Risk mitigating behaviours in people with inflammatory skin and joint disease during the COVID-19 pandemic differ by treatment type

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Risk mitigating behaviours in people with inflammatory skin and joint disease during the COVID-19 pandemic differ by treatment type: a cross-sectional patient survey

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Running head: Shielding behaviour in the pandemic in inflammatory skin and joint disease differs by treatment type

What is already known about this subject?

- At the beginning of the COVID-19 pandemic, patients with immune-mediated inflammatory diseases (IMIDs) on targeted systemic therapies were considered to be at higher risk of severe COVID-19. Subsequent clinician-reported registry data suggest targeted systemic therapy use is associated with fewer adverse COVID-19 outcomes compared to no systemic therapy.

What does this study add?

- We characterise shielding behaviour in 3,720 patients with IMIDs from a global self-report survey. Use of targeted systemic therapy associates with increased shielding behaviour, compared with standard systemics or no therapy, as do demographic risk factors for severe COVID-19 including male gender and obesity.

- Greater risk-mitigating behaviour among people with IMIDs receiving targeted therapies may contribute to the reported lower risk of adverse COVID-19 outcomes. Behaviour variation across treatment groups reinforces the need for clear evidence-based patient communication on risk mitigation strategies. These data may help inform updated public health guidelines as the pandemic continues.

Abstract

Objectives

Registry data suggest that people with immune-mediated inflammatory diseases (IMIDs) receiving targeted systemic therapies have fewer adverse COVID-19 outcomes compared to patients receiving no systemic treatments. We used international patient survey data to explore the hypothesis that greater risk-mitigating behaviour in those receiving targeted therapies may account, at least in part, for this observation.

Methods

Online surveys were completed by individuals with psoriasis (globally) or Rheumatic and Musculoskeletal Diseases (RMD) (UK only) between 4th May and 7th September 2020. We used multiple logistic regression to assess the association between treatment type and risk-mitigating behaviour, adjusting for clinical and demographic characteristics. We characterised international variation in a mixed effects model.

Results

Of 3,720 participants (2,869 psoriasis, 851 RMD) from 74 countries, 2,262 (60.8%) reported the most stringent risk-mitigating behaviour (classified here under the umbrella term 'shielding'). A greater proportion of those receiving targeted therapies (biologics and JAK inhibitors) reported shielding compared to those receiving no systemic therapy (adjusted odds ratio [OR] 1.63, 95% CI 1.35-1.97) and standard systemic agents (OR 1.39, 95% CI 1.22-1.56). Shielding was associated with established risk factors for severe COVID-19 (male sex [OR 1.14, 95% CI 1.05-1.24], obesity [OR 1.38, 95% CI 1.23-1.54], comorbidity burden [OR 1.43, 95% CI 1.15-1.78]), a primary indication of RMD (OR 1.37, 95% CI 1.27-1.48) and a positive anxiety or depression screen (OR 1.57, 95% CI 1.36-1.80). Modest differences in the proportion shielding were observed across nations.

Conclusions

Greater risk-mitigating behaviour among people with IMIDs receiving targeted therapies may contribute to the reported lower risk of adverse COVID-19 outcomes. The behaviour variation across treatment groups, IMIDs and nations reinforces the need for clear evidence-based patient communication on risk mitigation strategies and may help inform updated public health guidelines as the pandemic continues.

Introduction

The COVID-19 pandemic, caused by the highly infectious SARS-CoV-2 virus, represents an unprecedented global health crisis[1,2]. Death from COVID-19 is associated with male gender, older age, Asian/Black ethnicity, and coexisting conditions including cardiovascular disease and obesity[3,4]. Guided by international recommendations from the World Health Organization (WHO), public health risk mitigating measures such as social/physical distancing were introduced early in the pandemic to limit community transmission of COVID-19[5–8]. The WHO also recommended more stringent protection measures to reduce exposure risk in groups at higher risk of severe COVID-19[9]. This was referred to as 'shielding', and in the UK, was incorporated into Government policy where individuals classed as clinically extremely vulnerable were advised to physically isolate at home and avoid face-to-face interactions[7].

Informed by pre-COVID-19 observational studies on drug-related risks of serious infection[10–13], individuals with immune-mediated inflammatory diseases (IMIDs) receiving drugs that affect the immune system were considered at higher risk of severe COVID-19[14,15]. Whilst limited evidence has been published to date on drug-specific COVID-19 risks in IMIDs, rheumatoid arthritis, systemic lupus erythematosus and psoriasis were collectively suggested as risk factors for death using UK primary care data linked to hospital records from 17 million adults[3]. Global clinician-reported registry data in rheumatic diseases, psoriasis and inflammatory bowel disease have further suggested a differential risk of severe COVID-19 associated with different treatment types. In particular, use of targeted systemic therapies (biologics and Janus Kinase [JAK] inhibitors) was associated with a reduced risk of adverse COVID-19 outcomes, compared with no treatment or standard systemic agents[16–18]. It remains unclear if this is attributable to therapeutic modulation of the host antiviral immune and inflammatory response (i.e. biological mechanisms) or enhanced shielding behaviour in patients receiving targeted therapies (resulting in a lower infectious dose of SARS-CoV-2). There is an urgent need to address this knowledge gap since targeted and standard systemic therapies represent the mainstay of treatment in moderate to severe IMIDs.

Rheumatic and musculoskeletal diseases (RMDs) and psoriasis are common IMIDs that are closely related; psoriasis is the commonest immune-mediated skin disease associated with inflammatory arthritis, both conditions have a high prevalence of multimorbidity and are effectively treated with targeted and standard systemic therapies. We focused on RMDs and psoriasis as representative IMIDs and used global self-report survey data to explore the notion that individuals receiving different types of treatment exhibit distinct risk mitigating behaviours in the pandemic.

Methods

Study design, participants

Two online self-report surveys with aligned questions, permitting a combined analysis of data, were developed for people with psoriasis (Psoriasis Patient Registry for Outcomes, Therapy and Epidemiology of COVID-19 Infection *Me* [PsoProtect*Me*]*;* www.psoprotectme.org) and RMDs (COVID-19 Rheumatology Register [CORE-UK]; https://www.redcap02.medstats.org.uk/redcap/surveys/?s=LCA3L4JHXW). PsoProtect*Me* (available in 8 different languages) was promoted globally following its launch on 4th May 2020 and CORE-UK was subsequently launched on 12th June 2020 and promoted in the UK. The surveys were disseminated via social media, patient organisations (Table S1) and clinical networks. The eligibility criterion was any person (all ages) with a clinician-confirmed diagnosis of psoriasis (PsoProtect*Me*) or RMD (CORE-UK), irrespective of COVID-19 status (REC ref 20/YH/0135). Data were collected and managed using REDCap electronic data capture tools licensed to King's College London Division of Health and Social Care Research[19].

Variables

Minimum sufficient core sets of variables within the surveys were defined by our study group of clinicians, epidemiologists, health data researchers and patient representatives. Patient Health Questionnaire-2 (PHQ-2) and Generalized Anxiety Disorder 2-item scale (GAD-2) were used to screen for depression and anxiety, respectively; scores of 3 or more were positive. Adherence was assessed with a single item question which asked if the individual had stopped or delayed their medication in the pandemic.

Risk mitigating behaviour was assessed with the following question: '*Over the past 30 days, what methods have you been using to protect yourself from COVID-19?'*. Respondents could select any of the following options: (1) Shielding (quarantine, strict distancing from family members in the home); (2) Self-isolation (quarantine, staying home, avoiding others); (3) Social distancing (avoiding crowds and large groups of people); (4) Using gloves and/or masks during social interactions; (5) None. The most stringent risk-mitigating behaviour was classified under the umbrella term 'shielding', encompassing (1) shielding and (2) self-isolation. 'Shielding' was considered as a binary variable; any respondent who selected options (1) or (2) were coded as having shielded, and those selecting (3), (4) or (5) as having not shielded.

UK participants were also asked whether they were advised to shield using the following question; '*Did you receive a letter or text from the NHS asking you to take additional protective*

measures including to stay at home at all times and avoid all face-to-face contact for at least 12 weeks?'.

Statistical methods

Data were extracted on 7th September 2020 and analysed using Stata version 16. Continuous variables were reported using means and standard deviations (SD), and categorical/dichotomous variables as numbers and percentages. To account for partially completed surveys, respondents who completed more than 50% of variables were included. Individuals completing CORE-UK and PsoProtect*Me* were classified as having a primary diagnosis of RMD and psoriasis, respectively.

We characterised the demographic, socio-economic and disease-specific factors associated with the primary outcome of shielding behaviour in the pandemic. The key exposure measure was IMID treatment type in the pandemic, comprising 3 mutually exclusive categories:

(1) **Targeted therapy: biologics and JAK inhibitors** (TNF inhibitors: adalimumab, certolizumab pegol, etanercept, infliximab, golimumab; IL-17 inhibitors: brodalumab, ixekizumab, secukinumab; IL12/IL-23p40 or IL-23p19 inhibitors: guselkumab, risankizumab, tildrakizumab, ustekinumab; IL-6 inhibitors tocilizumab, sarilumab; JAK inhibitors: baricitinib, tofacitinib);

(2) **Standard systemic therapy** (methotrexate, ciclosporin, azathioprine, mycophenolate mofetil, fumaric acid esters/dimethylfumarate, sulfasalazine, leflunomide, acitretin, apremilast, chloroquine, hydroxychloroquine, prednisolone, tacrolimus);

(3) **No systemic therapy**.

Patients on combination targeted and standard systemic therapy were included in the targeted therapy group, and surveys with missing treatment data were excluded. Apremilast was included in the standard systemic therapy group since in clinician-reported registry analyses, it was not grouped with biologics (unlike JAK inhibitors)[17,18].

After excluding participants who self-reported current or prior confirmed/suspected COVID-19, associations with shielding status were assessed using: (a) a minimally adjusted logistic regression model including age and sex covariates; and (b) a fully adjusted model including a consensus list of covariates selected *a priori* as potentially influential on shielding behaviour on the basis of expert clinical opinion and existing evidence[20]. Treatment was included as a categorical variable in the fully adjusted model, with no systemic therapy as the reference group. Country of residence was included as a cluster variable. A count of the number of

comorbidities was generated. This was converted into a binary variable for analyses according to consensus clinical expert opinion of the study group: those with one or more comorbidity vs those with no comorbidities.

Two sensitivity analyses were performed on the fully adjusted multivariable regression models: (1) Multiple imputation using iterative chained equations with 20 sets of imputed data to account for missing covariate data; (2) Exclusion of respondents on no systemic therapy, with standard systemic therapy becoming the reference group. Adherence data was included as a covariate in this model.

As the COVID-19 pandemic progressed in countries over different time periods, we hypothesised that the impact of time on the relationship between treatment and shielding behaviour would vary between countries. To explore this, unadjusted estimates of shielding over time by treatment group were plotted for UK and non-UK survey respondents. Based on these plots we re-ran the multivariable model with UK respondents only including time as an interaction term with treatment, and as a fixed covariate, with a comparison of model fit. Time was converted to a binary variable, before or after 30th June. Shielding in the UK appeared to decrease after this date, which also coincided with the reopening of hospitality businesses (e.g. restaurants) across the UK.

To characterise international variations in shielding behaviour, a mixed effects logistic regression model was executed with country of residence as a random effect. The random effect captures the difference between national and overall sample means, enabling estimation of case-mix adjusted rates. The national effects on shielding were visualised using a caterpillar plot[21].

Results

Demographic, socio-economic and clinical characteristics of 3,720 study participants

Self-reported data from 3,720 individuals with a primary diagnosis of RMD (851, 22.9%) or psoriasis (2869, 77.1%) were available from 74 countries (including UK (2,578, 69.4%), Portugal (200, 5.4%), USA (165, 4.5%)) (demographic/clinical/socio-economic descriptions, Table 1). Survey completion rates were high, with a median of 94% of covariates of interest completed (interquartile range of 89 to 95). A total of 650 surveys (17%) had 100% data completion.

Two thousand two hundred and ninety-nine (61.8%) participants were not receiving a systemic agent for their psoriasis or RMD, 924 (24.8%) were receiving targeted therapies and 497 (13.4%) standard systemic agents. The three treatment groups had similar baseline characteristics including age, ethnicity, mean number per household and comorbidities. Non-adherence was also similar; 90 of 495 (18.2%) patients in the standard systemic therapy group reported non-adherence against medical advice, compared to 138 of 923 (15.0%) receiving targeted therapy. Of 257 (7.1%) participants who self-reported suspected or confirmed COVID-19, 80 (31.1%) were receiving a targeted therapy, 46 (17.9%) a standard systemic agent and 131 (51.0%) no systemic treatment. A lower proportion of those with COVID-19 reported shielding (143 of 257, 55.6%), compared to those without COVID-19 (2,051 of 3,352, 61.2%).

Risk mitigating behaviour differed by treatment type

Overall, 2,262 participants (60.8%) reported shielding. Of 1,632 participants self-reporting shielding in the UK, only 899 (55.1%) reported being specifically advised to shield (no data on shielding advice were available for non-UK participants). A greater proportion of those receiving targeted therapies (610 of 924, 66.0%) reported shielding compared with those receiving standard systemic agents (292 of 497, 58.8%) or no systemic therapy (1360 of 2299, 59.2%).

After excluding those with self-reported COVID-19, we used logistic regression models to investigate the observed differences in shielding by IMID treatment type. Compared to the reference group of no systemic therapy, an age and sex adjusted model for shielding behaviour estimated an odds ratio of 1.00 (95% CI 0.81 to 1.23) for those receiving standard systemic agents. In contrast, a significant association with shielding was observed for those receiving targeted therapies (OR 1.34, 95% CI 1.13 to 1.59) (Figure 1).

A fully adjusted multivariable logistic regression analysis was performed with a categorical treatment exposure variable: (1) targeted therapy; (2) standard systemic therapy; (3) no systemic therapy. The no systemic therapy group was used as the reference. Use of targeted therapy was associated with shielding compared to no systemic therapy (OR 1.63, 95% CI 1.35 to 1.97). Standard systemic therapy (OR 1.17, 95% CI 0.89 to 1.53) did not have a significant association with shielding. There were associations with shielding for RMD (OR 1.37, 95% CI 1.27 to 1.48), male sex (OR 1.14, 95% CI 1.05 to 1.24), comorbidity burden (OR 1.43, 95% CI 1.15 to 1.78), obesity (OR 1.37, 95% CI 1.23 to 1.54) and a positive anxiety or depression screen (OR 1.57, 95% CI 1.36 to 1.80) (Figure 2). In contrast, shielding was inversely associated with smoking (OR 0.73, 95% CI 0.63 to 0.85), full time employment (OR

0.66, 95% CI 0.49 to 0.88), >4 household members (OR 0.78, 95% CI 0.65 to 0.93) and key worker status (OR 0.55, 95% CI 0.44 to 0.68). No association was found with age (OR 1.00, 95% CI 0.99 to 1.00) or white ethnicity (OR 0.85, 95% CI 0.62 to 1.17).

Multivariable model sensitivity analyses

To account for missing data (Table 1), the multivariable model was rerun following multiple imputation. The magnitude and direction of associations did not change substantially (Table S2).

The model was also rerun excluding respondents on no systemic therapy, using standard systemic therapy as the reference group. The association between targeted therapy and shielding was preserved (OR 1.39, 95% CI 1.23 to 1.56). Therapy non-adherence was not associated with shielding (Table S3).

The influence of time (survey completion date) on shielding behaviour was explored across treatment groups. Estimated shielding behaviour generally decreased over time, however time had a differential impact in the UK (Figure S1) compared with non-UK countries (Figure S2). The multivariable model was therefore rerun with UK respondents only, first including time as a fixed covariate and secondly as an interaction term with treatment. The association between targeted therapy and shielding was preserved, with better model fit for the interaction term (further details in supplementary material).

The multivariable model was also rerun limiting shielding to only those who quarantined (i.e. option 1 of survey question on risk mitigating behaviour). The direction of the associations was preserved.

There was modest variation in risk mitigating behaviour across countries

A greater proportion of participants in the UK reported shielding compared to those elsewhere (63.3%, versus 55.0%). However, UK participants were also less likely to receive a targeted therapy (23.4%, versus 28.4%). A mixed effects model further showed modest variation around the sample mean in the proportion shielding in different countries, indicating broadly similar risk mitigating behaviours (Figure 3). Shielding was more prevalent in the UK, Canada and Argentina, but less prevalent in Portugal and Japan.

Discussion

We present global self-reported data on risk mitigating behaviours in 3,720 individuals with inflammatory joint and skin disease across 74 countries. Established risk factors for severe COVID-19 outcome including male sex, obesity and comorbidity burden were associated with stringent risk mitigating behaviour (classified here under the umbrella term 'shielding', encompassing self-reported shielding, quarantine, staying home or distancing within the home). Notably, use of targeted therapies (biologics and JAK inhibitors) was associated with shielding in comparison with no systemic therapy or standard systemic therapy. Although the differences in shielding behaviours across treatment groups in UK respondents were preserved when time was used as an interaction term, the observed decline in estimated shielding behaviour over time may help inform updated public health guidelines as the pandemic continues.

Our dataset is based on a large sample of individuals self-reporting RMD and psoriasis. Since there was no healthcare professional/record validation of survey responses, it is reassuring that key risk factors for severe COVID-19 in the general population such as male sex and obesity were associated with shielding. This is in keeping with public health messaging during the pandemic and indicates a representative and generalizable sample. Shielding was recommended in groups of individuals deemed at higher risk[7,9] on the premise that this would reduce the risk of COVID-19 transmission. More recently, evidence has emerged indicating shielding may also result in a less severe course of COVID-19 by reducing the frequency and intensity of exposures to SARS-CoV-2, thus lowering the infectious dose[22]. There is a growing body of evidence indicating that SARS-CoV-2 viral load positively correlates with disease severity[23,24], and that in animal models, greater SARS-CoV-2 dose at exposure correlates with higher viral load and worse outcomes[25].

Notably, increasing age was not associated with shielding behaviour in our dataset (despite an even spread of ages and 10.5% of our dataset being over age 70). This finding is in keeping with a recent international study of 8,317 individuals from the general population showing that age did not predict whether individuals took health precautions (mask wearing, social distancing, handwashing, staying home)[20]. Instead, beliefs that taking health precautions are effective and a concern for one's own health were important predictors. Consistent with this, we identified an association between shielding and anxiety/depression. A larger proportion of participants also reported shielding compared to those advised to shield, which may reflect the elevated rates of self-reported anxiety. Anxiety and depression has also been reported in previous observational studies, underscoring the mental health burden of the pandemic (which may at least in part be due to the impact of social isolation)[26–28]. While this finding suggests

accurate and representative data capture, more data are required on the severity and temporality of anxiety and depression.

Our study indicates a greater likelihood of shielding overall in individuals with a primary diagnosis of RMD compared with psoriasis, however the reasons underlying this are not clear. It may be attributable to differences in illness perception[29], use of treatments and prevalence of comorbidities. IMID-specific COVID-19 risks are unknown, and neither RMD nor psoriasis were included in WHO and national public health shielding recommendations per se[7,9]. The reasons underlying differences in shielding behaviours between treatment groups, including patient perceptions of COVID-19 risk, also warrant further study. Although there is a paucity of data on treatment-related beliefs in psoriasis, recent single centre cross-sectional patient survey data in inflammatory bowel disease indicate patients perceive biologics to be riskier than other therapies[29]. These perceptions may influence shielding behaviours and are important to address during patient-clinician interactions.

Our global data on shielding behaviour builds on the findings from a recent single centre audit of 1,693 UK patients with rheumatic diseases[26]. Forty six percent self-reported shielding, however shielding among different treatment groups was not explored. In line with our findings, the audit found that a lower proportion of individuals with COVID-19 shielded (39%) compared to those without COVID-19 (47%). Our study also complements emerging findings from international clinician-reported registries, indicating differences in COVID-19 outcomes between different treatment types. Among 600 patients with rheumatic diseases and COVID-19 reported to the COVID-19 Global Rheumatology Alliance registry[17], biologic/targeted synthetic systemic drug use was associated with lower odds of being hospitalized compared to patients receiving no systemic therapies. This effect was largely driven by TNF inhibitors since most patients on biologics were receiving this sub-group. A decreased risk of hospitalization or death was also associated with TNF inhibitor biologics compared with no treatment among 525 patients with inflammatory bowel disease and COVID-19 reported to SECURE-IBD[16]. In contrast, the standard systemics sulfasalazine or 5-aminosalicylate were associated with a higher risk of hospitalization or death. Our previous study of 374 patients with psoriasis and COVID-19 reported to the PsoProtect registry further suggested an association between biologics (pooled data on TNF, IL-17 and IL-23 inhibitors) and reduced risk of hospitalization, compared to standard systemic therapies[18]. Although exploration of possible biological mechanisms underlying these associations is warranted (e.g. cytokine-targeted biologics may attenuate a severe systemic inflammatory response to COVID-19[30]), our current study highlights shielding behaviour as an important unmeasured potential mediator in these datasets. The differences in shielding behaviours across treatments

supports the notion that greater protective shielding behaviour (resulting in a lower infectious dose of SARS-CoV-2) in those receiving targeted therapies may account, at least in part, for the observed associations. Thus, conclusions from clinician-reported registry data about medication-related COVID-19 risk should be interpreted in this context, and further research efforts are required to quantify potential mediation through shielding.

A greater proportion of participants from the UK reported shielding compared with those elsewhere, which may reflect cross-national differences in public health messaging. However, these data should be interpreted with caution since our dataset is dominated by UK participants. Due to limited capture of socioeconomic data, we were unable to fully adjust for this confounder in the analysis, however we did identify that household density and full-time employment were inversely associated with shielding. Both shielding behaviour and clinical decision making around systemic therapies globally (including access to medications) may be affected by socioeconomic variables such as income and education[31,32], which may in turn influence outcome of COVID-19[4]. Linkage between health, social, behavioural and employment data should thus be prioritised in future research.

Collecting data via an online survey may have limited participation to more tech-literate individuals and those more connected to media. The study sample was mostly female (as expected in survey-based studies), of white ethnicity, and self-reported their diagnoses, which further limits the generalizability of the results. Ascertainment bias may overestimate the overall proportion shielding, since those more concerned about COVID-19 risk may be more likely to participate. Our sample, in which a greater proportion reported receiving targeted therapies compared with standard systemic agents, may not be representative of patients receiving systemic therapies more broadly. A disparate group of medications is also classified together as standard systemic agents. Potential selection bias may be addressed through systematic recruitment of participants enrolled in pharmacovigilance registries. Future linkage to registry and healthcare records may also validate self-reported demographic and clinical characteristics.

Shielding of at-risk individuals remains a global public health priority. Our study indicates that use of targeted therapies is associated with shielding in individuals with RMD and psoriasis, compared to no systemic treatment or standard systemic agents. This may contribute to the reported lower risk of adverse COVID-19 outcomes associated with targeted therapies reported by IMID registries. The observed differences in shielding across treatment groups, IMIDs, nations and time may inform future updates of public health recommendations for COVID-19 risk mitigating behaviours. Capture and consideration of risk mitigating behaviour

is important in future studies of COVID-19 risk across people with IMIDs and on different types of systemic treatments.

Ethical Approval

Research approved by KCL research ethics committee (REC ref 20/YH/0135)

Data Sharing

Summary level data available on reasonable request.

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Table 1. Participant characteristics, by treatment.

	Total	No Systemic Therapy	Standard Systemic Therapy	Targeted Therapy	p-value	N Missing
	N=3,720	N=2,299	N=497	N=924		
Shielded (%)	2,262 (60.8%)	1,360 (59.2%)	292 (58.8%)	610 (66.0%)	<0.001	0
Advised to shield (%), UK only	1,092 (42.4%)	523 (31.6%)	164 (51.2%)	405 (67.2%)	<0.001	4
UK resident (%)	2,578 (69.4%)	1,656 (72.1%)	319 (64.6%)	603 (65.2%)	<0.001	7
Male gender (%)	1,174 (31.6%)	632 (27.5%)	158 (31.8%)	384 (41.6%)	<0.001	2
Age in years, mean (SD)	49.2 (15.0)	49.3 (15.7)	49.0 (14.8)	49.0 (13.2)	0.84	25
Ethnicity (%)					<0.001	0
White ethnicity	2,990 (80.4%)	1,856 (80.7%)	386 (77.7%)	748 (81.0%)		
Hispanic or Latino	158 (4.2%)	95 (4.1%)	29 (5.8%)	34 (3.7%)		
South Asian	127 (3.4%)	69 (3.0%)	23 (4.6%)	35 (3.8%)		
Japanese	90 (2.4%)	29 (1.3%)	18 (3.6%)	43 (4.7%)		
Black African/Caribbean/American	86 (2.3%)	68 (3.0%)	6 (1.2%)	12 (1.3%)		
Other	169 (4.5%)	182 (7.9%)	35 (7.0%)	52 (5.6%)		
BMI, mean (SD)	27.4 (6.1)	26.8 (5.8)	27.7 (6.0)	28.8 (6.5)	<0.001	301
Alcohol >14 units a week (%)	484 (13.6%)	291 (13.4%)	57 (12.0%)	136 (15.1%)	0.24	168
Current Smoker (%)	460 (13.1%)	259 (12.1%)	69 (14.6%)	132 (14.8%)	0.076	207
Full time employment (%)	1,664 (44.7%)	951 (41.4%)	223 (44.9%)	490 (53.0%)	<0.001	0
Number in household, mean (SD)	2.7 (1.7)	2.7 (1.6)	2.9 (1.8)	2.7 (1.8)	0.19	9
Key worker (%)	985 (26.6%)	585 (25.6%)	146 (29.4%)	254 (27.6%)	0.16	15
Diagnosis (%)					<0.001	54
Psoriasis	2,869 (78.3%)	1,539 (68.6%)	462 (93.0%)	868 (93.9%)		
Inflammatory arthritis	529 (14.4%)	465 (20.7%)	23 (4.6%)	41 (4.4%)		
Connective tissue disease	127 (3.5%)	113 (5.0%)	9 (1.8%)	5 (0.5%)		
Axial spondyloarthritis	85 (2.3%)	75 (3.3%)	1 (0.2%)	9 (1.0%)		
Other	56 (1.5%)	53 (2.4%)	2 (0.4%)	1 (0.1%)		
COVID-19 diagnosis (%)	257 (7.1%)	131 (5.8%)	46 (9.7%)	80 (9.0%)	<0.001	111
1 or more comorbidity (%)	1,651 (44.4%)	949 (41.3%)	224 (45.1%)	478 (51.7%)	<0.001	0
Anxiety (%)	958 (27.2%)	605 (28.1%)	138 (29.2%)	215 (23.9%)	0.032	197
Depression (%)	925 (26.2%)	593 (27.5%)	127 (26.9%)	205 (22.8%)	0.024	196

Table 1. 'Shielded' refers to participants who quarantined and self-isolated. Inflammatory arthritis included any participant with a diagnosis of rheumatoid arthritis or psoriatic arthritis. SD = standard deviation, BMI = body mass index, UK = United Kingdom.

**Box 1. Definition of 'shielding' in the analysis:**

- Self-reported shielding, quarantine, staying home or strict distancing within the home
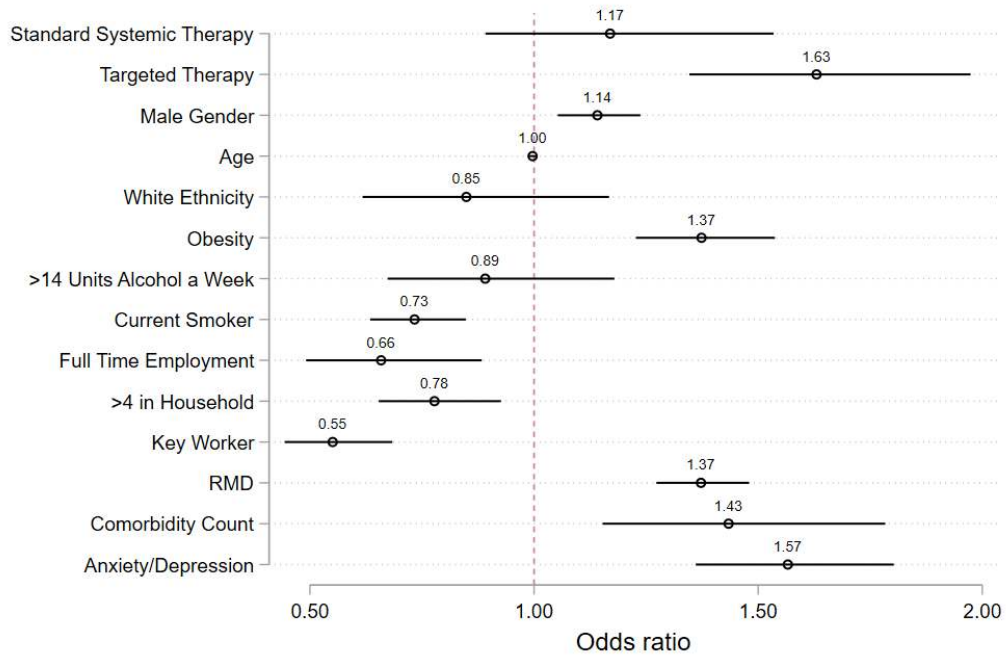
Figure legends

Figure 1. Each covariate was run as a predictor for shielding, adjusted for age and gender. Survey responders who were United Kingdom residents were asked if they received an NHS letter advising them to shield, which was associated with shielding, odds ratio of 4.7 (95% Confidence Interval 3.9 to 5.6). Standard therapy and biologic therapy were both compared to no systemic therapy as a reference group.   UK = United Kingdom. RMD = rheumatic and musculoskeletal disease.

Figure 2. Covariates were determined a priori by an expert panel of collaborators. Country of residence was included as a cluster variable. Biologic therapy was compared to no systemic therapy as a reference group. RMD = rheumatic and musculoskeletal disease.
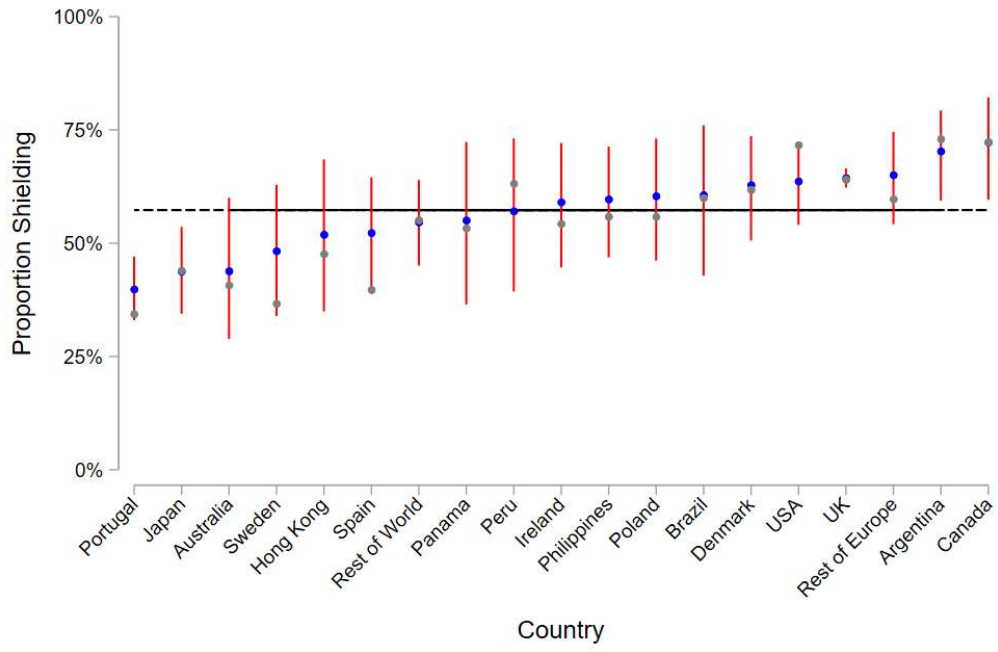
Figure 3. The grey markers are the observed national proportions of survey respondents who shielded. The blue markers are the predicted random national effect on shielding from a mixed effects model, with 95% confidence intervals in red. The black horizontal line represents the overall mean. UK = United Kingdom, USA = United States of America.
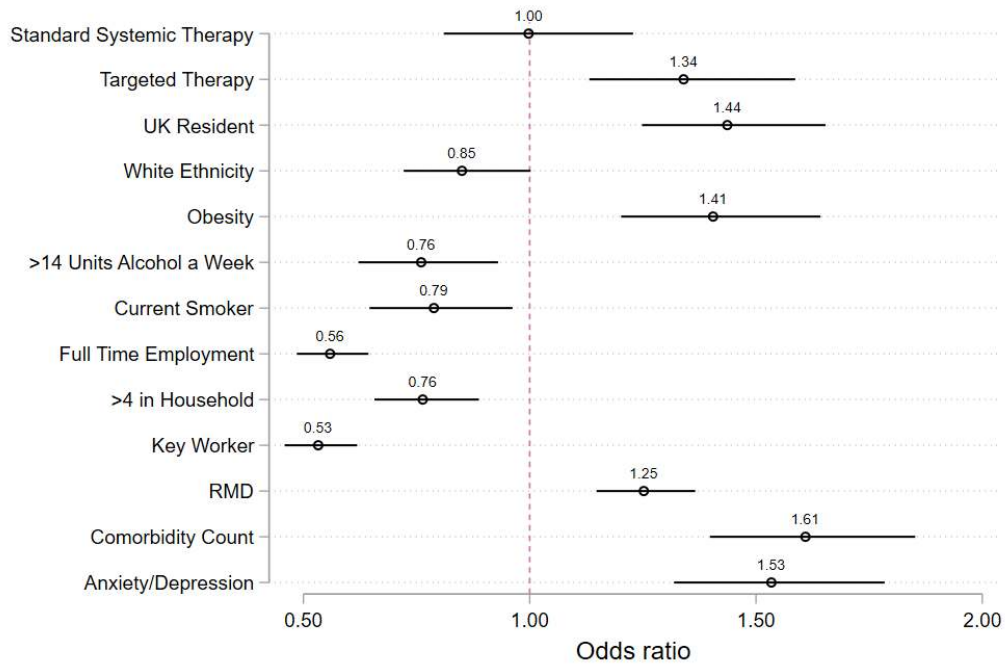
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