


BMJ Open Estimating the effect of South Africa travel restrictions in November 2021 on the SARS-CoV-2 Omicron outbreak in the Netherlands: a descriptive analysis and modelling study

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ABSTRACT

Background Governments used travel bans during the COVID-19 pandemic to limit the introduction of new variant of concern (VoC). In the Netherlands, direct flights from South Africa were banned from 26 November 2021 onwards to curb Omicron (B.1.1.529) importation.

Objectives This study retrospectively evaluated the effect of the South African travel ban and the timing of its implementation on subsequent Omicron infections in the Netherlands and, in order to help inform future decision-making, assessed alternative scenarios in which the reproduction number (R_0) and volume of indirectly imported cases were varied.

Design Descriptive analysis and modelling study.

Outcome measure Time (days) from 26 November 2021 to reach 10 000 cumulative Omicron infections in the Netherlands.

Methods To benchmark the direct importation rate of Omicron from South Africa, we used the proportion (n/N , %) of passengers arriving on two direct flights from South Africa to the Netherlands on 26 November 2021 with a positive PCR sequencing result for Omicron VoC infection. We scaled the number of directly-imported Omicron infections before and after the travel ban to the incidence in South Africa. We assumed that 10% of all cases continued to arrive via indirect routes, a 'failure rate' of 2% (ie, incoming Dutch citizens not adhering to quarantine on arrival) and an effective reproduction number (R_e) of Omicron of 1.3. In subsequent analyses, we varied, within plausible limits, the R_e (1.1–2.0) and proportion of indirectly-imported cases (0–20%).

Results Compared with no travel ban, the travel ban achieved a 14-day delay in reaching 10 000 Omicron cases, with an additional day of delay if initiated 2 days earlier. If all indirect importation had been prevented (eg, European-wide travel ban), a 21-day delay could have been achieved. The travel ban's effect was negligible if R_e was ≥ 2.0 and with a greater volume of ongoing importation.

Conclusions Travel bans can delay the calendar timing of an outbreak but are substantially less effective for pathogens where importation cannot be fully controlled

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This modelling study incorporates real-world epidemiological parameters in the specific context of the Netherlands in order to provide a detailed evaluation of Dutch travel restrictions to limit importation of the Omicron variant of concern (VoC) in November 2021.
- ⇒ A key strength of the study is that it combines descriptive analyses and mathematical modelling to estimate the public health impact of implemented measures in the Netherlands.
- ⇒ However, a limitation of our study is the substantial uncertainty around several key model parameters, for which robust data were lacking.
- ⇒ Our conclusions are not directly applicable to other contexts and pathogens but could be incorporated in a framework to guide future decision-making.

and tracing every imported case is unfeasible. When facing future disease outbreaks, we urge policy-makers to critically weigh up benefits against the known socioeconomic drawbacks of international travel restrictions.

INTRODUCTION

Travel-related restrictions are public health measures that can be used to limit the mobility of potentially infectious human hosts of a pathogen. Restrictions usually aim to prevent, reduce or delay importation of the pathogen into a susceptible population¹ and are implemented under the guidance of the WHO's International Health Regulations (IHR) (2005). The IHR are legally binding and were established to help detect, evaluate and appropriately respond to cross-border health threats, without subjecting essential international traffic and trade to unnecessary restrictions.² As such, building an evidence base for the effectiveness of travel bans, and the

parameters that influence their impact is central: first, to help inform future policy-makers who are often required to make rapid decisions with limited information, and second, to guide ongoing negotiations when forging the first global pandemic treaty.³ In this study, we retrospectively evaluate the impact of the travel restrictions implemented by the Dutch government on 26 November 2021 in response to the emergence of the Omicron subvariant (Pango lineage B.1.1.529) of SARS-CoV-2 and postulate how the results of this analysis may help guide decision-making during future disease outbreaks.

During the COVID-19 pandemic, many governments used bans on international (air) travel in the hope of restricting the entry of SARS-CoV-2 and its subvariants, including Omicron, into their respective countries.⁴ The Omicron subvariant was first detected in a sample collected on 11th November⁵ and initially raised global alarm due to numerous concerning features including mutations associated with escape of natural and vaccine-derived immunity,⁵ a steep rise in cases in South Africa in November suggesting superior transmissibility, and as yet insufficient evidence to demonstrate that Omicron resulted in a less severe clinical presentation⁶. As such, South African scientists promptly notified the WHO of the Omicron subvariant on 24 November 2021.⁷ After reviewing all available evidence, the WHO declared the Omicron subvariant a variant of concern (VoC) on 26 November 2021.

Following the WHO announcement, the Dutch government initiated a travel ban for flights from countries in Southern Africa (South Africa, Lesotho, Eswatini, Botswana, Malawi, Namibia, Zimbabwe and Mozambique). The aim of the travel ban was to limit the introduction of the Omicron variant in the Netherlands.⁸ When the measures were announced, two KLM Royal Dutch Airline flights—KL598 from Cape Town and flight KL592 from Johannesburg, carrying over 600 passengers in total—had already departed from South Africa to Schiphol Airport, Amsterdam. The local municipal public health service (GGD Kennemerland) and Regional Public Health Laboratory (Streeklaboratorium) in Haarlem coordinated testing of all passengers—also those in transit to other final destinations. In addition, isolation and quarantine locations were arranged for passengers who were unable to return to a home address (eg, non-Dutch residents or Dutch residents with unexposed household members). The travel ban lasted until 23:59 on 22 December 2021.

In the wake of concerns about why and how the travel ban was implemented (including criticism from the passengers disembarking from the two South African flights on 26 November⁹), the Ministry of Health, Welfare and Sport (VWS) commissioned a report which evaluated the logistics and communication channels of the government around the decision to initiate the travel ban.¹⁰ To date, however, an in-depth evaluation of the effect of the travel ban itself on the epidemiology of the subsequent Omicron outbreak is lacking. Weighing the public health impact of the travel ban against known disadvantages¹¹

helps establish an evidence base to help guide future decision-making. In this descriptive analysis and modelling study, we therefore aim to characterise the epidemiological context in which the decision to implement the travel ban was made; to assess the effect of the travel ban and its timing on days to 10 000 cumulative Omicron infections in the Netherlands; and to explore the effect of (1) the volume of Omicron importations via indirect routes and the days before the 26 November and (2) the reproduction number (R_e) of Omicron in the Netherlands, on the travel ban's impact.

METHODS

Data sources for descriptive analyses

To present the context for the situation in the Netherlands in the weeks prior to the implementation of the Omicron travel ban, epidemiological data and key events were identified. Data on notified cases, hospitalisations and intensive care unit (ICU) bed capacity were obtained from publicly available data from the National Institute for Public Health and the Environment (RIVM) COVID-19 data archive.¹² Information on additional key events was obtained from open-access WHO situational reports. These data were combined in a timeline in combination with data from the publicly-available Oxford Coronavirus Government Response Tracker.¹³ The Stringency Index is a measure of the severity of a government's response to COVID-19, incorporating nine response metrics (school closures; workplace closures; cancellation of public events; restrictions on public gatherings; closures of public transport; stay-at-home requirements; public information campaigns; restrictions on internal movements; and international travel controls). A higher score indicates a more stringent response (where 100=the strictest response possible).

Passenger test data

Testing of passengers arriving on the two KLM flights on 26 November 2021 was conducted by the Municipal Public Health Service of Kennemerland (GGD Kennemerland). Nasopharyngeal swabs were collected from all passengers on the two KLM flights on 26 November 2021, and molecular testing for SARS-CoV-2 was performed. Samples were first analysed at the Regional Public Health Laboratory (Streeklaboratorium) Haarlem and then re-tested at the RIVM reference laboratory. For the purpose of this study, fully anonymised test and sequencing results were obtained, as well as passengers' immune status (defined at that time by the government as valid proof of vaccination and/or recent recovery from COVID-19¹⁴) from the Municipal Public Health Service of Kennemerland. The confirmed number of individuals with Omicron infection arriving on 26 November 2021 was used to approximate the number of directly imported cases in our model and the range of values tested in sensitivity analyses. This range of values aimed to incorporate the uncertainty around the approximate number of directly imported

cases, recognising that some passengers testing positive were in transit and did not have Amsterdam as their final destination (thus not contributing to domestic transmission), while others may have tested negative but have been exposed on the flight or while waiting to be tested at the airport.

Model parameters: definitions and data sources

The travel ban was defined as a halt in all direct flights from South Africa to the Netherlands from 26 November 2021 onwards. Travel bans for other Southern African countries (Botswana, Lesotho, Mozambique, Namibia, Eswatini, Zimbabwe) were not included in our analyses as no direct flights to Amsterdam Schiphol Airport existed in 2021. An Omicron case was considered to be an individual infected with the Omicron SARS-CoV-2 subvariant with potential for transmission to others.

The John Hopkins 2019 Novel Coronavirus Visual Dashboard data repository and Global Initiative on Sharing All Influenza Data were used to represent the epidemiological situation of Omicron VoC in South Africa (see online supplemental figure S1). These data were used to estimate the number of imported cases avoided by the travel ban as well as the number of cases that were likely to have already been imported into the Netherlands prior to 26 November 2021, using the passenger test data from 26 November 2021 as a benchmark.

We included a 'leakage rate' in our model to reflect ongoing importation of Omicron cases despite the travel ban. The leakage rate was defined as the sum of the ongoing importation of Omicron cases via indirect routes and onward domestic transmission as a result of incoming infected Dutch citizens not adhering to quarantine advice (coined the 'failure rate' for the purpose of this study and defined, based on expert opinion from the local municipal health services, as 2%). For the rate of indirect importation, we used Amsterdam Schiphol Airport flight data.¹⁵ First, the mean proportion of all incoming passengers from January to October 2021 transiting via other airports was taken as a baseline. Next, the proportion of indirectly incoming passengers arriving via a European or Schengen area airport (Frankfurt Airport (FRA), London Heathrow Airport (LHR) or Paris Charles de Gaulle Airport (CDG)) in November 2021 was calculated. These proportions were multiplied, providing a best estimate of 10% for the proportion of incoming passengers who continued to arrive via European transit hubs from South Africa throughout the duration of the travel ban. For the 'failure rate', representing directly incoming passengers who were not blocked by the travel ban and contributed to secondary cases, stakeholder input from the Municipal Health Service of Kennemerland was used to estimate that for 2% of incoming passengers, either pre-departure testing did not detect all infections or the individuals failed to adhere to isolation measures within or outside of the household. Thus, the total 'leakage rate' in our main model was 12%. The reproduction number (R_e) of 1.3 was chosen for our main model as the estimated value

in mid-January 2022,¹⁶ when Omicron was the dominant VoC in the Netherlands, given that the value in November 2021 represented the spread of Delta VoC. The R_e value was based on epidemiological data from the whole Dutch population, thus taking into account transmission events and population immunity through vaccination. Taken together, these data sources and stakeholder input allowed our model to represent the specific situation of the Dutch travel ban on subsequent Omicron infections.

Model outcomes, structure and scenarios

The primary outcome in our model was the number of elapsed days from 26 November 2021 to 10 000 cumulative Omicron cases in the Netherlands. We chose a number of days as our primary end point to reflect the desired impact of travel bans on 'buying time' to prepare for an outbreak. Moreover, the threshold value of 10 000 cumulative cases was chosen to reflect the initial 6-week following initiation of the travel ban, when any effect would be most prominent; after this period, outbreak dynamics was expected to be largely influenced by the R_e of the pathogen as demonstrated in previous literature.^{17 18}

A generation interval model was created to estimate the impact of the travel ban on our primary outcome. Details of the model are presented in Supplementary Materials (online supplemental methodology figures SM1–SM5). Briefly, the model simulated the cumulative incidence of the Omicron variant within the Dutch population over 6 weeks after 26 November 2021. The Omicron variant was modelled to be gradually imported into the Netherlands at a rate proportional to the estimated daily prevalence in South Africa, spreading further within the Netherlands as defined by the chosen R_e for the model. Therefore, the sampling frame of passengers travelling to Amsterdam from South Africa was assumed to be the same across the modelled time period as on 26th November 2021. Mechanistically, the model transmits the Omicron variant across a homogeneous susceptible population at an initial rate of R_e , without accounting for Delta-Omicron competition. Because we only look at the period 6 weeks after the 26 of November, this is a realistic assumption because people in general are protected for at least 9 months after infection.¹⁹ To explore the effect of the timing of the travel ban, scenarios were defined in which the travel ban was implemented up to 2 days prior to 26 November (when Omicron was first notified to the WHO) and up to 14 days later (ie, if additional time had been taken to review the evidence or consult the OMT).

The relative contribution of the uncertainty around the parameters chosen in our main model was explored in subsequent analyses by considering several alternative plausible scenarios. First, alternative proportions of indirectly-imported cases were considered, namely 0% (ie, in the case of a travel ban spanning the European Union (EU)/Schengen Area, also blocking all passengers transferring via European transit hubs) and 20% (ie, approximate baseline rate of indirectly incoming

flights from South Africa prior to the travel ban). Second, we considered scenarios of both lower (ie, more stringent public health measures and/or higher vaccination coverage) and higher (ie, less stringent public health measures and/or lower vaccination coverage) values of R_c , although maintaining an $R_c > 1.0$. Finally, we explored the impact of different values of directly imported cases on 26 November to scale the model, ranging from 5 (ie, to incorporate the possibility that positive cases were in transit to another destination and therefore did not contribute to domestic transmission and/or that some positive PCR tests did not detect viable, infectious virus) to 30 (ie, to reflect possible in flight and airport transmission between passengers and possible under-detection of cases).

Patient and public involvement

Members of the public were not directly involved in the design or conduct of this study. However, a wide range of stakeholders who directly observed or coordinated the practical implementation of the travel restrictions and testing policy (including representatives from the Municipal Health Service of Kennemerland, the KLM Health Services and Amsterdam Airport Schiphol) were essential to the design, conduct and reporting of the research, and helped reflect on the public's perspective of the study context.

RESULTS

Epidemiological context and timeline of events prior to 26 November 2021

In early November, numerous public health regulations were re-introduced in the Netherlands due to increased incidence and hospital admission resulting from Delta VoC. As a result, the 2021 booster COVID-19 vaccination campaign, originally scheduled to start on 6 December 2021, was brought forward to start on 19 November (online supplemental figure S1). On 26 November, the number of ICU beds occupied by COVID-19 patients was 605/1016. The COVID-19 policy for entry into the Netherlands at the time of departure was that all incoming passengers needed to have at least one of: (i) an official negative test result (by PCR within 48 hours of departure, or rapid antigen test within 24 hours of departure), (ii) a recovery certification from an EU/Schengen country or (iii) a valid vaccination certificate (17). Fully vaccinated passengers on the two KLM flights with valid proof of vaccination were therefore exempt from predeparture testing, on the assumption that COVID-19 vaccination protected sufficiently against Omicron infection. All passengers arriving on the two direct flights from Johannesburg and Cape Town, South Africa, to Amsterdam Airport Schiphol on 26 November (including those in transit to other destinations and previously vaccinated individuals) were tested on arrival (the results of which are presented in online supplemental figure S2). Between January and October 2021, a median of 2626 (IQR: 2267–2856)

passengers arrived every month on direct flights from South Africa to Amsterdam Airport Schiphol¹⁵ and a median of 483 (IQR: 433–661; approximately 20% the volume of directly incoming passengers) travelled from South Africa to Amsterdam via indirect routes (transiting via other airports, in order of highest to lowest volume: LHR, CDG, Doha, FRA, Dubai and Istanbul, with approximately half of indirectly-incoming passengers transiting via a European hub).¹⁵

Passenger test data

Summary statistics of the PCR test data from passengers arriving on the two KLM flights on 26 November 2021 are presented in online supplemental figure S2. In total, 61/624 samples (10%) were positive for SARS-CoV-2; a minority of these individuals reported symptoms at the time of testing (9/61; 15%). On re-testing of the same samples at the RIVM reference laboratory, 22/61 samples remained positive, of which 16 were sequenceable, with 14/16 demonstrating mutations in keeping with Omicron infection. Given these findings, we used an approximate direct importation rate of 15 Omicron infections on 26 November 2021 in our model.

Impact of imposed travel ban

Without the travel ban but with the public health restrictions already in place in November 2021, our model estimated that it would have taken 22 days from 26 November 2021 to reach 10 000 cumulative Omicron infections in the Netherlands. Our model estimated that the travel ban achieved a 14-day delay in reaching 10 000 Omicron infections in the Netherlands, compared with no travel ban at all (ie, 36 days from 26th November instead of 22 days with no travel ban). The model also indicated that, if the travel ban had been initiated 1 day earlier, no further delay would have been achieved (figure 1), but that implementing the travel ban 2 days earlier (on 24 November, when South Africa first notified the WHO of Omicron detection) would have gained one additional day of delay (ie, 15-day delay; 37 days to reach cumulative 10 000 infections). Initiating the travel ban 7 days later than 26 November 2021 (on 3 December 2021) halved the delay gained by the travel ban (ie, 29 days to 10 000 infections; 7-day delay compared with no travel ban).

Modelling of alternative scenarios

In order to use the model to illustrate alternative plausible scenarios and assess the impact of uncertainty around the model parameters, the reproduction number (R_c) in the Dutch population and the volume of indirectly imported cases (ie, not affected by the travel ban) were varied within a range of plausible values. These analyses demonstrated that R_c was the most influential parameter on days to reaching 10 000 Omicron infections (figure 2): when defining R_c as 2.0 or greater, the effect of importation and timing of the travel ban was negligible. At lower R_c values, the travel ban's impact was accentuated, with the greatest impact observed early on in the outbreak (non-linear

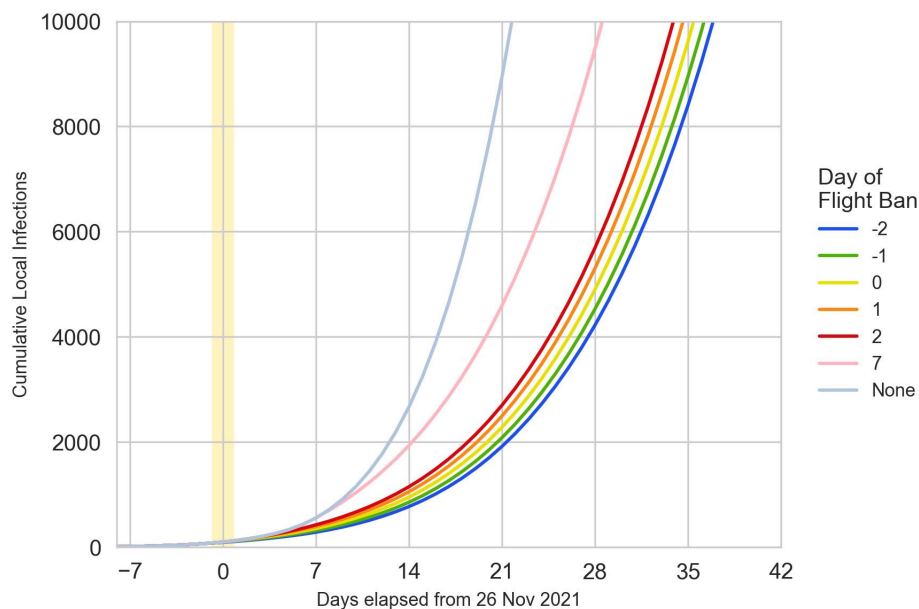


Figure 1 Model assumes an R_E of 1.3; direct importation scaling of 15 on 26 November 2021; indirect importation rate of 10%; and a ‘failure rate’ of travel ban on directly imported infections of 2%. Day of travel ban denotes the day of implementation of the travel ban, relative to 26 November 2021 (day 0).

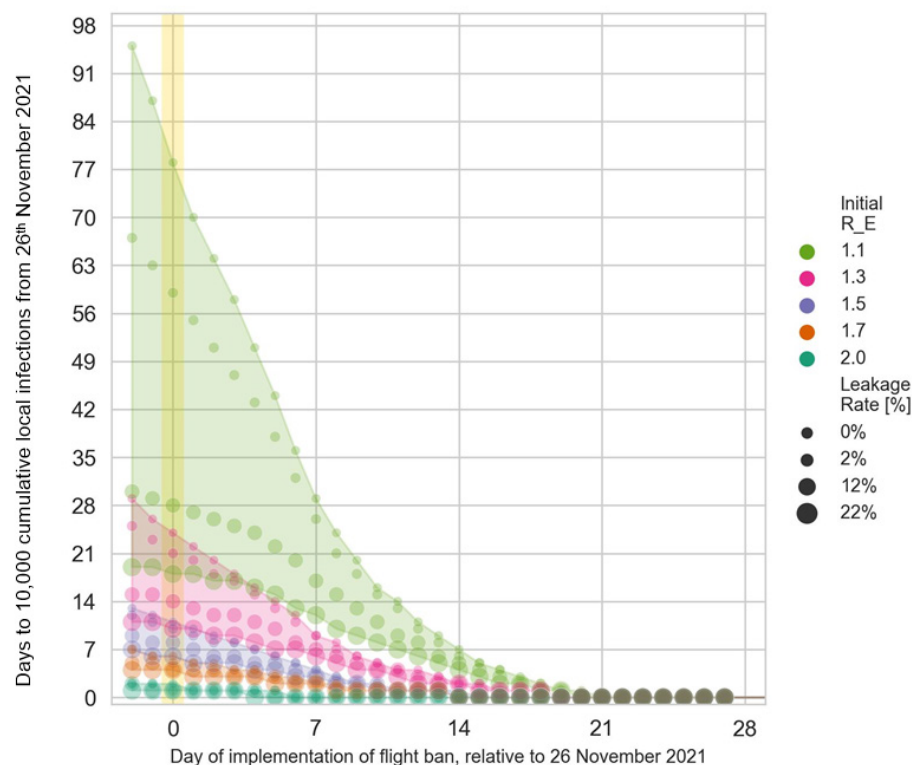


Figure 2 Model uses a direct importation rate of 15 Omicron infections on 26 November 2021 and is scaled over time to the epidemiology of the South Africa Omicron outbreak, assuming the sampling frame of passengers travelling to Amsterdam remained the same. The leakage rate (%) represents the sum of (i) the percentage of importations via an indirect route, therefore not affected by the travel ban, and (ii) the failure rate of the travel ban on directly imported infections, consistently defined as 2%. As such, the scenarios explored are: 0%, no indirect or direct importation; 2%, no indirect importation with a 2% failure rate; 12% and 10% indirect importation with a 2% failure rate (parameters of ‘base scenario’); 22% and 20% indirect importation with a 2% failure rate.

relationship) (figure 2). At an R_e value of 1.1, if the travel ban were to have been initiated on 26 November 2021, days to 10 000 cumulative Omicron infections was modelled to be 105 days if no direct or indirect importation took place, 86 days with no indirect importation but with a 2% failure rate and 55 days with 10% indirect importation with a 2% failure rate.

When assuming all indirect importation was prevented (eg, in a scenario of a European-wide travel ban) but a 2% failure rate persisted and with an R_e of 1.3, a delay of 3 weeks (21-day delay) was achieved, with an additional 3 days (24-day delay) if no failure existed. On the other hand, if indirect importation continued at pre-travel ban rates (ie, if flights via Dubai, Doha and Istanbul continued to arrive), the delay achieved in reaching 10 000 cumulative Omicron infections was reduced to 10 days (figure 2).

Finally, we considered alternative values for the number of directly imported cases on 26 November (Supplementary Figure SM4), recognising that the number of positive PCR tests among passengers on 26 November may have both under- and overestimated the true number of direct importations. When keeping all other parameters constant, a lower number of directly imported cases would have resulted in an under-estimation of the impact of the travel ban (eg, directly imported cases=5: delay=18 days, ie, +4 days compared with base scenario), while a higher number of directly imported cases would have resulted in an over-estimation of the impact of the travel ban (eg, directly imported cases=30: delay=11 days, ie, -3 days compared with base scenario) (Supplementary Figure SM4).

DISCUSSION

This study aimed to retrospectively evaluate the impact of the travel ban initiated by the Dutch government on 26 November 2021 on flights from South Africa and consider alternative scenarios in order to help guide future decision-making. Our analysis incorporated best estimates of real-world epidemiological parameters in order to reflect the uncertainties present at the time of decision-making in this specific scenario. It was estimated that the Dutch travel ban may have resulted in a 2-week delay in reaching 10 000 Omicron infections in the Netherlands compared with no travel ban. Minor additional benefit was gained by initiating the travel ban earlier (ie, prior to Omicron being declared a VoC) and delaying the initiation of the travel ban by 1 week halved the time gained to reach 10 000 cumulative Omicron infections. Additional analyses revealed that the R_e of Omicron, which is influenced by non-pharmaceutical interventions (NPIs), had far more influence on subsequent outbreak dynamics than the rate of either direct or indirect importation. This study therefore offers three key take-home messages. First, travel bans are most effective when initiated early in the course of an outbreak. In the case of a novel pathogen or subvariant, policy-makers may consider travel bans but should consider the extent of uncertainty around early

estimates of key epidemiological characteristics that may influence a travel ban's effect. Second, with lower R_e rates, the additional time gained by delaying importation may not offer additional benefit for preparations, especially if the pathogen is not particularly virulent. Finally, and perhaps most importantly in relation to Omicron VoC, which was more transmissible than previous SARS-CoV-2 subvariants, our analyses imply that when importation of a respiratory pathogen is likely to be inevitable or known to have already occurred, implementing public health and social measures to reduce the national R_e is more important than introducing international travel restrictions. In these situations, travel bans may only result at most in a modest delay of the outbreak's peak and often (based on previous evidence) result in negative socio-economic consequences that bring the proportionality of such measures into question, especially in light of IHR recommendations. It is crucial that WHO member states consider these observations, echoed by numerous other studies, when forging a well-informed and equitable international treaty to face future pandemics.

Travel-related public health measures may offer valuable time required to strengthen the capacity of healthcare services, initiate vaccination campaigns, increase stocks of medical equipment and devices and/or initiate clear and transparent communication with the public. However, it has been suggested that these measures, at most, delayed the inevitable importation of SARS-CoV-2 and were most effective in isolated nations (eg, island states¹⁷) at the very beginning or end of a specific outbreak.²⁰ At the beginning of the COVID-19 pandemic, strict travel restrictions in and out of Wuhan (a traditional 'cordon sanitaire', introduced on 23 January 2020)²⁰ aimed to contain SARS-CoV-2 transmission, preventing further spread within China and internationally. Modelling studies suggest that these severe measures had only a modest impact on epidemic progression, especially within China, and that NPIs to reduce the R_e (such as social distancing, early detection, hygiene and individual isolation/quarantine)²¹ were far more important in mitigating the pandemic. Similar conclusions have been made regarding early travel bans throughout the Southeast Asian continent.²² Despite these observations, travel restrictions were once again implemented as a public health intervention in the face of Omicron VoC. Our modelling study suggests a similar conclusion to previous analyses of travel restrictions at the beginning of the pandemic: namely, that while travel bans may result in a modest delay in calendar timing of a subsequent COVID-19 outbreak, other measures to reduce R_e had a greater impact on subsequent outbreak dynamics. This conclusion is echoed by numerous other studies,^{18 23–25} with one analysis suggesting that a short quarantine period with testing may often be as effective at limiting pathogen importation as complete travel bans.²⁶

It is important to note that the above conclusions are based on parameters specific to SARS-CoV-2 and are conditional on the fact that SARS-CoV-2 can result in pre- or asymptomatic transmission in a substantial proportion

of individuals, meaning that travel restrictions are often implemented once community transmission has already been established.^{20–22} Indeed, retrospective analyses of phylogenetic data demonstrated that all four VoCs prior to Omicron (Alpha, Beta, Gamma and Delta) had been introduced into the Netherlands prior to the initiations of any travel restrictions.²⁷ In addition, it later became apparent that vaccination was not effective at preventing against Omicron transmission, and therefore exempting vaccinated travellers from pre-departure testing is likely to have led to the importation of Omicron to the Netherlands several days prior to implementing the travel ban.²⁸ Taken together, our findings support the existing wider literature²⁹ that, for the mitigation of SARS-CoV-2 transmission and especially for a highly transmissible VoC such as Omicron, travel bans are consistently less effective than early detection in combination with rigorous source- and contact tracing and isolation/quarantine measures and are not appropriate in a context in which importation cannot fully be prevented.

This study did not set out to evaluate the impact of the travel ban on socio-economic, political or ethical outcomes. However, it is important to highlight the existing literature on adverse consequences of travel bans in order to help weigh expected costs and benefits of travel bans. Indeed, all public health and social measures may introduce infringement on human rights, present dilemmas pertaining to equity or have damaging socio-economic outcomes resulting from political and economic seclusion of the countries affected. The travel ban on Southern African countries had an adverse impact on the tourist industry, representing a major loss of revenue.³⁰ Inadvertently, these consequences may discourage countries from being transparent in their communication of new SARS-CoV-2 subvariants or other novel pathogens in the future, hindering timely action and undermining global health security. Ultimately, this counteracts the overall goals of the IHR, as adverse effects of travel restrictions may discourage countries from notifying the WHO of a new communicable disease outbreak, potentially delaying early appropriate actions. This raises concerns about whether the travel bans implemented during the COVID-19 pandemic represented the path with the least infringement³¹ as stipulated by the IHR.² It is therefore of vital importance that the potential benefits of international travel bans for mitigation of SARS-CoV-2 are carefully weighed up against their known negative consequences.

As we look forward from the COVID-19 pandemic and reflect on the 'lessons learnt', we argue that a comprehensive evaluation of the benefits and drawbacks of international travel restrictions is required. We suggest that such an evaluation should aim to stipulate the exact conditions (eg, the type of regulation, its optimal timing of implementation, existing pressures on healthcare and other epidemiological features of the pathogen in question) in which travel restrictions could be used effectively in the future and what steps must be taken to mitigate

their negative consequences. For instance, more severe measures may be proportional in the case of a more virulent pathogen with a higher hospitalisation and mortality rate than infection with Omicron SARS-CoV-2. In addition, a critical approach is required when suggesting suitable laboratory and/or clinical screening methods at border control, to optimise sensitivity and specificity for infectious cases to reduce unnecessary burden on passengers but also optimise for infection control. Incorporating such considerations and recommendations in the WHO's new pandemic treaty will help ensure future cross-border public health measures are implemented in a proportional manner, without undermining global health equity.

This study has several main strengths. First, real-world parameters were used in the model in order to closely reflect the situation in South Africa and the Netherlands at the time of the travel ban. Moreover, this study was a collaborative project involving key stakeholders, which helped to incorporate different data in the evaluation of the Dutch travel ban. However, our analyses also have limitations. First, we lacked empirical data on the number of individuals with Omicron infection arriving from South Africa in the days prior to the implementation of the travel ban, both from direct and indirect routes. As such, there are likely errors within the estimation of imported Omicron cases, the proportion of cases from direct and indirect entry and the chosen 'failure rate'. Most notably, the assumption of the importation being proportional to the prevalence in South Africa becomes less valid after the WHO announcement of Omicron as a VOC, as more stringent measures, such as pre-departure testing, were implemented, also for vaccinated passengers. Our estimate of 15 directly imported cases on 26 November may also be a conservative estimate, given that transmission may have occurred on the flight itself or when waiting to be tested on arrival. This suggests the impact of the travel ban may have been less than estimated in our model. On the other hand, some passengers who tested positive on 26 November may have been in transit to other destinations and therefore unlikely to have contributed to domestic transmission. As such, the estimate of 15 encompasses the possibility of both under- and over-estimation. However, this uncertainty is unlikely to substantially influence our conclusions as our sensitivity analysis demonstrated that the value of directly imported cases chosen for scaling the model had less influence than the R_e , the leakage rate and the timing of the travel ban. Another limitation is that we did not include parameters of pre-existing immunity and competing transmission with other variants (ie, Delta) in our model. This may have resulted in an underestimation of the absolute number of days to 10 000 cumulative Omicron infections; however, it would not have introduced bias. As such, the model was fit for purpose for studying the effect of the travel ban and comparing its efficacy over different scenarios of indirect importation and R_e values. Finally, the analyses focus on a respiratory pathogen with demonstrated transmissibility

during pre- or asymptomatic infection. The current analyses therefore lack external validity to pathogens with other routes of transmission, clinical presentation, virulence and pharmaceutical counter-measures.

Conclusions

This modelling study suggests that the travel ban implemented by the Dutch government on 26 November 2021 resulted in a modest delay in the calendar timing of the outbreak of the Omicron VoC. However, given that the importation of Omicron pre-dated the initiation of travel restrictions, we found that measures to reduce the R_e of the virus played a more important role in influencing its initial spread. Whether the estimated delay achieved was necessary and proportional given the negative consequences of the travel ban on the countries affected and the lower virulence of Omicron compared with Delta VoC should be studied further, as we reflect on the ‘lessons learnt’ from the pandemic and WHO member states aim to forge an international pandemic agreement.³² Generating an integrated rapid decision support tool or framework for adopting international travel restrictions in the face of incomplete and uncertain data (including epidemiological, social, economic and political factors) may help policy-makers weigh up risks and benefits in the future.

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