

RSV burden in infants (and children)

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Disclosures

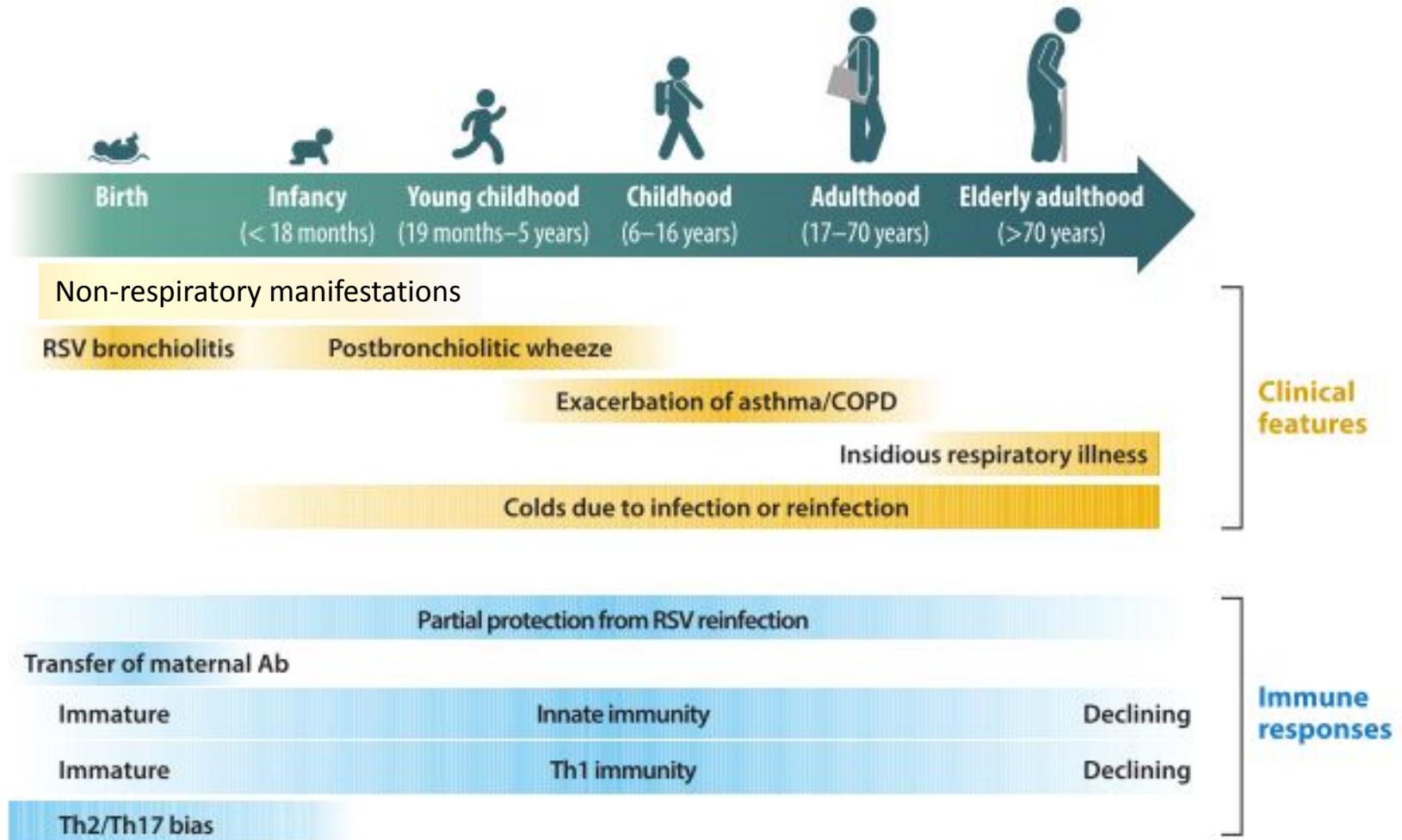
- SBD has previously received honoraria from MSD and Sanofi for taking part in RSV advisory boards and has provided consultancy and/or investigator roles in relation to product development for Janssen, AstraZeneca, Pfizer, Moderna, Valneva, MSD, iLiAD and Sanofi with fees paid to St George's, University of London.
- SBD is a member of the UK Department of Health and Social Care's (DHSC) Joint Committee on Vaccination and Immunisation (JCVI) RSV subcommittee and member of the Medicines and Healthcare products Regulatory Agency's (MHRA) Paediatric Medicine Expert Advisory Group (PMEAG), but the reviews expressed herein do not necessarily represent those of DHSC, JCVI, MHRA or PMEAG.
- Member of RESCEU Consortium

Outline

- Epidemiology
- Risk groups
- Costs
- Summary



Adaptation through life



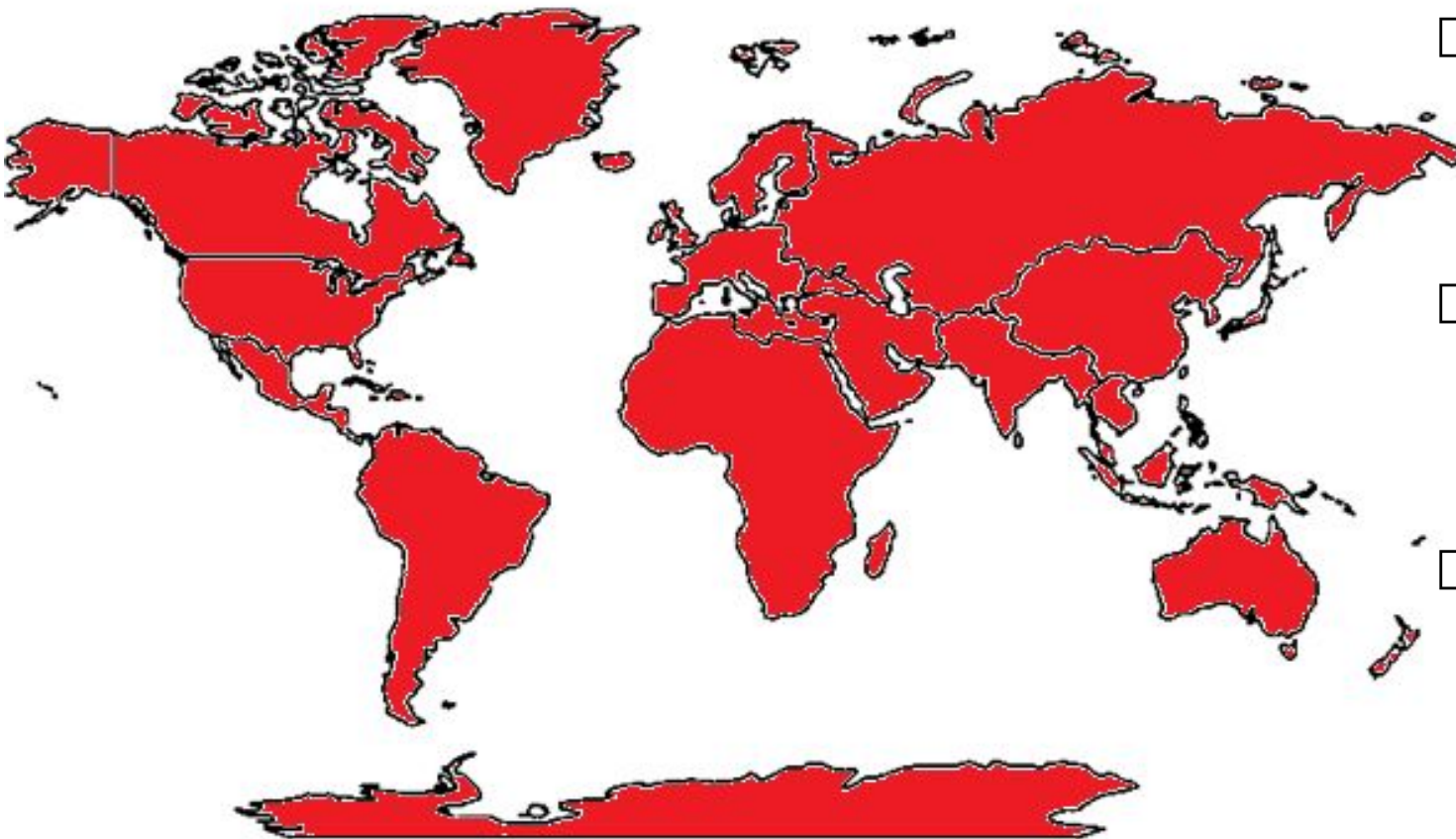
The problem....



© CBS News

Hospitalization: Infant Jude being treated for RSV, which annually kills over 200 children under the age of one in the United States

RSV ubiquity



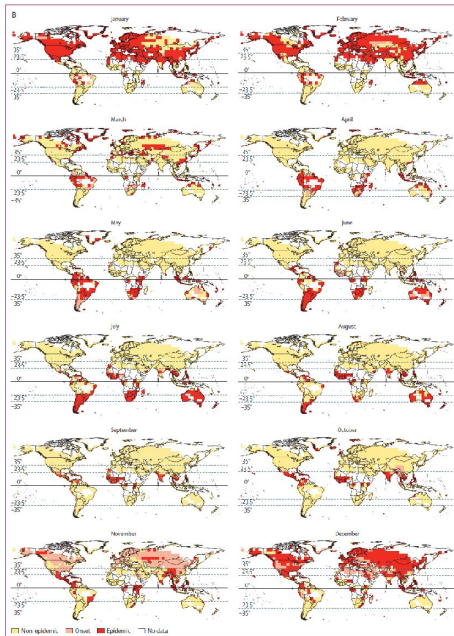
- All children infected by 3 years
- Repeated infections throughout life
- Incomplete immunity after natural infection

Global seasonality

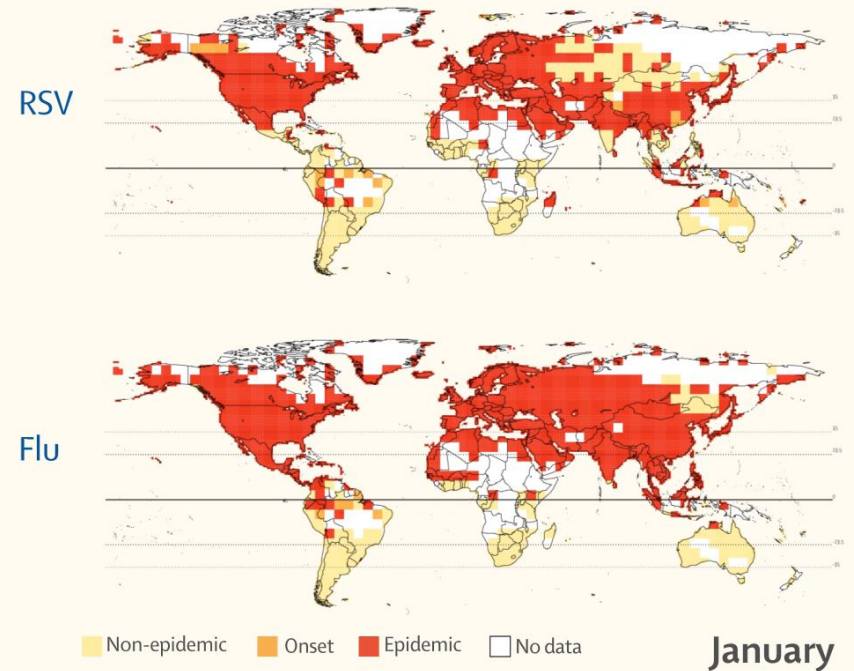
Global patterns in monthly activity of influenza virus, respiratory syncytial virus, parainfluenza virus, and metapneumovirus: a systematic analysis

You Li, Rachel M Reeves, Xin Wang, Quique Bassat, W Abdullah Brooks, Cheryl Cohen, David P Moore, Marta Nunes, Barbara Rath, Harry Campbell, Harish Nair, on behalf of the RSV Global Epidemiology Network and RESCEU investigators*

Lancet Glob Health 2019;
7: e1031-45



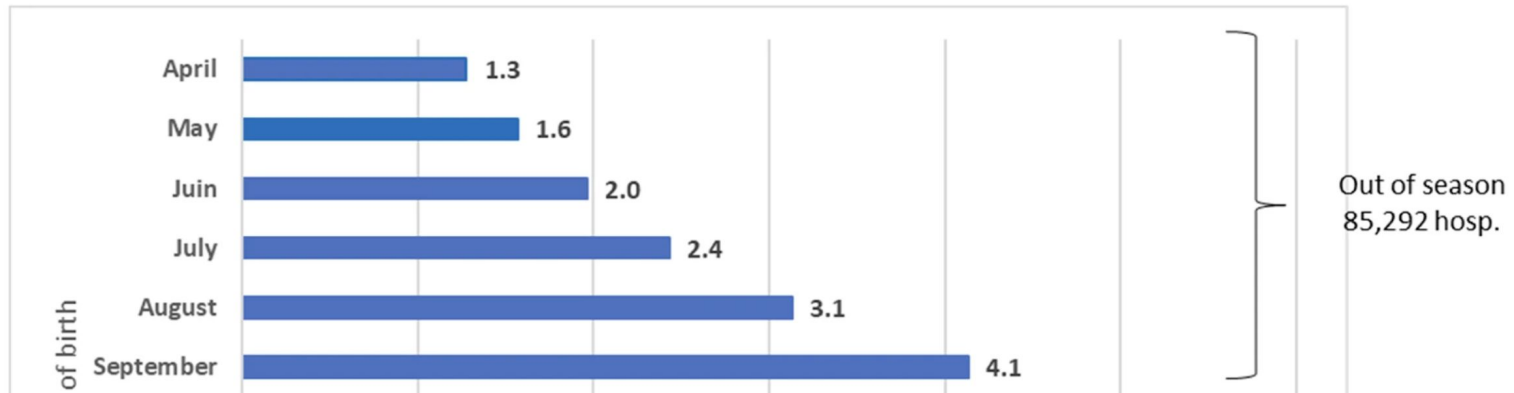
Predicted global changes in RSV and flu prevalence by month



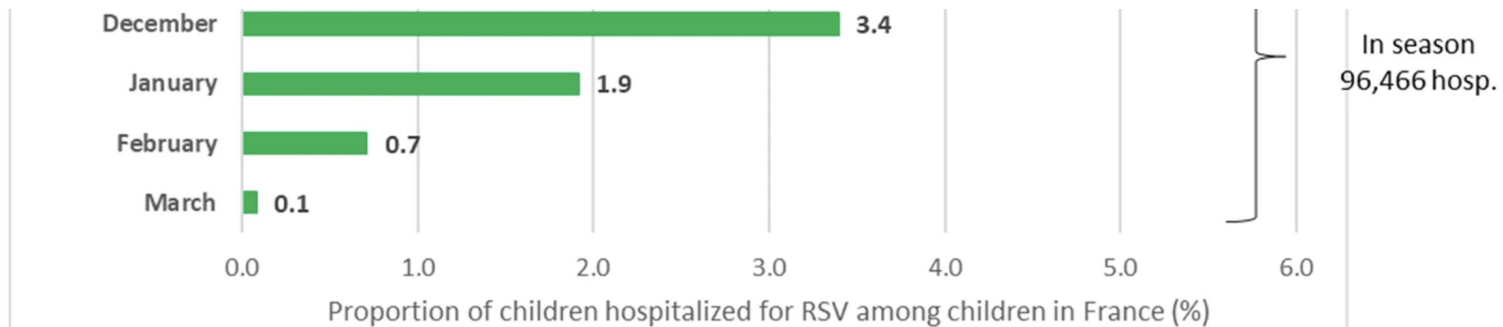
RSV=Respiratory syncytial virus; Flu=influenza virus

RSV Hospitalizations Among Infants and Children

From: [Economic and disease burden of RSV-associated hospitalizations in young children in France, from 2010 through 2018](#)



RSV-associated hospitalizations accounted for 28% of all-cause hospitalizations among children < 1 year old



Global data, 2019; <5-year-olds

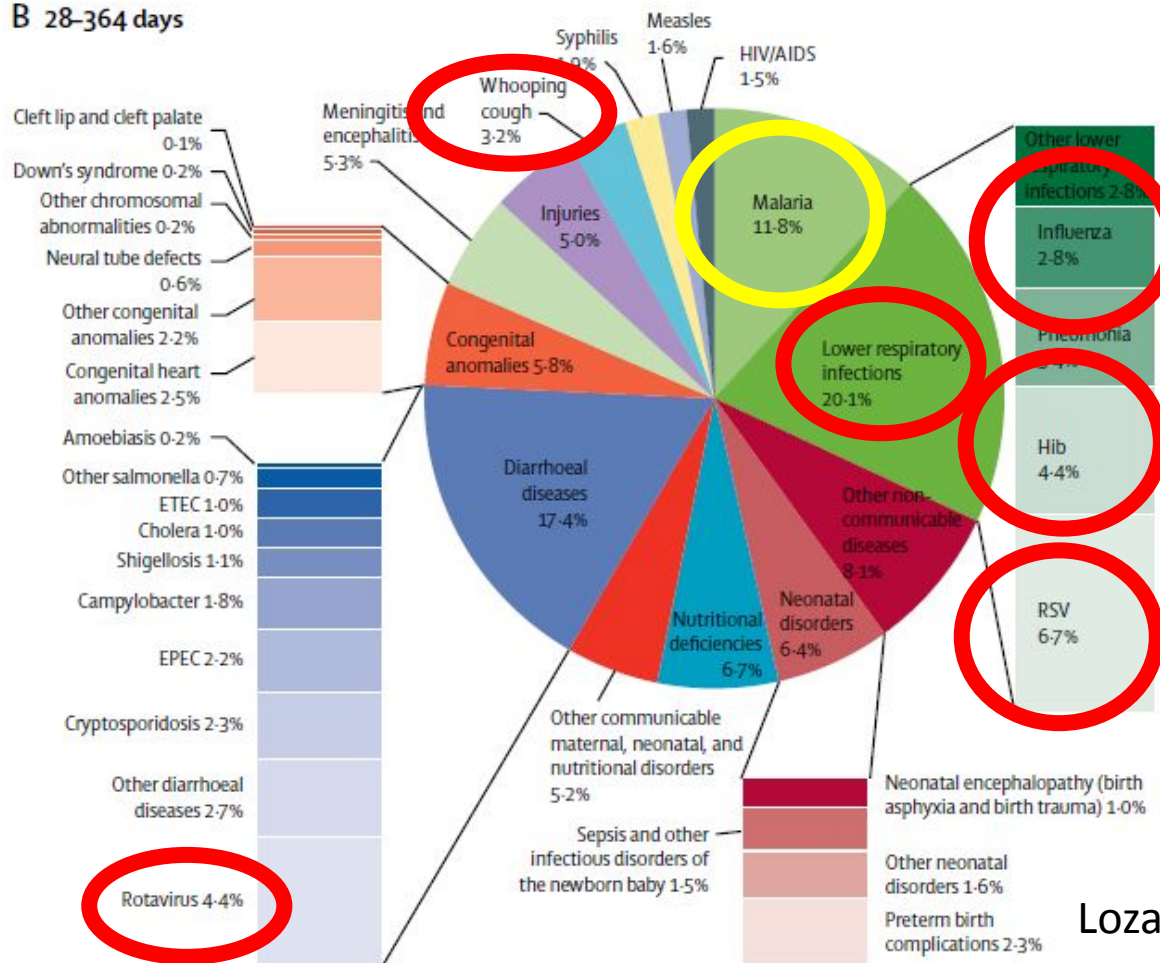
- 33.0 million RSV LRTIs (uncertainty range [UR] 25.4–44.6 million)
- 3.6 million RSV LRTI hospital admissions (2.9–4.6 million)
- 26,300 RSV LRTI in-hospital deaths (15,100–49,100)
- 101,400 RSV-attributable overall deaths (84,500–125,200)
- In infants aged 0–6 months:
 - 6.6 million RSV LRTIs (4.6–9.7 million)
 - 1.4 million RSV LRTI hospital admissions (1.0–2.0 million)
 - 13,300 RSV LRTI in-hospital deaths (6,800–28,100)
 - 45,700 RSV-attributable overall deaths (38,400–55,900)
- 2.0% of deaths in children <5yo (UR 1.6–2.4) and 3.6% of deaths in children 28 days to 6 months old (3.0–4.4) were attributable to RSV.
- >95% of RSV-associated LRTIs were in LMICs
- >97% of RSV-attributable deaths were in LMICs

Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis

You Li, Xin Wang, Dianna M Blau, Mauricio T Caballero*, Daniel R Feikin*, Christopher J Gill*, Shabir A Madhi*, Saad B Omer*, Eric A F Simões*, Harry Campbell, Ana Bernabeu Pariente, Darmaa Bardach†, Quique Bassat†, Jean-Sebastien Casalegno††, Giorgi Chakhunashvili†, Nigel Crawford†, Daria Danilenko†, Lien Anh Ha Do†, Marcela Echavarria†, Angela Gentile†, Aubree Gordon†, Terho Heikkinen†, Q Sue Huang†, Sophie Jullien†, Anand Krishnan†, Eduardo Luis Lopez†, Joško Markić†, Ainara Mira-Iglesias†, Hannah C Moore†, Jocelyn Moyes†, Lawrence Mwananyanda†, D James Nokes†, Faseeha Noordeen†, Evangeline Obodai†, Nandhini Palani†, Candice Ramerot†, Vahid Salimi†, Ashish Satavi†, Euri Seo†, Zakhar Shchomak†, Rosalyn Singleton†, Kirill Stolyarov†, Sonia K Stoszek†, Anne van Gottberg†, Danielle Wurzel†, Lay-Myint Yoshida†, Chee Fu Yung†, Heather J Zar†, Respiratory Virus Global Epidemiology Network§, Harish Nair, for the RESCEU investigators*

Global mortality

B 28-364 days



□ 33m new RSV ALRIs per year

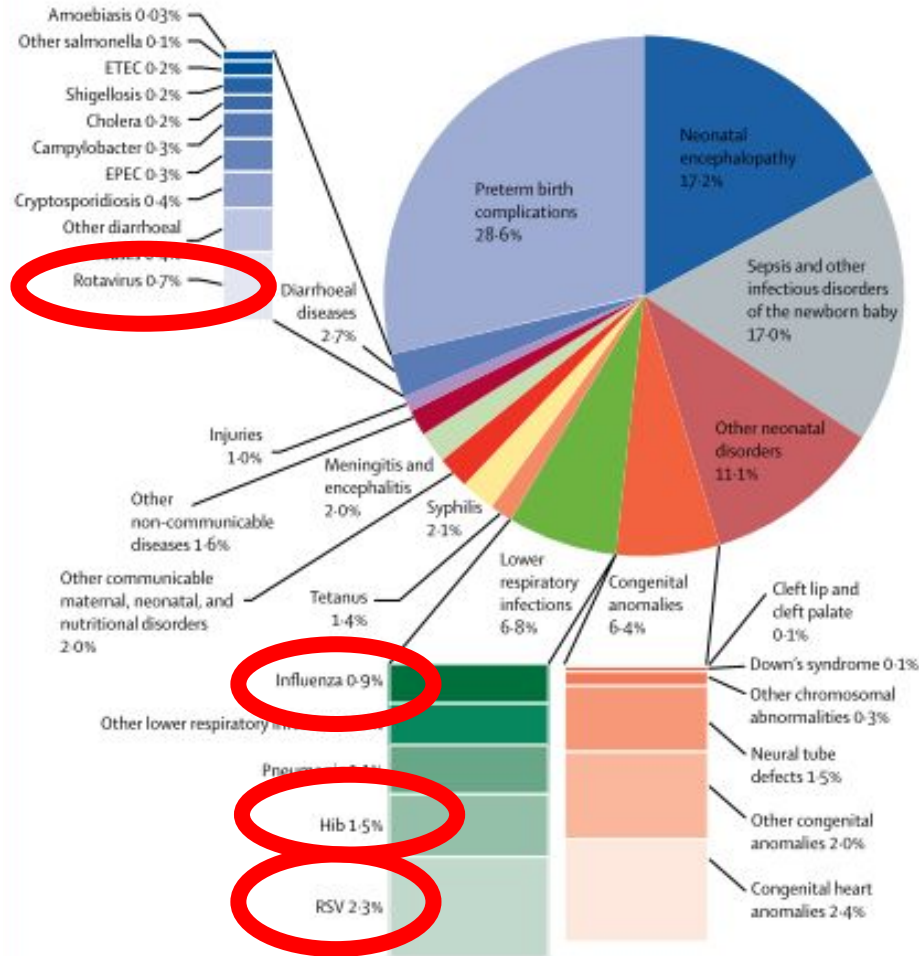
□ 84,500-125,200 RSV deaths in children <5 years old (>97% in LMIC)

Li et al, Lancet, 2022

Lozano et al, Lancet, 2012

Global mortality

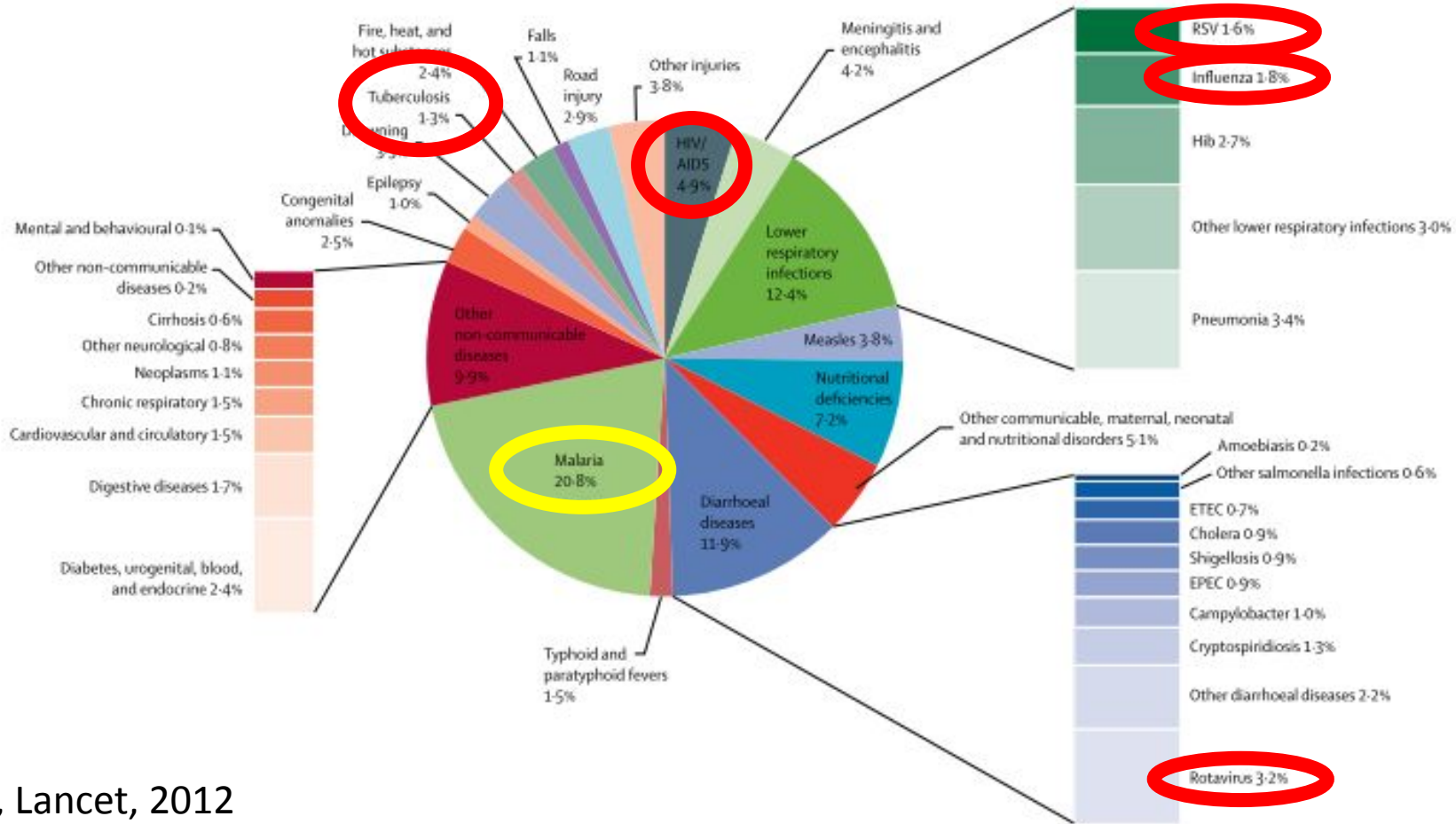
A 0-27 days



Lozano et al, Lancet, 2012

Global mortality

C 1-4 years



Lozano et al, Lancet, 2012

RSV

Globally, during a typical RSV season, across northern and southern hemispheres **a child under 5 is hospitalized every 5 seconds** as a result of RSV.^{1,2}



300 infants by the end
of this 25 min talk!



1. World Health Organization. Initiative for Vaccine Research: Acute Respiratory Infections. Last accessed May 2016.
2. World Health Organization. WHO Consultation on respiratory syncytial virus (RSV) vaccine development . Last accessed May 2016.



RSV

Across all ages,
EVERY 90 SECONDS
SOMEONE DIES
from RSV.^{1,2}

18 people by the end
of this 25 min talk!

1. World Health Organization. Initiative for Vaccine Research: Acute Respiratory Infections. Last accessed April 2016.
2. World Health Organization. WHO Consultation on respiratory syncytial virus (RSV) vaccine development [online].
http://www.who.int/immunization/research/meetings_workshops/rsv_vaccine_development/en/. Last accessed April 2016.

Table 3. Average RSV-Associated Hospitalizations per Age Group per Year

Country	0–2 mo (95% CI) ^a	3–5 mo (95% CI) ^a	6–11 mo (95% CI) ^a	12–35 mo (95% CI) ^b	36–59 mo (95% CI) ^b
EU-28 ^c	90 200 (83 923–96 476)	49 052 (45 328–52 776)	44 369 (40 529–48 208)	50 852 (45 249–56 456)	10 771 (9659–11 883)
Austria	1308 (1111–1505)	667 (558–775)	545 (432–658)	732 (563–902)	147 (112–182)
Belgium	2141 (1926–2446)	1122 (965–1302)	902 (816–1167)	1225 (972–1497)	306 (250–362)
Bulgaria	1374 (1111–1637)	667 (558–775)	545 (432–658)	732 (563–902)	147 (112–182)
Croatia	781 (632–930)	391 (325–457)	317 (251–383)	422 (336–508)	77 (59–95)
Cyprus	181 (145–217)	91 (73–109)	74 (60–88)	95 (77–113)	18 (13–22)
Czech Republic	2031 (1826–2236)	1016 (915–1117)	813 (737–889)	1016 (915–1117)	258 (209–308)
Denmark	846 (711–981)	423 (352–494)	338 (281–395)	423 (352–494)	199 (172–225)
Estonia	238 (205–271)	119 (102–136)	95 (81–109)	41 (112–170)	32 (25–38)
Finland	1122 (980–1264)	561 (489–633)	451 (394–508)	25 (501–750)	97 (71–124)
France	18 145 (16 336–19 952)	9075 (8368–9782)	7413 (6706–8120)	73 (5998–9148)	1704 (1368–2040)
Germany	12 977 (11 223–14 731)	6489 (5648–7330)	5207 (4506–5908)	50 (5802–8699)	1334 (1039–1629)
Greece	1895 (1670–2119)	948 (835–1061)	764 (670–854)	62 (661–1063)	193 (147–239)
Hungary	1748 (1521–1975)	874 (761–987)	703 (619–787)	76 (788–1164)	199 (161–237)
Ireland	1139 (980–1298)	569 (490–648)	451 (394–508)	50 (810–1091)	176 (146–206)
Italy	10 111 (8888–11 334)	5056 (4444–5668)	4045 (3533–4557)	75 (3387–5563)	1021 (787–1256)
Latvia	407 (353–459)	204 (177–231)	161 (139–183)	90 (148–232)	40 (32–48)
Lithuania	559 (485–633)	279 (240–318)	221 (189–253)	41 (179–304)	54 (42–67)
Luxembourg	96 (82–111)	48 (41–55)	38 (32–44)	64 (51–77)	12 (9–15)
Malta	69 (59–80)	35 (30–40)	27 (23–31)	47 (38–57)	11 (9–13)
Netherlands	2071 (1641–2502)	1036 (829–1243)	829 (661–997)	51 (292–1011)	398 (319–475)
Norway	811 (661–961)	406 (330–482)	325 (268–382)	12 (682–941)	61 (34–89)
Poland	6542 (5646–7439)	3271 (2800–3742)	2618 (2251–2985)	59 (2669–4249)	730 (557–903)
Portugal	1444 (1243–1645)	722 (621–823)	571 (490–652)	69 (590–949)	226 (185–268)
Romania	3300 (2830–3769)	1650 (1425–1875)	1275 (1092–1458)	40 (1150–1929)	389 (305–472)
Slovakia	1035 (900–1170)	518 (450–586)	415 (361–469)	31 (414–648)	98 (72–123)
Slovenia	399 (347–451)	199 (172–225)	159 (139–179)	25 (180–270)	48 (38–57)
Spain	7399 (6356–8442)	3699 (3165–4233)	2959 (2533–3385)	70 (1762–3578)	788 (585–992)
Sweden	1824 (1538–2110)	912 (769–1055)	726 (611–841)	29 (987–1471)	288 (237–339)
United Kingdom	12 333 (9291–15 375)	6167 (4625–7709)	5184 (3813–6555)	90 (7128–12 652)	2156 (1614–2698)

245,244 hospitalisations per year in children <5 years old in EU

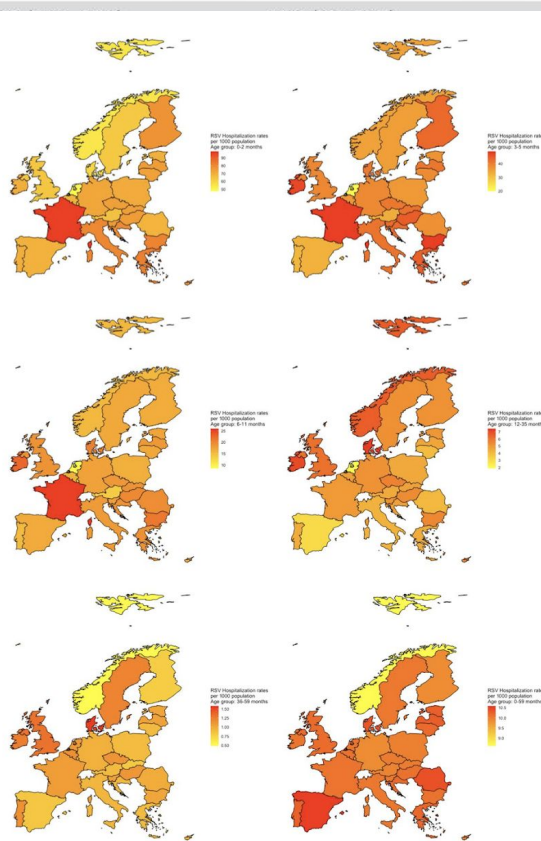
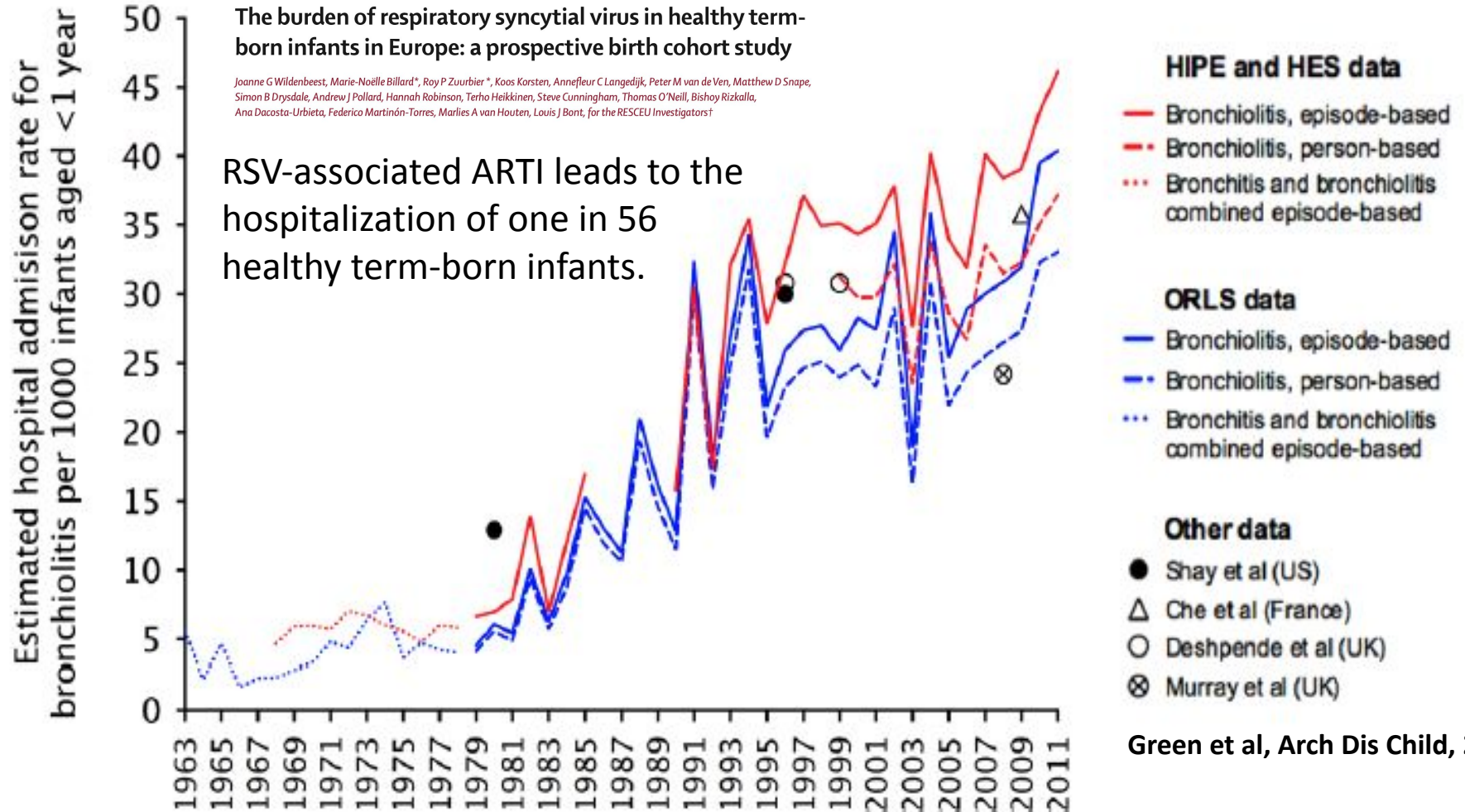


Figure 2. RSV-associated hospitalisation rates per 1000 population in 28 EU countries and Norway.

Abbreviations: CI, confidence interval; EU, European Union
^aRSV-associated hospitalization in these 3 age groups are €
^bRSV-associated hospitalization in these 2 age groups are €
^cIncludes the United Kingdom and excludes Norway.

eagues [15].
eagues [14].

Hospitalised infants



Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis

You Li, Xin Wang, Dianna M Blau, Mauricio T Caballero*, Daniel R Feikin*, Christopher J Gill*, Shabir A Madhi*, Saad B Omer*, Eric A F Simões*, Harry Campbell, Ana Bermejo Pariente, Darmaa Bardach†, Quique Bassat†, Jean-Sebastien Casalegno†‡, Giorgi Chakhunashvili†,*

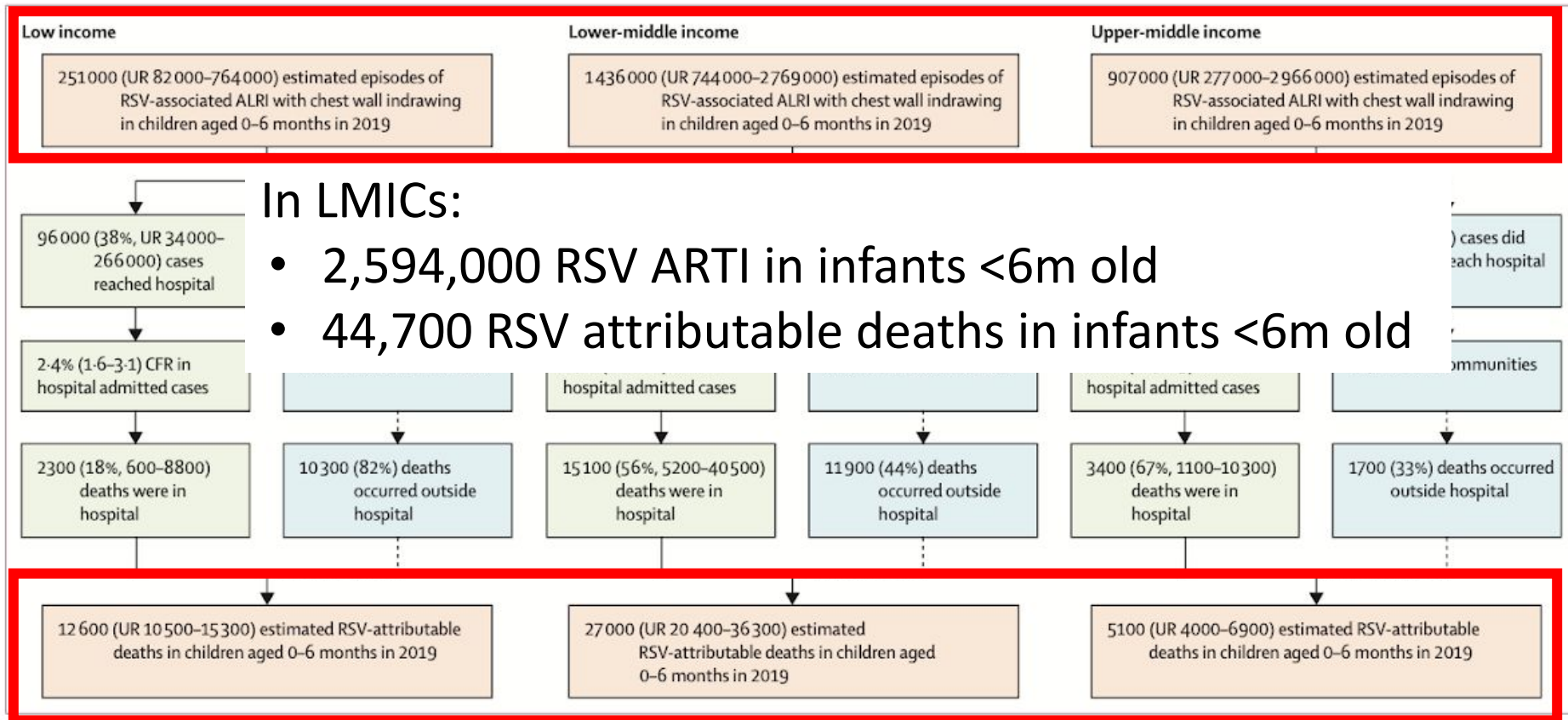
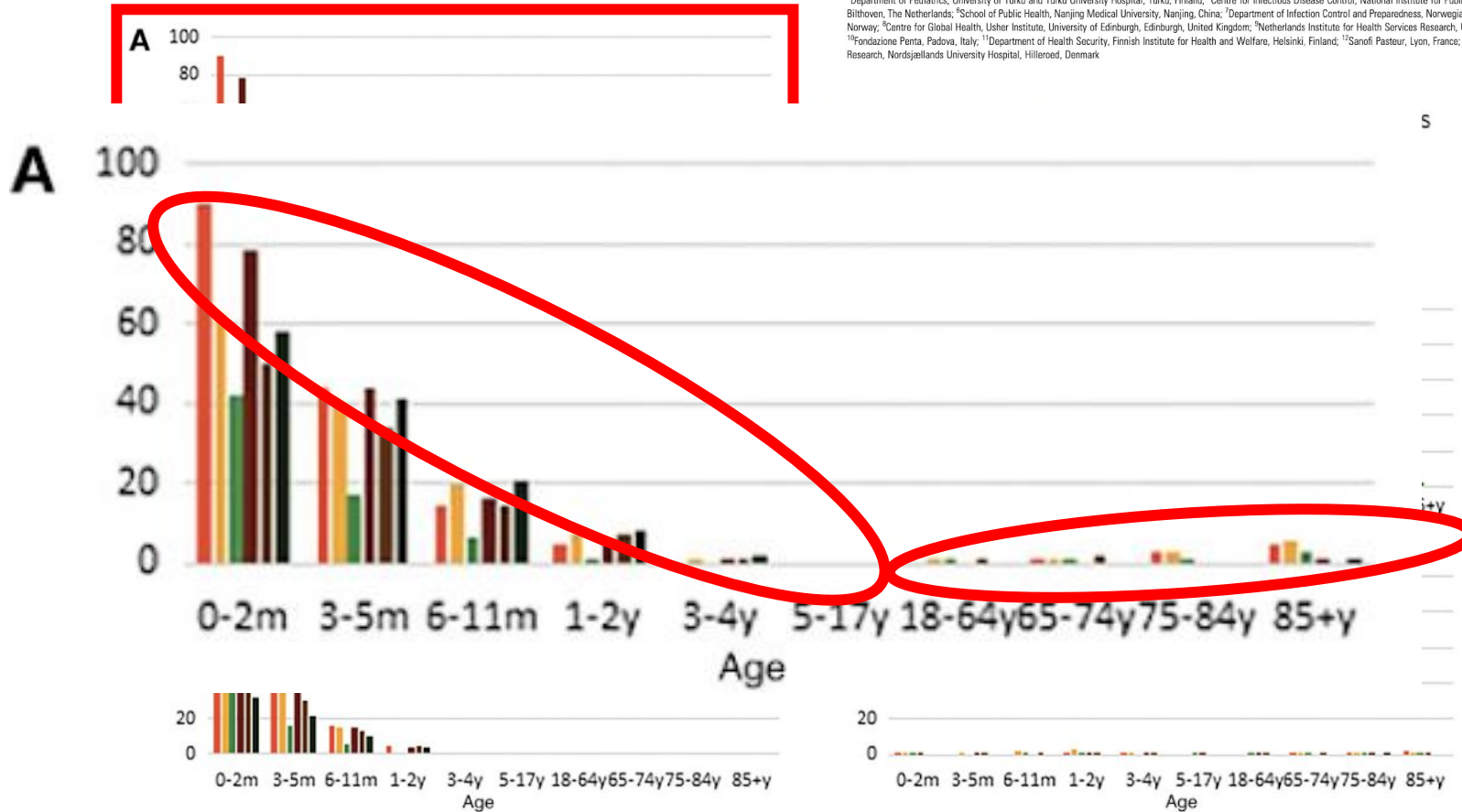


Figure 2: Burden of RSV-associated ALRI in infants aged 0–6 months in LMICs by severity and outcome including burden on health-care services
ALRI=acute lower respiratory infection. CFR=case fatality ratio. LMICs=low and middle income countries. RSV=respiratory syncytial virus. UR=uncertainty range.

Age-Specific Estimates of Respiratory Syncytial Virus-Associated Hospitalizations in 6 European Countries: A Time Series Analysis

Caroline K. Johannesen,^{1,6} Maarten van Wijhe,^{1,6} Sabine Tong,² Liliانا V. Fernández,³ Terho Heikkinen,⁴ Michiel van Boven,^{5,6} Xin Wang,⁶ Håkon Boås,⁷ You Li,^{8,9} Harry Campbell,^{8,9} John Paget,⁹ Luca Stona,¹⁰ Anne Teirlinck,² Toni Lehtonen,¹¹ Hanna Nohynek,¹¹ Mathieu Bangert,¹² and Thea K. Fischer,¹³ for the RESCEU Investigators¹

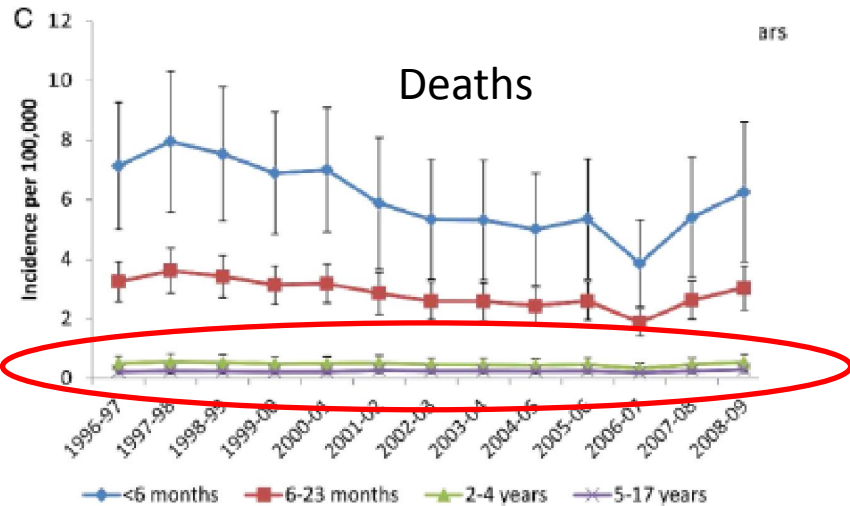
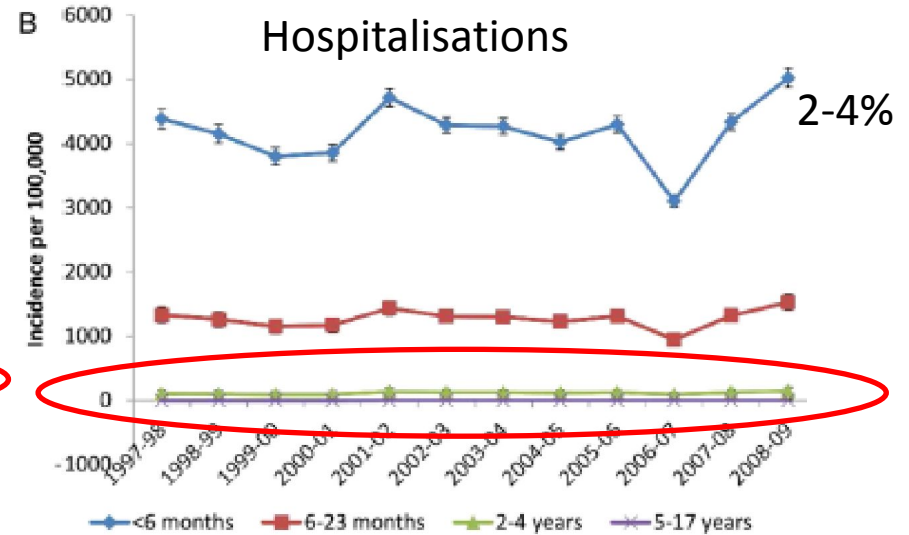
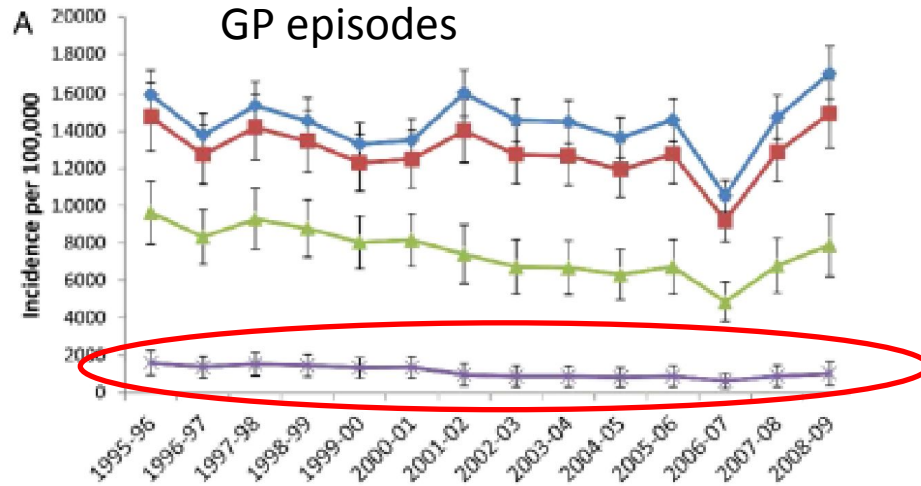
¹Statens Serum Institut, Copenhagen, Denmark; ²Sanofi, Chilly-Mazarin, France; ³Department of Methods Development and Analytics, Norwegian Institute of Public Health, Oslo, Norway; ⁴Department of Pediatrics, University of Turku and Turku University Hospital, Turku, Finland; ⁵Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, The Netherlands; ⁶School of Public Health, Nanjing Medical University, Nanjing, China; ⁷Department of Infection Control and Preparedness, Norwegian Institute of Public Health, Oslo, Norway; ⁸Centre for Global Health, Usher Institute, University of Edinburgh, Edinburgh, United Kingdom; ⁹Netherlands Institute for Health Services Research, Utrecht, The Netherlands; ¹⁰Fondazione Penta, Padova, Italy; ¹¹Department of Health Security, Finnish Institute for Health and Welfare, Helsinki, Finland; ¹²Sanofi Pasteur, Lyon, France; and ¹³Department of Clinical Research, Nordsjællands University Hospital, Hillerød, Denmark



S

Figure 2. Age-group-specific incidence rates of hospitalizations associated with respiratory syncytial virus per year per 1000: (A) all hospitalizations with respiratory infections, (B) hospitalizations with acute upper respiratory tract infection, (C) hospitalizations with pneumonia and influenza, (D) hospitalizations with bronchitis and bronchiolitis, (E) hospitalizations with unspecified lower respiratory infection.

RSV in older children (UK)



Green et al, ADC, 2015; Taylor et al, BMJ Open, 2016

Modelled estimates of hospitalisations attributable to respiratory syncytial virus and influenza in Australia, 2009–2017

Allen L. Nazareno^{1,2}  | David J. Muscatello¹ | Robin M. Turner³ |
James G. Wood¹ | Hannah C. Moore⁴ | Anthony T. Newall¹

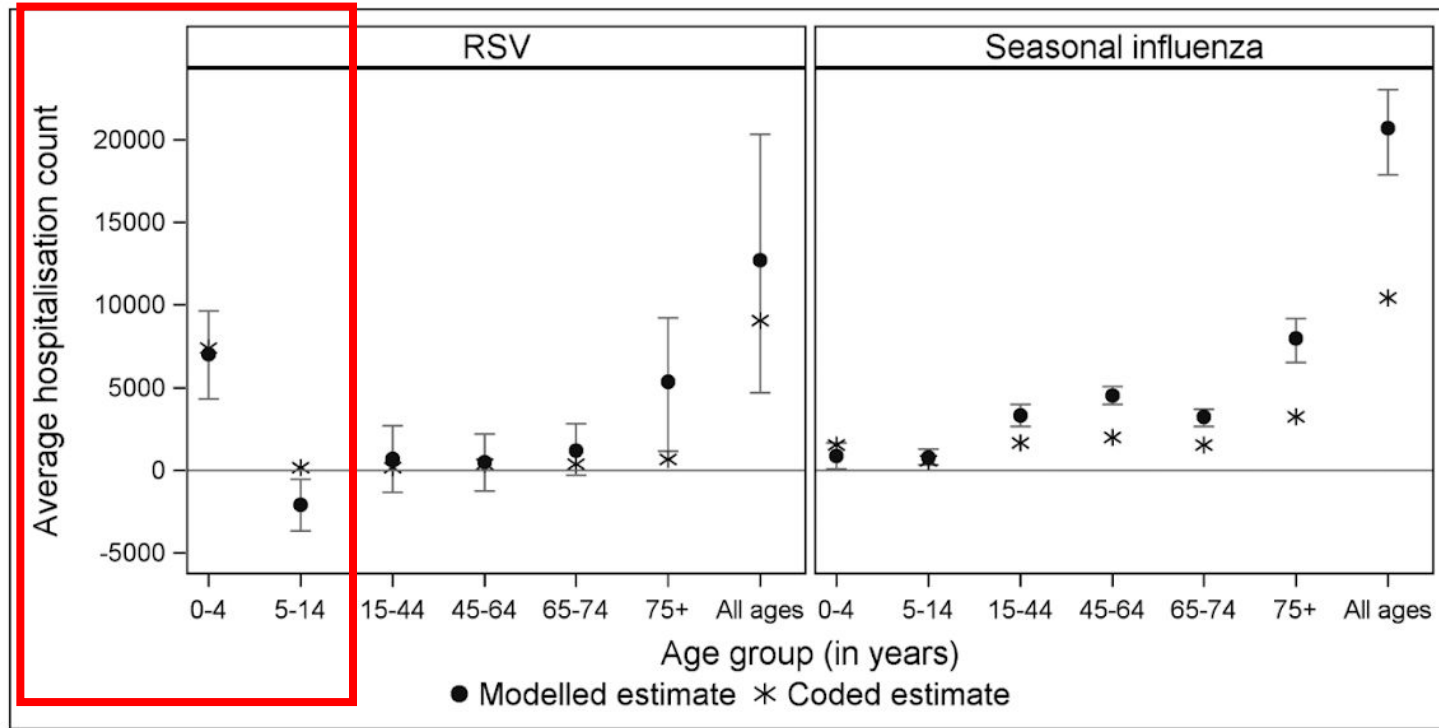


FIGURE 2 Comparison of the average annual estimate of modelled (attributable) and coded hospitalisations (any diagnosis field) from 2009 to 2017 for RSV and 2010 to 2017 for seasonal influenza, by age group, Australia. RSV, respiratory syncytial virus

High risk groups

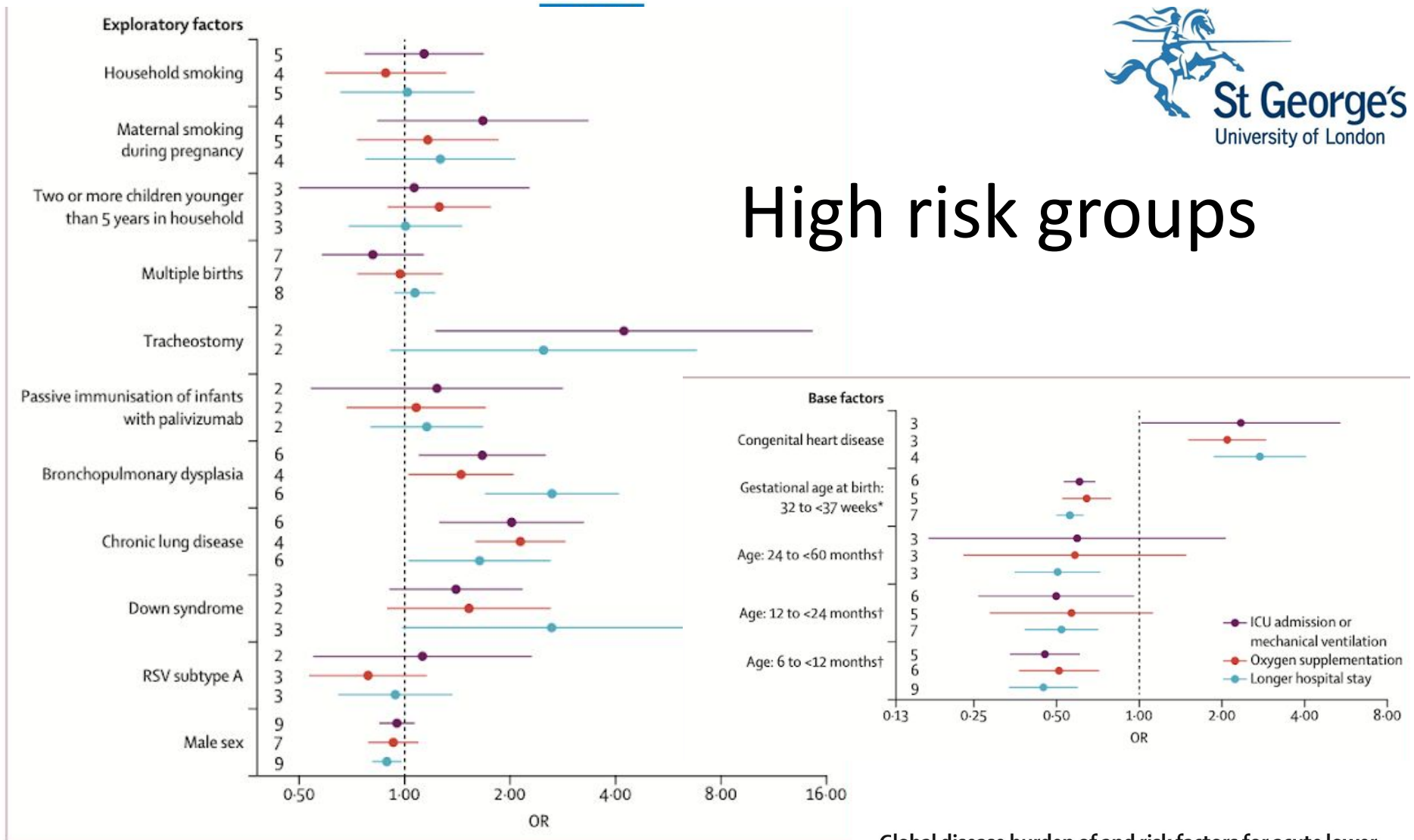


Figure 3: Risk factors for severe outcomes from RSV-associated ALRI requiring hospital admission
ORs calculated from meta-analysis results. Points indicate ORs and whiskers indicate 95% CIs. Base factors refer to factors that were fixed in individual regression models, determined a priori; exploratory factors refer to factors that were assessed individually in models with all base factors. Numbers on the left denote the number of studies contributing to the meta-estimates. Note that scales on the x axes differ between plots. ALRI=acute lower respiratory infection. ICU=intensive care unit. RSV=respiratory syncytial virus. OR=odds ratio. *With gestational age at birth of less than 32 weeks as reference. †With age between 0 months and less than 6 months as reference.

Global disease burden of and risk factors for acute lower respiratory infections caused by respiratory syncytial virus in preterm infants and young children in 2019: a systematic review and meta-analysis of aggregated and individual participant data

Xin Wang*, You Li*, Ting Shi, Louis J Bant, Helen Y Chu, Heather J Zar, Bhanu Wahi-Singh, Yiming Ma, Bingbing Cong, Emma Sharland, Richard D Riley, Jikui Deng, Josep Figueras-Aloy, Terho Heikkinen, Marcus H Jones, Johannes G Liese, Joško Markić, Asuncion Mejias, Marta C Nunes, Bernhard Resch, Ashish Satav, Kee Thai Yeo, Eric A F Simões, Harish Nair, Respiratory Virus Global Epidemiology Network†, for the RESCEU investigators†

Upper respiratory tract infections

Respiratory tract infections and viral causative agents in children

Disease	Adenoviruses	Coronaviruses	Enteroviruses	Influenza viruses	Parainfluenza viruses	RSV^a	Rhinoviruses
Common cold	+	++	++	++	+	+	+++
Tonsillitis	+++	-	++	+	+	+	-
Laryngitis	+	-	+	++	+++	+	+
Bronchitis	+	+	+	+++	++	+++	+
Bronchiolitis	+	+	+	++	++	+++	++
Pneumonia	+	+	+	+++	++	+++	++

Int J Pediatr Otorhinolaryngol. 2006 Aug; 70(8): 1333–1342.

- Acute otitis media developed in 103 (76.9%) of 134 infants with RSV infection.

J Infect Dis. 2021 Mar 3;223(5):811-817.

Research

Open Access

Extrapulmonary manifestations of severe respiratory syncytial virus infection – a systematic review

Michael Eisenhut



Hepatitis (46–49% of ventilated infants)



Elevated cardiac troponin levels (35–54% of ventilated infants)



Cardiac arrhythmias e.g. SVT, VT



Hyponatraemia (33%)



Local and generalized seizures, focal neurological abnormalities (overall 1.2% get neurological manifestations)



Central apnoeas (16–21% of admissions)

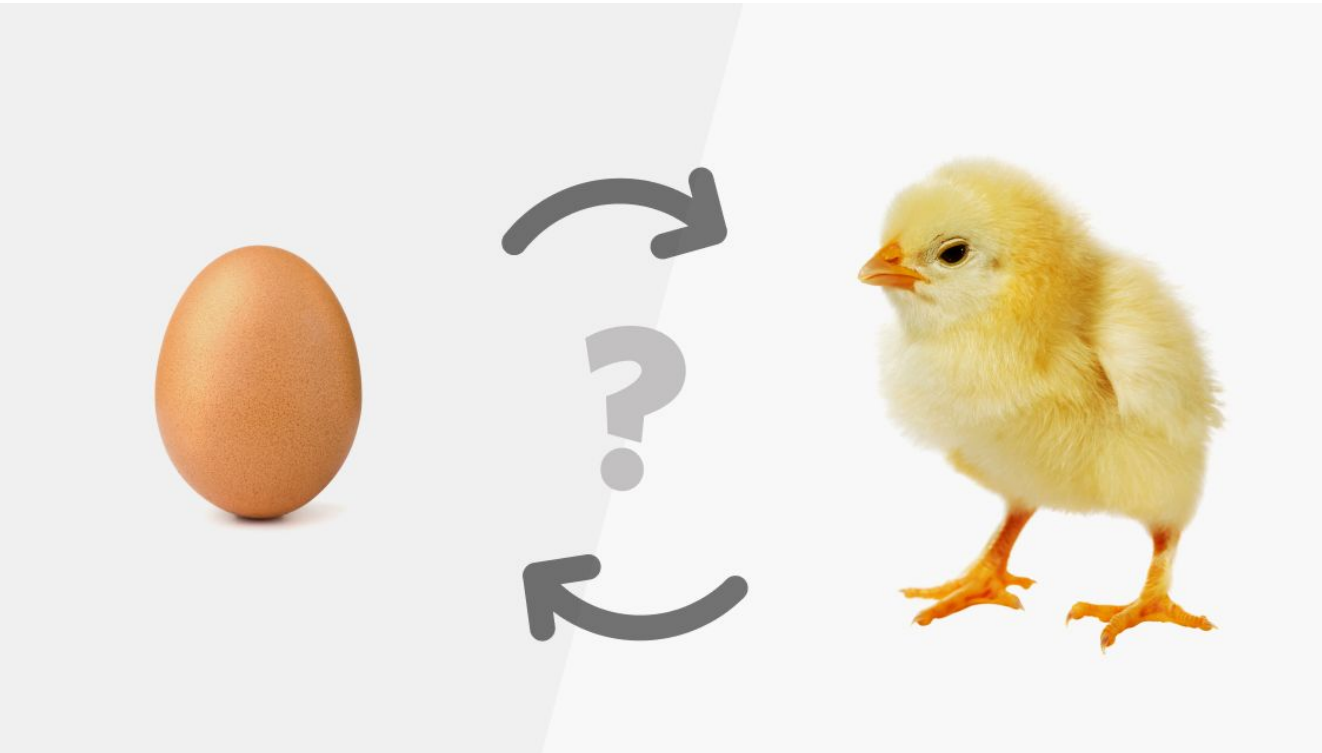
Association Between Respiratory Syncytial Virus-Associated Acute Lower Respiratory Infection in Early Life and Recurrent Wheeze and Asthma in Later Childhood

Ting Shi,^{1,a} Yujing Ooi,^{1,a} Ei Mon Zaw,¹ Natasa Utjesanovic,¹ Harry Campbell,^{1,e} Steve Cunningham,^{2,3} Louis Bont,^{4,5} and Harish Nair^{1,5,g}; for the RESCEU Investigators^b

¹Centre for Global Health, Edinburgh, The Netherlands

Table 1. Metaanalysis Group and Follow-up

Follow-up Age, mo
RSV vs no respiratory
<36
36–72
>72
RSV vs other pathogen
<36
36–72
>72
RSV vs rhinovirus
<36
36–72
>72



Stratified by Control

OR (95% CI)
...
...
2.95 (1.96–4.46)
...
1.28 (0.84–1.95)
0.54 (0.28–1.06)

<36	0	...	1	...
36–72	3	0.41 (0.20–0.83)	1	...
>72	0	...	1	...

Abbreviations: CI, confidence interval; OR, odds ratio; RSV, respiratory syncytial virus.

Quality of Life

Zhuxin Mao^{a,*}, Xiao Li^a, Ana Dacosta-Urbieto^{b,c,d}, Marie-Noëlle Billard^e, Joanne Wildenbeest^e, Koos Korsten^{f,g}, Federico Martín-Torres^{b,c,d}, Terho Heikkinen^h, Steve Cunninghamⁱ, Matthew D. Snape^j, Hannah Robinson^j, Andrew J. Pollard^j, Maarten Postma^{k,l,m}, Benoit Dervauxⁿ, Niel Hens^{a,o}, Louis Bont^{f,p}, Joke Bilcke^a, Philippe Beutels^a, for RESCEU investigators

• Of 1041 infants with a mean symptom duration of 10 days

Table 3
Average QALD loss of infants and caregivers

Category	Value
Infant	0.01
By healthcare resource use*	0.01
By country	0.01
By caregiver	0.01
Caregivers	0.01
By healthcare resource use	0.01
By country	0.01
By caregiver	0.01

* Two episodes did not have health confidence interval; Q1, first interquartile range

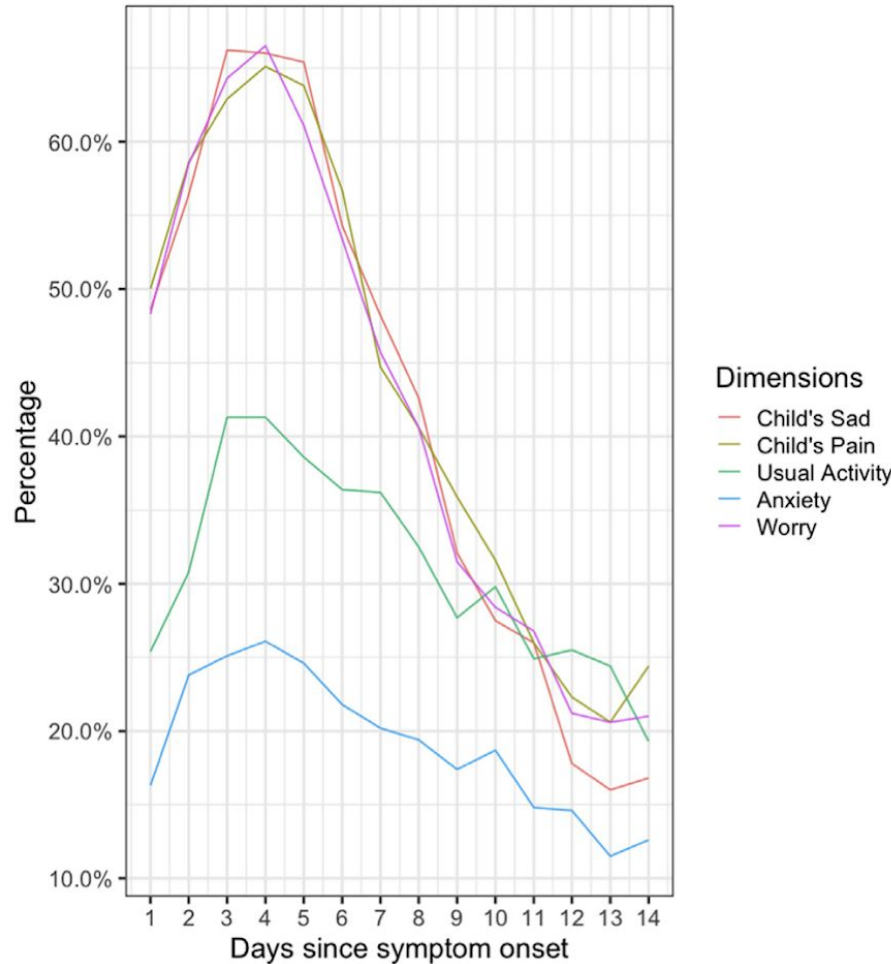


Fig. 2. Proportions of participants having any problem in 5 health dimensions (2 for children and 3 for caregivers).

problems with a

Dimension	Number
Child's Sad	180
Child's Pain	81
Usual Activity	90
Anxiety	7
Worry	36
Child's Sad	14
Child's Pain	76
Usual Activity	54
Anxiety	146
Worry	8
Child's Sad	164
Child's Pain	75
Usual Activity	81
Anxiety	6
Worry	33
Child's Sad	14
Child's Pain	69
Usual Activity	48
Anxiety	133
Worry	8

non-MA, non-medical attendance; CI, confidence interval

[Rand Health Q.](#) 2022 Nov; 10(1): 2.
Published online 2022 Nov 14.

PMCID: PMC9718057
PMID: [36484078](#)

The Burden of Respiratory Syncytial Virus: Understanding Impacts on the NHS, Society and Economy

[Francesco Fusco](#), [Lucy Hocking](#), [Stephanie Stockwell](#), [Margaretha Bonsu](#), [Sonja Marjanovic](#), [Stephen Morris](#), and [Jon Sussex](#)

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Short abstract

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Respiratory syncytial virus (RSV) is a significant burden on the healthcare system and on children and their parents and caregivers. We estimate RSV in children under 5 in the UK costs £80 million each year: £14 million of productivity losses, £1.5 million of out-of-pocket expenses for parents/carers, and £65 million of healthcare costs.

Economic costs

Cost of Respiratory Syncytial Virus-Associated Acute Lower Respiratory Infection Management in Young Children at the Regional and Global Level: A Systematic Review and Meta-Analysis



Shanshan Zhang,¹ Lily Zainal Akmar,¹ Freddie Bailey,¹ Barbara A. Rath,² Maren Alchikh,³ Brunhilde Schweiger,² Marilla G. Lucero,⁴ Leilani T. Nillos,⁴ Moe H. Kyaw,⁵ Alexia Kieffer,⁶ Sabine Tong,⁷ Harry Campbell,^{1,8} Philippe Beutels,⁹ and Harish Nair¹⁰; for the RESCEU Investigators^{*}

¹Centre for Global Health, Usher Institute, University of Edinburgh, Edinburgh, United Kingdom, ²Vienna Vaccine Safety Initiative, Berlin, Germany, ³National Reference Centre for Influenza, Robert Koch Institute, Berlin, Germany, ⁴Research Institute for Tropical Medicine, Alabang, Muntinlupa City, Philippines, ⁵Sanofi Pasteur, Swiftwater, Pennsylvania, USA, ⁶Sanofi Pasteur, Lyon, France, ⁷VIDATA Stats, Levallois-Perret, France, ⁸Universiteit Antwerpen, Antwerpen, Belgium, ⁹RESNET Foundation, Zeist, The Netherlands

- 41 studies; 365,828 RSV episodes (<5yo); mainly high-income countries
- The global cost of RSV ALRI management in young children in 2017 was estimated to be approximately **€4.82 billion** (95% CI, 3.47–7.93)
- (NB: There are ~680m children <5yo globally; **€7 per child**)
- 65% of these in LMICs countries; 55% due to hospitalization
- Average cost per episode:
 - **€3452 (95% CI, 3265–3639)** for inpatients without follow up
 - **€299 (95% CI, 295–303)** for outpatients without follow-up
 - **€8591 (95% CI, 8489–8692) and €2191 (95% CI, 2190–2192)** with 2y follow-up
- Known risk factors (preterm birth, congenital heart/lung disease, ICU admission) were associated with **€4160 (95% CI, 3237–5082)** increased cost of hospitalization.

Summary

- RSV is a cause of huge global morbidity and mortality in young children
 - >100,000 deaths in those <5y

- Those with co-morbidities at highest risk
 - Esp. prematurity and cardiac disease

- There is a massive healthcare and societal cost
 - €4.82 billion healthcare costs in those <5y

