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Same-day SARS-CoV-2 antigen test screening in an indoor mass-gathering live music event: a randomised controlled trial

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Summary

Background The banning of mass-gathering indoor events to prevent SARS-CoV-2 spread has had an important effect on local economies. Despite growing evidence on the suitability of antigen-detecting rapid diagnostic tests (Ag-RDT) for mass screening at the event entry, this strategy has not been assessed under controlled conditions. We aimed to assess the effectiveness of a prevention strategy during a live indoor concert.

Methods We designed a randomised controlled open-label trial to assess the effectiveness of a comprehensive preventive intervention for a mass-gathering indoor event (a live concert) based on systematic same-day screening of attendees with Ag-RDTs, use of facial masks, and adequate air ventilation. The event took place in the Sala Apolo, Barcelona, Spain. Adults aged 18–59 years with a negative result in an Ag-RDT from a nasopharyngeal swab collected immediately before entering the event were randomised 1:1 (block randomisation stratified by age and gender) to either attend the indoor event for 5 hours or go home. Nasopharyngeal specimens used for Ag-RDT screening were analysed by real-time reverse-transcriptase PCR (RT-PCR) and cell culture (Vero E6 cells). 8 days after the event, a nasopharyngeal swab was collected and analysed by Ag-RDT, RT-PCR, and a transcription-mediated amplification test (TMA). The primary outcome was the difference in incidence of RT-PCR-confirmed SARS-CoV-2 infection at 8 days between the control and the intervention groups, assessed in all participants who were randomly assigned, attended the event, and had a valid result for the SARS-CoV-2 test done at follow-up. The trial is registered at ClinicalTrials.gov, NCT04668625.

Findings Participant enrollment took place during the morning of the day of the concert, Dec 12, 2020. Of the 1140 people who responded to the call and were deemed eligible, 1047 were randomly assigned to either enter the music event (experimental group) or continue with normal life (control group). Of the 523 randomly assigned to the experimental group, 465 were included in the analysis of the primary outcome (51 did not enter the event and eight did not take part in the follow-up assessment), and of the 524 randomly assigned to the control group, 495 were included in the final analysis (29 did not take part in the follow-up). At baseline, 15 (3%) of 495 individuals in the control group and 13 (3%) of 465 in the experimental group tested positive on TMA despite a negative Ag-RDT result. The RT-PCR test was positive in one case in each group and cell viral culture was negative in all cases. 8 days after the event, two (<1%) individuals in the control arm had a positive Ag-RDT and PCR result, whereas no Ag-RDT nor RT-PCR positive results were found in the intervention arm. The Bayesian estimate for the incidence between the experimental and control groups was –0·15% (95% CI –0·72 to 0·44).

Interpretation Our study provides preliminary evidence on the safety of indoor mass-gathering events during a COVID-19 outbreak under a comprehensive preventive intervention. The data could help restart cultural activities halted during COVID-19, which might have important sociocultural and economic implications.

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Introduction

Mass-gathering events are associated with a high risk of spreading SARS-CoV-2.[1,2] Cultural activities such as sporting events, indoor gatherings, plays, or concerts have been identified as the most high-risk venues for SARS-CoV-2 transmission.[3] Health-care authorities have correspondingly reduced the capacity of the venues to prevent close contact between unknown attendees or have cancelled all events, despite the lack of scientific evidence for such increased risk.

Of all mass-gathering events banned during the COVID-19 pandemic, the closure of concert halls has had a remarkable impact on local economies. In 2019, music festivals had an estimated revenue of more than €5·5 billion in Spain and €2·5 billion in Catalonia. The cancellation and deferment of these events in 2020 resulted in substantial economic losses, and restrictions on their celebration or capacity remain in force in 2021.

One of the key factors that challenges the control of SARS-CoV-2 transmission in mass-gathering events is the

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For more on the **#YoMeCorono Initiative** see https://www.yomecorono.com/

Research in context

Evidence before this study

On March 30, 2021, we searched PubMed for articles published in English using the terms "mass-gathering event" and "COVID-19". The search returned 31 results, most of them corresponding to articles that either described mitigation plans or reported retrospective analyses of SARS-CoV-2 spread during mass-gathering events. None of the articles found reported the results of a controlled experiment in which preventive measures were used to create a safe environment during a mass-gathering event.

Added value of this study

To our knowledge, this is the first randomised clinical trial that assesses the risk of COVID-19 transmission in an indoor mass-gathering live concert done under comprehensive safety measures, including same-day SARS-CoV-2 screening with antigen-detecting rapid diagnostic tests (Ag-RDTs), compulsory N95 face mask wearing, and optimised air ventilation. Participants could sing and dance in the concert hall room, and no physical distancing was recommended. None of the 465 participants became infected, compared with two out of 495 in the control arm.

Implications of all the available evidence

Our study provides preliminary evidence on the effectiveness of same-day point-of-care screening with Ag-RDT, combined with face mask-wearing and active air ventilation, to create safe indoor environments with no need for physical distancing measures. Future studies with a larger capacity of attendees and assistants, and done during periods of increased transmission of COVID-19 are warranted.

difficulty in identifying individuals who can transmit the virus because they are infected with a high viral load, particularly asymptomatic or pre-symptomatic people with a high viral load.[4] SARS-CoV-2 transmissibility begins 2 to 3 days before symptom onset, and nearly half of the transmissions occur from asymptomatic individuals.[5]

The long turnaround time required for nucleic-acid amplification tests (NAATs)—including the gold standard real-time reverse transcriptase-PCR (RT-PCR)—for identifying SARS-CoV-2 in respiratory specimens creates difficulties in implementing mass testing strategies on the same day of the event. Alternatively, antigen-detecting rapid diagnostic tests (Ag-RDTs) have been proposed as suitable tools for point-of-care screening of individuals infected with SARS-CoV-2. The main advantages of Ag-RDTs include low price, absence of need for high-tech laboratory referral, and a short turnaround time to provide a result. Despite the overall lower sensitivity of Ag-RDTs than NAAT, a growing body of evidence indicates that they are suitable for identifying individuals who could potentially transmit the virus.[6–8]

Current evidence on Ag-RDT performance suggests that a point-of-care screening of contagious individuals, together with containment measures, such as the use of adequate facial masks and optimised ventilation, can create safe environments for mass-gathering events with low risk of SARS-CoV-2 spread. However, this approach has not been tested under controlled conditions. We did a randomised controlled trial to assess the effectiveness of a prevention strategy during a live indoor concert, under the hypothesis that same-day point-of-care screening of infected individuals and regular preventive measures would prevent an increased risk of SARS-CoV-2 transmission during the event.

Methods

Study design and participants

We did an open-label, randomised (1:1) clinical trial to assess the effectiveness of a comprehensive intervention to prevent SARS-CoV-2 spread during an indoor live concert (appendix 2 p 2). The study took place in the Sala Apolo, a concert venue in Barcelona, Spain. Study participants were recruited from a list of subscribers to news related to live music events; a call for enrolling in the study was done through non-official media, including WhatsApp, Telegram, and email. Eligible participants were adults aged 18–59 years with a negative result in an Ag-RDT from a nasopharyngeal swab collected in the morning of the day of the event (from about 12 h before the event began). Participants with known COVID-19 diagnosis within the 14 days before the event, relevant comorbidities (including hypertension, diabetes, or any type of cancer), or living with older people were excluded (appendix 2 p 3). The study protocol was approved by the Ethics and Clinical Research Committee of the Hospital Universitari Germans Trias in Badalona, Spain. All participants signed informed consent electronically, including the acceptance of not entering the event if allocated in the control arm. The study was done according to the Declaration of Helsinki and local legislation.

See Online for appendix 2

Randomisation and masking

Study participants with a negative result from Ag-RDT nasopharyngeal swab testing were randomly assigned (1:1) to either enter the indoor live event (experimental group) or not enter the event and return to normal life (control group). The computer-generated block randomisation (REDCap module) was stratified by age, gender, and previous COVID-19 episode reported in the questionnaire. Participants allocated to the experimental group also returned to normal life after the event. By the time of study conduct, mobility was constrained to the municipality, and indoor meetings of more than six people were banned. Face mask use was mandatory indoors and outdoors, except in the outdoor controlled smoking area.

The team of nurses that did the mass screening also did the computer-generated block randomisation using the REDCap module and sent the results of the allocation through the app installed on all participant smartphones. They had no further role in the trial.

This was an open-label study in which both participants and investigators knew to which groups participants had been randomly assigned.

Procedures

Before starting the music event, the health-care staff (45 nurses and one physician) collected nasopharyngeal swabs from all eligible participants in a screening structure set up outdoors in front of the concert venue, with 24 awnings. The mass screening started at 8:00 am and finished at 3:30 pm on the day the music event took place (Dec 12, 2020). The same nasopharyngeal specimen was used for in situ Ag-RDT (Panbio COVID-19 Ag Rapid Test, Abbott) and a transcription-mediated amplification test (TMA, Procleix Panther, Grifols). The result was reported after 15 min through the app installed in the smartphone of every participant. This immediate reporting of results allowed randomisation of individuals who could attend the live music event in the afternoon. The TMA result was reported 24–48 h after ending the event. All TMA-positive samples were re-tested by RT-PCR. The day after releasing the result, a study physician contacted all individuals with a positive TMA result by phone and screened their medical records to identify the exact date of a previous positive SARS-CoV-2 diagnostic test. All swabs with positive TMA results were assessed for viral isolation on cell culture.

All study participants were visited 8 days after the event for nasopharyngeal swab collection and TMA test (follow-up day 8 test). According to current evidence on SARS-CoV-2 kinetics, an assessment done on day 8 maximizes the likelihood of capturing infections caused during the live event.[5,9,10]

All participants installed two smartphone applications (apps). The Radar Covid application (a contact tracing app) was intended to capture close contacts of participants potentially infected during the concert. The Test-Wallet app was used to confidentially report the study test results (ie, Ag-RDT, TMA, and PCR) and fill in a health questionnaire before and 10 days after the event, and a satisfaction questionnaire for those attending the concert (appendix 2 pp 4–5). Data generated by the Test-Wallet app were encrypted using SHA-1 encryption and with 256-bit SSL security certificate. All SARS-CoV-2 positive results were reported into the public health electronic system and triggered quarantining measures and contact tracing studies.

Forehead body temperature was monitored at the entrance of the screening site and concert venue, where all participants received an N95 mask. Mask wearing was mandatory during the entire event. No physical distancing was required in the concert room (with a capacity of 900 people); singing and dancing were permitted. A smoking area was set up outdoors; the area had 20 people capacity and strict control of crowding and physical distancing. Masks could be removed in the outdoor smoking area due to physical distancing controlled by a security crew.

Drinks, including alcoholic beverages, were served only in the bar zone, located in an extra room with a capacity for 1600 people. Participants were asked to remove their face mask only when drinking. Movement within the venue was signposted, some sites of the venue were closed, and the direction of movement was controlled by the security crew that controlled any queue formation. Securities personnel oversaw all movements and acted, if necessary, to prevent queues in and around the venue foyer and toilets. Hydroalcoholic hand sanitizer gel was provided at multiple points in the venue.

The temperature of the dancing room and bar were maintained between 19·3 and 20·4 ºC during the event to facilitate wearing the mask and coats (the cloakroom was closed to avoid queues in front of it). Average carbon dioxide (CO_2) measurements before starting the event were 440 ppm in the dancing hall and 417 ppm in the bar room, both similar to those typically obtained in open air in the city. Public health safety guidance in force by the time of the event recommended not exceeding 800–1000 ppm during the event.[11]

The total surface area of the venue was 1024 m², which included 228 m² for the dancing hall, 381 m² for the bar hall, and 157 m² in the lobby. There were no exterior windows in the two respective halls; however, all access and exit doors remained open during the event, allowing additional fresh air from the inner courtyard.

The event, held in the Sala Apolo (Barcelona, Spain) on December 12, 2020, lasted for 5 h and included four performances: two DJ sessions and two live music acts. Besides the study participants and artists, 58 staff members (organizers, security, sound, light technicians, and bartenders) were inside the venue during the event. All of them were tested for SARS-CoV-2 using Ag-RDT at the same time points as the study participants.

Nasopharyngeal specimens were collected with flocked swabs in a viral universal transport medium (Deltalab SL, Barcelona, Spain). Samples were received at the laboratory and were processed immediately, inactivated, and analysed by TMA. All TMA-positive results were confirmed by RT-PCR assay to determine the cycle threshold (Ct) values (AllplexTM SARS-CoV-2, Seegene) using the software designed by the company. Leftover positives samples were conserved at –80°C.

Nasopharyngeal specimens with positive SARS-CoV-2 TMA results that had tested negative with Ag-RDT were analysed for viral isolation on cell culture. Vero E6 cells (ATCC CRL-1586) were cultured in Dulbecco's modified Eagle medium (DMEM) supplemented with 10% heat-inactivated fetal bovine serum (FBS), 100 U/mL penicillin, and 100 µg/mL streptomycin (Invitrogen). Two individuals with negative SARS-CoV-2 RT-PCR, and two viral stocks

For more on **R software** see https://www.gbif.org/tool/81287/r-a-language-and-environment-for-statistical-computing

previously isolated were cultured in triplicates as negative controls as previously described.[12] DMEM supplemented with FBS and penicillin/streptomycin were supplied to cells and inspected every 2 days for cytopathic effects. On day 7, cell supernatants were assayed with a high-sensitivity quantitative ELISA for SARS-CoV-2 nucleocapsid protein (ImmunoDiagnostics).

Outcomes

The primary outcome was to evaluate the risk of transmission of SARS-CoV-2 in a mass-gathering indoor music event with the implementation of safety strategies to reduce the spread of COVID-19. The primary efficacy endpoint was the difference in the incidence of RT-PCR-confirmed SARS-CoV-2 infection at 8 days between the control and the intervention groups. The primary outcome was assessed in the full analysis set, which included all participants who were randomly assigned, attended the event (in the experimental arm), and had a valid result for the SARS-CoV-2 test done on day 8.

Statistical analysis

We used a Bayesian beta-binomial model to analyse the number of infected cases in each group. This approach allows previous information to be included, which is useful when estimating the probability of rare events.[13,14]

The 7-day cumulative incidence observed in the city of Barcelona when the follow-up RT-PCR was done on day 8 after the live music event was about 1·3 cases per 1000 people, according to official data.[11] Considering this incidence, we estimated the ideal number of participants to be 1000 per study arm. However, this value underestimates the true rates due to the difficulty in recording asymptomatic cases. The study population had some exclusion and inclusion criteria that could influence this value. For the control group, the prior distribution chosen was a Beta (1·1, 400), with a median of 0·002, and the probability of values greater than 0·01 is approximately 2%. Uncertainty about the probability of infection among the experimental group was higher, and a Beta (1, 28·4) was chosen, with a probability of obtaining values greater than 0·1 around 5% as a prior distribution. For each group, the posterior median and the highest posterior density interval were calculated. Additionally, to compare the probabilities of infection between groups, the difference in their probabilities and its credible interval (CI) were calculated.

The negative predictive value of the Ag-RDT was estimated, taking as reference tests the RT-PCR and cell culture and using the Bayesian Markov Chain Monte Carlo (MCMC) method as proposed by Gelman and colleagues.[15] For the prevalence, a Beta (1·1, 400) was chosen again as a prior distribution, and the sensitivity and specificity are given with a non-informative Beta (1, 1) priors. The median and the highest posterior density CI were calculated for the negative predictive value.

The analyses were done with R and the Bayesian software JAGS.[16] The trial is registered at ClinicalTrials.gov, NCT04668625.

Role of the funding source

The study sponsor had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Participant enrolment and the live music event took place on Dec 12, 2020. A total of 1140 participants responded to the call released through social networks, were deemed eligible, and were invited to participate in the study. Of these, 93 individuals did not attend, and 1047 individuals turned out for the event and were screened for SARS-CoV-2 infection with Ag-RDT via a nasopharyngeal swab. All participants tested negative and were randomly assigned to either of the two trial arms (the experimental group to attend the music event, or the control group to not attend the event and continue with daily life). In the experimental group, 51 participants did not enter the live music event, and seven participants did not have a follow-up assessment, resulting in 465 participants with data assessed for the primary outcome. In the control group, 29 participants did not have a follow-up assessment, resulting in 495 participants with data assessed for the primary outcome (figure).

Participants included in the full analysis set had a mean age of 33·6 years (SD 8·6); 783 (82%) were men and 177 (18%) were women. Individuals in the intervention group spent a median of 2 h and 40 min inside the concert.

Of the 960 participants included in the full analysis set, all tested Ag-RDT negative in the baseline screening, and 28 (3%) had a positive TMA result (13 in the experimental group and 15 in the control arm). Of these 28, two (one in each arm) had a positive RT-PCR result (Ct 37 for both; table). The 14-day attack rate in Catalonia in the same calendar week (Dec 7–13, 2020) and population group was 220·7 cases per 100 000 inhabitants.[11] According to the interview by a physician and medical records review, all participants with positive TMA results had been previously diagnosed with COVID-19 within a median of 50 days (IQR 44–77) before the event. None of the 28 specimens with a positive TMA result showed a cytopathic effect on cell cultures, as measured with a quantitative ELISA 7 days post-inoculation. Conversely, control positive cultures showed evident cytopathic effect, and viral particles could be detected by ELISA.

None of the 465 participants in the experimental group became infected by SARS-CoV-2 (observed incidence 0%; estimated incidence 0·14%, 95% CI 0–0·61) versus two of 495 controls (0·31%, 0·04–0·73), as assessed by a positive RT-PCR test on day 8. The two participants in the control group with SARS-CoV-2 infection had positive Ag-RDT and RT-PCR (Ct values 26·3 and 28·3) results in

the follow-up assessment on day 8. Both had mild clinical disease and were reported to the health-care system. An epidemiological questionnaire and contact tracing were done. One of them had already been diagnosed 4 days after the randomisation had occurred. Except for the two individuals with positive RT-PCR and Ag-RDT tests, all individuals with a positive TMA result on day 8 had a history of a positive nasopharyngeal specimen (assessed either with TMA or RT-PCR) within the 52 days (IQR 45–81) before the event. The incidence difference, estimated using a Bayesian approach, did not reveal significant differences in incidence between the two groups. The Bayesian estimate for the incidence between the experimental and control groups was –0·15% (95% CI –0·72 to 0·44).

The negative predictive value of the Ag-RDT screening in this cohort of asymptomatic individuals was 99·9% (95% CI 99·5–100) for a positive RT-PCR, and 99·8% (99·3–100) for a positive viral culture.

The air concentration of CO_2 did not exceed the recommended threshold of 800 ppm at any time point during the event.[17] The number of complete air exchanges per h in the two rooms ranged from 11 to 13.

The median score of the questionnaire assessing satisfaction and enjoyment during the event, rated on a ten-point scale, was 8·63 (IQR 6–10). Most event attendees felt they could behave normally and non-constrained despite the safety measures (median score 8·08, IQR 5–10). They expressed their willingness to attend another activity with the same safety protocol (median score 9·29, IQR 9–10). There were neither disturbances nor interventions of security personnel aside from reminders of wearing the face mask during the event.

The staff crew inside the venue included 58 people (organizers, security, sound and light technicians, and bartenders). All of them had negative Ag-RDT and RT-PCR results at baseline and the follow-up visit on day 8.

Discussion

To our knowledge, this is the first randomised clinical trial that assesses the risk of COVID-19 transmission in an indoor mass-gathering live concert done under comprehensive safety measures, including same-day SARS-CoV-2 screening with Ag-RDTs, compulsory N95 face mask wearing, and optimised air ventilation. Participants were encouraged to sing and dance in the concert hall room, and no physical distancing was recommended. None of the 465 participants became infected, compared with two of 495 in the control arm.

High SARS-CoV-2 attack rates (53% of confirmed cases) following exposure at events involving people singing (eg, a choir practice) without face masks have been previously documented.[18] Airborne transmission was considered to be facilitated by close proximity (within 1·8 m) during practice and increased by the act of singing itself, and has subsequently been confirmed in other indoor events by high aerosol exposure indexes.[19] These superspreading events emphasised the importance of physical distancing, including avoiding large indoor

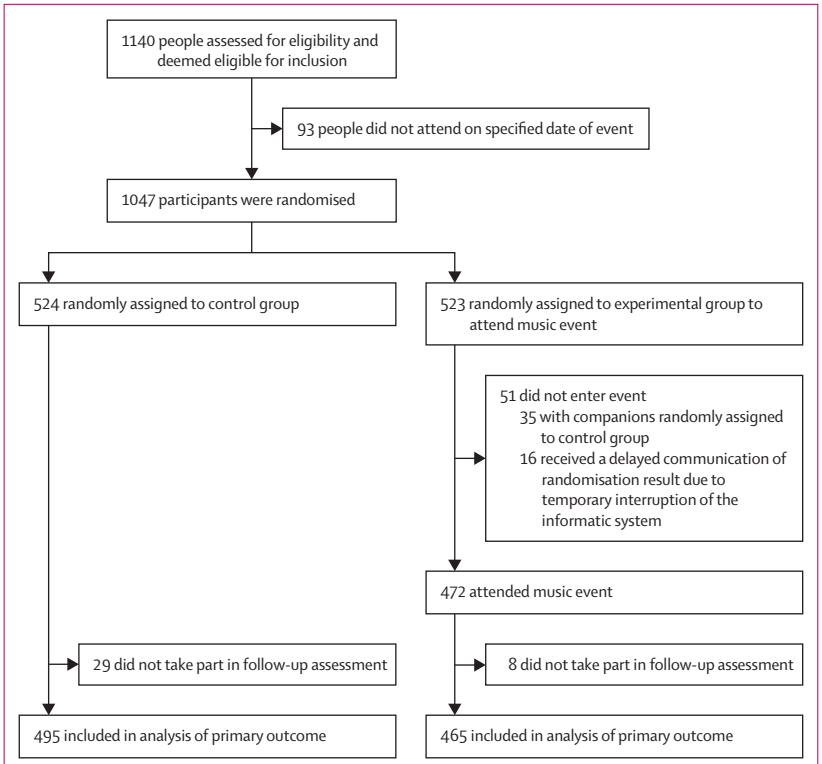

Figure: **Trial profile**

	Control group (n=495)	Experimental group (n=465)
Baseline screening		
Ag-RDT positive	0	0
TMA positive*	15 (3·0%)	13 (3%)
Cell culture positive	0	0
RT-PCR positive	1 (<1%)	1 (<1%)
Ct value	37	37
Follow-up assessment		
Ag-RDT positive	2 (0·4%)	0
TMA positive†	15 (3·0%)	12 (3%)
TMA positive at baseline	4	3
TMA negative at baseline	11	9
RT-PCR positive	2 (0·4%)	0
Ct value	26·3; 28·3	NA
Infected with SARS-CoV-2	2 (0·4%)	0

Ag-RDT=antigen-detecting rapid diagnostic tests. TMA=transcription-mediated amplification test. RT-PCR=real-time reverse transcriptase-polymerase chain reaction. Ct=cycle threshold. NA=not applicable. *Three TMA results in the control group were inconclusive. †One TMA result in the experimental group was inconclusive.

Table: **Virological assessment results for SARS-CoV-2 at baseline and day 8 after the event**

gatherings, and played a role in issuing restrictions against indoor cultural activities. Our study shows that the implemented safety measures can effectively diminish this risk.

A key intervention to remove physical distancing in this study was the screening of SARS-CoV-2 infection with Ag-RDTs immediately before entering the event. Despite their lower overall sensitivity than RT-PCR, Ag-RDTs have proven the ability to detect SARS-CoV-2 infection in respiratory specimens with Ct in RT-PCR below 25 (sensitivity of 100%) and below 30 (sensitivity 98·6%), regardless of age and the presence of symptoms.[6,20] Although the sensitivity of these tests decreases at Ct beyond this threshold, a growing body of evidence indicates that respiratory specimens with Ct values of more than 30 have a diminished infection capacity.[9,10,21,22] Therefore, the systematic screening of potential attendees to an indoor event is an excellent tool for ruling out SARS-CoV-2 infectious transmitters. In our real-life experience with the screening of asymptomatic individuals, Ag-RDTs had a negative predictive value of 99·9% for RT-PCR and 99·8% for viral culture, in agreement with previous reports.[23]

The use of Ag-RDTs for systematic screening purposes in mass gathering events has multiple advantages over NAATs, including the lack of need for laboratory referrals and short turnaround times to report the result. However, the low analytical sensitivity of these tests and the dynamics of SARS-CoV-2 infection suggest that a negative result with Ag-RDT can only rule out the potential for transmitting the virus within the few hours following the test.[6,7] Another consideration regarding this screening strategy is the controversy on whether tests done by non-trained people (including self-testing) achieve the same accuracy as that reported for tests done by health-care workers.[8]

The high sensitivity of NAAT is associated with the drawback of yielding positive results in respiratory specimens from individuals with past infection, albeit doubtful or no infectious capacity.[10] This is particularly pervasive in TMA-based tests, with a limit of detection as low as 60 copies per mL (by contrast with approximately 5000 copies per mL for RT-PCR) that allows identifying SARS-CoV-2 RNA remains some months after the COVID-19 episode.[24] Despite the fact that infectious viruses have not been recovered beyond 12 days in immunocompetent individuals, intestinal biopsies obtained from asymptomatic individuals 4 months after the onset of COVID-19 have revealed persistence of SARS-CoV-2 nucleic acids by in situ hybridisation of half of the samples.[25]

In line with these findings, various individuals (3% in our study) with a history of COVID-19 diagnosis (median of 50 days before the event) tested positive for TMA in our study despite a negative result in the Ag-RDT screening. Only 7% of those with positive TMA results had a positive RT-PCR test, all with Ct values of 37 or more, which was higher than the Ct cutoff associated with transmission risk. All had been diagnosed with COVID-19 a median of 50 days before the event and therefore had no potential for viral transmission (immunosuppressed participants were excluded). Unexpectedly, some TMA tests in our participants were positive in those with previously confirmed COVID-19 up to 5·5 months before the event. Notably, none of the TMA-positive samples from participants with a previous SARS-CoV-2 infection were associated with positive cell culture. Taken together, our findings suggest that high-sensitive techniques such as TMA are not suitable as screening tools for creating safe environments in indoor events because they would exclude people that have had COVID-19 in previous weeks or months, and those who have recovered and no longer have the potential to transmit the virus.

Aside from baseline screening, our intervention included other containment measures that might have contributed to the safety of the event. N95 mask-wearing was mandatory during the event, except when drinking (alcoholic beverages were allowed) or smoking. The lack of facial mask-wearing during indoor activities without physical distancing measures had been pointed out as a high-risk scenario for superspreading events.[18]

Other measures that potentially contributed to creating a safe environment included limited movement of participants inside the venue, avoidance of queues in restrooms and at entry or exit of the concert, the presence of dispensers of hydroalcoholic sanitizer gel, and controlled environment conditions. Limited air exchange in closed spaces is associated with an increased risk of SARS-CoV-2 transmission.[26] Multiple infection events that prompted the banning of massive gatherings[27] have been associated with inadequate ventilation.[28] In our study, all air flows and room ventilation were optimised in the indoor rooms, and air exchange was monitored during the entire event. CO_2 measurements were maintained below or around 800 ppm in the two crowded zones (dancing and bar areas). Notably, after the event, local authorities intensified the air quality recommendations beyond European guidelines;[17] according to the updated thresholds, air quality during our event would have been categorised as median or good, but not optimal. Therefore, in future mass-gathering indoor events, air ventilation would be set to maintain a maximum of 500 ppm (good quality) or 350 ppm (optimum quality).

The deployment of screening strategies such as the one used in our experiment is challenged by the need to test thousands of people within a few hours before the mass gathering event.[26] Therefore, organisational difficulties and costs should be considered. Because of these challenges, mHealth solutions such as the Test-Wallet smartphone app, designed to promptly manage Ag-RDT results while maintaining users' privacy, can substantially help to manage screening procedures and result delivery. When balancing the costs and benefits of the intervention, the public health implications of identifying and isolating

asymptomatic SARS-CoV-2-infected individuals of age groups that often remain undetected should also be considered.

The SARS-CoV-2 transmission results from our study must be placed in the context of the existing epidemiological situation at that time. The fourth round of the national longitudinal sero-epidemiological ENE-COVID study was done in Spain during November 16–29, 2020 (the closest date to the concert) with 51409 participants. According to the IgG results, the accumulative prevalence of participants with a positive result in the area of Barcelona was 12·4%, with 9·8% having a positive result during the fourth round. The day before the indoor event, 256 new COVID-19 cases were reported in the city of Barcelona (1·6 million people); the 14-day attack rate in Catalonia was 220·7 cases per 100000 inhabitants, and the number of active cases (during the past 14 days) was 16696, with 309388 cumulative cases and an effective growth potential (EGP) of 210 (of concern when >150).[11] The week after the concert (before the follow-up RT-PCR at day 8), EGP increased to 371. Because of the low number of COVID-19 cases expected given the epidemiological scenario, we considered the Bayesian estimate of the infection rate as an appropriate approach to the primary endpoint.

Our study has some limitations. First, participants could have modified their behaviour during the event due to their awareness of being observed, having signed an informed consent, and participating in a clinical trial. This phenomenon, known as the Hawthorne effect, is intrinsic to clinical trials and can limit the applicability of the results to a real-life scenario. However, in the post-event questionnaire, all participants stated normal behaviour during the event, without feeling under the scrutiny of security controls. Second, the planned number of participants (1000 per study arm) had to be halved due to restrictions issued by local health-care authorities. Our results encourage future studies with venues at an estimated full capacity. Finally, 16 participants did not attend the event because the result of the randomisation was communicated too close to the event and at that time they had already returned home. This delay was not due to the pace in the performance of screening tests but to a computer centre failure involving the block randomisation. Therefore, it should not effect Ag-RDT mass screening in future events.

In summary, our study provides the first approach to evidence building on the safety of indoor mass gathering events done during the COVID-19 outbreak without physical distancing measures and based on a comprehensive preventive intervention, including same-day screening with Ag-RDT, compulsory facial mask-wearing, and adequate ventilation. Ag-RDT screening was effective in identifying infectious individuals compared with RT-PCR and TMA. The results regarding virological assessment suggest that a baseline screening might allow easing some of the additional preventive measures, particularly in indoor events with preassigned seats (ie, theatres), associated with lower transmission risk. Besides the aforementioned limitations, our findings must be placed in the context of the evolving nature of the COVID-19 pandemic. Widespread vaccination campaigns, changes in local incidence, and the emergence of COVID-19 variants with higher transmissibility might shift the expected results of the intervention. Therefore, future trials done in different scenarios of the COVID-19 pandemic should confirm their safety and characterise the contribution of each of the preventive measures undertaken within the comprehensive intervention. Our findings pave the way to reactivate cultural activities halted during COVID-19, which could have important sociocultural and economic implications.

Contributors

BR, SV, BC, and JML conceived the project and designed the study. PS recruited participants and organised the venue framework. JP screened the virological tests of all participants. JT managed the database. XP and VN-P did the statistical analyses. IB and CC did the laboratory analyses on clinical samples. NI-U and DP-Z did the SARS-CoV-2 cell cultures. JT, JP, BR, and JML accessed and verified the data. BR and JML wrote the paper. All authors had the opportunity to discuss the results and comment on the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

PS is an employee and stockholder of Primavera Sound, sponsor of the study. All other authors declare no competing interests.

Data sharing

The complete de-identified participant data set will be available upon request to jtoro@flsida.org for researchers whose proposed use of the data has been approved, for any purpose. Data will be available with publication. If needed, requests will require the ethics committee approval of the University Hospital Germans Trias i Pujol in Badalona (Spain). Anonymised data are fully available on reasonable request from the corresponding author after approval by the hospital ethics committee.

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