Impact of COVID-19 lockdown on emergency asthma admissions and deaths: national interrupted time series analyses for Scotland and Wales

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ABSTRACT

Background The COVID-19 pandemic’s impact on people with asthma is poorly understood. We hypothesised that lockdown restrictions were associated with reductions in severe asthma exacerbations requiring emergency asthma admissions and/or leading to death.

Methods Using data from Public Health Scotland and the Secure Anonymised Information Linkage Databank in Wales, we compared weekly counts of emergency admissions and deaths due to asthma over the first 18 weeks in 2020 with the national averages over 2015–2019. We modelled the impact of instigating lockdown on these outcomes using interrupted time-series analysis. Using fixed-effect meta-analysis, we derived pooled estimates of the overall changes in trends across the two nations. We also investigated trends in asthma-related primary care prescribing and emergency department (ED) attendances in Wales.

Results Lockdown was associated with a 36% pooled reduction in emergency admissions for asthma (incidence rate ratio, IRR: 0.64, 95% CI: 0.49 to 0.83, p value 0.001) across both countries. There was no significant change in asthma deaths (pooled IRR: 0.57, 95% CI: 0.49 to 0.83, p value 0.001) across both countries. There was no significant increase in ED asthma attendances in Wales declined during lockdown (IRR: 0.85, 95% CI: 0.73 to 0.99, p value 0.03). A large spike of 121% more inhaled corticosteroids and 133% more oral corticosteroid prescriptions was seen in Wales in the week before lockdown.

Conclusions National lockdowns were associated with substantial reductions in severe asthma exacerbations leading to hospital admission across both Scotland and Wales, with no corresponding increase in asthma deaths.

INTRODUCTION

The emergence of the COVID-19 pandemic and resultant shift in focus of healthcare resource worldwide has led to the disruption of healthcare for people with chronic health conditions. Though much has been learnt about the risk of increased severity of COVID-19 conveyed by common comorbidities,1,2 little is yet known about the wider impact of the pandemic on those with chronic conditions such as asthma. Despite anecdotal concern early in the pandemic that SARS-CoV-2 may trigger asthma exacerbations in a similar manner to other respiratory viruses, and evidence of asthma being a risk factor for poor COVID-19 outcomes,3 initial reports from single centres have described a decrease in paediatric asthma-related emergency healthcare utilisation during the pandemic.4–7

In response to rising numbers of confirmed infections with SARS-CoV-2 in the UK, the UK Government announced a nationwide lockdown on 23 March 2020, with the key slogan ‘Stay at home. Protect the NHS. Save lives’.8 Messaging to avoid overwhelming the National Health Service (NHS) and fear of contracting SARS-CoV-2 in hospitals had an impact on patients’ willingness to seek emergency care.9 However, restrictions in movement10 and social contact with the resulting reduction in outdoor air pollution and exposure, and transmission of other respiratory viruses could have led to a true reduction in asthma exacerbations during the lockdown.

We sought to investigate the impact of the COVID-19 lockdown on severe asthma exacerbations leading to emergency hospital admissions in Scotland and Wales. We also examined deaths due to asthma because of concern that exacerbations may not have presented to the health systems and that this may therefore have manifested as increased deaths.
Asthma

METHODS
Data sources, populations and case definitions
The study was based on the entire populations of Scotland and Wales (the 2019 mid-year population estimates were 5,463,300 and 3,152,900, respectively). We accessed complete coverage person-level datasets from Public Health Scotland (PHS)\(^1\) and the Secure Anonymised Information Linkage (SAIL) Databank in Wales.\(^2\) PHS receives individual-level data from all general or acute specialties in NHS hospitals in Scotland. The SAIL Databank receives linkable, routinely collected data from all NHS hospitals in Wales and primary care data from approximately 76% of general practices (GP) with accompanying administrative data.

We defined two primary outcome measures relating to severe asthma exacerbations: asthma-related emergency hospital admission and death due to asthma. Emergency admissions for asthma were defined as those with a primary diagnosis of asthma recorded using J45 or J46 codes of the 10th revision of the International Statistical Classification of Diseases (ICD-10). These data were extracted from the Scottish Morbidity Record 01\(^3\) and the Patient Episodes Database for Wales. Deaths due to asthma were defined as those with asthma (ICD-10 codes J45 or J46) as the underlying cause of death in the National Records of Scotland deaths database\(^4\) or the Annual District Death Extract in SAIL. Mortality data are regularly checked and validated by the UK Office for National Statistics.

In an attempt to better understand the observed trends, we undertook further analyses of asthma-related emergency department (ED) attendances and asthma-related GP prescriptions in the SAIL Databank for Wales. We defined asthma-related ED attendances as those with a primary diagnosis of asthma (14A code) in the Emergency Department Dataset. We extracted inhaled and oral corticosteroid prescriptions for those diagnosed with asthma from the Welsh Longitudinal General Practice dataset.

The online supporting information contains a full list of clinical codes used.

Statistical analysis
We visualised weekly trends of asthma-related emergency admissions, deaths, ED attendances and GP-prescribed asthma medications for the first 18 calendar weeks in 2020 and corresponding national averages for the preceding 5 years.

We undertook interrupted time series analyses with a single change point of the 23 March (week 13) to investigate the impact of the UK lockdown on asthma admissions and deaths. We modelled the trends in the first 18 ISO weeks in 2020 and the corresponding 5-year averages (2015–2019) using Poisson generalised linear regression in R. The initial change point model in both the baseline period and 2020 had a pre-lockdown slope and intercept as well as an instantaneous change in intercept at the week of lockdown and a change in slope following lockdown. In the baseline period, we were anticipating no change in intercept and no change in slope at week 13. The final model is based on the baseline and 2020 data and includes a binary variable to differentiate the two periods together with interaction terms for the slopes and instantaneous effects of lockdown. These interaction terms were used to compare the slopes prior to lockdown in the baseline period with 2020; to compare the instantaneous change in intercept at lockdown in baseline with 2020 and to compare the change in slope post-lockdown in baseline with 2020. Residual plots have been used to check the linearity assumption and Breusch-Godfrey test was used to assess autocorrelation. Separate models were used in Scotland and Wales and z tests were used to compare the model coefficients between the two countries. We then used a fixed-effect meta-analysis to derive pooled estimates from their weighted averages. Data analysis was performed in R V 4.0.2.

Disclosure control procedures were applied before any data were released to investigators to prevent patient identification according to PHS and SAIL Information Governance regulations. We excluded two Health Boards in Scotland, Forth Valley and Greater Glasgow and Clyde, from analysis of admissions due to data incompleteness in 2020. All analyses were carried out using weekly data, but for disclosure control reasons only monthly data are presented for asthma deaths.

Patient and public involvement
This was an urgent public health research study in response to a public health emergency of international concern. This research was prioritised following discussion of the Asthma UK Centre for Applied Research Steering Committee, which included several patient and public involvement members, and the patient charity Asthma UK.

RESULTS
Emergency admissions
Emergency admissions for asthma in Scotland and Wales in 2020 were consistently lower than the 5-year averages since the beginning of the year (table 1).

In 2020, the average weekly admissions in weeks 13–18 decreased by 36.4 (48.7%) in Scotland and by 43.5 (69.9%) in Wales compared with the first 12 weeks. The average weekly admissions in weeks 13–18 decreased by 32.2 (45.8%) in Scotland and by 43.1 (69.8%) in Wales in 2020 compared with the 5-year average.

In 2020 before lockdown, admissions were consistently fewer than the 5-year averages and had comparable slopes in both countries (figure 1). The overall reduction pre-lockdown was comparable in Scotland (incidence rate ratio, IRR=0.84, 95% CI: 0.69 to 1.02) and Wales (IRR: 0.67, 95% CI: 0.53 to 0.83). The week-on-week reduction was significant in both countries (Scotland: IRR=0.97, 95% CI: 0.96 to 1.00; Wales: IRR=0.95, 95% CI: 0.93 to 0.97). Pre-lockdown admissions were falling faster than the 5-year average in Wales (IRR=0.97, 95% CI: 0.94 to 1.00) but not in Scotland (IRR=1.00, 95% CI: 0.97 to 1.02).

The declining trend appeared to start in mid-March. The first week of the lockdown (week 13) was, however, a statistically significant change point and was associated with an instantaneous drop in admissions in both countries (Scotland: IRR=0.59, 95% CI: 0.42 to 0.83; Wales: 0.70, 95% CI: 0.47 to 1.04; pooled effect: 0.64, 95% CI: 0.49 to 0.83, p value=0.001) compared with the same point for the 5-year average. There was no evidence that the drop in admissions was different between Scotland and Wales (ratio of IRRs=0.84, 95% CI: 0.50 to 1.41, p value=0.504).

The trend during the lockdown period declined further in Wales (IRR=0.82, 95% CI: 0.73 to 0.92) where it was steeper than the 5-year average (IRR=0.84, 95% CI: 0.73 to 0.95). However, it did not significantly change further in Scotland (IRR=1.04, 95% CI: 0.95 to 1.15) although it appeared to be increasing (figure 1). There was a statistically significant difference in the slope during the lockdown between Scotland and Wales (ratio of IRRs=1.25, 95% CI: 1.06 to 1.47, p value=0.008).


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\(^{4}\) Statistical analysis

\(^{5}\) RESULTS

\(^{6}\) Emergency admissions

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Deaths
The national lockdowns had no significant effects on asthma deaths. Asthma deaths in 2020 before lockdown were higher, although non-significantly, than the preceding 5-year average (Scotland: IRR=2.07, 95% CI: 0.78 to 5.50; Wales: IRR=1.14, 95% CI: 0.35 to 3.74, table 2 and figure 2).

There were no changes in asthma deaths at lockdown (Scotland: IRR=0.35, 95% CI: 0.07 to 1.68; Wales: IRR=0.12, 95% CI: 0.18 to 9.01; pooled IRR = 0.57, 95% CI: 0.17 to 1.94, p value=0.372).

There were no significant changes in the week on week trend in deaths (Scotland: IRR=0.75, 95% CI: 0.49 to 1.17; Wales: IRR=0.97, 95% CI: 0.68 to 1.38) during the lockdown weeks, compared with the non-lockdown period (weeks 1–12). The week on week pattern of deaths was the same in 2020 compared with the 5-year average in both Scotland and Wales.

ED attendances
In Wales, we were also able to examine asthma-related ED attendances, enabling us to further evaluate the impact of lockdown on emergency care. Before lockdown, ED attendances were overall 29% lower than the 5-year average (IRR=0.71, 95% CI: 0.53 to 0.94, table 3). The reduction was seen from the start of 2020 (figure 3). There was no statistically significant change at lockdown (IRR=0.78, 95% CI: 0.48 to 1.24). During lockdown, however, there was a significant week-on-week reduction which was steeper than in the preceding 5 years (IRR=0.85, 95% CI: 0.73 to 0.99).

Corticosteroid prescriptions
In Wales, there were spikes of 121% and 133% more GP prescriptions of inhaled and oral corticosteroids for people with asthma in the week preceding the lockdown when compared with the previous 5-year average (figure 4).

D I S C U S S I O N
Principal findings
To our knowledge, this is the first national-level analysis of the impact of the COVID-19 pandemic on severe asthma exacerbations and reveals substantial reductions in asthma exacerbations resulting in hospital admissions with no corresponding increases in asthma deaths.

Our interrupted time-series analysis has demonstrated a significant reduction in asthma admissions for the lockdown period by 36% (41% in Scotland and 30% in Wales). This finding is particularly striking given that, at the start of the pandemic, there was concern that SARS-CoV-2 may act as a trigger for asthma exacerbations, in a similar manner to other respiratory viruses.15

Comparison with other studies
Initial studies of asthma-related emergency healthcare utilisation during the pandemic have all reported a decline in attendances, but have been limited to single centre studies in the paediatric population.6 7 There have also been substantial reductions in non-COVID healthcare utilisation for an array of other emergency presentations reported worldwide.16 17 It was therefore important to determine to what extent decreased admission rates reflect a true decline in the incidence of these conditions versus simply a reduction in presentation at healthcare settings, which could manifest as increased deaths. Our cause-specific mortality data allowed us to explore this. We found no significant impact of the COVID-19 pandemic or lockdown on asthma deaths in Scotland or Wales when considering asthma as the underlying cause on death registration. The fact that we did not see any increase in deaths, and the accompanying ED data, are reassuring in this respect and suggests that the fall in admissions

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Table 1  Poisson models of emergency asthma admissions in 2020 and 5-year average

<table>
<thead>
<tr>
<th></th>
<th>Scotland</th>
<th>Wales</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>IRR (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Pre-lockdown intercept in 2020 compared with 5-year average</td>
<td>0.84 (0.69 to 1.02)</td>
<td>0.076</td>
</tr>
<tr>
<td>Week-on-week change in weeks 1–12</td>
<td></td>
<td></td>
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<tr>
<td>Five-year average</td>
<td>0.98 (0.97 to 1.00)</td>
<td>0.059</td>
</tr>
<tr>
<td>2020</td>
<td>0.97 (0.96 to 1.00)</td>
<td>0.032</td>
</tr>
<tr>
<td>2020 relative to 5-year average</td>
<td>1.00 (0.97 to 1.02)</td>
<td>0.768</td>
</tr>
<tr>
<td>Overall change in trend at week 13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Five-year average</td>
<td>0.97 (0.79 to 1.20)</td>
<td>0.800</td>
</tr>
<tr>
<td>2020</td>
<td>0.57 (0.44 to 0.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2020 relative to 5-year average</td>
<td>0.59 (0.42 to 0.83)</td>
<td>0.003</td>
</tr>
<tr>
<td>Week-on-week change in weeks 13–18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Five-year average</td>
<td>0.99 (0.93 to 1.05)</td>
<td>0.724</td>
</tr>
<tr>
<td>2020</td>
<td>1.03 (0.95 to 1.12)</td>
<td>0.432</td>
</tr>
<tr>
<td>2020 relative to 5-year average</td>
<td>1.04 (0.95 to 1.15)</td>
<td>0.400</td>
</tr>
</tbody>
</table>

IRR, incidence rate ratio.
represents—at least partly—a real reduction in severe asthma exacerbations.

There is currently only limited public availability of cause-specific mortality data for a few conditions.\textsuperscript{18, 19} The Office for National Statistics reported an excess of non-COVID asthma deaths in England and Wales.\textsuperscript{18} However, it considered any mention of asthma on the death certificate to be an asthma death, and care homes have seen the largest rise,\textsuperscript{18} raising the possibility that these increased numbers included people dying ‘with’ rather than ‘of’ asthma. Additionally, a proportion of these ‘non-COVID’ deaths could have had undiagnosed COVID-19, but quantifying this may prove impossible.

Potential explanations for our findings
Several factors could plausibly have contributed to a true decline in the incidence of severe asthma exacerbations during the lockdown. We have begun to examine these in our study, although there are likely to be a multitude of factors involved. Our analysis of GP prescription data in Wales—one of the first national-scale analyses of the impact of the pandemic on prescribing—found large spikes of inhaled and oral corticosteroid prescriptions for people with asthma in the week preceding the lockdown. While this may be partly due to stockpiling of preventer and rescue medication, this also provides some suggestive evidence for the intention to adhere to inhaled therapy regimes, implement self-management and manage exacerbations at home during the pandemic. Asthma exacerbations differ from other acute presentations such as stroke or acute coronary syndrome in that some people with asthma can implement self-management strategies to manage exacerbations, which reduce the need for emergency healthcare utilisation without detriment to their health.\textsuperscript{20} Pharmacy data during the pandemic in the USA have shown that dispensing did not increase for all medications, suggesting that reasons for increases seen are medication-specific or disease-specific.\textsuperscript{21}

Due to the UK Government mandating social distancing and school closures for the vast majority of children, advice regarding hand hygiene, and the ‘shielding’ of those with severe asthma, there is likely to have been a reduction in the transmission of respiratory infections other than SARS-CoV-2, which are the the most common triggers of asthma exacerbations.\textsuperscript{22} FluNet, a global surveillance system, reported a sharp decline in laboratory-confirmed influenza from late March 2020,\textsuperscript{24}

### Table 2 Poisson models of asthma deaths in 2020 and 5-year average

<table>
<thead>
<tr>
<th></th>
<th>Scotland IRR (95% CI)</th>
<th>P value</th>
<th>Wales IRR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-lockdown trend in 2020 compared with 5-year average</td>
<td>2.07 (0.78 to 5.50)</td>
<td>0.143</td>
<td>1.14 (0.35 to 3.74)</td>
<td>0.826</td>
</tr>
<tr>
<td>Week-on-week change in weeks 1–12</td>
<td>0.96 (0.87 to 1.06)</td>
<td>0.428</td>
<td>1.01 (0.90 to 1.14)</td>
<td>0.859</td>
</tr>
<tr>
<td>Five-year average</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>1.04 (0.95 to 1.14)</td>
<td>0.372</td>
<td>1.03 (0.92 to 1.16)</td>
<td>0.595</td>
</tr>
<tr>
<td>2020 relative to 5-year average</td>
<td>1.08 (0.95 to 1.24)</td>
<td>0.235</td>
<td>1.02 (0.87 to 1.20)</td>
<td>0.802</td>
</tr>
<tr>
<td>Overall change in trend at week 13</td>
<td>0.79 (0.60 to 5.32)</td>
<td>0.295</td>
<td>0.67 (0.14 to 2.66)</td>
<td>0.584</td>
</tr>
<tr>
<td>Five-year average</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2020</td>
<td>0.63 (0.21 to 1.93)</td>
<td>0.417</td>
<td>0.82 (0.21 to 2.90)</td>
<td>0.763</td>
</tr>
<tr>
<td>2020 relative to 5-year average</td>
<td>0.35 (0.07 to 1.68)</td>
<td>0.189</td>
<td>1.23 (0.18 to 9.01)</td>
<td>0.836</td>
</tr>
<tr>
<td>Week-on-week change in weeks 13–18</td>
<td>0.85 (0.62 to 1.78)</td>
<td>0.333</td>
<td>1.01 (0.67 to 1.52)</td>
<td>0.967</td>
</tr>
<tr>
<td>Five-year average</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>0.75 (0.49 to 1.17)</td>
<td>0.207</td>
<td>0.97 (0.68 to 1.38)</td>
<td>0.860</td>
</tr>
<tr>
<td>2020 relative to 5-year average</td>
<td>0.88 (0.51 to 1.52)</td>
<td>0.656</td>
<td>0.96 (0.56 to 1.64)</td>
<td>0.883</td>
</tr>
</tbody>
</table>

IRR, incidence rate ratio.

### Table 3 Poisson models of asthma-related emergency department attendances in Wales in 2020 and 5-year average

<table>
<thead>
<tr>
<th></th>
<th>IRR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-lockdown trend in 2020 compared with 5-year average</td>
<td>0.71 (0.53 to 0.94)</td>
<td>0.016</td>
</tr>
<tr>
<td>Week-on-week change in weeks 1–12</td>
<td>0.99 (0.96 to 1.01)</td>
<td>0.255</td>
</tr>
<tr>
<td>Five-year average</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>1.00 (0.97 to 1.03)</td>
<td>0.897</td>
</tr>
<tr>
<td>2020 relative to 5-year average</td>
<td>1.02 (0.98 to 1.06)</td>
<td>0.417</td>
</tr>
<tr>
<td>Overall change in trend at week 13</td>
<td>1.01 (0.76 to 1.34)</td>
<td>0.919</td>
</tr>
<tr>
<td>Five-year average</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>0.79 (0.53 to 1.15)</td>
<td>0.221</td>
</tr>
<tr>
<td>2020 relative to 5-year average</td>
<td>0.78 (0.48 to 1.24)</td>
<td>0.296</td>
</tr>
<tr>
<td>Week-on-week change in weeks 13–18</td>
<td>0.96 (0.89 to 1.04)</td>
<td>0.351</td>
</tr>
<tr>
<td>Five-year average</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>0.82 (0.72 to 0.93)</td>
<td>0.002</td>
</tr>
<tr>
<td>2020 relative to 5-year average</td>
<td>0.85 (0.73 to 0.99)</td>
<td>0.033</td>
</tr>
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</table>

IRR, incidence rate ratio.
with primary care physicians’ threshold to refer patients to hospital heightened due to reluctance to expose patients to SARS-CoV-2 in hospital. Fear of contracting SARS-CoV-2 infection has been identified as a key factor in delayed presentations and the significant reductions in emergency healthcare utilisation seen in other health conditions. However, those with chronic respiratory conditions may have been more likely to seek medical attention than other patient groups if experiencing an exacerbation, since they may fear worsening respiratory symptoms are COVID-19-related. Cough is one of the few presentations which has been reported as seeing a significant increase during the pandemic.

The reduction in asthma emergency admissions in 2020 was broadly comparable in Scotland and Wales. However, our findings also show differences in the trends between both countries. For example, the pre-lockdown slope was falling faster than the 5-year averages in Wales but not in Scotland. In addition, the slope after the introduction of lockdown, that is, during the weeks 13–18, was continuing to decrease in Wales whereas it was slightly increasing in Scotland. These differences might be due to environmental factors or differences in public health messaging, adherence to social distancing guidelines, and/or healthcare service between these two countries.

Lastly, the overall lower level of emergency admissions for asthma since the beginning of 2020 compared with the previous 5 years could be explained by the influenza season in 2019/2020 which occurred earlier than in the preceding 5 years.

Strengths and limitations of this study
This is the first national-level analysis of the impact of the COVID-19 pandemic on asthma-related emergency admissions and deaths, bringing together the paediatric and adult asthma populations across Scotland and Wales, thus enabling comparison between across two UK nations. We were able to perform near real-time population analyses, applying an interrupted time-series analysis to evaluate the intervention of instigating lockdown in the UK.

Our study has some limitations. First, the changes in asthma admission trends during lockdown do not necessarily imply causal effects, and the observed associations are likely to have been underpinned by a series of contributing factors which we could not measure, such as improvements in outdoor air quality and reductions in rates of transmission of other respiratory viruses. Second, the case definitions for asthma admissions and deaths have not been validated and may have variable accuracy. However, given that we were interested in trends over time rather than absolute numbers, and that coding practices are unlikely to have changed, this is unlikely to have significantly affected our findings. Third, we excluded two areas in Scotland from admissions figures due to data incompleteness, which might have affected the generalisability of our findings. That said, the consistent findings across the two nations provides supportive evidence for the likely generalisability of our findings. Finally, asthma deaths are relatively rare, and the small number of asthma deaths in both nations restricted our power to detect small changes in deaths during lockdown and also to adjust our models for various demographic, socioeconomic and other relevant covariates. We were also limited by the length of follow-up due to availability of data during lockdown in the two countries.
CONCLUSIONS AND POLICY IMPLICATIONS
In summary, there was a substantial decline in asthma emergency admissions across Scotland and Wales during UK lockdown with no corresponding increases in asthma deaths. We do not yet know to what degree the reduced numbers of emergency presentations of asthma in our study are due to improvements in asthma control or reductions in exposures to triggers during the pandemic versus avoidance of healthcare settings. We highlight several important areas for future investigation to understand underlying reasons, including positive drivers such as improved self-management and reduced exposure to respiratory pathogens and pollutants. It is crucial to assess the fuller impact of the study. CR reports grants from Medical Research Council and Public Health Scotland corresponding author and guarantor for this work and attests that all listed authors to study design and data interpretation. EV conducted the statistical analysis for the study.

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Contributors AS conceived the study. MAA, CR, AS, GAD and RAL contributed to study design and data interpretation. EV conducted the statistical analysis for Scotland. MAA conducted the statistical analysis for Wales and prepared the Tables and Figures. CR advised on statistical analysis. GAD, SS and MAA drafted the manuscript. GAD and AS commented critically on several drafts of the manuscript. All authors critically reviewed and approved the final version of the manuscript. MAA is corresponding author and guarantor for this work and attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Data availability statement The anonymised person-level data used in this study are held by Public Health Scotland (PHS) and the Secure Anonymised Information Linkage (SAIL) Databank and are restricted and not publicly available but can be accessed upon reasonable requests from PHS and SAIL. All proposals to use SAIL are carefully reviewed by an independent Information Governance Review Panel to ensure proper and appropriate use of data (https://www.sailedatabank.com/application-process). When approved, access is then provided through the SAIL Gateway, a privacy-protecting safe haven and a secure remote access system.

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