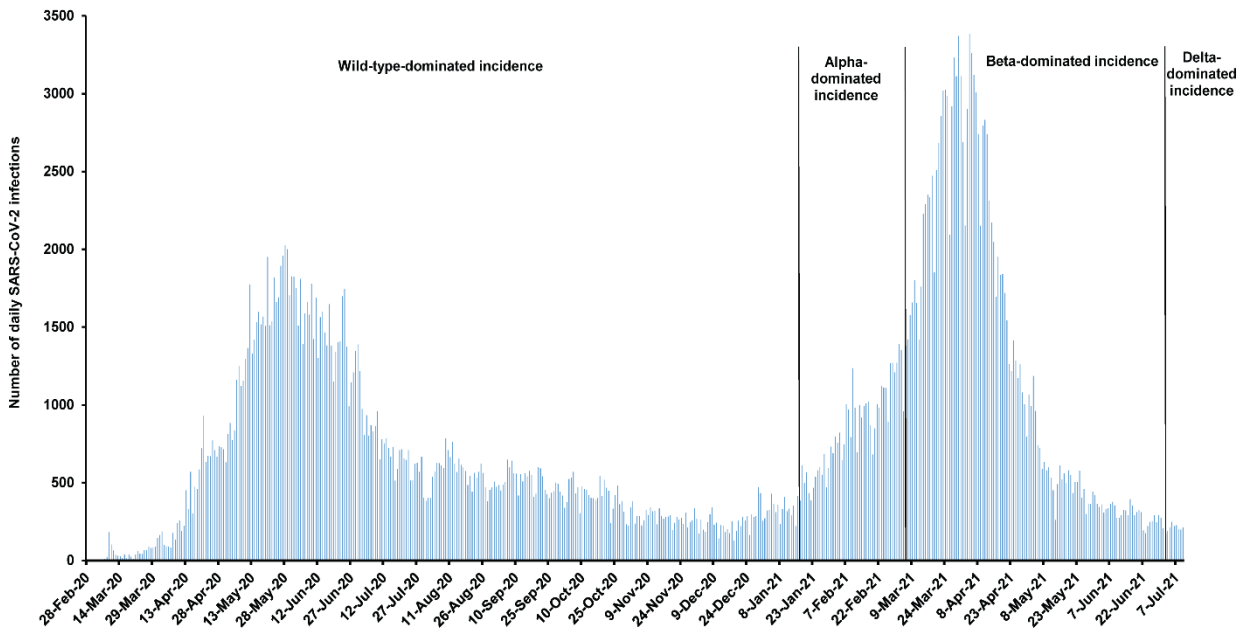


## Supplementary Information

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**Supplementary Fig. 1. Numbers of daily diagnosed SARS-CoV-2 infections during the study period.**



**Supplementary Table 1. Demographic characteristics of the study populations in the three pairwise comparisons between primary infections in unvaccinated individuals, BNT162b2-vaccine breakthrough infections, and mRNA-1273-vaccine breakthrough infections.**

| Characteristics                  | Study 1*                                       |                                          |         | Study 2*                                       |                                           |         | Study 3*                                 |                                           |         |
|----------------------------------|------------------------------------------------|------------------------------------------|---------|------------------------------------------------|-------------------------------------------|---------|------------------------------------------|-------------------------------------------|---------|
|                                  | Primary infections in unvaccinated individuals | BNT162b2-vaccine breakthrough infections | p-value | Primary infections in unvaccinated individuals | mRNA-1273-vaccine breakthrough infections | p-value | BNT162b2-vaccine breakthrough infections | mRNA-1273-vaccine breakthrough infections | p-value |
| <b>Median age (IQR) — years</b>  | 41 (34-52)                                     | 42 (34-53)                               | 0.082   | 35 (30-41)                                     | 35 (30-42)                                | 0.718   | 36 (31-43)                               | 36 (31-42)                                | 0.911   |
| <b>Age group — no. (%)</b>       |                                                |                                          |         |                                                |                                           |         |                                          |                                           |         |
| <20 years                        | 53 (1.3)                                       | 53 (1.3)                                 | 1.000   | 3 (1.1)                                        | 3 (1.1)                                   | 1.000   | --                                       | --                                        | 1.000   |
| 20-29 years                      | 439 (10.9)                                     | 439 (10.9)                               |         | 57 (21.5)                                      | 57 (21.5)                                 |         | 45 (19.8)                                | 45 (19.8)                                 |         |
| 30-39 years                      | 1,248 (30.9)                                   | 1,248 (30.9)                             |         | 118 (44.5)                                     | 118 (44.5)                                |         | 97 (42.7)                                | 97 (42.7)                                 |         |
| 40-49 years                      | 994 (24.6)                                     | 994 (24.6)                               |         | 65 (24.5)                                      | 65 (24.5)                                 |         | 62 (27.3)                                | 62 (27.3)                                 |         |
| 50-59 years                      | 675 (16.7)                                     | 675 (16.7)                               |         | 18 (6.8)                                       | 18 (6.8)                                  |         | 20 (8.8)                                 | 20 (8.8)                                  |         |
| 60-69 years                      | 458 (11.4)                                     | 458 (11.4)                               |         | 2 (0.8)                                        | 2 (0.8)                                   |         | 2 (0.9)                                  | 2 (0.9)                                   |         |
| 70+ years                        | 168 (4.2)                                      | 168 (4.2)                                |         | 2 (0.8)                                        | 2 (0.8)                                   |         | 1 (0.4)                                  | 1 (0.4)                                   |         |
| <b>Sex</b>                       |                                                |                                          |         |                                                |                                           |         |                                          |                                           |         |
| Male                             | 2,526 (62.6)                                   | 2,526 (62.6)                             | 1.000   | 209 (78.9)                                     | 209 (78.9)                                | 1.000   | 181 (79.7)                               | 181 (79.7)                                | 1.000   |
| Female                           | 1,509 (37.4)                                   | 1,509 (37.4)                             |         | 56 (21.1)                                      | 56 (21.1)                                 |         | 46 (20.3)                                | 46 (20.3)                                 |         |
| <b>Nationality<sup>†</sup></b>   |                                                |                                          |         |                                                |                                           |         |                                          |                                           |         |
| Bangladeshi                      | 290 (7.2)                                      | 108 (2.7)                                | <0.001  | 36 (13.6)                                      | 41 (15.5)                                 | <0.001  | 20 (8.8)                                 | 35 (15.4)                                 | <0.001  |
| Egyptian                         | 149 (3.7)                                      | 321 (8.0)                                |         | 1 (0.4)                                        | 13 (4.9)                                  |         | 13 (5.7)                                 | 13 (5.7)                                  |         |
| Filipino                         | 558 (13.8)                                     | 245 (6.1)                                |         | 16 (6.0)                                       | 15 (5.7)                                  |         | 7 (3.1)                                  | 12 (5.3)                                  |         |
| Indian                           | 1,173 (29.1)                                   | 855 (21.2)                               |         | 90 (34.0)                                      | 111 (41.9)                                |         | 70 (30.8)                                | 98 (43.2)                                 |         |
| Nepalese                         | 273 (6.8)                                      | 103 (2.6)                                |         | 24 (9.1)                                       | 8 (3.0)                                   |         | 19 (8.4)                                 | 6 (2.6)                                   |         |
| Pakistani                        | 185 (4.6)                                      | 109 (2.7)                                |         | 13 (4.9)                                       | 2 (0.8)                                   |         | 2 (0.9)                                  | 2 (0.9)                                   |         |
| Qatari                           | 412 (10.2)                                     | 1,258 (31.2)                             |         | 15 (5.7)                                       | 23 (8.7)                                  |         | 54 (23.8)                                | 17 (7.5)                                  |         |
| Sri Lankan                       | 137 (3.4)                                      | 41 (1.0)                                 |         | 5 (1.9)                                        | 16 (6.0)                                  |         | 5 (2.2)                                  | 14 (6.2)                                  |         |
| Sudanese                         | 103 (2.6)                                      | 122 (3.0)                                |         | 4 (1.5)                                        | 1 (0.4)                                   |         | 5 (2.2)                                  | 1 (0.4)                                   |         |
| Other nationalities <sup>‡</sup> | 755 (18.7)                                     | 873 (21.6)                               |         | 61 (23.0)                                      | 35 (13.2)                                 |         | 32 (14.1)                                | 29 (12.8)                                 |         |

Abbreviations: IQR, interquartile range.

\*Study groups were matched in a 1:1 ratio by sex, 10-year age group, reason for RT-qPCR testing, and RT-qPCR test calendar week.

<sup>†</sup>Nationalities were chosen to represent the most populous groups in the population of Qatar.

<sup>‡</sup>In Study 1, these comprise: 65 other nationalities in the primary infections and 60 in the BNT162b2-vaccine breakthrough infections; in Study 2: 18 other nationalities in the primary infections and 21 in the mRNA-1273-vaccine breakthrough infections; and in Study 3: 20 other nationalities in the BNT162b2-vaccine breakthrough infections and 16 in the mRNA-1273-vaccine breakthrough infections.

**Supplementary Table 2. Demographic characteristics of the study populations in three pairwise comparisons between primary infections in unvaccinated individuals, reinfections in unvaccinated individuals, BNT162b2-vaccine breakthrough infections, and mRNA-1273-vaccine breakthrough infections.**

| Characteristics                  | Study 4*                                       |                                          |         | Study 5*                                 |                                          |         | Study 6*                                  |                                          |         |
|----------------------------------|------------------------------------------------|------------------------------------------|---------|------------------------------------------|------------------------------------------|---------|-------------------------------------------|------------------------------------------|---------|
|                                  | Primary infections in unvaccinated individuals | Reinfections in unvaccinated individuals | p-value | BNT162b2-vaccine breakthrough infections | Reinfections in unvaccinated individuals | p-value | mRNA-1273-vaccine breakthrough infections | Reinfections in unvaccinated individuals | p-value |
| <b>Median age (IQR) — years</b>  | 33 (27-40)                                     | 33 (27-40)                               | 0.703   | 35 (30-42)                               | 35 (30-41)                               | 0.290   | 33 (27-38)                                | 33 (28-37)                               | 0.818   |
| <b>Age group — no. (%)</b>       |                                                |                                          |         |                                          |                                          |         |                                           |                                          |         |
| <20 years                        | 103 (6.1)                                      | 103 (6.1)                                | 1.000   | 9 (1.2)                                  | 9 (1.2)                                  | 1.000   | 1 (1.2)                                   | 1 (1.2)                                  | 1.000   |
| 20-29 years                      | 483 (28.7)                                     | 483 (28.7)                               |         | 174 (22.9)                               | 174 (22.9)                               |         | 27 (31.8)                                 | 27 (31.8)                                |         |
| 30-39 years                      | 664 (39.4)                                     | 664 (39.4)                               |         | 350 (46.0)                               | 350 (46.0)                               |         | 41 (48.2)                                 | 41 (48.2)                                |         |
| 40-49 years                      | 308 (18.3)                                     | 308 (18.3)                               |         | 160 (21.0)                               | 160 (21.0)                               |         | 12 (14.1)                                 | 12 (14.1)                                |         |
| 50-59 years                      | 104 (6.2)                                      | 104 (6.2)                                |         | 56 (7.4)                                 | 56 (7.4)                                 |         | 3 (3.5)                                   | 3 (3.5)                                  |         |
| 60-69 years                      | 20 (1.2)                                       | 20 (1.2)                                 |         | 8 (1.1)                                  | 8 (1.1)                                  |         | 1 (1.2)                                   | 1 (1.2)                                  |         |
| 70+ years                        | 4 (0.2)                                        | 4 (0.2)                                  |         | 4 (0.5)                                  | 4 (0.5)                                  |         | --                                        | --                                       |         |
| <b>Sex</b>                       |                                                |                                          |         |                                          |                                          |         |                                           |                                          |         |
| Male                             | 1,434 (85.1)                                   | 1,434 (85.1)                             | 1.000   | 648 (85.2)                               | 648 (85.2)                               | 1.000   | 68 (80.0)                                 | 68 (80.0)                                | 1.000   |
| Female                           | 252 (15.0)                                     | 252 (15.0)                               |         | 113 (14.9)                               | 113 (14.9)                               |         | 17 (20.0)                                 | 17 (20.0)                                |         |
| <b>Nationality<sup>†</sup></b>   |                                                |                                          |         |                                          |                                          |         |                                           |                                          |         |
| Bangladeshi                      | 168 (10.0)                                     | 178 (10.6)                               | <0.001  | 133 (17.5)                               | 73 (9.6)                                 | <0.001  | 12 (14.1)                                 | 12 (14.1)                                | 0.001   |
| Egyptian                         | 67 (4.0)                                       | 62 (3.7)                                 |         | 41 (5.4)                                 | 25 (3.3)                                 |         | 4 (4.7)                                   | 1 (1.2)                                  |         |
| Filipino                         | 138 (8.2)                                      | 90 (5.3)                                 |         | 42 (5.4)                                 | 54 (7.1)                                 |         | 4 (4.7)                                   | 3 (3.5)                                  |         |
| Indian                           | 572 (33.9)                                     | 521 (30.9)                               |         | 216 (28.4)                               | 269 (35.4)                               |         | 40 (47.1)                                 | 30 (35.3)                                |         |
| Nepalese                         | 193 (11.5)                                     | 324 (19.2)                               |         | 31 (4.1)                                 | 137 (18.0)                               |         | 1 (1.2)                                   | 11 (12.9)                                |         |
| Pakistani                        | 74 (4.4)                                       | 74 (4.4)                                 |         | 14 (1.8)                                 | 33 (4.3)                                 |         | 1 (1.2)                                   | 10 (11.8)                                |         |
| Qatari                           | 111 (6.6)                                      | 163 (9.7)                                |         | 229 (30.1)                               | 44 (5.8)                                 |         | 9 (10.6)                                  | 2 (2.4)                                  |         |
| Sri Lankan                       | 75 (4.5)                                       | 48 (2.9)                                 |         | 13 (1.7)                                 | 26 (3.4)                                 |         | 6 (7.1)                                   | 2 (2.4)                                  |         |
| Sudanese                         | 37 (2.2)                                       | 38 (2.3)                                 |         | 19 (2.5)                                 | 16 (2.1)                                 |         | 1 (1.2)                                   | 1 (1.2)                                  |         |
| Other nationalities <sup>‡</sup> | 251 (14.9)                                     | 188 (11.2)                               |         | 133 (17.5)                               | 73 (9.6)                                 |         | 7 (8.2)                                   | 13 (15.3)                                |         |

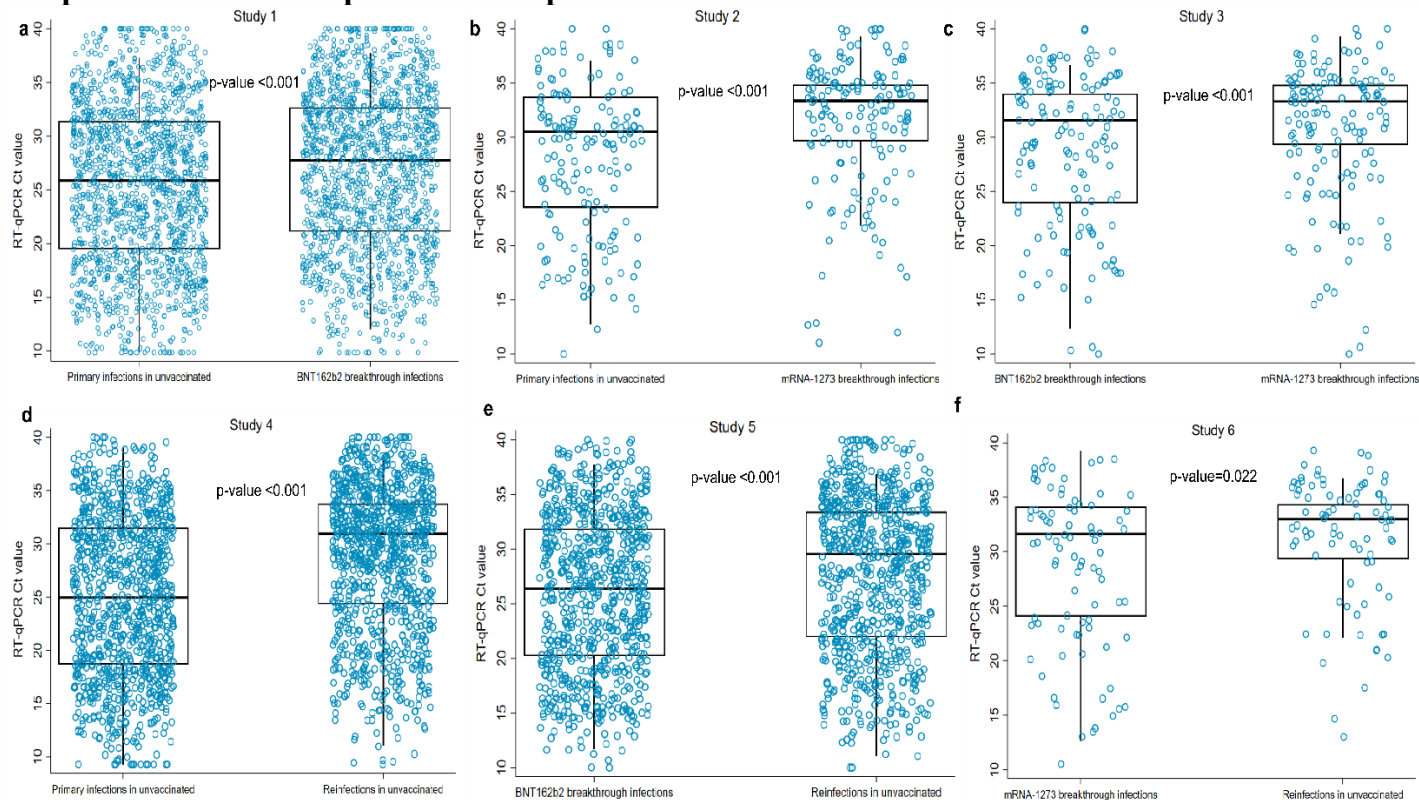
Abbreviations: IQR, interquartile range.

\*Study groups were matched in a 1:1 ratio by sex, 10-year age group, reason for RT-qPCR testing, and RT-qPCR test calendar week.

<sup>†</sup>Nationalities were chosen to represent the most populous groups in the population of Qatar.

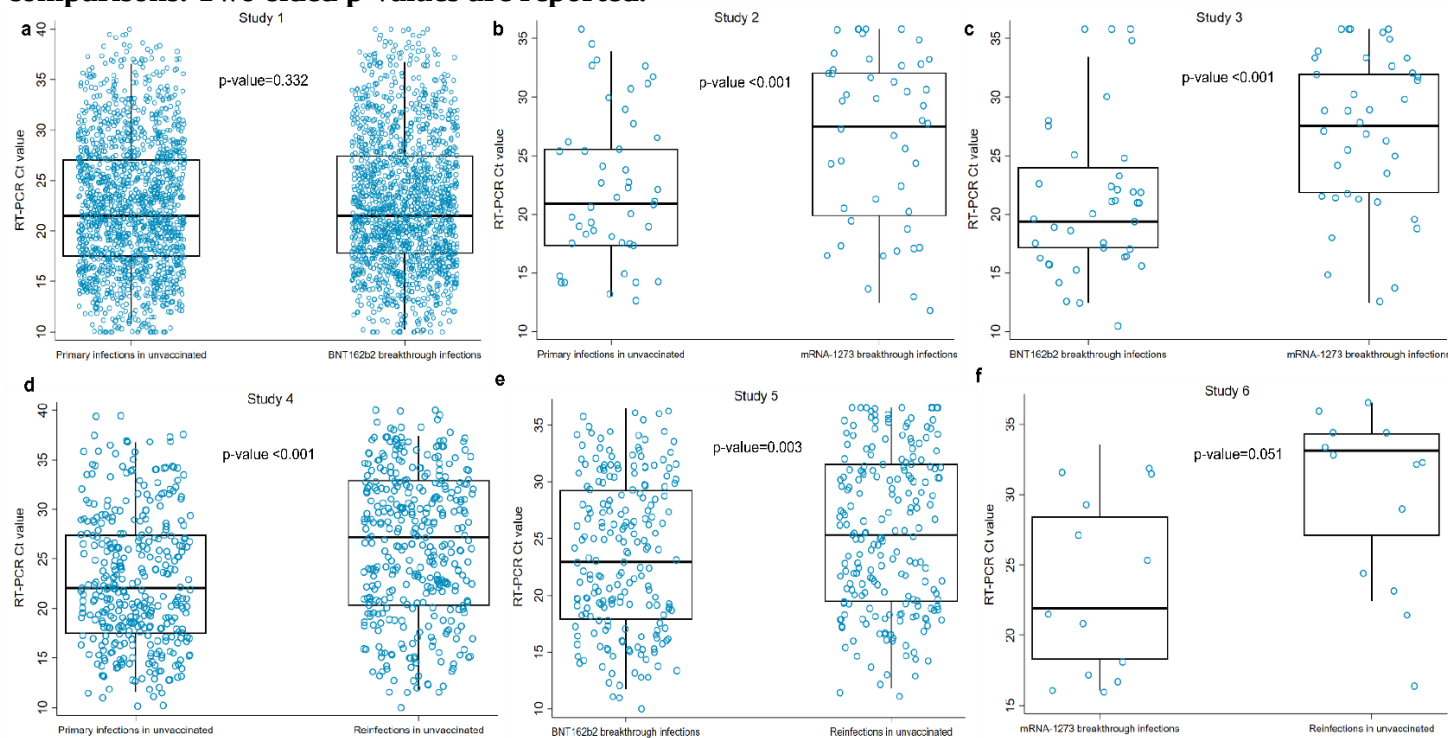
<sup>‡</sup>In Study 4, these comprise: 48 other nationalities in the primary infections and 37 in the reinfections; in Study 5: 28 other nationalities in the BNT162b2-vaccine breakthrough infections and 31 in the reinfections; and in Study 6: 10 other nationalities in the mRNA-1273-vaccine breakthrough infections and 6 in the reinfections.

**Supplementary Fig. 2. RT-qPCR Ct values in all confirmed infections, regardless of the reason for the RT-qPCR testing. Distribution of these Ct values (blue circles) in the six pairwise comparisons between primary infections in unvaccinated individuals, reinfections in unvaccinated individuals, BNT162b2-vaccine breakthrough infections, and mRNA-1273-vaccine breakthrough infections, panels 2a-2f. Figure 2a includes, in each comparison group, n=4,035 biologically independent samples, 2b includes n=265 biologically independent samples, 2c includes n=227 biologically independent samples, 2d includes n=1,686 biologically independent samples, 2e includes n=761 biologically independent samples, and 2f includes n=85 biologically independent samples, each over 1 experiment. Boxplots center lines indicate the median Ct values, box limits indicate the 25% and 75% quartiles, and whiskers indicate maximum and minimum observations within 1.5 of interquartile range. Paired t-tests were used to compare the difference in means between study groups, with no adjustment for multiple comparisons. Two-sided p-values are reported.**



Abbreviations: Ct, cycle threshold; RT-qPCR, real time reverse transcription polymerase chain reaction

**Supplementary Fig. 3. RT-qPCR Ct values in the symptomatic SARS-CoV-2 infections. Distribution of these Ct values (blue circles) in the six pairwise comparisons between primary infections in unvaccinated individuals, reinfections in unvaccinated individuals, BNT162b2-vaccine breakthrough infections, and mRNA-1273-vaccine breakthrough infections, panels 3a-3f. A symptomatic infection was defined as an RT-qPCR-positive test conducted because of clinical suspicion due to presence of symptoms compatible with a respiratory tract infection. Figure 3a includes, in each comparison group, n=1,566 biologically independent samples, 3b includes n=46 biologically independent samples, 3c includes n=39 biologically independent samples, 3d includes n=364 biologically independent samples, 3e includes n=204 biologically independent samples, and 3f includes n=13 biologically independent samples, each over 1 experiment. Boxplots center lines indicate the median Ct values, box limits indicate the 25% and 75% quartiles, and whiskers indicate maximum and minimum observations within 1.5 of interquartile range. Paired t-tests were used to compare the difference in means between study groups, with no adjustment for multiple comparisons. Two-sided p-values are reported.**



Abbreviations: Ct, cycle threshold; RT-qPCR, real time reverse transcription polymerase chain reaction

**Supplementary Table 3. STROBE checklist.**

Supplementary Table S1: STROBE checklist

|                          | Item No | Recommendation                                                                                                                                                                                    | Main Text                                                                               |
|--------------------------|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| Title and abstract       | 1       | (a) Indicate the study’s design with a commonly used term in the title or the abstract                                                                                                            | Abstract                                                                                |
|                          |         | (b) Provide in the abstract an informative and balanced summary of what was done and what was found                                                                                               | Abstract                                                                                |
| Introduction             |         |                                                                                                                                                                                                   |                                                                                         |
| Background/rationale     | 2       | Explain the scientific background and rationale for the investigation being reported                                                                                                              | Introduction paragraphs 1-4                                                             |
| Objectives               | 3       | State specific objectives, including any prespecified hypotheses                                                                                                                                  | Introduction paragraphs 3 & 5                                                           |
| Methods                  |         |                                                                                                                                                                                                   |                                                                                         |
| Study design             | 4       | Present key elements of study design early in the paper                                                                                                                                           | Methods (‘Data sources and study design’)                                               |
| Setting                  | 5       | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection                                                                   | Methods (‘Data sources and study design’) & Figure 1                                    |
| Participants             | 6       | (a) Give the eligibility criteria, and the sources and methods of selection of participants                                                                                                       | Methods (‘Data sources and study design’) & Figure 1                                    |
| Variables                | 7       | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable                                                          | Methods                                                                                 |
| Data sources/measurement | 8*      | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group              | Methods (‘Data sources and study design’ & ‘Statistical analysis’) & Supp. Tables 1 & 2 |
| Bias                     | 9       | Describe any efforts to address potential sources of bias                                                                                                                                         | Methods (‘Data sources and study design’ & ‘Statistical analysis’) & Table 3            |
| Study size               | 10      | Explain how the study size was arrived at                                                                                                                                                         | Methods (‘Data sources and study design’) & Figures 1-2                                 |
| Quantitative variables   | 11      | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why                                                                      | Methods (‘Statistical analysis’) & Supp. Tables 1 & 2                                   |
| Statistical methods      | 12      | (a) Describe all statistical methods, including those used to control for confounding                                                                                                             | Methods (‘Statistical analysis’)                                                        |
|                          |         | (b) Describe any methods used to examine subgroups and interactions                                                                                                                               | Methods (‘Statistical analysis’)                                                        |
|                          |         | (c) Explain how missing data were addressed                                                                                                                                                       | NA, see Methods (‘Data sources and study design’)                                       |
|                          |         | (d) If applicable, describe analytical methods taking account of sampling strategy                                                                                                                | Methods (‘Statistical analysis’)                                                        |
|                          |         | (e) Describe any sensitivity analyses                                                                                                                                                             | Methods (‘Statistical analysis’) & Table 3                                              |
| Results                  |         |                                                                                                                                                                                                   |                                                                                         |
| Participants             | 13*     | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | Results (‘Study populations’) & Figures 1-2                                             |
|                          |         | (b) Give reasons for non-participation at each stage                                                                                                                                              | Figures 1-2                                                                             |
|                          |         | (c) Consider use of a flow diagram                                                                                                                                                                | Figures 1-2                                                                             |
| Descriptive data         | 14*     | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders                                                          | Supp. Tables 1 & 2                                                                      |

|                          |     |                                                                                                                                                                                                              |                                                                                                                                                                 |
|--------------------------|-----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                          |     | (b) Indicate number of participants with missing data for each variable of interest                                                                                                                          | NA, see Methods ('Data sources and study design')                                                                                                               |
| Outcome data             | 15* | Report numbers of outcome events or summary measures                                                                                                                                                         | Results ('Differences in RT-qPCR Ct values in all confirmed infections' to 'Differences in RT-qPCR Ct values in symptomatic infections', & Tables 2-5           |
| Main results             | 16  | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | Results ('Differences in RT-qPCR Ct values in all confirmed infections' to 'Differences in RT-qPCR Ct values in symptomatic infections', Figure 3, & Tables 2-5 |
|                          |     | (b) Report category boundaries when continuous variables were categorized                                                                                                                                    | Supp. Tables 1 & 2                                                                                                                                              |
|                          |     | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period                                                                                             | NA                                                                                                                                                              |
| Other analyses           | 17  | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses                                                                                                               | Supplementary Figs. 2 & 3 & Tables 3-5                                                                                                                          |
| <b>Discussion</b>        |     |                                                                                                                                                                                                              |                                                                                                                                                                 |
| Key results              | 18  | Summarise key results with reference to study objectives                                                                                                                                                     | Discussion paragraphs 1-4                                                                                                                                       |
| Limitations              | 19  | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias                                                   | Discussion paragraphs 5-8                                                                                                                                       |
| Interpretation           | 20  | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence                                   | Discussion paragraph 9                                                                                                                                          |
| Generalisability         | 21  | Discuss the generalisability (external validity) of the study results                                                                                                                                        | Discussion paragraph 8                                                                                                                                          |
| <b>Other information</b> |     |                                                                                                                                                                                                              |                                                                                                                                                                 |
| Funding                  | 22  | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based                                                | Acknowledgements                                                                                                                                                |

Abbreviations: NA, not applicable; Supp, Supplementary Information.