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Review

SARS-CoV-2 (COVID-19) superspreader events

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SUMMARY

Background & objectives: A significant number of reported COVID-19 cases can be traced back to superspreader events (SSEs), where a disproportionally large number of secondary cases relative to the standard reproductive rate, R0, are initiated. Although a superspreader is an individual who undergoes more viral shedding and transmission than others, it appears likely that environmental factors have a substantial role in SSEs. We categorise SSEs into two distinct groups: 'societal' and 'isolated' SSEs.
Methods: We summarise SSEs that have occurred using multiple databases that have been cross referenced to ensure numbers are as reliable as we can ascertain. This enables more focussed and productive control of the current pandemic and future pandemics, especially as countries and regions ease lockdown restrictions.
Results and discussion: 'Societal' SSEs pose a significant threat as members of the event are free to mingle and can infect individuals in the outside community. On the other hand, 'isolated' SSEs can be effectively quarantined as only a few individuals can transmit the virus from the isolated community to the outside community, therefore lowering further societal infection.

Is it possible that the Rose Garden event at the White House was a superspreading event (SSE)? The term 'superspreading events' was initially coined in 2005 by Lloyd-Smith et al. 'in which certain individuals infected unusually large numbers of secondary cases'.[1] Now, a 'COVID-19 At The White House Contact Tracker' has been made publicly available,[2] we suggest that there seems to be an emergence of an SSE via the front two rows resulting in 11 positive members (including President Trump), 22 negative members and 74 unknowns, to the best of our knowledge. The source and date of infections will never be definitive but the data we have thus far indicates this was an SSE.

An SSE can act as a catalyst for outbreaks. To catalogue this further, we searched multiple available databases including PubMed and Nexis, using terms including "superspreader", "spreader", "COVID-19″, "SARS-CoV-2″, "clusters of infection" and "superspreader event". Table 1 includes reported SSEs, which had a total infection number per location of greater than 6. Data sources included many news agency articles, which have been cross-referenced to ensure that numbers presented were reliable, as much as we can ascertain.

While many attribute SSEs to individuals who shed more virus particles than normal, environmental conditions appear to outweigh this. The quick identification of the type of SSE an environment favours is pivotal in correct implementation of preventative measures to minimise greater infection. It is clear that in order to prevent future outbreaks, far more control needs to involve the prevention of 'societal' SSE's where environmental factors predominate, while rapid staff isolation in 'isolated' SSEs is key.

There is heterogeneity in the calculated R_0 for SARS-CoV-2, and as such, various predictions from the estimated R_0 need to be considered as a context-dependent variable with non-pharmaceutical interventions having a key role. Estimations, using epidemiological models that allow for heterogeneity, have now suggested that a population infection rate of ~40% (or even as low as 20%[3]) can help achieve herd immunity.[4,5] Virus particles in droplets from coughs and sneezes of an infected person can travel many metres by forming a turbulent multiphase gas cloud, protecting the droplets from evaporation.[6,7] Only a small viral load is thought to be needed to establish an infection; in other infections it has been thought that a single virus can initiate an infection,[8] and this could potentially apply to SARS-CoV-2. It is clear why large gatherings, without appropriate personal protective equipment (PPE), ventilation, and hygiene, create an environment for efficient transmission. In some settings, the long-range transmission of the virus between

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distant locations is viable due to air flows driven by: i) the opening of particular windows and doors, ii) through the mass movement of people and, iii) via ventilation systems.[9] In these scenarios, due to 'superspreading', the R_e can reach higher levels because of environmental conditions that favour transmission.

During recent outbreaks, SSEs played a significant part in the burst of new infections early on, facilitating the MERS-CoV outbreak in South Korea, and the 2014/15 Ebola crisis in Western Africa.[10] One of the most widely reported SSEs related to a UK citizen contracting the disease in Singapore, who subsequently infected 11 others while on a skiing trip in the French Alps, as well as further individuals upon return to England. It is notable here that one child infected while displaying symptoms did not transmit the virus when visiting 3 schools.[11] Clearly, children are less likely to develop severe complications from the disease, where a significant proportion are asymptomatic/or have subclinical symptoms[12] and a meta-analysis shows those <20 years have an odds ratio of 0.56 for being an infected contact compared to those who are older, indicating children are less susceptible compared to adults.[14] Evidence suggests children are not the primary source of infection in most household clusters as 9.7% of 31 transmission clusters identified were thought to have children as a paediatric index case.[13] Further, transmission between children does not play a vital role in the formation of SSEs with explanations including lower levels of ACE2 present in the nasal epithelium of children compared to adults.[15] However, children can be seen as a source of contagion[23] despite being asymptomatic. Those in lower socioeconomic backgrounds are of particular concern since multigenerational cohabitation is more common which leads to higher chance of spread to the vulnerable elderly population.[23]

In Table 1, the Singapore school SSE concerned a child transmitting the virus: of 26 cases identified, only staff members in the school were infected (as well as family members of a previously identified COVID-19 patient).[21] In Salt Lake City, Utah, 3 outbreaks in childcare facilities occurred where 54% of the cases were linked to children:12 children in the childcare facilities had COVID-19 with transmission to at least 26% of non-facility contacts.[81] Here, 2 out of the 3 asymptomatic children had transmitted the infection (1 mother had been hospitalised as she was presumably infected by her asymptomatic child).[81] Due to transmission from children to their household, sufficient testing of close contacts and children (regardless of symptoms) together with prompt test results may improve control of spread. Some estimates suggest that 80% of adults with the virus are aymptomatic.[82] Similarly, we do not know the testing protocol for US politicians and other attendees of the Rose Garden event. While it seems that transmission from children is rare, the difficulty in maintenance of social distancing between children in schools can permit SSEs to arise; it seems the same applies to adults in the Rose Garden.

Table 1 shows data suggesting that specific environments favour large clusters of infection. Table 1A summarises all of the recorded SARS-CoV-2 'societal' SSEs, where no controls could be implemented to prevent individuals from transmitting the virus to people in the outside, or wider, community after the event. Table 1B displays the recorded SARS-CoV-2 'isolated' SSEs, where isolation of the particular event appeared to effectively prevent further transmission. The categorisation of SSEs into 'isolated' and 'societal' is pivotal here, permitting an understanding of how future outbreaks can be effectively controlled. 'Societal' SSEs pose a significant threat as members of the event are free to mingle and can infect individuals in the outside community. On the other hand, 'isolated' SSEs can be quarantined as only a few individuals can transmit the virus from the isolated community to the outside community. Although those in 'isolated' superspreading environments can transmit SARS-CoV-2 to people in the outside community, the lower societal contact may lessen the resulting rate of infection in comparison to a COVID-19 outburst deriving from a 'societal' SSE. Thus, while the percentage of COVID-19 cases derived from SSEs is impossible to calculate, 'societal' SSEs act to intensify the infection rate of the outside community in comparison to 'isolated' SSEs.

While many consider aeroplanes a critical superspreading environment, few SSEs have been traced back to air travel. Most modern aircraft have High Efficient Particle Absorption-Filter (HEPA) systems installed, acting to mix fresh air with filtered recirculated air., able to remove particles below 0.1 μm in size.[24] One study demonstrated the air quality in the cabins/cockpits of 69 measurement flights was 'similar or better than what is observed in normal indoor environments'.[25] However, the close proximity of passengers to one another can facilitate the transmission of disease, which can be outlined via the recent outbreak on an Emirates flight to Hong Kong where 26 passengers tested positive,[26] and on a commercial airline flight from Tel Aviv to Frankfurt.[27] It appears that minimal transmission occurred on the plane, and the majority were infected prior to the flight.

On the Charles de Gaulle aircraft carrier, a total of 1081 out of 2300 onboard were infected.[26] Comparably, the SSE on the USS Theodore Roosevelt culminated in 1156 crew members testing positive.[29] Cramped indoor spaces, shared cabins and in particular, the lack of ventilation, combined with unfiltered, recirculated air conditioning aided the virus's reproduction rate. On the Diamond Princess, it was believed that passengers first transmitted COVID-19 to crew members at the beginning of the outbreak, and subsequent spread amongst the crew was localised to food service workers. An investigation illustrated 20 confirmed crew member cases out of 1068 crew members of which 15 were food service workers – the infection rate was likely intensified due to the crowded nature of the kitchens.[30]

Care homes have been associated with a significant number of SSEs. Historically, the most common pathogen to cause outbreaks in long term health facilities has been influenza, with some studies reporting a median infection rate of 33% across residents and 23% across staff during other epidemics.[17] Similarly, in a study, all 408 residents of a large Boston shelter for the homeless were tested for SARS-CoV-2 by PCR: of all who tested positive, 87.8% were asymptomatic, demonstrating that symptomatic screening may not be an effective way to prevent large clusters of infection.[18] Outbreaks in care homes and ships can be controlled more effectively via complete isolation. While workers can still transmit infection to the outside community, the resulting outbreaks from these 'isolated' SSEs can be effectively lessened through the identification of the environment and the establishment of appropriate protocols that can minimise societal infection, such as the implementation of staff isolation rooms.

A Bavarian COVID-19 outbreak, at the end of January 2020 permitted longitudinal study of transmission events, as well as secondary attack rates and the incubation period of the disease. A median incubation period of 4 days was observed, and while lower than the previously reported 5.2 days, the timely reporting of prodromal cases may have brought down the number. The investigation discovered that the secondary attack rate of household contacts was 10%, whereas the secondary attack rate of a household cohort was 75%. The decrease in percentage correlated to the isolation of symptomatic patients. Contact tracing revealed that the secondary attack rate of 217 non-household contacts was 5% and while low, more proactive isolation could have further prevented spread. This illustrates that substantial transmission occurred pre-symptomatically, as well as during prodromal symptoms.[19] A further study examined a total of 110 cases among 11 clusters, where 24.6% were primary cases that generated secondary cases. They demonstrated that the odds that a primary case transmitted COVID-19 in a closed environment was 18.7 times higher than in an open-air enviornement.[16]

Table 1A
SARS-CoV-2 'societal' superspreader events.

Setting	Country	Number of Sites	Total Infected	
Religious	South Korea	2	4531	[41]
Religious	Germany	2	171	[42, 43]
Religious	USA	3	150	[44–46]
Religious	Netherlands	1	102	[47]
Religious	Singapore	2	33	[48]
Religious	Hong Kong	1	19	[79]
Worker Dormitories	Singapore	17	1690	[48]
Work (Food Processing Plant)	Germany	1	1029	[49]
Work (Food Processing Plant)	USA	3	779	[50]
Work (Food Processing Plant)	Ghana	1	534	[51]
Work (Food Processing Plant)	UK	4	469	[52]
Work	Singapore	2	34	[48]
Work	China	3	25	[53–55]
School	France	1	133	[56]
School	Israel	1	130	[22]
School	New Zealand	1	96	[57]
School	Singapore	1	26	[21]
Shopping	Singapore	3	122	[48]
Shopping	China	3	44	[55, 58, 59]
Hospital	South Korea	1	118	[41]
Hospital	China	1	54	[60]
Hospital	Japan	2	20	[61]
Bar	Japan	6	100	[61]
Bar	Zurich	1	6	[38]
Bar	New Zealand	1	77	[62]
Bar	Germany	1	16	[63]
Bar	Austria	1	15	[64]
Bar	Hong Kong	4	106	[79]
Building Site	Singapore	3	90	[48]
Conference	USA	1	89	[65]
Conference	Japan	1	10	[61]
Sport	South Korea	1	65	[66]
Sport	Japan	2	20	[61]
Meal	Singapore	2	55	[48]
Meal	China	2	19	[67]
Aircraft	Dubai→Hong Kong	1	26	[26]
Skiing	France	1	11	[11]
Funeral	India	1	16	[77]
Wedding	Hong Kong	2	22	[79]
Bus riders	China	1	30	[80]
Household	China	5	39	[67–70]

Table 1B
SARS-CoV-2 'isolated' superspreader events.

Setting	Country	Clusters	Total Infected	
Navy Ship	USA	1	1156	[29]
Navy Ship	France	1	1081	[28]
Cruise Ship – Ruby Princess	N/A	1	662	[71]
Cruise Ship - Diamond Princess	N/A	1	620	[72]
Prison	USA	1	358	[73]
Elderly Care	USA	1	167	[74]
Elderly Care	Germany	1	74	[75]
Elderly Care	France	1	45	[75]
Elderly Care	Scotland	3	>30	[76]
Elderly Care	Italy	1	>27	[75]

Religious events are displayed at the top of Table 1A. The most notable SSE relating to a religious gathering involves the Shincheonji Church in Daegu, South Korea. An individual with the designated name 'patient 31′ was thought to be the source. The outbreak caused exacerbated infection rates in South Korea, leading the country to have the most confirmed cases at that time outside of mainland China[31]; over 5000 cases were related to the Shincheonji SSE.[32] Tightly packed church services and a ban on face masks exacerbated infection rates.[33] Singing probably played a role too as has been evident for choirs: in another event attended by 61 individuals in Washington, an attack rate of 53.3% to 86.7% occurred.[34] Similarly, the Haj is known to involve an environment which favours the transmission of infectious diseases as illustrated by the Neisseria meningitidis serogroup W135 outbreak of 2001, that had an attack rate of 25 cases/100,000 pilgrims.[35,36]

Worker dormitories, especially in Singapore, and meat processing plants in countries such as the USA have been critical sources of COVID-19 infections. Such examples can be attributed to confined spaces and poor ventilation. We speculate that air-conditioning lowers the relative humidity for a droplet expelled at body temperature (37^0C, or higher if febrile), allowing for a warm droplet to become a smaller droplet that can be suspended for longer, travel further, and penetrate deeper into the lung. If the temperature is lower than body temperature, then the difference in ambient versus body temperature results in a lower relative humidity for the droplet. Therefore, from the perspective of the droplet, the colder the ambient temperature, the lower the relative humidity and more evaporation is facilitated. Evaporation then shrinks the droplet to make it smaller and more likely to be aerosolised. In the case of Singapore, migrants were crammed into rooms with up to 20 people sleeping in confined spaces.[37] While it is tempting to state that the first step to preventing SSEs from occurring might be the quick identification and isolation of potentially infectious individuals, as asymptomatic or pre-symptomatic spread is often the norm, the reality is this is not going to be possible.[20]

Care facilities, religious gatherings, and hospitals have been the primary source of COVID-19 clusters and multiple SSEs can be traced back to gyms, bars and nightclubs. Alcohol-induced carefree attitudes, coupled with asymptomatic transmission, culminates in

a cramped indoor environment which facilitates transmission. A Zurich nightclub experienced an SSE, whereby, a single asymptomatic male infected 5 club visitors resulting in all 300 employees and visitors being placed under quarantine.[38] An investigation of clusters in Japan noted that many SSEs arose as a result of 'heavy breathing in close proximity', such as conversations in bars and karaoke parties.[39] Places that offer eating and drinking on-site may contribute to SSEs as "adults with positive SARS-CoV-2 test results were approximately twice as likely to have reported dining at a restaurant than those with negative results".[78] A total of 112 fitness dance-related COVID-19 cases was recorded at 12 different sports facilities in Cheonan, South Korea. The 'moist, warm atmosphere in a sports facility coupled with turbulent airflow generated by intense physical exercise could cause more dense transmission of isolated droplets' is relevant.[40] As aforementioned, while virus particles can travel significant distances, social distancing eliminates close contact and acts to reduce transmission through breathing. The images of closely packed individuals at the White House's Rose Garden suggest disregard for social distancing.

SSEs cannot be identified a priori but are a major route of presymptomatic or asymptomatic transmission. From these cases, we suggest that the quick identification of 'societal' and 'isolated' SSEs can allow us to more effectively tackle virus transmission. Members of 'isolated' SSEs that could potentially spread the virus to the outside community can be quarantined which could decrease the likelihood of a 'societal' SSE occurring. Use of contact tracing and testing could be beneficial in detecting these individuals to prevent a national lockdown. From our data, there are generally more 'societal' SSEs compared to 'isolated'. The data from 'isolated' SSEs suggest that SARS-CoV-2 is much more infectious and has a lower infection fatality rate than many suggest.

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Declaration of Competing Interest

JS' conflicts which are not relevant to this piece can be found at: https://www.nature.com/onc/editors. No other authors declare a conflict.

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