Comparison of COVID-19 outcomes among shielded and non-shielded populations:
A general population cohort study of 1.3 million

Bhautesh D Jani,* Frederick K Ho,* David J Lowe, Sean MacBride-Stewart, Frances S Mair, Jill P Pell

*Joint-first author

Bhautesh D Jani PhD
Clinical Senior Lecturer in General Practice and Primary Care
Institute of Health and Wellbeing, University of Glasgow,
Glasgow G12 9LX, UK
Bhautesh.jani@glasgow.ac.uk

Frederick K Ho PhD
Research Associate
Institute of Health and Wellbeing, University of Glasgow
Glasgow, G12 8RZ, UK
Frederick.Ho@glasgow.ac.uk

David J Lowe MSc
Consultant in Emergency Medicine,
Queen Elizabeth University Hospital, NHS Greater Glasgow and Clyde,
Glasgow, G52 4TF, UK
David.lowe@nhs.net

Sean MacBride-Stewart PhD
Lead Pharmacist (Medicines Management Resources)
Pharmacy Services
NHS Greater Glasgow and Clyde, G76 7AT, UK
Sean.MacBride-Stewart@ggc.scot.nhs.uk

Frances S Mair MD
Norie Miller Professor of General Practice
Institute of Health and Wellbeing, University of Glasgow,
Glasgow G12 9LX, UK
Frances.mair@glasgow.ac.uk

Jill P Pell MD
Henry Mechan Professor of Public Health
Institute of Health and Wellbeing, University of Glasgow,
Glasgow, G12 8RZ, UK
Jill.pell@glasgow.ac.uk

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Address for correspondence:
Professor Jill Pell
Director of the Institute of Health and Wellbeing
University of Glasgow
1 Lilybank Gardens
Glasgow G12 8RZ
United Kingdom
Jill.pell@glasgow.ac.uk

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Abstract

Background

Shielding (extended self-isolation) of people judged, a priori, to be at high-risk from COVID-19 has been used by some countries to protect the individuals and reduce demand on health services. It is unclear how well this strategy works in either regard.

Methods

A general population study was conducted using linked primary care, prescribing, laboratory, hospital and death records up to end of May 2020. Poisson regression models and population attributable fractions were used to compare COVID-19 outcomes by overall risk category, and individual risk criteria: confirmed infection, hospitalisation, intensive care unit (ICU) admission, population mortality and case-fatality.

Results

Of the 1.3 million population, 32,533 (2.47%) had been advised to shield, a further 347,374 (26.41%) were classified as moderate risk. Testing for COVID-19 was more common in the shielded (6.75%) and moderate (1.99%) than low (0.72%) risk categories. Referent to low-risk, the shielded group had higher risk of confirmed infection (RR 7.91, 95% 7.01-8.92), case-fatality (RR 5.19, 95% CI 4.12-6.53) and population mortality (RR 48.64, 95% 37.23-63.56). The moderate risk had intermediate risk of confirmed infection (RR 4.11, 95% CI 3.82-4.42) and population mortality (RR 26.10, 95% CI 20.89-32.60), but had comparable case-fatality (RR 5.13, 95% CI 4.24-6.21) to the shielded, and accounted for a higher proportion of deaths (PAF 75.27% vs 13.38%). Age ≥70 years made the largest contribution to deaths (49.53%) and was associated with an 8-fold risk of infection, 7-fold case-fatality and 74-fold mortality.

Conclusions
Shielding has not been effective at preventing deaths in those with highest risk. To be effective as a population strategy, shielding criteria would need to be widely expanded to include other criteria, such as the elderly.

**Keywords (MeSH terms):**

- Cohort studies; COVID-19; epidemiology; vulnerable populations
Background

Early in the COVID-19 pandemic, one of the greatest concerns was that the demand on health services would exceed capacity in terms of hospitalisations, admissions to intensive care units (ICU) and requirement for ventilation. Based on past experience, it was assumed that sub-groups of the population would have worse prognosis and, therefore, contribute disproportionately to adverse outcomes and healthcare demands.

Asian countries have generally relied solely on population-wide strategies. Early, widespread ‘test, trace, isolate’ strategies were made possible by higher testing capacity and a greater willingness to monitor and enforce compliance. In contrast, European countries have generally adopted a two-pronged approach, whereby general population interventions, such as physical distancing and hand hygiene, designed to reduce transmission in the population as a whole, have been supplemented by shielding of those assumed to be at higher risk. Notably, Sweden, an outlier in having not applied lock-down, nonetheless mandated shielding.

Studies suggest that shielding can have negative physical and psychological impact on those required to undertake strict isolation over a protracted period.

In the United Kingdom, a Shielded Patient List (initially referred to as the Vulnerable Patient List) was produced comprising two categories (Supplementary Table 1). The two groups have been labelled high risk, highest risk or clinically extremely vulnerable and moderate risk, at risk or clinically vulnerable by various UK organisations. For the purposes of this study they are referred to as shielded and moderate risk, with the remaining population labelled low risk. In the United Kingdom, the shielded group received individual letters strongly recommending that they self-isolate over a protracted period, by not leaving their...
homes and avoiding non-essential contact with their household members, and were provided
with support at home such as the delivery of food packages. The advice to the moderate risk
category was simply to be vigilant in adhering to the general population measures.

The definitions of high and moderate risk were based largely on expert opinion informed by
our understanding of previous viruses and the critical need for better definition of high risk
has been highlighted\(^7\). Studies are emerging of the individual risk factors associated with
COVID-19 outcomes. For example, among two million UK community-based app users self-
reported heart disease, kidney disease, lung disease, diabetes and obesity were associated
with self-reported hospital admission and respiratory support for COVID-19\(^8\). Similarly,
linkage of primary care records of 17 million people in England demonstrated that a wide
range of long-term conditions were associated with in-hospital death from COVID-19
including: respiratory, heart, liver and kidney disease, diabetes, cancers, stroke and organ
transplantation\(^9\). Unfortunately, the investigators did not have access to deaths in the
community. COVID-19 risk scores are being developed in an attempt to improve
identification of high risk individuals who would be advised to shield\(^10\) but attempts to
investigate the potential contribution of a shielding strategy to population-level outcomes and
healthcare demands have so far been limited to abstract mathematical modelling\(^11\–\19\).

The aims of this study were to compare those classified, a priori, as high risk (and therefore
advised to shield) and those classified as moderate and low risk, in terms of their individual
risk of COVID-19 infection and outcomes and the extent to which they accounted for
COVID-19 related outcomes at a population level.

Methods
We conducted a general population cohort study of all 1.3 million residents of NHS Greater Glasgow and Clyde (NHS GGC) in Scotland. The Community Health Index (CHI), a unique identifier attached to all health records in Scotland, was used to undertake individual-level record linkage via exact matching of nine databases: Community Health Index (CHI) register, NHS GGC Shielding List, Egton Medical Information Systems (EMIS) and Vision, Electronic Communication of Surveillance in Scotland (ECOSS), Prescribing Information System (PIS), Rapid Preliminary Inpatient Data (RAPID), and death certificates.

The CHI register provided sociodemographic information (age, sex, socioeconomic deprivation). Socioeconomic deprivation was derived from the Scottish Index of Multiple Deprivation (SIMD), an area-based measure derived from seven domains - income, education, health, employment, crime, housing, and access to services – which was categorised into general population quintiles. The Electronic Communication of Surveillance in Scotland (ECOSS) database collects laboratory data on infectious diseases, including test date and result. EMIS and Vision are the primary care electronic health record systems used in NHS GGC. Data are extracted using Albasoft software. The PIS collects data on all medications prescribed by community-based healthcare workers, including general practitioners. The RAPID database collects real-time data on every patient admitted to a general (i.e. non-psychiatric) hospital in Scotland including dates of admission and discharge, and type of ward (e.g. ICU) but does not record disease codes. Subsequently, the Scottish Morbidity Record 01 (SMR01) records the same information, in addition to disease codes. Death certificates provide the date and cause of death for all deaths, whether they occur in-
hospital or in the community. Follow-up data were available until the end of May 2020, before the recommendation to shield was lifted.

Supplementary Table 1 lists the criteria for the shielded and medium risk categories being applied in the United Kingdom at the time of data extraction. All remaining patients are categorised as low risk. The Scottish list of high-risk individuals is compiled, and regularly updated, centrally using data obtained from a number of sources including Albasoft extraction of general practice data, SMR01 (hospital admissions), SMR06 (cancer registry), national disease registries, and the PIS. The list is sent to individual general practitioners to check for completeness and accuracy, before letters are sent to patients with advice to shield. The NHS GGC Shielding List contains the validated data including the criterion satisfied. We ascertained people who met the criteria for moderate risk via Albasoft extraction of EMIS and Vision data and PIS data.

Separate models were conducted for two exposure variables: overall risk category (low, moderate or high) and the individual criteria for the moderate and high-risk categories. The four general population outcomes investigated were: confirmed COVID-19 infection; COVID-19 related hospitalisation; COVID-19 related ICU admission; COVID-19 related mortality. The three outcomes investigated among those with confirmed infection were; COVID-19 related hospitalisation; COVID-19 related ICU admission; and COVID-19 related case fatality.

Laboratory-confirmed cases were defined as patients who had a positive PCR test for COVID-19. Clinically-confirmed cases were defined as patients who either had a positive PCR test or who died from COVID-19 without testing. COVID-related deaths were defined
as deaths with International Classification of Diseases 10\textsuperscript{th} revision (ICD-10) code U07.1 or U07.2 recorded on the death certificate. COVID-related hospitalisation was defined as an SMR01 record of hospitalisation with an ICD code U07.1 or U07.2 or, for more recent admissions, a RAPID record of hospitalisation with a positive COVID-19 test taken between two weeks before and two days after admission to hospital. ICU admission during such hospitalisations was assumed to be COVID-related.

The sociodemographic characteristics of people were compared by risk category using chi-square tests. Poisson regression models with robust standard errors were used to compare the risk ratios (RR) for the high and moderate risk categories referent to the low risk category for each outcome in turn. The models were run univariately and then adjusted for sex and SIMD quintiles as potential confounders. Age was not included as a covariate because it was a moderate risk criterion. The models were re-run using the individual criteria for the high and moderate risk categories as the exposure variables, referent to the low risk category.

Population attributable fractions (PAFs) were calculated, from prevalence and adjusted RR, to determine the proportion of each outcome that could be attributed to being high and moderate risk, as well as the proportion due to each of the individual criteria. The PAFs of individual criteria were proportionally calibrated so that the sum of PAFs of individual criteria equated to the overall PAF of the relevant risk category. PAF confidence intervals were estimated using bootstrapping (x 1000).

Ethical approvals
The study was approved by the NHS Greater Glasgow and Clyde Primary Care Information Sharing Group and the NHS Greater Glasgow and Clyde Local Privacy Advisory Committee (LPAC) (Reference GSH/20RM005) and was covered by the generic Safe Haven Research Ethics Committee approval (GSH20RM005_COVID_Community).

Results

Of the 1,315,071 people registered with general practitioners in NHS Greater Glasgow and Clyde, 32,533 (2.47%) were recorded as requiring shielding and 347,374 (26.41%) were classified, a priori, as being at moderate risk. Of the 32,533 people in the shielded group, 18,147 (55.78%) had severe respiratory disease, 6,761 (20.78%) were on renal dialysis, 5,349 (16.44%) were on immunosuppressive therapies, 2,491 (7.66%) had specific cancers, 1,245 (3.83%) had received organ transplants, and less than five were pregnant and had severe heart disease. Of the 347,374 people classified as moderate risk, 160,215 (46.12%) had hypertension, 151,865 (43.72%) had chronic lung disease, 139,568 (40.18%) were at least 70 years of age, 64,358 (18.53%) had diabetes, 48,571 (13.98%) had heart disease, and 1,195 (0.34%) had a weakened immune system.

Shielded and moderate risk categories

Overall, 15,865 (1.21%) people had been tested for COVID-19. The likelihood of having been tested increased with age, was higher in women and was higher in the moderate-risk category and highest in the shielded group (Table 1). Overall, 3,348 (0.25%) people had confirmed COVID-19 infection. The likelihood of laboratory-confirmed COVID-19 infection followed similar patterns as testing. It increased with age, was higher in women, and was
highest in the shielded group and lowest in the low-risk category (Table 2). After adjustment for sex and deprivation quintile, the risk of laboratory-confirmed infection remained higher in the moderate-risk category and highest in the shielded group (Table 3).

Overall, 1,661 people were admitted to hospital for COVID-19. Within the general population, hospitalisations increased with age but were comparable between men and women (Table 2). Hospitalisations were more common in the moderate-risk category and most common in the shielded group (Table 2) and remained so after adjustment for sex and deprivation quintile (Table 3). Overall, 122 people were admitted to ICU wards for COVID-19. ICU admissions were significantly more common among people aged 45-64 years of age than among older people (Table 2). Compared with the low risk category, the shielded group were 18 times more likely to be hospitalised but only 4 times more likely to be admitted to ICU (Table 3). Overall, 1,027 (0.08%) people died from COVID-19. Within the general population, mortality increased with age but was similar in men and women (Table 2). Population mortality was higher in the moderate-risk category and highest in the shielded group (Table 2) and remained so after adjustment for sex and deprivation quintile (Table 3).

Among the sub-group with laboratory-confirmed (test-positive) COVID-19 infection, 1,661 (49.6%) were hospitalised. Hospitalisations increased with age but were comparable between men and women (Table 4). The moderate-risk category was more likely to be hospitalised and the shielded group most likely (Table 4) and remained so after adjustment for age and deprivation quintile (Table 5). Among the sub-group with laboratory-confirmed COVID-19 infection, ICU admissions were more common in men and more common in people aged 45-64 years than those older (Table 4). Low risk cases were more likely to be admitted to ICU than those in the moderate-risk category and shielded groups (Tables 4 & 5). Among the sub-
group with clinically-confirmed (test-positive or COVID-19 related death) COVID-19 infection, 1,027 (26.70%) died (Table 4). Case-fatality increased by age and was higher in men than women. It was lowest in the low-risk category but not significantly different in the moderate-risk category and shielded group (p=0.64) (Table 5).

The shielded group accounted for 8.58% of laboratory-confirmed COVID-19 infections, 15.45% of COVID-19 hospitalisations, 4.91% of ICU admissions and 13.38% of COVID-19 related deaths (Supplementary Table 2). The corresponding figures for the moderate risk category were 41.22%, 61.33%, 20.78% and 75.27%. To prevent at least 80% of deaths, 28.8% of the population would have had to receive the current level of shielding including those with five criteria currently classified as moderate risk (Supplementary Figure 1).

Individual risk criteria

Due to insufficient numbers, the models for individual risk criteria could not be run for pregnant women with severe heart disease or for COVID-19 related ICU admission in the high-risk category. All of the remaining individual risk criteria were associated with higher likelihood of being tested for COVID-19 (Table 1) and higher likelihood of having laboratory-confirmed infection (Table 2). They were all associated with higher risk of hospitalisation, population mortality (Table 3) and case-fatality (Table 5) independent of sex and deprivation quintile. Among the moderate-risk category criteria, age ≥ 70 years and weakened immune system had risks of population mortality (Table 3) and case-fatality (Table 5) that were at least as high as the overall shielded group. Apart from the 0.13% of people with relevant rare diseases and inborn errors of metabolism, the strongest associations were observed for those aged ≥ 70 years who were eight times more likely to have confirmed
infection (Table 3); seven times more likely to die following confirmation of infection (Table 5); and seventy four times as likely to die overall (Table 3) compared with those in low risk category. Being more than 70 years of age accounted for 17.45% of confirmed COVID-19 infections, 22.90% of COVID-19 related hospitalisations, and 49.53% of COVID-19 related deaths (Supplementary Table 2). Among those admitted to hospital for COVID-19, the likelihood of being admitted to ICU was significantly lower for all of the individual risk criteria included in the moderate risk category, other than diabetes (Table 5). In particular, hospitalised patients over 70 years of age were 14 times less likely to be admitted to ICU than low risk hospitalised patients (Table 5).

Discussion

The 2.47% of people who had been advised to shield were, nonetheless, eight times more likely to have confirmed infections than the low risk category, five times more likely to die following confirmed infection and 49 times more likely to die from covid-19 overall. Whilst selective testing of potential cases might explain the first outcome, it does not explain higher overall mortality which suggests that the shielding strategy has not been as effective as was hoped.

One quarter of the population were classified as moderate risk and not advised to shield. Nonetheless, they were four times more likely to have confirmed infections than the low risk category, five times more likely to die following confirmed infection and 26 times more likely to die overall, suggesting that consideration should be given to expanding the shielding criteria to include many currently classified as moderate risk. In particular, older age needs to
be considered since the elderly are both at high individual risk and contribute significantly to
population burden due to their relatively high numbers.

Paradoxically, people in the shielded and moderate risk categories were less likely to be
admitted to ICU following hospitalised for COVID-19 in spite of their poor prognosis.
Patients over 70 years were particularly unlikely to be admitted to ICU. This is likely to be
due to selective admission policies applied in order to avoid demand exceeding supply, as
experienced by some other countries. This finding reinforces the importance of prevention in
those with the worst prognosis.

Comparison with existing literature

Our finding of 26.41% percent of people satisfying the moderate risk criteria is consistent
with the limited existing evidence. A previous study linking English primary and secondary
care records on 3.9 million people reported that 20% of the population satisfied similar
criteria\textsuperscript{20}. Similarly, a study using data from the Global Burden of Diseases Study estimated
that 22% of the global population are at increased risk of severe COVID-19 disease\textsuperscript{21}. A USA
study using data from the Behavioral Risk Factor Surveillance System reported that 45.4% of
444,649 adults had one or more of a longer list of morbidities that may be associated with
higher risk from COVID-19\textsuperscript{22}. Another USA study estimated that 14.2% of participants in the
National Health Interview Survey had more than two-fold risk and 1.6% had more than 10-
fold risk\textsuperscript{23}.

The evidence on COVID-19 related complications among those people classified as high risk,
and therefore advised to shield, has mainly come from case series, expert opinions,
unpublished reports. Evidence from case reports found higher COVID-19 related complications among organ transplant recipients\textsuperscript{24,25}, patients receiving active cancer treatment (chemotherapy, radiotherapy or immunotherapy)\textsuperscript{26,27}, and patients with haematological cancers\textsuperscript{28}. Systematic review of case reports found higher COVID-19 complication risk among COPD patients, but the effect of COPD severity was not investigated\textsuperscript{29}. Patients with cystic fibrosis and sickle cell disease were regarded as high risk for COVID-19 complications based on expert opinions\textsuperscript{30,31}. While pregnant women with COVID-19 were found to have higher risk of poor maternal and perinatal outcomes\textsuperscript{32,33}, outcomes were not investigated specifically for pregnant women with heart disease. There was no evidence found for higher COVID-19 related complications for patients on various immunosuppressants\textsuperscript{34}. A large community study in England found strong association between severe asthma (hazard ratio 1.25) and COVID-19 related mortality but they did not investigate the risk of COVID-19 infection or hospitalisation\textsuperscript{9}.

In common with previous studies, we demonstrated that age was associated with one of the highest relative risks of death. Additionally, we showed the large extent to which age contributed to adverse outcomes at a population level with 79.14\% of deaths attributable to age $\geq 70$ years. The higher mortality in the elderly was mediated in part by their higher case-fatality but they also had a higher incidence of infection, possibly due to transmission within care homes. Their lower likelihood of being admitted to ICU once hospitalised for COVID-19 may have contributed to their higher case-fatality. Previous studies have reported that men are at highest risk of from COVID-19\textsuperscript{7}. Our study demonstrated that men are less likely than women to be tested for COVID-19, less likely have confirmed infection and slightly less likely to be hospitalised. They have comparable overall mortality from COVID-19, due to their lower incidence, but their case-fatality is significantly higher.
Strengths and Limitations

This study adds to the existing evidence of the possible effectiveness of a shielding strategy which is currently limited to mathematical modelling of population effects based on assumptions\textsuperscript{11–19}. Ours was a large-scale, unselected general population study. The data cover a period when shielding was in place. Linkage of primary care, laboratory, hospital and death data enabled us to examine a range of COVID-19 outcomes and study a range of exposure variables including the overall risk categories and their individual criteria. The datasets were linked using exact, rather than probabilistic, matching. We were able to adjust for potential sociodemographic confounders. The exposure data were collected prior to the outcomes occurring avoiding potential reverse causation and recall or recording bias. We did not have data on potential lifestyle confounding factors such as smoking and obesity, or ethnicity. We did not analyse multimorbidity or other potential risk factors not currently included in the high or moderate risk categories as the aim was to evaluate the current strategy. The shielding and moderate-risk criteria were correct at the time of extracting data but may be revised over time.

Implications of findings

Our findings suggest that our attempts to shield those at highest risk have not been as successful as hoped, with those advised to shield experiencing higher rates of infection and death. ICU provision has been successfully protected but via systematic exclusion of those with worse prognosis, rather than prevention of infection in those highest at risk. For shielding to be effective as a population level strategy, the current criteria would need to be
expanded since three-quarters of deaths were associated with moderate risk criteria for which
shielding has not hitherto been recommended. In our study, more than one-quarter of the
general population would have needed to be effectively shielded to prevent over 80% of
deaths. Since this is unlikely to be acceptable at a time when governments are under pressure
to ease lock-down restrictions, shielding is probably best viewed as an individual-level
intervention to be used alongside other population-wide interventions such as physical
distancing, face coverings and hand hygiene.
Availability of data and materials

The dataset supporting the conclusions of this article is available in the Glasgow Safe Haven
(https://www.nhsggc.org.uk/about-us/professional-support-sites/safe-haven/services/).

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Conflicts of interest

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Contributors

FH and BJ contributed equally and are joint-first authors. BJ and JP conceptualised the study,
interpreted the data, and wrote the first draft of the manuscript. FH analysed the data and
wrote the first draft of the manuscript. All other authors interpreted the data and critically
revised the manuscript. All authors approved the final submitted version of the manuscript.
BJ, FH, and JP serves as the guarantor of the manuscript and accepts full responsibility for
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**Table 1.** COVID-19 testing status by sociodemographic characteristics, risk category and risk criteria

|                         | COVID-19 testing status | N=1,299,206 | N=15,865 | P value |
|-------------------------|-------------------------|-------------|----------|---------|
|                         | Not tested              | n (%)       | Tested   |
| Age group (years)       |                         |             |          |         |
| 0-24                    | 355,238 (99.49)         | 1,822 (0.51)| <0.0001  |
| 25-44                   | 410,408 (99.22)         | 3,247 (0.78)|          |
| 45-64                   | 340,268 (98.65)         | 4,660 (1.35)|          |
| ≥65                     | 193,292 (96.92)         | 6,136 (3.08)|          |
| Sex                     |                         |             |          | <0.0001 |
| Male                    | 654,041 (99.01)         | 6,569 (0.99)|          |
| Female                  | 645,165 (98.58)         | 9,296 (1.42)|          |
| Deprivation quintile    |                         |             |          | <0.0001 |
| 1 (most deprived)       | 461,672 (98.67)         | 6,211 (1.33)|          |
| 2                       | 230,402 (98.75)         | 2,921 (1.25)|          |
| 3                       | 194,702 (98.90)         | 2,175 (1.10)|          |
| 4                       | 173,456 (98.93)         | 1,883 (1.07)|          |
| 5 (most affluent)       | 238,974 (98.89)         | 2,675 (1.11)|          |
| Risk category           |                         |             |          | <0.0001 |
| Low                     | 928,397 (99.28)         | 6,767 (0.72)|          |
| Moderate                | 340,473 (98.01)         | 6,901 (1.99)|          |
| Shielded                | 30,336 (93.25)          | 2,197 (6.75)|          |
| Moderate risk criteria  |                         |             |          | <0.0001 |
| Chronic respiratory disease | 149,325 (98.33)     | 2,540 (1.67)|          |
| Heart disease           | 46,728 (96.21)          | 1,843 (3.79)|          |
| Hypertension            | 156,286 (97.55)         | 3,929 (2.45)|          |
| Diabetes                | 62,482 (97.09)          | 1,876 (2.91)|          |
| Weakened immune system  | 1,140 (95.40)           | 55 (4.60)   |          |
| ≥70 years of age        | 134,305 (96.23)         | 5,263 (3.77)|          |
| Shielded criteria       |                         |             |          | <0.0001 |
| Severe respiratory disease | 17,146 (94.48)         | 1,001 (5.52)|          |
| Specific cancers        | 2,075 (83.30)           | 416 (16.70)|          |
| Pregnant with severe heart disease | <5           | 0          |          |
| Immunosuppressive therapy | 5,028 (94.00)        | 321 (6.00)  |          |
| Solid organ transplant  | 1,149 (92.29)           | 96 (7.71)   |          |
| Rare diseases and inborn errors of metabolism | 1,623 (91.95) | 142 (8.05) | <0.0001 |
| Renal dialysis          | 6,216 (91.94)           | 545 (8.06)  | <0.0001  |

N number
### Table 2. Crude, population-level COVID-19 outcomes by sociodemographic characteristics, risk category and risk criteria

| Confirmed COVID-19 infection | COVID-19 hospitalisation | COVID-19 ICU admission | COVID-19 mortality |
|------------------------------|--------------------------|------------------------|-------------------|
| Negative test/Not tested     | Positive test            |                        |                   |
| N=1,311,723 n (%)            | N=1,311,410 n (%)        | N=1,314,949 n (%)      | N=1,314,044 n (%) |
| Not admitted                 | Admitted                 | Not admitted           | Alive             |
|                              | P-value                  | Admitted               | Dead              |
|                              |                          | P-value                |                   |
| Age group (years)            |                          |                        |                   |
| 0-24                         | 356,944 (99.97)          | 116 (0.03)             | 357,041 (99.99)   |
|                              | 357,061 (100.00)         | 0                      | 357,060 (100.00)  |
| 25-44                        | 413,123 (99.87)          | 532 (0.13)             | 413,532 (99.97)   |
|                              | 413,643 (100.00)         | 12 (0.00)              | 413,647 (100.00)  |
| 45-64                        | 343,856 (99.69)          | 1,072 (0.31)           | 344,409 (99.95)   |
|                              | 344,846 (99.98)          | 82 (0.02)              | 344,838 (99.97)   |
| ≥65                          | 197,800 (99.18)          | 1,628 (0.82)           | 198,428 (99.50)   |
|                              | 199,400 (99.99)          | 28 (0.01)              | 198,499 (99.53)   |
| Sex                          |                          |                        |                   |
| Male                         | 659,203 (99.79)          | 1,407 (0.21)           | 660,525 (99.99)   |
|                              | 660,092 (99.92)          | 518 (0.08)             |                   |
| Female                       | 652,250 (99.70)          | 1,941 (0.30)           | 653,952 (99.92)   |
|                              | 653,925 (99.92)          | 509 (0.09)             |                   |
| Deprivation quintile         |                          |                        |                   |
| 1 (most deprived)            | 466,582 (99.72)          | 1,301 (0.28)           | 467,832 (99.99)   |
| 2                            | 232,710 (99.74)          | 613 (0.26)             | 233,302 (99.99)   |
| 3                            | 196,416 (99.77)          | 461 (0.23)             | 196,854 (99.99)   |
| 4                            | 174,933 (99.77)          | 400 (0.23)             | 175,329 (99.99)   |
| 5 (most affluent)            | 241,076 (99.76)          | 573 (0.24)             | 241,632 (99.99)   |
| Risk category                |                          |                        |                   |
| Low                          | 933,977 (99.87)          | 1,187 (0.13)           | 935,099 (99.99)   |
| Moderate                     | 345,552 (99.48)          | 1,822 (0.52)           | 347,325 (99.99)   |
| Shielded                     | 32,194 (98.96)           | 339 (1.04)             | 32,525 (99.98)    |
| Moderate risk criteria       |                          |                        |                   |
| Chronic respiratory disease  | 151,414 (99.70)          | 451 (0.30)             | 151,853 (99.99)   |
| Heart disease                | 48,176 (99.19)           | 395 (0.81)             | 48,564 (99.99)    |
| Hypertension                 | 159,267 (99.41)          | 948 (0.59)             | 160,189 (99.98)   |
| Diabetes                     | 63,903 (99.29)           | 455 (0.71)             | 64,335 (99.96)    |
| Weakened immune system       | 1,183 (99.90)            | 12 (1.00)              | 1,195 (100.00)    |
| ≥70 years of age             | 138,115 (98.96)          | 1,453 (1.04)           | 139,560 (99.98)   |
| Shielded group               |                          |                        |                   |
| Severe respiratory disease   | 17,981 (99.09)           | 166 (0.91)             | 18,142 (99.99)    |
| Specific cancers             | 2,452 (98.43)            | 39 (1.57)              | 2,462 (98.44)     |
| Pregnant, severe heart disease | <5                      | 0                     | 2,491 (100.00)    |
| Immunosuppressive therapy    | 5,285 (98.80)            | 64 (1.20)              | 5,346 (99.94)     |
| Solid organ transplant       | 1,226 (98.83)            | 17 (1.17)              | 1,240 (99.92)     |
| Rare diseases and IEM        | 1,725 (97.96)            | 36 (2.04)              | 1,764 (99.94)     |
| Renal dialysis               | 6,684 (98.86)            | 77 (1.14)              | 6,758 (99.96)     |

N number; IEM inborn errors of metabolism
Table 3. Associations* between risk categories and risk criteria and population-level COVID-19 outcomes

|                        | Confirmed COVID-19 infection |               | COVID-19 hospitalisation |               | COVID-19 ICU admission |               | COVID-19 mortality |               |
|------------------------|-------------------------------|---------------|--------------------------|---------------|------------------------|---------------|-------------------|---------------|
|                        | RR (95% CI)                   | P-value       | RR (95% CI)              | P-value       | RR (95% CI)            | P-value       | RR (95% CI)       | P-value       |
| Low                    | 1 (Reference)                 |               | 1 (Reference)            |               | 1 (Reference)          |               | 1 (Reference)     |               |
| Moderate               |                               |               |                          |               |                        |               |                   |               |
| Overall                | 4.11 (3.82-4.42)              | <0.0001       | 6.82 (6.07-7.66)         | <0.0001       | 2.06 (1.42-2.98)       | 0.0001        | 26.10 (20.89-32.60)| 0.0001        |
| Chronic respiratory disease | 2.31 (2.07-2.57)              | <0.0001       | 3.80 (3.24-4.45)         | <0.0001       | 1.15 (0.62-2.14)       | 0.65          | 3.92 (2.80-5.50)  | 0.0001        |
| Heart disease          | 6.54 (5.84-7.33)              | <0.0001       | 11.75 (10.02-13.77)      | <0.0001       | 1.92 (0.88-4.19)       | 0.1           | 26.30 (19.92-34.74)| 0.0001        |
| Hypertension           | 4.61 (4.23-5.02)              | <0.0001       | 8.09 (7.11-9.20)         | <0.0001       | 2.44 (1.55-3.84)       | 0.0001        | 15.87 (12.38-20.35)| 0.0001        |
| Diabetes               | 5.61 (5.03-6.24)              | <0.0001       | 10.6 (9.12-12.32)        | <0.0001       | 4.89 (3.04-7.88)       | <0.0001       | 16.42 (12.29-21.93)| 0.0001        |
| Weakened immune system | 7.81 (4.44-13.76)             | <0.0001       | 19.82 (10.60-37.07)      | <0.0001       |                        |               | 56.85 (25.14-128.55)| 0.0001        |
| ≥70 years of age       | 8.10 (7.50-8.74)              | <0.0001       | 15.12 (13.42-17.03)      | <0.0001       | 0.90 (0.43-1.86)       | 0.77          | 73.85 (59.45-91.75)| 0.0001        |
| Shielded               |                               |               |                          |               |                        |               |                   |               |
| Overall                | 7.91 (7.01-8.92)              | <0.0001       | 18.47 (15.79-21.59)      | <0.0001       | 3.67 (1.76-7.65)       | 0.0005        | 48.64 (37.23-63.56)| 0.0001        |
| Severe respiratory disease | 6.82 (5.79-8.02)              | <0.0001       | 16.59 (13.63-20.19)      | <0.0001       |                        |               | 53.52 (39.77-72.02)| 0.0001        |
| Specific cancers       | 12.16 (8.85-16.70)            | <0.0001       | 27.49 (18.87-40.04)      | <0.0001       |                        |               | 72.55 (42.83-122.88)| 0.0001        |
| Immunosuppressive therapy | 9.28 (7.23-11.92)             | <0.0001       | 22.08 (16.47-29.61)      | <0.0001       |                        |               | 52.86 (34.03-82.11)| 0.0001        |
| Solid organ transplant | 10.98 (6.82-17.67)            | <0.0001       | 28.18 (16.85-47.12)      | <0.0001       |                        |               | 63.06 (29.50-134.80)| 0.0001        |
| Rare diseases and IEM  | 15.95 (11.47-22.18)           | <0.0001       | 31.77 (21.06-47.91)      | <0.0001       |                        |               | 133.80 (83.50-214.41)| 0.0001        |
| Renal dialysis         | 8.76 (6.97-11.02)             | <0.0001       | 19.66 (14.90-25.94)      | <0.0001       |                        |               | 20.03 (11.04-36.36)| 0.0001        |

*adjusted for sex and deprivation quintile

RR relative risk; CI confidence interval; IEM inborn errors of metabolism
Table 4. Crude COVID-19 outcomes among confirmed cases by sociodemographic characteristics, risk category and risk criteria

|                           | COVID-19 hospitalisation |          | COVID-19 ICU admission |          | COVID-19 case-fatality |
|---------------------------|--------------------------|----------|------------------------|----------|------------------------|
|                           | N=3,348†                 |          | N=3,348†               |          | N=3,846‡               |          |
|                           | Not admitted N=1,687 n (%) | Admitted N=1,661 n (%) | P-value | Not admitted N=3,226 n (%) | Admitted N=1,122 n (%) | P-value | Alive N=2,819 n (%) | Dead N=1,027 n (%) | P-value |
| Age group (years)         |                          |          |                        |          |                        |          |                        |                      |          |
| 0-24                      | 97 (83.62)               | 19 (16.38) | <0.0001               | 116 (100.00) | 0                     | <0.0001 | 116 (100.00) 0 (0.00) | 526 (98.50) 8 (1.50) |
| 25-44                     | 410 (76.92)              | 123 (23.08) |                        | 520 (97.74) | 12 (2.26)              |         | 1,003 (91.77) 90 (8.23) |                      |          |
| ≥65                       | 630 (38.65)              | 1,000 (61.35) |                        | 990 (92.35) | 82 (7.65)              |         | 1,174 (55.83) 929 (44.17) |                      |          |
| Sex                       |                          |          |                        |          |                        |          |                        |                      |          |
| Male                      | 579 (41.12)              | 829 (58.88) | <0.0001               | 1,322 (93.96) | 85 (6.04)             | <0.0001 | 1,105 (68.08) 518 (31.92) |                      |          |
| Female                    | 1,108 (57.11)            | 832 (42.89) |                        | 1,904 (98.09) | 37 (1.91)             |         | 1,717 (77.10) 509 (22.90) |                      |          |
| Deprivation Quintile      |                          |          |                        |          |                        |          |                        |                      |          |
| 1 (most deprived)         | 566 (43.44)              | 737 (56.56) | <0.0001               | 1,250 (96.08) | 51 (3.92)             | 0.29    | 1,046 (70.34) 441 (29.66) |                      | 0.0004 |
| 2                         | 332 (54.07)              | 282 (45.93) |                        | 592 (96.57) | 21 (3.43)             |         | 531 (78.90) 142 (21.10) |                      |          |
| 3                         | 235 (50.98)              | 226 (49.02) |                        | 438 (95.01) | 23 (4.99)             |         | 394 (72.03) 153 (27.97) |                      |          |
| 4                         | 204 (51.00)              | 196 (49.00) |                        | 390 (97.50) | 10 (2.50)             |         | 341 (72.40) 130 (27.60) |                      |          |
| 5 (most affluent)         | 353 (61.61)              | 220 (38.39) |                        | 556 (97.03) | 17 (2.97)             |         | 507 (75.90) 161 (24.10) |                      |          |
| Risk category             |                          |          |                        |          |                        |          |                        |                      |          |
| Low                       | 792 (66.67)              | 396 (33.33) | <0.0001               | 1,122 (94.52) | 65 (5.48)             |         | 1,128 (93.15) 83 (6.85) |                      |          |
| Moderate                  | 820 (45.01)              | 1,002 (54.99) |                        | 1,773 (97.31) | 49 (2.69)             |         | 1,448 (64.36) 802 (35.64) |                      |          |
| Shielded                  | 78 (22.87)               | 263 (77.13) |                        | 331 (97.64) | 8 (2.36)              |         | 243 (63.12) 142 (36.88) |                      |          |
| Moderate risk criteria    |                          |          |                        |          |                        |          |                        |                      |          |
| Chronic respiratory disease | 205 (45.35)           | 247 (54.65) | 0.02                   | 439 (97.34) | 12 (2.66)             | 0.29    | 420 (88.79) 53 (11.21) | <0.0001 |
| Heart disease             | 149 (37.72)              | 246 (62.28) | <0.0001               | 388 (98.23) | 7 (1.77)              | 0.049   | 330 (74.16) 115 (25.84) | 0.7       |
| Hypertension              | 404 (42.57)              | 545 (57.43) | <0.0001               | 922 (97.26) | 26 (2.74)             | 0.10    | 836 (78.87) 224 (21.13) | <0.0001 |
| Diabetes                  | 161 (35.31)              | 295 (64.69) | <0.0001               | 432 (94.95) | 23 (5.05)             | 0.11    | 398 (80.73) 95 (19.27)  | <0.0001 |
| Weakened immune system    | 2 (16.67)                | 10 (83.33)  | 0.04                   | 12 (100.00) | 0                    | -       | 6 (50.00) 6 (50.00) | 0.13      |
| ≥70 years of age          | 587 (40.57)              | 867 (59.63) | <0.0001               | 1,445 (99.45) | 8 (0.55)             | <0.0001 | 1,035 (54.10) 878 (45.90) | <0.0001 |
| Shielding criteria        |                          |          |                        |          |                        |          |                        |                      |          |
| Severe respiratory disease | 33 (19.64)               | 135 (80.36) | <0.0001               | 165 (99.40) | 5                    | -       | 111 (55.78) 88 (44.22) | <0.0001 |
| Specific cancers          | 10 (25.64)               | 29 (74.36)  | 0.003                  | 39 (100.00) | 0                    | -       | 27 (62.79) 16 (37.21) | 0.16      |
| Pregnant, severe heart disease | -                       | -               | -                      | -         | -                    | -       | -                     | -         |
| Immunosuppressive therapy | 14 (21.88)               | 50 (78.12)  | <0.0001               | 61 (95.31) | 5                    | -       | 42 (62.69) 25 (37.31) | 0.07      |
| Solid organ transplant    | 2 (11.76)                | 15 (88.24)  | 0.09                  | 16 (94.12) | 5                    | -       | 11 (61.11) 7 (38.89)  | 0.37      |
| Rare diseases and IEM     | 12 (33.33)               | 24 (66.67)  | 0.06                   | 35 (97.22) | 5                    | -       | 23 (52.27) 21 (47.73) | 0.003     |
| Renal dialysis            | 20 (25.97)               | 57 (74.03)  | <0.0001               | 74 (96.10) | 5                    | -       | 66 (84.62) 12 (15.38) | 0.03      |

†laboratory-confirmed (test-positive) COVID-19 cases
‡clinically-confirmed (test-positive or COVID-19 on death certificate) COVID-19 cases
N number; IEM inborn errors of metabolism
Table 5. Associations* between risk categories and risk criteria and COVID-19 outcomes among confirmed cases

| Risk Category     | COVID-19 Hospitalisation N=3,348† | COVID-19 ICU Admission N=3,348† | COVID-19 Case-fatality N=3,846‡ |
|-------------------|-----------------------------------|----------------------------------|---------------------------------|
|                   | RR (95% CI) P-value               | RR (95% CI) P-value              | RR (95% CI) P-value              |
| Low               | 1 (Reference)                     | 1 (Reference)                    | 1 (Reference)                    |
| Moderate          |                                   |                                  |                                 |
| Overall           | 1.33 (1.22-1.46) <0.0001          | 0.38 (0.26-0.55) < 0.0001        | 5.13 (4.24-6.21) <0.0001         |
| Chronic respiratory disease | 1.56 (1.39-1.76) <0.0001             | 0.46 (0.25-0.86) 0.02             | 1.63 (1.22-2.18) 0.001            |
| Heart disease     | 1.60 (1.42-1.81) <0.0001          | 0.24 (0.11-0.53) 0.0004          | 3.57 (2.81-4.54) <0.0001         |
| Hypertension      | 1.54 (1.40-1.70) <0.0001          | 0.44 (0.28-0.69) 0.0004          | 3.06 (2.48-3.79) <0.0001         |
| Diabetes          | 1.71 (1.52-1.91) <0.0001          | 0.72 (0.45-1.18) 0.19            | 2.65 (2.06-3.40) <0.0001         |
| Weakened immune system | 2.43 (1.51-3.89) 0.0002               | -                                | 7.14 (3.54-14.39) <0.0001        |
| ≥70 years of age  | 1.37 (1.25-1.49) <0.0001          | 0.07 (0.04-0.15) < 0.0001        | 6.59 (5.46-7.96) <0.0001         |
| Shielded          |                                   |                                  |                                 |
| Overall           | 1.96 (1.74-2.21) <0.0001          | 0.33 (0.16-0.70) 0.004           | 5.19 (4.12-6.53) <0.0001         |
| Severe respiratory disease | 1.94 (1.67-2.25) <0.0001             | -                                | 6.23 (4.83-8.03) <0.0001         |
| Specific cancers  | 1.89 (1.42-2.51) <0.0001          | -                                | 5.04 (3.21-7.93) <0.0001         |
| Immunosuppressive therapy | 2.17 (1.74-2.71) <0.0001             | -                                | 5.19 (3.56-7.58) <0.0001         |
| Solid organ transplant | 2.33 (1.58-3.44) <0.0001             | -                                | 5.24 (2.73-10.07) <0.0001        |
| Rare diseases and IEM | 1.50 (1.10-2.05) 0.01               | -                                | 6.64 (4.42-9.96) <0.0001         |
| Renal dialysis    | 2.15 (1.74-2.65) <0.0001          | -                                | 2.20 (1.32-3.66) 0.003           |

*adjusted for sex and deprivation quintile
†laboratory-confirmed (test-positive) COVID-19 cases
‡clinically-confirmed (test-positive or COVID-19 on death certificate) COVID-19 cases
N number; RR relative risk; CI confidence interval; IEM inborn errors of metabolism