Gradual emergence followed by exponential spread of the SARS-CoV-2 Omicron variant in Africa

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The geographic and evolutionary origins of the SARS-CoV-2 Omicron variant (BA.1), which was first detected mid-November 2021 in Southern Africa, remain unknown. We tested 13,097 COVID-19 patients sampled between mid-2021 to early 2022 from 22 African countries for BA.1 by real-time RT-PCR. By November-December 2021, BA.1 had replaced the Delta variant in all African sub-regions following a South-North gradient, with a peak Rt of 4.1. Polymerase chain reaction and near-full genome sequencing data revealed genetically diverse Omicron ancestors already existed across Africa by August 2021. Mutations, altering viral tropism, replication and immune escape, gradually accumulated in the spike gene. Omicron ancestors were therefore present in several African countries months before Omicron dominated transmission. These data also indicate that travel bans are ineffective in the face of undetected and widespread infection.

By September 2022, over 6.5 million persons had died from coronavirus disease 2019 (COVID-19) (1). The true number of infections is probably much higher, particularly in Africa where the diagnostic capacities are low (2, 3). In Africa, the World Health Organization (WHO) estimates that only 14% of all SARS-CoV-2 infections are detected (4) and regional post-mortem data suggest the true COVID-19 death toll may be underestimated (5).

SARS-CoV-2 has evolved rapidly during intense transmission throughout the COVID-19 pandemic (6). The most pronounced viral change was the emergence of the Omicron variant (BA.1), which was first reported on 11 November 2021 in a patient from South Africa (Fig. 1A). Within a few weeks, BA.1 was reported in 87 countries (7), prevailing over Delta to become the predominant SARS-CoV-2 variant globally by the end of December 2021 (8). Divergent Omicron sublineages termed BA.2, BA.4 and BA.5 emerged globally months later than BA.1 (Fig. 1A). BA.1 has more than 50 non-synonymous mutations compared to ancestral SARS-CoV-2 strains, mostly located in the gene encoding the viral spike protein (9). Among the key BA.1 spike amino acid substitutions, the unique combination of K417N, S477N, E484A, and N501Y in the receptor-binding domain contributes to strong evasion of immune responses elicited by vaccination or prior infection, hinting at serotype properties of BA.1 relative to other variants (10–13). The BA.1 spike gene also harbors three mutations in the region encoding the furin cleavage site, likely facilitating proteolytic spike maturation (14). Finally, the BA.1 spike S2 subunit contains six unique amino acid substitutions which reduce cleavage efficiency by the transmembrane serine protease TMPRSS2, favoring BA.1 entry via the receptor-independent endosomal pathway and entailing increased replication of BA.1 in epithelial cells from the upper respiratory tract (15). Efficient immune evasion and infection of the upper respiratory tract are likely key to the explosive global spread of BA.1 (16).

In response to the emergence of BA.1, the United States of America, the European Union, and several other countries restricted travel for four to six weeks from Southern and Eastern African countries, including Botswana, Swaziland, Lesotho, Mozambique, Namibia, South Africa, and Zimbabwe, by the end of November 2021 (17). The direct economic loss in South Africa alone produced by these travel restrictions was roughly 600 million US dollars (18). However, where and when BA.1 originated remains unknown. Evolutionary reconstructions have projected an ancestor of BA.1 back to mid-2020 (19), which is consistent with preliminary data on eight partial BA.1-like sequences in samples from patients in Nigeria collected in August and September 2021 (20) and with 28 partial Omicron sequences available in the Global Initiative on Sharing Avian Influenza Data (GISAID) from samples collected between August and November 2021

in five different Western, Central and Eastern African countries. Lack of in-depth evolutionary analysis and epidemiological context for putative early Omicron sequences and regionally heterogeneous testing and reporting of Omicron infections have prevented definitive assessments of the spread of BA.1 in Africa. Here, we present the results of a diagnostic and evolutionary study to elucidate the emergence of BA.1 across Africa.

A real-time RT-PCR test was designed to be highly specific by targeting an BA.1-specific marker (spike 214 EPE insertion) which is near-absent in other Omicron lineages and a Delta-specific marker (spike deletion 157/158), achieving a diagnostic specificity of 98.7% for BA.1 and 99.8% for Delta according to GISAID data (table S1). The specificity of BA.1 detection was confirmed by the absence of the BA.1 marker in 545 SARS-CoV-2-positive respiratory samples from Benin, Western Africa, collected between January and April 2021 (21). In total, 13,097 samples from laboratory-confirmed COVID-19 patients from 22 African countries and 200 municipalities sampled during mid-2021 to early 2022 were included in this study (Fig. 1B and fig. S2).

South-North gradient of BA.1 spread in continental Africa

Across African countries, BA.1 replaced Delta as the predominant SARS-CoV-2 variant already by December 2021 (Fig. 2A, Delta fraction, and Fig. 2B, BA.1 fraction). Comparing continent-wide PCR data, BA.1 became the dominant variant (>50% detection) on 11 November (95% CI, −5/+3 days) in Southern Africa, 29 November (95% CI, −2/+1 days) in Western Africa, 1 December (95% CI, −2/+3 days) in continental Eastern Africa, 6 December (95% CI, −3/+3 days) in Central Africa, and 25 December (95% CI, −1/+1 days) in Northern Africa (Fig. 2C). The South-North gradient suggested by those data is consistent with the earliest known BA.1 spread in Southern Africa and recent genome-based analyses of SARS-CoV-2 in Africa (22). Delayed BA.1 introduction into Northern Africa is likely associated with reduced land connectivity imposed by the Sahara Desert (23). Similarly, border closure in Madagascar until late 2021 delayed BA.1 introduction until January 2022 (table S2). Across African countries, the median time between the first BA.1 detection and BA.1 predominance was 28 days (95% CI, 11–66.0) (Fig. 2D), which is comparable to high-income countries (9, 24). Combining all country-level data, the BA.1 effective reproduction number R_t peaked at 4.1 only five days after its first detection, which is consistent with an overall R_0 of 3.7 (95% CI, 3.3–4.1) reconstructed for SARS-CoV-2 variants in Africa (25) and an average R_t of 3.4 among countries in Africa, the Americas, Asia and Europe (26). In the combined country-level data, R_t dropped below 1 within 32 days after the detection of the first BA.1 case (Fig. 2E), likely due to widespread immunity following explosive BA.1

spread (*27*). This interpretation is in line with the steep increase of reported cases likely corresponding to and the short duration of the BA.1 wave in Africa (Fig. 2F) (*28*, *29*).

Occurrence of BA.1 ancestors across Africa during August 2021

Although BA.1 cases were first detected in South Africa and Botswana and knowing that our PCR data confirmed the earliest predominance of BA.1 in Southern Africa, the variant's geographic and evolutionary origin remains unclear. A systematic search among >6 million GISAID entries based on the BA.1-specific marker used in this study did not support existence of potential BA.1 ancestors outside of Africa (table S1 and fig. S2). In contrast, the earliest detection of BA.1-specific PCR signals in this study was among 25 patients sampled between August-September 2021 from six different Western and Eastern African countries (Mali, Benin, Kenya, Uganda, Ghana, and Niger) (table S2). For comparison, the first detection of BA.1-specific PCR signal in patients from Southern Africa only occurred two months later during November.

To confirm the early and widespread occurrence of potential Omicron ancestors outside of Southern Africa, near-full SARS-CoV-2 genome characterization was done in 247 BA.1-positive and -negative patient samples from Benin, Western Africa, and 424 patient samples from South Africa using a combination of deep sequencing- and PCR-based workflows. The genomic data generated de novo from both countries confirmed high specificity of around 98% of the BA.1 PCR test (table S3). Despite low virus concentrations, partial or near-complete SARS-CoV-2 genomes at a total genome coverage of 71.9% to 98.5% were recovered from five BA.1 PCR-positive samples from Benin sampled between 22 August and 27 October 2021 (termed Ben-1 to Ben-5) (table S4). Phylogenetic analyses in Maximum Likelihood and Bayesian frameworks (Fig. 3, A and B, and fig. S3) robustly identified them as proximal and more distant Omicron ancestors. The proximal Omicron ancestors (Ben-4 and Ben-5) contained 67.7% (42/62) and 75.0% (39/52) of the Omicron-defining mutations (*9*) that were covered by sequencing, sufficient to be classified as BA.1 using the widely used Nextclade and UShER algorithms (Fig. 3C). The distant Omicron ancestors (Ben-1–Ben-3) shared between 38.3% (23/60) and 66.7% (32/48) of BA.1-defining mutations and were classified as the parental lineage B.1.1 by Nextclade. Together with other Africa-derived BA.1-like sequence entries, the Omicron ancestors clustered in basal sister relationship between the Omicron clade *sensu strictu*, the BA.1 sublineage and Omicron ancestors belonging to the globally circulating B.1 lineage (Fig. 3, A and B). Phylogeographic analyses supported BA.1 origins in Western Africa preceding spread in Southern Africa (fig. S4), which was consistent with the PCR-based data (table S2).

Gradual evolution of Omicron across Africa

BA.1-defining mutations varied among distant and proximal Omicron ancestors that co-existed temporally, exemplified by Ben-1, -3 and -4 sampled at nearly identical time points during August 2021 in Cotonou, Benin (Fig. 3A), and Ben-5 and three GISAID sequence entries from neighboring Nigeria (*20*) (Fig. 3, A and B, and figs. S3 and S5). Together with evidence for recombination events in the receptor-binding domain of Benin-derived Omicron ancestors (fig. S6 and table S5), those data suggest a non-linear micro-evolutionary pattern of Omicron involving multiple ancestors existing across Western African regions over several months (fig. S5). Sequence comparisons of the distant and proximal Omicron ancestors from Benin suggested that Omicron accumulated immune escape mutations in the spike gene (*11*, *12*, *30*, *31*), consistent with antigenic drift driven by high levels of population immunity against prior SARS-CoV-2 variants in Africa (*32*). While the spike amino acid exchanges E484A and N501Y were present among all Omicron ancestors from Benin and most from GISAID, the occurrence of K417N and S477N varied among proximal Omicron ancestors from Benin and those available in GISAID. None of those individual mutations are specific for Omicron and they occur in diverse SARS-CoV-2 lineages (*22*) (Fig. 3C and fig. S5). Substitutions associated with immune escape may thus not fully explain Omicron emergence. Among the Omicron ancestors and the earliest known African Omicron strains (yellow nodes in Fig. 3, A and B), only the amino acid exchanges H655Y in the furin cleavage site and N969K in the S2 subunit (marked with asterisks in Fig. 3C) are shared by Omicron *sensu strictu* sequences in GISAID, the proximal Omicron ancestors Ben-4/Ben-5 and available GISAID sequence entries from potential Omicron ancestors (fig. S5). In contrast, these amino acid exchanges are absent in other SARS-CoV-2 lineages including the distant Omicron ancestors Ben-1/-2/-3 from Benin. Both amino acid substitutions are significantly associated with increased SARS-CoV-2 fitness in mathematical modeling (*33*) and are both present in >99% of all Omicron sequences and highly specific for Omicron in public databases (table S6). Those furin cleavage site and S2 mutations may thus represent key events during the evolution of Omicron beyond immune escape that deserve experimental investigation.

Finally, conjectures addressing the Omicron genealogy include its evolution in a non-human host (*34*) or in an immunocompromised individual (*35*, *36*), which would be consistent with the initial detection of Omicron in South Africa, which has a high HIV prevalence (*37*). In stark contrast, the mutation pattern of Omicron ancestors and Omicron strains deposited in public databases differed substantially from the SARS-CoV-2 mutation pattern in immunocompromised individuals (*38*) (fig. S7). Our data suggest prolonged and geographically widespread evolution of Omicron ancestors in

patients across Africa. Although partial evolution of Omicron ancestors in immunocompromised individuals or non-human animals cannot be excluded, Omicron did not evolve in a single infection event according to our continent-wide data. Eventually, highly transmissible BA.1 *sensu strictu* emerged, combining both efficient immune escape and tropism for the upper respiratory tract. Albeit the evolutionary origins of other Omicron sublineages than BA.1 remain uncertain, phylogenetically ancestral strains existing in Africa during 2021 suggest that diverse Omicron sublineages may share similar genealogy.

This study is limited by heterogeneous sampling in time and space and by lack of SARS-CoV-2 genomic data from all BA.1 PCR-positive patients. However, the PCR test was exhaustively validated in two African sub-regions and geographically widespread testing substantiates robustness of our findings.

In conclusion, our study clearly shows the need to strengthen and harmonize surveillance systems on a supranational level, establish strategic sampling frameworks, and the importance of sharing surveillance data (*39*) to allow efficient interventions. Without international surveillance and early detection travel bans have no epidemic containment value and can cause social and economic harm.

REFERENCES AND NOTES

1. World Health Organization, WHO Coronavirus (COVID-19) Dashboard; https://covid19.who.int.
2. A.-L. Sander, A. Yadouleton, A. Moreira-Soto, C. Tchibozo, G. Hounkanrin, Y. Badou, C. Fischer, N. Krause, P. Akogbeto, E. F. de Oliveira Filho, A. Dossou, S. Brünink, C. Drosten, M. A. J. Aïssi, M. Harouna Djingarey, M. Hounkpatin, M. Nagel, J. F. Drexler, An observational laboratory-based assessment of SARS-CoV-2 molecular diagnostics in Benin, Western Africa. *MSphere* **6**, e00979-20 (2021). doi:10.1128/mSphere.00979-20 Medline
3. E. Wilkinson, M. Giovanetti, H. Tegally, J. E. San, R. Lessells, D. Cuadros, D. P. Martin, D. A. Rasmussen, A. N. Zekri, A. K. Sangare, A.-S. Ouedraogo, A. K. Sesay, A. Priscilla, A.-S. Kemi, A. M. Olubusuyi, A. O. O. Oluwapelumi, A. Hammami, A. A. Amuri, A. Sayed, A. E. O. Ouma, A. Elargoubi, N. A. Ajayi, A. F. Victoria, A. Kazeem, A. George, A. J. Trotter, A. A. Yahaya, A. K. Keita, A. Diallo, A. Kone, A. Souissi, A. Chtourou, A. V. Gutierrez, A. J. Page, A. Vinze, A. Iranzadeh, A. Lambisia, A. Ismail, A. Rosemary, A. Sylverken, A. Femi, A. Ibrahimi, B. Marycelin, B. S. Oderinde, B. Bolajoko, B. Dhaala, B. L. Herring, B.-M. Njanpop-Lafourcade, B. Kleinhans, B. McInnis, B. Tegomoh, C. Brook, C. B. Pratt, C. Scheepers, C. G. Akoua-Koffi, C. N. Agoti, C. Peyrefitte, C. Daubenberger, C. M. Morang'a, D. J. Nokes, D. G. Amoako, D. L. Bugembe, D. Park, D. Baker, D. Doolabh, D. Ssemwanga, D. Tshiabuila, D. Bassirou, D. S. Y. Amuzu, D. Goedhals, D. O. Omuoyo, D. Maruapula, E. Foster-Nyarko, E. K. Lusamaki, E. Simulundu, E. M. Ong'era, E. N. Ngabana, E. Shumba, E. El Fahime, E. Lokilo, E. Mukantwari, E. Philomena, E. Belarbi, E. Simon-Loriere, E. A. Anoh, F. Leendertz, F. Ajili, F. O. Enoch, F. Wasfi, F. Abdelmoula, F. S. Mosha, F. T. Takawira, F. Derrar, F. Bouzid, F. Onikepe, F. Adeola, F. M. Muyembe, F. Tanser, F. A. Dratibi, G. K. Mbunsu, G. Thilliez, G. L. Kay, G. Githinji, G. van Zyl, G. A. Awandare, G. Schubert, G. P. Maphalala, H. C. Ranaivoson, H. Lemriss, H. Anise, H. Abe, H. H. Karray, H. Nansumba, H. A. Elgahzaly, H. Gumbo, I. Smeti, I. B. Ayed, I. Odia, I. B. Ben Boubaker, I. Gaaloul, I. Gazy, I. Mudau, I. Ssewanyana, I. Konstantinus, J. B. Lekana-Douk, J.-C. C. Makangara, J. M. Tamfum, J.-M. Heraud, J. G. Shaffer, J. Giandhari, J. Li, J. Yasuda, J. Q. Mends, J. Kiconco, J. M. Morobe, J. O. Gyapong, J. C. Okolie, J. T. Kayiwa, J. A. Edwards, J. Gyamfi, J. Farah, J. Nakaseegu, J. M. Ngoi, J. Namulondo, J. C. Andeko, J. J. Lutwama, J. O'Grady, K. Siddle, K. T. Adeyemi, K. A. Tumedi, K. M. Said, K. Hae-Young, K. O. Duedu, L. Belyamani, L. Fki-Berrajah, L. Singh, L. O. Martins, L. Tyers, M. Ramuth, M. Mastouri, M. Aouni, M. El Hefnawi, M. I. Matsheka, M. Kebabonye, M. Diop, M. Turki, M. Paye, M. M. Nyaga, M. Mareka, M.-M. Damaris, M. W. Mburu, M. Mpina, M. Nwando, M. Owusu, M. R. Wiley, M. T. Youtchou, M. O. Ayekaba, M. Abouelhoda, M. G. Seadawy, M. K. Khalifa, M. Sekhele, M. Ouadghiri, M. M. Diagne, M. Mwenda, M. Allam, M. V. T. Phan, N. Abid, N. Touil, N. Rujeni, N. Kharrat, N. Ismael, N. Dia, N. Mabunda, N. Y. Hsiao, N. B. Silochi, N. Nsenga, N. Gumede, N. Mulder, N. Ndodo, N. H. Razanajatovo, N. Iguosadolo, O. Judith, O. C. Kingsley, O. Sylvanus, O. Peter, O. Femi, O. Idowu, O. Testimony, O. E. Chukwuma, O. E. Ogah, C. K. Onwuamah, O. Cyril, O. Faye, O. Tomori, P. Ondoa, P. Combe, P. Semanda, P. E. Oluniyi, P. Arnaldo, P. K. Quashie, P. Dussart, P. A. Bester, P. K. Mbala, R. Ayivor-Djanie, R. Njouom, R. O. Phillips, R. Gorman, R. A. Kingsley, R. A. A. Carr, S. El Kabbaj, S. Gargouri, S. Masmoudi, S. Sankhe, S. B. Lawal, S. Kassim, S. Trabelsi, S. Metha, S. Kammoun, S. Lemriss, S. H. A. Agwa, S. Calvignac-Spencer, S. F. Schaffner, S. Doumbia, S. M. Mandanda, S. Aryeetey, S. S. Ahmed, S. Elhamoumi, S. Andriamandimby, S. Tope, S. Lekana-Douki, S. Prosolek, S. Ouangraoua, S. A. Mundeke, S. Rudder, S. Panji, S. Pillay, S. Engelbrecht, S. Nabadda, S. Behillil, S. L. Budiaki, S. van der Werf, T. Mashe, T. Aanniz, T. Mohale, T. Le-Viet, T. Schindler, U. J. Anyaneji, U. Chinedu, U. Ramphal, U. Jessica, U. George, V. Fonseca, V. Enouf, V. Gorova, W. H. Roshdy, W. K. Ampofo, W. Preiser, W. T. Choga, Y. Bediako, Y. Naidoo, Y. Butera, Z. R. de Laurent, A. A. Sall, A. Rebai, A. von Gottberg, B. Kouriba, C. Williamson, D. J. Bridges, I. Chikwe, J. N. Bhiman, M. Mine, M. Cotten, S. Moyo, S. Gaseitsiwe, N. Saasa, P. C. Sabeti, P. Kaleebu, Y. K. Tebeje, S. K. Tessema, C. Happi, J. Nkengasong, T. de Oliveira, A year of genomic surveillance reveals how the SARS-CoV-2 pandemic unfolded in Africa. *Science* **374**, 423–431 (2021). doi:10.1126/science.abj4336 Medline
4. WHO (World Health Organization, 2021), vol. 2022.
5. C. J. Gill, L. Mwananyanda, W. MacLeod, G. Kwenda, R. Pieciak, L. Etter, D. J. Bridges, C. Chikoti, S. Chirwa, C. Chimoga, L. Forman, B. Katowa, R. Lapidot, J. Lungu, J. Matoba, G. Mwinga, B. Mubemba, Z. Mupila, W. Muleya, M. Mwenda, B. Ngoma, R. Nkazwe, D. Nzara, N. Pawlak, L. Pemba, N. Saasa, E. Simulundu, B. Yankonde, D. M. Thea, Sustained high prevalence of COVID-19 deaths from a systematic post-mortem study in Lusaka, Zambia: one year later. medRxiv 2022.03.08.22272087 [Preprint] (2022). https://doi.org/10.1101/2022.03.08.22272087.
6. W. K. Jo, C. Drosten, J. F. Drexler, The evolutionary dynamics of endemic human coronaviruses. *Virus Evol.* **7**, veab020 (2021). doi:10.1093/ve/veab020 Medline
7. R. Viana, S. Moyo, D. G. Amoako, H. Tegally, C. Scheepers, C. L. Althaus, U. J. Anyaneji, P. A. Bester, M. F. Boni, M. Chand, W. T. Choga, R. Colquhoun, M. Davids, K. Deforche, D. Doolabh, L. du Plessis, S. Engelbrecht, J. Everatt, J. Giandhari, M. Giovanetti, D. Hardie, V. Hill, N.-Y. Hsiao, A. Iranzadeh, A. Ismail, C. Joseph, R. Joseph, L. Koopile, S. L. Kosakovsky Pond, M. U. G. Kraemer, L. Kuate-Lere, O. Laguda-Akingba, O. Lesetedi-Mafoko, R. J. Lessells, S. Lockman, A. G. Lucaci, A. Maharaj, B. Mahlangu, T. Maponga, K. Mahlakwane, Z. Makatini, G. Marais, D. Maruapula, K. Masupu, M. Matshaba, S. Mayaphi, N. Mbhele, M. B. Mbulawa, A. Mendes, K. Mlisana, A. Mnguni, T. Mohale, M. Moir, K. Moruisi, M. Mosepele, G. Motsatsi, M. S. Motswaledi, T. Mphoyakgosi, N. Msomi, P. N. Mwangi, Y. Naidoo, N. Ntuli, M. Nyaga, L. Olubayo, S. Pillay, B. Radibe, Y. Ramphal, U. Ramphal, J. E. San, L. Scott, R. Shapiro, L. Singh, P. Smith-Lawrence, W. Stevens, A. Strydom, K. Subramoney, N. Tebeila, D. Tshiabuila, J. Tsui, S. van Wyk, S. Weaver, C. K. Wibmer, E. Wilkinson, N. Wolter, A. E. Zarebski, B. Zuze, D. Goedhals, W. Preiser, F. Treurnicht, M. Venter, C. Williamson, O. G. Pybus, J. Bhiman, A. Glass, D. P. Martin, A. Rambaut, S. Gaseitsiwe, A. von Gottberg, T. de Oliveira, Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa. *Nature* **603**, 679–686 (2022). doi:10.1038/s41586-022-04411-y Medline
8. J. Hadfield, C. Megill, S. M. Bell, J. Huddleston, B. Potter, C. Callender, P. Sagulenko, T. Bedford, R. A. Neher, Nextstrain: Real-time tracking of pathogen evolution. *Bioinformatics* **34**, 4121–4123 (2018). doi:10.1093/bioinformatics/bty407 Medline
9. E. B. Hodcroft, CoVariants: SARS-CoV-2 Mutations and Variants of Interest (2021); https://covariants.org/.
10. S. H. Wilks, B. Mühlemann, X. Shen, S. Türeli, E. B. LeGresley, A. Netzl, M. A. Caniza, J. N. Chacaltana-Huarcaya, V. M. Corman, X. Daniell, M. B. Datto, F. S. Dawood, T. N. Denny, C. Drosten, R. A. M. Fouchier, P. J. Garcia, P. J. Halfmann, A. Jassem, L. M. Jeworowski, T. C. Jones, Y. Kawaoka, F. Krammer, C. McDanal, R. Pajon, V. Simon, M. S. Stockwell, H. Tang, H. van Bakel, V. Veguilla, R. Webby, D. C.

Montefiori, D. J. Smith, Mapping SARS-CoV-2 antigenic relationships and serological responses. bioRxiv 2022.01.28.477987 [Preprint] (2022). https://doi.org/10.1101/2022.01.28.477987.

11. L. Liu, S. Iketani, Y. Guo, J. F.-W. Chan, M. Wang, L. Liu, Y. Luo, H. Chu, Y. Huang, M. S. Nair, J. Yu, K. K.-H. Chik, T. T.-T. Yuen, C. Yoon, K. K.-W. To, H. Chen, M. T. Yin, M. E. Sobieszczyk, Y. Huang, H. H. Wang, Z. Sheng, K.-Y. Yuen, D. D. Ho, Striking antibody evasion manifested by the Omicron variant of SARS-CoV-2. *Nature* **602**, 676–681 (2022). doi:10.1038/s41586-021-04388-0 Medline

12. Q. Li, J. Nie, J. Wu, L. Zhang, R. Ding, H. Wang, Y. Zhang, T. Li, S. Liu, M. Zhang, C. Zhao, H. Liu, L. Nie, H. Qin, M. Wang, Q. Lu, X. Li, J. Liu, H. Liang, Y. Shi, Y. Shen, L. Xie, L. Zhang, X. Qu, W. Xu, W. Huang, Y. Wang, SARS-CoV-2 501Y.V2 variants lack higher infectivity but do have immune escape. *Cell* **184**, 2362–2371.e9 (2021). doi:10.1016/j.cell.2021.02.042 Medline

13. W. T. Harvey, A. M. Carabelli, B. Jackson, R. K. Gupta, E. C. Thomson, E. M. Harrison, C. Ludden, R. Reeve, A. Rambaut, S. J. Peacock, D. L. Robertson; COVID-19 Genomics UK (COG-UK) Consortium, SARS-CoV-2 variants, spike mutations and immune escape. *Nat. Rev. Microbiol.* **19**, 409–424 (2021). doi:10.1038/s41579-021-00573-0 Medline

14. G. Ye, B. Liu, F. Li, Cryo-EM structure of a SARS-CoV-2 omicron spike protein ectodomain. *Nat. Commun.* **13**, 1214 (2022). doi:10.1038/s41467-022-28882-9 Medline

15. B. Meng, A. Abdullahi, I. A. T. M. Ferreira, N. Goonawardane, A. Saito, I. Kimura, D. Yamasoba, P. P. Gerber, S. Fatihi, S. Rathore, S. K. Zepeda, G. Papa, S. A. Kemp, T. Ikeda, M. Toyoda, T. S. Tan, J. Kuramochi, S. Mitsunaga, T. Ueno, K. Shirakawa, A. Takaori-Kondo, T. Brevini, D. L. Mallery, O. J. Charles, J. E. Bowen, A. Joshi, A. C. Walls, L. Jackson, D. Martin, K. G. C. Smith, J. Bradley, J. A. G. Briggs, J. Choi, E. Madissoon, K. B. Meyer, P. Mlcochova, L. Ceron-Gutierrez, R. Doffinger, S. A. Teichmann, A. J. Fisher, M. S. Pizzuto, A. de Marco, D. Corti, M. Hosmillo, J. H. Lee, L. C. James, L. Thukral, D. Veesler, A. Sigal, F. Sampaziotis, I. G. Goodfellow, N. J. Matheson, K. Sato, R. K. Gupta; CITIID-NIHR BioResource COVID-19 Collaboration; Genotype to Phenotype Japan (G2P-Japan) Consortium; Ecuador-COVID19 Consortium, Altered TMPRSS2 usage by SARS-CoV-2 Omicron impacts infectivity and fusogenicity. *Nature* **603**, 706–714 (2022). doi:10.1038/s41586-022-04474-x Medline

16. J. A. Backer, D. Eggink, S. P. Andeweg, I. K. Veldhuijzen, N. van Maarseveen, K. Vermaas, B. Vlaemynck, R. Schepers, S. van den Hof, C. B. E. M. Reusken, J. Wallinga, Shorter serial intervals in SARS-CoV-2 cases with Omicron BA.1 variant compared with Delta variant, the Netherlands, 13 to 26 December 2021. *Euro Surveill.* **27**, 2200042 (2022). doi:10.2807/1560-7917.ES.2022.27.6.2200042 Medline

17. M. Mendelson, F. Venter, M. Moshabela, G. Gray, L. Blumberg, T. de Oliveira, S. A. Madhi, The political theatre of the UK's travel ban on South Africa. *Lancet* **398**, 2211–2213 (2021). doi:10.1016/S0140-6736(21)02752-5 Medline

18. D. Luke, in *Business Insider SA* (Business Insider SA, 2022).

19. S. Mallapaty, Where did Omicron come from? Three key theories. *Nature* **602**, 26–28 (2022). doi:10.1038/d41586-022-00215-2 Medline

20. C. Onwuamah, B. Iwalokun, R. Ahmed, E. Toye, O. Amoo, N. Ndodo, E. Momoh, A. Okwuraiwe, A. James, C. Okoli, C. Chukwu, J. Shaibu, M. Fowora, J. Fayemi, T. Onuigbo, M. Sunday, V. Ogbolu, M. Otuonye, N. Mba, R. Audu, O. Ezechi, A. Abayomi, I. Adetifa, B. Salako The trend of SARS-CoV-2 variants from July 2021 to Jan 2022 in metropolitan Lagos, the epicentre of the COVID-19 pandemic in Nigeria. Research Square [Preprint] (2022). https://www.researchsquare.com/article/rs-1602118/v1.

21. A. L. Sander, A. Yadouleton, E. F. de Oliveira Filho, C. Tchibozo, G. Hounkanrin, Y. Badou, P. Adewumi, K. K. René, D. Ange, S. Sourakatou, E. Sedjro, M. A. J. Aïssi, H. Fidelia, M. H. Djingarey, M. Nagel, W. K. Jo, A. Moreira-Soto, C. Drosten, O. Landt, V. M. Corman, B. Hounkpatin, J. F. Drexler, Mutations associated with SARS-CoV-2 variants of concern, Benin, Early 2021. *Emerg. Infect. Dis.* **27**, 2889–2903 (2021). doi:10.3201/eid2711.211353 Medline

22. H. Tegally, J. E. San, M. Cotten, M. Moir, B. Tegomoh, G. Mboowa, D. P. Martin, C. Baxter, A. W. Lambisia, A. Diallo, D. G. Amoako, M. M. Diagne, A. Sisay, A. N. Zekri, A. S. Gueye, A. K. Sangare, A.-S. Ouedraogo, A. Sow, A. O. Musa, A. K. Sesay, A. G. Abias, A. I. Elzagheid, A. Lagare, A.-S. Kemi, A. E. Abar, A. A. Johnson, A. Fowotade, A. O. Oluwapelumi, A. A. Amuri, A. Juru, A. Kandeil, A. Mostafa, A. Rebai, A. Sayed, A. Kazeem, A. Balde, A. Christoffels, A. J. Trotter, A. Campbell, A. K. Keita, A. Kone,

A. Bouzid, A. Souissi, A. Agweyu, A. Naguib, A. V. Gutierrez, A. Nkeshimana, A. J. Page, A. Yadouleton, A. Vinze, A. N. Happi, A. Chouikha, A. Iranzadeh, A. Maharaj, A. L. Batchi-Bouyou, A. Ismail, A. A. Sylverken, A. Goba, A. Femi, A. E. Sijuwola, B. Marycelin, B. L. Salako, B. S. Oderinde, B. Bolajoko, B. Diarra, B. L. Herring, B. Tsofa, B. Lekana-Douki, B. Mvula, B.-M. Njanpop-Lafourcade, B. T. Marondera, B. A. Khaireh, B. Kouriba, B. Adu, B. Pool, B. McInnis, C. Brook, C. Williamson, C. Nduwimana, C. Anscombe, C. B. Pratt, C. Scheepers, C. G. Akoua-Koffi, C. N. Agoti, C. M. Mapanguy, C. Loucoubar, C. K. Onwuamah, C. Ihekweazu, C. N. Malaka, C. Peyrefitte, C. Grace, C. E. Omoruyi, C. D. Rafaï, C. M. Morang'a, C. Erameh, D. B. Lule, D. J. Bridges, D. Mukadi-Bamuleka, D. Park, D. A. Rasmussen, D. Baker, D. J. Nokes, D. Ssemwanga, D. Tshiabuila, D. S. Y. Amuzu, D. Goedhals, D. S. Grant, D. O. Omuoyo, D. Maruapula, D. W. Wanjohi, E. Foster-Nyarko, E. K. Lusamaki, E. Simulundu, E. M. Ong'era, E. N. Ngabana, E. O. Abworo, E. Otieno, E. Shumba, E. Barasa, E. B. Ahmed, E. A. Ahmed, E. Lokilo, E. Mukantwari, E. Philomena, E. Belarbi, E. Simon-Loriere, E. A. Anoh, E. Manuel, F. Leendertz, F. M. Taweh, F. Wasfi, F. Abdelmoula, F. T. Takawira, F. Derrar, F. V. Ajogbasile, F. Treurnicht, F. Onikepe, F. Ntoumi, F. M. Muyembe, F. E. Z. Ragomzingba, F. A. Dratibi, F.-A. Iyanu, G. K. Mbunsu, G. Thilliez, G. L. Kay, G. O. Akpede, G. U. van Zyl, G. A. Awandare, G. S. Kpeli, G. Schubert, G. P. Maphalala, H. C. Ranaivoson, H. E. Omunakwe, H. Onywera, H. Abe, H. Karray, H. Nansumba, H. Triki, H. A. A. Kadjo, H. Elgahzaly, H. Gumbo, H. Mathieu, H. Kavunga-Membo, I. Smeti, I. B. Olawoye, I. M. O. Adetifa, I. Odia, I. B. Ben Boubaker, I. A. Muhammad, I. Ssewanyana, I. Wurie, I. S. Konstantinus, J. W. A. Halatoko, J. Ayei, J. Sonoo, J.-C. C. Makangara, J. M. Tamfum, J.-M. Heraud, J. G. Shaffer, J. Giandhari, J. Musyoki, J. Nkurunziza, J. N. Uwanibe, J. N. Bhiman, J. Yasuda, J. Morais, J. Kiconco, J. D. Sandi, J. Huddleston, J. K. Odoom, J. M. Morobe, J. O. Gyapong, J. T. Kayiwa, J. C. Okolie, J. S. Xavier, J. Gyamfi, J. F. Wamala, J. H. K. Bonney, J. Nyandwi, J. Everatt, J. Nakaseegu, J. M. Ngoi, J. Namulondo, J. U. Oguzie, J. C. Andeko, J. J. Lutwama, J. J. H. Mogga, J. O'Grady, K. J. Siddle, K. Victoir, K. T. Adeyemi, K. A. Tumedi, K. S. Carvalho, K. S. Mohammed, K. Dellagi, K. G. Musonda, K. O. Duedu, L. Fki-Berrajah, L. Singh, L. M. Kepler, L. Biscornet, L. de Oliveira Martins, L. Chabuka, L. Olubayo, L. D. Ojok, L. Deng, L. I. Ochola-Oyier, L. Tyers, M. Mine, M. Ramuth, M. Mastouri, M. ElHefnawi, M. Mbanne, M. I. Matsheka, M. Kebabonye, M. Diop, M. Momoh, M. D. L. Lima Mendonça, M. Venter, M. F. Paye, M. Faye, M. M. Nyaga, M. Mareka, M.-M. Damaris, M. W. Mburu, M. G. Mpina, M. Owusu, M. R. Wiley, M. Y. Tatfeng, M. O. Ayekaba, M. Abouelhoda, M. A. Beloufa, M. G. Seadawy, M. K. Khalifa, M. M. Matobo, M. Kane, M. Salou, M. B. Mbulawa, M. Mwenda, M. Allam, M. V. T. Phan, N. Abid, N. Rujeni, N. Abuzaid, N. Ismael, N. Elguindy, N. M. Top, N. Dia, N. Mabunda, N. Y. Hsiao, N. B. Silochi, N. M. Francisco, N. Saasa, N. Bbosa, N. Murunga, N. Gumede, N. Wolter, N. Sitharam, N. Ndodo, N. A. Ajayi, N. Tordo, N. Mbhele, N. H. Razanajatovo, N. Iguosadolo, N. Mba, O. C. Kingsley, O. Sylvanus, O. Femi, O. M. Adewumi, O. Testimony, O. A. Ogunsanya, O. Fakayode, O. E. Ogah, O.-E. Oludayo, O. Faye, P. Smith-Lawrence, P. Ondoa, P. Combe, P. Nabisubi, P. Semanda, P. E. Oluniyi, P. Arnaldo, P. K. Quashie, P. O. Okokhere, P. Bejon, P. Dussart, P. A. Bester, P. K. Mbala, P. Kaleebu, P. Abechi, R. El-Shesheny, R. Joseph, R. K. Aziz, R. G. Essomba, R. Ayivor-Djanie, R. Njouom, R. O. Phillips, R. Gorman, R. A. Kingsley, R. M. D. E. S. A. Neto Rodrigues, R. A. Audu, R. A. A. Carr, S. Gargouri, S. Masmoudi, S. Bootsma, S. Sankhe, S. I. Mohamed, S. Femi, S. Mhalla, S. Hosch, S. K. Kassim, S. Metha, S. Trabelsi, S. H. Agwa, S. W. Mwangi, S. Doumbia, S. Makiala-Mandanda, S. Aryeetey, S. S. Ahmed, S. M. Ahmed, S. Elhamoumi, S. Moyo, S. Lutucuta, S. Gaseitsiwe, S. Jalloh, S. F. Andriamandimby, S. Oguntope, S. Grayo, S. Lekana-Douki, S. Prosolek, S. Ouangraoua, S. van Wyk, S. F. Schaffner, S. Kanyerezi, S. Ahuka-Mundeke, S. Rudder, S. Pillay, S. Nabadda, S. Behillil, S. L. Budiaki, S. van der Werf, T. Mashe, T. Mohale, T. Le-Viet, T. P. Velavan, T. Schindler, T. G. Maponga, T. Bedford, U. J. Anyaneji, U. Chinedu, U. Ramphal, U. E. George, V. Enouf, V. Nene, V. Gorova, W. H. Roshdy, W. A. Karim, W. K. Ampofo, W. Preiser, W. T. Choga, Y. A. Ahmed, Y. Ramphal, Y. Bediako, Y. Naidoo, Y. Butera, Z. R. de Laurent, A. E. O. Ouma, A. von Gottberg, G. Githinji, M. Moeti, O. Tomori, P. C. Sabeti, A. A. Sall, S. O. Oyola, Y. K. Tebeje, S. K. Tessema, T. de Oliveira, C. Happi, R. Lessells, J. Nkengasong, E. Wilkinson; Africa Pathogen Genomics Initiative (Africa PGI), The evolving SARS-CoV-2 epidemic in Africa: Insights from rapidly expanding genomic surveillance. *Science* **378**, eabq5358 (2022). doi:10.1126/science.abq5358 Medline

23. E. Strano, M. P. Viana, A. Sorichetta, A. J. Tatem, Mapping road network communities for guiding disease surveillance and control strategies. *Sci. Rep.* **8**,

4744 (2018). doi:10.1038/s41598-018-22969-4 Medline

24. K. Sun, S. Tempia, J. Kleynhans, A. von Gottberg, M. L. McMorrow, N. Wolter, J. N. Bhiman, J. Moyes, M. du Plessis, M. Carrim, A. Buys, N. A. Martinson, K. Kahn, S. Tollman, L. Lebina, F. Wafawanaka, J. D. du Toit, F. X. Gómez-Olivé, T. Mkhencele, C. Viboud, C. Cohen, SARS-CoV-2 transmission, persistence of immunity, and estimates of Omicron's impact in South African population cohorts. *Sci. Transl. Med.* **14**, eabo7081 (2022). doi:10.1126/scitranslmed.abo7081 Medline

25. S. A. Iyaniwura, M. Rabiu, J. F. David, J. D. Kong, The basic reproduction number of COVID-19 across Africa. *PLOS ONE* **17**, e0264455 (2022). doi:10.1371/journal.pone.0264455 Medline

26. Y. Liu, J. Rocklöv, The effective reproductive number of the Omicron variant of SARS-CoV-2 is several times relative to Delta. *J. Travel Med.* **29**, taac037 (2022). doi:10.1093/jtm/taac037 Medline

27. H. Tegally, M. Moir, J. Everatt, M. Giovanetti, C. Scheepers, E. Wilkinson, K. Subramoney, Z. Makatini, S. Moyo, D. G. Amoako, C. Baxter, C. L. Althaus, U. J. Anyaneji, D. Kekana, R. Viana, J. Giandhari, R. J. Lessells, T. Maponga, D. Maruapula, W. Choga, M. Matshaba, M. B. Mbulawa, N. Msomi, Y. Naidoo, S. Pillay, T. J. Sanko, J. E. San, L. Scott, L. Singh, N. A. Magini, P. Smith-Lawrence, W. Stevens, G. Dor, D. Tshiabuila, N. Wolter, W. Preiser, F. K. Treurnicht, M. Venter, G. Chiloane, C. McIntyre, A. O'Toole, C. Ruis, T. P. Peacock, C. Roemer, S. L. Kosakovsky Pond, C. Williamson, O. G. Pybus, J. N. Bhiman, A. Glass, D. P. Martin, B. Jackson, A. Rambaut, O. Laguda-Akingba, S. Gaseitsiwe, A. von Gottberg, T. de Oliveira; NGS-SA consortium, Emergence of SARS-CoV-2 Omicron lineages BA.4 and BA.5 in South Africa. *Nat. Med.* **28**, 1785–1790 (2022). doi:10.1038/s41591-022-01911-2 Medline

28. K. Y. Oróstica, S. Contreras, A. Sanchez-Daza, J. Fernandez, V. Priesemann, Á. Olivera-Nappa, New year, new SARS-CoV-2 variant: Resolutions on genomic surveillance protocols to face Omicron. *Lancet Reg Health Am* **7**, 100203 (2022). doi:10.1016/j.lana.2022.100203 Medline

29. P. Elliott, O. Eales, N. Steyn, D. Tang, B. Bodinier, H. Wang, J. Elliott, M. Whitaker, C. Atchison, P. J. Diggle, A. J. Page, A. J. Trotter, D. Ashby, W. Barclay, G. Taylor, H. Ward, A. Darzi, G. S. Cooke, C. A. Donnelly, M. Chadeau-Hyam, Twin peaks: The Omicron SARS-CoV-2 BA.1 and BA.2 epidemics in England. *Science* **376**, eabq4411 (2022). doi:10.1126/science.abq4411 Medline

30. J. Wise, Covid-19: The E484K mutation and the risks it poses. *BMJ* **372**, n359 (2021). doi:10.1136/bmj.n359 Medline

31. Y. Cao, A. Yisimayi, Y. Bai, W. Huang, X. Li, Z. Zhang, T. Yuan, R. An, J. Wang, T. Xiao, S. Du, W. Ma, L. Song, Y. Li, X. Li, W. Song, J. Wu, S. Liu, X. Li, Y. Zhang, B. Su, X. Guo, Y. Wei, C. Gao, N. Zhang, Y. Zhang, Y. Dou, X. Xu, R. Shi, B. Lu, R. Jin, Y. Ma, C. Qin, Y. Wang, Y. Feng, J. Xiao, X. S. Xie, Humoral immune response to circulating SARS-CoV-2 variants elicited by inactivated and RBD-subunit vaccines. *Cell Res.* **31**, 732–741 (2021). doi:10.1038/s41422-021-00514-9 Medline

32. S. A. Madhi, G. Kwatra, J. E. Myers, W. Jassat, N. Dhar, C. K. Mukendi, A. J. Nana, L. Blumberg, R. Welch, N. Ngorima-Mabhena, P. C. Mutevedzi, Population immunity and Covid-19 severity with Omicron variant in South Africa. *N. Engl. J. Med.* **386**, 1314–1326 (2022). doi:10.1056/NEJMoa2119658 Medline

33. F. Obermeyer, M. Jankowiak, N. Barkas, S. F. Schaffner, J. D. Pyle, L. Yurkovetskiy, M. Bosso, D. J. Park, M. Babadi, B. L. MacInnis, J. Luban, P. C. Sabeti, J. E. Lemieux, Analysis of 6.4 million SARS-CoV-2 genomes identifies mutations associated with fitness. *Science* **376**, 1327–1332 (2022). doi:10.1126/science.abm1208 Medline

34. V. L. Hale, P. M. Dennis, D. S. McBride, J. M. Nolting, C. Madden, D. Huey, M. Ehrlich, J. Grieser, J. Winston, D. Lombardi, S. Gibson, L. Saif, M. L. Killian, K. Lantz, R. M. Tell, M. Torchetti, S. Robbe-Austerman, M. I. Nelson, S. A. Faith, A. S. Bowman, SARS-CoV-2 infection in free-ranging white-tailed deer. *Nature* **602**, 481–486 (2022). doi:10.1038/s41586-021-04353-x Medline

35. S. T. Sonnleitner, M. Prelog, S. Sonnleitner, E. Hinterbichler, H. Halbfurter, D. B. C. Kopecky, G. Almanzar, S. Koblmüller, C. Sturmbauer, L. Feist, R. Horres, W. Posch, G. Walder, Cumulative SARS-CoV-2 mutations and corresponding changes in immunity in an immunocompromised patient indicate viral evolution within the host. *Nat. Commun.* **13**, 2560 (2022). doi:10.1038/s41467-022-30163-4 Medline

36. S. A. Clark, L. E. Clark, J. Pan, A. Coscia, L. G. A. McKay, S. Shankar, R. I. Johnson, V. Brusic, M. C. Choudhary, J. Regan, Z. Li, A. Griffiths, I. Abraham, SARS-CoV-2 evolution in an immunocompromised host reveals shared neutralization escape mechanisms. *Cell* **184**, 2605–2617.e18 (2021). doi:10.1016/j.cell.2021.03.027 Medline

37. The World Bank Group, World Bank Open Data, Prevalence of HIV, total (% of population ages 15-49) (2022); https://data.worldbank.org/indicator/SH.DYN.AIDS.ZS.

38. S. Harari, M. Tahor, N. Rutsinsky, S. Meijer, D. Miller, O. Henig, O. Halutz, K. Levytskyi, R. Ben-Ami, A. Adler, Y. Paran, A. Stern, Drivers of adaptive evolution during chronic SARS-CoV-2 infections. *Nat. Med.* **28**, 1501–1508 (2022). doi:10.1038/s41591-022-01882-4 Medline

39. W. Preiser, S. Engelbrecht, T. Maponga, No point in travel bans if countries with poor surveillance are ignored. *Lancet* **399**, 1224 (2022). doi:10.1016/S0140-6736(22)00363-4 Medline

40. C. Fischer, Gradual emergence followed by exponential spread of the SARS-CoV-2 Omicron variant in Africa, version 1.4, Zenodo (2022); https://doi.org/10.5281/zenodo.7342478.

41. S. Engelbrecht, K. Delaney, B. Kleinhans, E. Wilkinson, H. Tegally, T. Stander, G. van Zyl, W. Preiser, T. de Oliveira, Multiple early introductions of SARS-CoV-2 to Cape Town, South Africa. *Viruses* **13**, 526 (2021). doi:10.3390/v13030526 Medline

42. F. Grabowski, M. Kochańczyk, T. Lipniacki, The spread of SARS-CoV-2 variant Omicron with a doubling time of 2.0-3.3 days can be explained by immune evasion. *Viruses* **14**, 294 (2022). doi:10.3390/v14020294 Medline

43. A. J. Drummond, M. A. Suchard, D. Xie, A. Rambaut, Bayesian phylogenetics with BEAUti and the BEAST 1.7. *Mol. Biol. Evol.* **29**, 1969–1973 (2012). doi:10.1093/molbev/mss075 Medline

44. P. Lemey, A. Rambaut, A. J. Drummond, M. A. Suchard, Bayesian phylogeography finds its roots. *PLOS Comput. Biol.* **5**, e1000520 (2009). doi:10.1371/journal.pcbi.1000520 Medline

45. F. Bielejec, G. Baele, B. Vrancken, M. A. Suchard, A. Rambaut, P. Lemey, SpreaD3: Interactive visualization of spatiotemporal history and trait evolutionary processes. *Mol. Biol. Evol.* **33**, 2167–2169 (2016). doi:10.1093/molbev/msw082 Medline

46. V. M. Corman, O. Landt, M. Kaiser, R. Molenkamp, A. Meijer, D. K. W. Chu, T. Bleicker, S. Brünink, J. Schneider, M. L. Schmidt, D. G. J. C. Mulders, B. L. Haagmans, B. van der Veer, S. van den Brink, L. Wijsman, G. Goderski, J.-L. Romette, J. Ellis, M. Zambon, M. Peiris, H. Goossens, C. Reusken, M. P. G. Koopmans, C. Drosten, Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill.* **25**, 2000045 (2020). doi:10.2807/1560-7917.ES.2020.25.3.2000045 Medline

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SUPPLEMENTARY MATERIALS

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Materials and Methods
Figs. S1 to S9
Tables S1 to S7
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MDAR Reproducibility Checklist
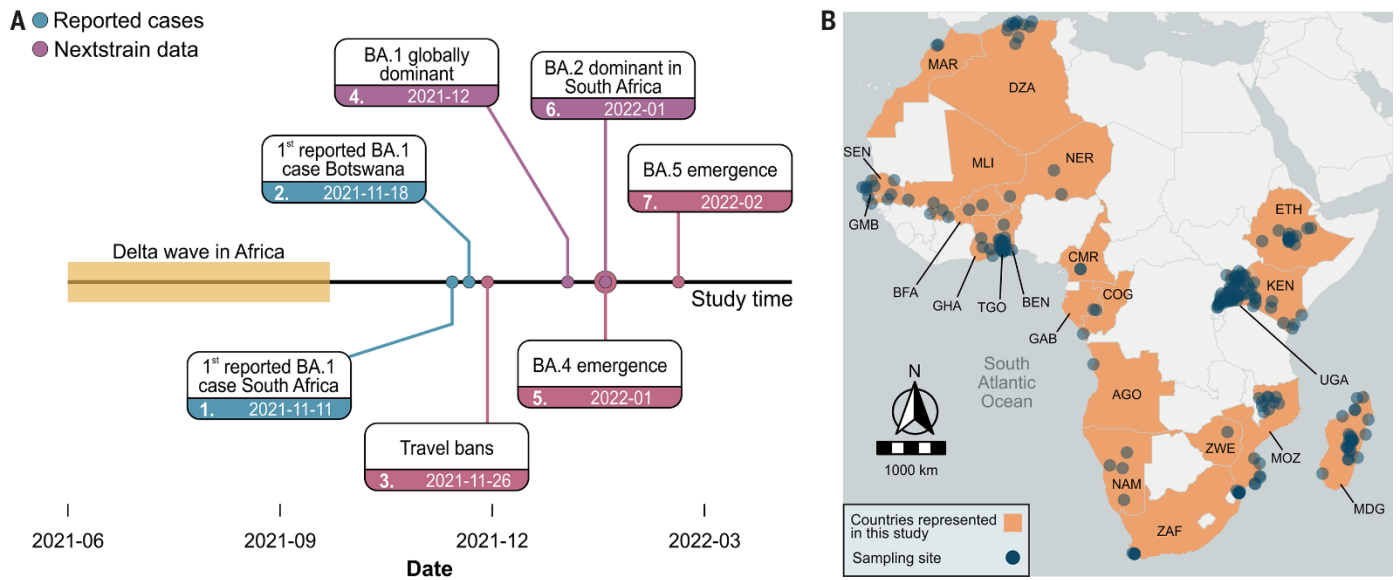
**Fig. 1. Study setup.** (**A**) Timeline of known events in the evolution and emergence of Omicron. (**B**) Geographic distribution of sampling sites and countries (alpha-3 country codes) represented in this study.
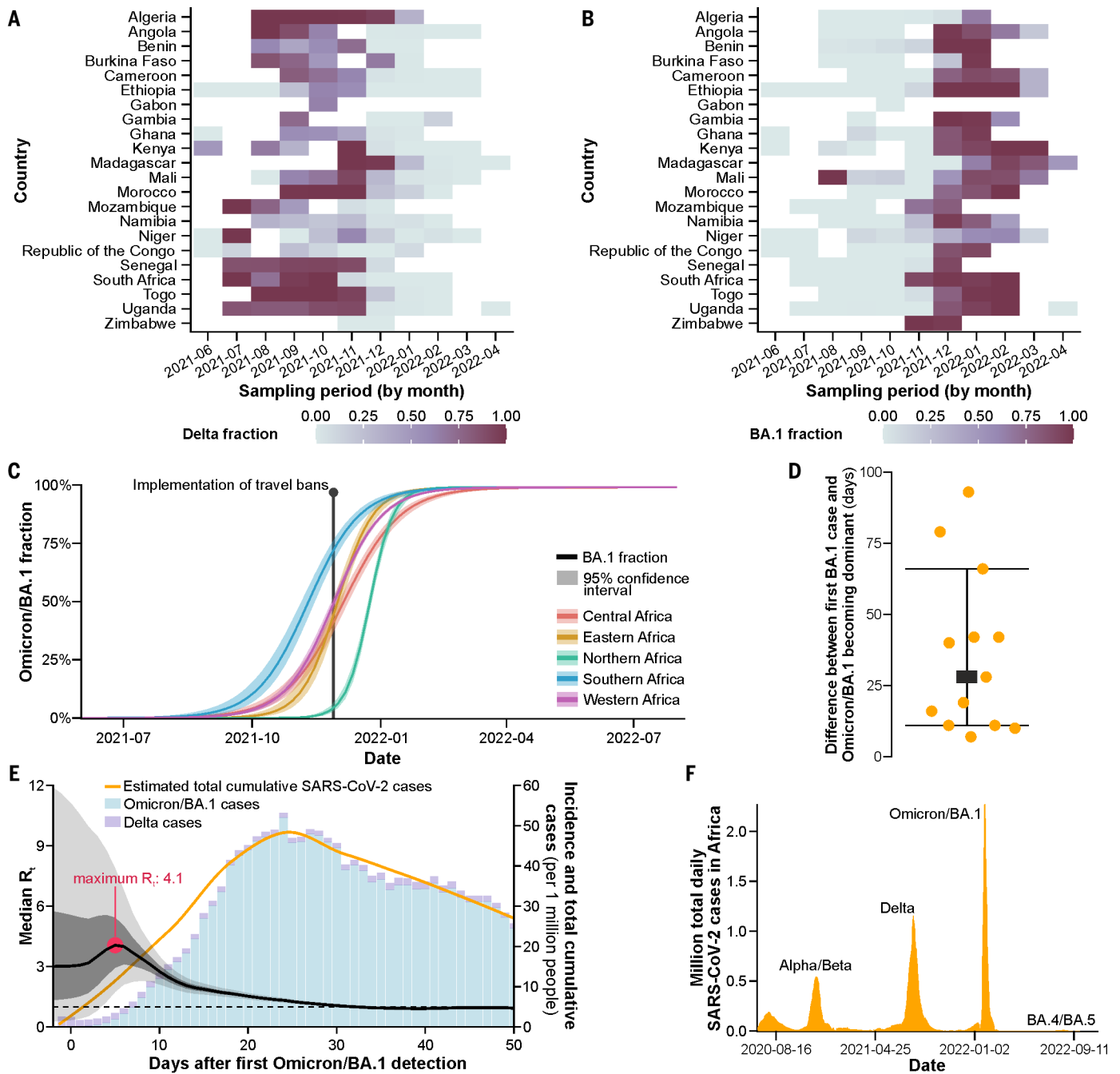
Fig. 2. Epidemiology of Omicron/BA.1 in Africa. (**A**) Fraction of samples positive for the Delta marker. (**B**) Fraction positive for the BA.1 marker. (**C**) Modeled increase in BA.1 fraction of all SARS-CoV-2 infections per African region based on PCR testing. (**D**) Days until BA.1 became the dominant SARS-CoV-2 variant after its first detection by PCR. (**E**) R_t and the incidence among countries represented in this study. (**F**) Daily reported SARS-CoV-2 cases in Africa (*28*).
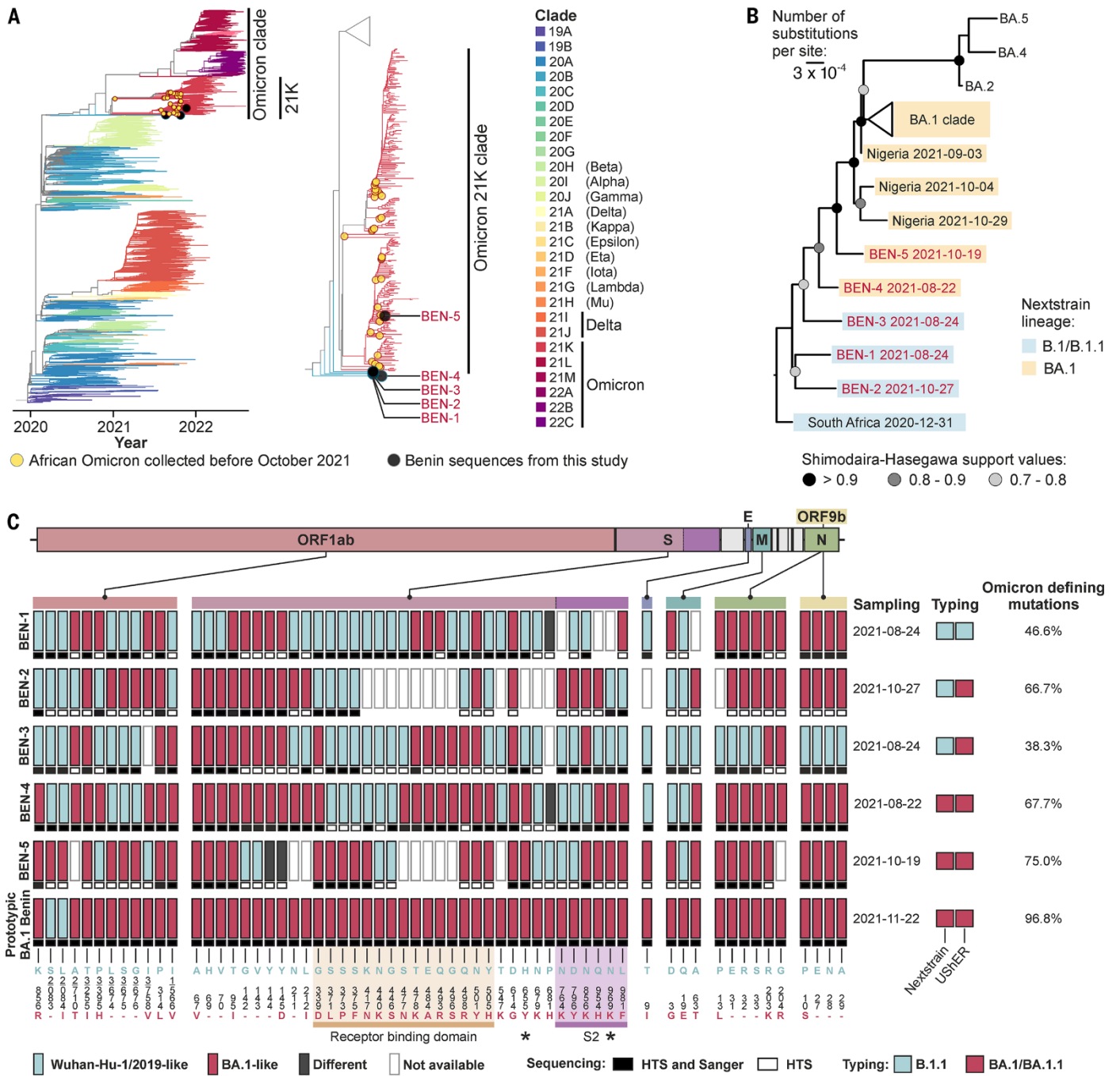
Fig. 3. Evolution of Omicron/BA.1 in Africa. (A) Time-resolved Nextstrain phylogeny of BA.1. (B) Approximate Maximum Likelihood phylogeny of African Omicron ancestors. (C) BA.1-defining mutations in samples from Benin (9). Asterisks, spike amino acid substitutions H655Y and N969K. HTS, high-throughput sequencing. Lineage assignment was conducted using the Nextclade (https://clades.nextstrain.org/) and UShER (https://genome.ucsc.edu/cgi-bin/hgPhyloPlace) online tools. Benin-derived sequences are available in GenBank (accession numbers OP537480-OP537485).

Gradual emergence followed by exponential spread of the SARS-CoV-2 Omicron variant in Africa

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