Research letter

Identifying importation points of the SARS-CoV-2 Omicron variant into the USA and potential locations of early domestic spread and impact

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On 26 November 2021, the World Health Organization designated a new SARS-CoV-2 variant of concern (VoC)—Omicron (B.1.1.529).1 As of December 12, it had been detected in 29 US states.2 We identified US airports that were the most likely initial importation points of the variant from South Africa and US domestic locations considered most susceptible to early spread and negative impacts on healthcare.

We analysed international air passenger volumes on flights that arrived in the US from South Africa in September 2021. The data were sourced from the International Air Transport Association (IATA) and comprised of anonymized, passenger-level flight itineraries from commercial and scheduled charter flights, accounting for ∼90% of global air travel volumes.3 This timeframe reflects the most recent data available at the time of writing and is expected to be representative of general travel patterns in more recent months. To identify US domestic locations where early spread most likely occurred, we applied a radiation model estimating where travellers likely dispersed post-arrival at US airports. We first generated a hexagonal grid covering the US; each hexagon has a side length of ∼25 km (0.6 mi) and an area of 1623 km² (626.6 mi²). The radiation model, as previously detailed,4 accounted for travel-times between airport-hexagon pairs and population sizes within each hexagon to estimate the probability of travelling to each hexagon from any commercial airport.5 We incorporated the aforementioned flight data to estimate the total volume of travellers, from all US airports on flights from South Africa, destined for each hexagon in the USA. We identified the 10 hexagons with the largest volume of travellers.

To evaluate local population risk to severe disease from COVID-19, we used data from the Centers for Disease Control and Prevention (CDC) on the percentage of each county’s total population that received two doses of a COVID-19 vaccine or one dose of a single-shot vaccine, as of December 1.6 We calculated a population-weighted average for the top 10 locations of early domestic spread and surrounding areas, defined as counties intersecting a 50 km (31.1 mi) buffer from each top 10 hexagon. As a surrogate for healthcare system capacity to accommodate increased hospitalization needs, we calculated the state-level COVID-19 hospitalization rates per 100 000 as of December 2 using the number of COVID-19 hospitalizations (adults and children)7 and 2019 population size from the US Department of Health & Human Services and the US Census Bureau, respectively.

As a sensitivity analysis, we identified the 10 US airports with the most air passengers in September 2021 from a broader set of African countries (South Africa, Namibia, Botswana, Lesotho, Eswatini (formerly Swaziland), Nigeria, Zambia, oxford, and Zimbabwe) with evidence of local transmission as of December 7 and/or in Southern Africa.

The 10 US airports with the most air passengers from South Africa were (in descending order): Newark Liberty International Airport, NJ (n = 920 passengers); Hartsfield-Jackson Atlanta International Airport, GA (n = 715); Los Angeles International Airport, CA (n = 659); John F. Kennedy International Airport, NY (n = 465); Chicago O’Hare International Airport, IL (n = 454); Washington Dulles International Airport, Washington DC (n = 436); Miami International Airport, FA (n = 424); Salt...
Table 1. Top 10 US metropolitan areas overlapping the 10 hexagons with the largest volume of travellers from South Africa expected to travel to a corresponding location after arriving at an US airport

| Rank | US metropolitan areas       | Estimated volume of air passenger travellers | Population-weighted average percentage of population who are fully vaccinated among counties within 50 km (31.1 mi) | State-level reporting of Omicron VoC, as of 12 December 2021 |
|------|----------------------------|---------------------------------------------|----------------------------------------------------------------------------------------------------|-------------------------------------------------------------|
| 1    | New York City, NY          | 806                                         | 68%                                                                                                 | Yes                                                         |
| 2    | Miami, FL                  | 372                                         | 70%                                                                                                 | Yes                                                         |
| 3    | Los Angeles, CA            | 342                                         | 61%                                                                                                 | Yes (first case detected in CA)                             |
| 4    | Washington DC              | 214                                         | 66%                                                                                                 | Yes                                                         |
| 5    | Atlanta, GA                | 172                                         | 51%                                                                                                 | Yes                                                         |
| 6    | Dallas-Fort Worth, TX      | 124                                         | 53%                                                                                                 | Yes                                                         |
| 7    | Salt Lake City, UT         | 108                                         | 56%                                                                                                 | Yes                                                         |
| 8    | Houston, TX                | 106                                         | 56%                                                                                                 | Yes                                                         |
| 9    | Minneapolis, MN            | 105                                         | 61%                                                                                                 | Yes                                                         |
| 10   | Chicago, IL                | 104                                         | 63%                                                                                                 | Yes                                                         |

*Defined as having received two doses of a COVID-19 vaccine or one dose of a single-shot COVID-19 vaccine, as of 1 December 2021.

Lake City International Airport, UT (n = 335); Minneapolis-St. Paul International Airport, MN (n = 328); San Francisco International Airport, CA (n = 320). Our sensitivity analysis yielded fairly consistent results, but differed in the addition of George Bush International Airport, TX; Dallas/Fort Worth International Airport, TX; and Logan International Airport, MA instead of Salt Lake City International Airport, UT; Minneapolis-St. Paul International Airport, MN; and San Francisco International Airport, CA. In Figure 1A–C, the 10 hexagons with the largest estimated volume of travellers from South Africa overlapped with the metropolitan areas of (in descending order): New York City, NY; Miami, FL; Los Angeles, CA; Washington DC; Atlanta, GA; Dallas-Fort Worth, TX; Salt Lake City, UT; Houston, TX; Minneapolis, MN; and Chicago, IL (Figure 1A, Table 1). Among these locations, the relatively lowest population-weighted average of full vaccination coverage were the local areas surrounding Atlanta, GA (51%); Dallas-Fort Worth, TX (53%); Houston, TX (56%); Salt Lake City, UT (56%) (Figure 1B, Table 1). Salt Lake City may be particularly vulnerable due to UT’s relatively high hospitalization rate per 100 000, as of December 2 (Figure 1C).

Our analysis exemplifies an importation risk assessment that offers highest value to decision-makers at the initial stages of an outbreak. Results highlight likely areas of initial importation and domestic spread to bolster surveillance and anticipate areas with risks to healthcare capacity. However, caveats and limitations must be noted. First, we assumed South Africa to be the primary source of importation as it was the first known epicentre, but Omicron may have emerged elsewhere and was spreading globally before the first known specimen was collected (November 9). Second, the radiation model did not account for factors like ticket prices or route that could influence one’s decision to arrive at a US airport far away from their final domestic destination. Third, we assumed that the Omicron variant spreads in areas with a high prevalence of the Delta variant, as other countries are experiencing. Fourth, we assumed that vaccination coverage could protect against severe disease at a similar level as observed for previous VoCs. Fifth, CDC data underestimated full-dose vaccination coverage and booster doses but overestimated first doses (the latter two unaccounted for in this manuscript). We

Figure 1. Maps of the US layered with data on: the modelled domestic destinations for travellers from South Africa post-arrival at a US airport in September 2021 (A) and county-level percentage of population who received two doses of a COVID-19 vaccine or one dose of a single-shot COVID-19 vaccine, as of 1 December 2021 depicted along a white–teal (low–high%) colour spectrum (B). Hexagons represent the estimated volume of travellers from South Africa expected to travel to a corresponding location after arriving at a US airport; darker, taller hexagons represent a larger volume. Red boxes denote the top 10 locations with the largest estimated volume of travellers. State-level COVID-19 hospitalizations per 100 000 are depicted along pink–purple (low–high) colour spectrum (C)
assumed consistency in the magnitude and direction of this systematic error across all counties. Furthermore, varying implementation/adherence to restrictions and increased population mobility associated with American holidays (i.e. Thanksgiving, Christmas) were not considered. These could influence which US areas were at highest risk of early spread. Finally, we did not account for immunity derived from previous infection, although T-cell responses appear to be conserved against the Omicron variant. Rather, we equated low vaccination coverage with susceptibility to severe COVID-19 disease.

Nevertheless, results highlighted metropolitan areas most likely to be locations for early introduction and spread of the Omicron variant in the USA with New York City, Miami, and Los Angeles leading. Several cities in GA, TX, oxford, and UT were particularly vulnerable to public health impacts given their relatively lower vaccination coverage.

**Authors’ contributions**
ATB, PAD, IIB and KK conceived the idea. NHA and JF conducted data analysis. CH contributed to writing. NHA, ATB, JF, PAD, IIB and KK interpreted data and contributed to writing.

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**Conflict of interest**
NHA, ATB, JF, PAD, CH and KK are employed at BlueDot, a social enterprise that develops digital technologies for public health. IIB has consulted for BlueDot.

**References**
1. Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern.
2. CDC. Omicron Variant: What You Need to Know. Centers for Disease Control and Prevention https://www.cdc.gov/coronavirus/2019-ncov/variants/omicron-variant.html (2021).
3. Passenger Intelligence Services (PaxIS). https://www.iata.org/en/services/statistics/intelligence/paxis/.
4. Tuite AR, Thomas-Bachli A, Acosta H et al. Infectious disease implications of large-scale migration of Venezuelan nationals. J Travel Med 2018; 25:tyay077.
5. Weiss DJ, Nelson A, Gibson HS et al. A global map of travel time to cities to assess inequalities in accessibility in 2015. Nature 2018; 553:333–6.
6. Centers for Disease Control and Prevention. COVID-19 Vaccinations in the United States, County. Data.CDC.gov https://data.cdc.gov/Vaccinations/COVID-19-Vaccinations-in-the-United-States-County/8xkx-amqh.
7. U.S. Department of Health & Human Services. COVID-19 Reported Patient Impact and Hospital Capacity by State Timeseries. Health-Data.gov https://healthdata.gov/Hospital/COVID-19-Reported-Patient-Impact-and-Hospital-Capa/g62h-syeh.
8. UK Health Security Agency. SARS-CoV-2 Variants of Concern and Variants under Investigation in England: Technical Briefing 31, Vol. 42, 2021.
9. Maggie Astor. C.D.C. Data May Inflate First Doses and Undercount Boosters. The New York Times https://www.nytimes.com/2021/12/11/health/cdc-revising-vaccination-data.html (2021).
10. Redd AD, Nardin A, Kared H et al. Minimal crossover between mutations associated with omicron variant of SARS-CoV-2 and CD8+ T cell epitopes identified in COVID-19 convalescent individuals. mBio 2022. https://doi.org/10.1128/mbio.03617-21.