Omicron strain spreads with the doubling time of 3.2—3.6 days in South Africa province of Gauteng that achieved herd immunity to Delta variant

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Abstract

Omicron, the novel, highly mutated SARS-CoV-2 Variant of Concern (belonging to the Pango lineage B.1.1.529), was first collected on November 8, 2021, in Gauteng province of South Africa. By the end of November 2021 it has spread towards fixation in Gauteng and was detected on all continents. Based on data collected till December 7, 2021, we showed the exponential growth of the Omicron variant over the four-week period in Gauteng (November 8–December 5, 2021) with the doubling time equal 3.38 day [CI 95%: 3.18–3.61 day]. Log–linear regression suggests that the spread began around October 10, 2021, however due to stochasticity in the initial spread this estimate is likely inaccurate. Phylogenetic analysis indicates that the Omicron strain started to diverge in between October 28 and November 5, 2021. This implies that the hidden spread of Omicron before October 10, 2021 (which would suggest slower strain growth) is unlikely. The very short doubling time of Omicron in Gauteng, a province that has reached herd immunity to the Delta variant (implied by the decrease of the weekly number of cases between July and October, 2021, at no significant mobility restrictions), suggests that Omicron will cause abrupt outbreaks of COVID-19 epidemics across the world, and will become the (temporarily) dominant strain.
Introduction

Omicron, the novel SARS-CoV-2 Variant of Concern (Pango lineage B.1.1.529, Nextstrain clade identifier 21K, first collected in Gauteng province of South Africa, November 8, 2021 GISAID sequence accession ID: EPI_ISL_6913995) is characterized by 30 amino acid substitutions, three small deletions and one small insertion in the spike protein compared to the original SARS-CoV-2 virus\(^1\). Altogether, Omicron has 51 amino-acid mutations, and its closest known epigenetic sister has 15 mutations (GISAID sequence accession ID: EPI_ISL_622806) with only 9 common mutations, implying the distance of 42 mutations from the last common ancestor (based on the phylogenetic tree generated by Nextstrain). The collection date of the Omicron epigenetic sister, September 13, 2020, suggests more than a year of evolution in an isolated niche, possibly in an immunocompromised host, but more data is necessary to rule out or confirm the existence of hidden branches (see Ref.\(^2\) for discussion). The lineage started spreading rapidly in Gauteng province in November 2021, reaching fixation by the end of that month and causing an abrupt epidemic outbreak in the province. Based on GISAID data\(^3\) and Gauteng province data on daily COVID-19 cases\(^4\), both accessed on December 7, 2021, we estimated the Omicron strain doubling time, and the strain divergence date.

Results

The Delta variant (lineage B.1.617.2) became the dominant variant in Gauteng in June 2021, causing an epidemic wave that peaked at the beginning of July 2021, Fig. 1A. Between July and October 2021, the weekly number of COVID-19 cases has been decreasing, despite no significant reduction of population mobility at workplaces and retail & recreation centers, Fig. 1B (see Methods). The appearance of the Omicron variant, has caused a rapid

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\(^1\)Implications of the further emergence and spread of the SARS-CoV-2 B.1.1.529 variant of concern (Omicron) for the EU/EEA-first update, ECDC, [https://www.ecdc.europa.eu/en/publications-data/covid-19-threat-assessment-spread-omicron-first-update](https://www.ecdc.europa.eu/en/publications-data/covid-19-threat-assessment-spread-omicron-first-update) (visited on 12/07/2021).

\(^2\)Kupferschmidt K. (2021) *Science* **374**, 1179–1179.

\(^3\)Shu Y. & McCauley J. (2017) *Eurosurveillance* **22**, 30494.

\(^4\)Marivate V. & Combrink H. M. (2020) *Data Science Journal* **19**, 1–7; Marivate V. *et al.*, *Coronavirus disease (COVID-19) case data - South Africa* (Zenodo, Mar. 2020).
Table 1: Data used for Fig. 1C.

| Week of 2021 | Cases | All genomes | Omicron genomes | Estimated Omicron cases |
|--------------|-------|-------------|-----------------|------------------------|
| 43 (Oct 25–Oct 31) | 625   | 3           | 0               | 0.0                    |
| 44 (Nov 1–Nov 7)   | 491   | 4           | 0               | 0.0                    |
| 45 (Nov 8–14)     | 762   | 23          | 21              | 695.7                  |
| 46 (Nov 15–21)    | 2549  | 167         | 160             | 2442.2                 |
| 47 (Nov 22–28)    | 10,938| 13          | 13              | 10,938.0               |
| 48 (Nov 29–Dec 5) | 50,612| 0           | 0               | 50,612.0*              |

*Assuming that all cases are Omicron infections.

epidemic outbreak (Fig. 1A). In Fig. 1C we show the exponential growth of Omicron variant in weeks 45–48, 2021 (November 8–December 5). Omicron cases were estimated as a product of the proportion of Omicron genomes to all collected genomes in a given week and the respective weekly number of total COVID-19 confirmed cases (see Table 1). Since data on genomes collected in week 48, 2021 are not yet available, we have assumed that in that week all Gauteng cases are from Omicron infections. This method, in contrast with analyzing only the proportion of new strain genomes, enabled us to follow Omicron growth after its fixation in weeks 46–47, of 2021. The weekly Omicron multiplication rate was estimated to be equal to 4.20 [CI 95%: 3.84–4.60] corresponding to the doubling time equal 3.38 day [CI 95%: 3.18–3.61 day]. The log–linear regression suggests that the Omicron exponential growth has started around October 10, 2021, however the initial epidemic growth is highly stochastic and may be heavily disturbed by the appearance of superspreaders in the cascade of infections. The profile of mutation accumulation in Fig. 1D indicates that the Omicron strain started diverging between October 28 and November 5, 2021 (95% CrI), with average mutation accumulation rate equal 0.47/week [CrI 95%: 0.38–0.57], which is in good agreement with the average SARS-CoV-2 mutation accumulation rate equal 0.45/week (based on the Nextstrain estimate as of December 7, 2021).

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6 Kochańczyk M. et al. (2020) Royal Society Open Science 7, 200786.
7 Hadfield J. et al. (2018) Bioinformatics 34, 4121–4123.
8 https://nextstrain.org/ncov/gisaid/global?l=clock.
**Figure 1:** Growth and divergence of the Omicron strain.  
**A** Weekly aggregated cases of Omicron, Delta and other variants in the Gauteng province in South Africa.  
**B** Weekly averaged mobility in workdays in the Gauteng province in workplaces and retail & recreation centers.  
**C** Exponential growth of the Omicron strain in weeks 45–48, 2021 (November 8–December 5) in the Gauteng province.  
**D** Accumulation of mutations on the Omicron strain worldwide based on Nextstrain phylogenetic tree. The green line shows the mutation accumulation trend determined by the linear regression assuming Poisson distribution of the number of mutations in a give time. The 95% credible interval is shown by the light green rectangle.

**Discussion**

We have demonstrated the exponential growth of the Omicron strain in the South African province of Gauteng in the four-week period from November 8 to December 5, 2021, with the doubling time equal 3.38 day [CI 95%: 3.18–3.61 day]. Based on the mutation accumulation profile we found that the Omicron strain started diverging between October 28 and November 5, 2021, which is after October 10, the date suggested by log–linear regression of the number of weekly cases. The discrepancy can be explained by the occurrence of a su-
perspreading event or events at the beginning of November that could have caused a sharp growth of Omicron infections before the more regular exponential growth has started. This is also suggested by the fact that before the week of November 8–15, in which 61 Omicron genomes were collected worldwide, no Omicron genomes were found. The estimated date of divergence between October 28 and November 5, 2021, in conjunction with the lack of detected Omicron genomes before November 8, implies that circulation of Omicron in October or September 2021 (which could potentially explain the abrupt outbreak) is unlikely.

Before the Omicron outbreak, the Delta variant was the dominant strain in Gauteng, and between July and October the COVID-19 epidemic was receding without significant mobility reduction, suggesting that the population of Gauteng has reached herd immunity to the Delta variant. The population-level immunity has been apparently overcome by the Omicron variant. Omicron accumulated more than 30 mutations in its spike protein, with 15 substitutions in the receptor binding domain (RBD, residues 319—541) alone. Many of these RBD mutations are thought to decrease potency of neutralizing antibodies. This is in line with the recent study which demonstrated that the spread of the Omicron variant increased substantially the hazard ratio for reinfection versus primary infection.

The Omicron doubling time found here to be in range 3.18–3.61 days for the Gauteng province is larger but comparable to the doubling times during the first COVID-19 pandemic outbreaks in spring 2020 that were found in range between 1.86 and 2.88 for China, Italy, France, Germany, Spain, UK, Switzerland and New York State. Such short Omicron doubling time implies that it will likely outcompete the Delta variant, become (temporarily) the dominant strain and cause epidemic outbreaks across the world. These outbreaks may be hard to control by the current vaccines (as already suggested by abrupt growths of Omicron).

9Implications of the further emergence and spread of the SARS-CoV-2 B.1.1.529 variant of concern (Omicron) for the EU/EEA—first update, ECDC, https://www.ecdc.europa.eu/en/publications-data/covid-19-threat-assessment-spread-omicron-first-update (visited on 12/07/2021).
10Callaway E. & Ledford H. (2021) Nature 600, 197–199.
11Pulliam J. R. et al. (2021) medRxiv, 10.1101/2021.11.11.21266068 10.1101/2021.11.11.21266068.
cron cases in Denmark\textsuperscript{12} and UK\textsuperscript{13} with 69% and 77% vaccination rates respectively) as well as by lockdowns due to increasing lockdown fatigue.

**Methods**

All used data were retrieved on December 7, 2021. The Omicron strain divergence date and mutation accumulation rate were determined by the linear regression assuming Poisson distribution of the number of mutations in a given time point. The Omicron phylogenetic tree was accessed from Nextstrain (https://nextstrain.org). The Omicron weekly cases where estimated based on GISAID data and the Gauteng province COVID-19 cumulative cases (DSFSI at University of Pretoria, https://github.com/dsfsi/covid19za/tree/master/data) corrected from 8099 to 605 for November 23, 2021 using the information from South African National Institute for Communicable Diseases (NICD) (https://www.nicd.ac.za/latest-confirmed-cases-of-covid-19-in-south-africa-23-november-2021). According to the information provided by NICD the difference results from retrospective addition of 7494 antigen tests. The mobility in Gauteng province was accessed from COVID-19 Community Mobility Reports from Google (https://www.google.com/covid19/mobility). The weekly average was calculated based on workday days.

**Data availability**

We analyzed publicly available genome datasets retrieved from GISAID, https://www.gisaid.org and Community Mobility Reports https://www.google.com/covid19/mobility/. Cases data for Gauteng can be found in daily reports from the National Institute for Communicable Diseases https://www.nicd.ac.za as aggregated by University of Pretoria https://github.com/dsfsi/covid19za.\textsuperscript{12} Status på omikron-varianten (B.1.1.529) pr. 08.12.21, https://www.ssi.dk/aktuelt/nyheder/2021/status-pa-omikron-varianten-b11529-pr-071221.\textsuperscript{13} Variant of concern: Omicron, VOC-21NOV-01 (B.1.1.529), https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1038404/Technical_Briefing_30.pdf.
Author contributions

Conceptualization, Frederic Grabowski, Marek Kocharczzyk and Tomasz Lipniacki; Data curation and Software, Frederic Grabowski; Investigation, Frederic Grabowski and Marek Kocharczzyk; Supervision, Marek Kocharczzyk and Tomasz Lipniacki; Visualization, Frederic Grabowski; Writing – original draft, Tomasz Lipniacki; Writing – review & editing, Marek Kocharczzyk.

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Competing interests

The authors have no competing interests.