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Original Research paper

The impact of primary care supported shielding on the risk of mortality in people vulnerable to COVID-19: English sentinel network matched cohort study

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S U M M A R Y

Objectives: To mitigate risk of mortality from coronavirus 2019 infection (COVID-19), the UK government recommended ‘shielding’ of vulnerable people through self-isolation for 12 weeks.

Methods: A retrospective cohort study using a nationally representative English primary care database comparing people aged >= 40 years who were recorded as being advised to shield using a fixed ratio of 1:1, matching to people with the same diagnoses not advised to shield (n = 77,360 per group). Time-to-death was compared using Cox regression, reporting the hazard ratio (HR) of mortality between groups.

Results: We found a time-varying HR of mortality between groups. In the first 21 days, the mortality risk in people shielded was half those not (HR = 0.50, 95%CI:0.41–0.59, p < 0.0001). Over the remaining nine weeks, mortality risk was 54% higher in the shielded group (HR = 1.54, 95%CI:1.41–1.70, p < 0.0001). Beyond the shielding period, mortality risk was over two-and-a-half times higher in the shielded group (HR = 2.61, 95%CI:2.38–2.87, p < 0.0001).

Conclusions: Shielding halved the risk of mortality for 21 days. Mortality risk became higher across the remainder of the shielding period, rising to two-and-a-half times greater post-shielding. Shielding may be beneficial in the next wave of COVID-19.

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Introduction

In England, COVID-19-related excess mortality largely occurred between weeks 12 to 22 of the year 2020 and primarily affected people age 45 years and older (Fig. 1). 1–4 Insufficient protection for care home staff and residents, 5–7 exacerbation of existing health inequalities 8,9 and missed diagnoses of common conditions including cancer, particularly haematological malignancies and cardiovascular disease, 10 may all have exacerbated mortality alongside the large number of COVID-19–related deaths. 11–14 Effective clinical interventions include the finding that corticosteroids may play a role in alleviating the implicated pathologic inflammatory response, reducing mortality in critically ill patients. 15,16 Mitigating actions for infection prevention included advising those deemed extremely likely to be vulnerable to COVID-19 to self-isolate, termed ‘shielding,’ for 12 weeks. 17

Shielding, and the need to protect the vulnerable was initially announced on 12th March and subsequently implemented across the NHS as a three-step process. Firstly, national datasets were searched to identify individuals at ‘high risk,’ of developing complications following COVID-19 infection, based on criteria agreed by the UK’s Chief Medical Officers. Secondly, primary care data were

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searched centrally (data are held by NHS Digital) using these clinical criteria, and the people identified sent a letter advising them they were on the Shielded Patient List (SPL). This process was not without problems, with some patients having died and others not considering themselves vulnerable. General practitioners (GPs) then added and subtracted patients from this list of people at ‘high risk’. GPs then contacted their patients to confirm or add them to the ‘high risk’ category, or to let them know they were reclassified as ‘medium’ or ‘low’ risk. Template letters were provided to support this process. GPs coded into computerised medical records (CMR) those they considered ‘high risk’. The first letter to GPs was on 21st March, with a follow-up on 3rd April, with a request this work was completed by 14th April, all dates well within COVID-19’s first wave mortality peak (these dates correspond to International Standards Organisation (ISO) weeks 12, 14 and 16, Fig. 1).

We carried out this study to test whether recommending those at ‘high risk’ to shield may have been effective and reduced mortality. We analysed whether people in the ‘high risk’ category, aged 40 years or older, receiving shielding advice reinforced by their GP, reduced the risk of mortality compared with a matched cohort of people not advised to shield.

Data for the study were extracted between International Standards Organisation (ISO) Weeks 12–39 (16/3/2020–27/9/2020), giving a maximum observation period of 195 days depending on the date GPs contacted their patient with shielding advice. We report the study according to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidance.

Population and settings

We included people aged 40 years old and above, registered with general practices who are part of the Oxford-Royal College of General Practitioners (RCPG) Research and Surveillance Centre (RSC), a nationally representative population (N = 3,994,125). Our exposed group were people flagged as ‘high risk’ of COVID-19 and needing to shield for 12 weeks. We started our observation period from 16th March 2020. People were included from the date when the ‘high risk’ code was recorded in their CMR. Patients entered the cohort on the index date when the shielding code was first added to their electronic health record, with matched controls added from the same date.

Method

Study design

Our primary analysis was a matched cohort study to compare the risk of mortality in those who were at ‘high risk’ and advised to shield compared with those who were not, using propensity-matched controls. We also conducted a sensitivity analysis using an exact matched cohort. Our outcome measure was hazard ratio (HR) of mortality between the two groups using Cox’s proportional hazards model, adjusted for baseline covariates.

We constructed three mutually exclusive follow-up periods, estimating distinct hazard ratios for the shielding effect in each follow-up period, because we found the hazard of mortality changed over time. We divide the 12-week shielding period into the first three weeks (0–21days), and subsequent nine weeks (22–84 days), then the remainder of our period of observation.

Fig. 1. Mortality in people aged ≥45 years old per 100,000 of the English primary care sentinel network population by international standards organisation (ISO) week, comparing this year’s death rate with that for the previous five years. The peak in mortality, weeks 12 to 22, coincides with the first wave of the COVID-19 pandemic. 

Our primary outcome was all-cause mortality during the study period. We measured time-to-event from the date a ‘high risk’ term was included in a patient’s record until death, the study observational period ends (195 days) or the participant is censored, in this study de-registered from their general practice. Our primary variable of interest is if people were flagged as ‘high risk’ of COVID-19 complications and recommended to shield.

Variables for analysis included a wide range of demographic and clinical risk groups thought to impact on COVID-19.

We included the following sociodemographic variables: sex, age, ethnicity divided into Asian, White, and Black, Mixed and Other, using an ontology to maximise case identification, household size as determined based upon a pseudonymised household key derived from identical addresses, practice-level urban-rural status as derived from Lower Layer Super Output Area (LSOA, a geographical subunit with a minimum population of 1,000), socioeconomic status using the Index of Multiple Deprivation (IMD) quintiles (we combined the two most deprived quintiles as there

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are almost no lowest quintile people in rural areas), body mass index (BMI) using World Health Organisation categorisation of overweight (25–29Kg/m²), obese (BMI 30–34Kg/m²) and severely obese (BMI ≥ 35Kg/m²), and smoking status divided into current, ex-smokers and non-smokers. We also added possible surrogate markers of complexity care. These included recording if individuals were care home residents, if the patient has a care plan (patient-held summaries of health and care needs, generally provided to people with more complex needs), or polypharmacy, where we divided prescriptions into 1–2, 3–4, or 5 or more different long-term medications. We defined polypharmacy as 5 or more.

We included the following clinical risk groups as they may have been associated with an increased mortality rate: hypertension, chronic kidney disease (CKD) defined as stages 3–5, rheumatoid arthritis, heart disease (including acute myocardial infarction, atrial fibrillation and congestive cardiac failure), stroke (haemorrhagic and ischaemic), haematological malignancy (including Hodgkin's lymphoma, non-Hodgkin's lymphoma, leukaemia, myeloma), learning disability and an immunocompromised state (excluding malignancy) due to taking medication for inflammatory conditions, chronic respiratory disease (including asthma) and chronic obstructive pulmonary disease (COPD). We included the use of steroid inhalers in the last 6 months and use of inhaled bronchodilators in the last 6 months as steroids may impact on disease progression.

Comparator

Each patient advised to shield was matched to a non-shielded patient in a 1:1 fixed ratio. People were matched on the basis of propensity scores and on the following exact matching variables: sex, age (banded), ethnicity (banded), house size (banded), asthma diagnosis and history of inhaler use in the 6 months prior to the study start date (both steroid inhalers and inhaled bronchodilators). The propensity score used the exact matching baseline variables listed above plus the following study variables: smoking status, care home status, history of a care plan in the two years prior to the study start date.

Outcomes

We report unadjusted rates of survival comparing the unsheltered (n = 1348,354), and shielded (n = 97,963). We report HRs in our matched cohort between shielded people and propensity-matched controls, reporting separate HRs for any periods where there was a marked difference in risk.

Statistical methods

Propensity scores (the likelihood of being given a code for shielding) were estimated using logistic regression. We fitted the propensity score model by using baseline characteristics at the individual start date for all patients, the date their ‘high risk’ code was recorded in their record. To mitigate effects of immortal time bias, study entry date of unshielded individuals coincided with their shielded counterpart. Matching was based on both exact matching variables and distance within a calliper (setting a calliper width at 0.2 of the standard deviation of the logit of the propensity score). We used descriptive statistics to characterise the study cohort (Table 1). Differences were quantified using standardised mean differences (SMD), with a score under 0.1 indicating good balance. Crude mortality incidence rates with 95% confidence intervals were calculated.

To generate hazard ratios, we used Cox’s proportional hazards model, adjusted for baseline covariates, fitting two models: the base model and an adjusted model. The base model included the shielding status indicator variable only. The adjusted model included exact matching variables, all variables used in the propensity score, and, in a sensitivity analysis, groups based on quintiles of propensity scores. We tested the proportional hazards assumption for the adjusted survival model and we accommodated deviation from the proportional hazards assumption by fitting piece-wise constant coefficients for the shielding status in three contiguous follow up periods evaluated posthoc. Epochs that were derived identified time periods where there were non-time-varying effects. The follow-up period was divided in 84 days (to account for the 12-week recommended shielding period) and beyond 84 days. Iterative halving of these two sets of follow-up periods till the proportional hazards assumption was not violated led to the three epochs of: 0–21 days, 22–84 days, and greater than 84 days.

We carried out a sensitivity analysis fitting a survival model to an exact matched cohort comparing people recommended to shield (n = 24,752) and those not (n = 61,566).

We also report the crude mortality in the people GPs regarded from high to moderate or low risk (see also Supplementary Materials).

Ethical approval

The RCGP RSC’s work concerning SARS-CoV-2 has been approved by Public Health England’s Caldicott Guardian Committee as fitting under Regulation 3 of the Health Service Control Patient Information Regulations 2002. The study was approved by RCGP.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation nor writing of the manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

We identified 1,446,317 patients aged 40 years or more in the RCGP RSC population fully registered on 16th March 2020. Of these 97,963 (6.77%) were recommended to shield. A propensity-matched cohort was created for 77,360 of these patients; the shielded and non-shielded groups were well matched at baseline (Table 1).

We describe the time from the recommendation to shield being made to patients being contacted by their GP. We report overall unadjusted and adjusted mortality rates, then how the risk of mortality varied with time, and which elements of the model appeared to be associated with mortality.

Exposure to the recommendation to shield

The first shielding letter was issued to GPs on Saturday 21st March 2020. Following the start of implementation from 22nd March 2020, many patients were notified directly of the need to shield. This was augmented by GPs notifying patients who needed to shield and coding they had done so. A quarter of patients were notified by their GP within 4 days of receiving this request, half in 24 days and 75% within 30 days (Fig. 2). The mean duration was 26.5 days. The target date for completion was Tuesday 14th April (day 24) and half were completed by then. Half of these recommendations to shield would have been received before the pandemic peaked (week 16, 1319th April), and three-quarters before the excess peak in mortality was over (Figs. 1 and 2).
## Table 1
Distribution of propensity score matching variables for matched cohorts within RCGP RSC cohort, sociodemographic and clinical covariates.

| Variable                  | Category                  | Shielded Percentage (%) | Not Shielded Percentage (%) |
|---------------------------|---------------------------|-------------------------|-----------------------------|
| **Socio-demographic variables:** |                           |                         |                             |
| Sample size               |                           | 77,360                  | 77,360                      |
| Sex                       | Female                    | 41,675                  | 41,675                      |
|                           | Male                      | 35,685                  | 35,685                      |
| Age Band                  | 40–64                     | 30,375                  | 30,375                      |
|                           | 65–74                     | 19,993                  | 19,993                      |
|                           | 75+                       | 26,992                  | 26,992                      |
| Ethnicity                 | White                     | 69,824                  | 69,824                      |
|                           | Asian                     | 3,813                   | 3,813                       |
|                           | Black/Mixed/Other         | 3,723                   | 3,723                       |
| IMD quintile              | 1                         | 28,440                  | 28,440                      |
|                           | 2                         | 15,405                  | 15,405                      |
|                           | 3                         | 16,031                  | 16,031                      |
|                           | 4                         | 17,484                  | 17,484                      |
| Household dwelling size   | 1                         | 26,032                  | 26,032                      |
|                           | 2–4                       | 45,760                  | 45,760                      |
|                           | 5–8                       | 3,964                   | 3,964                       |
|                           | 9+                        | 1,604                   | 1,604                       |
| Urban Rural Indicator     | Rural                     | 13,783                  | 13,783                      |
|                           | Urban                     | 63,577                  | 63,577                      |
| BMI band                  | Normal weight             | 25,942                  | 23,869                      |
|                           | Overweight                | 26,853                  | 27,797                      |
|                           | Obese                     | 20,669                  | 21,958                      |
| Smoking Status            | Active Smoker             | 11,568                  | 11,590                      |
|                           | Ex-smoker                 | 48,202                  | 48,395                      |
|                           | Non-smoker                | 17,590                  | 17,375                      |
| Care Home Residency Status| No                        | 76,121                  | 76,113                      |
|                           | Yes                       | 1,390                   | 1,547                       |
| Care Plan within last 2 years| No                     | 72,952                  | 72,929                      |
|                           | Yes                       | 4,408                   | 4,431                       |
| Polypharmacy              | 1–2                       | 6,327                   | 6,298                       |
|                           | 3–4                       | 7,229                   | 7,414                       |
|                           | 5 or more                 | 63,604                  | 63,648                      |
| **Clinical covariates:**  |                           |                         |                             |
| Hypertension              | No                        | 36,092                  | 36,106                      |
|                           | Yes                       | 41,688                  | 41,254                      |
| Chronic Kidney Disease (Stages 3–5) | No | 62,366                  | 62,708                      |
|                           | Yes                       | 14,994                  | 14,652                      |
| Rheumatoid Arthritis      | No                        | 72,128                  | 72,128                      |
|                           | Yes                       | 5,232                   | 5,232                       |
| Heart disease             | Acute Myocardial Infarction| No                     | 72,061                      |
|                           | Yes                       | 5,299                   | 5,655                       |
| Atrial Fibrillation       | No                        | 67,763                  | 68,071                      |
|                           | Yes                       | 9,597                   | 9,289                       |
| Congestive Cardiac Failure| No                        | 70,595                  | 70,698                      |
|                           | Yes                       | 6,765                   | 6,662                       |
| Stroke                    | Haemorrhagic Stroke       | 76,420                  | 76,367                      |
|                           | Yes                       | 940                     | 993                         |
| Ischaemic Stroke          | No                        | 76,059                  | 75,958                      |
|                           | Yes                       | 1,301                   | 1,402                       |
| Chronic Respiratory Disease| Asthma Diagnosis       | No                     | 55,887                      |
|                           | Yes                       | 21,473                  | 21,473                      |
| COPD Diagnosis            | No                        | 62,132                  | 61,676                      |
|                           | Yes                       | 15,228                  | 15,684                      |
| Chronic Lung Disease      | No                        | 65,801                  | 65,136                      |
|                           | Yes                       | 11,559                  | 12,224                      |
| Inhaled Bronchodilators in last 6 months | No | 55,646                  | 56,672                      |
|                           | Yes                       | 21,714                  | 20,688                      |
| Steroid Inhalers in last 6 months | No | 58,276                  | 59,436                      |
|                           | Yes                       | 19,084                  | 17,924                      |
| Malignancy                | Hodgkin’s Lymphoma       | 77,348                  | 77,350                      |
|                           | Yes                       | 12                     | 10                          |
| Non-Hodgkin’s Lymphoma    | No                        | 77,196                  | 77,230                      |
|                           | Yes                       | 164                     | 130                         |
| Leukaemia                 | No                        | 77,252                  | 77,302                      |
|                           | Yes                       | 108                     | 58                          |
| Myeloma                   | No                        | 77,312                  | 77,311                      |
|                           | Yes                       | 48                      | 29                          |
| Immunocompromised         | No                        | 74,972                  | 75,279                      |
|                           | Yes                       | 2,388                   | 2,081                       |
| Learning Disability       | No                        | 76,725                  | 76,628                      |
|                           | Yes                       | 635                     | 732                         |
Mortality risk associated with shielding status

Our unadjusted analysis showed people at ‘high risk’ from COVID-19, who were recommended to shield had an overall increased risk of all-cause mortality (HR 2.13 95% CI 1.95–2.33; p < 0.0001, Table 2). After adjustment, people recommended to shield still had higher all-cause mortality than those not recommended (HR=1.70, 95%CI: 1.60–1.80, p < 0.0001, Table 3B).

Time-varying effect of shielding on mortality

While overall recommendation to shield is associated with increased all-cause mortality across the whole study period, there was considerable variation over time (Fig. 3).

In the first 21 days following GP recommendation to shield, there was a halving of the risk of mortality compared to the matched control population (HR=0.4952, p < 0.0001). However, the risk of all-cause mortality increased in the remaining nine weeks of proposed shielding, rising to one-and-a-half times that of the control population (HR=1.5449 , p < 0.0001). After the shielding period ended, mortality in the shielding group was substantially higher, over two-and-a-half times that of controls (HR= 2.6143, p < 0.0001, Table 3A).

We report the association of individual variables with mortality as these may inform which variables to include in any future shielding intervention (Table 3B).

Across sociodemographic factors, male gender, age, deprivation (where the most deprived two quintiles were at greater risk), living alone or in large (including likely communal) dwellings, and polypharmacy were associated with greater risk. The greatest risks were age 75-years and older (HR = 3.17, 95%CI:2.86–3.50, p < 0.0001), households of 9 or more, which is likely to include residential homes (HR = 2.74, 95%CI:2.38–3.15, p < 0.0001) and polypharmacy (HR = 2.63, 95%CI:2.13–3.24, p < 0.0001). Asian ethnicity and obesity were associated with lower risk (Table 3B).

Cardiovascular disease, CKD, atrial fibrillation and heart failure were associated with greater risk; whereas this was not the case for hypertension and people who have had myocardial infarctions. People who have had a haemorrhagic stroke were at greater risk, whereas those with ischaemic strokes were not.

Asthma diagnosis was associated with lower risk, whereas COPD was associated with an increased risk of mortality. Interestingly those prescribed an inhaled bronchodilator were at increased risk of mortality (HR = 1.1748, 95%CI:1.0734–1.2858, p < 0.001), whereas those prescribed a steroid inhaler had a lower risk of mortality (HR=0.880, 95%CI:0.798–0.971, p=0.011).

Among haematological malignancies, people diagnosed with Hodgkin’s lymphoma were at particularly high risk (HR = 12.24, 95%CI:4.58–32.67, p < 0.0001), though the confidence interval is wide. There was also increased risk in other lymphoma’s but not demonstrated for leukaemia or myeloma.

People who risk being immunocompromised, outside of those with malignancies, were not at increased risk.

The sensitivity analysis, a complete cases survival analysis, reported similar findings. The people who GPs regraded to moderate or low risk had a similar mortality to those not advised to shield (Supplementary Materials).

Discussion

Principal findings

Recommendation to shield was associated with a short-term effect in reducing the risk of mortality in the shielded population, compared with matched controls. However, the protective effect lasted less than twelve weeks. At the end of the shielding period, mortality HR for the shielded group rose to more than two-and-a-half times that of the matched group. Additionally, we have associations with increased mortality, which may help improve the design of any future interventions.

Implications

Shielding may provide a short-term decrease in the risk of mortality, but the intervention as delivered across the first wave of the pandemic may be insufficient. However, it is impossible to know whether this group would have had a different relative risk had they not been shielded; or if the matched controls might have benefited more.

GPs’ assessment of the greater risk of mortality appears to have face validity; notwithstanding these cohorts were matched for sociodemographic factors and clinical conditions, the individuals picked out for shielding overall had a greater risk of mortality. Similarly, those GPs reclassified as medium or low risk had a similar unadjusted mortality to those not advised to shield (Supplementary Materials). Given the negative consequences of shielding (on physical and mental health, not accessing vital medical care, etc.), policymakers should carefully consider the extent to which
Table 3
(A) Base Model Hazard ratios for base survival models of matched cohort.

| Hazard Ratio (HR) | Lower 95% confidence interval | Upper 95% confidence interval | Probability p |
|------------------|-------------------------------|-------------------------------|--------------|
| Shielding Status follow-up 0–21 days | 0.4952 | 0.4144 | 0.5918 | < 0.0001 |
| Shielding Status follow-up 22–84 days | 1.5449 | 1.408 | 1.6952 | < 0.0001 |
| Shielding Status follow-up 85–195 days | 2.6143 | 2.3831 | 2.868 | < 0.0001 |

(B) Fully adjusted model Hazard ratios for fully adjusted survival models of matched cohort.

| Hazard Ratio (HR) | Lower 95% confidence interval | Upper 95% confidence interval | Probability p |
|------------------|-------------------------------|-------------------------------|--------------|
| Shielding Category (ref No) | 1.6090 | 1.6000 | 1.8020 | < 0.0001 |
| Shielding Status follow-up 0–21 days | 0.4918 | 0.4116 | 0.5878 | < 0.0001 |
| Shielding Status follow-up 22–84 days | 1.5243 | 1.389 | 1.6727 | < 0.0001 |
| Shielding Status follow-up 85–195 days | 2.587 | 2.3579 | 2.8383 | < 0.0001 |
| Sex (ref level: female) | 1.3670 | 1.2866 | 1.4524 | < 0.0001 |
| Age Band (ref level 40–64) | 65–74 | 1.8311 | 1.6470 | 2.0358 | < 0.0001 |
| Ethnicity (ref level White) | 75+ | 3.1662 | 2.8636 | 3.2008 | < 0.0001 |
| Deprivation Status (Quintiles) | Q3 | 0.7003 | 0.5895 | 0.8320 | < 0.0001 |
| Q4 | 0.8494 | 0.7092 | 1.0172 | 0.0760 |
| Q5 (least deprived) | 0.8762 | 0.8086 | 0.9495 | 0.0013 |
| Household Dwelling Size (ref level one individual) | 2–4 | 0.8889 | 0.8325 | 0.9491 | 0.0004 |
| 5–8 | 1.4356 | 1.2351 | 1.6686 | < 0.0001 |
| 9 or more individuals | 2.7377 | 2.3814 | 3.1474 | < 0.0001 |
| Urban-Rural Practice (ref Level Rural) | Urban | 0.9911 | 0.9173 | 1.0708 | 0.8207 |
| BMI Band (ref level Normal weight) | Overweight | 0.6847 | 0.6397 | 0.7328 | < 0.0001 |
| Obese | 0.5904 | 0.5445 | 0.6402 | < 0.0001 |
| Severely Obese | 0.7345 | 0.6214 | 0.8682 | 0.0003 |
| Polypharmacy (ref level: 1 or 2 drugs) | 3,4 medications | 1.2827 | 0.9941 | 1.6549 | 0.0556 |
| 5 or more medications | 2.6265 | 2.1278 | 3.2421 | < 0.0001 |
| Clinical condition, reference: absence | Hypertension | 0.9332 | 0.8744 | 0.996 | 0.0375 |
| Chronic Kidney Disease (Stages 3–5) | Heart disease | 1.2741 | 1.1932 | 1.3606 | < 0.0001 |
| Acute Myocardial Infarction | 1.0594 | 0.9663 | 1.1615 | 0.2188 |
| Atrial Fibrillation | 1.2075 | 1.1220 | 1.2994 | < 0.0001 |
| Congestive Cardiac Failure | 1.5792 | 1.4577 | 1.7109 | < 0.0001 |
| Stroke | Haemorrhagic Stroke | 1.3072 | 1.0869 | 1.5721 | 0.0044 |
| Ischaemic Stroke | 1.0418 | 0.8914 | 1.2175 | 0.6066 |
| Chronic Respiratory Disease | Asthma Diagnosis | 0.7309 | 0.6698 | 0.7976 | < 0.0001 |
| COPD | 1.1789 | 1.0480 | 1.3263 | 0.0061 |
| Chronic Lung Disease | 0.8730 | 0.7712 | 0.9883 | 0.0318 |
| Inhaled Bronchodilators in last 6 months | 1.1748 | 1.0734 | 1.2858 | 0.0005 |
| Steroid Inhalers in last 6 months | 0.8804 | 0.7982 | 0.9712 | 0.019 |
| Haematological Malignancy | Hodgkin's lymphoma | 12.236 | 4.5836 | 32.6645 | < 0.0001 |
| Non-Hodgkin's Lymphoma | 2.1391 | 1.2383 | 3.0951 | 0.0064 |
| Leukaemia | 1.3382 | 0.637 | 2.8113 | 0.4417 |
| Myeloma | 2.2025 | 0.915 | 5.3017 | 0.0781 |
| Immunosuppressed (excluding malignancy) | 0.8255 | 0.6744 | 1.0105 | 0.0630 |
| Rheumatoid Arthritis | 0.6934 | 0.5974 | 0.8049 | < 0.0001 |
| Learning Disability | 1.2309 | 0.9161 | 1.6539 | 0.1680 |
high risk patients should be asked to shield in future waves of the pandemic. It is possible that these results, combined with others could allow a more focussed approach.

Comparison with the literature

There is a dearth of analyses as to whether shielding should be part of our response to future waves of COVID-19. Segmentation of the population to enable shielding of the extremely clinically vulnerable individuals whilst the wider population returns to normalcy has been suggested. It has also been proposed that shielding for 38 weeks alongside mask-wearing and social distancing may see up to 62% reduction in mortality. Whilst lockdown is effective, it has immense socioeconomic impact and may exacerbate existing social inequalities, and whilst local level responses are a nuanced alternative, how shielding might be incorporated is far from clear. Those we identify at greatest risk might be more selectively shielded. Many of our findings are corroborated. There is other evidence suggesting that age is the overwhelmingly dominant factor for mortality risk (those ≥ 45 years old saw increased mortality risk of 20 – 35% compared to those < 45, with 0–14% increased risk).

We have previously reported the association of chronic disease with mortality, which has also been reported in other studies. We reported the increased risk of mortality associated with care homes, which too has been found by other groups. The association with living conditions has also been reported, given that transmission of infectious disease is assumed to be density-dependent.

The effectiveness of shielding may be questioned when mortality in care home communities has been high. There are important ethical considerations when shielding, with a balance required between the risk of disease transmission and the mental and cognitive health effects of isolation, particularly with the lack of visitors.

The challenge is to develop specific and structured rationalised shielding policy that is relevant to an individual’s circumstances which extends to their immediate support system and employers and is not jeopardised by financial or professional obstacles.

Government guidance regarding shielding has been deemed vague and not behaviourally specific. There must be consideration as to what extent shielding is realistic for those who cannot shield due to work and family commitments. GPs have had a significant role in recommending shielding. NHS Digital reported at the end of the shielding period that 30.1% of the additional recommendations to shield have come from GPs. GPs have also deducted 14.7% of people from the ‘high risk’ list; suggesting a significant impact on the shaping of the list.

Strengths and limitations

The strengths of this study include a large population size (n=1,446,317) which has a large proportion of shielded individuals in the sample (6.77%), and that both the unadjusted and fully adjusted models yielded similar results.

Limitations include that routine clinical data does not contain much information about the variation in disease severity. The difference between the GP-nominated group to shield and the matched controls might be accounted for by disease severity. Whilst we looked to include surrogates for this, such as having a care plan and polypharmacy, the people who GPs recommended to shield had worse mortality of the latter period after the end of shielding.

The mean time from symptom onset to death in COVID-19 is 17.8 days. It might be questioned whether there was time for shielding to work. However, with intention to recommend shielding announced by the government prior to commencement and with the delay prior to GPs contacting and coding high risk patients, GPs’ action was reinforcement, as opposed to the only element, of the intervention. With a mean 26.5-day delay in time for shield coding addition, the meantime for symptom onset to death would have been accounted for.

The study of shielding classification does not imply full compliance with shielding guidelines. The analysis would have benefited from including an indicator of previous engagement in preventative healthcare. This would provide an approximate indication as to the likelihood of the patient to engage and comply with
shielding, as well as disease management, in partnership with their care team. Finally, whilst we appreciate that mortality risk for the shielded group was greater in the longer term, we feel that is unlikely that recommendation to shield resulted in this later greater risk of mortality. The greater mortality rate corresponds with the summer months where there was little community transmission, thus this may represent the overall greater risk of mortality of the shielded group, reflecting the validity of their GPs’ clinical judgement.

**Call for further research**

Additional analyses should urgently examine whether there was a genuine early reduction in mortality and if the intervention were more intensive whether this would have a sustained effect. Behavioural research into how compliance can be enacted and maintained as well as psychological and economic research into how to maintain mental health and to execute shielding without inducing financial stress can be supportive towards implementing a more holistic course of action.

**Conclusions**

The initial three-week period of shielding following contact from their GP was associated with half the mortality risk compared with matched controls. After this period, any benefit disappeared, and the shielding group has a 50% higher risk of mortality. At the end of the 12-week shielding period, those asked to shield had an increased risk of mortality over two-and-a-half times more than controls, a constant difference they maintained across the summer. These data are challenging to interpret, but it is plausible that shielding had an initial very positive effect, that then partially wore off, followed by a reversion to a higher rate of mortality. The associations from this observational study should be urgently tested on another dataset, and the reinstatement of more targeted shielding should be considered in the emergent second wave of COVID-19.

**Data sharing**

The RCGP RSC data set can be accessed by researchers, approval is on a project-by-project basis (www.rcgp.org.uk/rsc). Ethical approval by an NHS Research Ethics Committee is needed before any data release/other appropriate approval. Researchers wishing to directly analyse the patient-level pseudonymised data will be required to complete information governance training and work on the data from the secure servers at the University of Surrey. Patient-level data cannot be taken out of the secure network. We encourage interested researchers to attend the short courses on how to analyse primary-care data/RCGP RSC data offered twice a year.

**Declaration of Competing Interest**

Sdel is the director of RCGP RSC. He has unrelated projects funded by GSK, Seqirus and has been a member of Global Advisory Boards for Seqirus and Sanofi. FDRH reports personal fees from Novartis and Boehringer Ingelheim and grants from Pfizer. All other authors declare no competing interests.

**CRediT authorship contribution statement**

**Azmaeen Zarif:** Conceptualization, Investigation, Writing - original draft, Writing - review & editing, Formal analysis. **Mark Joy:** Conceptualization, Investigation, Validation, Writing - review & editing, Formal analysis. **Julian Sherlock:** Data curation, Validation, Writing - review & editing, Formal analysis. **James P Sheppard:** Investigation, Writing - review & editing, Formal analysis. **Oluwafunmi Akinyemi:** Writing - review & editing, Formal analysis. **Clare R Bankhead:** Writing - review & editing, Formal analysis. **Alexandra Deeks:** Writing - review & editing, Formal analysis. **Filipa Ferreira:** Writing - review & editing, Formal analysis. **Nicholas Jones:** Investigation, Writing - review & editing, Formal analysis. **Harshana Liyanage:** Writing - review & editing, Formal analysis. **Dylan McGagh:** Conceptualization, Data curation, Writing - review & editing, Formal analysis. **Brian Nicholson:** Investigation, Writing - review & editing, Formal analysis. **Manasa Tripathy:** Writing - review & editing, Formal analysis. **Cecilia Okusi:** Writing - review & editing, Formal analysis. **Richard Hobbs:** Writing - review & editing, Formal analysis. **Simon de Lusignan:** Conceptualization, Investigation, Validation, Writing - review & editing, Formal analysis.

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**Supplementary materials**

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2021.04.033.

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