Risk of winter hospitalisation and death from acute respiratory infections in Scotland: national retrospective cohort study

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Abstract

Objectives

We undertook a national analysis to characterise and identify risk factors for acute respiratory infections (ARIs) resulting in hospitalisation during the winter period in Scotland.

Design

A population-based retrospective cohort analysis

Setting

Scotland

Participants

5.4 million residents in Scotland

Main outcome measures

Cox proportional hazard models were used to estimate adjusted hazard ratios (aHR) and 95% confidence intervals (CIs) for the association between risk factors and ARI hospitalisation.

Results

Between September 1, 2022 and January 31, 2023, there were 22,284 (10.9% of 203,549 with any emergency hospitalisation) ARI hospitalisations (1,759 in children and 20,525 in adults) in Scotland. Compared to the reference group of children aged 6-17 years, the risk of ARI hospitalisation was higher in children aged 3-5 years (aHR=4.55 95%CI (4.11-5.04)). Compared to 25-29 years old, the risk of ARI hospitalisation was highest amongst the oldest adults aged ≥80 years (7.86 (7.06-8.76)). Adults from more deprived areas (most deprived vs least deprived, 1.64 (1.57-1.72)), with existing health conditions (≥5 vs 0 health conditions, 4.84 (4.53-5.18)) or with history of all-cause emergency admissions (≥6 vs 0 previous emergency admissions 7.53 (5.48-10.35)) were at higher risk of ARI hospitalisations. The risk increased by the number of existing health conditions and previous emergency admission. Similar associations were seen in children.

Conclusions

Younger children, older adults, those from more deprived backgrounds and individuals with greater numbers of pre-existing conditions and previous emergency admission were at increased risk for winter hospitalisations for ARI.

Introduction

Acute respiratory infections (ARI) constitute a substantial disease burden, particularly in young children and older adults.[1, 2] The Global Burden of Disease (GBD) Study 2019 estimated that, in 2019, lower respiratory tract infections (LRIs) caused 628,338 deaths (95% uncertainty interval [UI] 513,848-775,433) in children younger than 5 years, 613,468 deaths (526,059-698,564) in adults older than 70 years, and over 1.6 million deaths in people of all ages, worldwide.[3]

Many health systems internationally, including the National Health Services (NHS) in the UK, face considerable pressures each year over the winter period, particularly being driven by the seasonal increases in ARI. These increases in ARI typically begin with the start of the new school year and extend throughout the winter period. In addition to the usual surge in demand for care associated with ARI, the NHS was under unprecedented pressure last winter (2022-23) as a result of the ongoing COVID-19 pandemic, NHS staff absences and vacancies, and the cost-of-living crisis.[4] Last year, there were in addition major concerns about increases in the incidence and severity of respiratory syncytial virus (RSV) as seen in parts of the United States and Europe.[5] In summary, the ongoing health system pressures are substantial during winter and therefore there is policy interest in trying to understand who might be most likely to be admitted to hospital. This would help to inform targeted preventive actions (such as vaccination, optimising care for individuals with pre-existing conditions).

During the pandemic, we created the Early Pandemic Evaluation and Enhanced Surveillance of COVID-19 (EAVE II) national COVID-19 surveillance platform, which has been used to identify and predict children and adults at increased risk of serious COVID-19 outcomes leading to hospitalisation and death. Following an urgent commission from the Department of Health and Social Care, we repurposed the EAVE II platform to characterise and identify risk factors predicting those at risk of hospitalisation associated with ARI during the winter period across Scotland.

Methods

Study design

EAVE II is a Scotland-wide COVID-19 surveillance platform that has been used to track and forecast the epidemiology of COVID-19, inform risk stratification assessment, and investigate vaccine effectiveness and safety.[6-10] It comprises national health-care datasets on 5·4 million people (~99% of the Scottish population) deterministically linked through the Community Health Index (CHI) number, which is a unique identifier for each population member and used in all healthcare contacts across NHS Scotland.

We used the EAVE II platform to describe the demographic profile of people of different age groups who had hospital admissions associated with ARI (henceforth 'ARI hospitalisation'). We also undertook a national population-based observational cohort analysis to investigate risk factors of ARI as well as the risk factors for common respiratory pathogens associated ARI (influenza, RSV and SARS-CoV-2), stratified by age groups. The cohort baseline was March 1, 2020 (when the COVID-19 pandemic started in Scotland) thus our cohort included individuals who were at least three years old. This analysis was based on all 5,021,056 people in the EAVE II linked dataset on September 1, 2022. The study period was September 1, 2022 to January 31, 2023.

Data sources

The national datasets linked using CHI numbers were primary care (demographics and clinical history), the Scottish Morbidity Record (which records hospitalisation data), the Scottish Intensive Care Society Audit Group (which records intensive care unit (ICU) admissions), and National Records of Scotland (which records mortality data). A data linkage diagram is available at Figure S1. All individuals were

followed from September 1, 2022 until the date of ARI hospitalisation, date of death or end of follow-up (January 31, 2023), whichever came first.

Outcomes

Our primary outcome was ARI hospitalisation. We defined ARI hospitalisation as the first hospital emergency admission during the study period with an International Classification of Diseases, Tenth Revision (ICD-10) code for respiratory infections in any position of the first episode (admitted due to or with respiratory infections). We also looked at common respiratory pathogens (I.e. influenza, RSV and SARS-CoV-2) related ARI hospitalisation, defined by ICD-10 code. The full list of ICD-10 codes for ARI is available in Table S1.

Our secondary outcomes were ARI related length of hospital stay, ICU admission and death. ICU admission was defined as admission to ICU after ARI hospitalisation. Death was defined as any cause of death within 28 days of ARI hospitalisation. Follow-up time for individuals who were hospitalised within 28 days prior to the cohort end date was extended to allow 28 days of follow-up after hospitalisation. For the primary outcome (ARI hospitalisation), we also applied a strict definition in a sensitivity analysis, which was a hospital emergency admission with an ICD-10 code for respiratory infections in the first position of the first episode.

Covariates

We included age, sex, ethnicity, urban/rural areas, Scottish Index of Multiple Deprivation (SIMD), number of previous all-cause emergency hospitalisation (for any reason) in the six months prior to September 1, 2022, number of risk groups (co-morbidities), Health Board, body mass index (BMI), vaccination for COVID-19 (at any time; number of doses) and influenza vaccination (during study period) as the covariates. Socioeconomic status was determined using the SIMD.[11] The SIMD is a measure of deprivation in areas typically comprising 700-800 people, that captures multiple dimensions of socioeconomic disadvantage. We used quintiles of SIMD, where quintile 1 refers to the most deprived and quintile 5 refers to the least deprived. SIMD was assigned according to residential postcode. Risk groups (co-morbidities) were defined by those used in the QCOVID risk prediction algorithm, which consists of 30 clinical characteristics identified from primary care records that are known to be associated with increased risk of serious COVID-19 outcomes in adults (Box 1).[12] For the analysis of children, we excluded risk groups that were not relevant to the paediatric population (i.e. care home/homeless (no children in the cohort were classified as homeless over the study period), chronic obstructive pulmonary disease, coronary heart disease, dementia, Parkinson's disease) and BMI (due to different measurement for children with substantial percentage of missing data, 95%).

Statistical analysis

We developed the statistical analysis plan for this work in advance which is available at https://www.ed.ac.uk/usher/eave-ii/connected-projects/winter-respiratory-pressures-in-scotland/project-outputs/statistical-analysis-plan.

A Cox proportional hazard was used to model the time to ARI hospitalisation and to derive the adjusted hazard ratios (aHR) and 95% confidence intervals (CIs) for the association between risk factors and ARI hospitalisation. This model eliminated the need to model the underlying temporal trends, which was incorporated into the baseline hazard. To improve the efficiency of the analysis, the cox model was fitted to a subset of the data – all the cases who had experienced an emergency ARI hospitalisation and, for each case, 10 randomly selected controls who did not have an emergency ARI hospitalisation during the study period. Sample weights were then used to weight the analysis sample back to the full population. The 10:1 ratio was predetermined and the sampling of the original cohort was a simple random sample without replacement.

Age, sex, socioeconomic status, number of risk groups (defined above), and number of previous emergency hospitalisations within six months prior to September 1, 2022 were included as adjustments. Ethnicity (due to 14.6% missing data in cases, and 29.0% in controls), Health Board, COVID-19 and influenza vaccination were not included in the modelling in our main analysis. A small number of individuals had missing data for urban/rural areas (0.6%) and SIMD (0.6%), and they were excluded from the analysis. Some individuals were also missing BMI data (7.8%), which we imputed using multiple imputations. Similarly, Cox proportional hazard models were fitted to estimate the association between risk factors and specific common respiratory pathogens (RSV, influenza and SARS-CoV-2) related hospital admission. ARI hospitalisations which were not RSV, influenza and SARS-CoV-2 related were censored at the first admission for the pathogen specific models. All controls were censored at the end of the study.

A multivariable logistic regression model was conducted to estimate the association between risk factors and ARI related prolonged hospital stay (a hospital stay longer than five days – the median length of stay for ARI hospitalisations). Patients who died in the interim were included in the multivariable logistic regression analysis for prolonged hospital stay. Odds ratio (OR) and 95% CI was generated. All analyses were carried out in two age groups (i.e. 3-17 years vs. ≥18 years, respectively) as the risk profiles between these groups may have been different.

For other secondary outcomes (i.e. ICU admission or death), we calculated the percentage of ICU admission among individuals hospitalised with ARI and the percentage of all cause deaths among individuals hospitalised with ARIs (in-hospital case fatality ratio), respectively.

A pre-specified sensitivity analysis was carried out using a strict definition for ARI hospitalisation where ARI was the primary cause of hospitalisation. We also looked at Electronic Communication of Surveillance in Scotland (ECOSS), which is a national database for all virology testing, to estimate the number of laboratory-confirmed influenza and SARS-CoV-2 cases in comparison to those identified using ICD-10 codes. Another two sensitivity analyses were conducted including ethnicity or smoking status in the Cox modelling. Smoking status data were based on March 2020 and for individuals with no data on smoking, we classified them as unknown, and we assumed that there has been no change since then. Sensitivity analyses adjusting for either influenza vaccination status or SARS-CoV-2 vaccination status were also conducted when looking at outcomes of influenza hospitalisation or SARS-CoV-2 hospitalisation.

The Cox proportional hazards models used sampling weights to correct for the size of the registered general practice population being greater than the population in Scotland (some due to individuals who had recently moved). These weights were derived by matching the age and sex numbers in the general practice data to the Scottish population data (from 2011 Scotland census). This adjustment ensured that the denominators in the tables matched the Scottish population.

Use of reporting guideline

We followed the Reporting of Studies Conducted using Observational Routinely-collected Data (RECORD) and Strengthening the Reporting of Observational studies in Epidemiology (STROBE) checklists[13, 14] to guide transparent reporting of this cohort study (Table S2).

Data availability

Analyses were carried out in R (version 3.6.1). A data dictionary covering the datasets used in this study can be found at https://github.com/EAVE-II/EAVE-II-data-dictionary. All code developed for this analysis is available in our GitHub repository: https://github.com/EAVE-II/winter_pressures_code. The data used in this study are sensitive due to individual patient-level data and will not be made publicly

available. We will deposit the meta-data information in the Health Data Research Innovation Gateway on publication.

Ethics and permissions

Ethical approval was obtained from the National Research Ethics Service Committee, Southeast Scotland 02 (reference number, 12/SS/0201). The Public Benefit and Privacy Panel Committee of Public Health Scotland approved the linkage and analysis of the de-identified datasets for this project (1920-0279).

Patient and Public Involvement

We have patient and public involvement engagement throughout the project. The details are available in Supplementary Materials Tables S3 and S4.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or the writing of the report.

Results

5,021,056 individuals aged at least three years old across Scotland were included in this analysis. Overall, there were 22,284 (10.9% of 203,549 with any first emergency hospitalisation) ARI emergency first admissions during September 1, 2022 and January 31, 2023 (1,759 in children and 20,525 in adults). 1,804 (7.5%) were upper respiratory infections, 5,609 (23.3%) were unspecified lower respiratory infections, 11,986 (49.9%) were influenza/pneumonia, 4,280 (17.8%) were COVID-19, 227 (0.9%) were bronchiolitis and 138 (0.6%) were RSV. 7,997 (35.9%) had multiple respiratory infection categories listed above. Among 22,284 ARI hospitalisation, the median age was 72.5 (interquartile range 56.0, 82.4) years. 53.2% of them were female and 46.8% male. 13.1% of them were older adults aged 75-79 years old and 33.8% were at least 80 years old. About 25.6% of them (22,284) did not have any existing conditions as defined by the QCOVID prediction algorithm.[12] Most people (74.1%) did not have any all-cause emergency admissions in the past six months prior to September 1, 2022. Among the 22,284 people admitted to hospitals with ARI across Scotland during the study period, 1,126 (5.1%) were admitted to ICU (86 children and 1040 adults) and 1,660 (7.4%) died (all adults); 1,605 (7.2%) were readmitted to hospitals following discharge from their first ARI hospitalisation. A data flow diagram showing the number of individuals included at different stages is available in Figure 1. More baseline demographic characteristics on the study population are available in Table 1. Details on individuals with ARI hospitalisation including first admissions and readmissions are available in Table S5. We also compared the ARI hospitalisation to other causes emergency hospitalisation during the study period (Table S6). The cumulative incidence of ARI hospitalisation in children and adults was plotted in Figure S2. Number of ARI hospitalisation over time is shown in Figure S3. When we compared number of ARI hospitalisation over time to emergency admissions due to other health conditions, we have observed a peak in ARI hospitalisation while there was no peak for other health conditions associated emergency admission during the same study period (Figure S4).

Adults

In the Cox modelling results for adults with ARI (Table 2), older adults aged ≥45 years old were found to be at an increased risk of ARI hospitalisation compared to adults aged 25-29 years old. The HRs increased with age with overlapping confidence intervals. The highest HR was found in adults aged at least 80 years old (aHR=7.86, 95% CI 7.06-8.76). Adults from increasingly deprived areas had increased risk of ARI hospitalisation (with overlapping confidence intervals): most deprived vs least

deprived, 1.64 (1.57-1.72). Adults with existing conditions showed a much higher risk than those without existing conditions, and the more existing conditions they had the higher the risk was (with overlapping confidence intervals): ≥5 vs 0 health conditions, 4.84 (4.53-5.18). Similarly, adults with a history of all-cause emergency admissions had a much higher risk of ARI hospitalisation than those without, and the more previous emergency admissions they had the higher the risk of ARI hospitalisation was: ≥6 vs 0 previous emergency admissions 7.53 (5.48-10.35). Adults underweight (BMI <18.5) or severely obese (≥40) showed slightly higher risks of ARI hospitalisation. Adults with BMI 25.0-34.9 had slightly reduced risks of ARI hospitalisation. Adults from urban areas had slightly increased risk of ARI hospitalisation. Similar results and trends were found when looking specifically at influenza and SARS-CoV-2 respiratory pathogens (Table 2). Due to the small number of events for RSV when stratified by different variables, Cox modelling was not conducted.

Length of hospital stay was five days or less for 52.7% of patients. The multivariable logistic regression results showed that in adults, those aged at least 35 years old were associated with prolonged ARI related longer hospital stay (>5 days) and the association increased by age (Table S7). The OR (95% CI) was highest in those aged at least 80 years old (9.30 (6.98-12.64)). Those underweight (BMI <18.5), from most deprived areas, with 1-4 previous emergency admissions or from urban areas were at slightly higher risk of prolonged hospital stay. However, we did not find associations between adults with existing conditions or who had at least five previous emergency admissions and ARI related prolonged hospital stay.

Children

In the Cox modelling results for children with ARI (Table 3), children aged 3-5 years old were at increased risk of ARI hospitalisation: aHR 4.55 (4.11-5.04) compared to children aged 6-17 years old. Similarly, children from more deprived areas, with existing conditions or with history of all-cause emergency admissions were at increased risk of ARI hospitalisation. The more existing conditions or previous emergency admissions they had, the higher the risk. Children from urban areas had slightly increased risk of ARI hospitalisation. Due to the limited number of events for specific respiratory pathogen associated ARI when stratified by different variables, Cox modelling was not carried out.

Sensitivity analysis

In the sensitivity analysis using the strict definition of ARI hospitalisation (ARI as the primary cause of hospital admission), 14,612 people were admitted to hospitals with ARI across Scotland during the study period (1,534 children and 13,941 adults). The median age was 71.5 (interquartile range 53.5, 81.6) years old. All baseline demographic characteristics were similar to those when using the broad definition (Table S8). Among the 14,612 ARI hospitalisations across Scotland, 719 (4.9%) were admitted to ICU (71 children and 648 adults) and 1,008 (6.9%) died (all adults).

Sensitivity analysis – adults

The Cox modelling showed similar results on risk of ARI hospitalisation in adults (Tables S9 and S10), being increased by age, higher in those from more deprived areas, with existing conditions or a history of all-cause emergency admissions. Adults underweight (BMI <18.5) or severely obese (≥40) or from urban areas similarly showed slightly higher risk of ARI hospitalisation. Similar findings were observed for influenza or SARS-CoV-2 associated ARI hospitalisation in adults (Table S9). Another sensitivity analysis comparing laboratory-confirmed influenza and SARS-CoV-2 cases to those identified using ICD-10 codes has shown that 2,984 -2,749 cases of SARS-CoV-2 associated ARI hospitalisation in adults during our study period. The results of the Cox model for influenza and COVID-19 associated ARI hospitals showed similar findings when using laboratory-confirmed data in comparison to ICD-10 codes (Table S11). Another sensitivity analysis including ethnicity in the Cox modelling has shown similar results for all variables and within ethnicity “unknown” group seemed

to have a lower risk (compared to "White" group) (Table S12). Sensitivity analysis including smoking status in the Cox modelling has shown similar results for all variables and within the smoking status, adults who were current smokers or ex-smokers had a higher risk of ARI hospitalisation (1.59 (1.51-1.66) and 1.26 (1.22-1.31) respectively, in comparison to non-smokers (Table S13). Similar findings were found for influenza or SARS-CoV-2 associated ARI hospitalisation. Cox modelling for influenza or SARS-CoV-2 related ARI hospitalisation after adjusting for influenza or SARS-CoV-2 vaccination is available in Tables S14-S15. The risk of influenza hospitalisation was lower in those with influenza vaccines (0.76 (0.73-0.80)). The risk of SARS-CoV-2 hospitalisation was -and fourth or fifth dose vaccines (0.64 (0.58-0.71)) and 0.83 (0.73-0.93) respectively), in comparison to those unvaccinated or had first or two dose vaccines.

Sensitivity analysis – children

The results for children using the strict definition of ARI hospitalisation were similar to the main analyses of using broad definition (Table S10).

Discussion

We provide national evidence of important predictors for hospitalisations due to ARI during the winter 2022-23. Children and adults from more deprived areas, those with existing health conditions and with a history of all-cause emergency admissions experienced an increased risk of ARI hospitalisations in Scotland. Younger children and older adults were at particularly at higher risk. Urban areas were also associated with a slight increased risk of ARI hospitalisation. The results were similar whether a broad definition for ARI (a hospital admission due to or associated with ARI) or strict definition for ARI (a hospital admission due to ARI) was used. Influenza or SARS-CoV-2 associated ARI in adults had similar risk factors. However, the length of hospital stay among adults was less affected by these risk factors except for age and underweight. In addition, we have also shown the impact of smoking on the risk of ARI hospitalisation and the impact of influenza or SARS-CoV-2 vaccines on the risk of influenza or SARS-CoV-2 hospitalisation.

Our study has several strengths. We undertook a national population-level study assessing the risk of ARI hospitalisations among people of different age groups in Scotland. We developed a national linked dataset and created a platform that allowed rapid access to and analysis of data from routinely collected electronic health records and national databases. Therefore, our study potentially has lower risk of recall or misclassification bias. The use of a large population aided study power, facilitating precise estimates of HRs for ARI associated hospital admission or ORs for prolonged hospital stay stratified by different variables. We are likely to have excellent generalisability across the UK and potentially other countries with similar demographics and health systems.

Our study has several limitations. It is noteworthy that since we only included a five-month study period, there were low absolute numbers of events for RSV related ARI hospitalisations in adults and RSV/influenza/SARS-CoV-2 related ARI hospitalisations in children. These low numbers precluded the opportunity for further investigations into the severe outcomes of these specific respiratory pathogens and highlighted the need for laboratory diagnosis of these respiratory pathogens. RSV is one of the important viral pathogens identified in older adults with ARI and is increasingly recognised as a cause of illness in high-risk adults, including those with chronic lung and heart disease.[15, 16] RSV is also one of the most common pathogens responsible for ARI in young children and contributed to over 3 million hospital admissions in children under five years old annually across the world.[17] With RSV vaccines in children and older adults being developed and planned internationally,[18] more research assessing the risk profiles of RSV related ARI including in-hospital and post-discharge complications would be needed to inform and support decisions on vaccination priorities among high-risk populations. There was a lack of more granular data on the reason for admission, so we used both broad and strict definitions for our main outcome – ARI hospitalisation (hospital admission due to or

associated with ARI vs. hospital admission due to ARI) and the results were comparable. Regarding the adjustment of risk groups among children, we only included risk groups that were defined by the QCOVID prediction algorithm[12] (which was based on adult population), so we may have missed some important paediatric risk groups. There may also have been different healthcare seeking behaviours and lower threshold for hospital admission (influenced by physician and hospital factors) in children and adults with existing health conditions, which may have resulted in higher risk of hospital admissions with ARI. Our main analysis did not include some potentially important predictors (such as smoking status) due to these data being somewhat out of date (being updated to March 2020 only). However, our sensitivity analysis including smoking status has shown that current smokers and ex-smokers (compared to non-smokers) both had higher risk of ARI hospitalisation and influenza or SARS-CoV-2 associated ARI hospitalisation. Our main analysis did not include influenza or SARS-CoV-2 vaccination in the Cox modelling either due to the fact that there were no mechanisms for these vaccines to have effect on for non-specific outcomes (non-influenza/SARS-CoV-2 hospitalisation). However, our sensitivity analysis including vaccination status has shown that adults with influenza vaccines or SARS-CoV-2 vaccines had lower risk of influenza hospitalisation or SARS-CoV-2 hospitalisation.

Similar findings have been reported in the literature. The risk factors for influenza associated ARI hospitalisation included age <5 and ≥65 years old, diabetes, heart diseases and chronic respiratory diseases during the 2018/2019 winter season in Yemen.[19] Prematurity, presence of a chronic illness, oxygen saturation < 90%, and atelectasis and consolidation on chest X-rays were associated with an increased ARI related length of hospital stay based on the viral surveillance of children with ARI in two main hospitals in Northern Jordan, Irbid, during the winter of 2016.[20] Also, the presence of chronic obstructive pulmonary disease (COPD), other chronic disease and being housebound were found to be independent risk factors associated with winter hospital admissions among older people presenting with ARI.[21] Our study has added robust and generalisable evidence using population level data and quantified associations between demographic and clinical risk factors and ARI hospitalisation in both children and adults. Building on this work, it is important for more detailed characterisation of potential modifiable risk factors for specific respiratory pathogen associated ARI hospitalisation and to investigate underlying mechanisms that predispose such populations to these increased risks.

Our findings lay the foundations for the development and validation of winter respiratory risk prediction models in children and adults. Scotland currently uses the Scottish Patients at Risk of Readmission and Admission (SPARRA V3) risk prediction tool,[22] but it was developed for use prior to the pandemic (last iteration in 2011), does not use data from GP primary care data (except for prescription records), provides an assessment of risk over a 12-month horizon for highest risk of admission/readmission, is only for use in adults aged ≥16 years and predicts any type of admission without distinguishing specific types. The model has different performance depending on the condition.[23] Thus, developing a more targeted SPARRA-like risk prediction model would be needed. We will be able to use this to identify practices/areas of the country that contain the largest numbers of high-risk individuals which could then inform the allocation of resources with the aim of improving the delivery of care.

In conclusion, this national analysis has provided the first detailed characterisation of individuals with ARI contributing NHS compound winter pressure in Scotland. We identified individuals who were at greatest risk of being admitted to hospitals with ARI and lay the foundations for new risk prediction tools in children and adults, which can be used to target interventions and resources to those most at risk. Moreover, the unique data resources available to us through EAVE II provided insights into predicting and forecasting emergency NHS use for the UK as a whole.

Contributors

AS, CR, and TS conceived this study. AS, CR, TS and TM commented on the paper, oversaw the analysis, and edited the final manuscript. TS and AS led the writing of the paper. TM led the data analysis with support from CR, BS and AF. All authors contributed to the study design. All authors contributed to drafting the paper and revised the manuscript for important intellectual content. All authors had final responsibility for the decision to submit for publication.

Declaration of interests

AS and CR are members of the Scottish Government's CMO COVID-19 Advisory Group. AS and CR are members of NERVTAG's risk stratification subgroup. CR is a member of SPI-M. AS was a member of AstraZeneca's Thrombotic Thrombocytopenic Advisory Group and the Scottish Government's Standing Committee on Pandemics. SVK was co-chair of the Scottish Government's Expert Reference Group on Ethnicity and COVID-19. IR is a member of Scientific Advisory Panel on COVID-19 of the Government of Croatia and the President of the International Society of Global Health. All roles are unremunerated. All other co-authors report no conflict of interests.

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1 **Table 1: Baseline characteristics of the cases with ARI hospitalisation, selected controls and eligible controls without ARI**
2 **hospitalisation from the Scottish population**

Variable	Level	Cases	Controls	Full Population
All		22284	222840	4998772
Age	Mean (standard deviation)	65.6 (24)	44.6 (22.8)	44.6 (22.8)
	Median (interquartile range)	72.5 (56,82.4)	44.5 (25.7,62)	44.5 (25.7,61.9)
Number of Risk Groups	0	5699 (25.6%)	133906 (63.9%)	3195309 (63.9%)
	1	5352 (24.0%)	50267 (24.0%)	1197439 (24.0%)
	2	4439 (19.9%)	16311 (7.8%)	389051 (7.8%)
	3	3172 (14.2%)	5624 (2.7%)	135680 (2.7%)
	4	1927 (8.6%)	2156 (1.0%)	51768 (1.0%)
	≥5	1695 (7.6%)	1271 (0.6%)	29525 (0.6%)
Sex	Female	11865 (53.2%)	107306 (51.2%)	2561551 (51.2%)
	Male	10419 (46.8%)	102228 (48.8%)	2437221 (48.8%)
Age Groups (years)	3-5	896 (4.0%)	5648 (2.7%)	135310 (2.7%)
	6-17	863 (3.9%)	26894 (12.8%)	637394 (12.8%)
	18-24	427 (1.9%)	15518 (7.4%)	373455 (7.5%)
	25-29	364 (1.6%)	12940 (6.2%)	311123 (6.2%)
	30-34	397 (1.8%)	14222 (6.8%)	337104 (6.7%)
	35-39	449 (2.0%)	13998 (6.7%)	339234 (6.8%)
	40-44	458 (2.1%)	13655 (6.5%)	333720 (6.7%)
	45-49	482 (2.2%)	13014 (6.2%)	309699 (6.2%)
	50-54	811 (3.6%)	15356 (7.3%)	366700 (7.3%)
	55-59	1151 (5.2%)	16590 (7.9%)	389812 (7.8%)
	60-64	1534 (6.9%)	15238 (7.3%)	364695 (7.3%)
	65-69	1741 (7.8%)	13174 (6.3%)	309985 (6.2%)
	70-74	2276 (10.2%)	11460 (5.5%)	268762 (5.4%)
	75-79	2914 (13.1%)	9528 (4.5%)	226550 (4.5%)
	≥80	7521 (33.8%)	12300 (5.9%)	295228 (5.9%)
COVID-19 Vaccination Status	Unvaccinated	2414 (10.8%)	37712 (18.0%)	894038 (17.9%)
	1st Dose >14 days	448 (2.0%)	7362 (3.5%)	177871 (3.6%)
	2nd Dose >14 days	1542 (6.9%)	27206 (13.0%)	653529 (13.1%)
	3rd Dose >14 days	7994 (35.9%)	115904 (55.3%)	2761678 (55.2%)
	4th Dose >14 days	9215 (41.4%)	20143 (9.6%)	483534 (9.7%)
	5th Dose >14 days	671 (3.0%)	1207 (0.6%)	28122 (0.6%)
Influenza Vaccination Status	Unvaccinated	11753 (52.7%)	118391 (56.5%)	2830373 (56.6%)
	0 - 14 days	1187 (5.3%)	364 (0.2%)	8503 (0.2%)
	>14 days	9344 (41.9%)	90780 (43.3%)	2159896 (43.2%)
Urban/Rural Classification	Rural	3752 (16.8%)	40431 (19.3%)	958830 (19.2%)

	Urban	18532 (83.2%)	169103 (80.7%)	4039942 (80.8%)
SIMD quintiles	1 – Most deprived	3138 (14.1%)	41561 (19.8%)	991130 (19.8%)
	2	6035 (27.1%)	42619 (20.3%)	1021100 (20.4%)
	3	5122 (23.0%)	41758 (19.9%)	996473 (19.9%)
	4	4288 (19.2%)	41283 (19.7%)	977798 (19.6%)
	5 – Least Deprived	3701 (16.6%)	42313 (20.2%)	1012271 (20.3%)
ICU Admission	Adult ICU Admission	1012 (4.5%)	400 (0.2%)	9274 (0.2%)
	Children ICU Admission	88 (0.4%)	< 5 (0.0%)	66 (0.0%)
	No ICU Admission	21184 (95.1%)	209132 (99.8%)	4989432 (99.8%)
Deaths	Yes	1660 (7.4%)	777 (0.4%)	17910 (0.4%)
	No	20624 (92.6%)	208757 (99.6%)	4980862 (99.6%)
Length of Hospital Stay (days)	0	0	205673 (98.2%)	4906647 (98.2%)
	1	4055 (18.2%)	1027 (0.5%)	25306 (0.5%)
	2	2575 (11.6%)	583 (0.3%)	13922 (0.3%)
	3-4	5122 (23.0%)	914 (0.4%)	21812 (0.4%)
	5-9	4319 (19.4%)	635 (0.3%)	14312 (0.3%)
	10-19	3284 (14.7%)	366 (0.2%)	9064 (0.2%)
	≥20	2929 (13.1%)	336 (0.2%)	7709 (0.2%)
Number of previous admissions*	0	16523 (74.1%)	202858 (96.8%)	4841196 (96.8%)
	1	3728 (16.7%)	5489 (2.6%)	129925 (2.6%)
	2	1267 (5.7%)	860 (0.4%)	20197 (0.4%)
	3	431 (1.9%)	224 (0.1%)	4911 (0.1%)
	4	172 (0.8%)	61 (0.0%)	1547 (0.0%)
	5	79 (0.4%)	25 (0.0%)	538 (0.0%)
	≥6	84 (0.4%)	17 (0.0%)	458 (0.0%)
Ethnicity	Asian	337 (1.5%)	5261 (2.5%)	126062 (2.5%)
	Black	66 (0.3%)	1297 (0.6%)	31739 (0.6%)
	Mixed	60 (0.3%)	1472 (0.7%)	33524 (0.7%)
	White	18492 (83.0%)	139574 (66.6%)	3333646 (66.7%)
	Other	74 (0.3%)	1100 (0.5%)	26544 (0.5%)
	Unknown	3255 (14.6%)	60831 (29.0%)	1447257 (29.0%)
Health Board	NHS Ayrshire and Arran	1754 (7.9%)	12709 (6.1%)	307607 (6.2%)
	NHS Borders	400 (1.8%)	4031 (1.9%)	96177 (1.9%)
	NHS Dumfries and Galloway	812 (3.6%)	5886 (2.8%)	141258 (2.8%)
	NHS Fife	1050 (4.7%)	13735 (6.6%)	328683 (6.6%)
	NHS Forth Valley	1028 (4.6%)	11397 (5.4%)	268695 (5.4%)
	NHS Grampian	1930 (8.7%)	22300 (10.6%)	531963 (10.6%)
	NHS Greater Glasgow and Clyde	5656 (25.4%)	46480 (22.2%)	1115443 (22.3%)

	NHS Highland	828 (3.7%)	12626 (6.0%)	300571 (6.0%)
	NHS Lanarkshire	3115 (14.0%)	26170 (12.5%)	618786 (12.4%)
	NHS Lothian	3784 (17.0%)	35126 (16.8%)	838759 (16.8%)
	NHS Orkney	83 (0.4%)	805 (0.4%)	18637 (0.4%)
	NHS Shetland	63 (0.3%)	856 (0.4%)	20861 (0.4%)
	NHS Tayside	1691 (7.6%)	16548 (7.9%)	392020 (7.8%)
	NHS Western Isles	90 (0.4%)	866 (0.4%)	19312 (0.4%)

Data are n (%). * Number of previous admissions was within six-month period prior to September 1, 2022. ARI: Acute Respiratory Infection. SIMD: Scottish Index of Multiple Deprivation. ICU: Intensive Care Unit.

5 **Table 2: Adjusted hazard ratios of hospitalisation with acute respiratory infections in adults aged ≥18 years old**

Variable	Level	ARI hospitalisation		Influenza hospitalisation		SARS-CoV-2 hospitalisation	
		No. of events	HR (LCI, UCI)	No. of events	HR (LCI, UCI)	No. of events	HR (LCI, UCI)
Sex	Female	11041	1.00	6173	1.00	2179	1.00
	Male	9484	1.06 (1.03, 1.09)	5393	1.08 (1.04, 1.12)	2017	1.18 (1.11, 1.26)
Age (years)	18-24	427	1.01 (0.88, 1.16)	123	0.68 (0.54, 0.86)	49	1.05 (0.69, 1.59)
	25-29	364	1.00 (1.00, 1.00)	154	1.00	40	1.00
	30-34	397	0.97 (0.84, 1.11)	189	1.09 (0.88, 1.34)	62	1.38 (0.93, 2.05)
	35-39	449	1.07 (0.94, 1.23)	218	1.24 (1.01, 1.52)	71	1.55 (1.05, 2.29)
	40-44	458	1.10 (0.96, 1.26)	247	1.40 (1.15, 1.72)	81	1.78 (1.22, 2.59)
	45-49	482	1.21 (1.06, 1.38)	285	1.68 (1.39, 2.05)	76	1.74 (1.19, 2.55)
	50-54	811	1.59 (1.41, 1.80)	482	2.25 (1.88, 2.70)	140	2.53 (1.78, 3.60)
	55-59	1151	1.98 (1.76, 2.22)	684	2.77 (2.33, 3.30)	223	3.56 (2.55, 4.99)
	60-64	1534	2.58 (2.30, 2.89)	920	3.64 (3.07, 4.31)	287	4.49 (3.23, 6.26)
	65-69	1741	3.10 (2.77, 3.47)	1084	4.52 (3.81, 5.35)	352	5.86 (4.22, 8.14)
	70-74	2276	4.09 (3.66, 4.57)	1376	5.87 (4.97, 6.95)	476	8.25 (5.96, 11.41)
	75-79	2914	5.34 (4.78, 5.97)	1709	7.46 (6.31, 8.82)	650	11.58 (8.39, 15.99)
	≥80	7521	7.86 (7.06, 8.76)	4095	10.47 (8.88, 12.35)	1689	18.62 (13.53, 25.62)
SIMD quintiles	1 - Most deprived	5582	1.64 (1.57, 1.72)	3241	1.75 (1.64, 1.86)	1008	1.51 (1.37, 1.68)
	2	4757	1.38 (1.32, 1.45)	2687	1.41 (1.33, 1.51)	1010	1.44 (1.30, 1.59)
	3	3937	1.24 (1.18, 1.30)	2177	1.25 (1.17, 1.34)	841	1.27 (1.14, 1.42)
	4	3376	1.13 (1.07, 1.19)	1886	1.15 (1.08, 1.24)	729	1.17 (1.05, 1.30)
	5 - Least deprived	2873	1.00	1575	1.00	608	1.00
Number of risk groups	0	4293	1.00	2197	1.00	814	1.00
	1	5090	1.93 (1.85, 2.01)	2877	2.11 (1.99, 2.23)	1026	2.00 (1.82, 2.20)
	2	4365	2.90 (2.77, 3.03)	2473	3.22 (3.03, 3.43)	929	3.05 (2.76, 3.38)
	3	3155	3.74 (3.55, 3.94)	1814	4.38 (4.08, 4.70)	687	4.21 (3.75, 4.72)

	4	1927	4.19 (3.94, 4.46)	1149	5.16 (4.75, 5.60)	407	4.74 (4.14, 5.43)
	≥5	1695	4.84 (4.53, 5.18)	1056	6.57 (6.01, 7.18)	333	5.24 (4.51, 6.08)
BMI	<18.5	861	1.52 (1.40, 1.65)	569	1.76 (1.59, 1.95)	187	1.71 (1.45, 2.01)
	18.5 – 24.9	6372	1.00	3649	1.00	1319	1.00
	25 – 29.9	6698	0.87 (0.84, 0.90)	3736	0.83 (0.80, 0.87)	1367	0.84 (0.78, 0.91)
	30 – 34.9	3899	0.92 (0.88, 0.95)	2113	0.84 (0.80, 0.89)	782	0.89 (0.81, 0.97)
	35 – 39.9	1324	1.04 (0.97, 1.11)	755	0.98 (0.90, 1.07)	270	1.02 (0.89, 1.17)
	≥40	1371	1.11 (1.05, 1.18)	744	1.01 (0.93, 1.10)	271	1.13 (0.98, 1.29)
Number of Previous Admissions	0	15104	1.00	8542	1.00	3003	1.00
	1	3544	2.80 (2.69, 2.92)	1970	2.91 (2.75, 3.07)	785	3.43 (3.15, 3.74)
	2	1193	3.81 (3.56, 4.08)	692	4.28 (3.90, 4.69)	250	5.02 (4.34, 5.80)
	3	391	4.97 (4.38, 5.63)	203	5.28 (4.44, 6.29)	87	7.68 (5.96, 9.89)
	4	154	5.39 (4.38, 6.63)	80	5.60 (4.21, 7.46)	32	8.69 (5.68, 13.29)
	5	72	7.67 (5.71, 10.30)	42	8.93 (6.03, 13.23)	25	22.08 (13.34, 36.54)
	≥6	67	7.53 (5.48, 10.35)	37	8.34 (5.36, 12.99)	14	11.98 (7.23, 19.86)
Urban/Rural Classification	Rural	3496	1.00	1930	1.00	729	1.00
	Urban	17029	1.17 (1.12, 1.21)	9636	1.20 (1.14, 1.26)	3467	1.24 (1.14, 1.34)

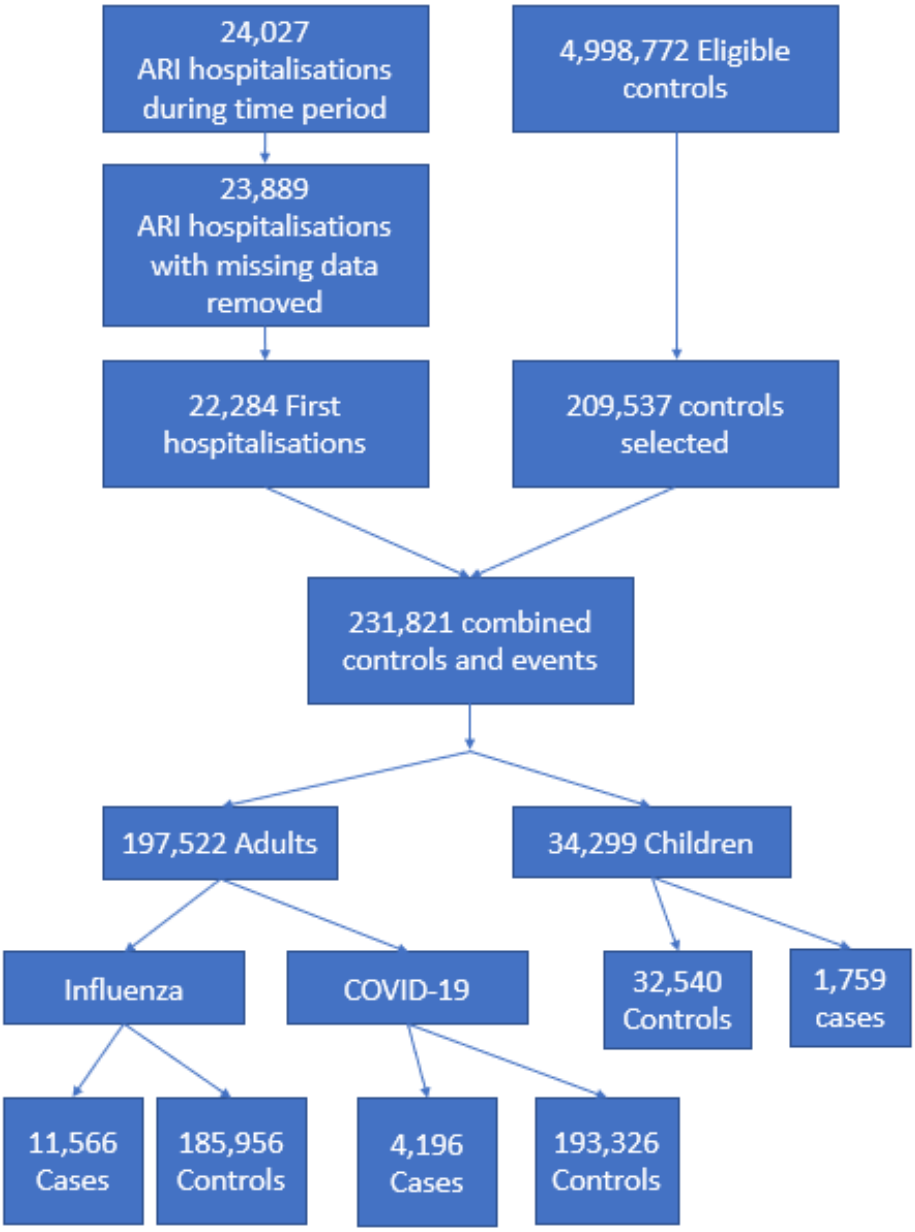
HR: Hazard Ratio. LCI: Lower Confidence Interval. UCI: Upper Confidence Interval. Hazard ratios were derived using cox proportional hazard model adjusting for age, sex, socioeconomic status, number of risk groups, and number of previous emergency hospitalisations within six months prior to September 1, 2022. BMI: Body Mass Index. SIMD: Scottish Index of Multiple Deprivation.

Table 3: Adjusted hazard ratios of hospitalisation with acute respiratory infections in children aged 3-17 years old

Variable	Level	ARI Hospitalisation	
		Number of events	HR (LCI, UCI)
Sex	Female	824	1.00
	Male	935	1.03 (0.94, 1.14)
Age Group (years)	3 - 5	896	4.55 (4.11, 5.04)
	6 - 17	863	1.00
SIMD quintiles	1 - Most deprived	453	1.24 (1.06, 1.44)
	2	365	1.19 (1.01, 1.39)
	3	351	1.35 (1.15, 1.58)
	4	325	1.16 (0.99, 1.36)
	5 - Least deprived	265	1.00
Number of risk groups	0	1406	1.00
	1	262	2.24 (1.95, 2.57)
	2	74	3.76 (2.86, 4.94)
	3	17	7.61 (4.54, 12.75)
	4	0	NA
	≥5	0	NA
Number of previous admissions	0	7	1.00
	1	17	4.60 (3.91, 5.41)
	2	453	8.64 (6.54, 11.43)
	3	365	17.88 (13.38, 23.91)
	4	351	16.75 (9.95, 28.18)
	5	325	7.57 (3.78, 15.15)
	≥6	265	49.23 (32.33, 74.96)
Urban/Rural Classification	Rural	256	1.00
	Urban	1503	1.33 (1.17, 1.52)

HR: Hazard Ratio. LCI: Lower Confidence Interval. UCI: Upper Confidence Interval. Hazard ratios were derived using cox proportional hazard model adjusting for age, sex, socioeconomic status, number of risk groups, and number of previous emergency hospitalisations within six months prior to September 1, 2022. SIMD: Scottish Index of Multiple Deprivation. NA: Not Available.

Figure 1: Data flow diagram for the ARI hospitalisation Cox modelling*



*24,027 includes 1,605 individuals with readmissions and 138 individuals with missing information on Urban/Rural Classification, SIMD quintiles and Health Board.