Empirical evidence on the efficiency of bidirectional contact tracing in COVID-19

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Abstract

Despite ubiquitous rollout of contact tracing to counteract the spread of COVID-19, few countries have been spared from widespread community transmission, highlighting the need for more effective tracing strategies[1,2]. Standard contact tracing practice identifies, quarantines and tests persons exposed to an infected person during the contagious period, assumed to start two days before symptom onset or diagnosis[3,4]. Backward contact tracing intends to identify the source of the infection and persons infected by the same source, either by extending the contact tracing window or investigating suspected source events. These approaches have shown promise in modelling studies, but lack empirical data supporting their efficiency[5–7]. In the first large cohort study on backward contact tracing for COVID-19, we found that extending the contact tracing window backward by 5 days increased the number of identified contacts by 49.2%. The risk of infection amongst these additional contacts was similar to contacts exposed during the standard tracing window and significantly higher than symptomatic individuals in a control group, leading to an increase of 42.0% in cases identified through contact tracing. The risk was not limited to attendees of suspected source events. Our results imply an urgent need to implement backward contact tracing globally.

Introduction

The role of contact tracing in COVID-19

Case-based interventions such as case isolation, contact tracing and quarantine are crucial in controlling the ongoing COVID-19 pandemic while reducing the need for indiscriminate contact reductions with high economic cost[2,8].

Contact tracing aims to identify and interrupt transmission chains by isolating infected patients and quarantining those at risk from infection. More infections are prevented, and epidemic control is improved, if the identification of patients and contacts at risk is rapid and comprehensive[9–11].

Worldwide investments in contact tracing programs and research on the topic have not prevented repeated resurgence of community transmission of COVID-19, underscoring the urgent need for improved knowledge on the effective implementation of this key public health measure[1,12].

Forward contact tracing

Forward contact tracing of an index case (the person diagnosed with COVID-19 undergoing contact tracing) intends to interrupt onward transmission from child cases (persons infected by the index case) by quarantining contacts the index case has encountered during their infectious period[5–7]. In the light of substantial asymptomatic and presymptomatic transmission, the infectious period is generally assumed to start 2 days prior to onset of symptoms or diagnosis, whichever came first[3,4,13–15]. In addition to child cases, any practical forward tracing strategy probably identifies the parent case (the infector of the index

case) and sibling cases (infected by the same parent case) some of the time, especially if traced contacts are immediately tested[7]. Forward contact tracing is the main focus in most jurisdictions and has shown its ability to decrease COVID-19 transmission[3,4,16].

Backward contact tracing

Backward contact tracing, or bidirectional contact tracing, which combines both approaches, specifically aims to identify the parent case and sibling cases. Through iterative subsequent contact tracing, a larger fraction of the transmission chain is detected[5,6]. Effective backward contact tracing requires that contacts are tested immediately after their identification and their contacts traced if the test is positive[7].

Backward contact tracing is particularly promising in COVID-19 because a small proportion of index cases, the so-called superspreaders, generate the majority of secondary infections[6,17–24]. This phenomenon favours allocating resources to the identification of source cases and events, as a high rate of infection can be expected amongst individuals exposed to the same source. Endo et al estimate bidirectional contact tracing to result in 2-3 times the number of subsequent cases averted compared to forward contact tracing alone in a simple branching model for COVID-19[5]. Kojaku et al show backward contact tracing to be highly effective in terms of the number of prevented cases per quarantine when running an SEIR (Susceptible-Exposed-Infectious-Removed) model on synthetic and empirical contact networks, even if contact tracing comprehensiveness is low[6].

The real world implementation of bidirectional contact tracing can be broadly subdivided into a source event approach and an extended contact tracing window approach. (Figure 1)

Several countries have rolled out an approach focusing on “source events”, which are events where the index case is suspected to have contracted COVID-19. The identification of such an event leads to the screening of attendants at risk, which usually includes more individuals than the direct contacts of the index case under investigation[25–27]. This is because the risk at these events is not directly related to the index case, but to an unknown parent case. High positivity rates are reported for attendants of such source events[28]. This approach is reliant on the identification of multiple infected cases at the same event, by pooling of contact tracing data from different index cases, and it fails when no clear source event can be identified during contact tracing.

Another approach is to extend the contact tracing window back in time and to systematically refer all close contacts for quarantine and testing both as soon as possible and after an incubation period. This is based on the assumption that, if the tracing window is extended backward by at least the incubation period, the parent case can be identified, as well as sibling cases seen by both the index case and the parent case. Iterative tracing of the identified cases identifies further infections thereafter[7].

Several modelling studies underscore the benefits of extending the contact tracing window for COVID-19. Bradshaw et al show in a stochastic branching-process model that extending the contact tracing

window from 2 to 6 days before onset or diagnoses improves the reduction in the effective reproduction number by 85%-275% when using manual contact tracing only (performed by humans rather than through digital means)[7]. Their findings are robust to contextual factors such as case ascertainment rate, test sensitivity, basic reproduction number and the percentages of asymptomatic, pre-symptomatic and environmental transmission. Fyles et al also show in a branching process model that an extended contact tracing window results in a linear decrease in the growth rate up until around 8 to 10 days prior to symptom onset or diagnosis[11].

Hypothesis and research question

Therefore, whilst there is evidence from modelling studies pointing at the benefits of backward contact tracing, no study has evaluated the efficiency in practice. The positivity rate of screened contacts has been proposed as an indicator for efficient allocation of testing and quarantine[29,30].

In this cohort study we determined the positivity rate of additional close contacts (for the purpose of this article this includes co-attendants of high risk events of up to 20 persons) identified in an extended contact tracing window, starting 7 days before onset of symptoms or diagnosis. This window was chosen to generally include the source event [31,32]. The study ran from February to May 2021, in the context of a dedicated test and trace system targeting a population of about 33,000 largely unvaccinated higher education students in the city of Leuven, Belgium.

We tested the hypothesis that the positivity rate amongst additional contacts in the extended tracing window would be at least as high as amongst a control group of patients attending the test centre for symptoms suggestive of COVID-19. In a first subgroup analysis, we explored how far back the contact tracing window should extend, by calculating the positivity rate of identified contacts grouped by day of last exposure. Our second hypothesis was that the risk would not be limited to possible source events identified at the time of the tracing interview. Therefore, the second subgroup analysis compared our strategy to a source investigation approach, by subgrouping according to presence at suspected source events.

Results

Study cases and contacts

Our test and trace program started in September 2020 and is still active at the time of writing. Due to gradual improvements in organisation and data collection, there was a marked increase in the ratio of contacts with outcome data after the initial months of the program. The study period was chosen from 1st February 2021 to 31st May 2021, which was after the initial set-up phase of the program, and included both an upward and a downward trend in country-wide infection rates.

14,917 students underwent RT-qPCR testing at our centre in this period (3.8 tests per 1,000 persons daily), resulting in 498 students with a new diagnosis of COVID-19. A further 231 positive RT-qPCR test results of

students in the study population were reported to us from external sources, resulting in a total of 729 cases. 36 (4.9%) of these were interpreted as a past infection or false positive by the treating physician, leaving 693 actual cases (14-day incidence of 245 per 100,000). Six cases (0.9%) were considered lost to follow-up, because they could never be contacted by the contact tracing team, and 28 (4.1%) were excluded because data on presence of symptoms was missing. Therefore, 659 index cases remained in the analysis (Extended data Fig. 2)

72.5% of index cases self-reported being symptomatic at the time of testing. Index cases had a mean age of 21.4 years (SD: 3.60 years, missing data 15.0%) and were 51.1% male (missing data 12.1%).

Contact tracing of the index cases resulted in 3,971 case-contact pairs (mean 6.0 contacts per case), of which 956 (24.1%) were excluded because the contact person already had a positive test result 0 to 60 days before the positive test of the index case. Another 324 (10.7%) contacts were excluded because they already had a known exposure to a different infected individual within 7 days before the tracing interview. Finally, 288 contacts (10.7%) were lost to follow-up.

The resulting 2,403 contacts were divided into two groups. The standard tracing window group, which would have been identified through standard practice, consisted of 1610 individuals in close contact with the index case in the period from 2 days before onset or test until the contact tracing interview. The study group consisted of 793 additional contacts in the extended tracing window, i.e. their last close interaction with the index case was 3 to 7 days before onset or test.

We did not collect demographic data on contacts of index cases.

The control group consisted of all 1,461 students who attended our test centre for the first time with self-reported symptoms suggestive of COVID-19 as the main reason for their test.

There was a slightly higher percentage of women in the control group (56.5%, missing data 3.0%) while the mean age was similar to the other groups (22.0 years; SD 3.84 years, missing data 3.0%). The temporal distribution of individuals in the study and control groups is shown in Extended Data Fig. 1.

High risk of infection in the extended tracing window

By extending the contact tracing window, 49.2% more contacts at risk and 42.0% more cases were identified, compared to standard contact tracing practice alone.

The risk of infection in the standard and extended tracing window groups was similar, namely 17.1% in the former (CI 15.3-19.1%) and 14.6% in the latter (CI 12.2-17.3%). The risk in the extended tracing window group was significantly higher (risk ratio 2.23, CI 1.72-2.88, $p<0.0001$) than the risk of 6.5% (CI 5.3-7.9%) in the control group, demonstrating the relative efficiency of extending the contact tracing window to 7 days prior to symptom onset or test (Figure 2).

Contacts in the standard and extended tracing window groups were subgrouped by their last day of contact with the index case, relative to symptom onset or test. The results show that the number of additional identified close contacts per day decreased markedly as the tracing window was extended backward. The risk of infection varied from 9.6% to 19.2%, and the confidence interval lower bound did not drop below 4.3% for any of these subgroups in the extended tracing window. For day 3, 4 and 5 before onset or test, the risk was significantly higher than the control group ($p<0.05$).

The risk is not limited to suspected source events

An important consideration when deciding between a source investigation approach and an extended tracing window is the risk of infection for contacts not present at suspected source events. A suspected source event was identified for 80.6% of index cases. If the contact tracing interview failed to suggest a source event, the risk of infection for extended tracing window contacts was 17.1% (CI 11.9-23.6%). If a source event was identified, the risk was around 4 times higher for contacts who attended the event (absolute risk 27.4%, CI 21.5-33.9%) compared to those who did not. The latter group still had a risk of 6.9% (CI 4.6-9.8%), which was similar to the symptomatic control group but not significantly higher. *(Figure 2)*

Risk by relationship type

In a final explorative subgroup analysis, extended tracing window contacts were grouped according to relationship type with the index case. The majority of identified contacts were either family (28.5%), fellow residents in student housing (12.3%), or friends (48.4%). Each of these three groups had a significantly increased infection risk as compared to the symptomatic control group. The other subgroups lacked sufficient numbers for statistical power.

Discussion

This study lays out a strategy for backward contact tracing which markedly improves the effectiveness of contact tracing in the setting of COVID-19. It identifies an additional 43.5% of cases not detected through the contact tracing protocol used in most jurisdictions, gains which are likely to have a major impact on epidemic control[7]. The results contradict perceptions on cost efficiency, which continue to hamper the broader introduction of backward contact tracing as a standard mitigation strategy.

Our approach was to extend the contact tracing window back in time from 2 to 7 days before symptom onset or test, and to systematically refer all identified close contacts in this period for testing, as well as co-attendees of high risk events. This allowed parent cases, sibling cases and additional child cases to be identified quickly as direct contacts of the index case.

Our data show that only 49.2% more contacts at risk are identified by extending the contact tracing window backward by 5 additional days. This could be explained by recall decay or by recurring contacts with the same individuals.

Crucially, contacts last encountered during the extended tracing window had a higher risk of testing positive compared to symptomatic patients in the same population, who would be tested according to most protocols globally. These results were independent of whether they were friends, family or fellow residents of the index case.

The high positivity rate observed in contacts last seen before the contagious period can be explained by several mechanisms. First, the index case may have become contagious more than 2 days before symptom onset or test. Second, the source case is likely to be amongst these earlier contacts. Third, due to a proven individual propensity to shed live virus and an above average number of social interactions, the source case is likely to have initiated other infections among the index's contacts[6,31]. Fourth, more distant relatives in the transmission tree could be detected due to wider circulation in an index case's social circle. Fifth, recall decay may cause index cases to forget contacts with whom they had shorter, fewer and less close interactions. There may also be a more intentional tendency to mention only those contacts who the index case considers at risk.

A question that arises is whether it is worthwhile to quarantine and test a contact in the extended tracing window, if a source event was identified which the contact at hand did not attend. Our results show that the risk of infection for such a contact (6.9%, CI 4.7-9.7%) is only a quarter of that of source event attendees, but still similar to the symptomatic control group. It is also higher than the threshold positivity rates of 5% and 4% that the World Health Organisation (WHO) and European Centre for Disease Control (ECDC) recommended as target indicator for comprehensive testing, when considering all tests performed in a population[32,33].

These results speak in favour of simply referring all close contacts in the extended tracing window for testing and quarantine, even if they were not present at the suspected source event.

Additionally, we show that jurisdictions favouring the implementation of a source investigation strategy would do well to switch to an extended contact tracing window approach when no clear source event is identified at the time of the contact tracing interview (hybrid strategy, Figure 3).

The study has several limitations. First, it took place in the setting of moderate general contact restrictions, which altered social patterns significantly and likely increased the efficiency of identifying source individuals by decreasing the number of contacts in general and casual contacts in particular, which are harder to identify through manual contact tracing. Second, index cases were young adults in tertiary education, whose socio-economic status and contact patterns may differ significantly from other age and social groups, limiting generalisability[34]. Third, the population was almost entirely unvaccinated, the effects of which on transmission risk are only starting to emerge[35,36]. Fourth, the main variant circulating in the population at the time was the alpha strain, with lower transmissibility than the delta variant now dominant in most parts of the world. Fifth, we acknowledge that a testing and contact tracing program is a complex public health intervention, and the particular methods of implementation and contextual factors have a major impact on its overall effectiveness.

Our results indicate that in the context of significant community transmission of COVID-19 and in the presence of moderate contact restrictions, there is a marked added benefit, at low relative cost, to extending the contact tracing window to at least 7 days before symptom onset or test of the index case.

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Methods

Study design and context

In this cohort study we investigated the risk of contracting COVID-19 for contacts traced in an extended contact tracing window. Their risk was compared to a control group of patients from the target population, who were tested for self-reported symptoms of COVID-19 in the same period (Extended data Fig 1). A second reference group consisted of contacts exposed to an index case during the standard “forward” contact tracing window. The main outcome measure was a positive test in the 14 days after the last contact with the index case, or - for the control group - after the onset of symptoms.

The study was performed in the context of a dedicated test and trace system for a target population of an estimated 32,965 higher education students residing in the city of Leuven, Belgium. A low-threshold test centre offered free RT-qPCR tests upon self-referral, while a team of contact tracers performed manual bidirectional contact tracing. The program relied heavily on community involvement and benefited from maximum integration of testing and tracing from a human process and information technology (IT) point of view. We elaborate on the operational aspects in a published testing and contact tracing protocol[37].

The study protocol was approved by the Ethics Committee Research UZ / KU Leuven. Informed consent was waived as the data gathered did not exceed what was required for the purpose of safeguarding public health.

We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[38].

Study participants

Students attached to one of Leuven's tertiary education facilities were included in the study if they either had a positive RT-qPCR test result from 1st February until 31st May 2021at the KU Leuven test centre or if they were reported to the tracing team as having had a positive RT-qPCR test result elsewhere and had recently resided in or had come into contact with others in the city of Leuven.

Cases were excluded if the treating physician interpreted the result as falsely positive, or as a past infection with COVID-19. Cases who could not be contacted by the tracing team after repeated attempts were also excluded, as well as cases where information on symptom onset was missing.

Cases were asked about all their close interactions with contact persons in the period from 7 days before symptom onset or test until the time of the contact tracing interview.

Contacts were included as a close contact if they were reported by the index case as having had either direct physical contact, an interaction at less than 1.5 meters without face masks, an interaction at less than 1.5 meters for more than 15 minutes, or an interaction without face masks for more than 15 minutes. Also included as close contacts were co-attendants at a "high risk event" of up to 20 attendees, defined as fitting at least 2 of the following 3 criteria: crowding (at least 5 individuals belonging to at least two households), close contact (<1,5 meters without masks) and closed environment (indoor).

We excluded contacts already identified as exposed within 7 days before the contact tracing interview to a previously diagnosed index case.

Contacts who had already tested positive on the same day as the index case or up to 60 days before, were also excluded. All other contacts were advised to quarantine while undergoing RT-qPCR testing as soon as possible and, if the test was negative, seven days after the last exposure to a positive case.

Contacts were assigned to either the standard tracing window group, a reference group mirroring standard practice, or to the extended tracing window group, based on when their last close contact with the index case took place.

As a control group, we selected all students who attended the test centre for the first time during the study period, and who self-reported symptoms suggestive for Covid-19 as the reason for their test. Only the first test was included, to reduce selection bias towards students with a lower threshold for testing.

Data sources

For cases and contacts tested in our test centre, RT-qPCR test results were reported directly by the laboratory. Students who tested positive elsewhere were reported by the government contact tracing teams, by the infected students themselves or by their contacts attending the test centre. The date of onset of symptoms was reported by the index case when attending the test centre and confirmed when being called by the contact tracing team.

For each of their listed close contacts, we asked the index case about the dates and nature of their interactions, and the type of their relationship. Cases could supply this information using an online web form, and were contacted by telephone for confirmation and clarification during a thorough interview. Contacts were grouped into events if multiple people were present at the same time. These contact data were coded into a customized version of *Go.Data*, an outbreak investigation tool developed by the WHO and GOARN (Global Outbreak Alert and Response Network) partners[39].

Test dates and results of contacts who were tested outside of our test centre were obtained by telephone. This information was coded into *Go.Data* in a similar fashion.

Variables

Contacts were assigned one of three possible outcomes. “Infected” includes those contacts who were diagnosed with COVID-19 1 to 14 days after the diagnosis of the index case. “Not infected” denotes other contacts who underwent an RT-qPCR or antigen test with a negative result 1 to 7 days after their last contact with the index case. All other contacts were considered “lost to follow-up”.

The day of last contact was defined as the difference in days between the last date of interaction with the index case on the one hand, and on the other hand either the date of the positive test or the date of onset of symptoms, whichever was earlier.

Each contact of an index case was assigned a relationship type from the following list: partner, family, friend, fellow resident, acquaintance, fellow student or other.

Suspected source events were defined as events which, at the time of the contact tracing interview with the index case, were identified as the likely source of the infection, because the index case knew that an individual was present with a confirmed infection or suggestive symptoms. If the index case had been in

quarantine since travelling from abroad, travel was considered the source event and travel companions were considered present. Multiple suspected source events were taken into account per index case if applicable.

Study size

The data feeding into this study were gathered in the light of the ongoing public health response for COVID-19. The exact study period was chosen from February onwards since gradual improvements in data gathering - through updates of the IT infrastructure and human capacity building - allowed for follow-ups of all contacts to be consistently recorded from February onwards. The end of the study period marks the end of the academic semester, at which point testing and case numbers fell precipitously. The resulting number of cases and contacts is a consequence of the epidemiological trajectory within the study period.

Statistical methods

Positivity rates were calculated with two-sided 95% confidence intervals according to the Clopper-Pearson method. Small-sample adjusted risk ratios were determined with two-sided normal approximation 95% confidence intervals.

Missing demographic data was ignored in the calculations and the amount of missing data reported. Contacts with missing outcome data were considered lost to follow-up.

Cases and contacts lost to follow-up were not included in the analysis.

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Declarations

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Author contributions

JR, KN, CG and EA conceived and designed the analysis. CG, JR, KN and SG collected the data. SG contributed data. CG and JR performed the analysis. JR and CG wrote the paper. KN and EA critically reviewed the paper.

Competing interest declaration

None of the authors has competing interests to declare.

Additional information

The data that support the findings of this study are available on request from the corresponding author (Joren Raymenants). The data are not publicly available because they could compromise research participant privacy.

Supplementary Information is available for this paper.

Correspondence and requests for materials should be addressed to: Joren Raymenants.

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Figures

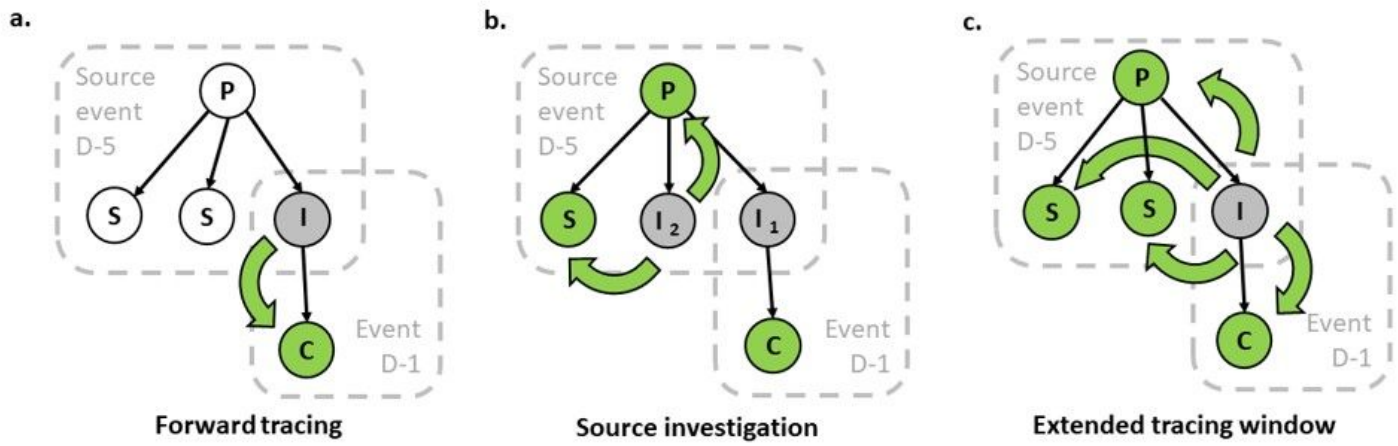

Figure 1

Schematic representation of contact tracing strategies. Thin black and thick green arrows indicate the directions of transmission and contact tracing respectively. I: index case. C: child case. P: parent case. S: sibling case. White circle: undetected case. Grey circle: case detected through symptomatic screening. Green circle: case detected through contact tracing (a) When an index case is diagnosed, the child case at event D-1 is identified through standard forward tracing. A source investigation would fail at this stage, because there is no indication of further infections at the source event. (b) Source investigation does succeed when a second index case I2 is diagnosed independently of the initial index case I1. As the source event becomes clear due to identification of multiple infections, all attendants are traced. (c) An extended tracing window quickly identifies parent, sibling and child cases as direct contacts of the first index case.

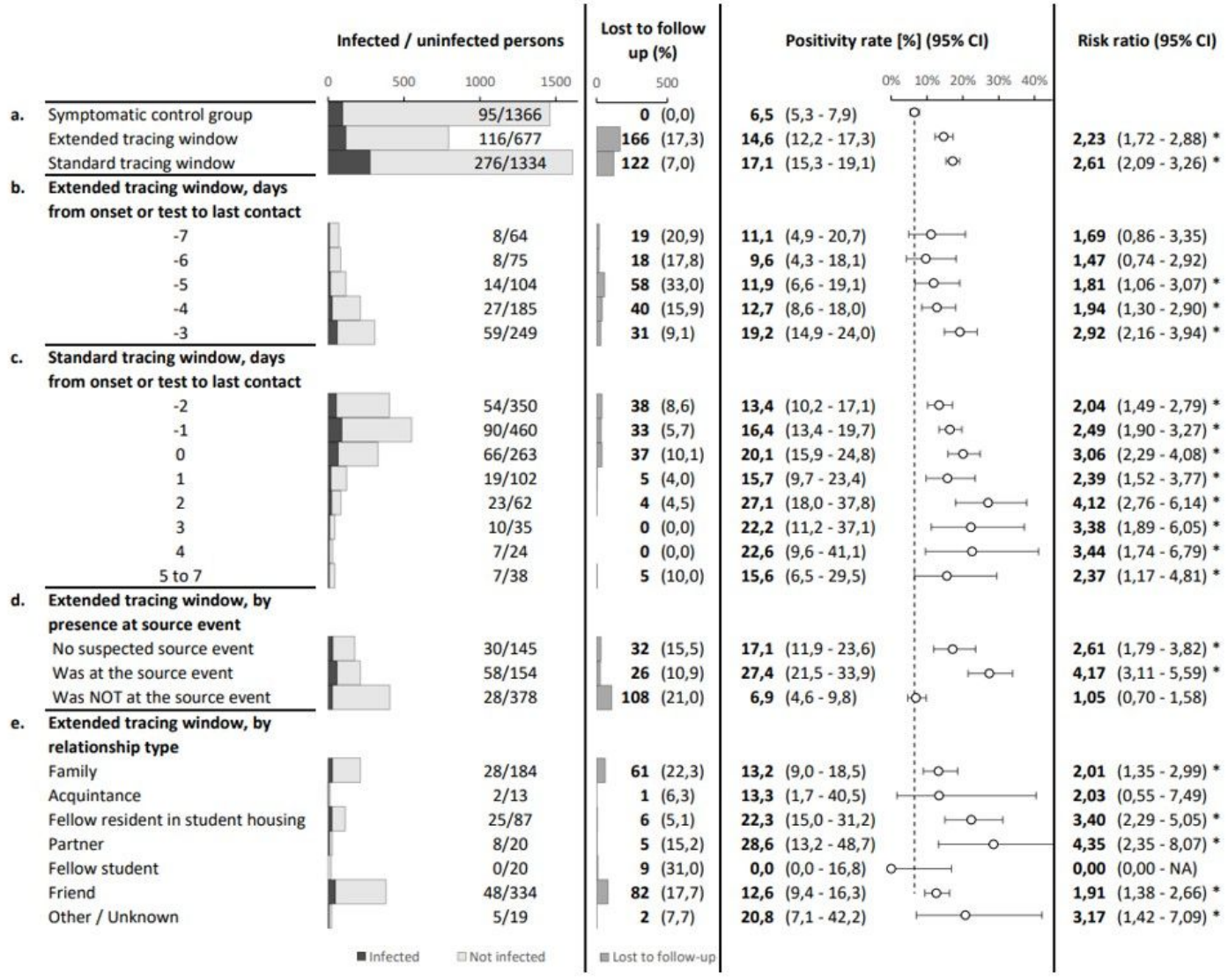

Figure 2

Outcomes, positivity rates and risk ratios for contacts of index cases. The dotted line indicates the positivity rate in the control group. The error bars indicate 95% confidence intervals. * indicates a

statistically significant difference in comparison to the control group ($p<0.05$). Section (a) tests the main hypothesis by comparing the extended tracing window to the symptomatic control group. Subgroups by the numbers of days from onset or test of the index case to the last interaction with the index case are shown in section (b) and (c) for the extended and standard tracing windows respectively. Section (d) shows subgroups according to presence at suspected source events, and subgroups by relationship type are shown in panel (e).

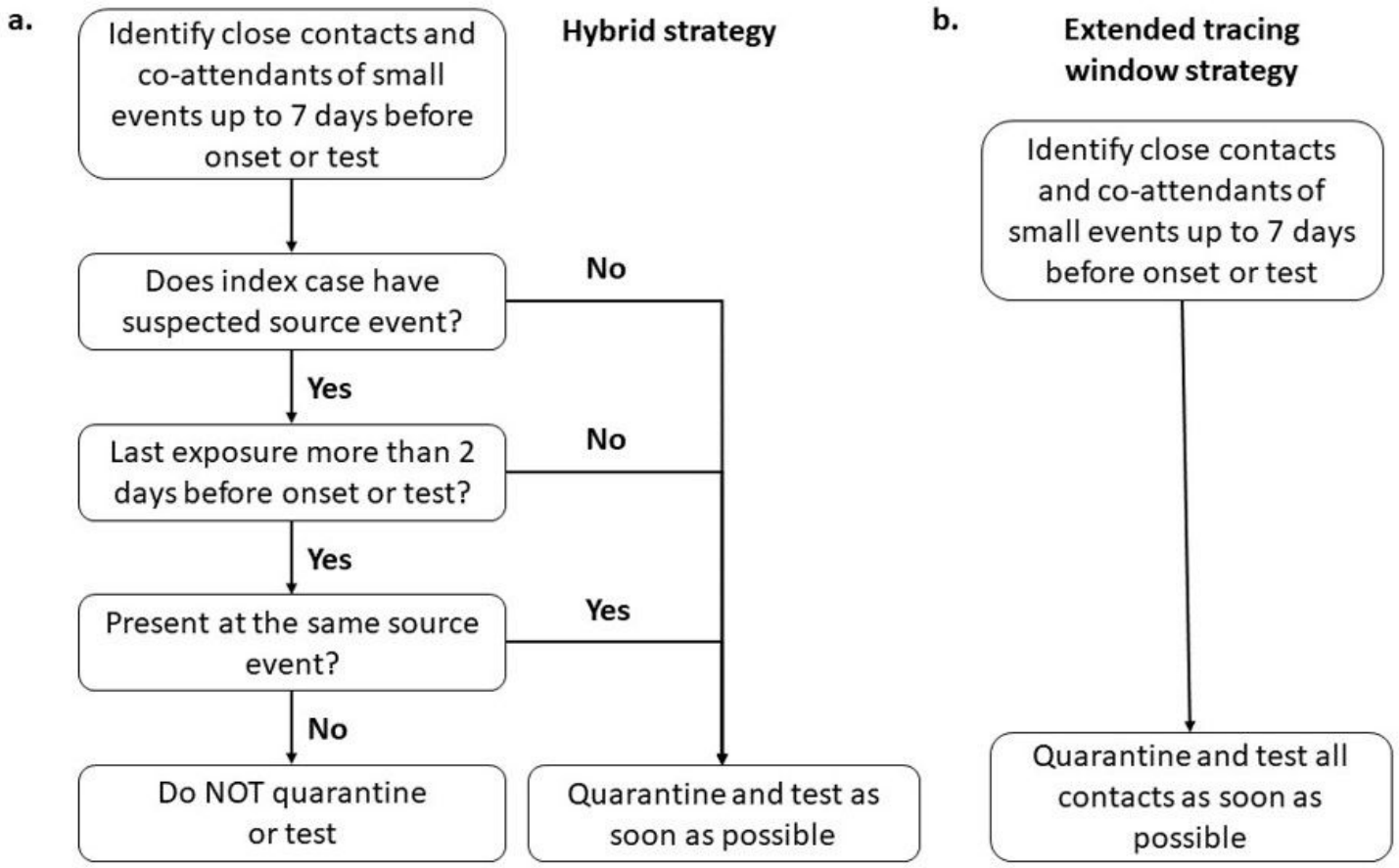

Figure 3

Schematic representation of two possible strategies for backward contact tracing, based on our results. Panel a shows a hybrid strategy, which avoids testing contacts in the extended tracing window who were not present at the suspected source event. Panel b shows an extended tracing window strategy with systematic testing of all contacts.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- ExtendedData.docx