can be used (eg, buprenorphine, half-life 24 h) or even synthesised.

I declare no competing interests.

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Tale of three seeding patterns of SARS-CoV-2 in Saudi Arabia

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Human mobility patterns are determinants of disease transmission. This is particularly relevant for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission in Saudi Arabia (population 34 million), which experiences three types of population movements. First is the international and domestic movement of pilgrims in Saudi Arabia. On average each month about 1 million incoming pilgrims from 180 countries merge with about 1 million Saudi-national Sunni pilgrims (75% of the Saudi population) in Saudi Arabia's two holy sites and the nearest entry port of Jeddah.[1] Second is the returning Shiite Saudi-national pilgrims (4·9 million Shiite population in Saudi Arabia) who travel to Iran and Iraq for pilgrimage. Men and women older than 60 years are overrepresented among pilgrims. Third is routine travel to and from Saudi Arabia by Saudis, permanent residents, and non-pilgrim visitors for commerce and tourism, estimated to be about 3 million people each month.

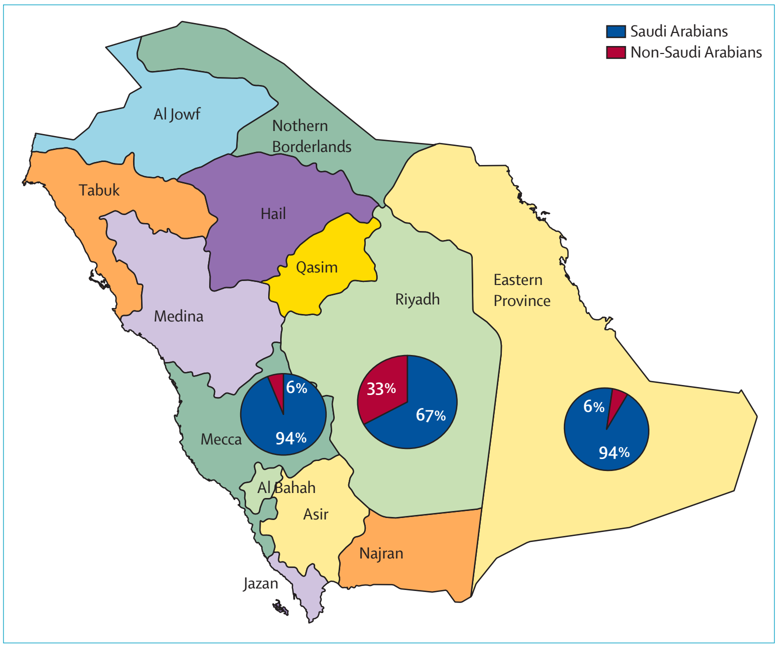

Figure: **COVID-19 distribution in Saudi Arabia on March 15, 2020, by nationality**
COVID-19=coronavirus disease 2019.

We observed three outbreak seeding patterns in Saudi Arabia in the early phase of the coronavirus disease 2019 (COVID-19) epidemic that match the three types of population movements (figure). First, transmission related to international pilgrims in holy sites in Mecca and Medina region, largely among the non-Saudi population (49 [94%] of 52 cases). Second, transmission among returning Saudi Shiite pilgrims in the eastern province, affecting mostly Saudi citizens (45 [94%] of 48 cases). Third, general non-specific spread by routine international travel in the political and diplomatic hub of Riyadh province, mostly among the Saudi population (12 [67%] of 18 cases). The remaining provinces of Saudi Arabia did not have COVID-19 cases in the early phase. Of the three seeding patterns, by April 2, 2020, the second had the greatest affect on accelerating domestic transmission in Saudi Arabia, with highest acceleration of cases seen in the eastern region (99 cases per 100 000). Per 100 000 population, Mecca and Riyadh had 17 cases and eight cases, respectively, on April 2.

Saudi Arabia's ten quarantined student evacuees from China were reported on Feb 16 to have tested negative for SARS-CoV-2.[2] The country's suspension of pilgrimage visas for international visitors on Feb 27 and for all people by March 4 probably helped delay detection of the first case in the Mecca region until March 10. Saudi Arabia implemented comprehensive pandemic mitigation efforts[3] incrementally during March 8–21.

In the early phase of the epidemic, the high proportion of COVID-19 diagnoses in the Riyadh region that were among Saudi nationals (67%) might have resulted from entry restrictions on non-Saudi people and increases in returning Saudi citizens who might have been exposed overseas. The outbreak in the eastern region was reported on March 10 among four returning Saudi pilgrims. Saudi Arabia had not recognised the impact of Qom pilgrimage[4] on SARS-CoV-2 transmission in eastern Saudi Arabia until then. The country's attempt to identify and quarantine returning Saudi pilgrims proved inefficient initially owing to non-direct routes of travel to Saudi Arabia through Gulf Cooperation Council countries. Saudi Arabia then encouraged returning citizens to voluntarily declare travel to Iran and repatriated stranded citizens using special flights.

Saudi Arabia mitigated international and domestic superspreader transmission of SARS-CoV-2 in its international pilgrim sites with early restrictions of access to its holy sites. Saudi Arabia was unsuccessful in limiting transmission among returning Saudi nationals who participated in an unmitigated superspreader event. The ongoing domestic transmission in the country is largely fueled by returning Saudi-national pilgrims.

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COVID-19 and the difficulty of inferring epidemiological parameters from clinical data

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Knowing the infection fatality ratio (IFR) is crucial for epidemic management: for immediate planning, for balancing the life-years saved against those lost to the consequences of management, and for considering the ethics of paying substantially more to save a life-year from the epidemic than from other diseases. Impressively, Robert Verity and colleagues[1] rapidly assembled case data and used statistical modelling to infer the IFR for COVID-19. We have attempted an in-depth statistical review of their paper, eschewing statistical nit-picking, but attempting to identify the extent to which the (necessarily compromised) data are more informative about the IFR than are the modelling assumptions. First, the data.

Individual-level data for outside China appear problematic because different countries have differing levels of ascertainment and different disease-severity thresholds, even for classification as a case. The data's use in IFR estimation would require model-ascertainment parameters that are country specific, about which we have no information. Consequently, these data provide no useful information on the IFR.

Repatriation flight data provide the sole information on the prevalence in Wuhan, China (excepting the lower bound of confirmed cases). 689 foreign nationals who were eligible for repatriation are doubtfully representative of the susceptible population of Wuhan. Hence, seeing how to usefully incorporate the six positive cases from this sample is difficult.

Case mortality data from China provide an upper bound for the IFR, and with extra assumptions these data also supply information on how the IFR varies with age. Because prevalence is unknown, the data contain no information for estimating the absolute IFR magnitude.

Because of extensive testing, the outbreak on the *Diamond Princess*, the quarantined cruise liner (used only for validation by Verity and colleagues) supplies data on infections and symptomatic cases, with fewer ascertainment problems. These data appear directly informative about the IFR, although the comorbidity load on the *Diamond Princess* is unlikely to fully represent any population of serious interest (perhaps having fewer individuals with very severe but more with mild comorbidities).

Second, the modelling assumptions, in which we see two primary problems. The first problem is that Verity and colleagues correct the Chinese case data by assuming that ascertainment differences across age groups determine case rate differences. Outside of Wuhan, the authors replace observed case data by the cases that would have occurred if each age group had the same per-capita observed case rate as the 50–59 years age group. The authors assume complete ascertainment for this age group. These are very strong modelling assumptions that will greatly affect the results, but the published uncertainty bounds reflect no uncertainty about these assumptions. In Wuhan, the complete ascertainment assumption is relaxed by introducing a parameter, but one for which the data appear uninformative, so the results will be driven by the assumed uncertainty.

The second problem is that, generically, Bayesian models describe uncertainty both in the data and in prior beliefs about the studied system. Only when data are informative about the targets of modelling can we be sure that prior beliefs play a small role in what the model tells us about the world. In this case, the data are especially uninformative: we suspect