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Rebound in asthma exacerbations following relaxation of COVID-19 restrictions: a longitudinal population-based study (COVIDENCE UK)

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ABSTRACT

Background The imposition of restrictions on social mixing early in the COVID-19 pandemic was followed by a reduction in asthma exacerbations in multiple settings internationally. Temporal trends in social mixing, incident acute respiratory infections (ARI) and asthma exacerbations following relaxation of COVID-19 restrictions have not yet been described.

Methods We conducted a population-based longitudinal study in 2312 UK adults with asthma between November 2020 and April 2022. Details of face covering use, social mixing, incident ARI and severe asthma exacerbations were collected via monthly online questionnaires. Temporal changes in these parameters were visualised using Poisson generalised additive models. Multilevel logistic regression was used to test for associations between incident ARI and risk of asthma exacerbations, adjusting for potential confounders.

Results Relaxation of COVID-19 restrictions from April 2021 coincided with reduced face covering use ($p<0.001$), increased frequency of indoor visits to public places and other households ($p<0.001$) and rising incidence of COVID-19 ($p<0.001$), non-COVID-19 ARI ($p<0.001$) and severe asthma exacerbations ($p=0.007$). Incident non-COVID-19 ARI associated independently with increased risk of asthma exacerbation (adjusted OR 5.75, 95% CI 4.75 to 6.97) as did incident COVID-19, both prior to emergence of the omicron variant of SARS-CoV-2 (5.89, 3.45 to 10.04) and subsequently (5.69, 3.89 to 8.31).

Conclusions Relaxation of COVID-19 restrictions coincided with decreased face covering use, increased social mixing and a rebound in ARI and asthma exacerbations. Associations between incident ARI and risk of severe asthma exacerbation were similar for non-COVID-19 ARI and COVID-19, both before and after emergence of the SARS-CoV-2 omicron variant.

Study registration number NCT04330599.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The imposition of COVID-19 lockdowns was followed by reductions in asthma exacerbations in multiple settings internationally. Impacts of relaxing these restrictions have not yet been described, and the relative influence of SARS-CoV-2 versus other respiratory pathogens on risk of asthma exacerbation remains unclear.

WHAT THIS STUDY ADDS

⇒ This population-based longitudinal study in 2312 UK adults with asthma shows that lifting COVID-19 restrictions coincided with decreased face covering use, increased social mixing and a rebound in acute respiratory infections (ARIs) and asthma exacerbations. Associations between incident ARI and risk of asthma exacerbation were similar for non-COVID-19 ARI and COVID-19, both before and after emergence of the SARS-CoV-2 omicron variant.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings highlight the potential for interventions such as face covering use to reduce risk of asthma exacerbation and provide reassurance that COVID-19 is not significantly more likely to trigger asthma exacerbations than other ARI.

INTRODUCTION

Asthma is an inflammatory airways disease that affects more than 300 million people globally.[1] Episodes of progressive worsening of symptoms, termed exacerbations, are the major cause of morbidity and mortality in this condition. Viral respiratory infections are the most common precipitants of asthma exacerbations in both children and adults.[2]

COVID-19, an infectious disease caused by SARS-CoV-2), emerged in Wuhan, China, in late 2019, and rapidly spread globally.[3] In the absence of an effective vaccine or treatments, social distancing measures, such as lockdowns, were legislated globally. Imposition of these measures was associated with decreased social mixing, reduced transmission of SARS-CoV-2 and other acute respiratory pathogens[4] and reductions in asthma exacerbations.[5 6] Although COVID-19 has been reported to associate with increased inhaler use and poorer symptom control in people with asthma,[7] the relative influence of COVID-19 versus non-COVID-19 acute respiratory infection (ARI) on risk of asthma

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exacerbation has yet to be evaluated. Moreover, there are limited data relating to whether relaxation of restrictions was associated with a rebound in ARIs and asthma exacerbations.

A retrospective cohort study using data from an English national primary care database from January 2016 to October 2021 reported that asthma exacerbation rates were substantially lower between the second quarter of 2020 and the third quarter of 2021 than before the pandemic (2016–2019).[8] Although this study did not formally demonstrate an increase in incidence of exacerbations over the course of 2021, a trend towards an increase in mean exacerbation rate from the first to the third quarter of 2021 was observed, a period that coincided with relaxation of COVID-19 restrictions in the UK. However, since the study was conducted using routinely collected data, it was not possible to establish whether changes in risk of asthma exacerbation over time were temporally associated with changes in behaviours affecting viral transmission. Moreover, follow-up did not extend to cover the period following emergence of the omicron variant of SARS-CoV-2, which became dominant in December 2021. This is an important knowledge gap, given concerns that the omicron variant may be more tropic to the upper airway and therefore potentially more likely than earlier variants to precipitate asthma exacerbations.[9] We therefore sought to characterise changes in behaviours influencing respiratory viral transmission following relaxation of restrictions and to establish whether changes in these behaviours coincided with increases in COVID-19, non-COVID-19 ARI and asthma exacerbations, using data from a prospective population-based longitudinal study of COVID-19 in the UK population (COVIDENCE UK).[10] We also conducted multivariable analysis to determine the relative influence of COVID-19 and non-COVID-19 ARI on risk of asthma exacerbations, with additional stratification to determine whether the strength of association between COVID-19 and asthma exacerbations changed after the emergence of the omicron variant of SARS-CoV-2, as the dominant circulating variant in December 2021.

METHODS

Study design and setting and approvals

COVIDENCE UK is a population-based longitudinal study investigating risk factors for, and impacts of, COVID-19 and other ARI.[10] Full details of study design are reported elsewhere.[11–17] Briefly, from 1 May 2020 to 6 October 2021, UK residents aged ≥16 years were invited via a national media campaign to complete a detailed online baseline questionnaire capturing self-reported information relating to their sociodemographic characteristics, occupation, lifestyle, quality of life, weight, height, longstanding medical conditions, medication use, vaccination status, diet and supplemental micronutrient intake. Follow-up on-line questionnaires capturing behaviours potentially influencing risk of acquiring or transmitting ARI, incident ARI symptoms, results of reverse transcription PCR (RT-PCR) and antigen testing for respiratory viruses, incident exacerbations of asthma and chronic obstructive pulmonary disease and doses of SARS-CoV-2 vaccine received were completed at monthly intervals.

Participants

Inclusion criteria for the current analysis were participation in COVIDENCE UK; self-report of doctor-diagnosed asthma at baseline with ongoing use of at least one prescribed asthma treatment and/or at least one severe asthma exacerbation (definition below) in the 12 months prior to enrolment; and completion of at least 1 monthly follow-up questionnaire between 12 November 2020 (when details of asthma exacerbations were first included in monthly follow-up questionnaires) and 21 April 2022 inclusive. Exclusion criteria were self-report of a positive RT-PCR or antigen test for SARS-CoV-2, ongoing or prior

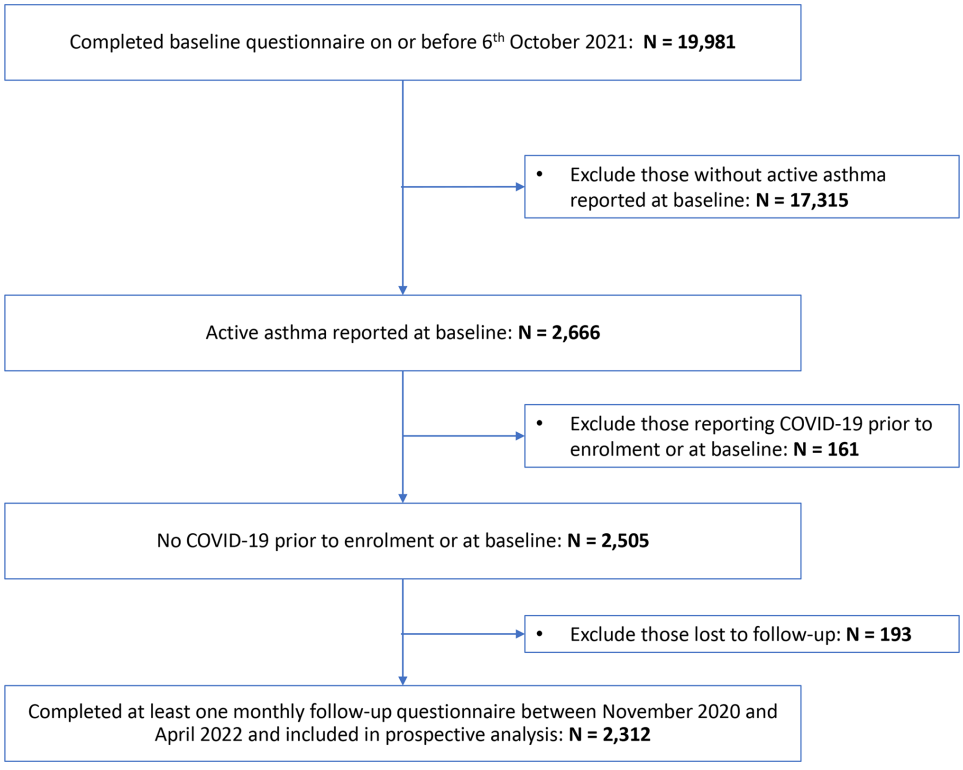

Figure 1 Participant flow.

Table 1 Participant characteristics at baseline and events during follow-up

Baseline characteristics	
Sex, n (%)	
Male	570 (24.7)
Female	1742 (75.3)
Age, years	
Median (IQR) (range)	60 (49–67) (16–88)
Mean (SD)	58.9 (12.3)
Ethnicity, n (%)	
Black/African/Caribbean/black British	11 (0.5)
Mixed/multiple ethnic groups	34 (1.5)
South Asian*	43 (1.9)
White	2191 (94.7)
Other	33 (1.4)
Index of multiple deprivation, quartile, n (%)†	
4 (least deprived)	586 (25.4)
3	587 (25.4)
2	563 (24.4)
1 (most deprived)	570 (24.7)
Current tobacco smoking, n (%)	
Yes	123 (5.3)
No	2189 (94.7)
Educational attainment, n (%)†	
Primary/secondary	229 (9.9)
Higher/further (A levels)	332 (14.4)
College/university	999 (43.2)
Postgraduate	748 (32.4)
Self-reported general health, n (%)	
Poor	148 (6.4)
Fair	450 (19.5)
Good	730 (31.6)
Very good	749 (32.4)
Excellent	235 (10.2)
Body mass index, kg/m^2	
Mean (SD)	27.4 (6.1)
<25	952 (41.2)
25–30	732 (31.7)
>30	624 (27.0)
Missing	4 (0.0)
≥1 severe asthma exacerbation‡ in 12 months pre-enrolment, n (%)	
Yes	320 (13.8)
No	1992 (86.2)
Asthma treatment, n (%)†	
Reliever only§	694 (30.0)
ICS±reliever¶	686 (29.7)
LAB±ICS or reliever**	916 (39.6)
Monoclonal antibody††	14 (0.6)
Events during follow-up	
SARS-CoV-2 vaccination (primary course)	
ChAdOx1 (Oxford/AstraZeneca) only	1205 (52.1)
BNT162b2 (Pfizer) only	724 (31.3)
Other/mixed regimen	79 (3.4)
Unvaccinated	304 (13.1)
≥1 severe asthma exacerbation, n (%)‡	
Yes	411 (17.8)
No	1901 (82.2)
≥1 episode of COVID-19, n (%)‡‡	
Yes	656 (28.4)
No	1656 (71.6)
≥1 episode of non-COVID-19 ARI, n (%)§§	
Yes	1115 (48.2)
No	1197 (51.8)

*Self-defined as Indian, Pakistani, Bangladeshi or Sri Lankan.
†Missing data: index of multiple deprivation (n=6), educational attainment (n=4) and asthma treatment (n=2).
‡Defined as an asthma exacerbation requiring treatment with systemic corticosteroids and/or precipitating emergency department attendance or hospital admission in the 12 months preceding enrolment to COVIDENCE UK.
§Inhaled short-acting beta-agonist or anticholinergic.
¶Regular use of ICS±reliever inhaler, but no LAB or monoclonal antibody treatment.
**Regular use of LAB±ICS or reliever inhaler but no monoclonal antibody treatment.
††Monoclonal antibody treatment, with or without any other treatment.
‡‡Confirmed with positive reverse transcription PRC (RT-PCR) or antigen swab test for SARS-CoV-2.
§§Defined as self-report of doctor-diagnosed or symptom-defined ARI associated with at least one negative RT-PCR or antigen test result for SARS-CoV-2 and no positive RT-PCR or antigen test results for SARS-CoV-2.
ARI, acute respiratory infection; ICS, inhaled corticosteroid; LAB, long-acting bronchodilator inhaler.

chronic symptoms attributed to prior SARS-CoV-2 infection (long COVID) or hospitalisation for COVID-19 either prior to enrolment or at baseline.

Variables

Behavioural variables

Face covering use was categorised as the proportion of participants who reported that they had 'Always (100% of the time)' used a face covering while in an indoor public place in the week prior to questionnaire completion. Visits to shops, visits to other indoor public places, indoor visits to/from other households and public transport use were categorised as the proportion of participants who reported one or more such events in the week prior to questionnaire completion. Travel outside the UK was categorised as the proportion of participants who reported foreign travel in the month prior to questionnaire completion.

Respiratory variables

Severe asthma exacerbations were defined as those requiring treatment with systemic corticosteroids and/or precipitating emergency department attendance or hospital admission. COVID-19 was defined as self-report of COVID-19 confirmed by a positive RT-PCR or antigen test result for SARS-CoV-2. Episodes of COVID-19 were imputed as being due to the omicron SARS-CoV-2 variant if they occurred from 16 December 2021 onwards (ie, the date on which the UK Health Security Agency reported omicron to be the dominant SARS-CoV-2 variant in the UK).[7] Non-COVID-19 ARI was defined as self-report of a general practitioner or hospital diagnosis of pneumonia, influenza, bronchitis, tonsillitis, pharyngitis, ear infection, common cold or other upper or lower respiratory infection and/or self-report of a symptom-defined ARI associated with at least one negative RT-PCR or antigen test results for SARS-CoV-2 and

no positive RT-PCR or antigen test results for SARS-CoV-2. Symptom-defined episodes of ARI were identified using modified Jackson criteria for upper respiratory infection,[18] modified Macfarlane criteria for lower respiratory infection[19] and a triad of cough, fever and myalgia for influenza-like illness.[20] Full details of algorithms employed are presented in online supplemental table S3.

Potential confounders

The following factors were identified a priori as potential confounders of relationships between incident ARI and asthma exacerbation: duration of follow-up (number of months postenrolment), sex (male vs female, defined by sex assigned at birth), age (years), ethnic origin (white vs minority ethnic), current tobacco smoking (yes vs no), educational attainment (primary/secondary school vs higher/further education (A-levels) vs college/university vs postgraduate), body mass index (<25 vs 25–30 vs >30 kg/m^2), asthma treatment level (use of reliever inhaler only vs use of inhaled corticosteroid (ICS)±reliever inhaler vs use of a long-acting bronchodilator inhaler±ICS or reliever inhaler vs monoclonal antibody therapy with or without any other treatment), history of severe asthma exacerbation in the 12 months prior to enrolment (yes vs no), index of multiple deprivation (IMD) 2019 score (assigned according to participants' postcodes and categorised into quartiles), self-reported general health (poor vs fair vs good vs very good vs excellent) and SARS-CoV-2 vaccination status (primary vaccination course completed vs not completed).

Data sources and measurement

All variables previously mentioned were derived from responses to baseline and monthly online questionnaires, as detailed in online supplemental tables S1 and S2, respectively.

Bias

Selection bias was minimised by use of a national media campaign to enrol participants from the general population. Detection bias was minimised by using a uniform approach (online questionnaires) to capture outcomes in exposed versus unexposed individuals. Observation bias was minimised as a result of participants being unaware of the specific hypotheses being tested in this analysis. Recall bias was minimised by frequent (monthly) administration of follow-up questionnaires.

Study size

Details of the sample size calculation for the COVIDENCE UK study are presented elsewhere.[16] The current analysis was pragmatic in nature, including all participants meeting the study-specific eligibility criteria described previously with no sample size specified.

Statistical analysis

We used univariable Poisson generalised additive models to explore temporal changes in face covering use, social mixing behaviours, ARI and severe asthma exacerbations over time (November 2020–April 2022). Univariable models were plotted to visualise the penalised regression splines over time

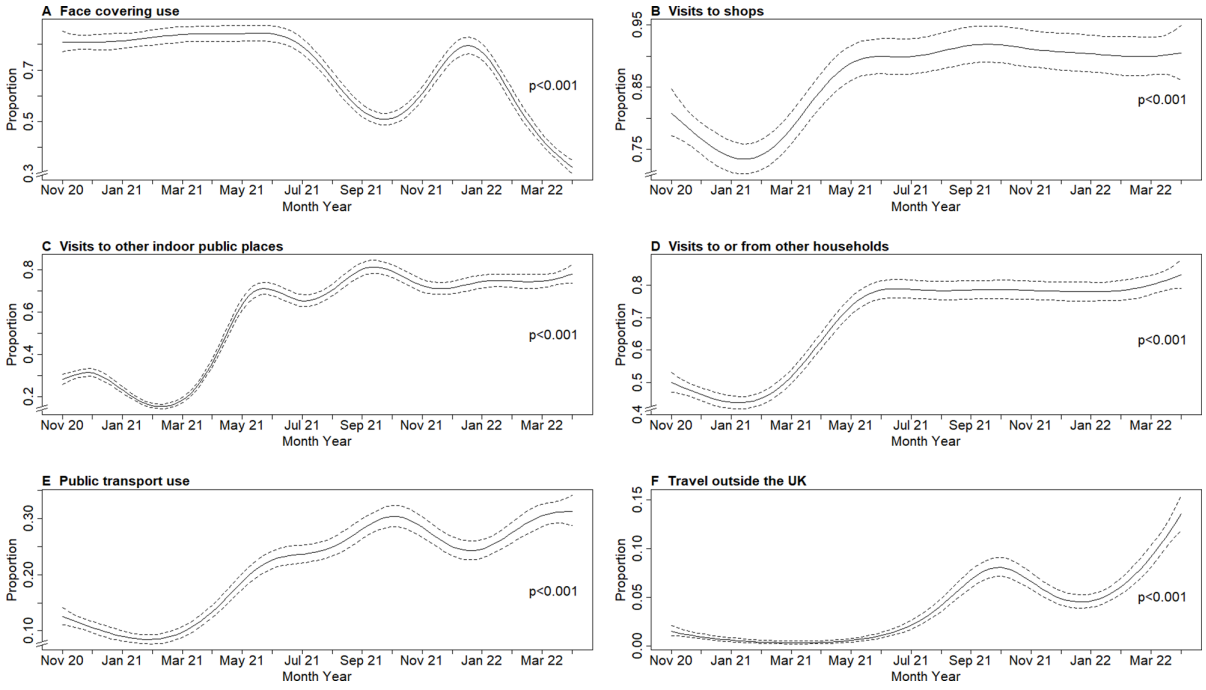

Figure 2 Temporal trends in behaviours potentially influencing risk of acquiring or transmitting acute respiratory infections from November 2020 to April 2022. (A) Proportion of participants using a face covering 100% of the time when visiting an indoor public place in the week prior to completion of monthly follow-up questionnaire. (B) Proportion of participants visiting shops at least once in the week prior to completion of monthly follow-up questionnaire. (C) Proportion of participants visiting an indoor public place other than a shop at least once in the week prior to completion of monthly follow-up questionnaire. (D) Proportion of participants making or receiving at least one indoor visit to another household in the week prior to completion of monthly follow-up questionnaire. (E) Proportion of participants using public transport at least once in the week prior to completion of monthly follow-up questionnaire. (F) Proportion of participants travelling outside the UK at least once in the month prior to completion of monthly follow-up questionnaire. All plots are from univariable generalised additive models; p values refer to temporal changes in proportions over the study period. Solid and dotted lines show means and 95% CIs, respectively.

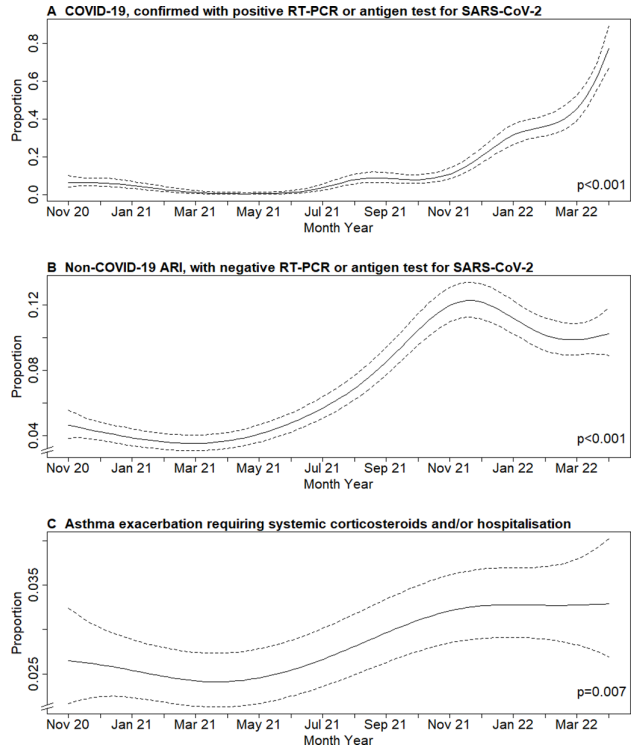

Figure 3 Temporal trends in incident acute respiratory infections and asthma exacerbations from November 2020 to April 2022. (A) RT-PCR-confirmed or antigen test-confirmed COVID-19. (B) Episodes of acute respiratory infection symptoms associated with a negative RT-PCR or antigen test result for SARS-CoV-2. (C) Episodes of severe asthma exacerbation. All plots are from univariable generalised additive models; p values refer to temporal changes in proportions over the study period. Solid and dotted lines show means and 95% CIs, respectively.

(month-year), with transformation of y-axes onto the response scale. Means with 95% CIs of proportions experiencing each outcome were displayed. A fully adjusted multilevel logistic generalised linear model was applied to calculate adjusted ORs (aORs) for associations between incident ARI and severe asthma exacerbations. Adjusted models included age, sex, ethnicity, tobacco smoking status, educational attainment, body mass index, IMD 2019 quartile, self-defined general health, SARS-CoV-2 vaccination status, asthma treatment level and asthma exacerbation history prior to enrolment as covariates. Random effects of unique participant identifier were included in all models to account for within-participant variability. Missing data were assumed to be missing completely at random and were handled with listwise deletion in the generalised linear mixed models to obtain unbiased estimates. All statistical analyses were conducted using R V.4.1.1, with mixed effects models conducted using R-package lme4 v1.1–30.

RESULTS

A total of 19 981 UK residents aged 16 years or more completed the COVIDENCE UK baseline questionnaire between 1 May 2020 and 6 October 2021, of whom 2666 reported having doctor-diagnosed asthma with ongoing use of a prescribed asthma treatment. Of these, 2312 (86.7%) reported no episodes of COVID-19 before or at enrolment and completed at least 1 monthly follow-up questionnaire (figure 1). Table 1 presents baseline characteristics of participants contributing data to statistical analyses: 75.3% were female, median age was 60 years (IQR 49–67), 94.7% were of white ethnic origin and 13.8% reported at least one severe asthma exacerbation in the 12 months prior to enrolment. Follow-up was from November 2020 to April 2022, during which 411 (17.8%) participants reported at least one severe asthma exacerbation, 656 (28.4%) reported at least one positive RT-PCR or antigen swab test result for SARS-CoV-2 and 1115 (48.2%) reported at least one episode of ARI symptoms associated with a negative RT-PCR or antigen swab test result for SARS-CoV-2 (table 1).

Figure 2 presents generalised additive model plots illustrating changes in a range of behaviours potentially influencing risk of acquiring or transmitting ARI over the study period. Statistically significant temporal fluctuations were seen in proportions of participants reporting face covering use ($p<0.001$), visits to shops ($p<0.001$), visits to other indoor public places ($p<0.001$), making or receiving indoor visits to or from other households ($p<0.001$), using public transport ($p<0.001$) or travelling outside of the UK ($p<0.001$). The period during which more stringent restrictions were imposed (November 2020–March 2021) coincided with more frequent use of face coverings and reduced social mixing behaviours. Conversely, periods during which restrictions were relaxed (April–November 2021 and February–April 2022) coincided with less frequent face covering use and increased social mixing behaviours. The period immediately following emergence of omicron as the dominant variant of SARS-CoV-2 in the UK (December 2021–January 2022) coincided with increased face covering use, reduced public transport use and less frequent travel outside the UK.

Figure 3 presents generalised additive model plots illustrating changes in incident ARI and asthma exacerbations over the study period. Statistically significant temporal fluctuations were seen in proportions of participants reporting COVID-19 ($p<0.001$), non-COVID-19 ARI ($p<0.001$) and asthma exacerbations ($p=0.007$). The proportion of participants reporting COVID-19 at each monthly questionnaire began to increase from June 2021, climbing more steeply from December 2021. By contrast, the proportion of participants reporting non-COVID-19 ARI increased from March to November 2021 but dipped from December 2021 onwards. The proportion of participants reporting asthma exacerbations increased more gradually from March 2021 and levelled off from January 2022 onwards.

Table 2 presents results of univariable and multivariable analysis of potential determinants of severe asthma exacerbation. Incident non-COVID-19 ARI associated with increased odds of reporting an asthma exacerbation after adjustment for multiple potential sociodemographic and clinical confounders (aOR 5.75, 95% CI 4.75 to 6.97). Similarly, incident COVID-19 associated with increased odds of severe asthma exacerbation, both prior to dominance of the omicron variant of SARS-CoV-2 in December 2021 (aOR 5.89, 95% CI 3.45 to 10.04) and subsequently (aOR 5.69, 95% CI 3.89 to 8.31). Independent associations with increased odds of reporting an asthma exacerbation were also seen for participants receiving more intensive asthma treatment versus use of a reliever inhaler only (for long-acting bronchodilator therapy, aOR 1.94, 95% CI 1.36 to 2.78; for monoclonal antibody asthma therapy, aOR 7.24, 95% CI 2.36 to 22.18); for those who reported an asthma attack in the 12 months prior to enrolment versus those who did not (aOR 5.01, 95% CI 3.67 to 6.85); and for those who reported less good general health ('good' vs 'excellent', aOR 1.99, 95% CI 1.04 to 3.80; 'fair' vs 'excellent', aOR 3.17, 95% CI 1.64 to 6.16; 'poor' vs 'excellent', aOR 4.57, 95% CI 2.19 to 9.55).

Table 2 Determinants of severe asthma exacerbation risk

	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)*	P value
Follow-up duration, months	1.03 (1.02 to 1.05)	<0.001	0.99 (0.97 to 1.02)	0.438
Sex				
Female	1.00 (Ref)	–	1.00 (Ref)	–
Male	0.81 (0.58 to 1.12)	0.205	1.11 (0.81 to 1.52)	0.512
Age, years	0.99 (0.98 to 1.00)	0.072	1.01 (1.00 to 1.02)	0.202
Ethnicity				
White	1.00 (Ref)	–	1.00 (Ref)	–
Other	1.01 (0.53 to 1.91)	0.976	1.25 (0.69 to 1.52)	0.461
Current tobacco smoking				
No	1.00 (Ref)	–	1.00 (Ref)	–
Yes	1.96 (1.11 to 3.45)	0.020	1.34 (0.78 to 2.31)	0.290
Educational attainment				
Postgraduate	1.00 (Ref)	–	1.00 (Ref)	–
College/university	1.32 (0.95 to 1.83)	0.095	1.05 (0.77 to 1.42)	0.774
Higher/further (A levels)	1.57 (1.02 to 2.41)	0.042	1.09 (0.72 to 1.64)	0.688
Primary/secondary	1.22 (0.74 to 2.02)	0.442	1.06 (0.66 to 1.70)	0.820
Body mass index, kg/m²				
<25	1.00 (Ref)	–	1.00 (Ref)	–
25–30	1.22 (0.87 to 1.70)	0.253	1.12 (0.82 to 1.54)	0.468
≥30	2.18 (1.57 to 3.03)	<0.001	1.36 (0.98 to 1.87)	0.062
Asthma treatment				
Reliever only†	1.00 (Ref)	–	1.00 (Ref)	–
ICS±reliever‡	1.51 (1.02 to 2.24)	0.041	1.24 (0.84 to 1.83)	0.299
LAB±ICS or reliever§	3.67 (2.58 to 5.21)	<0.001	1.94 (1.36 to 2.78)	<0.001
Monoclonal antibody¶	53.47 (16.39 to 174.46)	<0.001	7.24 (2.36 to 22.18)	0.004
Asthma exacerbation pre-enrolment**				
No	1.00 (Ref)	–	1.00 (Ref)	–
Yes	8.75 (6.55 to 11.70)	<0.001	5.01 (3.67 to 6.85)	<0.001
Index of multiple deprivation, quartile				
Q4 (least deprived)	1.00 (Ref)	–	1.00 (Ref)	–
Q3	0.96 (0.65 to 1.41)	0.826	0.96 (0.66 to 1.38)	0.807
Q2	1.10 (0.75 to 1.63)	0.618	1.04 (0.72 to 1.49)	0.845
Q1 (most deprived)	1.35 (0.92 to 1.98)	0.121	1.02 (0.71 to 1.47)	0.900
Self-reported general health				
Excellent	1.00 (Ref)	–	1.00 (Ref)	–
Very good	1.70 (0.91 to 3.19)	0.096	1.73 (0.90 to 3.31)	0.098
Good	2.85 (1.54 to 5.28)	0.001	1.99 (1.04 to 3.80)	0.037
Fair	5.90 (3.15 to 11.03)	<0.001	3.17 (1.64 to 6.16)	0.001
Poor	12.23 (6.08 to 24.61)	<0.001	4.57 (2.19 to 9.55)	<0.001
Primary course of SARS-CoV-2 vaccination				
No	1.00 (Ref)	–	1.00 (Ref)	–
Yes	1.35 (1.13 to 1.61)	0.001	1.12 (0.84 to 1.48)	0.466
Incident COVID-19				
No	1.00 (Ref)	–	1.00 (Ref)	–
Yes, before December 2021	4.09 (2.22 to 7.53)	<0.001	5.89 (3.45 to 10.04)	<0.001
Yes, on/after December 2021	4.17 (2.77 to 6.27)	<0.001	5.69 (3.89 to 8.31)	<0.001
Incident non-COVID-19 ARI				
No	1.00 (Ref)	–	1.00 (Ref)	–
Yes	4.53 (3.72 to 5.52)	<0.001	5.75 (4.75 to 6.97)	<0.001

*Mutually adjusted for all independent variables displayed.
†Inhaled short-acting beta-agonist or anticholinergic.
‡Regular use of ICS±reliever inhaler, but no LAB or monoclonal antibody treatment.
§Regular use of LAB±-ICS or reliever inhaler, but no monoclonal antibody treatment.
¶Monoclonal antibody treatment, with or without any other treatment.
**Defined as reporting at least one asthma exacerbation requiring treatment with systemic corticosteroids and/or precipitating emergency department attendance or hospital admission in the 12 months preceding enrolment to COVIDENCE UK.
ARI, acute respiratory infection; ICS, inhaled corticosteroid; LAB, long-acting bronchodilator inhaler; Ref, referent category.

DISCUSSION

We report findings of the first study to compare the influence of COVID-19 versus non-COVID-19 ARI on risk of asthma exacerbation and to investigate the strength of association between COVID-19 and asthma exacerbation before and after emergence of the omicron variant of SARS-CoV-2. We show that relaxation of COVID-19 restrictions in the UK from April 2021 coincided with reduced use of face coverings, increased social mixing and increases in COVID-19, non-COVID-19 ARI and severe asthma exacerbations. Incident ARI were strongly associated with increased risk of severe asthma exacerbations after adjustment for multiple potential confounders. However, the strength of such associations was similar for non-COVID-19 ARI and for COVID-19, both before and after emergence of the omicron variant of SARS-CoV-2.

Our findings support those of others who have investigated temporal trends in COVID-19 and asthma exacerbations over the course of the pandemic[5 6 8 21] and extend them substantively by the addition of granular repeated-measures data capturing month-to-month changes in behaviours and non-COVID-19 ARI over an 18-month period spanning the lockdown of winter 2020–2021, the subsequent relaxation of restrictions and the emergence of the omicron variant of SARS-CoV-2. With regard to behaviours, our findings are broadly consistent with national data from the UK reporting good compliance with recommendations on use of coverings and reduced social mixing during early 2021, with increases in visiting and travel starting from April 2021.[22] The temporal trends in COVID-19 reported here are also consistent with national data, which report increases in COVID-19 notifications from mid-2021, with sharp increases from November/December 2021,[23] coinciding with the emergence of omicron as the dominant variant of SARS-CoV-2 in the UK.[24] Similarly, national surveillance data show increases in cases of influenza, influenza-like illnesses and other respiratory viruses in 2021/2022 compared with 2020/2021, although incidence continued to remain lower than before the pandemic.[25]

Our findings also complement those of a retrospective cohort study conducted using data from an English national primary care database,[8] which reported a trend towards an increase in mean asthma exacerbation rate over the course of 2021. Our demonstration that COVID-19 associates strongly with risk of severe exacerbation is in keeping with findings of a mixed-methods analysis reporting an association between COVID-19 and increased inhaler use in a cohort of adults with asthma.[26] Given concerns that the omicron variant of SARS-CoV-2 may be more likely to precipitate asthma exacerbations than earlier variants,[9] our finding that the strength of associations between COVID-19 and asthma exacerbation was not increased following emergence of the omicron variant is reassuring.

Our study has several strengths. The large size of our dataset, incorporating multiple repeated measures, afforded a high degree of power to detect temporal changes in behaviours and impacts of ARI on risk of asthma exacerbation. We captured episodes of non-COVID-19 ARI as well as COVID-19 across an extended period, which allowed us to compare the influence of different causes of ARI and different variants of SARS-CoV-2 on risk of asthma exacerbation. Availability of detailed information on multiple factors associating with exposures and outcomes of interest allowed us to perform adjusted analyses to minimise potential for confounding. The prospective longitudinal nature of the study allows us to rule out reverse causation as an explanation for associations observed, and the population-based approach to recruitment with inclusion of participants with different degrees of asthma severity enhances the generalisability of our findings.

Our study also has some limitations. No asthma outcome data were collected prior to November 2020, so information from before the pandemic and its early phases are lacking. All data are self-reported; however, participants were not aware of the hypotheses tested in these analyses, which reduces the risk of reporting bias. Variants of SARS-CoV-2 were imputed based on the date on which COVID-19 arose: this could lead to a degree of misclassification, although this is limited by the rapidity with which the omicron variant replaced the delta variant in the UK.[24] Adherence to ICS improved early in the pandemic, which may have contributed to declines in the asthma exacerbation rate during that period.[27] Increases in exacerbation risk following relaxation of restrictions may reflect declining ICS adherence as concerns receded. However, we lacked information on participants' adherence to asthma medication and cannot therefore evaluate this possibility. Our definition of non-COVID-19 ARI included symptom-defined events and was not validated against RT-PCR or other laboratory testing within this study; however, we have previously validated symptom-defined ARI against RT-PCR in a similar study population.[28] Women and older people were over-represented in our study population as compared with those in another population-based cohort of UK adults with asthma identified using electronic healthcare records,[29] which might have implications for generalisability of our findings. Finally, we highlight that temporal associations between trends in behaviours, infections and asthma exacerbations should not necessarily be interpreted as being causal, given the observational nature of our study.

In conclusion, this large prospective population-based study shows for the first time that relaxation of COVID-19 restrictions in the UK coincided with increased risk of COVID-19 and non-COVID-19 ARI, which in turn associated independently with increased risk of severe asthma exacerbations. The strength of associations between incident ARI and asthma exacerbation were similar for non-COVID-19 ARI and COVID-19, both before and after emergence of omicron as the dominant variant of SARS-CoV-2 in the UK.

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Competing interests RAL declares membership of the Welsh Government COVID19 Technical Advisory Group. AS is a member of the Scottish Government Chief Medical Officer's COVID-19 Advisory Group and its Standing Committee on Pandemics. He is also a member of the UK Government's NERVTAG's Risk Stratification Subgroup. All other authors declare that they have no competing interests.

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