



EUROPE



The burden of respiratory syncytial virus

Understanding impacts on the NHS, society and economy

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Preface

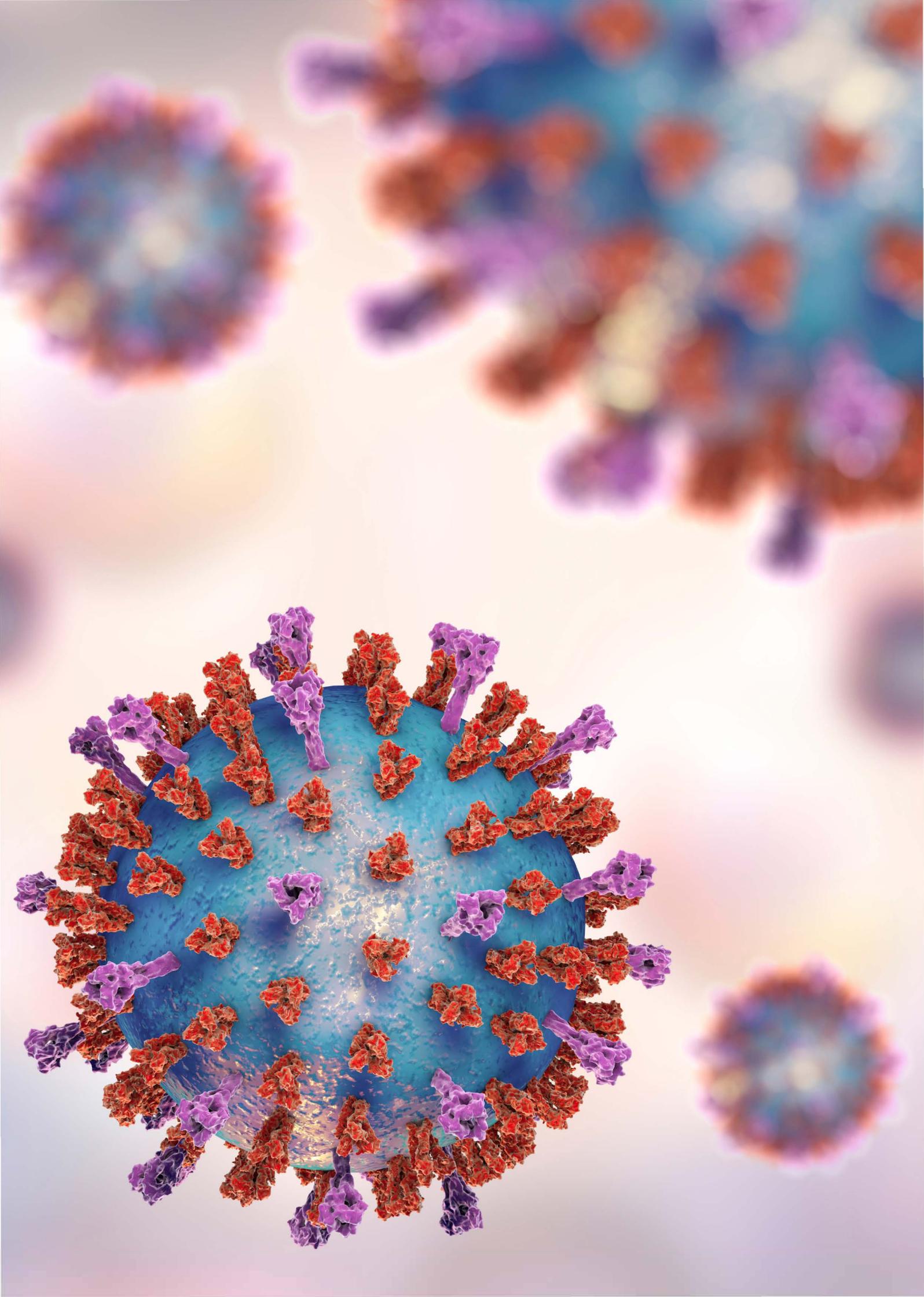
This report presents an assessment of the societal burden imposed by respiratory syncytial virus (RSV) in the United Kingdom (UK) by researchers from RAND Europe and the University of Cambridge (collaborators in the Cambridge Centre for Health Services Research). The report can be read on a standalone basis but is supported by detailed Annexes published in a separate document.

RSV is a common respiratory virus affecting large numbers, mainly children, every year. The burden of RSV has many dimensions, including ill-health for children with the virus (potentially leading to hospitalisation, intensive care and even death in severe cases), the emotional and practical burden on affected families and carers and its impact on economic productivity, and the costs of providing healthcare.

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assurance standards. This work is intended to inform the public good and should not be taken as a commercial endorsement of any product or service. RAND Europe is a not-for-profit policy research organisation that helps to improve policy and decision making through research and analysis. The University of Cambridge Primary Care Unit delivers research and education to reduce the burden of ill health. RAND Europe and the University of Cambridge have a long-standing collaboration through the Cambridge Centre for Health Services Research, which aims to inform health policy and practice by developing methods for measuring the quality of care and evaluating ways to improve its safety, effectiveness, efficiency and experience. For further information about this research, please contact:

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Summary

This study describes and quantifies where possible, the UK burden of Respiratory Syncytial Virus (RSV) in children aged up to five, their families and carers, and the healthcare system and economy. RSV is a common virus prevalent among infants and young children that causes acute lower respiratory tract infections such as pneumonia and bronchiolitis.

The evidence presented here is from a recent literature review (29 papers) and published data relevant to the UK. Both sources informed our economic model, which estimates the costs to the National Health Service (NHS) and the wider costs in terms of productivity losses of parents/carers. Costs are expressed in 2020/21-financial-year price terms and estimated from UK data for 2019 (the last pre-COVID-19 pandemic year) that approximated £80 million in annual healthcare costs and productivity losses to the economy from RSV in children younger than five. This figure is equivalent to a mean total cost per child below five presenting to the NHS with RSV of £97. Just over £14 million of the £80 million annual cost is due to productivity losses, about £1.5 million to out-of-pocket costs incurred by parents/carers, and the remaining nearly £65 million to healthcare costs. The estimated costs are the consequence, in part, of an estimated 467,230 General Practice (GP) visits and 33,937 hospitalisations per year in the UK for children aged under five with RSV.

In 2019 we estimate
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and productivity losses to
the economy from RSV in
children younger than five

Based on our modelling, the number of deaths of children aged up to five attributable to RSV is relatively small but still amounts to an estimated 33 per year in the UK. Although the healthcare consequences of RSV are short-term for the majority of cases, there are long term sequelae for some, including poorer respiratory health in later life.

Infants aged 0–6 months represent about 10% of the total population of children under five yet account for 33% of the total annual cost estimate. Children in the first six months of their lives are responsible for nearly half of the hospitalisation costs (including outpatient costs) of RSV cases in children under five in the UK, including outpatient costs. We estimate that children aged 0–12 months incur 49% of the total annual cost of RSV in children under five. We conclude that RSV has a much larger burden on infants during their first year of life than any subsequent age.

Our modelling also illustrates that although babies born prematurely account for 19% of the total RSV cost burden, the RSV cost burden of babies born at term totals more than four times as much (though the cost per child is much less). When considering the cost burden of RSV, it would be a mistake to focus primarily on pre-term infants.

This report also presents additional material on the burden of RSV in children under five identified in the literature review concerning the health impacts on affected children and the nature of parental and familial burden of caring for a young child with RSV.

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Abbreviations

Can\$	Canadian Dollar
GBP	British Pound
GP	General Practice
ICU	Intensive Care Unit
NHS	National Health Service
QALY	Quality-adjusted life years
REA	Rapid Evidence Assessment
RSV	Respiratory Syncytial Virus
UK	United Kingdom
US	United States

1 Study context and aims

This study describes and quantifies the burden of Respiratory Syncytial Virus (RSV) in the United Kingdom (UK) in children aged up to five, their families and carers, and the healthcare system and economy. The evidence presented derives from a literature review, published data and our economic model of costs to the National Health Service (NHS) and lost parent/carer productivity.

RSV is a common virus that causes acute lower respiratory tract infections such as pneumonia and bronchiolitis [1]. It is recognised as one of the most common causes of acute respiratory tract infections in children under five years [2]. Symptoms usually involve fever, nasal congestion, runny nose and wheezing [3]. Certain high-risk groups are more prone to severe disease with higher morbidity and mortality rates, such as premature infants and infants with an underlying medical condition [4, 5]. However, otherwise-healthy infants constitute a significant proportion of hospitalised patients, not only at-risk infants [6].

While RSV is usually a short-term infection that fully resolves, health impacts may sometimes persist in the long-term (potentially for decades), manifesting as conditions such as asthma and wheezing [7, 8]. The quality of life for children with RSV and their parents and other carers can be affected by their symptoms, disruptions associated with hospitalisation and treatment, and the

emotional strain of having a sick child [9]. There are evidence gaps regarding the economic impacts of RSV on parents/carers due to labour-productivity losses (days lost from work and reduced productivity while at work) and out-of-pocket expenses incurred by the family/carers of a child with RSV in the UK. As well as the health and social burden of RSV for patients and their families, the medical support children with RSV require (whether hospitalised or not) has substantial cost implications for the healthcare system. These include costs associated with using NHS 111 (the NHS urgent telephone and online advice service), primary care visits, hospitalisation costs (e.g. bed days, medical intervention/treatment and Intensive Care Unit [ICU] admission) and associated outpatient attendances. Although existing literature addresses hospitalisation costs, evidence on other healthcare costs is sparse.

We calculated estimates to address some of the quantitative evidence gaps around healthcare costs and productivity impacts of RSV in the UK and synthesised our findings from the broader literature on RSV in young children, including qualitative evidence. Despite recognising that RSV can have diverse impacts on the healthcare system, society and the economy, evidence on the nature and degree of burden in the UK is fragmented and incomplete. The identified studies use various age-group categorisations, timeframes

and measures for specific types of impact, employing varied methodologies for calculating estimates. Moreover, very few studies consider the impact of RSV on children under five at the UK level (often focusing on individual nations, particularly England and Scotland). Consequently, there is a need for research to synthesise insights from previous studies and enrich evidence on the burden of RSV in the UK. This is important for a well-rounded and comprehensive understanding of the impact and distribution of the RSV burden.

Against this backdrop, this study aimed to:

- Bring together insights from recent literature and conduct economic modelling to help understand the burden of childhood RSV in the UK, specifically on children aged up to five;
- Consider diverse areas of burden, including the NHS (primary and secondary care burden), patients and their parents/carers' health and well-being, and the wider UK economy.

1.1. Reader's guide

Chapter 2 briefly describes the study methods, while chapter 3 brings together and summarises the results, where we first discuss the burden on children with RSV and the impact on their family/carers. We then discuss the quantified annual costs of RSV in the UK on the NHS and the economy regarding lost economic productivity. We end with an overview of the opportunities identified from the literature that could help reduce the burden of RSV.

2 Method

The study consisted of two main components: a literature review and economic modelling. This section outlines the methods used, with full details provided in the accompanying Annexes document. We quantitatively modelled healthcare and productivity costs (due to parent/carer time away from work) and estimated parents/carers' out-of-pocket expenses. Additional RSV burdens, including the risk of death and reduced quality of life of children with RSV and their parents/carers, are presented based on the evidence available in the literature.

We undertook the literature review using Rapid Evidence Assessment (REA) methodology, which provides a rapid but systematic approach to evidence gathering by placing specific limits on the search scope to enable a focused review in a limited timeframe [10]. The REA entailed the following steps: (1) search-strategy development; (2) database searching in PubMed; (3) screening and prioritisation of hits to enable paper selection; (4) data extraction from selected papers; and (5) evidence analysis and synthesis. The REA included papers on RSV in children up to 18 years, but most articles focused on children under five (see Annexes A and C for further detail). We focused on children under 18 to ensure no relevant articles were missed, e.g. those with either unspecified or broad age ranges (under-fives and older). We reviewed 29

papers in detail, extracting information from them for the present study.

The REA identified numerous papers reporting relevant information on the economic impact of RSV on UK children younger than five. However, since only two manuscripts contained all the key information for our economic modelling analysis [11, 12], we sourced our key modelling data from a single publication to preserve the data's internal validity and avoid discrepancies due to differing methodologies. We selected the 2017 paper by Cromer and colleagues [11] as our modelling starting point as it did not rely on expert elicitation, considered RSV explicitly alongside all other respiratory pathogens, and permitted subgroup analysis differentiating pre-term and term infants. Based on the information available in the literature, we were able to extend the quantification of the costs of RSV in UK children aged under five to cover all hospitalisation costs, outpatient costs, General Practice (GP) costs and NHS 111 costs. We were also able to add lost-productivity costs due to parents/carers of children with RSV being absent from work.

We performed the analysis in four steps (further details are provided in Annex B). First, we extracted data from Cromer et al. on resource use (e.g. NHS 111 calls, GP visits, hospitalisations, outpatient attendances) and

events (e.g. deaths) for the English population [11]. Second, we extrapolated the data from Cromer et al. to the UK population. Third, we performed a Monte Carlo simulation to synthesise the model's parameters and obtain an estimate of the burden of RSV in the UK. Finally, we tested the robustness of the results by varying key parameter/assumption values.

3 Key insights into the burden of RSV in the UK

In this chapter, we first provide the main results of the quantitative modelling of the healthcare costs, productivity impacts and out-of-pocket expenses for parents/carers that result from RSV. We then describe all parts of the burden of RSV from a societal perspective based on the evidence presented in the published literature reviewed.

3.1. Modelled estimates of healthcare, productivity and out-of-pocket costs are substantial

Based on data for 2019, we estimate that the annual healthcare costs and productivity losses to the UK economy resulting from RSV in children younger than five totalled approximately £80 million (in 2020/21 price terms), equivalent to a mean total cost per child under five presenting to the NHS with RSV of £97. Approximately 80% (nearly £65 million) of the total annual cost is attributable to direct healthcare costs (e.g. hospital admissions and outpatient attendances). However, just over £14 million is due to productivity losses and about £1.5 million to parents/carers' out-of-pocket costs.

The estimated productivity cost to the UK economy is £14.2 million annually. This estimate is based on the assumption that parents/carers of children aged up to six months would not need to take time off work

as at least one parent/carer is likely to be at home with a child that young. However, we anticipate this assumption may be too simplistic as a parent/carer at work may take time off even if there is a parent/carer already at home (or at the hospital) with the child. Therefore, we may be underestimating the productivity impact for this age group. Consequently, we have also estimated the productivity cost to the UK based on the assumption that parents/carers of children aged less than six months also lose time at work. Based on this assumption, the resulting UK annual productivity cost increased by £7.4 million to £21.6 million, with the total cost (including healthcare costs) increasing to £87.7 million annually.

The average annual cost per child is significantly higher for children under six months (£344) than for children aged between six months and five years (£72). We estimate that children aged 0–12 months incur nearly half (49% - £39.5 million) of the total annual cost of RSV in children aged under five years. We conclude that the burden of RSV is significantly larger for infants during their first year of life than for any subsequent ones. These estimated costs mainly comprise direct healthcare utilisation, with an estimated 467,230 GP visits per year and 33,937 hospitalisations in the UK for children aged five and under. Full details of the different cost categories estimated and the split between

children aged up to six months and those between six months and five years are set out in Table 5 in Annex B.

Although relatively small, the number of deaths of children aged up to five attributable to RSV still amounts to an estimated 33 deaths per year. Although the healthcare consequences are short-term in most cases, there are long term sequelae for some, including poorer respiratory health in later life (as discussed below).

The following sections provide further details, drawn from the literature, on the impact of RSV on the child, their parents/carers/family, and the healthcare system.

3.2. RSV can damage a child's health and is fatal in some cases

3.2.1. Mortality

Using evidence from the literature, we estimate that an average of 33 children under five years old die from RSV in the UK each year. The number of children who become ill with RSV each year is estimated to be high, with approximately 467,230 GP attendances each year. This figure is expected to be an underestimate as it is unlikely that all cases reach primary or secondary care (indeed, the NHS estimates that almost all children are infected with RSV by the time they are two years old [13]).

3.2.2. Short-term impact on children's health

Children diagnosed with RSV experience a range of symptoms as a result of their infection

Children diagnosed with RSV face a range of respiratory-related symptoms, sometimes simultaneously. These include cough, cold and flu symptoms, bronchiolitis, wheeze, asthma

exacerbation, low blood oxygen levels and allergies [14-17]. In addition to respiratory symptoms, otitis media (ear inflammation or infection) is also common in children with RSV in the UK, especially in younger children [12, 15, 17]. One 2016 study estimated 125,487 otitis media cases per RSV season in UK children aged 0–17 years, with most cases occurring in children aged between six months and four years [17]. Other RSV-related symptoms in children include cardiovascular issues, electrolyte imbalances and neurological issues, which appear more likely in children with more severe RSV infections [16].

Outside the UK, evidence for acute bronchiolitis suggests that apnoea (the temporary cessation of breathing, primarily during sleep) occurs at a higher rate in pre-term infants and children with comorbidities than in otherwise-healthy children [16]. However, there is limited evidence on the differential impact of various RSV-associated symptoms in otherwise-healthy children and pre-term infants or children with comorbidities. This limits the capacity to draw firm conclusions about this aspect of RSV's burden.

Children with RSV may need to miss days of day-care and school

UK and international evidence on the rates and scale of absence **from early years day-care or school** (if the child is school-aged) due to RSV infection is scarce [17]. One paper from Finland suggests that 65% of children under three years with RSV miss at least one day of day-care, with a mean duration of three days [17]. The lack of estimates on missed day-care/school for children in the UK meant we could not incorporate this measure into our economic model. However, we included the impact of lost productivity for parents/carers taking time off to be with their sick child (as reported in Section 3.1).

Children with RSV experience a loss of quality of life due to their infection

Evidence from England suggests that children under five with RSV face quality-adjusted life-year (QALY) losses due to the infection, although few studies explore the scale of this impact [18]. The evidence suggests a modest average impact on QALYs at the individual level in most cases due to the illness's short duration [18]. QALY losses also vary depending on whether healthcare is sought or not [18].

3.2.3. The impact on long-term health and quality of life

Respiratory issues can persist for an extended period after the RSV infection has resolved, manifesting as a wheeze, asthma, bronchiolitis, poor lung function and allergies [16, 19, 20]. While the evidence suggests a possible link between RSV in childhood and later development of other health issues (such as asthma), the level of risk and the most at-risk groups are not clear from the reviewed literature. For some conditions, such as asthma, estimates varied across studies and age groups [16, 19, 20]. An international review from 2016 notes that recurrent wheezing may be up to three times higher for children with a history of RSV infection than children with no RSV history [16]. In a cohort study of nearly 750,000 Scottish children, RSV-related hospitalisation before the age of two was an independent risk factor for **asthma** through to age 18, with a 2–3 times higher risk for children hospitalised with RSV than those who were not [19]. According to this study, the most significant risk for asthma admission was at age seven [19]. Evidence from studies in a Swedish context in a review by Díez-Domingo et al. [16] also suggests a link between RSV in early years and childhood asthma, suggesting that the risk is nearly 22 times higher at 13 months follow-up, five times higher at 13 years follow-up, and four times higher at 18 years

follow-up. A systematic review covering diverse settings internationally (one of which includes the UK) indicates a 2.64 times higher risk of asthma outcomes for children with a history of RSV lower respiratory tract infection than children without [20].

Multiple studies suggest a link between childhood RSV and later-life asthma. However, the lack of robust data on the proportion of respiratory illness in older children due to RSV early in life makes the additional burden difficult to estimate within this study's scope (which is limited to RSV in children under the age of five years).

3.3. Impacts on families from a child under five having RSV include loss of workdays and work productivity, reducing their quality of life and emotional well-being and increasing out-of-pocket expenses

3.3.1. The economic impact on families

The results of the literature review reveal that parents or carers of children hospitalised with RSV may need to **miss work and, even when at work, may suffer productivity losses** due to caring for the child with RSV or parents contracting RSV from their child [17, 18, 21-24]. Estimates for days lost from work vary across countries and studies and depend partly on the age of the affected child, although we found no UK estimates in the literature we reviewed. However, there is some UK evidence on the impact of parents and older siblings needing to take time off work or school due to contracting RSV from their child or younger sibling [18]. Hodgson et al. conducted a surveillance study of 122 children aged under five years with RSV in England. They found that 16.6% of siblings aged 15+ and parents took time off school or work due to suspected RSV infection (median

of two days) after sharing a household with a confirmed RSV case [18].

Based on international evidence, parents/carers of children with RSV tend to lose less than two weeks of work [17, 22]. However, parents/carers of children under three years may need to miss more workdays than parents/carers of children aged 3–17 to care for the child and visit the hospital (in hospitalised cases) [17]. For parents of hospitalised children, taking time off work may remain necessary post-discharge to care for the child, who may not be back to full health [24]. The literature suggests that re-arranging work commitments or taking days off from work is likely to impose the most important financial burden on parents [21].

Our economic model estimates productivity losses for parents/carers because of the child's GP visits, outpatient appointments or hospitalisation. For children under five years, we estimate that total productivity losses due to GP visits and outpatient appointments cost £7.3 million per year and £6.9 million per year for hospitalisations. As well as lost workdays, parents/carers may be less productive at work if they have a child unwell with RSV [21, 22]. While these studies did not explore why parent/care productivity may be affected, it could be assumed multiple factors may be at play, including the emotional impacts of worries about the child's health, concerns over any financial impacts, or other physical or organisational factors. Since evidence on this aspect of productivity loss in the UK was lacking, it was not included in our model estimates. Similarly, the economic model did not include cost estimates of the impacts of RSV transmission to family members from a child under five.

The families of children hospitalised with RSV may lose time they would otherwise devote to activities beyond paid work because of

hospital visits. They may also face disruptions to their normal day-to-day routines [22, 24, 25]. However, evidence on the scale of this impact is minimal, especially in a UK context. A study from the United States (US) found that parents of pre-term infants aged under one face greater disruption to family routines with an infant hospitalised with RSV than parents of infants born to term, although the reasons are not clear [24].

There is minimal evidence on the impact of a child's RSV on parents'/carers' out-of-pocket expenses. One paper found that parents in Canada pay approximately Can\$737 (£560 in 2011 GBP) in out-of-pocket expenses when their child under one is hospitalised with RSV. They specify that these out-of-pocket expenses include transport, childcare for other children and home support [22]. These costs may well apply to other geographies, including the UK. However, their scale is likely to differ considerably given the nature of the healthcare systems and the distances travelled. We found no evidence on the extent and nature of out-of-pocket expenses associated with RSV in the UK. Consequently, our economic model includes a rough estimate for the UK based on evidence from Germany and the Netherlands [26] suggesting £1.5 million in out-of-pocket costs for the families of children aged up to five with RSV.

3.3.2. Quality-of-life impacts on families

There is some limited evidence that the quality of life and emotional well-being of siblings and parents/carers who contract RSV from a younger child can also be impaired [18, 23], with older siblings often missing days from school [18]. A surveillance study in England found that 84% of siblings aged 5–14 with suspected RSV reported anxiety or depression, 76% had their usual activities impacted by RSV symptoms and 72% reported pain or discomfort. For siblings aged 15+ or parents/

carers with suspected RSV, 36% reported anxiety or depression, 54% had their usual activities impacted by RSV symptoms and 36% reported pain or discomfort [18]. On average, these negative impacts on siblings/parents/carers' health-related quality of life last days rather than months. When pooling the results of all parents and siblings (aged 5 years and older) together, the authors estimated a modest average QALY loss for this age group at 1.950×10^{-3} QALYs per RSV episode for those who did not seek healthcare and 1.543×10^{-3} QALYs for those who did [18]. The small scale of QALY loss per episode reflects the short duration of most such episodes: although the loss of quality of life is substantial, it does not last long due to the nature of the infection.

Hospitalisation of children with RSV can also contribute to poor emotional health for parents through stress, anxiety, distress and feelings of helplessness, which can last beyond the child's discharge [21-25]. A range of factors can cause these feelings, including feeling guilty for not noticing their child's illness earlier, concern about infection transmission, fears of how quickly a child's state can decline, worries over recovery/survival, re-infection and readmission, delays accessing care due to living in a rural area, sleep deprivation, challenges keeping family informed, missing work, feeling stuck at the hospital, witnessing painful/invasive procedures and concerns over providing care at home [21-25]. While emotional health can improve over time, evidence suggests these feelings can persist for weeks after discharge [24, 25].

Parent/carer perceptions of suboptimal interactions with healthcare professionals and a lack of sufficient information provision can also contribute to feelings of stress, anxiety and helplessness [21, 25]. However, the frequency of suboptimal experiences of parent-healthcare professional interactions is unclear.

In addition, there is minimal evidence from the UK on this topic.

3.4. RSV in under-fives creates a significant burden for the healthcare system in terms of NHS 111 calls, GP visits and hospitalisation

3.4.1. NHS 111 calls and GP visits

Children with RSV place a significant burden on primary and community care, including a significant percentage of calls to NHS 111 related to respiratory conditions [27, 28] and GP visits [11, 12, 16, 18, 28]. One study analysed data on 2 million calls to NHS 111 in England relating to respiratory issues (out of 18.2 million total calls made to NHS 111) during two RSV seasons. The results showed that 43% of all respiratory calls per week were associated with RSV (408 out of 948 respiratory calls per week), the highest proportion of any respiratory pathogen analysed for the study [27]. Nearly half of these RSV calls were for children aged five and under [27]. Our economic model estimated that there are over 467,000 calls to NHS 111 each year due to RSV in children under five years, costing £0.7 million in total. Calls to NHS 111 for RSV can cause a significant burden to an already stretched NHS 111 service. One study indicates that higher numbers of RSV calls contributed to exceeding the medium intensity threshold for cough-related calls over two weeks in 2017–18 [28].

Modelling studies from the UK and England suggest that 11–16% of GP visits for respiratory diseases in children are associated with RSV [11, 12]. Our economic model estimated over 467,230 GP visits due to RSV in under-fives per year in the UK, costing £15.7 million. The number of GP visits for RSV varies seasonally, meaning that infants born in certain months of the year may be at higher

risk of needing to visit a GP [11, 12]. One study in an English context estimated that the GP consultation rate for RSV is 27.4 per 100 births for children born in November compared to 13.9 for children born in March [11].

3.4.2. Hospitalisations, including readmissions and outpatient appointments

Although the hospitalisation rate for children with RSV is moderate – ranging from 21.9/1,000 to 35.1/1,000 for infants aged under one in the UK [29-31], depending on the study and geographical context – the overall scale of the burden is significant given the high prevalence of RSV among young children. However, estimates of this burden vary substantially across studies, geographical contexts and age groups in the UK. Our model estimated 33,937 hospitalisations per year due to RSV in under-fives in the UK. Including the associated ICU costs and outpatient attendances, this amounts to a total estimated annual cost of £48.2 million for RSV hospitalisations for under-fives.

Multiple UK and international studies indicate that children born prematurely [29, 30, 32] or with underlying comorbidities [29, 32] face a greater risk of hospitalisation for RSV than children born at term or without comorbidities. A cohort study of nearly 624,000 children aged under two in Scotland found that pre-term children were significantly more likely to require RSV hospitalisation than children born at term (5% vs 2%) [32]. In addition, comorbidities were found in 7% of children under two hospitalised for RSV compared to 1% of those not hospitalised with RSV, a statistically significant difference [32]. In a study of children under three in Scotland, 19% of the 4,966 RSV admissions in children with known gestational age were among children who were premature or had an underlying chronic condition [29].

The risk of hospitalisation due to RSV may also be higher in patients from a lower socioeconomic background. Hardelid et al. [29] conducted a study in Scotland of over 5,000 patients aged up to three hospitalised with RSV. This study found that patients who were premature or of lower gestational age, with younger mothers and with delayed or incomplete vaccine schedules (all of which are associated with lower socioeconomic status) were more likely to be hospitalised with RSV.

Hospitalisation rates also vary by season. Multiple studies highlight RSV peaks during the winter months [11, 30-33], with hospital admissions highest between October and January. In Scotland, Thwaites et al. [32] found that 92% of RSV hospitalisations in children under two occurred from October to March, representing 9% of all admissions in this age group. In England, Reeves et al. [31] report that 80–90% of bronchiolitis admissions in children aged 0–4 years were from November to January, with admission peaking in early December [30]. Furthermore, Cromer et al. [11] estimated that 70% of all hospital admissions from October to January in England for acute respiratory reasons were children under six months with RSV.

The majority of studies exploring the length of post-admission hospital stays found that the median length of stay was 2–4 days in the UK and globally [14, 19, 32, 33], although non-UK evidence suggests this could be up to 13–15 days for the most severe cases [16]. Reeves et al. [30] used lab surveillance and hospital admissions data of children under one to explore the number of bed days associated with RSV. They estimated that almost 60,000 bed days are required per year for children under one with RSV in England. Of these, 31% were for less than one day, accounting for 5% of all RSV-associated bed days. In addition, the authors estimated that 74% of RSV admissions in children under one were for children under

six months, accounting for 80% of annual RSV-associated bed days [30]. Length of stay is likely longer for children born prematurely or with underlying conditions [29]. For example, a birth cohort study of over 5,000 Scottish children aged under three hospitalised for RSV found that the median length of stay was significantly longer for premature infants and children with underlying chronic conditions: three days compared to an overall median of two days [29].

The presence of comorbidities increases the average length of stay. Children with a chronic condition made up only 11% of RSV-associated admissions but 20% of bed days [29]. One modelling study in England identified that of all RSV hospital admissions for children under one, only 5% were considered high-risk due to prematurity or comorbidities. However, this group of children accounted for 21% of total bed days.

The longer-term respiratory impacts of RSV in children (e.g. wheezing and asthma) create additional cost burdens for the healthcare system. In the UK, a paper in Scotland found that significantly more patients with RSV in their first two years of life were hospitalised for asthma during later childhood than the control group without a history of RSV (8% versus 2%) [19]. The same study also found that a significantly higher proportion of RSV cases required more than one hospital admission for asthma than controls (44% compared to 35%). This finding suggests that children with a history of RSV may face more severe asthma in the long term and thus incur more healthcare costs [19].

Data on ICU admissions of the very sickest children hospitalised vary significantly across studies and geographical contexts. Data from Scotland suggest that ICU admission may be required in around 4% of children under two admitted to hospital with RSV [19, 32]. International evidence suggests a higher

proportion for pre-term infants and infants with specific comorbidities such as congenital heart disease [16, 22]. In our modelling, we used the rates provided by Cromer et al. [11]: 1.8% of at-term hospitalised cases requiring ICU admission and 9% of pre-term cases.

Readmissions for children with RSV add further burden to the healthcare system in terms of bed days and cost. Research in a Scottish setting suggests that just under a fifth of hospitalised cases (19%) in children aged under two result in readmissions [32]. Based on a study in England and Wales, half of the readmissions for RSV for children aged 0–4 were within nine days of initial discharge [34]. The same study found that the average length of stay on readmission among children with underlying conditions/multiple diagnoses increases significantly relative to otherwise-healthy children [34]. Since readmissions are part of the total number of hospitalisations referred to earlier, we included their costs in our estimate of the total costs of hospitalisations.

3.4.3. Medical interventions and support

Antibiotic prescriptions are common for children with RSV in both primary and secondary care in the UK and elsewhere, usually for bacterial co-infections [35]. One study of around 3.7 million children aged up to 17 years in the UK found that over 416,000 prescriptions for antibiotics were written in primary care per RSV season [12]. The same study found that roughly 8% of children under six months and 12% aged 6–23 months received antibiotics to treat RSV-associated infection in an average RSV season [12]. Our economic model excluded the cost of prescribing antibiotics for RSV-associated bacterial infections as this is a secondary impact/cost of treating a non-RSV infection.

Evidence suggests that children hospitalised with RSV are highly likely to require supplemental oxygen. Some children may also

require other respiratory support [16, 22, 33], although UK data from the literature included in this study on these issues are limited. Paul et al. (2017) reviewed the testing and intervention requirements of 162 children under two admitted to one hospital with RSV in England and found that 36 (22%) required respiratory support [33].

Children with RSV may require a range of other interventions, such as chest x-rays, admission to high-dependency care units, intravenous fluids, inhalers and antipyretics [16, 33].

3.5. Opportunities for improvement

The literature analysed in this study referred to various ways efforts to reduce the health, economic and wider societal impacts of RSV could be improved. Although such efforts are not the subject of our (current cost burden) study, we mention them here as potential prospects for ameliorating the future burden.

Some studies suggested that improving RSV immunisations could reduce RSV transmission and reduce illness severity, hospitalisations and antibiotic prescriptions [11, 14, 17, 28, 29, 36]. One global systematic review estimated that a successful maternal/newborn vaccine programme could prevent up to 1.1 million RSV-associated hospital admissions and 22,000 inpatient deaths globally [14].

Vaccination programmes could be broadened to offer protection for older children, reducing hospital admissions and the risk of subsequent future health issues [17, 29].

Besides immunisations, other efforts to reduce RSV transmission (such as the use of other prophylaxis, public health campaigns and infection control measures) could also help prevent RSV infections and hospitalisations, reducing morbidity and mortality [16]. The literature also flags the importance of educating parents/carers on hygiene measures to prevent RSV transmission, such as hand washing and self-isolation – particularly for parents with premature babies – and support for recognising early RSV symptoms [16, 23].

The literature also suggests that the development of antivirals targeted at RSV could help reduce infection incidence, length and severity, including subsequent health impacts such as otitis media and bacterial co-infection requiring antibiotics [17, 37].

Finally, the literature notes how important it is that healthcare professionals answer parents/carers and families' questions and provide timely and understandable updates on their hospitalised child and clear guidance on caring for them after discharge. Such measures can be expected to reduce the burden of anxiety and distress on parents/carers and families [21, 23, 25].

4 Discussion and conclusion

We have taken a broad societal perspective to assess the burden of RSV in the UK for children aged under five. As well as costs to the healthcare system, our assessment includes productivity costs and out-of-pocket costs for families/carers, plus the loss of health and, in some cases, loss of life associated with RSV. We used a mixed-methods approach, quantifying the UK cost burden in financial terms where data were available from the literature. Based on the literature review, we have also described other aspects of the RSV burden that contribute to the total burden on the NHS, the UK economy and society in general, and the parents/carers and families of the children concerned. Evidently, the overall burden of RSV in children aged under five in the UK is substantial.

Our quantitative modelling of costs in financial terms goes beyond any previous work by:



Providing costs on a UK basis;



Adding the costs of productivity losses to the UK economy due to parents/carers' absence from work; and



Including the costs of NHS 111 calls and outpatient attendances in the estimates of health system costs.

We based our estimates on data in the literature, starting from the work of Cromer

and colleagues [29]. Inevitably there are uncertainties in these estimates, such as the number of RSV cases that present per year to healthcare professionals. We report on several sensitivity tests in Annex B. However, the quantified cost burden remains in the same order of magnitude.

Our model's cost estimates likely underestimate the total costs per year due to RSV in children aged under five in the UK for the following reasons:



The cost consequences of longer-term sequelae that affect a child's health beyond the initial episode of RSV are not included;



The impact costs of RSV transmission to parents/carers or siblings from a child aged under five have not been modelled due to insufficient data;



While we have estimated productivity losses due to a parent/carer's absence from work to be with their sick child or take them to a GP, we were unable to estimate the impact of their lower productivity when at work. Since we know that having a child sick with RSV causes stress to the parents/carers, lower productivity at work seems a likely consequence.

Our quantitative model estimated the proportion of the total RSV burden associated with children in the first six months of their lives versus those in the next four-and-a-half years. The model also estimated the relative proportion of the RSV burden associated with premature babies versus other babies. Infants aged 0–6 months represent about 10% of the total population of children under five years, yet they account for 33% of the total quantified annual cost estimate (£26.4 million out of £80.2 million). Children in the first six months of their life are responsible for nearly half (48%) of hospitalisation (including outpatient) costs: £23.1 million out of £48.2 million. Our modelling also illustrated that while premature babies account for 19% of the total RSV cost burden (£15.5 million out of £80.2 million), the RSV cost burden from babies born at term totals more than four times as much (although the cost per child is much less).

It would thus be a mistake to focus primarily on pre-term infants when considering the RSV cost burden. The results presented from the literature review concerning mortality and

quality-of-life impacts and the nature of the burden on parents and families of caring for a young child with RSV are also important, even when unquantified.

We conclude that the societal burden of RSV in children aged up to five years in the UK is substantial. The financial costs amount to £65 million of NHS costs per year, £14 million of productivity losses to the economy in terms of lost workdays and another £1.5 million in out-of-pocket costs for parents/carers (all financial estimates are in 2020/21-financial-year price terms). An estimated 33 children aged five years and younger die from RSV annually in the UK. Many children experience reduced quality of life during the illness, and their parents/carers and families experience corresponding emotional stress. While our analysis estimated a considerable loss of QALYs (3,137), this estimate is conservative since for some of the children with RSV the consequences are longer term, which may result in an increased risk of respiratory and other conditions later in life able to impair their quality of life.

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