

101034339 – PROMISE

Preparing for RSV Immunisation and Surveillance in Europe

WP1 – WP RSV Epidemiology and Impact of COVID-19

D1.6 RSV healthcare burden in young children and the elderly in 6 European countries before and since the emergence of the COVID-19 pandemic

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Definitions

- **Participants** of the PROMISE Consortium are referred to herein according to the following codes:
 1. **UEDIN.** The University of Edinburgh (United Kingdom)
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 3. **UA.** Universiteit Antwerpen (Belgium)
 4. **Imperial.** Imperial College of Science, Technology and Medicine (United Kingdom)
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 20. **Novavax.** Novavax, Inc. (United States)
 21. **Pfizer.** Pfizer Limited (United Kingdom)
 22. **AZ.** AstraZeneca AB (Sweden)

- **Grant Agreement.** (Including its annexes and any amendments) The agreement signed between the beneficiaries of the action and the IMI2 JU for the undertaking of the PROMISE project (Grant Agreement No. 101034339).
- **Project.** The sum of all activities carried out in the framework of the Grant Agreement.
- **Work plan.** Schedule of tasks, deliverables, efforts, dates and responsibilities corresponding to the work to be carried out, as specified in Annex I to the Grant Agreement.
- **Consortium.** The PROMISE Consortium, comprising the above-mentioned participants.
- **Consortium Agreement.** The agreement concluded amongst PROMISE participants for the implementation of the Grant Agreement. The agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

Abbreviations

Acronym / Abbreviation	Meaning
APC	Admitted Patient Care
ARI	Acute Respiratory Infection
CI	Confidence Interval
COVID-19	Coronavirus Disease 2019
CRS	Civil Registration System
ECOSS	Electronic Communication of Surveillance in Scotland
HES	Hospital Episode Statistics
ICD-10	International Classification of Disease - 10 th edition
ICU	Intensive Care Unit
ILI	Influenza-Like Illness
IMI	Innovative Medicines Initiative
LOS	Length of Stay
LRTI	Lower Respiratory Tract Infection
MBR	Medical Birth Registry
NHS	National Health Services
NPI	Non-Pharmaceutical Intervention
NPR	National Patient Registry
PCR	Polymerase Chain Reaction
OPCS-4	Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures, Fourth Revision
RSV	Respiratory Syncytial Virus
RTI	Respiratory Tract Infection
SD	Standard Deviation
SMR	Scottish Morbidity Record
URTI	Upper Respiratory Tract Infection
WP	Work Package

Abstract

Background

Respiratory syncytial virus (RSV) causes severe disease, especially among the very young and the elderly. Awareness regarding RSV and its post-COVID epidemiology is key to understanding its burden and implementing healthcare measures that could reduce pressure on healthcare systems. Despite its importance, RSV is not systematically tested for, making its real burden hard to quantify. Here we present preliminary data on RSV hospitalisations between 2016-2022 in Denmark, England, Finland, Spain-Valencia and Scotland. The study, aimed to assess various aspects of RSV burden in Europe, including the impact(s) of COVID-19 on RSV hospitalisations. The outcomes of this study aim to help inform public health decisions regarding RSV immunisation opportunities, as well as contribute to raising disease awareness.

Methods

We conducted a retrospective study of respiratory tract infection (RTI) admissions, RSV-coded admissions and RSV-laboratory-confirmed admissions using routinely collected hospital admissions data from five countries (Denmark, England, Finland, the Netherlands, and Scotland), and a prospective hospital-based surveillance network in one country (Spain-Valencia region).

Insights

This report gives insights on the impact of COVID-19 on RSV epidemiology and healthcare practices at hospital settings. No significant change in terms of coding was observed related to COVID-19, meaning relying only on ICD-10 codes to estimate hospital RSV burden is strongly underestimating the real RSV-related burden. In terms of RSV epidemiology, we observed changes following COVID-19 in some age groups, notably in older children: 2+ years old. It will be interesting to pursue the monitoring in more seasons and in more settings to assess if this increase is punctual or long-term, and to what extent it could be associated with non-pharmaceutical intervention (NPI) impacts following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emergence.

In addition, this report demonstrates that by utilising routinely collected healthcare data and a standardised methodology for data collection, we can estimate and compare hospital admissions related to RSV in both children and adults across various European countries. Incorporating national-level data offers the advantage of facilitating informed regulatory decisions regarding RSV immunisation strategies and the possibility of monitoring the impact of the newly authorised RSV interventions on reducing RSV-associated hospitalisations in the coming years. However, a limitation of this study is the existence of poor coding practices – with no sensible better coding following COVID-19 emergence – and coding biases depending on the age and local practices, as well as a limited understanding of RSV testing practices/coverage in many countries and hospital settings, which makes the data hard to interpret for research purposes. These results also emphasise the need to test more systematically, as that would also contribute to better monitoring of RSV burden especially in the older adult age groups. Nonetheless, we observed consistent patterns and seasonal variations across all countries, underscoring that these data are suitable for providing insights into RSV epidemiology at the European level.

1. Introduction

Human respiratory syncytial virus (RSV) is a common cause of acute respiratory infections and can cause severe outcomes in the very young, elderly and in high-risk groups [1-3]. In 2019, it was estimated that RSV caused approximately 33 million cases of lower respiratory tract infections (LRTIs) globally in children under five years, leading to around 3.6 million hospitalisations and approximately 100,000 attributable deaths [3]. RSV infection is nearly universal by the age of 2 years, with around 50% of the infections occurring in infants under 6 months. In older adults ≥ 60 years, a recent systematic review and meta-analysis suggests that RSV may have led to around 470,000 hospitalisations and 33,000 in-hospital deaths in high-income countries in 2019 [4]. However, these estimates are based on limited data as currently RSV is not systematically tested for in clinical practice, especially in older adults [5-7].

The Respiratory Syncytial virus Consortium in Europe (RESCEU) project was an Innovative Medicines Initiative (IMI) funded project under the EU's Horizon 2020 program for 5 years (from 2017 to 2021) [8]. The goal was to assemble existing routinely collected RSV healthcare data to inform policymaking and regulatory decisions. Task 1 in Work Package (WP2) focused on assessing the healthcare burden of RSV among children younger than 5 years of age in 8 EU countries (Denmark, Netherlands, Finland, England, Scotland, Italy, France, and Norway) during 2000-2016 [5]. From RESCEU, new gaps in evidence emerged, such as the burden across other age groups and data on severity of the disease (e.g., intensive care unit (ICU) admissions and morbidity).

The coronavirus disease 2019 (COVID-19) pandemic and the subsequent stringent non-pharmaceutical interventions (NPIs) had significant short-term impacts in lowering all respiratory virus circulation [9, 10]. This reduction is known to have had a substantial impact on RSV epidemiology including the burden on health care systems and its seasonality. Studies have reported that public health measures implemented to control the COVID-19 pandemic have contributed to a dramatic decline in RSV infections and hospitalisations in 2020 in both hemispheres [11-19]. However, due to the concurrent implementation of control measures by countries to mitigate the COVID-19 pandemic, individual evaluation of the impacts of these measures on RSV epidemiology has been challenging [20, 21]. Given the recent market authorisation of new RSV immunisation products for infants (nirsevimab - Beyfortus[®], Sanofi and AstraZeneca), older adults (Arexvy – GSK) or both pregnant women and older adults (Abrysvo[™] - Pfizer), it is imperative to understand how COVID-19 has impacted RSV burden and to gather more data across all age groups for effectiveness studies of these new RSV disease prevention options.

The Preparing for RSV Immunisation and Surveillance in Europe (PROMISE) project was funded under the IMI for 30 months (beginning 01 November 2021) to build on, exploit, and add value to the significant achievements of RESCEU to prepare for the imminent introduction of RSV interventions and understand COVID-19 changes in RSV burden [22]. From existing national-level routine health data, including disease registries and surveillance networks, the aim of PROMISE WP1 Task 1.2 was to provide direct estimates of RSV healthcare burden in all age groups, including young children and older adults, by estimating changes in frequency and burden of RSV-associated illnesses in six European countries: Scotland, England, Finland, Denmark, Netherlands, which also participated in RESCEU, and the Spain-Valencia region before and during the COVID-19 pandemic (from 2016 to 2023).

2. Deliverable structure

The outcomes presented in this report have been divided into the following sections: first we present the methods used which are common across all age groups. We then present in two independent sections the main outcomes of the analysis of children below 5 years of age (*section 4.1*) and the main outcomes of the analysis of older children and adults (*section 4.2*). Additional analyses concerning the whole study population and associated general discussion are presented *afterwards* (*section 4.3*).

3. Methods

Collection of data was standardised using a common data collection template and common definitions. Sometimes country-specificities prevented the use of a general definition for some of the outcomes, this is then detailed afterwards. All analyses were performed in R (version 4.3.1) using common programming scripts to ensure a certain level of results comparability between countries despite the heterogeneity of healthcare utilisation and data sources.

3.1 Study design

We conducted a retrospective study of respiratory tract infection (RTI) admissions, RSV-coded admissions and RSV laboratory-confirmed admissions using routinely collected hospital admissions data from five countries (Denmark, England, Finland, the Netherlands, and Scotland), and a prospective hospital-based surveillance network in one country (Spain-Valencia region).

3.2 Study population

National hospital registries containing individual-level patient data on all hospital admissions were used for Denmark, England, Finland, the Netherlands, and Scotland (see sections 3.6.1 - 3.6.5). In Spain-Valencia, data from a regional prospective hospital-based surveillance network was used (see section 3.6.6). Hospital admissions with any mention of RTI using ICD-9-CM or ICD-10 codes (full list available in section 3.8) were extracted in Denmark, England, Finland, the Netherlands, and Scotland. In Spain-Valencia, all hospital admissions via an emergency room that met preliminary inclusion criteria and were compatible with an influenza-like-illness (ILI) case definition (see section 3.6.6) were included.

3.3 Definitions

A hospital admission was defined as any hospitalisation lasting more than 12 hours (8 hours in Spain-Valencia, any duration for England). Scheduled or routine admissions were excluded. Patients with admissions 28 days following any previous admission for the same diagnosis were excluded (30 days in Spain-Valencia). A hospital admission was considered completed upon hospital discharge or death. In England, ICU admissions were also available. Mortality data, when available, was defined as any death during or after hospitalisation where the primary or secondary causes of death included one of the diagnoses from section 3.8. If the death occurred out of hospital, we only considered deaths that occurred within 14 days after the end of the hospitalisation (except in Spain-Valencia and in England, where no follow-up of patients was made after discharge).

The following hospital admission types were defined:

- 1) Hospital admissions with any ICD-9-CM or ICD-10 code related to an RTI (full list of codes in section 3.6), are referred to from here on as RTI or RTI-coded admissions. An exception to this was in Spain-Valencia, where RTI admissions correspond to influenza-like illness (ILI) admissions in patients ≥ 5 years old (see section 3.6.6 for more details).
- 2) RSV-coded admissions were defined as those RTI admissions including any RSV-associated ICD-9-CM or ICD-10 code (4801, 46611, 0796, J12.1, J20.5, J21.0, B97.4).
- 3) In countries with access to laboratory results, hospital admissions with an RSV lab-confirmed polymerase chain reaction (PCR) positive test were included (referred to from here on as RSV-confirmed admissions). An admission with an RSV lab-confirmed record was classified as RSV-confirmed if the laboratory test was performed within -7 to $+2$ dates of the hospitalisation.

Each of these hospitalisation types were classified by the following diagnosis groups: upper respiratory tract infection (URTI), lower respiratory tract infection (LRTI) stratified by bronchitis & bronchiolitis, pneumonia & influenza, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 or unspecified LRTI (section 3.8).

High-risk patients were also identified in four countries (Denmark, England, Finland, and Spain-Valencia). Risk factors were defined for three age categories independently: children below 1 year of age, children between 1 and 4 years and patients ≥ 5 years. The classification was done according to country-specific availability of the risk categories as described in section 3.9.

3.4 Study period

The study period was chosen to cover full calendar years before and after the COVID-19 pandemic (2016/18 to 2022/23); country-specific study periods are described in section 3.7. A year was defined starting from ISO week 27 of one given year to ISO week 26 of the following year. In Spain-Valencia, data was adjusted to the RSV circulation period to allow comparisons across surveillance years with different active surveillance periods (see section 3.6.6). A calendar year is referred to from here on as surveillance year or season.

3.5 Data analysis

Data from all ages was analysed and stratified by the following age groups: 0-2 months, 3-5 months, 6-11 months, 1-2 years, 3-4 years, 5-17 years, 18-64 years, 50-64 years (only in Finland, Scotland, and Spain-Valencia), 65-74 years, 75-84 years and ≥ 85 years. Age was calculated as the person's age at the time of each hospitalisation event. The in-hospital length of stay (LOS) in days was estimated from admission and discharge dates. It included the ICU stay or the transfer to another hospital, if any. Median and interquartile ranges were calculated by hospitalisation type, age group, diagnosis, risk category, country, and year. Denmark, Finland, the Netherlands, and Scotland could not provide real counts when the associated number was below 5 due to data privacy compliancy. In these cases, the final number was artificially set to 2.

Rates for RTI admissions, RSV-coded admissions or RSV-confirmed admissions were calculated in each age group for each country using the 01 January population (Denmark, Finland, the Netherlands, and Spain-Valencia) or mid-year population (England, Scotland) stratified by age groups. In all countries, only the overall population for children under 1 year was known, so it was assumed that 25% were aged between 0 and 2 months, 25% between 3 and 5 months and 50% between 6 and 11 months. In Spain-Valencia, the population was multiplied by the RSV circulation duration in years in each surveillance year to compensate for the difference in active surveillance duration between seasons (section 3.6.6). In Scotland and England, no population data for the 2022/23 season was available, so the population was assumed to be as the 2021/22 season. Rates were computed per 1,000 person-years for children below 5 years and per 100,000 person-years for persons above 5 years due to the observed difference of frequency. The 95% confidence intervals (CIs) were estimated using a Poisson exact method.

In order to analyse in a qualitative manner a change due to COVID-19, i.e., a difference observable since the start of the COVID-19 pandemic, we performed several statistical tests. First, we computed the average incidence rate by hospitalisation outcome (all hospitalisations, hospitalisation including an ICU stay, and hospitalisation leading to death), category (RTI-coded, RSV-coded, and RSV-confirmed), country and age group, for the pre-COVID and post-COVID periods. The pre-COVID period covered seasons from 2016 (2017 for England and Scotland) to 2019. The post-COVID period covered the 2021-2022 season for Denmark and Scotland and 2021-2023 seasons for England, Finland, and Spain-Valencia. We considered 2019/2020 and 2020/2021 not to be representative, as strong NPI measures were in place and, therefore, were removed from this

analysis. We computed a metric that we will call afterwards “ChangeProxy” to represent the change as the proportion of the difference between post- and pre-COVID averages, compared to the pre-COVID average period. We then leveraged Kruskal-Wallis test, a non-parametric test enabling comparisons of data sets whatever their distribution. We performed an initial series of nine tests to analyse if the ChangeProxy metric differed depending on the country, considering all age groups together but considering separately each hospitalisation outcome and category. ICU data being only present for England, the associated tests were withdrawn. Spain-Valencia data were not included in these tests as changes in hospital admission policies and procedures after COVID-19 may explain some of the differences observed. The effect of these changes had to be quantified before performing any statistical test. We then performed a second series of tests to directly assess a difference within the incidence rates between pre- and post-COVID periods, grouping the data by hospitalisation outcome, category, and age group.

3.6 National registries

Denmark

The Danish data is based on the Danish National Patient Registry (NPR) [23-26]. The NPR provides nationwide longitudinal registration of detailed administrative and clinical data [23-26]. For each patient contact, one primary and numerous, optional, secondary diagnoses are recorded. For this study, data on all admissions with an RSV diagnosis were gathered from 2016 to 2023. Linkage to RSV-positive laboratory confirmations was possible through data from the national clinical microbiological database, where data from all microbiological tests are stored. This data was provided by Statens Serum Institute through the KIDS database. Patients identified in DNPR were also linked to the Medical Birth Registry (MBR), as well as the Civil Registration System (CRS) to obtain additional and missing information. The MBR contains data on all births in Denmark since 1973 including background information on the circumstances of the birth. No information on SARS-CoV-2 was available. When the number of admissions or deaths was below 5, information was provided as “<5” and treated in the analysis as 2 to enable display on one hand and aggregation over multiple values of the other hand (2.5 rounded to integer for confidence interval function). Demographic data for population estimates were collected from Statistics Denmark [27].

England

Hospitalisation and death data were collected from the England Hospital Episode Statistics (HES) [28] database that monitors >98% of England’s population and gathers information related to the patient and their clinical course in the hospital. HES is a reimbursement dataset that facilitates secondary care provider reimbursement from local health commissioners. HES contains details of inpatient, including ICU, admissions in a dataset called Admitted Patient Care (APC), from National Health Service (NHS) hospitals in England. Patient secondary care activity is longitudinally linked across all NHS hospitals. The information within HES is collected across services as part of the Commissioning Data Sets. Data are submitted monthly to NHS Digital for processing and is made available as the Secondary Uses Service dataset which can be used for non-clinical purposes, such as research and planning health services. In HES, APC diagnoses are recorded using the ICD-10 and procedures performed using the Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures, fourth revision (OPCS-4). Inpatient admissions may have up to 20 ICD-10 diagnoses, of which one is the primary cause of admission, investigation, or treatment, and the remaining 19 codes are secondary diagnoses codes. The same is available for procedures with up to 20 OPCS-4 codes. ICU episodes can be level two (high dependency) and level three (intensive organ support and/or nursing care). ICU episodes can occur multiple times during the same overnight admission as patient care is escalated and de-escalated. When a patient dies during a hospital stay this is recorded in the HES APC dataset as an inpatient death. However, deaths that occur among patients outside of the inpatient setting are not recorded in this dataset.

Mothers and infants cannot be linked in the dataset.

To exclude scheduled admissions, the HES admission method field was used, and all hospitalisations that were labelled as “Waiting list”, “Booked”, or “Planned” were excluded. The exclusion criterion for admissions shorter than 12 hours was not applied, as the admission duration in HES can only be calculated in whole days. Admissions coded as COVID-19 that occurred prior to 01 March 2020 were excluded, as these were likely to be coding errors. Where the age was missing, it was imputed using information from any other admissions for that person where the age was recorded. From this, an approximate date of birth was calculated and then used to calculate an approximate age at the time of the admission with the missing age. When nothing was available to impute age, the admission was counted in the “Overall” age group category only.

The earliest occurrence of each risk factor was identified for each person, using all HES admissions, including non-RTI admissions. People were considered to have that risk factor from that point forward. Any admission occurring at or after the risk factor was first observed was counted under that risk factor.

For risk factors, the gestational age of each infant was calculated, using the gestational age field from HES that is recorded during the birth episode. All subsequent admissions up to the age of 5 years were classified using this value. Additionally, the use of mechanical ventilation and oxygen at the time of birth was calculated for each person, using the birth resuscitation fields in HES (considered as yes when modalities “Invasive ventilation or nebuliser therapy” or “Non-invasive/other respiratory support”). All subsequent admissions up to the age of 5 years were classified using this value. Admissions were not included if the person did not receive resuscitation at birth.

The population comes from various United Kingdom censuses from the National Office for Statistics: for 2021/2022 the population described in Census 2021 [29], for previous seasons’ populations the mid-year census of the year, i.e., week 27 of the surveillance year [30]. For 2022/2023, as the census was not yet publicly available at the time of the study, we assumed the same population for mid-2022 as the one in mid-2021 to compute the incidence, which is expected to have low bias on the outcomes as the population is not varying a lot over years as observed in Supp Fig SC1.

Finland

The Finnish data is based primarily on two nationwide registers maintained by the Finnish Institute for Health and Welfare (THL): the Finnish Care Register for Health Care (HILMO) and the National Infectious Diseases Register (NIDR). HILMO covers individual level clinical and administrative data from inpatient care, specialised outpatient care and day surgeries from both hospitals and other institutions. Each registered event has a symptom-cause pair of primary diagnoses and similar pairings of optional secondary diagnoses, all of which have been recorded using the ICD-10 classification since 1996. For this study the data from HILMO was gathered from 2016 to 2023. The NIDR captures records of selected microbiological findings and related diagnoses that all laboratories and physicians are obliged to report under the Communicable Disease Act. All positive test results for RSV, influenza A virus and influenza B virus are included in the register, though there is no denominator information on the total number tested.

General demographic records and dates of death for the study population were obtained from the Population Information System which is maintained by Statistics Finland. Risk group variables for infants were collected from Medical Birth Register (MBR). The MBR dataset covers only the years 2018-2020. The linkage of data from different registers was carried out using unique personal identification codes.

Scotland

In Scotland, we used the Scottish Morbidity Record (SMR01) and Electronic Communication of Surveillance in Scotland (ECOSS) registries containing individual-level patient data on all inpatient and day cases in hospitals and laboratory cases. We used the continuous inpatient stay (CIS) marker to group admissions belonging to the same episode; for example, transfers from one hospital or significant facility to another were included as the same admission. The period of data availability was between January 2017 to June 2023, and we only integrated cases within the defined surveillance seasons (week 27 of year Y to week 26 of year Y+1). Age groups for children were computed differently than for other areas: 0-1y and 2-4y. The study was approved by the Public Benefit and Privacy Panel for Health and Social Care (HSC-PBPP), and data were provided by the electronic Data Research and Innovation Services (eDRIS) [31, 32].

Netherlands

The Dutch Hospital Data (DHD) registration collects, manages and processes hospital data and manages standards for its registration. The used data sources were LBZBASISTAB and LBZDIAGNOSENTAB for the years 2016 to 2021. All diagnoses were recorded using ICD-10 classification. The demographic database from Statistics Netherlands (CBS) GBAPERSONTAB was used to link data on gender and birth date to the admitted patients. Linkage to RSV-positive confirmations was not possible for this study. This non-public microdata were provided by Statistics Netherlands [33].

Spain-Valencia

In Spain-Valencia, patient information was collected through the Valencia Hospital Surveillance Network for the Study of influenza and other Respiratory Viruses (VAHNSI), an active prospective hospital-based surveillance network (~1 million catchment population; 21% of the total Valencia population). The network is coordinated by the Vaccine Research Department of FISABIO-Public Health and has been described previously [34-37]. Patients had to fulfil the following criteria to be included in the study: being hospitalised via an emergency room with a diagnosis compatible with an RTI, reside in the catchment area of one of the participating hospitals for at least 6 months, non-institutionalised, not discharged from a previous hospital admission in the last 30 days and give their (or their legally authorised representative) written consent. Patients ≥ 5 years old were included if, upon admission they met symptoms compatible with ILI, defined as the presence of at least one respiratory symptom (cough, sore throat or shortness of breath) with an onset within 7 days prior to admission [38]. For patients under 5 years no specific symptomatology was required but symptoms had to have appeared no more than 7 days before hospitalisation.

The participating hospitals were the following:

Hospital	Surveillance years	Catchment size
General Castellón	All	279,111
La Fe	All	284,152
Dr. Peset	All	272,842
General Alicante	Until 2019/20	271,120
La Marina Baixa	2021/22 and 2022/23	184,076

As VAHNSI is a surveillance network initially setup to cover influenza seasons, monitoring did not occur throughout the whole year and the duration of the monitoring was also different across seasons. Therefore, data was adjusted to the RSV circulation period in each of the surveillance years to allow data comparison across years with a different surveillance length. Circulation was defined as the weeks between the first of at least two consecutive weeks with two or more RSV

cases and the week prior to the first of at least two consecutive weeks without RSV cases considering the PCR results of included patients from all ages. The loss of RSV confirmed cases after adjusting the data to the circulation period seasons is negligible. The duration in weeks of each surveillance year was calculated as the total number of epidemiological weeks in each RSV circulation period. The population was adjusted to the length of the RSV circulation period in years (approximated as 1 year; ~ 52.143 weeks). **Table 1** describes the Spain-Valencia RSV circulation period in each surveillance year. Due to the COVID-19 pandemic no data was collected during season 2020/2021. During 2021/22 there were two RSV circulation periods (from W43 to W05 and from W13 to W26) and data from both circulations have been used here.

Table 1. Data collection period per surveillance year in Spain-Valencia.

Surveillance year	RSV-circulation starts	RSV-circulation ends	N weeks	Length in years
2016/17	2016-W45	2017-W11	18	0.34
2017/18	2017-W44	2018-W17	25	0.48
2018/19	2018-W44	2019-W14	22	0.42
2019/20	2019-W44	2020-W11	19	0.36
2021/22**	Circ1: 2021-W43 Circ2: 2022-W13	Circ1: 2022-W05 Circ2: 2022-W26	28	0.54
2022/23	2022-42	2023-12	22	0.42

** Two RSV circulation periods

No follow-up of patients was done after hospital discharge.

The study protocol was approved by the Ethics Research Committee of the Dirección General de Salud Pública-Centro Superior de Investigación en Salud Pública (DGSP-CSISP). All subjects signed written informed consent prior to their inclusion in the study.

3.7 Data availability

Table 2 summarises the data availability of each of the participating countries.

Table 2. Data availability in each of the participating countries.

Data availability	Scotland	England	The Netherlands	Finland	Denmark	Spain-Valencia
Population coverage	National	National	National	National	National	~21% Spain-Valencia region
Denominator population of <5-year-olds [Mean (range) over study period]	269,985 (255,437, 282,106)	3,237,439 (3,076,950, 3,384,926)	865,110 (857,626, 872,289)	259,746 (238,282, 287,537)	305,496 (298,063, 311,412)	19,021 (15,921, 22,825)
Denominator population of ≥5-year-olds [Mean (range) over study period]	5,184,235 (5,142,694, 5,224,463)	52,998,194 (52,234,505, 53,413,095)	16,445,983 (16,233,094, 16,644,470)	5,269,632 (5,215,760, 5,325,688)	5,506,549 (5,450,706, 5,562,008)	439,991 (356,277, 528,473)
Years available for this study	2017-2022	2017-2023	2016-2021	2016-2023	2016-2022	2016-2023 (except 2020/21)
Linkage to RSV laboratory confirmations	Yes	No	No	Yes	Yes	Yes

Coding system	ICD10	ICD10	ICD10	ICD10	ICD10	ICD-9, ICD10
Maximum number of diagnosis codes per record	6	20	No maximum	No maximum	No maximum	3
Mortality data	No	Yes	No	Yes	Yes	Yes
ICU admissions	No	Yes	No	No	No	No
Risk group identification	No	Yes	No	Yes	Yes	Yes

3.8 List of ICD codes

In **Table 3**, the list of ICD-10 and ICD-9 codes used to identify RTI and RSV-coded (in red) hospitalisations. The codes are shown together with their corresponding diagnosis group classification.

Table 3. List of ICD-10 and ICD-9 codes used in this study, with RTI codes in black and RSV codes in red.

Diagnosis classification	ICD-10	ICD-9
Acute upper respiratory tract infection (URTI)	J00 J02.0 J02.8 J02.9 J03.0 J03.8 J03.9 J04.0 J04.1 J04.2 J05.0 J05.1 J06.0 J06.8 J06.9	460 4610 4611 4612 4613 4618 4619 462 463 46400 46401 46410 46411 46420 46421 46430 46431 4644 46450 46451 4650 4658 4659
Pneumonia & Influenza (LRTI)	J09 J10.0 J10.1 J10.8 J11.0 J11.1 J11.8 J12.0 J12.1 J12.2 J12.3 J12.8 J12.9 J13 J14 J15.0 J15.1 J15.2 J15.3 J15.4 J15.5 J15.6 J15.7 J15.8 J15.9 J16.0 J16.8 J17.0 J17.1 J17.2 J17.3 J17.8 J18.0 J18.1 J18.2 J18.8 J18.9	4800 4801 4802 4803 4808 4809 481 4820 4821 4822 48230 48231 48232 48239 48240 48241 48249 48281 48282 48283 48284 48289 4829 4830 4831 4838 4841 4843 4845 4846 4847 4848 485 486 4870 4871 4878 514
Bronchiolitis & Bronchitis (LRTI)	J20.0 J20.1 J20.2 J20.3 J20.4 J20.5 J20.6 J20.7 J20.8 J20.9 J21.0 J21.1 J21.8 J21.9 J40	4660, 46611 , 46619
Unspecified LRTI	J22	5198 (not exact map)
SARS-CoV-2/COVID-19	U07.1, U07.2, U08-10	-
RSV-specific codes	B97.4	0796

3.9 Risk-group categories

Table 4 shows the risk groups per age category used in countries with available data to identify high-risk patients. A hospital admission was classified as high-risk if patients met at least one of the

categories shown (*note that there were significant country-specific differences*). Low-risk admissions were classified as such when none of the categories shown in each age category were present. **Table 5** shows the ICD-10 codes used to identify each of the categories in health records. In Spain-Valencia, the risk classification was made according to the interview by the field researchers for each of the included patients.

Prematurity refers to a gestational age below 37 weeks.

Table 4. Risk categories used to identify high-risk patients in each country.

Age category	Country	Available risk categories*
Children <1 year	Denmark**	APGAR SCORE:1-7, Birthweight ≤ 2.5kg, Birthweight > 4 kg, maternal smoking during pregnancy, prematurity
	Finland***	APGAR SCORE:1-7, Birthweight ≤ 2.5kg, Birthweight > 4 kg, maternal smoking during pregnancy, prematurity, oxygen use or mechanical ventilation at birth
	England	Prematurity
	Spain-Valencia***	Birthweight ≤ 2.5kg, Birthweight > 4 kg, prematurity, non-breastfed
Children 1-4 years	Denmark	Broncho pulmonary Dysplasia, Congenital Heart Disease, Cystic Fibrosis, Down Syndrome
	Finland	Broncho pulmonary Dysplasia, Congenital Heart Disease, Cystic Fibrosis, Down Syndrome
	England	Bronchopulmonary Dysplasia, Congenital Heart Disease, Cystic Fibrosis, Down Syndrome, Prematurity
	Spain-Valencia****	Prematurity
≥ 5 years	Denmark	Asthma, Diabetes, Heart failure, Immunosuppression
	Finland	Asthma, COPD, Diabetes, Heart failure, Immunosuppression, Obesity
	England	Asthma, COPD, Diabetes, Heart failure, Immunosuppression, Obesity
	Spain-Valencia****	ACVD (incl. heart failure), Asthma, Bronchiolitis (incl. COPD and bronchitis), Diabetes, Immunosuppression, Obesity

*In each country, patients were classified as high-risk if they had a record in any database of at least one of these categories. Low-risk patients were classified as such when there was no record of any of these categories available.

** In Denmark, the registry called ‘medical birth records’ was used for maternal smoking. There is a binary variable called ‘Maternal smoking’. Some data were missing in this variable, but they were assumed to be missing mostly when negative. The variable was collected from medical/antenatal records by the midwife attending the birth.

*** In Finland, all the risk groups for children under the age of 1 year were identified from the (Finnish) Medical Births Register. MBR covers a multitude of different variables of all kinds of different pre- and post-natal characteristics, including ones for maternal smoking status, oxygen use and mechanical ventilation. All of these variables are coded using register-level standards.

**** In Spain-Valencia, risk classification was made according to the data based on the interview performed by the field researchers for each of the patients.

Table 5. ICD-10 codes used to identify risk categories, when applicable.

Age group	Risk category	ICD-10
Children <1 year	Maternal smoking during pregnancy	NA
	Oxygen use or mechanical ventilation at birth	NA



	Birthweight ≤ 2500 g	P07.0, P07.1, P05.0, P05.1
	Birthweight > 4000 g	P08.0, P08.1
	Prematurity	P07.2, P07.3, or from gest. age/birthweight or other variable in birth records
	APGAR score: 1-7	P21.0, P21.1
	Non-breastfed	O92.5
Children 1-4 years	Prematurity	As above
	Down Syndrome	Q90
	Congenital Heart Disease	Q20-Q26
	Bronchopulmonary Dysplasia	P27.1
	Cystic Fibrosis	E84
≥5 years	COPD (not asthma)	J40-J44, J47
	Asthma	J45-J46
	Heart failure	I50
	Diabetes	E10-E14
	Immunosuppression	B20-B24, O98.7, Z21, C00-C99, D37-D48
	Obesity	E66.9

4. Outcomes

Table 6 shows the overall number of hospitalisations in each of the three defined hospitalisation types: RTI, RSV-coded and RSV-confirmed for each country. Overall, between 1.7% and 11.7% of all admissions were related to RSV.

Table 6. Total number (%) of RTI hospital admissions, RSV-coded admissions and RSV-confirmed admissions in each country over the whole study period. Shown is the sum of admissions per hospitalisation type in each country over the whole study period.

Country	Population Mean (\pm SD)	RTI N	RSV-coded N (%)	RSV-confirmed N (%)
England	56,235,632 (+/- 338.867)	5,457,398	94,682 (1.7%)	NA
Netherlands	17,311,092 (+/- 146.431)	568,723	13,571 (2.4%)	NA
Denmark	5,812,045 (+/- 40,458)	284,779	5,942 (2.1%)	8,320(2.9%)
Finland	5,529,377 (+/- 19,650)	389,734	13,475 (3.5%)	15,759 (4.0%)
Scotland	5,458,500 (+/- 20,947)	361,276	10,131 (2.8%)	13,434 (3.7%)
Spain-Valencia	459,012 (+/- 60,215)	11,386	661 (5.8%)	1,336 (11.7%)

In the next sub-sections, data stratified by patients under 5 years of age (4.1), ≥ 5 years of age (4.2) and common additional information (4.3) are shown.

4.1 Burden in young children

Background

RSV is a leading cause of hospitalisations in children [2], notably infants below 1 year old [1] and including healthy term-born newborns, where RSV is estimated to cause around 1 hospitalisation per 60 births in high-income countries [39]. Overall, RSV was estimated to have caused 841,000 hospitalisations for infants aged 0-2 months (mo), 579,000 for 3-5 mo, 683,000 for 6-11 mo and 827,000 for children 1-4 years worldwide in 2019 [3]. In addition to overload of the healthcare systems, deaths are also substantial: 101,400 deaths were estimated to be RSV-attributable for children below 5 years [3]. With the emergence of new prevention measures and several additional options in development, accurate estimates of the current burden of RSV in hospital healthcare are critical, to adequately leverage these preventative measures, and then measure their effectiveness afterwards. This work brings a multi-country perspective that will complement prior work done in some specific countries [40] and over a shorter period of time during the COVID-19 pandemic [9].

Data analysis

Data analysis for children was the same as for adults. The only difference was in risk groups, where we had two specific categories for young children: infants below 1 year, in order to assess specificities related to their young age and the fact they will be facing their first RSV season, if infected by RSV, and children between 1 and 4 years of age as we considered the potential risk factors were not the same as adults.

Summary of results

Hospitalisation burden overall

RSV-coded hospital admissions incidence ranged from no incidence (2020/2021, Finland, 0-2 mo, 3-5mo and 3-4 yrs) to 108 hospital admissions per 1000 children per surveillance year (Valencia, 2017/2018, 0-2mo). When excluding 2019/2020 and 2020/2021 that were strongly impacted by NPIs, incidences were 38.6 ± 23.6 RSV-coded hospital admissions per 1000 children per surveillance year (mean \pm SD) for 0-2mo, 21.0 ± 13.1 for 3-5mo, 6.6 ± 3.5 for 6-11mo, 2.0 ± 1.3 for 1-2y and 0.4 ± 0.4 for 3-4y. For RSV lab-confirmed, it ranged from no incidence (Finland, 2020/2021, 0-2 mo, 3-5mo, 6-11mo and 3-4 yrs) to 111 hospital admissions per 1000 children (Valencia, 2018/2019, 0-2mo), with a mean of 16 ± 22 .

RSV-coded ICU admissions represented on average $5\% \pm 7\%$ [Min/Max: 0;50] of RSV-coded hospital admissions. RSV-coded deaths following a hospital episode (Denmark, Finland) and/or during hospitalisation (England, Spain-Valencia) represented 0.5% of hospitalisations on average (SD=3.5, min=0, max=40).

Table SC1 provides the comprehensive overview of observed hospitalisations before and after SARS-CoV-2 emergence per country, age group, diagnosis group and risk group.

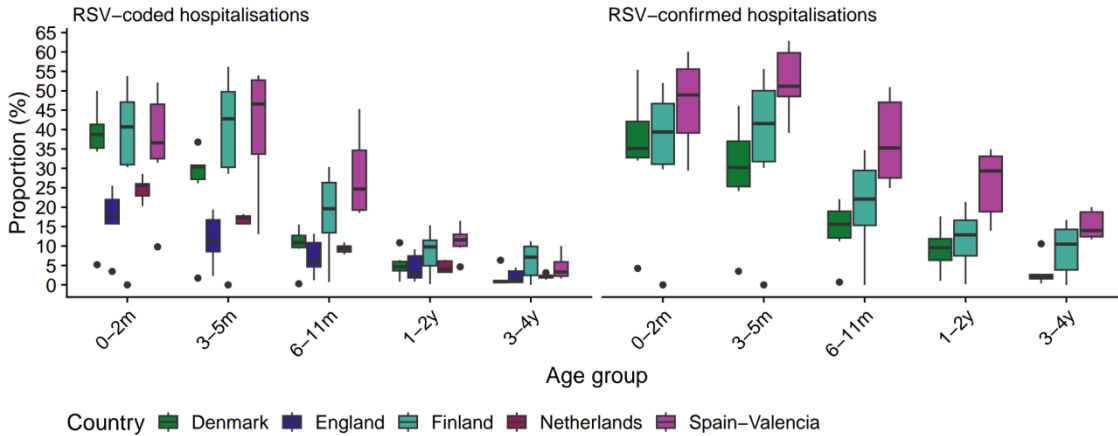


Figure C1 – Proportion of RTI hospital admissions that are RSV-coded (panel A, on the left) and RSV-confirmed (panel B, on the right), per age group (x-axis) and country (colour)

Figure C1 shows heterogeneities in the proportion of RTI admissions that are RSV-coded and RSV-confirmed across countries that are often higher than between seasons but also show some common trends. First, there are more RSV-confirmed hospitalisations than RSV-coded hospitalisations, for all areas where data are available. Then, except for Netherlands, the burden is similar between 0-2m and 3-5m – for Denmark not shown if considering only RSV-coded, but shown when considering RSV-confirmed.

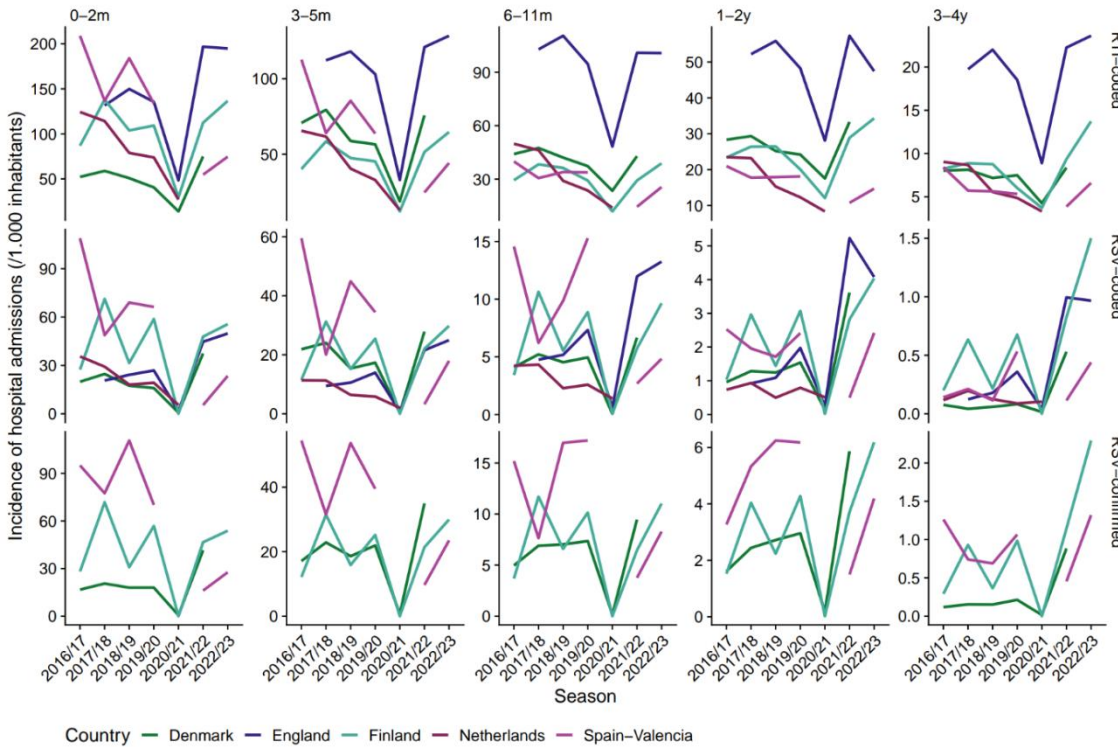


Figure C2 – Hospital admissions rates in children below 5 years of age. The incidence of hospital admissions per 1,000 children of same age (y-axis) per surveillance year (x-axis) is shown for each country (colour), age group (vertical subpanels) and each hospitalisation type (rows): 1) all RTI-hospital admissions 2) all RSV-coded admissions and 3) laboratory-confirmed RSV admissions. Note that each individual panel has a different y-axis scale to allow for readability and that for Spain-Valencia, no data was collected in 2020/2021, explaining the “broken” line.

Figure C2 shows that for all age groups and all countries (except Spain-Valencia where monitoring was paused in 2020/2021), hospital burden for all respiratory viruses in children below 5 years decreased substantially in the 2020/21 season, and notably for RSV-attributable admissions (either RSV-coded or RSV-confirmed). For 0-2mo, 3-5mo and 6-11mo, the RSV visible hospital burden (coded and confirmed) returned to a level similar to that observed before the COVID-19 pandemic start, except in Spain-Valencia where it is observed to be lower. Denmark, England, and Finland show higher incidence rate post 2020/2021 for children aged 1-2 years, and England and Finland

also for children aged 3-4 years.

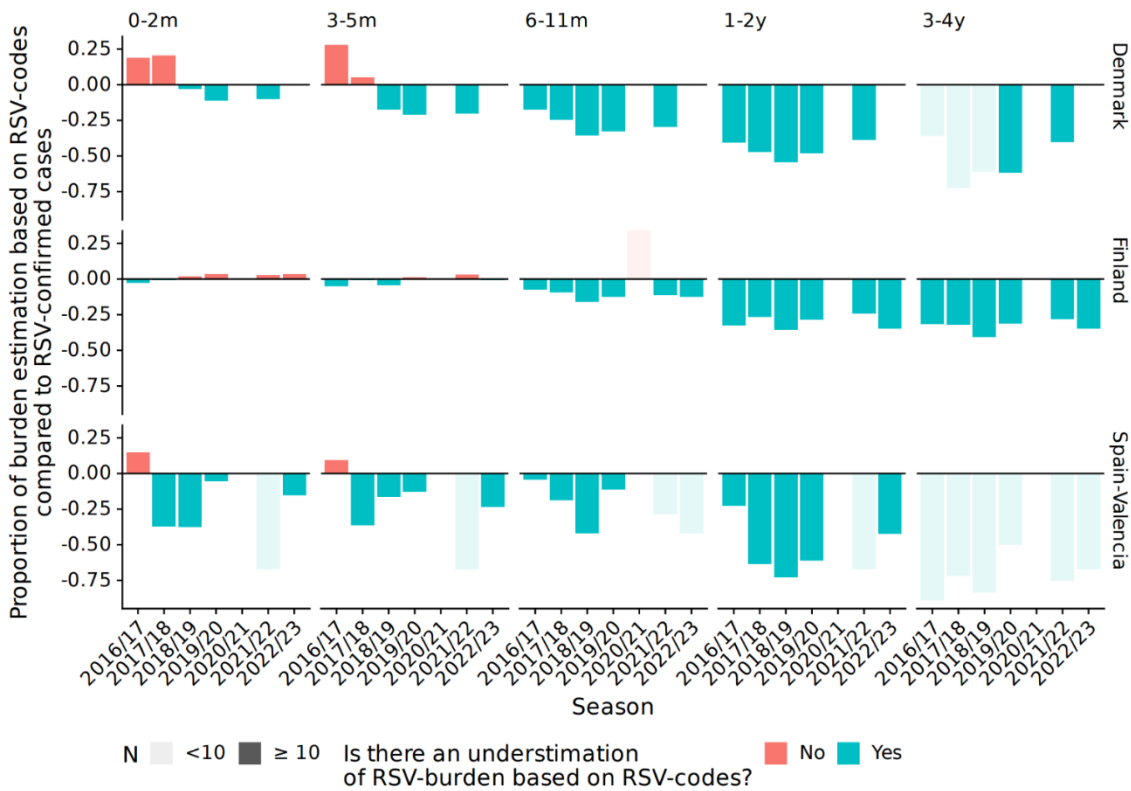


Figure C3 – Evaluation of the evolution of RSV-coding practice compared to RSV-confirmation practice per country and season, computed as the proportion of RSV-coded cases that are RSV-confirmed, centred on 0 for readability (y-axis). For example, if the metric is equal for 0.25, it means there are 25% more RSV-coded hospital admissions than RSV-confirmed hospital admissions. This metric was computed by surveillance year (x-axis), by age group (vertical sub-panels) and by country (horizontal sub-panels). Bars with a pale colour indicate less robust data as there were fewer than 10 hospital admissions for that season and that country. Colours indicate if there is an underestimation (blue: yes, and red: no) to facilitate readability.

Figure C3 shows that there are more RSV-confirmed cases than RSV-coded hospital admissions except for Finland for infants below 6 months, although only in Spain-Valencia RSV-testing is performed systematic. No significant change of trend is observable with these data following the COVID-19 pandemic, trends are consistent with the pre-COVID surveillance years.

We observe in Figure C4 that differences in incidence between the pre- and post-COVID time periods is stable over age groups for RTI-coded patients, but for RSV-coded patients, the change increases with age. For RSV-confirmed hospitalisations, there are less data, but we still observe an increase of difference for children aged 3-4 years. For other age groups, the heterogeneity is more country-specific and does not highlight a general trend.

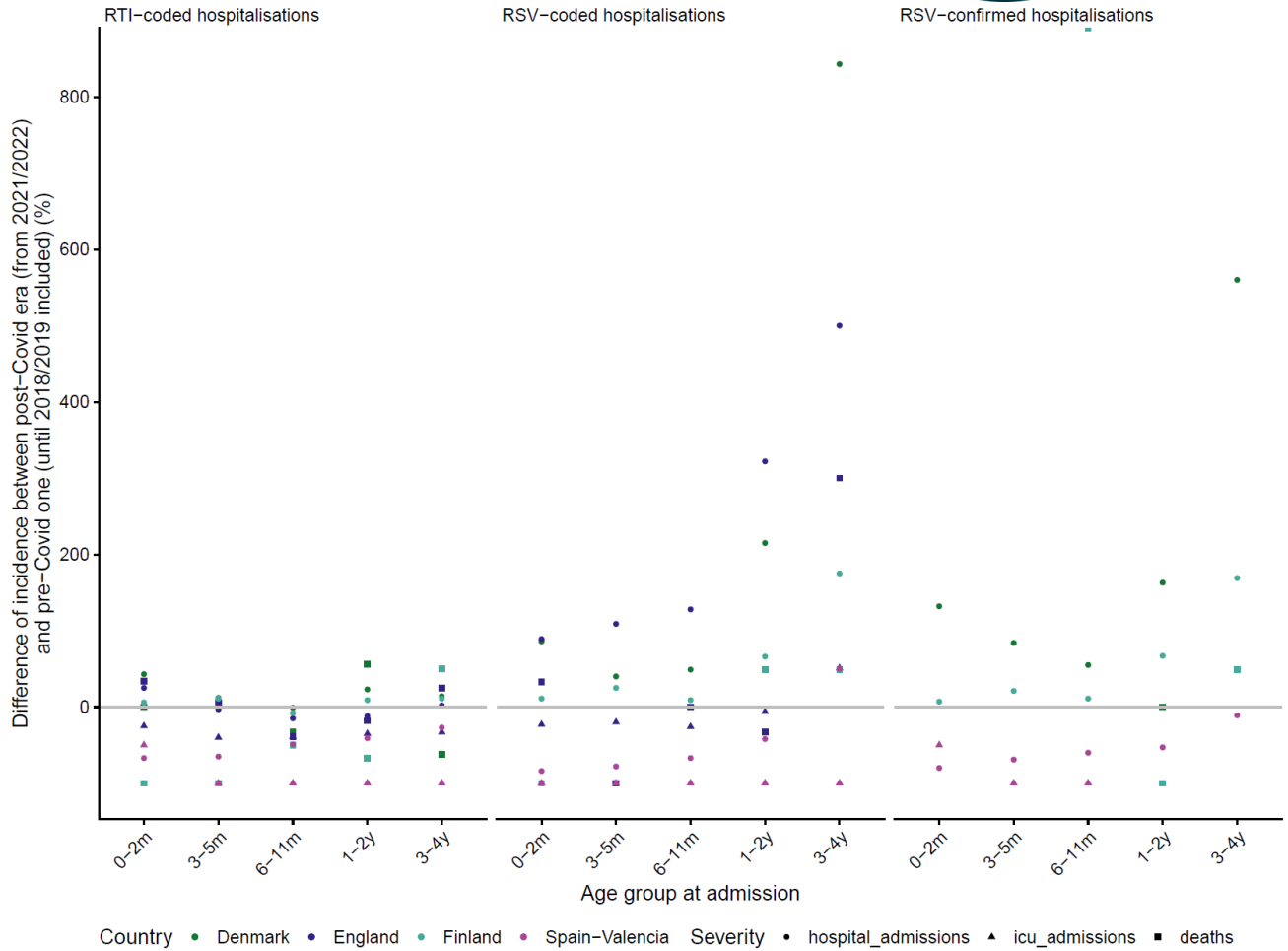


Figure C4 – Evolution of incidence after COVID-19 pandemic for children below 5 years of age, stratified by category of hospitalisations (vertical subpanels, from left to right, RTI-coded, RSV-coded, and RSV laboratory-confirmed), coloured by country and shaped by severity of the hospital stay (hospitalisation only in general ward, including an ICU stay or leading to death). The metric is the ChangeProxy defined in section 3.5.

Kruskal-Wallis tests considering all the age groups together and looking for differences per country does not show a significant trend; there are no significant trends for any of the settings combinations between hospitalisation category (RTI, RSV-coded or RSV-confirmed) and severity (hospital admissions or deaths).

When considering directly the difference in incidences for all countries combined, we observe significant differences between before and since COVID-19 emergence for:

- RSV-coded hospital admissions of children aged 6-11mo, 1-2y, and 3-4y with a p-value <0.001, RSV-coded hospital admissions for other age groups (0-2mo, 3-5mo),
- RSV laboratory-confirmed cases of children aged 1-2y and 3-4y, and
- RTI hospital admissions of children aged 1-2y and 3-4y with a p-value <0.05.

To inform if the change for 1-2y and 3-4y could be considered different or similar between all hospitalisations regardless of hospitalization severity, we performed a final test considering each of these two age groups separately, focusing on the hospital admissions cohort: for both age groups, there is a significant difference depending on the patient record (RTI-coded, RSV-coded, and RSV-confirmed) – p-value <<0.001.

Severity of admissions

Lengths of stay

As illustrated in Figure C5, the length of stay for RTI-coded cases is shorter than for RSV-coded or RSV-confirmed patients in Denmark, England, Netherlands. In Finland and in Spain-Valencia, this is only observed for 0-2mo. With current data, no sustainable change in the pre- and post-COVID-19 era seems to have occurred: only some punctual fluctuations are observed, e.g., in 2020/21 a small increase in the duration of stay in Denmark, or due to a country-specific trend, e.g., the decrease of length of stay in England for children aged 3-4 years.

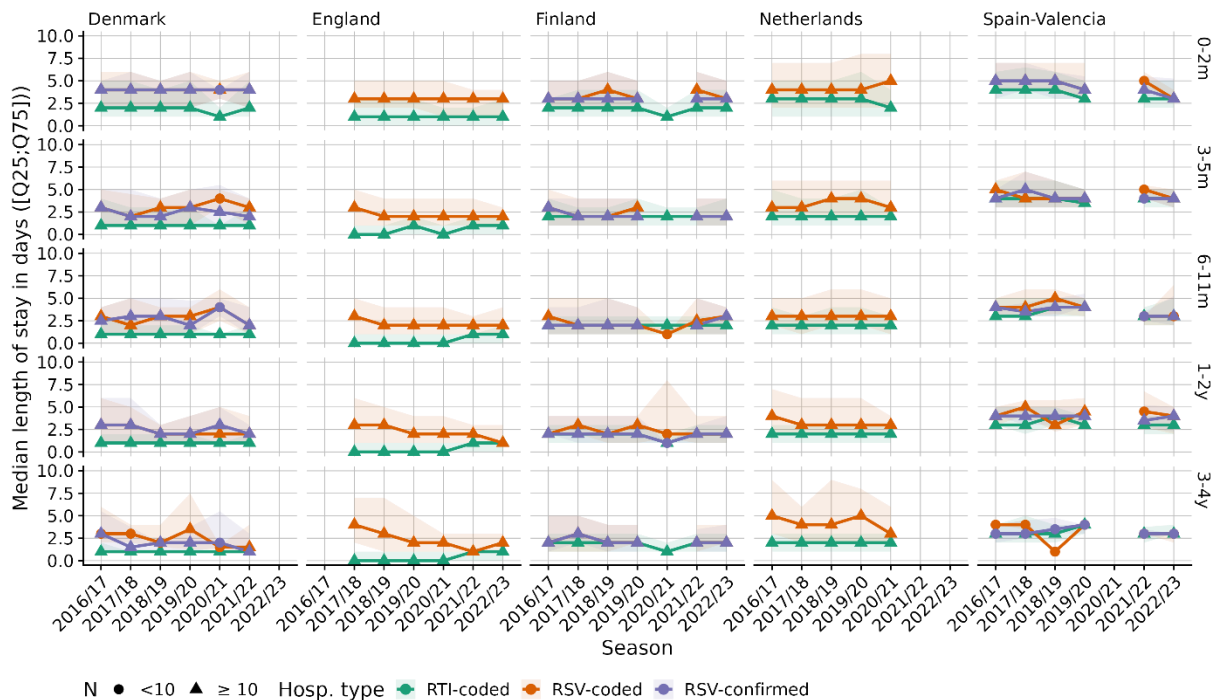


Figure C5 – Lengths of stay among patients below 5 years of age. Median length of stay (y-axis) and 25/75 quartiles (shadow area) of all hospital admissions per country, age group and surveillance year (x-axis). Each hospitalisation type is shown with a different colour (green: RTI-coded, orange: RSV-coded and violet: RSV-confirmed admissions). If the estimate is based on fewer than 10 patients the shape is represented as a dot, whereas if the estimate is based on more than 10 patients the shape is represented as a triangle.

ICU admissions

In England, ICU admissions data was available and is summarised in Table TC1. RSV-coded ICU admissions represent from 2 to 20% of RSV-coded hospital admissions, depending on the age group and the surveillance year. Before COVID-19 emergence, the average over age groups and surveillance years was 12.1±4.1% and after COVID-19 emergence it was 3.8±2.2%. The highest RSV-coded ICU admission average numbers were observed in the 0-2mo age group both before and after COVID-19 (570 and 438, respectively). The numbers ranged from 30 to 161 in the other age groups. All the age groups show a higher proportion of RTI-coded that are RSV-coded than for patients older than 5 years (Table SA1). Bronchitis & bronchiolitis were the most frequent diagnosis groups among patients in the ICU RSV-coded admissions, and the change of diagnosis is small, especially comparing to changes of diagnosis for RTI-coded.

Table TC1. Average number and proportion of ICU admissions of patients below 5 years of age. Shown are all RTI-admissions and RSV-coded admissions that ended in an ICU admission by age group, diagnosis group and risk group stratified by before COVID-19 (2016/17 to 2018/19) and after COVID-19 (2021/22 to 2022/23). Shown is the average (± SD) of all admissions belonging to each category before and after COVID-19. Percentage corresponds to the % of RSV-coded ICU admissions compared to RTI-coded ICU admissions.

		England	
	COVID-19	RTI-coded	RSV-coded
Per age group			
0-2m	Before	1267 (1152,1382)	570 (481,659), 45%
	After	948 (510,1386)	438 (245,631), 46.2%
3-5m	Before	535 (519,551)	138 (130,146), 25.8%
	After	318 (191,445)	110 (68,152), 34.6%
6-11m	Before	812 (756,868)	140 (136,144), 17.2%
	After	498 (336,660)	104 (59,149), 20.9%
1-2y	Before	1354 (1271,1437)	161 (155,167), 11.9%
	After	882 (447,1317)	151 (68,234), 17.1%
3-4y	Before	530 (466,594)	30 (24,36), 5.7%
	After	354 (256,452)	46 (18,74), 13%
Per diagnosis			
Bronchitis & Bronchiolitis	Before	1647 (1479,1815)	725 (658,792), 44%
	After	1204 (787,1621)	586 (384,788), 48.7%
LRTI	Before	870 (806,934)	46 (44,48), 5.3%
	After	494 (323,665)	32 (17,47), 6.5%
URTI	Before	538 (486,590)	10 (9,11), 1.9%
	After	199 (182,216)	6 (4,8), 3%
Pneumonia	Before	862 (861,863)	46 (41,51), 5.3%
	After	449 (343,555)	41 (26,56), 9.1%
SARS-CoV-2	After	178 (79,277)	2 (0,4), 1.1%
More than one diagnosis	Before	552 (482,622)	186 (185,187), 33.7%
	After	451 (329,573)	157 (104,210), 34.8%
Per risk group			
<1y - low risk	Before	1783 (1698,1868)	578 (525,631), 32.4%
	After	1220 (680,1760)	473 (265,681), 38.8%
<1y - high risk	Before	830 (729,931)	270 (245,295), 32.5%
	After	544 (357,731)	180 (109,251), 33.1%
1-4y - low risk	Before	1480 (1400,1560)	133 (95,171), 9%
	After	768 (421,1115)	110 (41,179), 14.3%
1-4y - high risk	Before	404 (177,631)	58 (21,95), 14.4%
	After	470 (284,656)	86 (43,129), 18.3%

Deaths

No death was reported in Spain-Valencia. Deaths for Denmark, England and Finland are detailed in Table TC2 by age group, diagnosis group and risk group.

Table TC2. Average number and proportion of deaths of patients below 5 years of age. Shown are all RTI-admissions, RSV-coded admissions and RSV-confirmed admissions that ended in death by age group, diagnosis group and risk group stratified by before COVID-19 (2016/17 to 2018/19) and after COVID-19 (2021/22 to 2022/23). Shown is the average (\pm SD) of all admissions belonging to each category before and after COVID-19. Percentage corresponds to the % of RSV-coded deaths compared to RTI-coded deaths.

	COVID-19	Denmark			England		Finland			Spain-Valencia	
		RTI-coded	RSV-coded	RSV-confirmed	RTI-coded	RSV-coded	RTI-coded	RSV-coded	RSV-confirmed	RTI-coded	RSV-coded
Per age group											
0-2m	Before	2 (NA,NA)	NA, NA%	NA, NA%	22 (16,28)	3 (2,4), 13.6%	2 (2,2)	1 (0,2), 50%	0 (0,0), 0%	0 (0,0)	0 (0,0), NaN%
	After	2 (NA,NA)	2 (NA,NA), 100%	2 (NA,NA), 100%	30 (28,32)	4 (4,4), 13.3%	0 (0,0)	0 (0,0), NaN%	0 (0,0), NaN%	0 (0,0)	0 (0,0), NaN%
3-5m	Before	2 (2,2)	NA, NA%	NA, NA%	16 (15,17)	1 (1,1), 6.2%	1 (0,2)	0 (0,0), 0%	0 (0,0), 0%	0 (0,0)	0 (0,0), NaN%
	After				16 (11,21)	0 (0,0), 0%	0 (0,0)	0 (0,0), NaN%	0 (0,0), NaN%	0 (0,0)	0 (0,0), NaN%
6-11m	Before	3 (1,5)	2 (NA,NA), 66.7%	2 (2,2), 66.7%	30 (19,41)	2 (1,3), 6.7%	2 (2,2)	0 (0,0), 0%	0 (0,0), 0%	0 (0,0)	0 (0,0), NaN%
	After	2 (NA,NA)	NA, NA%	NA, NA%	18 (15,21)	2 (1,3), 11.1%	1 (0,2)	0 (0,0), 0%	1 (0,2), 100%	0 (0,0)	0 (0,0), NaN%
1-2y	Before	9 (7,11)	NA, NA%	2 (NA,NA), 22.2%	34 (31,37)	4 (3,5), 11.8%	6 (4,8)	1 (0,2), 16.7%	1 (0,2), 16.7%	0 (0,0)	0 (0,0), NaN%
	After	14 (NA,NA)	2 (NA,NA), 14.3%	2 (NA,NA), 14.3%	28 (25,31)	3 (2,4), 10.7%	2 (2,2)	1 (0,2), 50%	0 (0,0), 0%	0 (0,0)	0 (0,0), NaN%
3-4y	Before	5 (1,9)	NA, NA%	NA, NA%	16 (15,17)	0 (-1,1), 0%	1 (0,2)	1 (0,2), 100%	1 (0,2), 100%	0 (0,0)	0 (0,0), NaN%
	After	2 (NA,NA)	NA, NA%	NA, NA%	20 (17,23)	2 (2,2), 10%	2 (2,2)	1 (0,2), 50%	1 (0,2), 50%	0 (0,0)	0 (0,0), NaN%
Per diagnosis											
Bronchitis & Bronchiolitis	Before	2 (2,2)	2 (NA,NA), 100%	2 (NA,NA), 100%	14 (13,15)	4 (4,4), 28.6%	2 (2,2)	0 (0,0), 0%	0 (0,0), 0%		
	After	45 (NA,NA)	NA, NA%	2 (NA,NA), 4.4%	10 (9,11)	4 (4,4), 40%	1 (0,2)	0 (0,0), 0%	1 (0,2), 100%		
LRTI	Before				25 (22,28)	1 (1,1), 4%	0 (0,0)	0 (0,0), NaN%	0 (0,0), NaN%		
	After				16 (12,20)	1 (1,1), 6.2%	0 (0,0)	0 (0,0),	0 (0,0),		

								NaN%	NaN%		
URTI	Before	34 (25,43)	NA, NA%	2 (2,2), 5.9%	6 (5,7)	0 (-1,1), 0%	2 (0,4)	0 (0,0), 0%	0 (0,0), 0%		
	After	25 (25,25)	NA, NA%	NA, NA%	4 (3,5)	0 (0,0), 0%	1 (0,2)	0 (0,0), 0%	0 (0,0), 0%		
Pneumonia	Before	38 (14,62)	4 (4,4), 10.5%	2 (NA,NA), 5.3%	56 (52,60)	2 (2,2), 3.6%	7 (4,10)	1 (0,2), 14.3%	1 (-1,3), 14.3%		
	After	25 (25,25)	7 (7,7), 28%	7 (7,7), 28%	50 (44,56)	4 (2,6), 8%	3 (2,4)	2 (2,2), 66.7%	1 (0,2), 33.3%		
SARS-CoV-2	After				12 (11,13)	0 (-1,1), 0%	0 (0,0)	0 (0,0), NaN%	0 (0,0), NaN%		
More than one diagnosis	Before				16 (10,22)	2 (1,3), 12.5%	5 (3,7)	1 (0,2), 20%	1 (0,2), 20%		
	After				18 (16,20)	2 (1,3), 11.1%	2 (2,2)	0 (0,0), 0%	0 (0,0), 0%		
Per risk group											
<1y - low risk	Before	7 (2,12)	NA, NA%	8 (NA,NA), 114.3%	42 (31,53)	4 (4,4), 9.5%	5 (3,7)	1 (0,2), 20%	0 (0,0), 0%		
	After	4 (4,4)	2 (NA,NA), 50%	2 (NA,NA), 50%	39 (38,40)	3 (2,4), 7.7%	1 (0,2)	0 (0,0), 0%	1 (0,2), 100%		
<1y - high risk	Before	13 (8,18)	2 (NA,NA), 15.4%	2 (NA,NA), 15.4%	26 (20,32)	2 (1,3), 7.7%	1 (0,2)	0 (0,0), 0%	0 (0,0), 0%		
	After				25 (24,26)	4 (2,6), 16%	1 (0,2)	0 (0,0), 0%	0 (0,0), 0%		
1-4y - low risk	Before	10 (5,15)	2 (NA,NA), 20%	2 (NA,NA), 20%	35 (31,39)	3 (2,4), 8.6%	4 (2,6)	1 (0,2), 25%	1 (-1,3), 25%		
	After	84 (84,84)	5 (NA,NA), 6%	5 (NA,NA), 6%	29 (25,33)	3 (3,3), 10.3%	3 (2,4)	2 (2,2), 66.7%	1 (0,2), 33.3%		
1-4y - high risk	Before	52 (34,70)	2 (NA,NA), 3.8%	NA, NA%	15 (7,23)	2 (1,3), 13.3%	2 (2,2)	1 (0,2), 50%	1 (0,2), 50%		
	After	8 (8,8)	NA, NA%	6 (NA,NA), 75%	19 (15,23)	2 (1,3), 10.5%	3 (2,4)	0 (0,0), 0%	0 (0,0), 0%		

Discussion

These results confirm the continued substantial burden of RSV RTI hospitalisations in Europe, with a particularly high burden continuing to affect the youngest age groups over all seasons, and an increased burden in toddler and pre-schoolers since COVID-19 emergence. Morbidity and mortality are also high in young children and older adults, specifically in infants aged 0-2 months and adults ≥ 85 years with 5% of RSV-coded hospital admissions involving an ICU stay, and 0.6% of RSV-coded hospitalisations resulting in an RSV-coded death during or shortly after the hospital stay overall.

As RSV is not systematically tested for when clinically suspected, it is challenging to establish the true burden of RSV directly from available metrics, and challenging to determine how available metrics can help identify the true burden. We evaluated two different metrics: hospitalisation records with an RSV-related code, and hospitalisations with an associated RSV positive laboratory test. Spain-Valencia (Spain) is the only area where every included patient was systematically tested for RSV. We observed that even with systematic testing, there were fewer RSV-coded patients than RSV lab-positive patients. These results highlight that on top of the lack of systematic testing, a change in practice to more accurately code patient records that would help better assess the true burden of RSV. This is confirmed by Danish and Finnish outcomes, where we also observed a higher proportion of patients that are RSV-confirmed than are RSV-coded. We did not investigate in this study what codes were used for patients positive for RSV, but this work has been done previously for adults [41]. These results also emphasise the need to test more systematically, as that would also contribute to better monitoring of RSV burden. The observed variability across countries underlies the need to harmonise coding practices to facilitate a harmonised European-level framework for RSV monitoring.

The COVID-19 pandemic and its associated NPIs triggered a demonstrable impact from an epidemiological point of view. First, there was a reduction in hospitalisation in 2020/2021 for all age groups likely due to the reduced circulation of non-COVID respiratory viruses, which was expected and shows the strong effectiveness of such measures, consistently with other published works [9]. Second, children who should have faced their first or second RSV season during that period – as virtually all children will have had at least one RSV infection by the age of 2 [42]– seem to have been more susceptible to a severe form of the disease, as there was a significant increase of RSV-coded and RSV-confirmed cases for those aged 1-2. These results, similar to what was observed in other countries [9], raise questions regarding the root cause: an increased virus circulation? An increased trend to hospitalise? An immune system less efficient when meeting the virus later, or without having been seasonally exposed and then reinforced (immunity debt hypothesis)? This latest option should be explored further as currently only few studies investigated that possibility [43], as it would explain with what was observed for England and Finland for 3-4 years too. In a recent publication [44], the increase of RSV cases observed in the paediatric population after COVID-19 was attributed to the increase in RSV testing, rather than changes in viral circulation and the immunity debt hypothesis. This should be explored collecting exhaustive test data, as we only had one of our studied area, Spain-Valencia, where testing was systematic and so normally stable over seasons but where other parameters evolved preventing to do this analysis for this site too. In Spain-Valencia, changes in hospital admission policies and procedures could explain why incidence rates have not returned to similar levels after COVID-19 as before the pandemic, contrary to the pattern observed in other countries. However, the precise reason is still unclear until more up-to-date data becomes available. Moreover, overall RSV-coding practices seem to have been impacted based on available data, to be confirmed where data are available for a longer time period than 1 or

2 seasons after the COVID pandemic.

In terms of the impact of COVID-19 on severe outcomes of RSV hospitalisation, ICU data were lacking from most countries to enable a multi-country comparison for RSV-coded ICU admissions. The availability and collection methods for RSV-coded deaths were also too different to enable a robust comparison. This study nonetheless provides the opportunity to share these data, which may provide insights on study design for future studies, on top of providing figures that are useful to represent the situation in their respective countries.

Additional material

Table SC1. Average number and proportion of all admissions of patients below 5 years of age. Shown are all RTI-admissions, RSV-coded admissions and RSV-confirmed admissions by age group, diagnosis group and risk groups stratified by before COVID-19 (2016/17 to 2018/19) and after COVID-19 (2021/22 to 2022/23). Shown is the average (\pm SD) of all admissions belonging to each category before and after COVID-19.

		Denmark			England		Finland			Netherlands		Scotland			Spain-Valencia		
	COVI D-19	RTI-coded	RSV-coded	RSV-confirmed	RTI-coded	RSV-coded	RTI-coded	RSV-coded	RSV-confirmed	RTI-coded	RSV-coded	RTI-coded	RSV-coded	RSV-confirmed	RTI-coded	RSV-coded	RSV-confirmed
Per age group																	
0-2m	Before	834 (768,900)	319 (262,376), 38.2%	284 (254,314), 34.1%	22693 (20996,243 90)	3608 (3262,3954) , 15.9%	1379 (1058,17 00)	547 (240,854), 39.7%	550 (240,860), 39.9%	4505 (3446,556 4)	1177 (788,1566) , 26.1%	NA	NA	NA	159 (145,17 3)	67 (49,85) , 42.1%	86 (72,100) , 54.1%
	After	1191 (NA,NA)	595 (NA,NA), 50%	660 (NA,NA), 55.4%	28352 (28155,285 49)	6834 (6311,7357) , 24.1%	1464 (1363,15 65)	609 (586,632), 41.6%	591 (571,611), 40.4%	NA	NA	NA	NA	NA	52 (50,54)	11 (3,19), 21.2%	18 (14,22), 34.6%
3-5m	Before	1077 (917,123 7)	316 (246,386), 29.3%	302 (256,348), 28%	18583 (18234,189 32)	1613 (1517,1709) , 8.7%	613 (502,724)	243 (111,375), 39.6%	249 (119,379), 40.6%	2381 (1786,297 6)	412 (288,536), 17.3%	NA	NA	NA	78 (67,89)	36 (22,50) , 46.2%	42 (34,50), 53.8%
	After	1205 (NA,NA)	443 (NA,NA), 36.8%	556 (NA,NA), 46.1%	18056 (17285,188 27)	3365 (3017,3713) , 18.6%	683 (619,747)	304 (260,348), 44.5%	301 (250,352), 44.1%	NA	NA	NA	NA	NA	28 (22,34)	8 (1,15), 28.6%	13 (7,19), 46.4%
6-11m	Before	1377 (1294,14 60)	143 (126,160), 10.4%	195 (160,230), 14.2%	34400 (33248,355 52)	1602 (1535,1669) , 4.7%	872 (779,965)	164 (71,257), 18.8%	184 (82,286), 21.1%	3554 (2577,453 1)	308 (208,408), 8.7%	NA	NA	NA	63 (62,64)	18 (13,23) , 28.6%	24 (16,32), 38.1%

	After	1364 (NA,NA)	212 (NA,NA), 15.5%	301 (NA,NA), 22.1%	29177 (29147,292 07)	3652 (3390,3914) , 12.5%	799 (693,905)	180 (127,233), 22.5%	204 (142,266), 25.5%	NA	NA	NA	NA	NA	32 (25,39)	6 (5,7), 18.8%	10 (6,14), 31.2%
1-2y	Before	3351 (3130,35 72)	142 (117,167), 4.2%	276 (199,353), 8.2%	72668 (69521,758 15)	1352 (1199,1505) , 1.9%	2778 (2664,28 92)	198 (87,309), 7.1%	284 (143,425), 10.2%	7154 (5516,879 2)	250 (174,326), 3.5%	NA	NA	NA	150 (138,16 2)	16 (14,18) , 10.7%	41 (25,57), 27.3%
	After	4107 (NA,NA)	446 (NA,NA), 10.9%	724 (NA,NA), 17.6%	64154 (55606,727 02)	5700 (4704,6696) , 8.9%	3015 (2557,34 73)	328 (236,420), 10.9%	474 (293,655), 15.7%	NA	NA	NA	NA	NA	88 (84,92)	10 (2,18), 11.4%	19 (9,29), 21.6%
3-4y	Before	917 (859,975)	7 (5,9), 0.8%	17 (15,19), 1.9%	28687 (26697,306 77)	208 (156,260), 0.7%	1017 (987,104 7)	41 (12,70), 4%	62 (21,103), 6.1%	2728 (2058,339 8)	51 (36,66), 1.9%	NA	NA	NA	54 (48,60)	1 (0,2), 1.9%	7 (5,9), 13%
	After	1041 (NA,NA)	66 (NA,NA), 6.3%	110 (NA,NA), 10.6%	29193 (27964,304 22)	1248 (1223,1273) , 4.3%	1128 (861,139 5)	114 (71,157), 10.1%	168 (94,242), 14.9%	NA	NA	NA	NA	NA	40 (32,48)	2 (1,3), 5%	6 (2,10), 15%
0-1y	Before	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	6854 (6701,70 07)	1214 (1090,133 8), 17.7%	1281 (1278,128 4), 18.7%	NA	NA	NA
	After	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	5364 (3516,72 12)	1280 (1237,132 3), 23.9%	1432 (1365,149 9), 26.7%	NA	NA	NA
2-4y	Before	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	7413 (7395,74 31)	384 (383,385), 5.2%	626 (559,693), 8.4%	NA	NA	NA
	After	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	6282 (4064,85 00)	532 (504,560), 8.5%	766 (671,861), 12.2%	NA	NA	NA

Per diagnosis																	
Bronchitis & Bronchiolitis	Before	2061 (1860,2262)	679 (598,760), 32.9%	569 (484,654), 27.6%	42557 (39455,45659)	6530 (6090,6970), 15.3%	3161 (2748,3574)	973 (518,1428), 30.8%	1021 (564,1478), 32.3%	5877 (4732,7022)	1849 (1357,2341), 31.5%	4886 (4786,4986)	1399 (1312,1486), 28.6%	1354 (1295,1413), 27.7%	234 (191,277)	108 (71,145), 46.2%	137 (126,148), 58.5%
	After	2914 (2914,2914)	1471 (1471,1471), 50.5%	1475 (1475,1475), 50.6%	47580 (46116,49044)	14680 (14379,14981), 30.9%	3542 (3195,3889)	1186 (1116,1256), 33.5%	1268 (1124,1412), 35.8%	NA	NA	4270 (3101,5439)	1460 (1443,1477), 34.2%	1524 (1483,1565), 35.7%	90 (70,110)	29 (14,44), 32.2%	49 (35,63), 54.4%
LRTI	Before	8 (6,10)	NA, NA%	2 (2,2), 25%	27703 (25661,29745)	331 (303,359), 1.2%	32 (31,33)	1 (-1,3), 3.1%	4 (1,7), 12.5%	842 (602,1082)	27 (20,34), 3.2%	1126 (948,1304)	44 (41,47), 3.9%	147 (130,164), 13.1%	23 (11,35)	3 (3,3), 13%	3 (1,5), 13%
	After	17 (17,17)	NA, NA%	4 (4,4), 23.5%	23181 (19420,26942)	1322 (1111,1533), 5.7%	22 (19,25)	1 (0,2), 4.5%	3 (2,4), 13.6%	NA	NA	1087 (661,1513)	96 (81,111), 8.8%	186 (143,229), 17.1%	4 (4,4)	NA, NA%	2 (NA,NA), 50%
URTI	Before	3473 (3110,3836)	9 (6,12), 0.3%	131 (109,153), 3.8%	88239 (87870,88608)	178 (131,225), 0.2%	1762 (1719,1805)	15 (3,27), 0.9%	60 (29,91), 3.4%	9914 (7755,12073)	85 (56,114), 0.9%	7598 (7384,7812)	88 (80,96), 1.2%	303 (289,317), 4%	30 (17,43)	2 (1,3), 6.7%	10 (6,14), 33.3%
	After	3990 (3990,3990)	10 (10,10), 0.3%	347 (347,347), 8.7%	65772 (65065,66479)	882 (817,947), 1.3%	1274 (1209,1339)	16 (13,19), 1.3%	66 (60,72), 5.2%	NA	NA	5714 (4028,7400)	195 (177,213), 3.4%	409 (380,438), 7.2%	11 (10,12)	NA, NA%	2 (2,2), 18.2%
Pneumonia	Before	1668 (1508,1828)	227 (175,279), 13.6%	260 (230,290), 15.6%	11211 (10328,12094)	222 (220,224), 2%	1094 (1006,1182)	71 (26,116), 6.5%	107 (44,170), 9.8%	3116 (2497,3735)	94 (59,129), 3%	657 (582,732)	65 (47,83), 9.9%	102 (96,108), 15.5%	113 (92,134)	16 (6,26), 14.2%	31 (21,41), 27.4%
	After	1600 (1600,1600)	242 (242,242), 15.1%	339 (339,339), 21.2%	11282 (8595,13969)	734 (729,739), 6.5%	936 (640,1232)	120 (53,187), 12.8%	172 (87,257), 18.4%	NA	NA	574 (534,614)	60 (52,68), 10.5%	79 (58,100), 13.8%	68 (43,93)	8 (5,11), 11.8%	11 (7,15), 16.2%

SARS-CoV-2	After	NA	NA	NA	8850 (6776,10924)	25 (23,27), 0.3%	484 (403,565)	2 (2,2), 0.4%	7 (6,8), 1.4%	NA	NA	1000 (464,1536)	4 (4,4), 0.4%	19 (7,31), 1.9%	15 (6,24)	NA, NA%	2 (NA,NA), 13.3%
More than one diagnosis	Before	NA	NA	NA	7110 (6568,7652)	910 (904,916), 12.8%	607 (570,644)	132 (76,188), 21.7%	138 (82,194), 22.7%	573 (505,641)	143 (122,164), 25%	NA	NA	NA	33 (27,39)	18 (9,27), 54.5%	17 (11,23), 51.5%
	After	NA	NA	NA	11337 (10913,11761)	2228 (2022,2434), 19.7%	830 (715,945)	208 (154,262), 25.1%	222 (157,287), 26.7%	NA	NA	NA	NA	NA	17 (12,22)	2 (NA,NA), 11.8%	7 (5,9), 41.2%
Other diagnosis	Before	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	133 (113,153)	29 (1,57), 21.8%	35 (13,57), 26.3%
	After	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	68 (55,81)	4 (3,5), 5.9%	9 (6,12), 13.2%
Per risk group																	
<1y - low risk	Before	2396 (2234,2558)	559 (485,633), 23.3%	565 (510,620), 23.6%	63324 (62089,64559)	5431 (5123,5739), 8.6%	2371 (1649,3093)	802 (328,1276), 33.8%	829 (346,1312), 35%	NA	NA	NA	NA	NA	145 (130,160)	62 (50,74), 42.8%	79 (60,98), 54.5%
	After	3574 (3574,3574)	1191 (1191,1191), 33.3%	1454 (1454,1454), 40.7%	62852 (62852,62852)	11405 (10554,12256), 18.1%	2394 (1658,3130)	888 (581,1195), 37.1%	894 (580,1208), 37.3%	NA	NA	NA	NA	NA	67 (53,81)	16 (3,29), 23.9%	26 (13,39), 38.8%
<1y - high risk	Before	878 (779,977)	217 (177,257), 24.7%	214 (181,247), 24.4%	12353 (10390,14316)	1392 (1191,1593), 11.3%	493 (- 35,1021)	152 (18,286), 30.8%	155 (17,293), 31.4%	NA	NA	NA	NA	NA	155 (141,169)	59 (35,83), 38.1%	72 (63,81), 46.5%
	After	186 (186,186)	59 (59,59), 31.7%	63 (63,63), 33.9%	12734 (12191,13277)	2446 (2165,2727), 19.2%	553 (27,1079)	204 (- 11,419), 36.9%	202 (- 9,413), 36.5%	NA	NA	NA	NA	NA	45 (44,46)	8 (4,12), 17.8%	14 (14,14), 31.1%

1-4y - low risk	Before	3132 (2960,3304)	97 (84,110), 3.1%	203 (164,242), 6.5%	94182 (94045,94319)	1248 (1206,1290), 1.3%	3476 (3375,3577)	207 (98,316), 6%	307 (162,452), 8.8%	NA	NA	NA	NA	NA	179 (170,188)	13 (11,15), 7.3%	41 (31,51), 22.9%
	After	4636 (4636,4636)	460 (460,460), 9.9%	755 (755,755), 16.3%	75667 (69573,81761)	5232 (4447,6017), 6.9%	3824 (3268,4380)	394 (299,489), 10.3%	578 (397,759), 15.1%	NA	NA	NA	NA	NA	112 (104,120)	10 (3,17), 8.9%	20 (7,33), 17.9%
1-4y - high risk	Before	1118 (1050,1186)	48 (40,56), 4.3%	87 (55,119), 7.8%	7174 (2174,12174)	312 (64,560), 4.3%	319 (288,350)	32 (15,49), 10%	38 (19,57), 11.9%	NA	NA	NA	NA	NA	26 (17,35)	5 (2,8), 19.2%	7 (2,12), 26.9%
	After	506 (506,506)	52 (52,52), 10.3%	79 (79,79), 15.6%	17680 (16456,18904)	1717 (1481,1953), 9.7%	320 (284,356)	47 (32,62), 14.7%	64 (37,91), 20%	NA	NA	NA	NA	NA	16 (12,20)	3 (NA,NA), 18.8%	6 (5,7), 37.5%

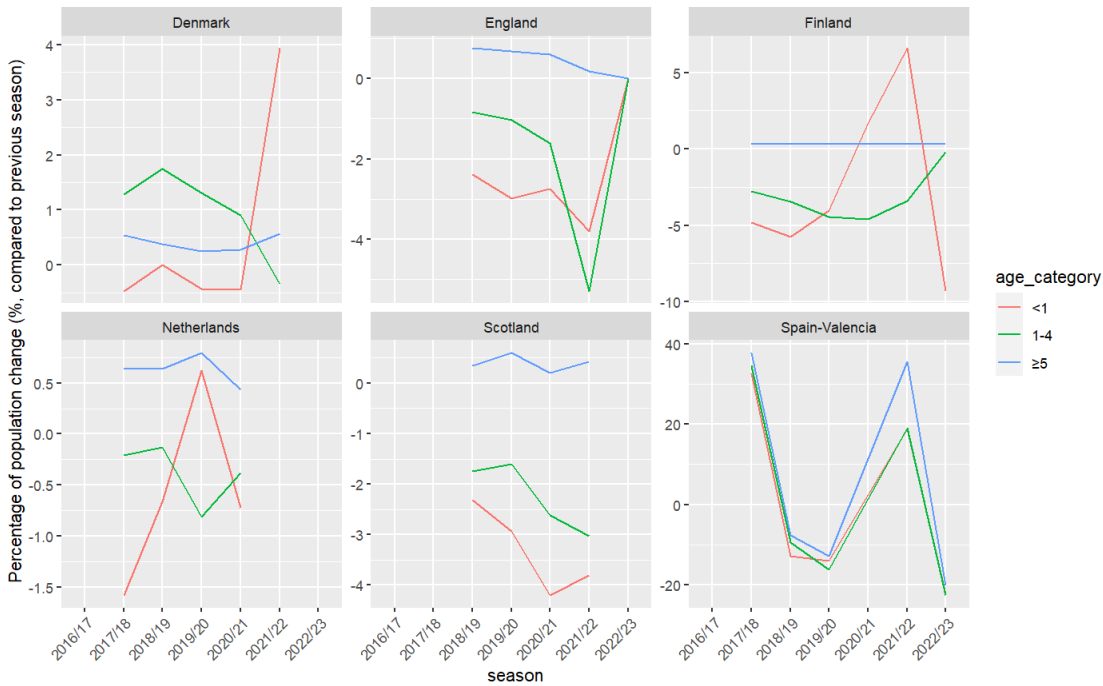


Figure SC1 – Evolution of population over seasons per country and age group. Age groups were simplified - leveraging those used for risk groups analysis- for the figure as trends are the same when using the smaller age groups used all along the analysis except for risk groups, and it improves readability.

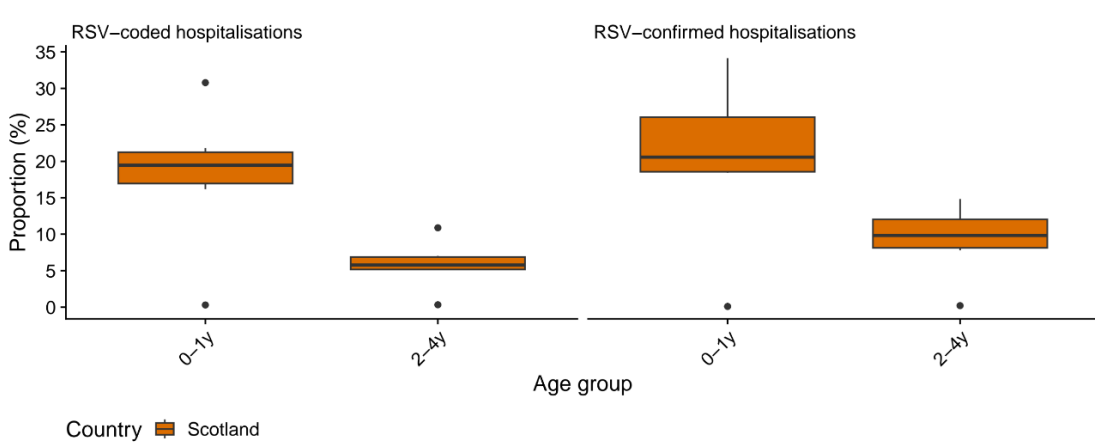


Figure SC2 – Proportion of RTI hospital admissions that are RSV-coded (panel A, on the left) and RSV-confirmed (panel B, on the right), per age group (vertical sub-panels), Scotland.

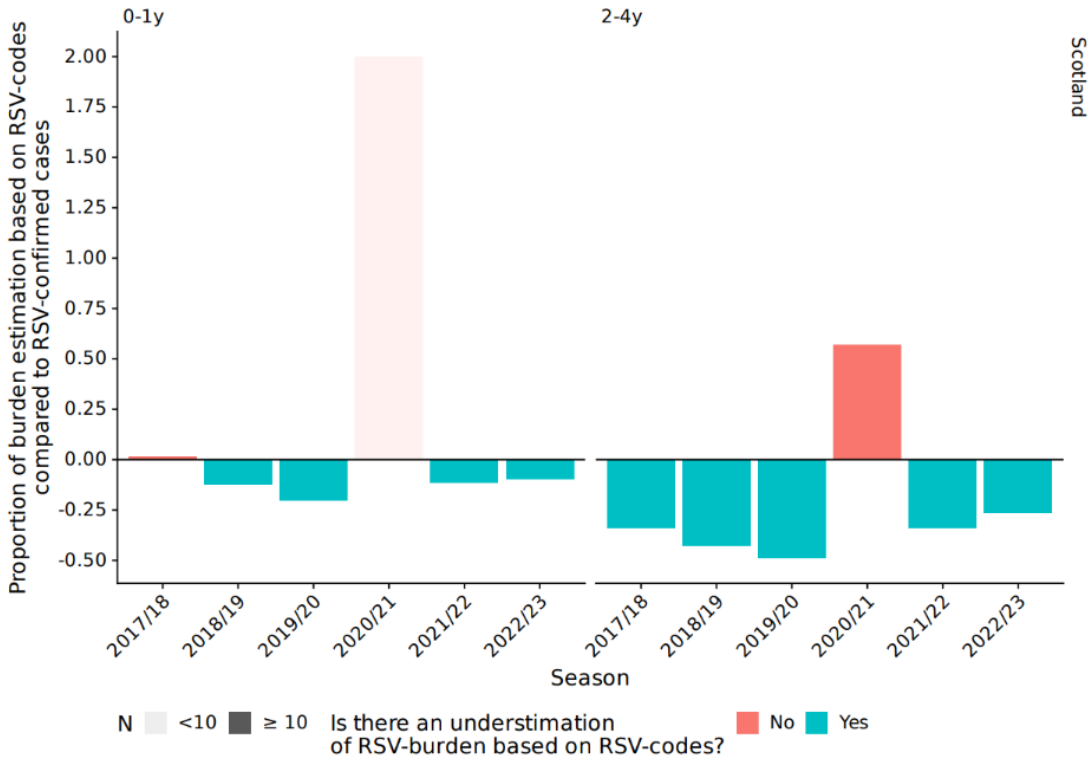


Figure SC3 – Evaluation of the evolution of RSV-coding practice compared to RSV-confirmation practice per country and season, computed as the proportion of RSV-confirmed cases that are RSV-confirmed, centred on 0 for readability. If the metric is equal for 0.25 for example, it means there are 25% more RSV-coded hospital admissions than RSV-confirmed hospital admissions. Bars with a pale colour indicate less robust data as there were fewer than 10 hospital admissions for that season and that country.

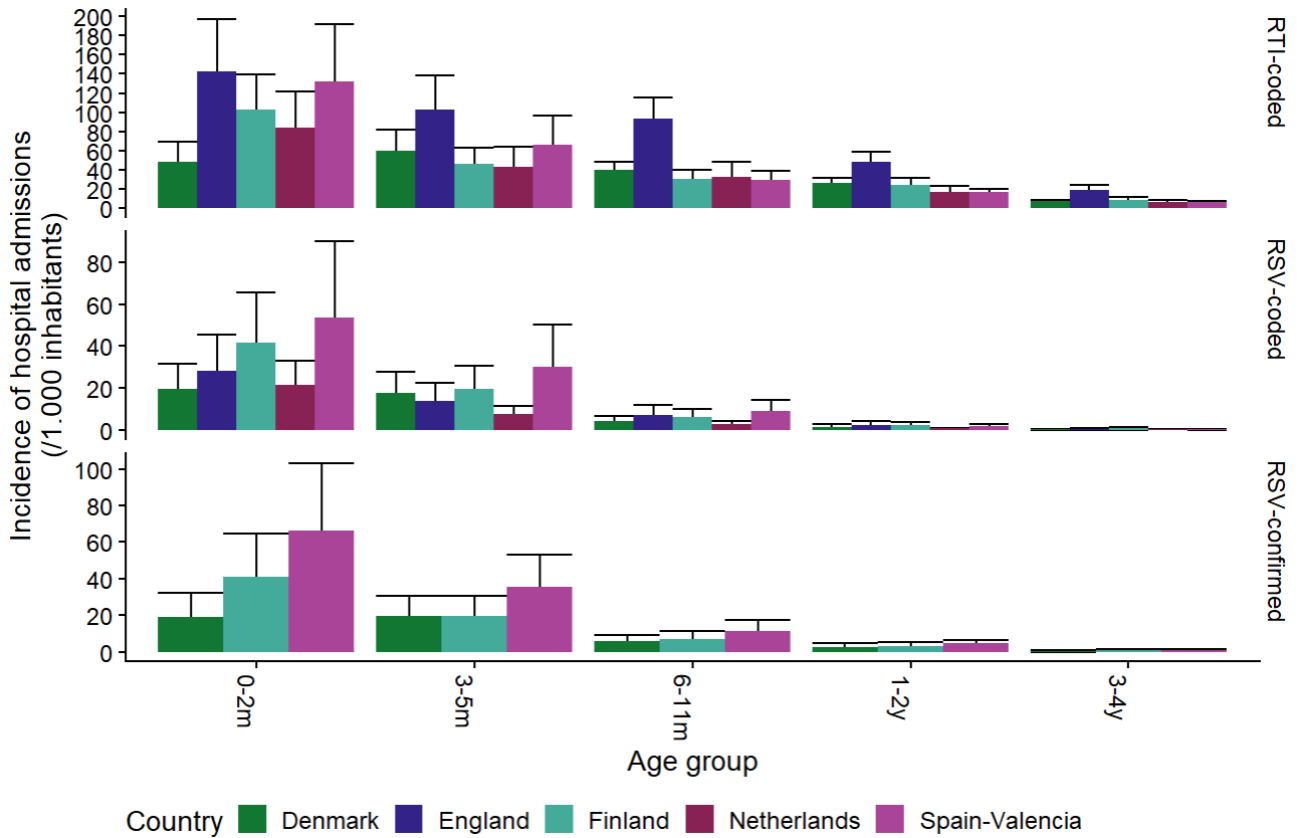


Figure SC4 – Average incidence of hospital admissions of patients below 5 years per 1,000 inhabitants. The average incidence per 1,000 inhabitants (y-axis) over all available surveillance years is shown per age group (x-axis) and country (colours) for each hospitalisation type. The error bars indicate the standard deviation.

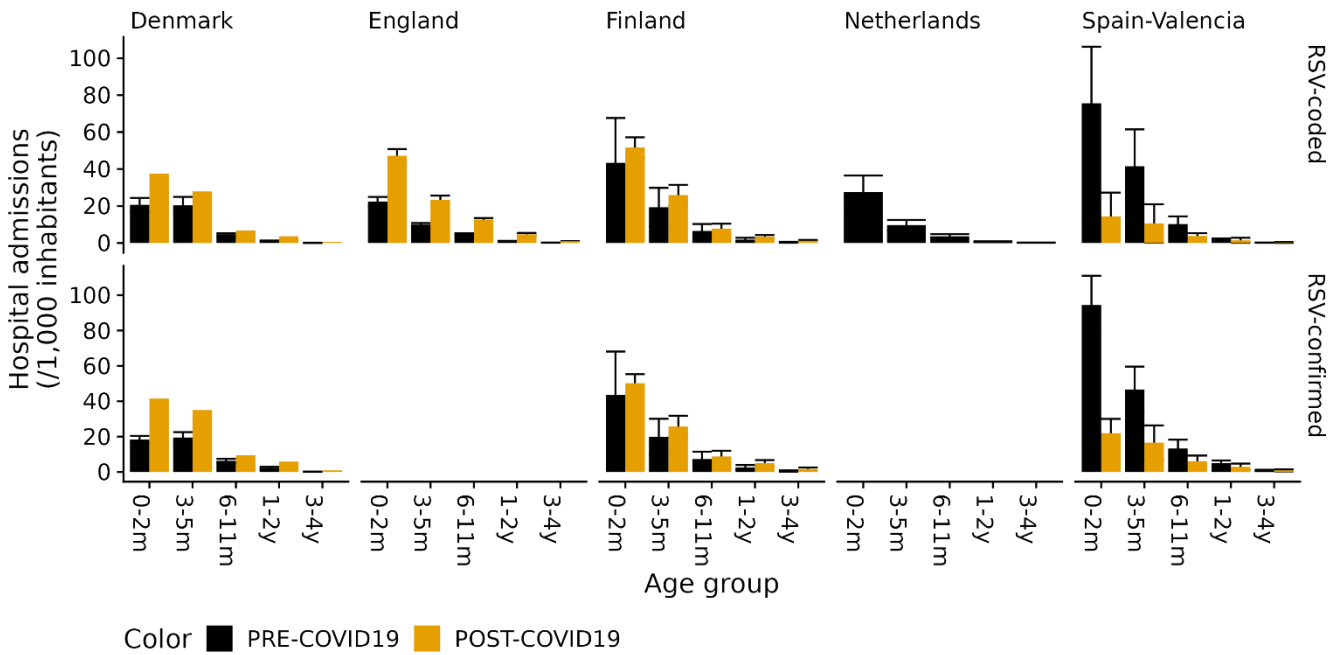


Figure SC5 – Average incidence per 1,000 person-years during the pre-COVID-19 period (2016-2019, black bars) and during the post-COVID-19 period (2021-2023, yellow bars). The average incidence per 100,000 inhabitants (y-axis) stratified by after/during COVID-19 is shown per age group (x-axis) and country (subpanels) for RSV-coded and RSV-confirmed admissions. The error bars indicate the standard deviation. 2019/20 and 2020/21 data have not been included in this table to remove potential NPI’s effects introduced during the COVID-19 pandemic.

4.2 Older children and adults burden

Background

The impact of RSV on older adults is not as well understood as in young children, although early research dating back to 1993 already noted its significance, comparing it to that of influenza's burden in this demographic [45]. Recent findings have revealed a higher hospitalisation incidence than previously acknowledged, particularly among adults with underlying health conditions, immunocompromised or of advanced age [46-53]. RSV is also known to exacerbate conditions such as asthma, COPD or heart failure and to lead to severe outcomes, such as pneumonia, hospitalisation, myocardial infarction or death [54-57]. A recent systematic review and meta-analysis suggests that RSV may have led to around 470,000 hospitalisations and 33,000 in-hospital deaths among individuals aged 60 and above in high-income countries in 2019 [4]. This positions RSV as a notable cause of hospitalisations among older adults. Still, determining the true incidence of RSV-related hospitalisations in older adults remains challenging due to a lack of routine testing for RSV in hospitals and the absence of dedicated surveillance systems. With the recent market approval of vaccines for adults ≥ 60 years of age (Arexvy - GSK and Abrysvo™ - Pfizer) [58-60], it has become more crucial than ever to have accurate burden estimates to assist in immunisation strategies and monitor the vaccines' impact and effectiveness.

Using a similar approach as previously employed in RESCEU [5, 6], where routinely collected health records from various European countries were utilised to understand the burden of RSV disease in young children, we present findings on RSV hospitalisation rates, associated RSV ICU admissions, mortality data, and LOS among patients aged 5 years and older in six European countries. We compare admission rates across countries and age groups and provide estimates before and after the COVID-19 pandemic.

Methods

The study design, study population and data analysis have been described in section 3 of this report. Age has been stratified by the following age groups: 5-17 years, 18-64 years, 65-74 years, 75-84 years and ≥ 85 years. In some countries (Finland, Spain-Valencia, and Scotland) some additional age groups (18-49 years and 50-64 years) were included.

Summary of results

Admission rates by season, country, and age group

Average annual RTI hospitalisation admission rates ranged from 94 to 496 before COVID-19 (seasons 2016/17 - 2018/19) and 47 to 512 after COVID-19 (seasons 2021/22 - 2022/23) per 100,000 adults aged 5-17 years. Average rates ranged between 160 to 641 per 100,000 adults aged 18-64 years before COVID-19 and 95 to 791 after COVID-19, between 908 to 2195 per 100,000 adults aged 65-74 years before COVID-19 and 361 to 2359 after COVID-19, between 1938 to 5353 per 100,000 adults aged 75-84 years before COVID-19 and 676 to 5577 after COVID-19 and between 3939 to 12684 per 100,000 adults ≥ 85 years before COVID-19 and 1489 to 13011 after COVID-19 (Figure A1). The average annual RTI hospitalisation rates were highest in adults aged 85 years or older and lowest in the 5-17-year age group in all countries (Figure A1). A drop in admission rates was seen across all countries during 2020/21. Overall RTI admission rates were always highest in England and lowest in Spain-Valencia (although *in Spain-Valencia, RTI admissions were those meeting ILI criteria only and seasons were restricted to the RSV circulation period*).

Average RSV-coded hospitalisation rates ranged from 0 to 4.4 before COVID-19 (seasons 2016/17 - 2018/19) and 0.9 to 9 after COVID-19 (seasons 2021/22 - 2022/23) per 100,000 adults aged 5-17 years. Average rates ranged between 0.7 to 4.7 per 100,000 adults aged 18-64 years before COVID-19 and 1 to 5 after COVID-19, between 0 to 25 per 100,000 adults aged 65-74 years before COVID-19 and 5 to 25 after COVID-19, between 6 to 66 per 100,000 adults aged 75-84 years before COVID-19 and 13 to 45 after COVID-19 and between 7 to 166 per 100,000 adults \geq 85 years before COVID-19 and 20 to 116 after COVID-19 (Figure A1).

Average RSV-confirmed hospitalisation rates ranged from 0.5 to 10 before COVID-19 (seasons 2016/17 - 2018/19) and 2 to 17 after COVID-19 (seasons 2021/22 - 2022/23) per 100,000 adults aged 5-17 years. Average rates ranged between 1.8 to 7 per 100,000 adults aged 18-64 years before COVID-19 and 2 to 6 after COVID-19, between 10 to 45 per 100,000 adults aged 65-74 years before COVID-19 and 6 to 29 after COVID-19, between 20 to 148 per 100,000 adults aged 75-84 years before COVID-19 and 25 to 54 after COVID-19 and between 44 to 260 per 100,000 adults \geq 85 years before COVID-19 and 51 to 127 after COVID-19 (Figure A1).

As previously described in some EU countries (Finland, Norway and Denmark) [5], here we also observed that in Finland, England, Scotland, and Spain-Valencia a high RSV admission rate in a given year was followed by a low RSV admission rate the next year. A drop in RSV admission rates was seen across all countries during 2020/21. The incidence of RSV-coded/RSV-confirmed admissions ranged between 0 and 1.6 per 100,000 in 2020/21 considering all countries and age groups. In Scotland and England there was a substantial decrease in RTI admissions in the 5-17-year age group during the pandemic which was not so sharp in other countries and age groups. From 2021/22 onwards, the general trend across all countries and age groups implies that rates are returning to levels similar to those pre-pandemic (Supplementary Tables SA2 and SA3). In Scotland and England, a higher incidence of RSV-coded admissions is observed after 2020/21 in the 5-17-year age group, as well as for the rest of age groups in England (Figure A1, Supplementary Table SA2 and SA3).

The highest RSV-confirmed admission rates were observed in Finland and Spain-Valencia. In Spain-Valencia, all patients were systematically tested for RSV, but in Finland testing denominator data was not known. Supplementary Table SA1 describes the average number of RTI-admissions, RSV-coded admissions and RSV-confirmed admissions in each age group and country stratified by before and after COVID-19. The percentage of admissions belonging to each of the diagnosis and risk groups described in sections 3.8 and 0 are shown in Supplementary Figures S1 - S6 and Supplementary Table SA1 for each country.

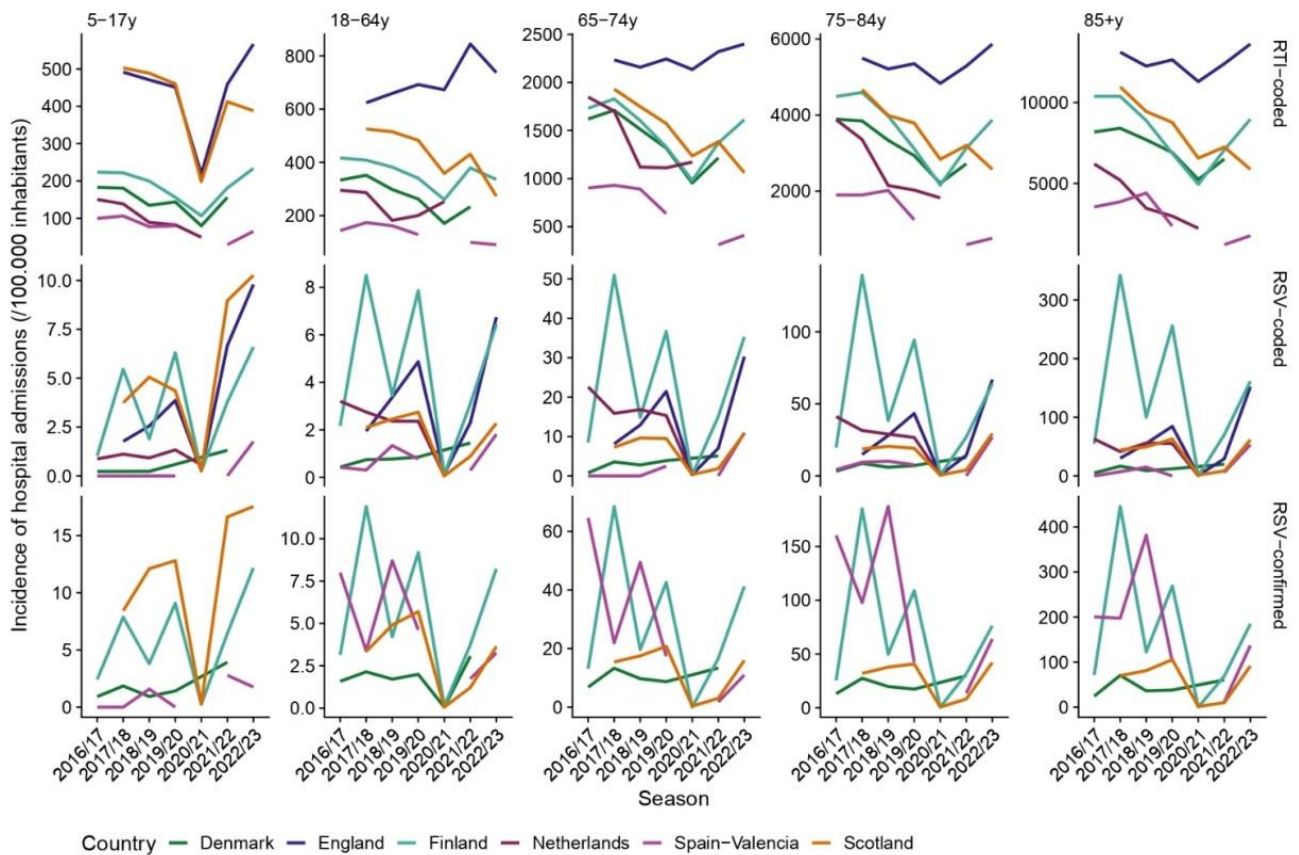


Figure A1. Hospitalisation admission rates in patients 5 years of age and above. The hospital admissions rates per 100,000 persons-year (y-axis) per surveillance year (x-axis) is shown for each country (colour), age group (vertical subpanels) and hospitalisation type: A) RTI admissions B) RSV-coded admissions and C) RSV admissions with a laboratory confirmed result for RSV. Note that each individual panel has a different y-axis scale to allow for readability. A summary figure with identical y-axis scales for all age groups can be found in Supplementary Figure SA2.

RSV-coding practices

In countries with RSV-coded and RSV-confirmed data we estimated the proportion of RSV-admission rates that would be underestimated when only relying on RSV-codes (Figure A2). We performed this exercise to estimate if relying on RSV-codes would be a good proxy of the real RSV hospitalisation burden, as most countries have access to this information only. In Denmark, Finland, Scotland, and Spain-Valencia and across all age groups using RSV-codes resulted in an underestimation between 100% and 5% in older children and adults. Only in Finland during 2020/21 in adults ≥ 85 years of age the number of RSV-coded hospitalisations was 1.8% higher than the number of RSV-confirmed hospitalisations.

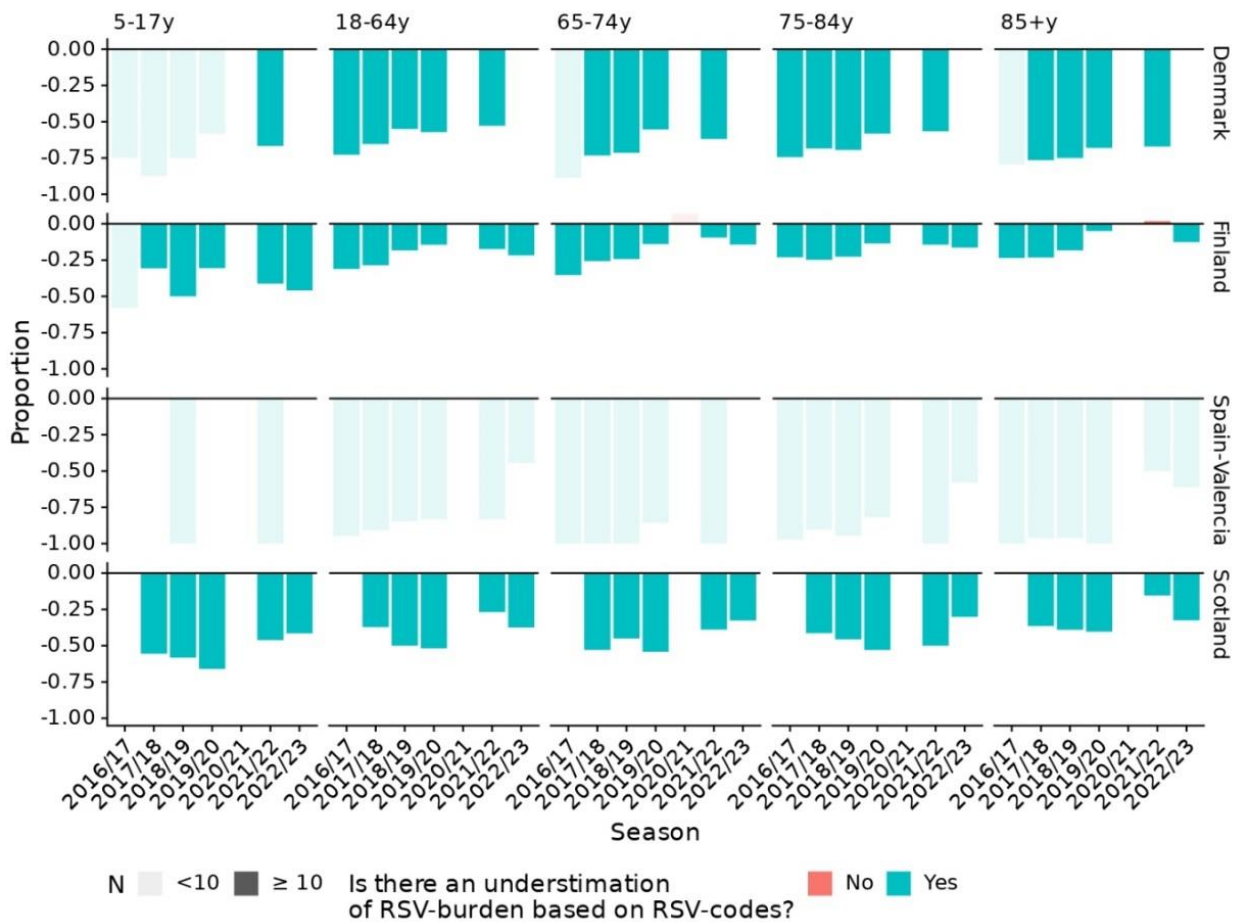


Figure A2. Underestimation of RSV-burden when relying on RSV-coding practices in patients of 5 years of age or older. The proportion of hospitalisations underestimated when using RSV-codes as a reference compared to RSV-confirmed cases is shown in the x-axis for countries with both types of data available (vertical sub-panels) and per age group (panels). Colours indicate if there is an underestimation (blue: yes, and red: no). Shades indicate the number of patients available for the estimation (<10 light shade and ≥10 dark shade).

Severity of admissions

Lengths of stay

Figure A3 shows the median LOS of each hospitalisation type, age group and country. No significant differences can be seen between seasons in all countries and age groups, except in Scotland and England where a longer LOS could be observed in some age groups during 2020/21 in RSV-coded and RSV-confirmed admissions. Across countries, the average RTI median LOS for the 5-17-year age group ranged between 1 and 3.2 days, in the 18-64-year age group between 1.5 and 5.7 days, in the 65-74-year age group between 2 and 6 days, in the 75-84-year age group between 2 and 7.5 days and in the ≥ 85 years age group between 2 and 9.2 days. The average RSV-coded median LOS for the 5-17-year age group ranged between 2.4 and 5 days, in the 18-64-year age group between 1.8 and 12.1 days, in the 65-74-year age group between 2.1 and 5.8 days, in the 75-84-year age group between 3.3 and 7.9 days and in the ≥85 years age group between 2 and 7.9 days. The average RSV-confirmed median LOS for the 5–17-year age group ranged between 1.6 and 3.5 days, in the 18-64-year age group between 1.7 and 5.5 days, in the 65-74-year

age group between 4.2 and 6.2 days, in the 75-84-year age group between 2.8 and 6.4 days and in the ≥ 85 years age group between 3.7 and 6.6 days. The variability between seasons was higher in the RSV-coded/confirmed hospitalisations compared to RTI, but the number of admissions for LOS estimation was higher in RTI hospitalisations. In most countries, RSV-related hospitalisations (confirmed or coded) led to longer hospitalisation stays on average in the 5-17-year age group, but not in the rest of the age groups.

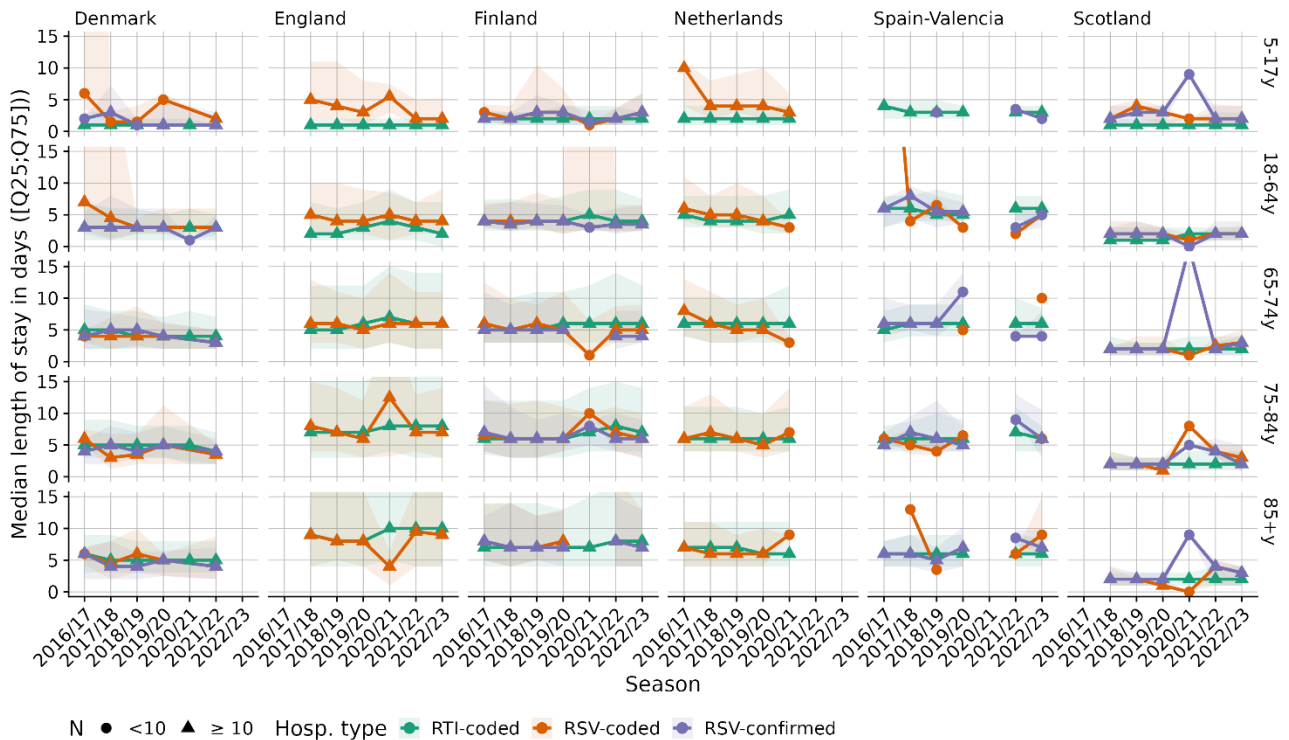


Figure A3. Length of stay among patients 5 years of age or older. Median LOS (y-axis) and 25/75 quartiles (shadow area) of all hospital admissions per country, age group and surveillance year (x-axis). Each hospitalisation type is shown with a different colour (green: RTI admissions, orange: RSV-coded and violet – RSV-confirmed admissions). If the estimate is based on fewer than 10 patients the shape is represented as a dot, whereas if the estimate is based on more than 10 patients the shape is represented as a triangle. Outliers (18-64 age group and RSV-coded in Spain-Valencia: 52 days [1 patient] and 65-74 age group and RSV-confirmed in Scotland [2 patients]: 18 days) are not shown to allow for readability of the graph.

ICU admissions

In England, ICU admissions data was available and is summarised in Table A1. The highest RSV-coded ICU admissions rates compared to RTI ICU admissions were observed in the 5-17-year age group both before and after COVID-19 (2.7% and 3.8%, respectively). The proportion of RSV-coded ICU admissions compared to RTI ICU admissions ranged from 0.6% to 0.3% in the rest of the age groups. Bronchitis & bronchiolitis was the most frequent diagnosis group among patients admitted to ICU.

Table A1. Average number and proportion of ICU admissions of patients of 5 years of age or older. Shown are all RTI-admissions, RSV-coded admissions and RSV-confirmed admissions that ended in an ICU admission by age group, diagnosis group and risk group stratified by before COVID-19 (2016/17 to 2018/19) and after COVID-19 (2021/22 to 2022/23). Shown is the average (± SD) of all admissions belonging to each category before and after COVID-19.

	England
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Age group	COVID-19	RTI-admissions	RSV-coded
5 - 17 years	Before	1262 (1243,1281)	34 (26,42), 2.7%
	After	943 (643,1243)	36 (22,50), 3.8%
18 - 64 years	Before	12468 (12176,12760)	65 (42,88), 0.5%
	After	10318 (4931,15705)	47 (40,54), 0.5%
65 - 74 years	Before	7372 (7040,7704)	46 (39,53), 0.6%
	After	4939 (2664,7214)	22 (19,25), 0.4%
75 - 84 years	Before	6338 (6145,6531)	27 (16,38), 0.4%
	After	3716 (2336,5096)	12 (8,16), 0.3%
≥ 85 years	Before	1996 (1899,2093)	5 (5,5), 0.3%
	After	882 (628,1136)	5 (4,6), 0.6%
Bronchitis & Bronchiolitis	Before	55 (46,64)	4 (2,6), 7.3%
	After	100 (98,102)	8 (7,9), 8%
Unspecified LRTI	Before	1590 (1238,1942)	20 (19,21), 1.3%
	After	3736 (3624,3848)	18 (15,21), 0.5%
URTI	Before	278 (237,319)	1 (0,2), 0.4%
	After	587 (554,620)	4 (3,5), 0.7%
Pneumonia & Influenza	Before	11662 (9415,13909)	53 (50,56), 0.5%
	After	24615 (24528,24702)	109 (81,137), 0.4%
SARS-COV-2	Before	NA	
	After	2023 (1402,2644)	2 (1,3), 0.1%
2+ diagnosis	Before	5161 (1278,9044)	14 (11,17), 0.3%
	After	372 (346,398)	12 (8,16), 3.2%
Low	Before	17270 (14884,19656)	94 (79,109), 0.5%
	After	10404 (5014,15794)	50 (44,56), 0.5%
High	Before	12166 (10129,14203)	84 (50,118), 0.7%
	After	10394 (6187,14601)	72 (65,79), 0.7%

Mortality

In Denmark, England, Finland, and Spain-Valencia mortality data was available and is summarised in Table A2.

Table A2. Average number and proportion of deaths of patients of 5 years of age or older. Shown are all RTI admissions, RSV-coded admissions and RSV-confirmed admissions that ended in death by age group, diagnosis group and risk group stratified by before COVID-19 (2016/17 to 2018/19) and after COVID-19 (2021/22 to 2022/23). Shown is the average (\pm SD) of all admissions belonging to each category before and after COVID-19.

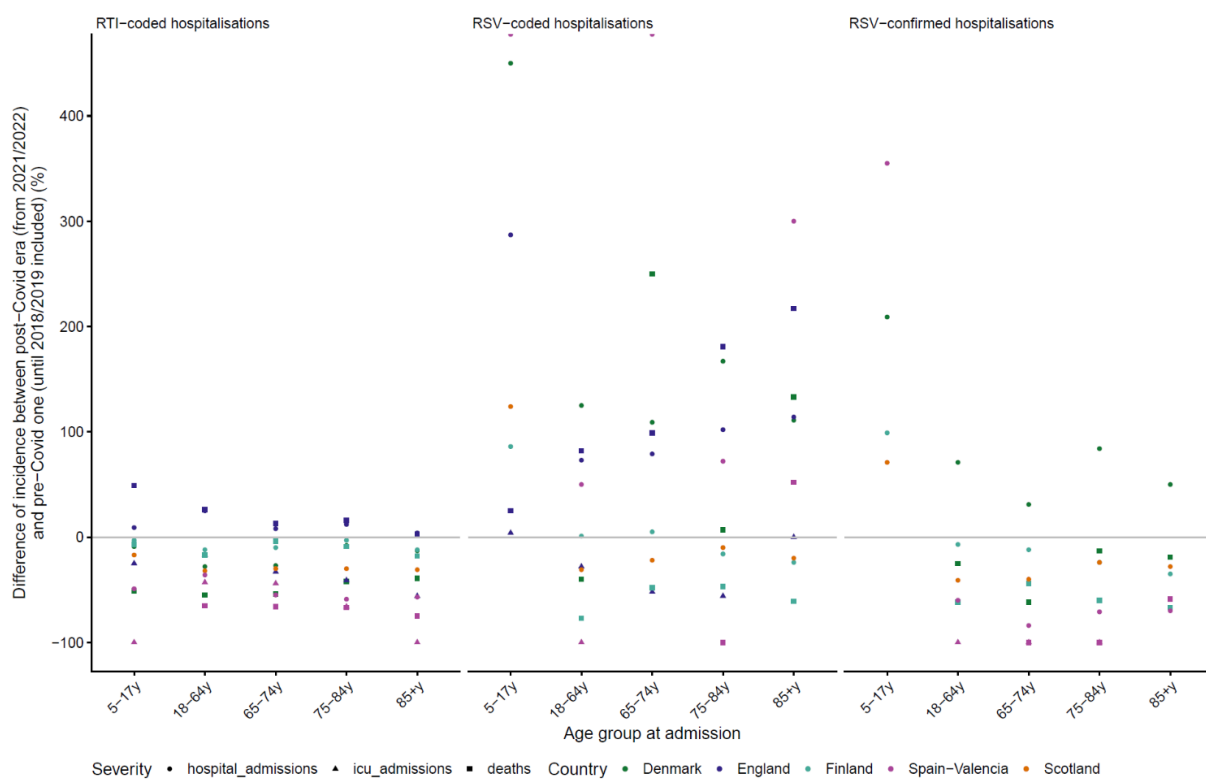
		England		Denmark			Finland			Spain-Valencia		
Age group	COVID-19	RTI-admissions	RSV-coded	RTI-admissions	RSV-coded	RSV-confirmed	RTI-admissions	RSV-coded	RSV-confirmed	RTI-admissions	RSV-coded	RSV-confirmed
5 - 17 years	Before	76 (65,87)	2 (1,3), 2.6%	23 (21,25)	2 (+/- NA), 8.7%	2 (2,2), 8.7%	7 (6,8)	0 (0,0), 0%	0 (0,0), 0%	0 (0,0)	0 (0,0), 0%	0 (0,0), 0%
	After	112 (111,113)	2 (-2,6), 1.8%	11 (+/- NA)	0 (0,0), 0%	NA, NA%	6 (4,8)	0 (0,0), 0%	0 (0,0), 0%	0 (0,0)	0 (0,0), 0%	0 (0,0), 0%
18 - 64 years	Before	8391 (8159,8623)	30 (29,31), 0.4%	820 (717,923)	3 (1,5), 0.4%	13 (12,14), 1.6%	481 (456,506)	4 (1,7), 0.8%	5 (1,9), 1%	6 (3,9)	0 (0,0), 0%	0 (0,0), 0%
	After	10550 (9182,11918)	54 (12,96), 0.5%	368 (+/- NA)	2 (+/- NA), 0.5%	10 (+/- NA), 2.7%	402 (175,629)	1 (0,2), 0.2%	2 (2,2), 0.5%	2 (2,2)	0 (0,0), 0%	0 (0,0), 0%
65 - 74 years	Before	12660 (12048,13272)	43 (40,46), 0.3%	1651 (1496,1806)	2 (2,2), 0.1%	26 (16,36), 1.6%	995 (967,1023)	7 (-1,15), 0.7%	8 (-2,18), 0.8%	13 (11,15)	0 (0,0), 0%	1 (-1,3), 7.7%
	After	14282 (13243,15321)	86 (15,157), 0.6%	754 (+/- NA)	7 (+/- NA), 0.9%	10 (+/- NA), 1.3%	958 (550,1366)	4 (2,6), 0.4%	4 (0,8), 0.4%	4 (2,6)	0 (0,0), 0%	0 (0,0), 0%
75 - 84 years	Before	24388 (22683,26093)	54 (40,68), 0.2%	2915 (2626,3204)	5 (3,7), 0.2%	39 (23,55), 1.3%	1910 (1767,2053)	13 (-1,27), 0.7%	20 (-3,43), 1%	27 (18,36)	0 (-1,1), 0%	1 (0,2), 3.7%
	After	28196 (28170,28222)	152 (4,300), 0.5%	1698 (+/- NA)	5 (+/- NA), 0.3%	34 (+/- NA), 2%	1736 (1049,2423)	7 (0,14), 0.4%	8 (0,16), 0.5%	9 (5,13)	0 (0,0), 0%	0 (0,0), 0%

85 years	Before	34054 (30409,37699)	69 (49,89), 0.2%	3215 (2963,3467)	3 (1,5), 0.1%	42 (18,66), 1.3%	2559 (2396,2722)	30 (3,57), 1.2%	38 (-4,80), 1.5%	48 (26,70)	0 (-1,1), 0%	4 (3,5), 8.3%
	After	35145 (34267,36023)	219 (- 19,457), 0.6%	1964 (+/- NA)	7 (+/- NA), 0.4%	34 (+/- NA), 1.7%	2110 (1313,2907)	12 (3,21), 0.6%	12 (1,23), 0.6%	12 (8,16)	0 (-1,1), 0%	2 (0,4), 16.7%
Diagnosis groups												
Bronchitis & Bronchiolitis	Before	111 (100,122)	2 (1,3), 1.8%	92 (67,117)	13 (6,20), 14.1%	14 (6,22), 15.2%	89 (81,97)	14 (3,25), 15.7%	12 (2,22), 13.5%	5 (5,5)	1 (+/- NA), 20%	0 (0,0), 0%
	After	113 (107,119)	6 (1,11), 5.3%	39 (39,39)	22 (22,22), 56.4%	22 (22,22), 56.4%	30 (13,47)	4 (2,6), 13.3%	4 (2,6), 13.3%	2 (+/- NA)	0 (0,0), 0%	0 (0,0), 0%
Unspecified LRTI	Before	7410 (6893,7927)	16 (14,18), 0.2%	189 (133,245)	0 (0,0), 0%	6 (6,6), 3.2%	55 (50,60)	0 (0,0), 0%	0 (0,0), 0%	5 (2,8)	0 (0,0), 0%	1 (+/- NA), 20%
	After	5528 (5396,5660)	35 (7,63), 0.6%	78 (78,78)	0 (0,0), 0%	0 (0,0), 0%	30 (17,43)	0 (0,0), 0%	0 (0,0), 0%	1 (1,1)	0 (0,0), 0%	0 (0,0), 0%
URTI	Before	150 (147,153)	0 (-1,1), 0%	111 (93,129)	0 (0,0), 0%	5 (3,7), 4.5%	50 (38,62)	0 (0,0), 0%	1 (0,2), 2%	2 (1,3)	0 (0,0), 0%	0 (0,0), 0%
	After	127 (105,149)	4 (0,8), 3.1%	51 (51,51)	0 (0,0), 0%	0 (0,0), 0%	18 (11,25)	0 (0,0), 0%	1 (0,2), 5.6%	0 (0,0), 0%	0 (0,0), 0%	0 (0,0), 0%
Pneumonia & Influenza	Before	71182 (67142,75222)	136 (114,158), 0.2%	19869 (19052,2068 6)	51 (22,80), 0.3%	289 (180,398), 1.5%	6117 (5821,6413)	35 (8,62), 0.6%	54 (2,106), 0.9%	42 (26,58)	1 (+/- NA), 2.4%	2 (1,3), 4.8%
	After	55067 (52398,57736)	305 (89,521), 0.6%	10298 (10298,1029 8)	86 (86,86), 0.8%	218 (218,218), 2.1%	3054 (1769,4339)	12 (5,19), 0.4%	14 (5,23), 0.5%	14 (7,21)	0 (0,0), 0%	1 (+/- NA), 7.1%
SARSCOV-2	Before	NA										
	After	8019 (7926,8112)	5 (0,10), 0.1%				1566 (1382,1750)	0 (0,0), 0%	5 (4,6), 0.3%	13 (13,13)	0 (0,0), 0%	0 (0,0), 0%
2+ diagnosis	Before	683 (622,744)	12 (12,12), 1.8%				121 (101,141)	10 (3,17), 8.3%	10 (3,17), 8.3%			
	After	19350	76 (14,138),				920	7 (2,12),	8 (4,12),	20 (20,20)	0 (0,0),	0 (0,0), 0%

		(15255,23445)	0.4%				(704,1136)	0.8%	0.9%		0%	
Risk groups												
Low	Before	38246 (27949,48543)	92 (81,103), 0.2%	4099 (3868,4330)	7 (4,10), 0.2%	71 (36,106), 1.7%	1265 (1184,1346)	10 (5,15), 0.8%	14 (3,25), 1.1%	17 (14,20)	0 (0,0), 0%	0 (0,0), 0%
	After	28146 (27301,28991)	136 (4,268), 0.5%	2179 (2179,2179)	35 (35,35), 1.6%	58 (58,58), 2.7%	1080 (698,1462)	3 (2,4), 0.3%	5 (4,6), 0.5%	3 (0,6)	0 (0,0), 0%	0 (0,0), 0%
High	Before	41322 (37208,45436)	106 (64,148), 0.3%	16321 (15634,17008)	57 (26,88), 0.3%	248 (159,337), 1.5%	4685 (4468,4902)	44 (7,81), 0.9%	58 (3,113), 1.2%	77 (49,105)	1 (1,1), 1.3%	6 (4,8), 7.8%
	After	60140 (59484,60796)	377 (6,748), 0.6%	8442 (8442,8442)	73 (73,73), 0.9%	194 (194,194), 2.3%	4130 (2933,5327)	18 (5,31), 0.4%	22 (7,37), 0.5%	24 (16,32)	1 (+/- NA), 4.2%	3 (+/- NA), 12.5%

Differences pre- and post-COVID-19

We first analysed possible differences triggered by the COVID-19 pandemic using the following approach: we computed the difference of the incidence of admissions before and after the pandemic, normalising by the incidence before the pandemic (Figure A4). The seasons pre-COVID were defined as all seasons without any COVID-19 circulation (until 2018/19) and seasons post-COVID were considered those from 2021/22 onwards. We considered 2019/2020 and 2020/2021 as outliers due to the strong COVID-19 circulation and the country-specific non-pharmaceutical interventions implemented to mitigate COVID-19's impact. Hence, we considered these seasons to not be representative of the post-COVID era. A qualitative difference could be observed across all age groups in the RSV-coded hospitalisations, with the strongest change observed in the 5-17year age group both in RSV-coded hospitalisations as well as RSV-confirmed hospitalisations.



FigureA4. Change of incidence of admissions before and after COVID-19 for patients aged 5 years of age and older, stratified by category of hospitalisations (vertical subpanels, from left to right, RTI-coded, RSV-coded, and RSV-laboratory confirmed), coloured by country and shaped by severity of the hospital stay (hospitalisation only in general ward, including an ICU stay or leading to deaths). The metric is the ChangeProxy defined in section 3.5.

Kruskal-Wallis test considering all the age groups together and looking for differences between countries shows significant differences, for all the hospitalisation categories (RTI, RSV-coded or RSV-confirmed) and severities (hospital admissions or deaths), except for RSV-confirmed deaths, in opposite to children where no difference was observed.

When considering the incidences directly and taking all countries together, we observe significant changes only in the 5-17-year age group for RSV-coded hospital admissions with a p-value <0.01 and in the 5-17-year age group for RSV-confirmed hospital admissions with a p-value <0.05.

Discussion

Here we have further explored the use of routinely collected healthcare data in 5 European countries, and the use of a hospital-based surveillance network to study RSV-associated hospitalisations. Despite the heterogeneity of data sources, we find similar age admission patterns in all countries, with the highest incidence observed in adults ≥ 85 years of age (Supplementary Figure SA2). COVID-19 caused an overall decrease of RSV-associated hospitalisations in all countries, but rates are returning to pre-COVID-19 levels, with a similar slope in most countries (except in Spain-Valencia).

In pre-COVID-19 seasons (2016/17 - 2018/19) the average annual number of RSV-related (coded or confirmed) admissions compared to RTI admissions ranged from 0.5% to 2.2% in adults 5-17 years of age, from 0.4 - 4.0%, in adults 18-64 years of age ranged from 0.2 - 4.0%, in adults 65-74 years from 0.5 - 4.7%, in adults 75-84 years from 0.4 to 7.5% and in adults ≥ 85 from 0.3 - 6.6%. In post-COVID-19 seasons (2021/22 - 2022/23) the average annual number of RSV-related (coded or confirmed) admissions compared to RTI admissions ranged from 1.6 to 5.2% in adults 5-17 years of age, from 0.6 - 2.5%, in adults 18-64 years of age ranged from 0.2 - 4.0%, in adults 65-74 years from 0.8 - 1.9%, in adults 75-84 years from 0.7 to 5.4% and in adults ≥ 85 from 0.7 - 4.6%. During 2020/21 the average annual number of RSV-related (coded or confirmed) admissions compared to RTI admissions ranged from 0 to 1.2% across all age groups. The only age group with a significant increase of RSV-related admissions after COVID-19 is the 5-17-year age group.

These rates are informative for an overall picture of trends, but country-specific nuances were observed. Country differences could be attributed to differences in RSV circulation, coding/testing practices and/or healthcare utilisation patterns. Scotland and England had very similar RTI and RSV-coded admission patterns in the 5-17-year age group, but RTI admissions were notably lower in the Scottish data. RTI admissions were notably lower in Spain-Valencia as inclusion criteria in Spain-Valencia were restricted to patients meeting ILLI criteria and follow-up was done during the RSV circulation period only. Finland, England, Scotland, and the Netherlands showed similar RSV-coded admission trends which could reflect similarities in Nordic healthcare systems and coding practices. A higher incidence of RSV-confirmed admissions was observed in countries with robust access to laboratory data (Finland and Spain-Valencia; in the latter, PCR testing was systematically performed in all patients). Biennial peaks of RSV admissions were observed in Finland, Spain-Valencia, Scotland and in Denmark as previously described for Finland and Denmark [5].

Obtaining laboratory results is often difficult, and even when available, testing denominators are often not known. Consequently, evaluating RSV testing practices is challenging and RSV-coding practices become the best available proxy to estimate RSV burden. In countries with both types of data available, we estimated that, in adults, relying on RSV codes led to an underestimation between 100% and 5% of RSV admission rates. Despite the existing underestimation we observed similar patterns between RSV-coded admissions and RSV-confirmed admissions in Scotland, Finland, and Denmark across all age groups, suggesting that RSV-coded admissions could be used as an indicator of RSV epidemiology when laboratory data is not available or challenging to access. Relying on laboratory data also has its limitations. In older adults, variations in clinical specimen collection methods and diagnostic tests can lead to an underestimation of at least 2.2 times the real disease burden [61, 62]. In Spain-Valencia, the data collection method differed from the rest of the countries as it was based on an active surveillance network initially set up for influenza surveillance. Data in each season was adjusted to the RSV circulation period and the admission rates were shown per 100,000 adults during the RSV circulation period. Hence, estimates cannot

be directly compared to the rest of the countries, although similar trends were observed. In terms of RSV-confirmed cases, Finland and Spain-Valencia showed similarities in seasonality, rates and age distribution of RSV-confirmed cases despite being based on two different data collection methods. This demonstrates that despite its limitations the use of routinely collected national health data can give a good overview of RSV trends and epidemiology in older adults.

Additional material

Table SA1. Average number and proportion of all admissions of patients of 5 years of age or older. Shown are all RTI-admissions, RSV-coded admissions and RSV-confirmed admissions by age group, diagnosis group and risk groups stratified by before COVID-19 (2016/17 to 2018/19) and after COVID-19 (2021/22 to 2022/23). Shown is the average (\pm SD) of all admissions belonging to each category before and after COVID-19.

	COVI D-19	England		Netherlands		Denmark			Finland			Scotland			Spain-Valencia		
		RTI	RSV-coded	RTI	RSV-coded	RTI	RSV-coded	RSV-confirmed	RTI	RSV-coded	RSV-confirmed	RTI	RSV-coded	RSV-confirmed	RTI	RSV-coded	RSV-confirmed
5 - 17 years	Before	41111 (40289,41933)	185 (136,234), 0.5%	3169 (2327,4011)	24 (21,27), 0.8%	1434 (1187,1681)	2 (2,2), 0.1%	11 (6,16), 0.8%	1693 (1594,1792)	22 (3,41), 1.3%	37 (15,59), 2.2%	3718 (3656,3780)	33 (26,40), 0.9%	77 (57,97), 2.1%	57 (43,71)	0 (0,0), 0%	0 (-1,1), 0%
	After	44606 (37978,51234)	716 (524,908), 1.6%	NA	NA	1311 (+/- NA)	11 (+/- NA), 0.8%	33 (+/- NA), 2.5%	1638 (1352,1924)	41 (25,57), 2.5%	74 (42,106), 4.5%	3080 (2948,3212)	74 (67,81), 2.4%	132 (127,137), 4.3%	29 (18,40)	0 (-1,1), 0%	2 (1,3), 6.9%
18 - 64 years	Before	216660 (207718,225602)	898 (556,1240), 0.4%	26896 (20341,33451)	293 (250,336), 1.1%	11467 (10534,12400)	23 (16,30), 0.2%	63 (53,73), 0.5%	13155 (12521,13789)	154 (44,264), 1.2%	210 (54,366), 1.6%	17600 (17354,17846)	77 (69,85), 0.4%	140 (103,177), 0.8%	464 (351,577)	2 (0,4), 0.4%	19 (11,27), 4.1%
	After	271297 (245283,297311)	1552 (474,2630), 0.6%	NA	NA	8237 (+/- NA)	51 (+/- NA), 0.6%	108 (+/- NA), 1.3%	11576 (10608,12544)	154 (77,231), 1.3%	194 (91,297), 1.7%	11894 (8124,15664)	54 (21,87), 0.5%	82 (24,140), 0.7%	298 (231,365)	3 (0,6), 1%	8 (6,10), 2.7%
65 - 74 years	Before	121223 (119079,123367)	582 (392,772), 0.5%	28969 (22315,35623)	343 (282,404), 1.2%	10443 (9808,11078)	15 (6,24), 0.1%	64 (43,85), 0.6%	11583 (10883,12283)	168 (13,323), 1.5%	228 (22,434), 2%	10442 (9796,11088)	48 (38,58), 0.5%	94 (85,103), 0.9%	299 (223,375)	2 (0,4), 0.7%	14 (8,20), 4.7%
	After	131280 (128150,134410)	1038 (123,1953), 0.8%	NA	NA	7645 (+/- NA)	32 (+/- NA), 0.4%	84 (+/- NA), 1.1%	10410 (9312,11508)	176 (78,274), 1.7%	202 (82,322), 1.9%	7279 (5916,8642)	38 (1,75), 0.5%	56 (2,110), 0.8%	188 (165,211)	3 (0,6), 1.6%	6 (3,9), 3.2%
75 - 84 years	Before	172590	694	31120	338	12814	21 (11,31),	70 (44,96),	15609	235	310	14224	64 (59,69),	114	401	0 (0,0),	19

	re	(169289,175891)	(382,1006), 0.4%	(23038,39202)	(283,393), 1.1%	(12232,13396)	0.2%	0.5%	(14614,16604)	(7,463), 1.5%	(5,615), 2%	(12801,15647)	0.4%	(99,129), 0.8%	(327,475)	0%	(12,26), 4.7%
	After	193230 (179031,207429)	1406 (119,2693), 0.7%	NA	NA	11830 (+/- NA)	56 (+/- NA), 0.5%	129 (+/- NA), 1.1%	15102 (12262,17942)	198 (78,318), 1.3%	234 (89,379), 1.5%	10015 (8474,11556)	58 (-4,120), 0.6%	87 (4,170), 0.9%	182 (175,189)	2 (-2,6), 1.1%	3 (0,6), 1.6%
≥85 years	Before	172292 (165185,179399)	582 (337,827), 0.3%	19486 (14383,24589)	211 (169,253), 1.1%	9772 (9376,10168)	12 (5,19), 0.1%	53 (24,82), 0.5%	14384 (13279,15489)	242 (16,468), 1.7%	311 (14,608), 2.2%	12512 (11305,13719)	58 (53,63), 0.5%	92 (81,103), 0.7%	544 (452,636)	2 (1,3), 0.4%	41 (29,53), 7.5%
	After	178562 (166759,190365)	1246 (52,2440), 0.7%	NA	NA	8511 (+/- NA)	26 (+/- NA), 0.3%	79 (+/- NA), 0.9%	12718 (10508,14928)	184 (81,287), 1.4%	202 (71,333), 1.6%	8616 (7341,9891)	46 (-3,95), 0.5%	66 (-10,142), 0.8%	222 (216,228)	4 (-2,10), 1.8%	12 (2,22), 5.4%
Diagnosis groups																	
Bronchitis & Bronchiolitis	Before	9236 (9062,9410)	106 (85,127), 1.1%	3398 (2556,4240)	196 (162,230), 5.8%	462 (396,528)	20 (12,28), 4.3%	19 (13,25), 4.1%	4168 (3799,4537)	398 (103,693), 9.5%	418 (111,725), 10%	302 (286,318)	22 (20,24), 7.3%	17 (11,23), 5.6%	147 (113,181)	2 (1,3), 1.4%	20 (8,32), 13.6%
	After	6428 (5889,6967)	212 (133,291), 3.3%	NA	NA	352 (352,352)	58 (58,58), 16.5%	50 (50,50), 14.2%	1490 (1273,1707)	320 (196,444), 21.5%	315 (181,449), 21.1%	201 (168,234)	18 (12,24), 9%	16 (12,20), 8%	38 (26,50)	3 (3,3), 7.9%	6 (3,9), 15.8%
Unspecified LRTI	Before	185619 (183873,187365)	662 (431,893), 0.4%	2084 (1474,2694)	69 (46,92), 3.3%	520 (343,697)	2 (+/- NA), 0.4%	7 (4,10), 1.3%	1328 (1249,1407)	2 (-1,5), 0.2%	8 (4,12), 0.6%	21374 (20457,22291)	98 (78,118), 0.5%	194 (153,235), 0.9%	185 (56,314)	0 (0,0), 0%	22 (9,35), 11.9%
	After	131182 (122852,139512)	1238 (559,1917), 0.9%	NA	NA	304 (304,304)	NA	4 (4,4), 1.3%	640 (625,655)	0 (0,0), 0%	7 (6,8), 1.1%	12494 (10903,14085)	94 (52,136), 0.8%	156 (90,222), 1.2%	51 (45,57)	1 (+/- NA), 2%	2 (1,3), 3.9%
URTI	Before	73256 (73125,73387)	152 (93,211), 0.2%	13946 (10735,17157)	214 (177,251), 1.5%	2384 (2200,2568)	NA	7 (6,8), 0.3%	5846 (5699,5993)	5 (2,8), 0.1%	44 (16,72), 0.8%	6312 (6142,6482)	26 (23,29), 0.4%	54 (36,72), 0.9%	38 (15,61)	0 (0,0), 0%	9 (4,14), 23.7%
	After	59903 (49539,70267)	252 (160,344), 0.4%	NA	NA	2205 (2205,2205)	NA	19 (19,19), 0.9%	2706 (2428,2984)	5 (2,8), 0.2%	34 (19,49), 1.3%	4155 (3686,4624)	36 (29,43), 0.9%	62 (56,68), 1.5%	3 (1,5)	0 (0,0), 0%	1 (+/- NA), 33.3%
Pneumonia &	Before	446002 (440997,4510)	1250 (877,1623),	89215 (71026,107)	661 (610,712),	42187 (40199,441)	51 (29,73), 0.1%	226 (158,294),	56598 (53911,592)	428 (115,741),	683 (173,1193),	30508 (28907,321)	128 (125,131),	250 (243,257),	1001 (751,125)	7 (7,7), 0.7%	30 (22,38),

Influenza		07)	0.3%	404)	0.7%	75)		0.5%	85)	0.8%	1.2%	09)	0.4%	0.8%	1)		3%	
	After	340649 (304196,377102)	2186 (720,3652), 0.6%	NA		34307 (34307,34307)	116 (116,116), 0.3%	346 (346,346), 1%	30145 (29100,31190)	453 (270,636), 1.5%	587 (338,836), 1.9%	24022 (20092,27952)	123 (36,210), 0.5%	189 (61,317), 0.8%	647 (599,695)	11 (5,17), 1.7%	15 (10,20), 2.3%	
SARSCOV-2	Before	NA																
	After	171158 (146191,196125)	62 (16,108), 0%	NA		NA			20357 (18266,22448)	3 (2,4), 0%	22 (10,34), 0.1%	13589 (8567,18611)	9 (6,12), 0.1%	26 (18,34), 0.2%	183 (69,297)	1 (+/-NA), 0.5%	1 (+/-NA), 0.5%	
2+diagnosis	Before	9109 (8606,9612)	118 (106,130), 1.3%	997 (835,1159)	67 (61,73), 6.7%	NA			1636 (1505,1767)	139 (37,241), 8.5%	148 (39,257), 9%	NA			57 (27,87)	0 (0,0), 0%	6 (3,9), 10.5%	
	After	108105 (83858,132352)	459 (136,782), 0.4%	NA		NA			7684 (7368,8000)	126 (77,175), 1.6%	134 (79,189), 1.7%	NA			225 (93,357)	4 (4,4), 1.8%	3 (2,4), 1.3%	
Risk groups																		
Low	Before	422235 (361404,483066)	1453 (1126,1780), 0.3%	NA			11764 (11134,12394)	14 (9,19), 0.1%	63 (40,86), 0.5%	18469 (17243,19695)	212 (44,380), 1.1%	299 (63,535), 1.6%	NA			391 (326,456)	1 (+/-NA), 0.3%	14 (9,19), 3.6%
	After	363637 (357093,370181)	2248 (635,3861), 0.6%	NA			10851 (10851,10851)	42 (42,42), 0.4%	119 (119,119), 1.1%	16497 (15998,16996)	174 (115,233), 1.1%	242 (150,334), 1.5%	NA			262 (246,278)	7 (+/-NA), 2.7%	4 (0,8), 1.5%
High	Before	301640 (245240,358040)	1487 (675,2299), 0.5%	NA			34120 (32245,35995)	60 (37,83), 0.2%	198 (145,251), 0.6%	37954 (36388,39520)	608 (152,1064), 1.6%	797 (200,1394), 2.1%	NA			1572 (1231,1913)	5 (1,9), 0.3%	98 (64,132), 6.2%
	After	455338 (439048,471628)	3710 (657,6763), 0.8%	NA			26633 (26633,26633)	133 (133,133), 0.5%	313 (313,313), 1.2%	34948 (31373,38523)	578 (329,827), 1.7%	664 (361,967), 1.9%	NA			686 (681,691)	10 (-2,22), 1.5%	30 (8,52), 4.4%

Table SA2. RSV-coded admission rates and 95% CI per 100,000 person-years per age group, country and surveillance year.

Surveillance year	Age group	Denmark	Finland	Netherlands	Spain-Valencia	England	Scotland
2016/17	5-17y	0.2 [0-0.8]	1 [0.4-2]	0.9 [0.5-1.3]	0 [0-7.3]	NA	NA
2017/18	5-17y	0.2 [0-0.8]	5.5 [4-7.4]	1.1 [0.7-1.6]	0 [0-5.4]	1.8 [1.5-2.1]	3.7 [2.5-5.4]
2018/19	5-17y	0.2 [0-0.8]	1.9 [1.1-3.1]	0.9 [0.6-1.4]	0 [0-5.8]	2.6 [2.2-2.9]	5.1 [3.6-6.9]
2019/20	5-17y	0.6 [0.2-1.4]	6.3 [4.7-8.3]	1.3 [0.9-1.9]	0 [0-6.7]	3.9 [3.5-4.3]	4.4 [3-6.1]
2020/21	5-17y	NA	0.3 [0-0.9]	0.6 [0.3-1]	NA	0.3 [0.2-0.4]	0.3 [0-0.9]
2021/22	5-17y	1.3 [0.7-2.3]	3.8 [2.6-5.4]	NA	0 [0-5.1]	6.7 [6.1-7.2]	9 [7-11.3]
2022/23	5-17y	NA	6.6 [4.9-8.7]	NA	1.8 [0-9.8]	9.8 [9.1-10.5]	10.3 [8.1-12.8]
2016/17	18-64y	0.4 [0.2-0.7]	2.2 [1.7-2.7]	3.2 [2.9-3.6]	0.4 [0-2.3]	NA	NA
2017/18	18-64y	0.7 [0.5-1.1]	8.5 [7.5-9.6]	2.7 [2.4-3.1]	0.3 [0-1.7]	1.9 [1.8-2.1]	2.1 [1.6-2.6]
2018/19	18-64y	0.8 [0.5-1.1]	3.4 [2.8-4.1]	2.4 [2.1-2.7]	1.3 [0.4-3.4]	3.4 [3.2-3.6]	2.5 [2-3]
2019/20	18-64y	0.9 [0.6-1.2]	7.9 [6.9-8.9]	2.4 [2.1-2.7]	0.8 [0.1-2.8]	4.9 [4.6-5.1]	2.7 [2.2-3.4]
2020/21	18-64y	NA	0.1 [0-0.3]	0.1 [0-0.1]	NA	0.1 [0.1-0.2]	0.1 [0-0.2]
2021/22	18-64y	1.4 [1.1-1.9]	3.1 [2.5-3.8]	NA	0.3 [0-1.6]	2.3 [2.1-2.5]	0.9 [0.6-1.3]
2022/23	18-64y	NA	6.4 [5.6-7.4]		1.8 [0.6-4.2]	6.7 [6.5-7]	2.3 [1.8-2.8]
2016/17	18-49y	NA	NA	NA	NA	NA	NA
2017/18	18-49y						1.1 [0.7-1.7]
2018/19	18-49y						1.5 [1-2.1]
2019/20	18-49y						1.6 [1.2-2.3]
2020/21	18-49y						0.1 [0-0.3]

2021/22	18-49y						0.4 [0.2-0.8]
2022/23	18-49y						1.3 [0.8-1.8]
2016/17	50-64y	NA	NA	NA	1.3 [0-7.5]	NA	NA
2017/18	50-64y				0 [0-3.6]		4 [2.9-5.4]
2018/19	50-64y				4.1 [1.1-10.6]		4.3 [3.2-5.7]
2019/20	50-64y				1.2 [0-6.5]		4.9 [3.7-6.4]
2020/21	50-64y				NA		0.2 [0-0.6]
2021/22	50-64y				0.8 [0-4.6]		1.8 [1.1-2.8]
2022/23	50-64y				5.2 [1.7-12.1]		4.3 [3.1-5.6]
2016/17	65-74y				0.8 [0.3-1.8]		8.5 [6.4-11]
2017/18	65-74y	3.6 [2.3-5.3]	50.9 [45.7-56.6]	15.9 [14.1-17.8]	0 [0-7.4]	8.1 [7.4-8.9]	7.3 [5.2-9.9]
2018/19	65-74y	2.8 [1.6-4.4]	14.9 [12.1-18]	16.8 [15-18.8]	0 [0-7.9]	12.9 [12-13.9]	9.6 [7.3-12.5]
2019/20	65-74y	3.9 [2.5-5.7]	36.6 [32.3-41.4]	15.3 [13.6-17.2]	2.5 [0.1-13.8]	21.4 [20.3-22.7]	9.5 [7.2-12.4]
2020/21	65-74y	NA	0.3 [0-1]	0.1 [0-0.4]	NA	0.4 [0.2-0.6]	0.3 [0-1.2]
2021/22	65-74y	5.1 [3.5-7.2]	15.1 [12.3-18.2]	NA	0 [0-6.5]	7 [6.3-7.8]	1.8 [0.9-3.3]
2022/23	65-74y	NA	35.3 [31-40]	NA	11 [3.6-25.6]	30.3 [28.9-31.8]	10.7 [8.3-13.7]
2016/17	75-84y	3.3 [1.7-5.9]	19.6 [15.3-24.8]	41.2 [37.2-45.4]	4.3 [0.1-24.1]	NA	NA
2017/18	75-84y	8.6 [5.8-12.3]	139.2 [127.2-152]	31.5 [28.1-35.2]	9.5 [2-27.7]	14.9 [13.6-16.3]	18.7 [14.3-24]
2018/19	75-84y	6 [3.8-9.1]	38.4 [32.3-45.3]	29 [25.8-32.5]	10.2 [2.1-29.8]	28 [26.2-29.9]	20.5 [15.9-26]
2019/20	75-84y	7.2 [4.8-10.4]	94.2 [84.6-104.6]	26.7 [23.6-29.9]	7.7 [0.9-27.9]	43.3 [41.1-45.6]	19.2 [14.8-24.5]
2020/21	75-84y	NA	0.5 [0.1-1.8]	0.5 [0.1-1.1]	NA	0.5 [0.3-0.8]	0.6 [0.1-2.1]
2021/22	75-84y	12.9 [9.7-16.7]	27 [22.3-32.5]	NA	0 [0-10]	14.3 [13.1-15.6]	4 [2.2-6.8]
2022/23	75-84y	NA	63.8 [56.6-71.7]	NA	27 [11.6-53.1]	66.8 [64.1-69.6]	29.4 [24-35.7]
2016/17	85+y	5 [1.8-10.9]	54.6 [43.2-68.1]	62.9 [55.3-71.4]	0 [0-36.9]	NA	NA
2017/18	85+y	16.6 [10.1-	342.1 [312.7-373.4]	41.5 [35.4-48.3]	7.1 [0.2-39.3]	30.2 [27.3-33.3]	44.3 [33.3-57.8]

		25.6]					
2018/19	85+y	9 [4.5-16.2]	100.3 [84.8-117.8]	56.2 [49.1-64]	15 [1.8-54.1]	55.3 [51.4-59.4]	49.4 [37.8-63.5]
2019/20	85+y	12.1 [6.8-19.9]	255.6 [230.7-282.4]	55.2 [48.3-62.9]	0 [0-31]	84.5 [79.7-89.4]	62.9 [49.9-78.3]
2020/21	85+y	NA	0 [0-2.4]	0.5 [0.1-1.7]	NA	0.9 [0.4-1.5]	1.6 [0.2-5.6]
2021/22	85+y	19.9 [13-29.2]	70.4 [57.9-84.8]	NA	6.1 [0.2-33.8]	29.3 [26.5-32.3]	8.4 [4.2-15]
2022/23	85+y	NA	161.5 [142.4-182.5]	NA	53.3 [21.4-109.7]	152.3 [145.8-159]	61.7 [49-76.7]

Table SA3. RSV lab-confirmed admission rates and 95% CI per 100,000 persons-year per age group, country and surveillance year.

Surveillance year	Age group	Denmark	Finland	Spain-Valencia	Scotland
2016/17	5-17y	0.9 [0.4-1.8]	2.4 [1.5-3.8]	0 [0-7.3]	NA
2017/18	5-17y	1.9 [1.1-3]	7.9 [6-10.1]	0 [0-5.4]	8.4 [6.5-10.8]
2018/19	5-17y	0.9 [0.4-1.8]	3.8 [2.6-5.4]	1.6 [0-8.8]	12.1 [9.7-14.9]
2019/20	5-17y	1.4 [0.7-2.5]	9.1 [7.1-11.4]	0 [0-6.7]	12.8 [10.4-15.6]
2020/21	5-17y	NA	0.3 [0-0.9]	NA	0.3 [0-0.9]
2021/22	5-17y	3.9 [2.7-5.5]	6.4 [4.8-8.5]	2.8 [0.3-10.1]	16.6 [13.9-19.8]
2022/23	5-17y	NA	12.2 [9.9-14.9]	1.8 [0-9.8]	17.5 [14.7-20.8]
2016/17	18-64y	1.6 [1.2-2.1]	3.1 [2.6-3.8]	8 [4.8-12.5]	NA
2017/18	18-64y	2.1 [1.7-2.7]	11.9 [10.8-13.1]	3.4 [1.7-6.1]	3.3 [2.8-4]
2018/19	18-64y	1.7 [1.3-2.2]	4.2 [3.5-5]	8.7 [5.7-12.7]	4.9 [4.2-5.7]
2019/20	18-64y	2 [1.6-2.5]	9.2 [8.2-10.3]	4.6 [2.4-8.1]	5.7 [4.9-6.6]
2020/21	18-64y	0.1 [0-0.2]	0.1 [0-0.3]	NA	0.1 [0-0.2]
2021/22	18-64y	3.1 [2.5-3.7]	3.7 [3.1-4.5]	1.7 [0.6-3.8]	1.2 [0.9-1.6]
2022/23	18-64y	NA	8.2 [7.3-9.3]	3.3 [1.5-6.2]	3.6 [3-4.3]
2016/17	18-49y	NA	NA	NA	NA
2017/18	18-49y				1.7 [1.2-2.4]
2018/19	18-49y				2.8 [2.1-3.6]
2019/20	18-49y				3.4 [2.7-4.2]
2020/21	18-49y				0.1 [0-0.3]
2021/22	18-49y				0.6 [0.3-1]
2022/23	18-49y				2.2 [1.6-2.9]
2016/17	50-64y	NA	NA	20.2 [11.3-33.4]	NA

2017/18	50-64y			7.8 [3.4-15.3]	6.6 [5.2-8.3]
2018/19	50-64y			20.7 [12.7-32]	9.1 [7.5-11.1]
2019/20	50-64y			11.7 [5.6-21.6]	10.3 [8.5-12.3]
2020/21	50-64y			NA	0.2 [0-0.6]
2021/22	50-64y			3.3 [0.9-8.5]	2.4 [1.6-3.5]
2022/23	50-64y			8.3 [3.6-16.3]	6.4 [5-8.1]
2016/17	65-74y	6.8 [5-9.2]	13.1 [10.4-16.2]	64.6 [41-97]	NA
2017/18	65-74y	13.3 [10.6-16.4]	68.5 [62.4-75]	22 [11-39.3]	15.4 [12.3-19]
2018/19	65-74y	9.7 [7.5-12.4]	19.6 [16.5-23.2]	49.4 [31.3-74.1]	17.5 [14.2-21.3]
2019/20	65-74y	8.7 [6.6-11.3]	42.6 [37.9-47.7]	17.3 [7-35.7]	20.8 [17.2-24.8]
2020/21	65-74y	NA	0 [0-0.5]	NA	0.3 [0-1.2]
2021/22	65-74y	13.3 [10.6-16.5]	16.6 [13.8-19.9]	1.8 [0-9.8]	3 [1.8-4.8]
2022/23	65-74y	NA	41.2 [36.6-46.3]	11 [3.6-25.6]	16 [12.9-19.5]
2016/17	75-84y	13 [9.4-17.5]	25.5 [20.5-31.3]	160.4 [112.9-221]	NA
2017/18	75-84y	27.3 [22.1-33.4]	185 [171.2-199.7]	97.8 [66.5-138.8]	31.9 [26.1-38.6]
2018/19	75-84y	19.7 [15.4-24.8]	49.7 [42.7-57.5]	187.2 [141-243.7]	37.7 [31.4-44.9]
2019/20	75-84y	17.3 [13.4-21.9]	108.9 [98.6-120.1]	42.5 [21.2-76]	40.7 [34.2-48.1]
2020/21	75-84y	NA	0.5 [0.1-1.8]	NA	0.6 [0.1-2.1]
2021/22	75-84y	29.6 [24.7-35.2]	31.5 [26.4-37.4]	13.6 [4.4-31.6]	8.1 [5.4-11.7]
2022/23	75-84y	NA	76.3 [68.4-84.9]	64 [38.5-100]	42.1 [35.5-49.5]
2016/17	85+y	24.2 [16.2-34.8]	71.4 [58.2-86.7]	200.3 [122.3-309.3]	NA
2017/18	85+y	70.4 [56.2-87]	445.4 [411.8-481]	197.5 [131.2-285.4]	69.8 [55.7-86.3]
2018/19	85+y	36.2 [26.3-48.6]	122.6 [105.4-141.8]	381.7 [284.2-501.9]	81.1 [65.9-98.6]
2019/20	85+y	37.8 [27.8-50.3]	268.9 [243.3-296.3]	100.8 [52.1-176]	105.4 [88.3-124.9]
2020/21	85+y	NA	0 [0-2.4]	NA	1.6 [0.2-5.6]



2021/22	85+y	60.5 [47.9-75.4]	69.1 [56.8-83.4]	12.1 [1.5-43.8]	9.9 [5.3-16.9]
2022/23	85+y	NA	184.8 [164.3-207.1]	136.9 [81.2-216.4]	91.4 [75.8-109.3]

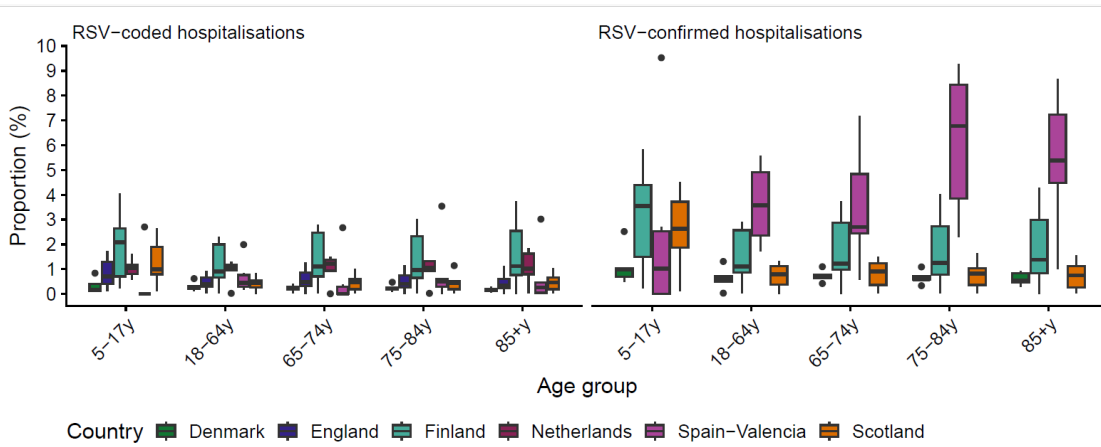


Figure SA1. Boxplot of the proportion of RSV-coded and RSV-confirmed hospitalisations over all RTI hospitalisations. The median and quartiles of the percentage of hospital admissions (y-axis) with an RSV code (first panel) or RSV-confirmed (second panel) from all RTI admissions over all seasons is shown per country (colours) and age group (x-axis).

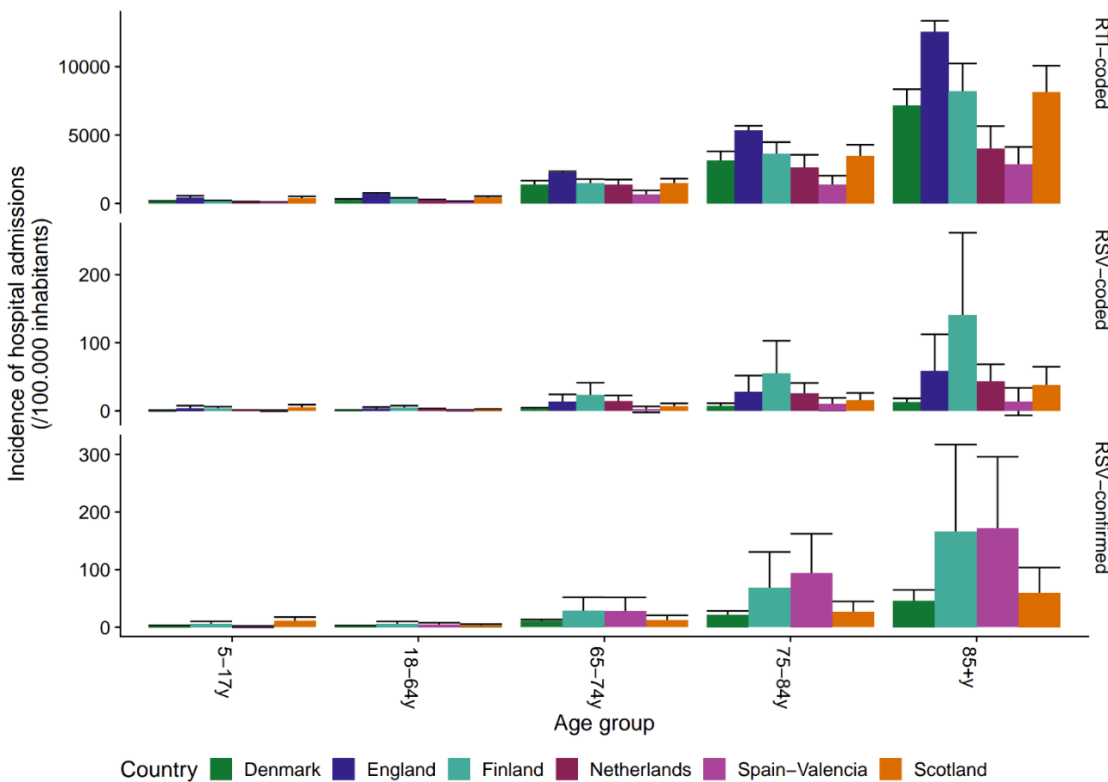


Figure SA2. Average incidence per 100,000 person-years. The average incidence per 100,000 inhabitants (y-axis) over all available surveillance years is shown per age group (x-axis) and country (colours) for each hospitalisation type. The error bars indicate the standard deviation.

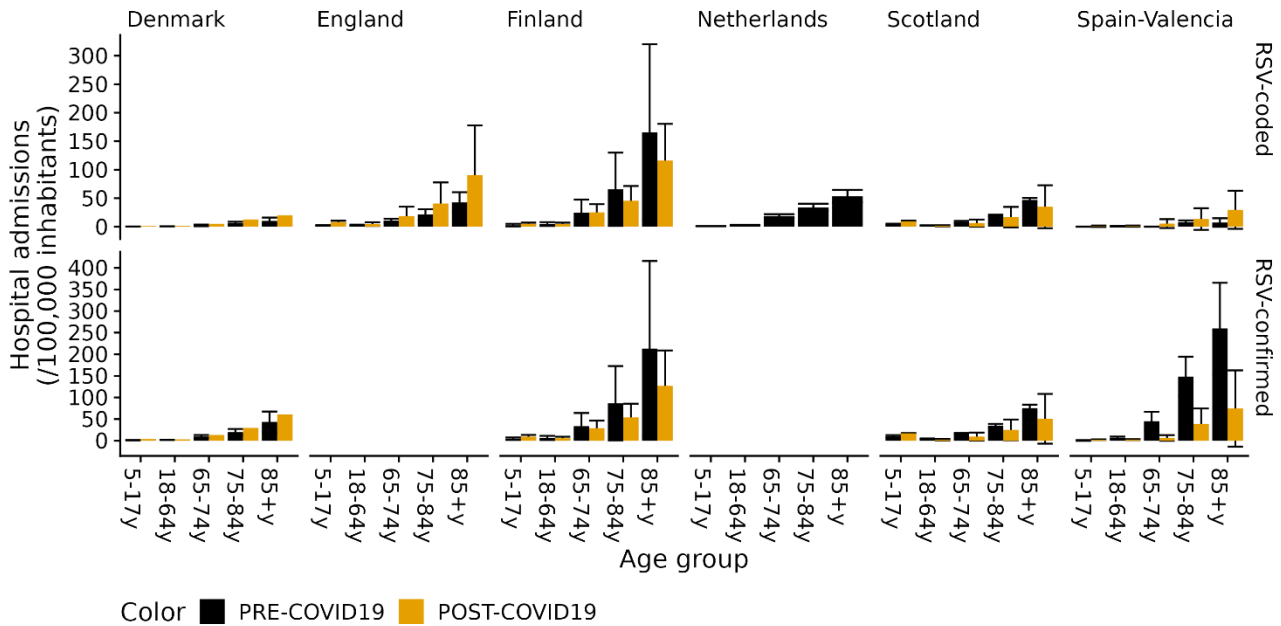


Figure SA3. Average incidence per 100,000 person-years during the pre-COVID-19 period (2016-2019, black bars) and during the post-COVID-19 period (2021-2023, yellow bars). The average incidence per 100,000 inhabitants (y-axis) stratified by after/during COVID-19 is shown per age group (x-axis) and country (subpanels) for RSV-coded and RSV-confirmed admissions. The error bars indicate the standard deviation. 2019/20 and 2020/21 data have not been included in this table to remove potential NPI effects introduced during the COVID-19 pandemic.

Data on additional age groups

In Finland, Scotland and Spain-Valencia additional age groups were available: 18-49 years (Finland and Scotland only) and 50-64 years. In Finland, the population data for these age groups was not available; hence, the incidence of admissions was not estimated.

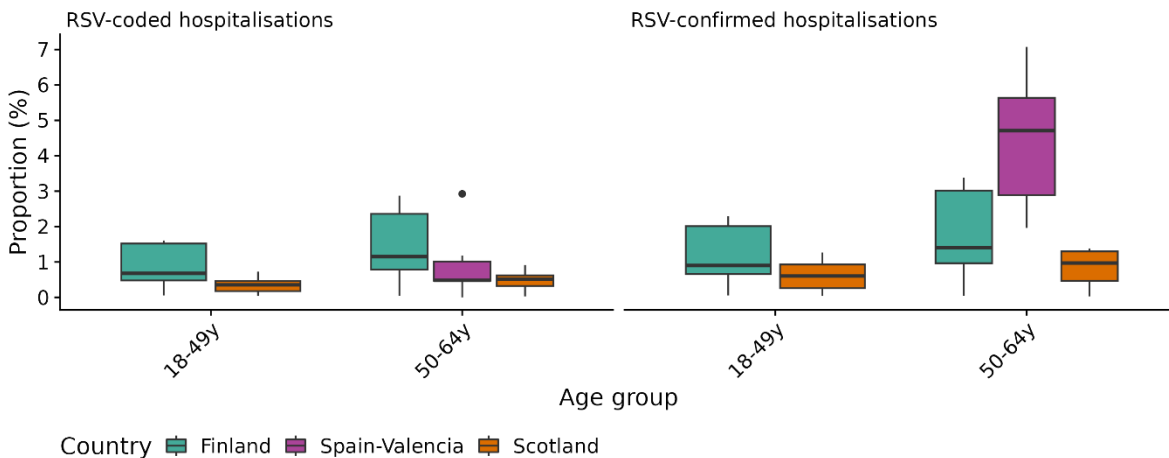


Figure SA4. Boxplot of the proportion of RSV-coded and RSV-confirmed hospitalisations. The median and quartiles of the percentage of hospital admissions (y-axis) with an RSV code (first panel) or RSV-confirmed (second panel) from all RTI admissions over all seasons is shown per country (colours) and age group (x-axis).

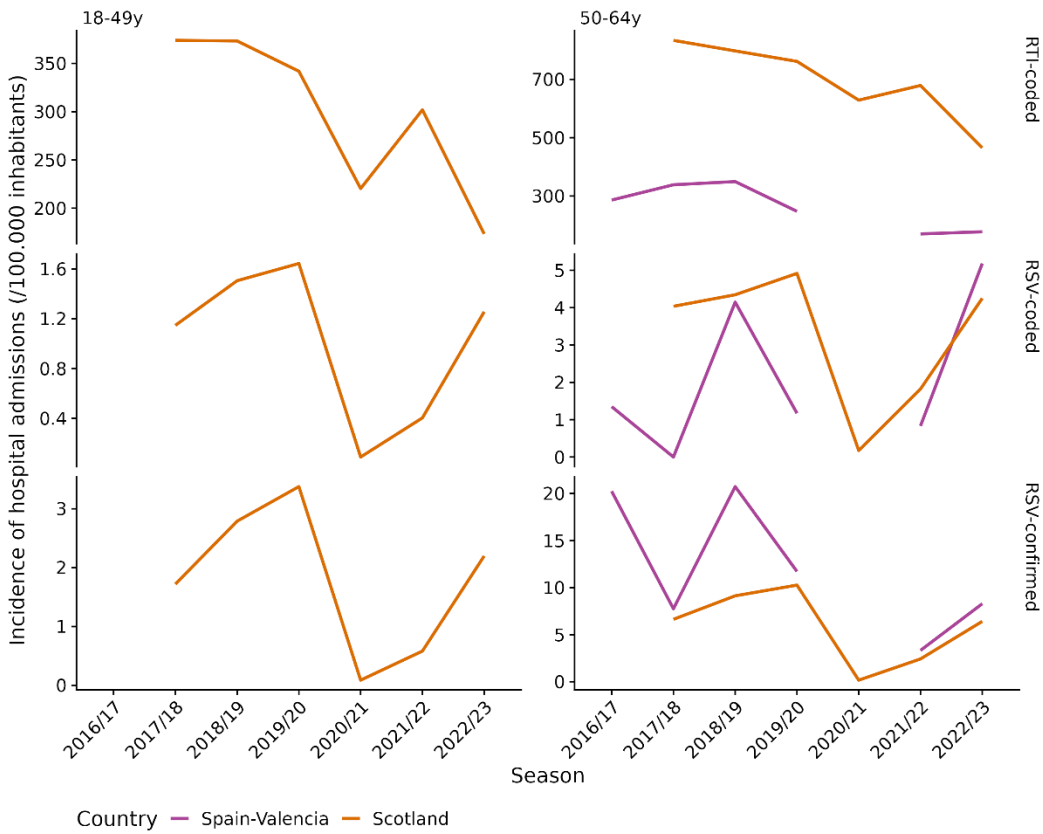


Figure SA5. Hospitalisation admission rates in patients 50-64 years of age and above. The incidence of hospital admissions per 100,000 adults (y-axis) per surveillance year (x-axis) is shown in Spain-Valencia (pink) and Scotland (orange) for each hospitalisation type: A) Incidence of all RTI admissions B) Incidence of all RSV-coded admissions and C) Incidence of laboratory-confirmed RSV admissions.

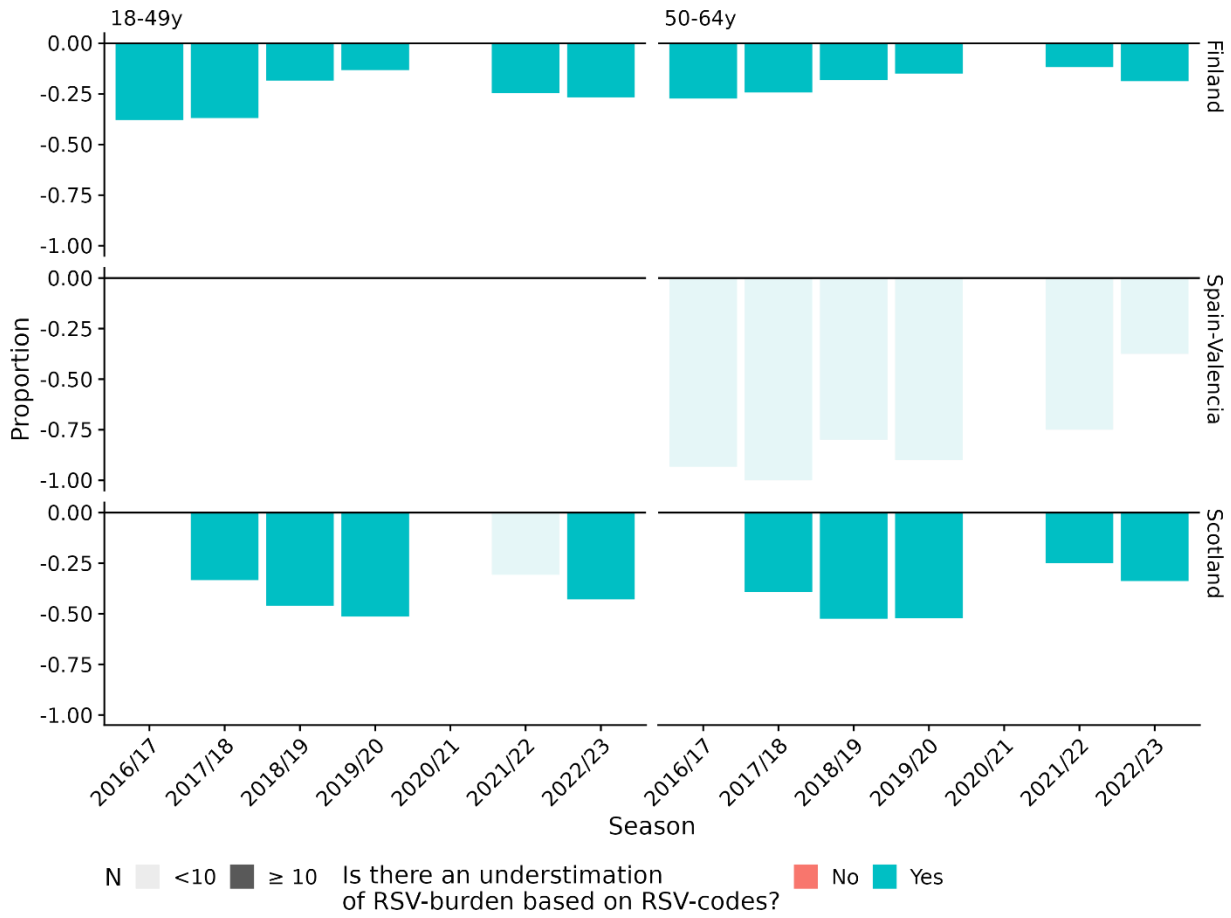


Figure SA6. Underestimation of RSV-burden when relying on RSV-coding practices in the 18-49-year and 50-64-year age groups. The proportion of hospitalisations underestimated when using RSV-coding as a reference compared to RSV-confirmed cases for estimating RSV-hospitalisation admissions is shown in the x-axis for countries with both types of data available (vertical sub-panels) and per age group (panels). Colours indicate if there is an underestimation (blue: yes, and red: no). Shades indicate the number of patients available for the estimation (<10 light shade and ≥10 dark shade).

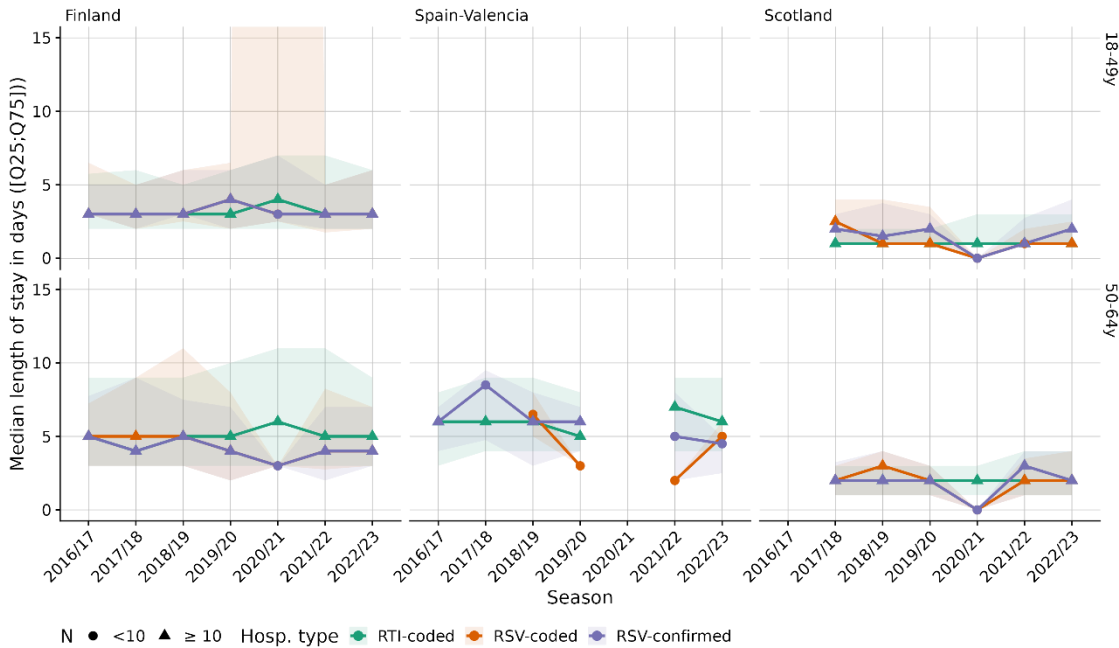


Figure 1SA7. Lengths of stay among patients 18-49 years and 50-64 years of age. Median LOS (y-axis) and 25/75 quartiles (shadow area) of all hospital admissions per country, age group and surveillance year (x-axis). Each hospitalisation type is shown with a different colour (green: RTI admissions, orange: RSV-coded and violet: RSV-confirmed admissions). If the estimate is based on fewer than 10 patients the shape is represented as a dot, whereas if the estimate is based on more than 10 patients the shape is represented as a triangle.

Table SA4. Average number and proportion of all admissions of patients 18-49 years and 50-64 years. Shown are all RTI-admissions, RSV-coded admissions and RSV-confirmed admissions by age group, diagnosis group and risk groups stratified by before COVID-19 (2016/17 to 2018/19) and after COVID-19 (2021/22 to 2022/23). Shown is the average (± SD) of all admissions belonging to each category before and after COVID-19.

Age group	COVID-19	Finland			Scotland			Spain-Valencia		
		RTI	RSV-coded	RSV-confirmed	RTI	RSV-coded	RSV-confirmed	RTI	RSV-coded	RSV-confirmed
18 - 49 years	Before	5700 (5390,6010)	45 (13,77), 0.8%	68 (15,121), 1.2%	8454 (8421,8487)	30 (24,36), 0.4%	51 (34,68), 0.6%	NA		
	After	5268 (4383,6153)	57 (33,81), 1.1%	77 (43,111), 1.5%	5298 (3271,7325)	18 (5,31), 0.3%	31 (6,56), 0.6%			
50 - 64 years	Before	7455 (7099,7811)	108 (30,186), 1.4%	141 (38,244), 1.9%	9146 (8932,9360)	47 (44,50), 0.5%	88 (67,109), 1%	299 (223,375)	2 (0,4), 0.7%	14 (8,20), 4.7%
	After	6308 (6225,6391)	98 (45,151), 1.6%	117 (48,186), 1.9%	6596 (4853,8339)	35 (15,55), 0.5%	51 (18,84), 0.8%	188 (165,211)	3 (0,6), 1.6%	6 (3,9), 3.2%

Table SA5. Average number and proportion of deaths of patients 18-49 years and 50-64 years. Shown are all RTI-admissions, RSV-coded admissions and RSV-confirmed admissions that ended in death by age group, diagnosis group and risk group stratified by before COVID-19 (2016/17 to 2018/19) and after COVID-19 (2021/22 to 2022/23). Shown is the average (\pm SD) of all admissions belonging to each category before and after COVID-19.

		Finland			Spain-Valencia		
Age group	COVID-19	RTI admissions	RSV-coded	RSV-confirmed	RTI admissions	RSV-coded	RSV-confirmed
18 - 49 years	Before	69 (61,77)	1 (0,2), 1.4%	1 (0,2), 1.4%	NA		
	After	72 (44,100)	0 (0,0), 0%	1 (0,2), 1.4%			
50 - 64 years	Before	481 (456,506)	4 (1,7), 0.8%	5 (1,9), 1%	5 (3,7)	0 (0,0), 0%	0 (0,0), 0%
	After	402 (175,629)	1 (0,2), 0.2%	2 (2,2), 0.5%	2 (2,2)	0 (0,0), 0%	0 (0,0), 0%

4.3 Supplementary material on the whole population

In Supplementary Figures S1 – S6, the percentage of admissions corresponding to a given diagnosis group is shown for each country, all age groups (children and adults), hospitalisation types and surveillance year. A variability in diagnosis groups per age group, hospitalisation type and across countries can be observed. We observed a high proportion of bronchitis & bronchiolitis diagnoses in RTI admissions in children under 5 years of age in all countries; however, with increasing age pneumonia & influenza were the most common diagnosis group (in Scotland and England a high proportion of RTI admissions in older adults were classified as unspecified LRTI as well). This pattern is slightly different in RSV-coded/RSV-confirmed admissions, where a higher proportion of admissions were classified as bronchitis & bronchiolitis in all age groups. However, pneumonia & influenza was still the most common diagnosis group in older adults in most countries.

We observed that the proportion of pneumonia & influenza diagnoses, as well as bronchitis & bronchiolitis diagnoses, consistently increased with age for RSV-confirmed and RSV-coded hospital admissions across all countries. The following age groups had a consistent diagnosis presence for bronchitis & bronchiolitis which represented $88\pm 12\%$ of diagnoses for 0-2m, 3-5m and 6-11m, $63\pm 15\%$ for 1-2y, $50\pm 19\%$ for 3-4y and $25\pm 22\%$ for 5+y. Differences were the Netherlands where 1-2y were closer to those below 1 year than in other countries ($76\pm 5\%$), England for 3-4 years that were closer to ≥ 5 years than in other countries ($18\pm 3\%$) and Spain-Valencia where ≥ 85 years presented a high percentage of such diagnoses for RSV-confirmed hospital admissions ($44\pm 31\%$).

We observed a difference in terms of diagnosis between RSV-coded and RSV-confirmed admissions for URTI diagnosis. In Denmark, URTI diagnosis was more present when hospital admissions were RSV-confirmed ($13\pm 8\%$) compared to RSV-coded ($2\pm 3\%$). The observed trend was similar in Spain-Valencia ($39\pm 53\%$ vs $13\pm 10\%$) and in Finland – but less marked where URTI diagnosis represented $6\pm 7\%$ of all diagnoses for RSV-confirmed hospital admissions vs $2\pm 3\%$ of all diagnoses for RSV-coded admissions; this second figure is mostly due to the 5-17-year age group where 13% of RSV-coded diagnoses were URTI diagnoses on average over seasons vs 1% in other age groups. Differently, URTI diagnoses were present in England and in the Netherlands among RSV-coded hospital admissions, but there were no RSV-confirmed cases to compare. URTI diagnoses were also similar for RSV-coded and RSV-confirmed admissions in Spain-Valencia ($11\pm 11\%$ vs $14\pm 15\%$, respectively). Regarding the impact of COVID-19, some differences of diagnosis classifications were observed during 2020/21 but in the following year(s) pre-COVID

patterns of diagnosis returned. Any relevant change in diagnosis group classification will need to be assessed with more data post-COVID.

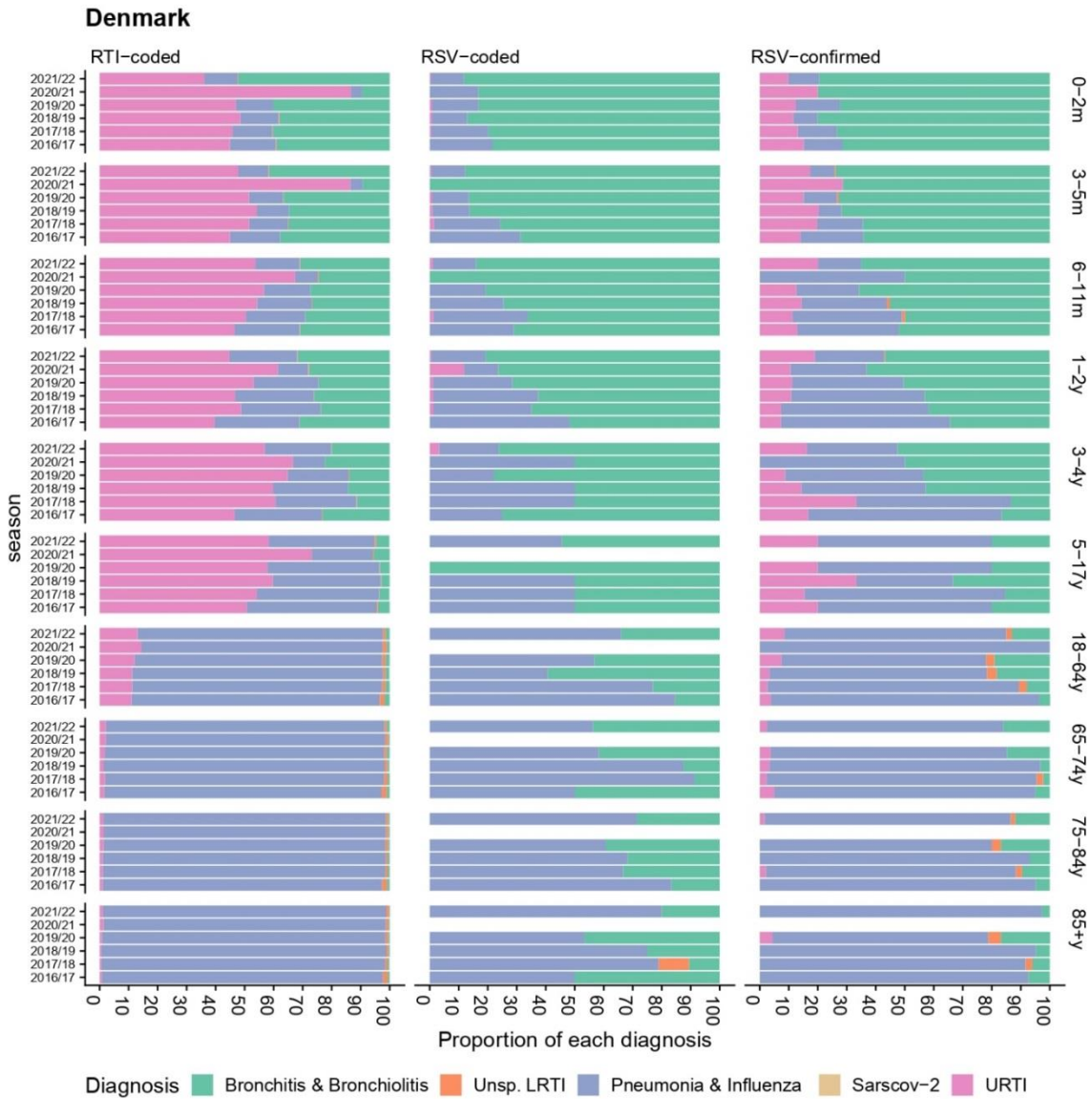


Figure S1. Percentage of each diagnosis group in Denmark per hospitalisation type and age group.

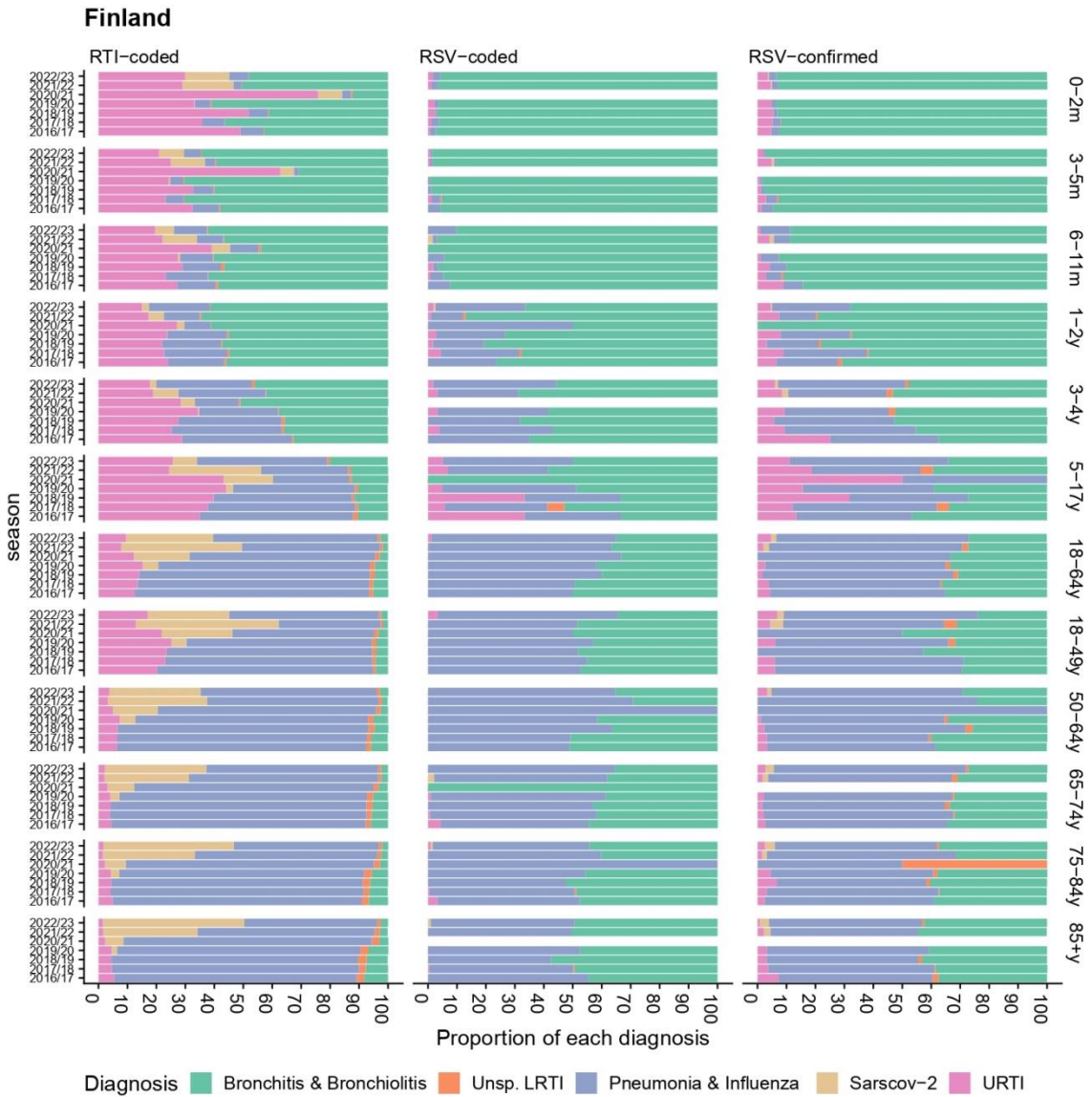


Figure S2. Percentage of each diagnosis group in Finland per hospitalisation type and age group.



Figure S3. Percentage of each diagnosis group in Netherlands per hospitalisation type and age group.

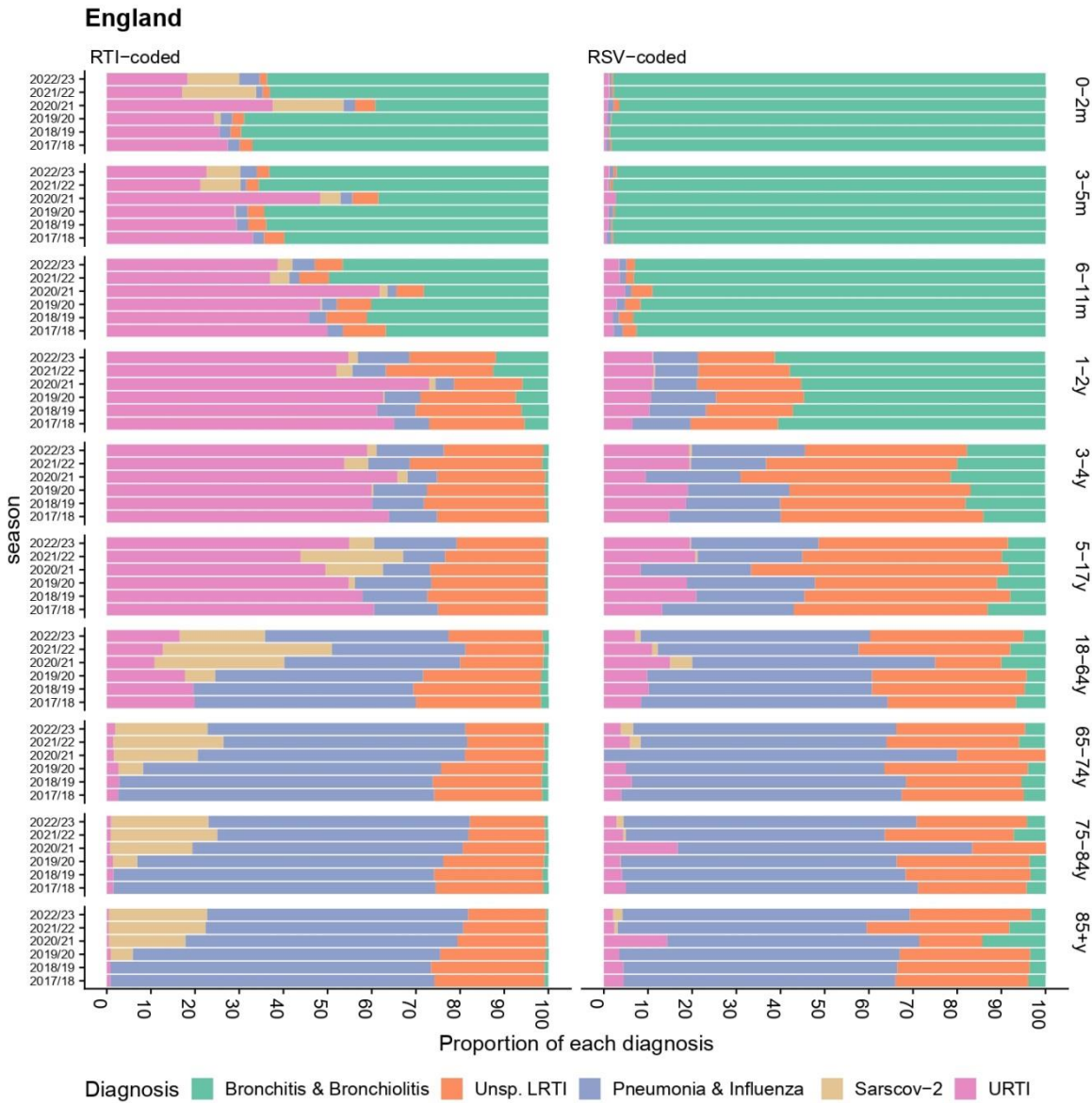


Figure S4. Percentage of each diagnosis group in England per hospitalisation type and age group.

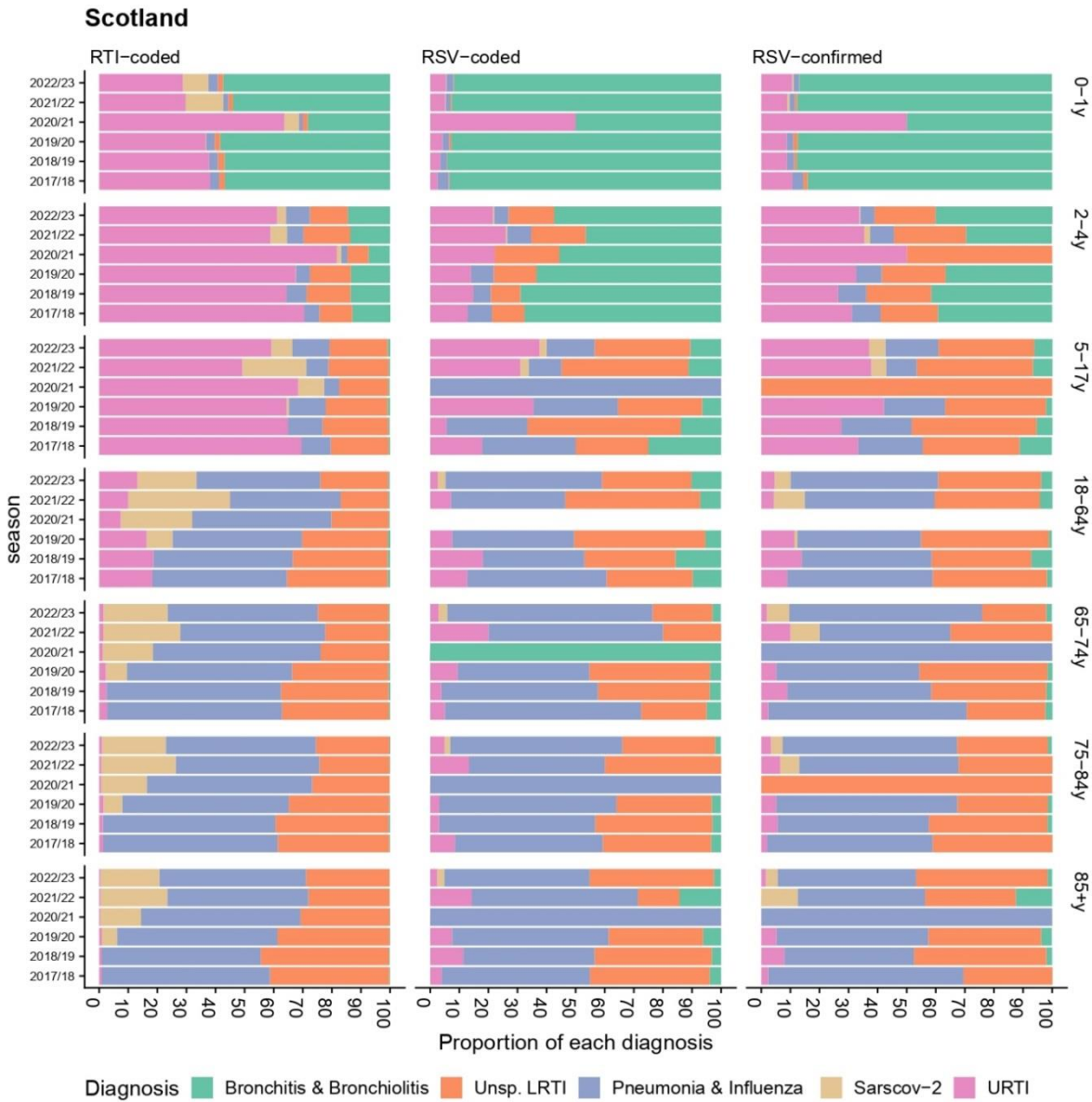


Figure S5. Percentage of each diagnosis group in Scotland per hospitalisation type and age group.

Spain-Valencia

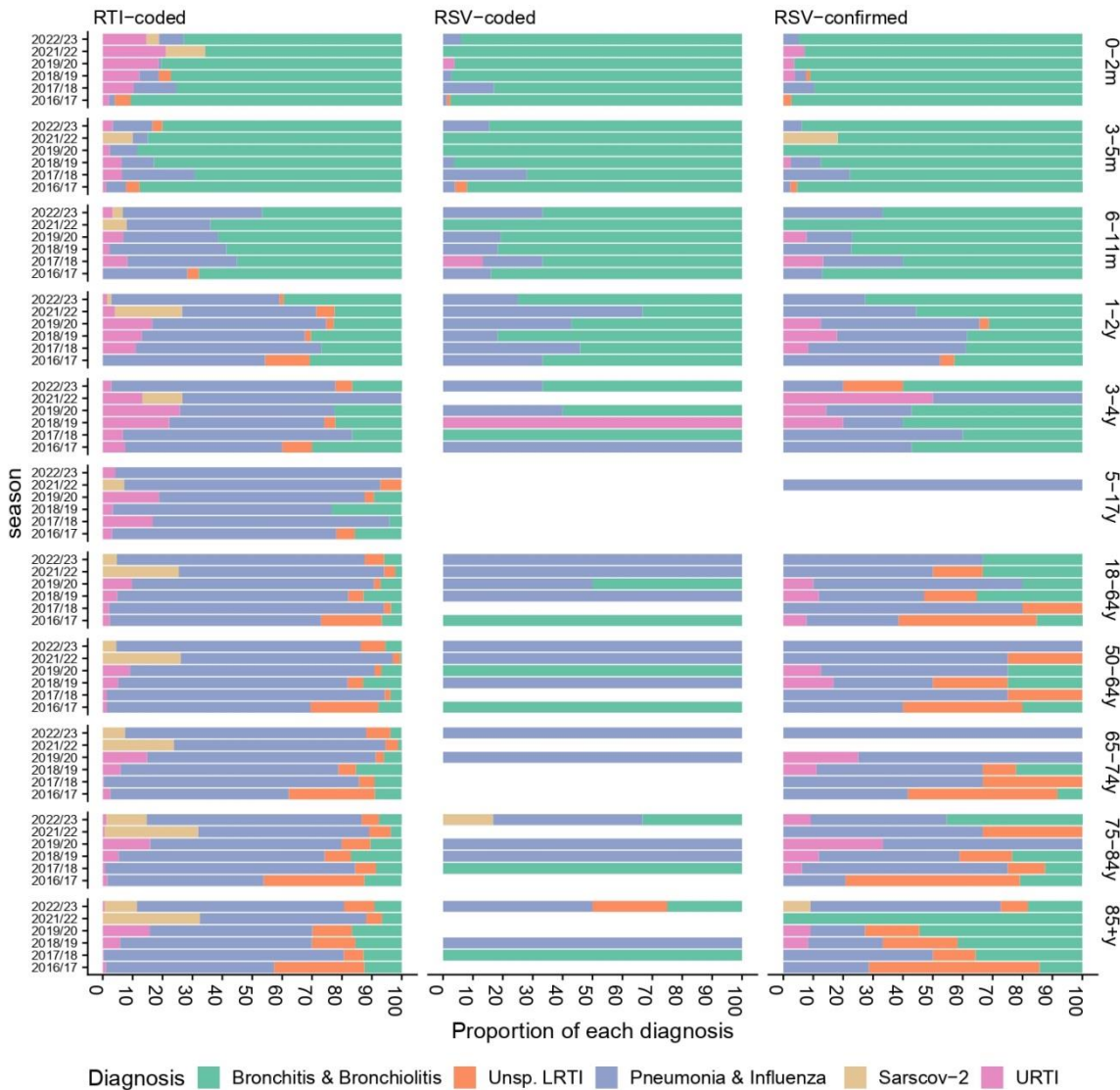


Figure S6. Percentage of each diagnosis group in Spain-Valencia per hospitalisation type and age group.

Supplementary Figure S7 shows the proportion of high- and low-risk patients (as defined in section 3.9) per age group, country, hospitalisation type and surveillance year. We observed a similar prevalence of high-risk patients in RSV-confirmed hospital admissions and in RSV-coded hospital admissions, respectively; $28 \pm 19\%$ vs $29 \pm 22\%$ for <1 year of age, $16 \pm 9\%$ vs $22 \pm 11\%$ for 1-4 years of age and $78 \pm 9\%$ vs $73 \pm 16\%$ for patients ≥ 5 years old. We then observed a strong heterogeneity between age groups, with patients ≥ 5 years old being hospitalised more frequently when being at high risk, except in England (54%).

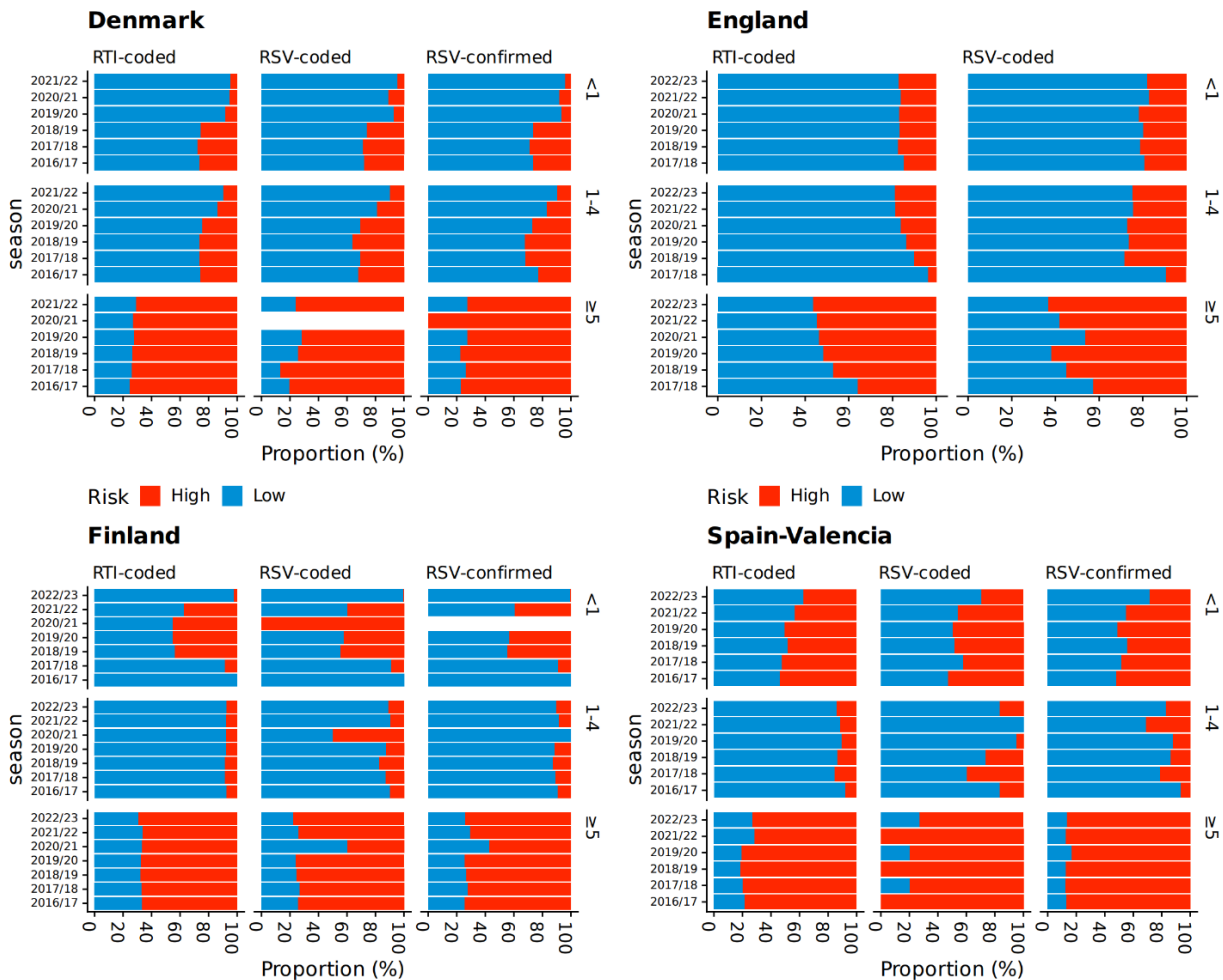


Figure S7. Proportion (%) of low and high-risk patients in each country, hospitalisation type and surveillance year. The proportion (x-axis) of low- and high-risk patients (red: high and blue: low) is shown per hospitalisation type (panels), age category (vertical panels) and surveillance year (y-axis).



Task1.2_data_collecti
on_template.xlsx

Document 1 – Template used to harmonise data collection and be able to leverage common script to analyse the data. A double left-click on it will open it.

5. General conclusions

This report demonstrates that by utilising routinely collected healthcare data and a standardised methodology for data collection, we can estimate and compare hospital admissions related to RSV in both children (section 4.1) and adults (section 4.2) across various European countries. Incorporating national-level data offers the advantage of facilitating informed regulatory decisions regarding RSV immunisation strategies and the possibility to monitor the impact of the newly authorised RSV vaccines on reducing RSV-associated hospitalisations in the coming years. However, a limitation of this study is the existence of poor coding practices, and coding biases depending on the age, as well as a limited understanding of RSV testing practices/coverage in many countries and hospital settings, which makes the data hard to interpret for research purposes.

Nonetheless, we observed consistent patterns and seasonal variations across all countries, underscoring that these data are suitable for providing insights of RSV epidemiology at the European level.

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Contributions:

Ombeline Jollivet: Paediatric burden

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Both contributed equally to the analysis and delivery of the report.

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