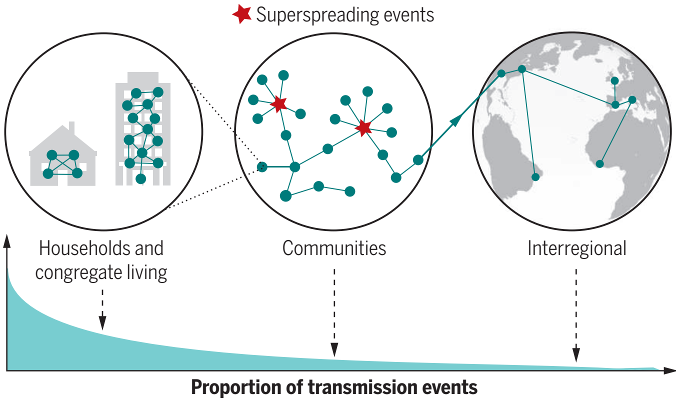
A mode of transmission need not be frequent to be important, and regardless of the cause, overdispersion has considerable implications. First, overdispersion means that most infected individuals who enter a community will not transmit, so many introductions may occur before an epidemic takes hold; likewise, overdispersion also increases the probability of disease extinction as the epidemic recedes and fewer people are infected (*11*). When large transmission events do occur, epidemics can expand rapidly, but as the epidemic grows, overdispersion will matter less to the trajectory until incidence decreases and case counts are low again. Second, overdispersion gives transmission networks "scale-free" properties, in which connectivity in the network is dominated by a few highly connected nodes. Compared with networks with more evenly distributed connections, the connectivity of scale-free networks is less sensitive to random node removal but more susceptible to targeting of highly connected nodes (*11*).

If transmission is highly overdispersed, broad and untargeted interventions may be less effective than expected, whereas interventions targeted at settings conducive to superspreading (such as mass gatherings and hospitals) may have an outsized effect. Although some determinants of overdispersion may not be amenable to targeted interventions, others related to occupation or setting could be. For example, rapidly improved infection control procedures within health care facilities played a critical role in containing the nascent SARS-CoV pandemic of 2003.

Intercity, interregional, and international spread are also essential to sustain the pandemic, even if long-distance transmission events are rare (see the figure). Only a small number of such long-distance connections are needed to create a "small world" network in which only a few infection events can transmit the virus between any two individuals worldwide. This is one reason why early travel bans could not stop the global spread of SARS-CoV-2, although they may have slowed the pandemic. However, travel restrictions can work: Extreme measures in China played an important part in achieving domestic suppression of the virus.

SARS-CoV-2 spread across spatial scales

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is mostly transmitted within households and household-like settings. A decreasing proportion of transmission events take place at increasing spatial scales, but these events become more critical for sustaining the pandemic.



Phylogenetic data provide some insight into global connectivity and the scale at which intercommunity mixing is most relevant to spread. Major SARS-CoV-2 clades are present in all global regions. Within the United States, where interstate travel continued during lockdowns, the mix of viral lineages was similar across states (*15*). This suggests that viral lineages spread quickly throughout the country and that reintroductions are highly probable should an area achieve local elimination of the virus.

The engines of the SARS-CoV-2 pandemic—household and residential settings, community, and long-distance transmission—have important implications for control. Moving from international to household scales, the burdens of interventions are shared by more people; there are few international travelers, but nearly everyone lives in households and communities. Measures to reduce household spread may appear particularly challenging, but because they directly affect so many, they need not be perfect. Household mask use and partitioning of home spaces, isolation or quarantine outside the home, and, in the future, household provision of preventive drugs could have large effects even if they offer only modest protection. Conversely, control measures at larger spatial scales (for example, interregional) must be widely implemented and highly effective to contain the virus. Indeed, few nations have managed to curb infection without stay-at-home orders and business closures, particularly after community transmission is prevalent.

The impact of accumulated SARS-CoV-2 immunity on transmission will vary across spatial scales. Any immunity conferred by infection or vaccination mitigates transmission in households or communities in near-direct proportion to the number of potential infectees that become immune, plus ancillary benefits due to herd immunity. However, because of overdispersion and small-world network properties, the ability for the virus to spread between communities is less sensitive to accumulating immunity. If even a few regions exist with a sufficient proportion of susceptible individuals to support viral spread, SARS-CoV-2 can continue to circulate in humans.

More is learned about SARS-CoV-2 transmission every day, and important uncertainties remain. The relative risk of transmission in different community settings, such as restaurants and retail stores, is still unclear, as is the impact of mitigation measures in these contexts. It is still unknown how seasonality and heterogeneities in the population distribution and duration of immunity will affect future transmission dynamics. Filling these and other knowledge gaps will clarify how the engines of transmission interact to drive the pandemic—and how best to fight back. ■

REFERENCES AND NOTES

1. Q. Bi *et al.*, *Lancet Infect. Dis.* **20**, 911 (2020).
2. Y. J. Park *et al.*, *Emerg. Infect. Dis.* **26**, 10 (2020).
3. J. M. Read *et al.*, *Proc. Biol. Sci.* **281**, 1785 (2014).
4. Z. J. Madewell *et al.*, *medRxiv* 2020.07.29.20164590 [Preprint] 1 August 2020.
5. Q. J. Leclerc *et al.*, *Dataset*, Figshare (2020).
6. H. Njuguna *et al.*, *MMWR Morb. Mortal. Wkly. Rep.* **69**, 26 (2020).
7. X. He *et al.*, *Nat. Med.* **26**, 672 (2020).
8. S. Lee *et al.*, *JAMA Intern. Med.* 10.1001/jamainternmed.2020.3862 (2020).
9. L. Hamner *et al.*, *MMWR Morb. Mortal. Wkly. Rep.* **69**, 19 (2020).
10. C. Stein-Zamir *et al.*, *Euro Surveill.* **25**, 29 (2020).
11. J. O. Lloyd-Smith *et al.*, *Nature* **438**, 355 (2005).
12. B. Gamage *et al.*, *Am. J. Infect. Control* **33**, 114 (2005).
13. D. A. T. Cummings *et al.*, *Clin. Infect. Dis.* ciaa900 (2020).
14. S. Paynter, *Epidemiol. Infect.* **143**, 1110 (2015).
15. J. Hadfield *et al.*, *Bioinformatics* **34**, 4121 (2018).

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