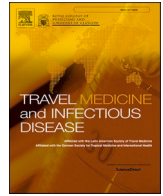




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Tracking and controlling the spatiotemporal spread of SARS-CoV-2 Omicron variant in South Africa

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ABSTRACT

Background: South Africa is the focus of the current epidemic caused by Omicron. Understanding the spatiotemporal spread of Omicron in South Africa and how to control it is crucial to global countries.

Methods: To explore the spatiotemporal spread of Omicron in 9 provinces in South Africa, a province-level geographic prediction model of COVID-19 symptom onset risk, is proposed.

Results: It has been found that i) The spatiotemporal spread was relatively slow during the first stage and following the emergence of Omicron in Gauteng. The spatial spread of Omicron accelerated after it had become the dominant variant, and continued to spread from Gauteng to the neighboring provinces and main transport nodes. ii) Compared with current Alert Levels 1–4 in all provinces, the imposition of lockdown in the high-onset-risk Gauteng together with the Alert Level 1 in other 8 provinces, was found to more effectively control the spread of Omicron in South Africa. Moreover, it can reduce the spread of the Omicron epidemic in the provinces where main international airports are located to other parts of the world. iii) Due to declining vaccine efficiency over time, even when the daily vaccination rates in each province increased by 10 times, the daily overall onset risk was only reduced by 0.34%–7.86%.

Conclusions: Our study has provided a comprehensive investigation concerning the spatiotemporal dynamics of Omicron and hence provided scientific findings to enable a contribution which will assist in controlling the spatiotemporal spread of Omicron by integrating the prevention measures and vaccination.

1. Introduction

The new Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant (B.1.1.529) had spread to more than 100 countries and territories around the world since it was first detected in South Africa on November 9th, 2021 [1,2]. And Omicron is becoming, or already has become, dominant in several countries [3]. This variant contains >30 spike protein amino acid mutations that possibly are associated with increased transmissibility, severity, and capacity for immune escape [4–6]. It has been found that Omicron variant may lead to more significant escape from immune protection elicited by previous SARS-CoV-2 infection and perhaps even by existing Coronavirus disease 2019 (COVID-19) vaccines [7–10]. Thus, Omicron was designated as variant of concern (VOC), by the World Health Organization (WHO) on November 26th, 2021 [11]. To assist more countries to effectively prevent the emergence of the Omicron variant, it is crucial to explore both factors relating to its emergence and also the manner of its spread [12].

Likewise, how to effectively control the spatiotemporal spread of the Omicron by the means of the integration of the non-pharmaceutical interventions (NPIs) measures and the vaccination should be investigated [13]. South Africa, the country in which Omicron caused a new surge in COVID-19 cases [14], has been thus, chosen regarding the exploration of the spatial dynamics of the Omicron spread and thereby further enabling a subsequent investigation regarding how to effectively control such a spread by the integration of vaccination and NPI measures. It has become clear that an exploration to find the means to effectively control the Omicron epidemic the impact on normal social and economic activities is to be reduced.

South Africa announced its withdrawal from the third wave of the COVID-19 infection at the end of September [15]. The control measures were thereby relaxed from October 1st 2021 by adjusting Alert Level 2 to Alert Level 1 [15]: i) the hours of the curfew were changed; ii) the maximum number of large gatherings was promoted; iii) the sale of alcohol – for both off-site and on-site consumption – was permitted.

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However, the emergence of Omicron quickly destroyed the potential of the success of the defeat of the above third wave of the epidemic. The mean number of 280 COVID-19 cases in South Africa per day during the week before the detection of Omicron, increased to 800 cases per day in the following week. COVID-19 cases were increasing rapidly in South Africa [7]. The early doubling time in the Omicron wave is higher than that of the previous three waves [7]. Sequencing data suggests that Omicron had become the dominant variant in South Africa by November 2021 [16]. Data from South Africa's largest private health insurer suggest that more than 90% of newly sequenced infections in South Africa now involve the Omicron variant. After the outbreak caused by Omicron, it was decided for South Africa to remain on Coronavirus Alert Level 1 and to increase the current low vaccination rate [17].

During critical times, the province-level weighted kernel density estimation (WKDE) model [18,19] was proposed to enable the prediction of the spatiotemporal COVID-19 symptom onset risk, and further to explore the spread of Omicron in 9 provinces of South Africa. The original WKDE model had been applied to explore the spread of Alpha (B.1.1.7) before [20]. In order to more comprehensively estimate Omicron's transmissibility under the impact of vaccination and control measures, i) The daily human mobility [21], ii) time-varying vaccination rate and vaccination efficiency [22], iii) daily COVID-19 effective reproductive number R [23], iv) weekly respiratory pathogens surveillance reports [24], v) weekly levels of SARS-CoV-2 in wastewater treatment plants [25], vi) weekly COVID-19 cases admitted to sentinel hospital surveillance sites [26], vii) the weekly percentage testing positive [27], and viii) daily social distancing level factors [20] in 9 provinces were incorporated to enhance the original WKDE model. Based on the onset risk prediction results, the spatiotemporal spread of Omicron under different scenarios with different epidemic alert levels and vaccination rate levels was simulated. The spatiotemporal data of the daily COVID-19 cases in 9 provinces of South Africa from October 1st, 2021, to December 5th, 2021, are utilized in the development of this study [28].

2. Methods

2.1. Data sources

A total of 127,205 COVID-19 cases with spatiotemporal information in South Africa during the period from October 1st, 2021, to December 5th, 2021, were collected from official reports by the National Institute For Communicable Diseases (NICD) in South Africa [28]. In addition, to quantify the daily human mobility and the impact of the social distancing control level on the COVID-19 epidemic in all 9 provinces,

daily human mobility trend data from September 1st, 2021, to December 5th, 2021, provided by Apple Map were used (Fig. 1) [21]. Until December 5th, 2021, the COVID-19 vaccines used in South Africa were Janssen (Johnson & Johnson) and Pfizer-BioNTech vaccines. In order to measure the impact of vaccination on the COVID-19 epidemic, daily vaccination rates in all of the 9 provinces of South from February 17th, 2021, to December 5th, 2021, were used (Fig. 2) [22]. The vaccination rate in these instances, refers to the receipt of a Johnson & Johnson single dose or Pfizer-BioNTech 2 doses. The effectiveness of Johnson & Johnson and Pfizer-BioNTech vaccines over time is based on the previous study about examining SARS-CoV-2 infection by vaccination status in 780,225 veterans in United States (US) during the period February 1st, 2021 to October 1st, 2021 [29]. According to this study, vaccine effectiveness against infection risk (VE-I) continued to decline over time [23]. VE-I at the sixth month had declined to 13.1% for Johnson & Johnson, and 43.3% (95% CI: 41.9%–44.6%) for Pfizer-BioNTech [23]. In addition, i) daily COVID-19 effective reproductive number R in all 9 provinces [23], ii) weekly respiratory pathogens surveillance reports [24], iii) weekly percentage testing positive [27], iv) weekly levels of SARS-CoV-2 in wastewater in wastewater treatment plants [25], and v) weekly COVID-19 cases admitted to sentinel hospital surveillance sites [26] from October 1st, 2021, to December 5th, 2021 were also collected from official reports by the NICD in South Africa.

2.2. An enhanced WKDE model for predicting the onset risk of COVID-19 symptoms at the province-level

The SARS-CoV-2 has been found to have a high viral load and transmissibility around the date of symptom onset [30,31]. Therefore, it is necessary to adopt appropriate data-driven spatiotemporal models to dynamically and individually assess the onset risk level. Shi et al. developed an intercity scale extended WKDE model [18,19]. The model performs retrospective analysis based on the spatiotemporal information of onset cases to infer the infection date of each onset case, and further infer the spatial distribution (that is, the kernel density surface) of the infected risk of people by the onset cases at a past date, and finally predict the distribution of onset risk in a future date. In addition, according to the transmission law of COVID-19 (i.e., mainly through direct, indirect, or close contact between people), the dynamic flow of people data was introduced into the model to improve the accuracy of prediction [18,19]. The improved model is called an extended WKDE model. This data-driven spatial prediction method can reduce the dependence on theoretical assumptions and environmental parameters, which is suitable for the current stage when the transmission characteristics of COVID-19 are not very clear.

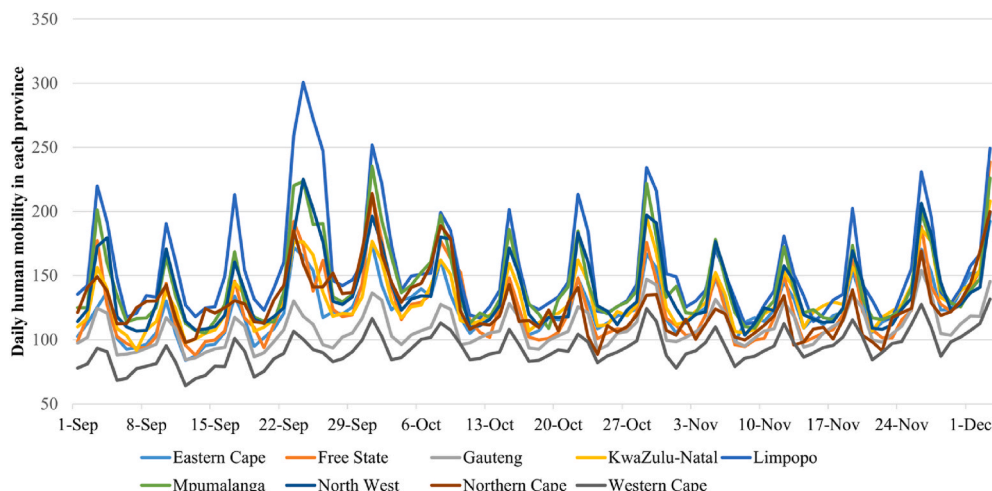


Fig. 1. The daily variation of the human mobility in the 9 provinces of South Africa from September 1st, 2021 to December 5th, 2021.

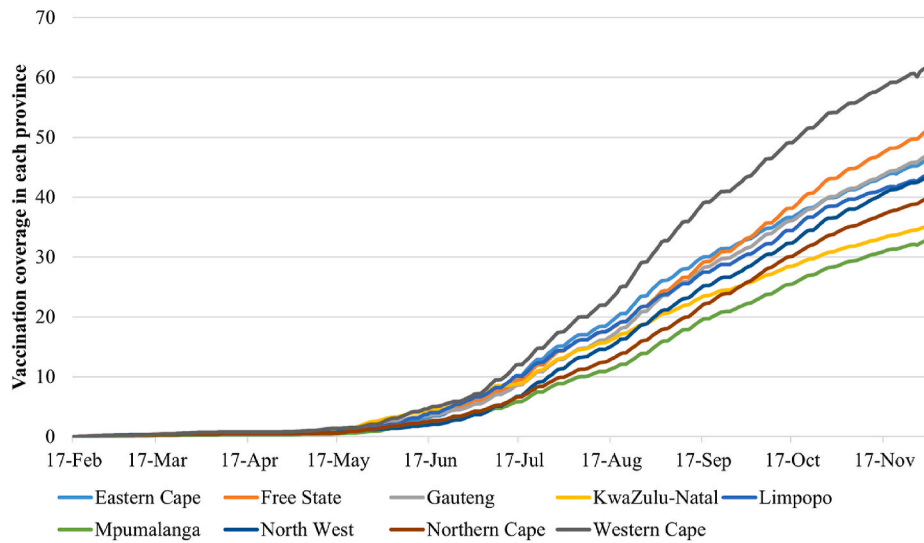


Fig. 2. The daily variation rates of the COVID-19 vaccination rates in the 9 provinces of South Africa from February 17th, 2021 to December 5th, 2021.

As a further development of the original extended WKDE model, the province-level WKDE model, proposed in this study, includes the following three steps [18,19]:

- a) Conducting a retrospective analysis of the historical existence likelihood of the infection in each provincial location in which an onset case had been present;
- b) Making inferences regarding the historical existence likelihood of the infection in the entire region;
- c) Making predictions regarding the epidemic onset risk in the entire region on a given day, in the near future.

The main difference between the province-level WKDE model and the original extended WKDE model was that at step b) of the model, the historical existence likelihood of an infection in a random location in the entire region was formulated as follows [18,19]:

$$P_{Infection}(S, t_i) = n(t_i)^{-1} \sum_{j=1}^{n(t_i)} R(S, t_i) \times (1 - VE(S, t_i) \times Vp(S, t_i)) \times Waterlevel(S, t_i) \times Influenzapositive(S, t_i) \times Testpositive(S, t_i) \times Sentinelcase(S, t_i) \times MSD(S, t_i) \times M(S, t_i) \times P_{Infection}(L_j, t_i) \times Kh(S - L_j) \tag{1}$$

where $P_{Infection}(S, t_i)$ is the probability of any individual, infected with COVID-19, infecting others in a random location, S , in the city on day t_i ; $R(S, t_i)$ denotes COVID-19 effective reproductive number in the province containing the location S , on day t_i ; $VE(S, t_i)$ denotes the vaccine efficiency in the province containing the location S , on day t_i ; $VP(S, t_i)$ is the proportion of the population who, on day t_i , have been fully vaccinated in the province containing the location S ; $Water_{level}(S, t_i)$ denotes the SARS-CoV-2 levels in influent (untreated) wastewater in the province containing the location S , on day t_i ; $Influenzapositive(S, t_i)$ denotes the influenza positive cases in the province containing the location S , on day t_i ; $Testpositive(S, t_i)$ denotes the percentage testing positive in the province containing the location S , on day t_i ; $Sentinelcase(S, t_i)$ denotes the COVID-19 admissions to sentinel hospital surveillance sites in the province containing the location S , on day t_i ; L_j is the j -th location among the provincial places in which the onset cases resided; $P_{Infection}(L_j, t_i)$ denotes the probability that one onset case was infected on day t_i in a location L_j ; and $Kh(S - L_j)$ denotes a Gaussian kernel between locations S , and L_j . The values of $P_{Infection}(L_j, t_i)$, $Kh(S - L_j)$, and h were

determined in earlier model procedures.

$M(S, t_i)$ denotes the human mobility factor at location S , on day t_i , calculated as [18,19].

$$M(S, t_i) = i^{-1} M_k \tag{2}$$

where M_k denotes the daily human mobility of the province containing location S , on day t_k , prior to t_i .

$M_{SD}(S, t_i)$ denotes the social distancing level factor in the province on day t_i , calculated as follow [20]:

$$MSD(S, t_i) = i^{-1} \sum_{k=1}^i \frac{M_k}{M_{t0}} \tag{3}$$

where M_k denotes the daily human mobility in a province containing the location S , on day t_k prior to t_i ; M_{t0} is the average value of the daily human mobility data in the specific province before the COVID-19 outbreak date; and denotes the daily social distancing amount in a

province containing location S , on day t_k prior to t_i .

In particular, for the new scenario of the Alert Level 2 for all 9 provinces in South Africa, the daily human mobility $M(S, t_i)$ and social distancing level factors $M_{SD}(S, t_i)$ for 9 provinces, were set as usual from September 12th to October 1st, 2021 (The stage where the Alert Level 2 was implemented before). For the new scenario of the Alert Level 3 for all 9 provinces in South Africa, the daily human mobility $M(S, t_i)$ and social distancing level factors $M_{SD}(S, t_i)$ for 9 provinces, were set as usual from July 25th to September 11th, 2021 (The stage where the Alert Level 3 was implemented before). For the new scenario of the Alert Level 3 for all 9 provinces in South Africa, the daily human mobility $M(S, t_i)$ and social distancing level factors $M_{SD}(S, t_i)$ for 9 provinces, were set as usual, from June 27th to July 24th, 2021 (The stage at which the Alert Level 4 was implemented before). For the new scenario of the Alert Level 5 in Gauteng, together with Alert Level 1 in the remaining 8 provinces in South Africa, the daily human mobility $M(S, t_i)$ and social distancing level factor $M_{SD}(S, t_i)$ in Gauteng, were set as 0, the daily human mobility $M(S, t_i)$ and social distancing level factor $M_{SD}(S, t_i)$ in 8 other provinces,

were set as usual.

Finally, the predicted risk in each location was divided by the maximum predicted risk among all locations on a specific date and thereby standardized to a value of between 0 and 1 [18,19]. Different levels of onset risk were established as follows [18,19]: low onset risk [0–0.2], low-medium onset risk [0.2–0.4], medium onset risk [0.4–0.6], medium-high onset risk [0.6–0.8], and high onset risk [0.8–1]. The reliability of the predicted COVID-19 onset risk was evaluated using its spatial significance, i.e., the percentage of onset cases on a future predicted date, that would occur in the areas with a predicted onset risk greater than 0.8 (identified as onset hotspots).

Table 1
Level 1–5 epidemic alert in South Africa [32].

The alert level of the epidemic	Specific measures
Level 1	<ul style="list-style-type: none"> • Every person is confined to his or her place of residence from 00H00 until 04H00 daily. • The wearing of a face mask is mandatory for every person when in a public place • Attendance of a funeral and cremation is limited to 100 persons or less. • A distance of at least one and a half metres from each other when in common spaces. • Social, political and cultural gatherings are permitted but limited to 750 persons or less for indoor venues and 2000 persons or less • Night clubs are closed to the public • Bus and taxi services may not carry more than 70% of the licensed capacity for long distance travel
Level 2	<ul style="list-style-type: none"> • Every person is confined to his or her place of residence from 23H00 until 04H00 daily. • The wearing of a face mask is mandatory for every person when in a public place. • Attendance of a funeral and cremation is limited to 50 persons or less • A distance of at least one and a half metres from any other person • Social, political and cultural gatherings are permitted but limited to 250 persons or less for indoor venues and 500 persons or less for outdoor venues • Night clubs are closed to the public. • Bus and taxi services may not carry more than 70% of the licensed capacity for long distance travel
Level 3	<ul style="list-style-type: none"> • Every person is confined to his or her place of residence from 22H00 until 04H00 daily • The wearing of a face mask is mandatory for every person • Attendance of a funeral and cremation is limited to 50 persons or less • A distance of at least one and a half metres from any other person • Social, political and cultural gatherings are permitted but limited to 50 persons or less for indoor venues and 100 persons or less for outdoor venues • Night clubs are closed to the public • Bus and taxi services may not carry more than 70% of the licensed capacity for long distance travel
Level 4	<ul style="list-style-type: none"> • Every person is confined to his or her place of residence from 21H00 until 04H00 daily • Schools and institutions of higher education will be closed for contact classes • Attendance of a funeral and cremation is limited to 50 persons or less • All gatherings are prohibited
Level 5	<ul style="list-style-type: none"> • Lockdown • Every person is confined to his or her place of residence, unless strictly for the purpose of performing an essential service, obtaining an essential good or service, collecting a social grant, pension or seeking emergency, life-saving, or chronic medical attention • All commuter transport services including passenger rail services, bus services, taxi services, e-hailing services, maritime and air passenger transport are prohibited

2.3. Specific measures for level 1 to 5 epidemic alert in South Africa

After the COVID-19 outbreak, South Africa mainly adopted Level 1–5 epidemic alert. A series of epidemic prevention measures such as social distancing, mask-wearing/partitions, crowd controls, imposition of Lockdown has been adopted under different epidemic prevention levels [32]. The specific measures taken under Level 1–5 epidemic alert are as Table 1 shown.

3. Results

3.1. How the SARS-CoV-2 Omicron variant spread spatiotemporally

The COVID-19 symptom onset risk in 9 provinces in South Africa, during the whole process of SARS-CoV-2 lineage Omicron emergence together with its spread, was first predicted and analyzed using the province-level WKDE model. A total of 127,205 COVID-19 onset cases with spatiotemporal information in South Africa during the period from October 1st, 2021, to December 5th, 2021, were used in the model [28]. The prediction accuracy of the enhanced WKDE model at the province-level was over 80%, as regards the prediction of the symptom onset risk during the following seven days (Fig. 3). The predicted accuracy of the enhanced WKDE model for the next 14 days is 13.30%–

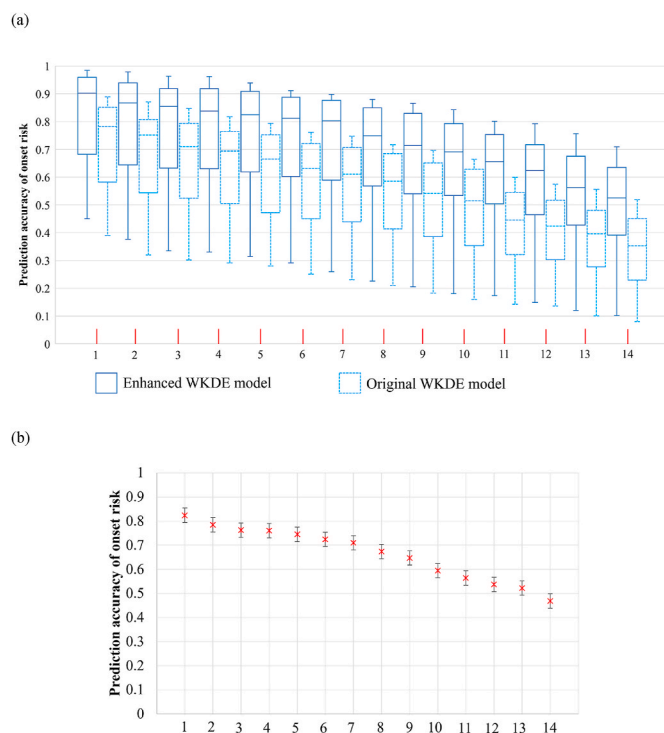


Fig. 3. The accuracy of the predicted risk of COVID-19 symptom onset by province-level WKDE models, and 95% confidence interval of the prediction accuracy [18,19]. (a) The accuracy of the predicted risk of COVID-19 symptom onset by the enhanced and original WKDE models. The predicted onset risk is a normalized value between 0 and 1, hence, indicating risk relative to the highest predicted risk among all locations, on the date for which the risk of symptom onset is predicted, hereafter termed “the prediction date”. The prediction accuracy is defined as the percentage of the onset cases in those areas in which the predicted onset risk was higher than 0.8 on the decided prediction date. The time interval denotes the period between the base date and the date of prediction. The horizontal line in the box denotes the median, while the lower and upper edges of the box represent the respective first and third quartiles. The lines emanating from the box a) upwards and b) downwards, represent the respective maximum and minimum values. (b) The 95% confidence interval of the mean accuracy of the predicted risk of COVID-19 symptom onset by province-level WKDE models.

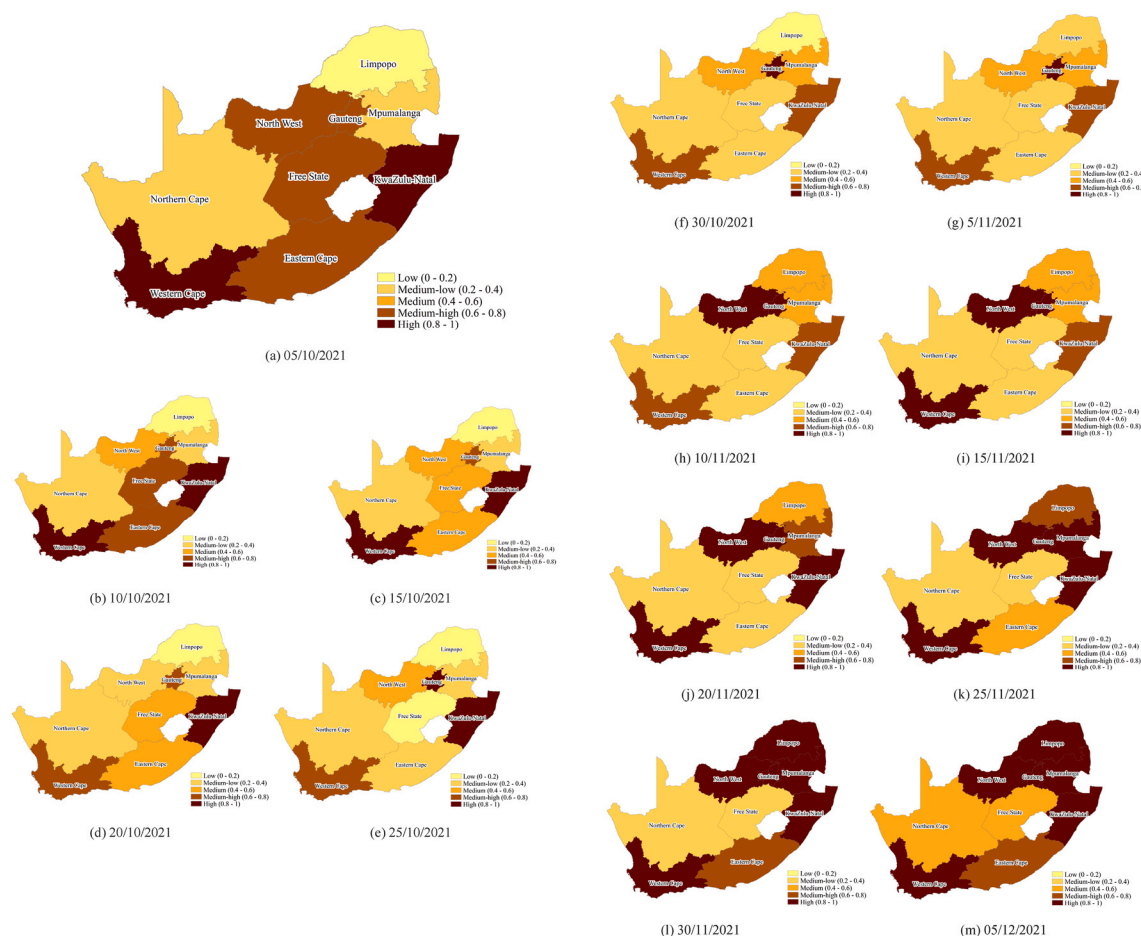


Fig. 4. Predicted risk of COVID-19 symptom onset across 9 provinces in South Africa (a–i) The predicted onset risk during the study period from October 1st, 2021 to December 5th, 2021. The predicted COVID-19 symptoms onset risk was generated using the province-level WKDE model.

32.85% higher than that of the original WKDE model (Fig. 3a). Such an out-performance should be attributed to the incorporation of i) The daily human mobility, ii) time-varying vaccination rate and vaccination efficiency, iii) daily COVID-19 effective reproductive number R, iv) weekly respiratory pathogens surveillance reports, v) weekly levels of SARS-CoV-2 in wastewater treatment plants, vi) weekly COVID-19 cases admitted to sentinel hospital surveillance sites, vii) the weekly percentage, testing positive, and viii) the daily social distancing level factors at the province-scale.

The emergency and spread of Omicron are described by the spatio-temporal variation of the predicted risk of COVID-19 symptom onset as follows (Fig. 4). From the beginning of October, it is seen that except for Gauteng, the onset risk levels of the other eight provinces were either

mostly decreased or remained unchanged. For example, Western Cape and KwaZulu-Natal, which previously were at high risk of symptom onset, had been reduced to areas within the medium-high onset risk category (Fig. 4f). Unlike these eight provinces, the onset risk of COVID-19 symptoms in Gauteng continued to increase. By the end of October, this area became the only one at high-onset-risk (Fig. 4f). Based on the previous comparison of different Omicron genomes, it was seen that the Omicron virus had, in fact, possibly begun to appear in Gauteng Province in early October. It had previously been seen that the spatiotemporal trend was relatively slow during the early stage, after its initial emergence. By the end of October, its main spread area remained within Gauteng Province. According to South Africa’s official report, the earliest detection of Omicron in South Africa was in Gauteng [27], hence

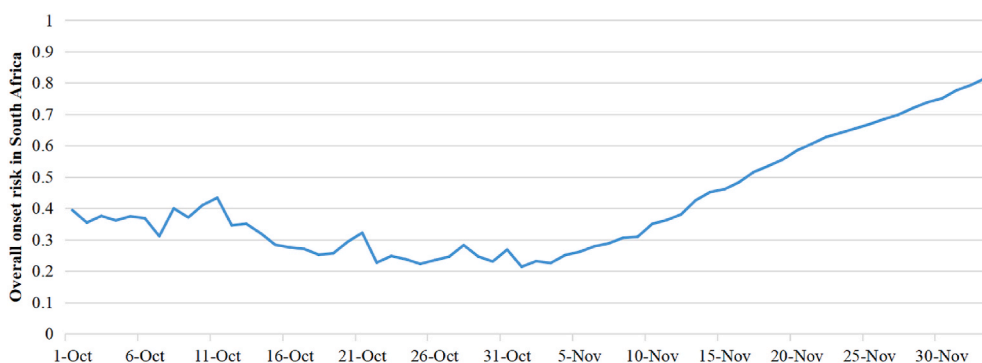


Fig. 5. Daily overall risk of COVID-19 symptom onset in South Africa from October 1st, 2021 to December 10th, 2021.

supporting this study's analysis concerning the aspect established by the appearance of Omicron. Meanwhile, in October, following the downward trend of the onset risk in the other eight provinces, apart from Gauteng, the overall onset risk in South Africa fell from 0.39 to 0.21, namely, a 45% reduction (Fig. 5). Hence, it could be determined that although the Delta variant was still dominant during October [33], the epidemic, which it caused was, in fact, gradually decreasing.

Sequencing data suggests that Omicron had, in fact, become the dominant variant in South Africa by November 2021 [16]. From the variations in the spatiotemporal distribution of onset risk in November, the spread of Omicron accelerated from the point in which it had been acknowledged as the dominant variant. Starting from the Gauteng province, the center of the epidemic, and as could be expected, the initial spread was to the neighboring provinces, namely, North West, Mpumalanga, and Limpopo followed by the two main nodes in the transport network in South Africa - Western Cape and KwaZulu-Natal (Fig. 4j-k). These provinces accounted for 81.30% of the total population of South Africa [34], and their contribution to South Africa's GDP accounted for 85.15% [35]. Notably, South Africa's main airports and railway stations are in these provinces. By the end of November, all the neighboring provinces then became at high-onset-risk (Fig. 4l). The epidemic caused by Omicron was relatively mild in the sparsely populated provinces of Northern Cape (the largest and most sparsely populated province in South Africa) and Free State. Until the end of November, these two provinces remained at medium-low onset risk (Fig. 4l). Overall, however, it was clear that onset risk in South Africa still rapidly increased by more than 2.57 times from 0.21 on November 1st, 2021 to 0.75 on November 30th, 2021 (Fig. 5). Despite South Africa remaining at Alert Level 1 and accelerating vaccination at the end of November, Omicron still continued the spatiotemporal spread trend, with an overall onset risk in South Africa increasing to 0.81 by December 5th, 2021.

3.2. How to control the spatiotemporal spread of Omicron effectively by integrating epidemic alert measures and vaccination

According to the above analysis of Omicron's spatiotemporal spread, the continued Alert Level 1 from November 28th, 2021 does not seem to have been effective as regards the prevention or slowing down of the epidemic in South Africa. During the week of November 29th to December 5th, South Africa's cases increased by 111% from the previous week. Hence, based on the predicted risk of the COVID-19 symptom onset in the 9 provinces of South Africa, the impact of each epidemic alert level on the spread of Omicron was further analyzed to explore methods necessary to better control the epidemic more effectively. This impact was analyzed and the results compared, based on five scenarios: i) existing scenario under the Alert Level 1 in all 9 provinces; ii) the new scenario under Alert Level 2 in all 9 provinces; iii) the new scenario under the Alert Level 3 in all 9 provinces; iv) 4 the new scenario of Alert Level 4 in all 9 provinces; v) the new scenario of Alert Level 5 (i.e., lockdown) in Gauteng province together with Alert Level 1 for the remaining 8 provinces. The latter four new scenarios were to be simulated from November 26th, 2021.

The daily overall onset risk in South Africa in the above five scenarios was further used to analyze the effect of the different alert levels. Alert Level 5 in Gauteng, together with Alert Level 1 in the remaining 8 provinces have the most obvious suppression of the overall onset risk in South Africa. Compared with that under the current Alert Level 1, approximately 14 days after Alert Level 5 in Gauteng, together with Alert Level 1 in the remaining 8 provinces were implemented, the daily overall onset risk decreased by 1.72%–15.34% (Fig. 6a). The daily reduction of the predicted overall onset risk in South Africa, under the Alert Level 2, 3, 4, was only in 1.08%–4.38%, 1.31%–6.97%, 1.43%–9.43% (Fig. 6a). Although more stringent measures have been adopted in other 8 provinces other than Gauteng, the suppression effect of Alert Level 2, 3, 4 on the overall onset risk was relatively limited.

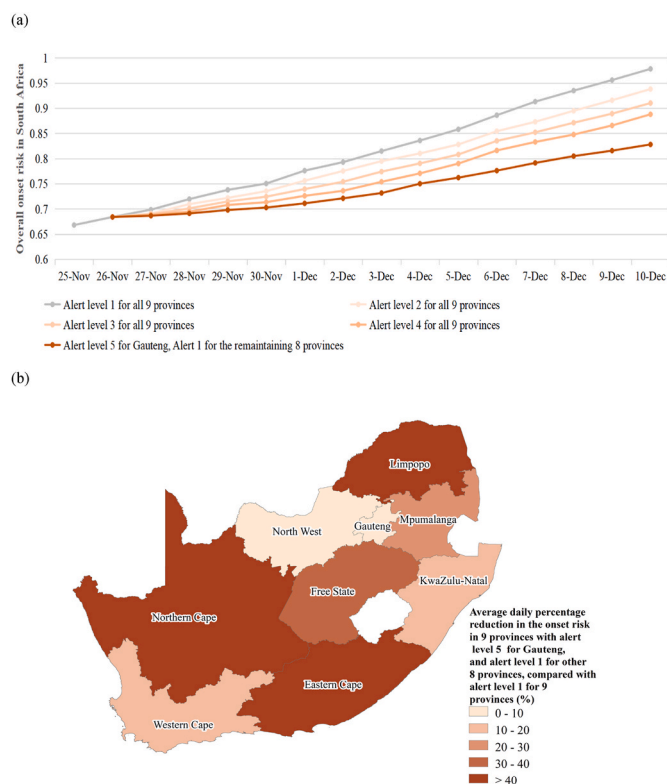


Fig. 6. The risk of COVID-19 symptom onset in the five epidemic alert scenarios (i.e., the current Alert Level 1 in all 9 provinces, Alert Level 2 in all 9 provinces, Alert Level 3 in all 9 provinces, Alert Level 4 in all 9 provinces, and Alert Level 5 in Gauteng together with Alert Level 1 in other 8 provinces) from October 27th, 2021 to December 10th, 2021. (a) The overall onset risk in the five epidemic alert scenarios. The plotted values were computed with the predicted risk of COVID-19 symptom onset in the four epidemic alert scenarios. (b) The average daily percentage reduction in the onset risk in 9 provinces, regarding the scenario of the Alert Level 5 for Gauteng together with Alert Level 1 for the remaining 8 provinces, when compared with the scenario of the current Alert Level 1 for the entire South Africa region.

Furthermore, in the new scenario of Alert Level 5 in Gauteng together with Alert Level 1 in the remaining 8 provinces, the spatial differences in the reduction of onset risk in various provinces have also been further explored (Fig. 6b). It can be seen that after the implementation of Alert level 5 (lockdown) in Gauteng province, the daily onset risk in i) its neighboring provinces, and ii) provinces with close communication with it, has, to a certain extent, decreased. In particular, although continuing to maintain the original Alert level 1 there, the daily onset risk in KwaZulu-Natal and West Cape provinces (South Africa's second and third largest economies are also international traffic hotspots) have an average reduction of 11.57% and 13.81% (Fig. 6b). This is very positive for maintaining normal social and economic activities in South Africa. More importantly, it is also conducive to controlling the Omicron epidemic spread to other countries and regions. Moreover, by controlling further spread of Omicron from Gauteng to the above traffic hotspot provinces, it has obviously played an obvious role in reducing the daily onset risk in those provinces adjacent to such traffic hotspot provinces. For example, the daily onset risk in Northern Cape and Eastern Cape provinces, which border KwaZulu-Natal and the West Cape provinces, have an average reduction of 48.13% and 41.42% (Fig. 6b). Such a reduction is crucial not only in enabling control of the Omicron infection spread locally, but also, and in particular, its spread in a larger area.

As of December 5th, 2021, the total number of individuals, 33.33%–62.49% of the population by province, received a Johnson & Johnson single dose or Pfizer-BioNTech 2 doses in South Africa's 9 provinces

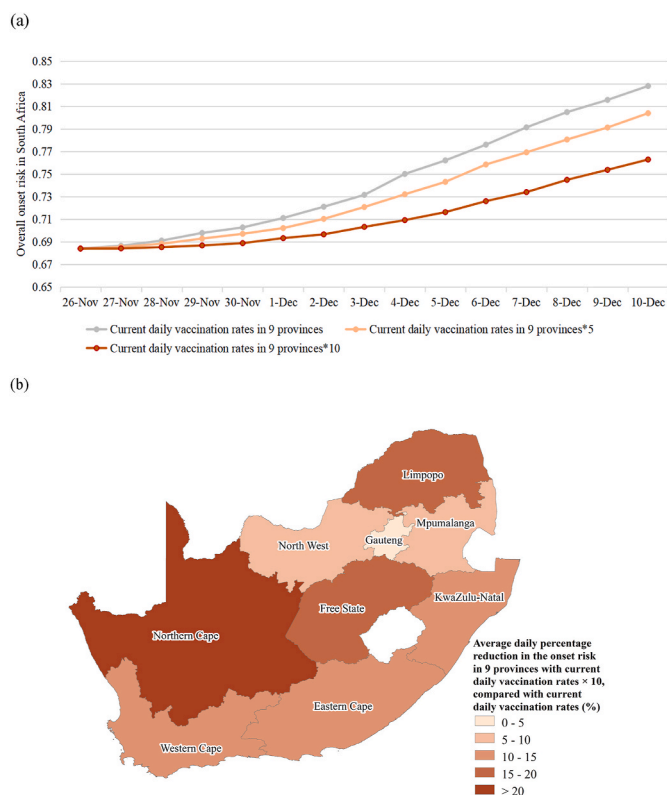


Fig. 7. The risk of COVID-19 symptom onset with the current daily vaccination rates, 5 times the vaccination rates, 10 times the vaccination rate at the Alert Level 5 for Gauteng together with Alert Level 1 for the remaining 8 provinces from November 27th, 2021 to December 10th, 2021. (a) The overall onset risk with the current daily vaccination rates, 5 times the vaccination rates, and 10 times the vaccination rates in the scenario of Alert Level 5 for Gauteng, together with Alert Level 1 for the remaining 8 provinces. The plotted values were computed from the predicted risk of COVID-19 symptom onset in 9 provinces of South Africa. (b) The average daily percentage reduction in the onset risk in 9 provinces of South Africa with 10 times the current daily vaccination rates, compared with the current daily vaccination rates in the scenario of Alert Level 5 for Gauteng, together with Alert Level 1 for the remaining 8 provinces.

[22]. From current early research, it is suggested that two doses of the vaccine may still offer protection against severe disease caused by the Omicron strain. Thus, based on the previous judgment that the most effective control measure – Alert Level 5 for Gauteng together with Alert Level 1 for the remaining 8 provinces (Fig. 6a), how to strengthen vaccination to further curb the spread of Omicron was simulated. The simulation was conducted in i) the current daily vaccination rates in 9 provinces, ii) 5 times the current daily vaccination rates in 9 provinces, and iii) 10 times the current daily vaccination rates in 9 provinces.

The temporal variation of the daily overall onset risk values in South Africa, under the current vaccination rates, namely, 5 times the current vaccination rates, and 10 times the current vaccination rates, were explored to reflect the effect of the improved vaccination rates (Fig. 7a). A constant lower daily overall onset risk was found after increasing the current vaccination rates 5 times to 10 times., it was found, that when the daily vaccination rate in each province was increased by 5 times, the daily overall onset risk in South Africa decreased by 0.14%–3.02%. When the daily vaccination rate in each province was increased by 10 times, the daily overall onset risk in South Africa was reduced by 0.34%–7.86%. Of interest is that, with 10 times the current daily vaccination rates, the overall onset risk in South Africa would be likely to be reduced, hence reaching the medium-high risk level. In general, although vaccination did have some effect on curbing the epidemic in South Africa, this reduction appears to have some limitations. Such

limitations may be because more than 1.61 million people have been fully vaccinated for more than 6 months. At that time, the VE-I was very limited. Furthermore, the onset risk in all the 9 provinces, which had 10 times the current daily vaccination rates, on the same date, was obviously lower than that with the current daily vaccination rates (Fig. 7b). On the basis of the aforementioned Alert Level 5 lockdown measures in Gauteng Province, in addition to the average daily onset risk reduction of 23.52% in Northern Cape province in remote areas, increasing daily vaccination rates further reduced the daily onset risk in Western Cape and KwaZulu-Natal. The latter were at important traffic nodes. The daily onset risk in these two provinces was further reduced by 13.48% and 12.67%.

4. Discussion

So far, as Omicron becomes the dominant variant in many countries, all of us need to take extra precautions [36,37]. WHO calls on all countries to take all effective measures to prevent the spread of Omicron [36,37]. Thus, this study has provided an analysis of the spatiotemporal dynamics of the Omicron spread throughout the 9 provinces of South Africa, to describe the mechanism of the spatial spread of Omicron in an increased in-depth manner. Of importance, in this respect, is that, the proposed province-level WKDE model has been used to enable the prediction of the risk of COVID-19 symptom onset, to retrospectively analyze the entire dynamic process of the Omicron spatiotemporal spread in South Africa. Methods regarding how to control the spatiotemporal spread of Omicron by means of the integration of epidemic prevention measures. In this respect vaccination levels are also analyzed.

By incorporating new factors like the vaccine efficiency for estimating Omicron's transmissibility better, the enhanced WKDE model has achieved a higher accuracy with more than 80% in the onset risk prediction of the associated following 7 days. In this respect, the whole process of emergency and spread of Omicron in South Africa is analyzed by the means of onset risk prediction. The results shown in this study include: i) the Omicron virus may begin to appear in Gauteng in early October. The spatiotemporal spread was relatively slow in the early stage after the emergence of Omicron. ii) the spatial spread of Omicron accelerated after it became the dominant variant. Starting from the Gauteng province, the center of the epidemic, the virus first spread to the neighboring provinces and before spreading to main nodes in the transport network in South Africa. The above details can act as a guide to enable more countries and regions find and thereby prepare methods to enable the prevention of the emergence and spread of Omicron, and thereby more effectively, cutting possible networks of spread.

Through the simulation and comparison of how to control the spread of Omicron under different scenarios with different levels of epidemic prevention measures and vaccination rates, this study has also provided a scientific reference for areas attacked by SARS-CoV-2 variants. Hence the results regarding recorded attempts to control the spatiotemporal spread of Omicron in 9 provinces of South Africa, show that:

- 1) Compared with the implementation of current alert measures 1–4 in the whole of South Africa, imposing Alert Level 5 (i.e., lockdown) in the high onset risk province Gauteng could possibly more effectively control the spatiotemporal spread of Omicron [38]. The onset risk is more likely to be reduced, by up to 48.13% throughout all provinces. In other provinces, the current lowest Alert Level 1 could be taken to reduce the impact on further normal socioeconomic activities and public services. The above is very important for South Africa or any area which is facing an economic downturn. Such measures would control further aggravation of the spatial spread of Omicron and hence benefit the normal economic activities of the wider region [39].
- 2) If the COVID-19 vaccination rate in each province was raised from the current daily vaccination rates to 5 times, and 10 times, the

spatiotemporal spread of Omicron could be controlled more effectively by further reducing the onset risk up by up to 23.52% throughout all provinces, especially in important economic provinces at the nodes of the transportation network. However, increased vaccination seems to be limited in reducing the overall risk level in South Africa. This may be because more than 1.61 million people have been fully vaccinated for more than 6 months. At this time, VE-I had declined to very low. Therefore, it is very necessary to vaccinate these 1.6 million people with booster doses as soon as possible [40, 41].

This study has aimed to provide a comprehensive investigation concerning the spatiotemporal dynamics of SARS-CoV-2 Omicron variant and hence provides scientific findings to enable a contribution which will assist in controlling the spatiotemporal spread of Omicron by integrating the prevention measures and vaccination.

Data availability

The datasets generated and analyzed during this study are available from the corresponding author on reasonable request.

Code availability

The MATLAB scripts developed and used in this study are available from the corresponding author on reasonable request.

CRedit authorship contribution statement

Chengzhuo Tong: collected the data, developed the computation models, wrote the manuscript, Writing – original draft, and helped interpreted the results. **Wenzhong Shi:** conceived and designed the study, interpreted the results, and helped develop the computation models, analyze the data, and write the manuscript, Writing – original draft. **Anshu Zhang:** helped develop the computation models, analyze the data, and write the manuscript, Writing – original draft. **Zhicheng Shi:** wrote the manuscript, Writing – original draft, and helped collect the data, analyze the data and interpret the results.

References

- [1] World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19. <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-14-december-2021>. [Accessed 22 December 2021].
- [2] delRio C, Omer SB, Malani PN. Winter of omicron—the evolving COVID-19 pandemic. *JAMA* 2021;n3104. <https://doi.org/10.1001/jama.2021.24315>.
- [3] Shanmugaraj B, Malla A, Khorattanakulchai N, Phoolcharoen W. SARS-CoV-2 omicron variant: could it be another threat? *J Med Virol* 2021. <https://doi.org/10.1002/jmv.27532>.
- [4] Torjesen I. Covid-19: omicron may be more transmissible than other variants and partly resistant to existing vaccines, scientists fear. *BMJ* 2021;375:n2943. <https://doi.org/10.1136/bmj.n2943>.
- [5] Kandeel M, Mohamed MEM, Abd El-Lateef HM, Venugopala KN, El-Beltagi HS. Omicron variant genome evolution and phylogenetics. *J Med Virol* 2021. <https://doi.org/10.1002/jmv.27515>.
- [6] Kazymbay B, Ahmad A, Mu C, Mengdesh D, Xie Y. Omicron N501Y mutation among SARS-CoV-2 lineages: in-silico analysis of potent binding to tyrosine kinase and hypothetical repurposed medicine. *Trav Med Infect Dis* 2021;1022242. <https://doi.org/10.1016/j.tmaid.2021.102242>.
- [7] Karim SSA, Karim QA. Omicron SARS-CoV-2 variant: a new chapter in the COVID-19 pandemic. *Lancet* 2021;398:2126–8. [https://doi.org/10.1016/S0140-6736\(21\)02758-6](https://doi.org/10.1016/S0140-6736(21)02758-6).
- [8] Torjesen I. Covid restrictions tighten as omicron cases double every two to three days. *BMJ* 2021;n3051. <https://doi.org/10.1136/bmj.n3051>.
- [9] Ai J, Zhang H, Zhang Y, Lin K, Zhang Y, Wu J, et al. Omicron variant showed lower neutralizing sensitivity than other SARS-CoV-2 variants to immune sera elicited by vaccines after boost. *Emerg Microb Infect* 2021;1–24. <https://doi.org/10.1080/22221751.2021.2022440>.
- [10] Zhang X, Wu S, Wu B, Yang Q, Chen A, Li Y, et al. SARS-CoV-2 Omicron strain exhibits potent capabilities for immune evasion and viral entrance. *Signal Transduct Target Ther* 2021;6:10–2. <https://doi.org/10.1038/s41392-021-00852-5>.
- [11] World Health Organization. Update on omicron. <https://www.who.int/news/item/28-11-2021-update-on-omicron>. [Accessed 9 December 2021].
- [12] Poudel S, Ishak A, Perez-Fernandez J, Garcia E, León-Figueroa DA, Romaní L, et al. Highly mutated omicron variant sparks significant concern among global experts – what is known so far? *Trav Med Infect Dis* 2022;45:102234. <https://doi.org/10.1016/j.tmaid.2021.102234>.
- [13] Hallett S. We need increased targeted measures now to slow the spread of omicron. *BMJ* 2021;n3133. <https://doi.org/10.1136/bmj.n3133>.
- [14] Dyer O. Covid-19 : South Africa's surge in cases deepens alarm over omicron variant. *BMJ* 2021;375:n3013. <https://doi.org/10.1136/bmj.n3013>.
- [15] Government of South Africa. Coronavirus COVID-19 alert level 1. <https://www.gov.za/covid-19/about/coronavirus-covid-19-alert-level-1>. [Accessed 9 December 2021].
- [16] National Institute for Communicable Diseases. SARS-CoV-2 sequencing update 8 December 2021. 2021.
- [17] Government of South Africa. President Cyril Ramaphosa : address on South Africa's response to coronavirus COVID-19 pandemic. <https://www.gov.za/speeches/president-cyril-ramaphosa-address-south-africas-response-coronavirus-covid-19-pandemic-28>. [Accessed 9 December 2021].
- [18] Shi W, Tong C, Zhang A, Shi Z. A spatial and dynamic solution for how to allocate the COVID-19 vaccine in the Context of limited supply. *Commun Med* 2021;1:1–14. <https://doi.org/10.1038/s43856-021-00023-1>.
- [19] Shi W, Tong C, Zhang A, Wang B, Shi Z, Yao Y, et al. An extended Weight Kernel Density Estimation model forecasts COVID-19 onset risk and identifies spatiotemporal variations of lockdown effects in China. *Commun Biol* 2021;4:1–11. <https://doi.org/10.1038/s42003-021-01677-2>.
- [20] Tong C, Shi W, Zhang A, Shi Z. Tracking and controlling the spatiotemporal spread of SARS-CoV-2 lineage B.1.1.7 in COVID-19 reopenings. *GeoHealth* 2021. <https://doi.org/10.1029/2021GH000517>. e2021GH000517.
- [21] Apple. COVID-19 - mobility trends reports (South Africa). 2021.
- [22] National Department of Health in South Africa. Latest vaccine statistics. <https://sacoronavirus.co.za/latest-vaccine-statistics/>. [Accessed 11 December 2021].
- [23] National Institute for Communicable Diseases. The daily COVID-19 effective reproductive number (R) in South Africa. <https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/covid-19-special-reports/the-initial-and-daily-covid-19-effective-reproductive-number-in-south-africa/>. [Accessed 11 December 2021].
- [24] National Institute for Communicable Diseases. Weekly respiratory pathogens surveillance report. <https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/weekly-respiratory-pathogens-surveillance-report-week/>. [Accessed 11 December 2021].
- [25] National Institute for Communicable Diseases. Wastewater-based epidemiology for Sars-Cov-2 wastewater-based epidemiology surveillance in South Africa for Sars-Cov-2 surveillance in surveillance in South Africa. <https://www.nicd.ac.za/disease-s-a-z-index/disease-index-covid-19/surveillance-reports/weekly-reports/waste-water-based-epidemiology-for-sars-cov-2-in-south-africa/>. [Accessed 11 December 2021].
- [26] National Institute for Communicable Diseases. Covid-19 sentinel hospital surveillance Update. <https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/weekly-hospital-surveillance-datcov-update/>. [Accessed 11 December 2021].
- [27] National Institute for Communicable Diseases. COVID-19-Testing-Summary. <https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/weekly-testing-summary/>. [Accessed 11 December 2021].
- [28] National Institute for Communicable Diseases. Latest confirmed cases OF COVID-19 IN South Africa. <https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/national-covid-19-daily-report/>. [Accessed 11 December 2021].
- [29] Cohn BA, Cirillo PM, Murphy CC, Krigbaum NY, Wallace AW. SARS-CoV-2 vaccine protection and deaths among US veterans during 2021. *Science* 2021. <https://doi.org/10.1126/science.abm0620>. 0620:6.
- [30] Adam DC, Wu P, Wong JY, Lau EHY, Tsang TK, Cauchemez S, et al. Clustering and superspreading potential of SARS-CoV-2 infections in Hong Kong. *Nat Med* 2020;26:1714–9. <https://doi.org/10.1038/s41591-020-1092-0>.
- [31] Walsh KA, Jordan K, Clyne B, Rohde D, DrummondL, Byrne P, et al. SARS-CoV-2 detection, viral load and infectivity over the course of an infection. *J Infect* 2020;81:357–71. <https://doi.org/10.1016/j.jinf.2020.06.067>.
- [32] Government of South Africa. About coronavirus COVID-19. <https://www.gov.za/covid-19/about>. [Accessed 11 December 2021].
- [33] National Institute for Communicable Diseases. SARS-CoV-2 sequencing Update 26 November 2021. https://www.nicd.ac.za/wp-content/uploads/2021/11/Update-of-SA-sequencing-data-from-GISAID-26-Nov_Final.pdf. [Accessed 11 December 2021].
- [34] Government of South Africa. Midyear population estimate 2019. <https://www.statssa.gov.za/publications/P0302/P03022019.pdf>. [Accessed 11 December 2021].
- [35] Government of South Africa. GDP by provinces. <http://www.statssa.gov.za/?p=12056>. [Accessed 11 December 2021].
- [36] Luo M, Liu Q, Wang J, Gong Z. From SARS to the Omicron variant of COVID-19: China's policy adjustments and changes to prevent and control infectious diseases. *Biosci Trends* 2021. <https://doi.org/10.5582/bst.2021.01535>. 2021.01535.
- [37] World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19. <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-22-december-2021>. [Accessed 22 December 2021].

- [38] Iacobucci G. Covid-19: Government ignores scientists' advice to tighten restrictions to combat omicron. *BMJ* 2021;n3131. <https://doi.org/10.1136/bmj.n3131>.
- [39] Choudhary OP, Dhawan M, Priyanka. Omicron variant (B.1.1.529) of SARS-CoV-2: threat assessment and plan of action. *Int J Surg* 2021;97:106187. <https://doi.org/10.1016/j.ijisu.2021.106187>.
- [40] Li X. Omicron: call for updated vaccines. *J Med Virol* 2021. <https://doi.org/10.1002/jmv.27530>. 0–2.
- [41] Iacobucci G. Covid-19: GPs are told to postpone routine care to focus on vaccine boosters in response to omicron. *BMJ* 2021;375:n3083. <https://doi.org/10.1136/bmj.n3083>.