RSV profylakse med maternel vaccine eller langvarige monoklonale antistoffer: Datagrundlag

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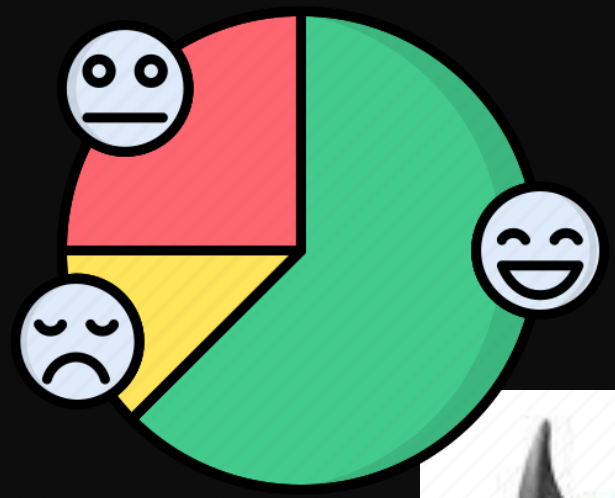

Historik

- Vaccineafprøvning til spædbørn 1969 medførte forværret RSV-sygdom inkl. 2 dødsfald, som med sikkerhed kunne tilskrives alvorlig RSV
- Brugen af palivizumab, et monoklonalt antistof som skal gives ved cirka 5 månedlige injektioner, har været begrænset af høj pris, besværlig administration og begrænset effekt
  - 1998 Impact RSV Study Group: 55% reduktion af RSV-indlæggelse blandt præmature < 35 GA, 78% uden BPD, 39% med BPD
  - 2003 Cardiac Study Group: 45% reduktion af RSV-indlæggelse blandt børn med hæmodynamisk betydende medfødt hjertesygdom

Nirsevimab (Beyfortus)

Study design, number of participants and year	Primary effect results	Secondary effect results	Safety	Funds	Designation, PMID and comments
RCT, N=8058, 1:1, infants ≥ 29 GA, one season, published 2024	RSV LRTI hospitalisation: 11/4037 (0.3%) vs. 60/4021 (1.5%) = 83.2 efficacy	”Very severe” (SAT < 90% and oxygen) 75.7% Germany 74.2%	Day 31. Serious AE 2.2 vs. 1.7, 1 related	Sanofi Astra Zeneca	HARMONIE, PMID: 38157500 Drysdale Europe, open-label, exclusion criteria, 2022/2023 RSV sæson
RCT, N=3012, 2:1, ≥ 35 GA, 150 days, published 2023	Medically attended RSV LRTI: 24/2009 (1.2%) vs. 54/1003 (5.4) = 76.4% efficacy	RSV LRTI hospitalisation 76.8%	Related adverse events 1.3 vs. 1.5%	Sanofi Astra Zeneca	MELODY, PMID: 37018470 Muller Multiplicity
RCT, N=1490, 2:1, ≥ 35 GA, 150 days, published 2022	Medically attended RSV LRTI: 12/994 (1.2%) vs. 25/496 (5.0%) = 74.5% efficacy	RSV LRTI hospitalisation 62.1%	Serious AE 6.8% vs. 7.3%	MEDIMMUNE Astra Zeneca Sanofi	MELODY, PMID: 35235726, Hammitt Antidrug antibodies, high RSV rate, exclusion criteria
RCT, N=1453 2016-2017, 2:1, preterm 29-34 GA, published 2020	Medically attended RSV LRTI: 25/969 (2.6%) vs. 46/484 (9.5%) = 70.1% efficacy	RSV LRTI hospitalisation 78.4%	Serious AE 11.2% vs. 16.9, 2 vs. 3 deaths	Sanofi Astra Zeneca	MELODY, PMID: 32726528, Griffin PMID: 38219024 follow-up for enhanced RSV PMID: 37095249 follow-up for natural immunity to RSV
Observational population-based cohort, N=10259, 9408 got nirsevimab, published 2024	RSV hospitalisation: 16/851 (1.9%) vs. 30/9408 (0.3%) = 82.0 effectiveness	Severe RSV LRTI 86.9% 69.2% LRTI 66.2% against all-cause hospitalisation	NA	Sanofi Astra Seneca	NIRSE-GAL PMID: 38701823 Healthy-wealthy vaccinée bias. Non-comparable comparison groups

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HARMONIE – selection og supeior popultation?

125 **Methods**

126 **Participants**

127 Healthy infants ≤12 months old, born ≥29 weeks gestational age entering their first
128 RSV season (born either in-season or out-of-season [see footnote to Table 1][17-19])
129 were eligible for inclusion. Exclusion criteria included eligibility to receive
130 palivizumab to minimize interference with routine practice; the intention was to
131 recruit a wide range of infants not currently eligible for RSV prophylaxis with
132 palivizumab. Other inclusion and exclusion criteria are described in the
133 supplementary appendix.

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Exclusion criteria

- Meets national or other local criteria to receive commercial palivizumab.
- Any fever (≥38.0°C, regardless of route) or acute illness within 7 days prior to randomization.
- Any history of lower respiratory tract infection (LRTI) or active LRTI prior to, or at the time of, randomization.
- Known history of RSV infection or active RSV infection prior to, or at the time of, randomization.
- Any drug therapy (chronic or other) within 7 days prior to randomization or expected receipt during the trial with the exception of: (a) multivitamins and iron; (b) infrequent use of over-thecounter medications for the systemic treatment of common childhood symptoms (e.g., pain relievers) that may be permitted according to the judgment of the investigator.
- Any current or expected receipt of immunosuppressive agents, including steroids (except for the use of topical steroids according to the judgment of the investigator).
- History of receipt of blood, blood products, or immunoglobulin products, or expected receipt through the duration of the trial.
- Receipt of any investigational drug.
- Known renal impairment.
- Known hepatic dysfunction, including known or suspected active or chronic hepatitis infection.
- History of chronic lung disease/bronchopulmonary dysplasia.
- Clinically significant congenital anomaly of the respiratory tract.
- Chronic seizure or evolving or unstable neurologic disorder.
- Congenital heart disease (CHD), except for children with uncomplicated CHD (e.g., patent ductus arteriosus, small septal defect).
- Prior history of a suspected or actual acute life-threatening event.
- Known immunodeficiency, including human immunodeficiency virus (HIV).
- Mother with HIV infection (unless the child has been proven to be not infected).
- Any known allergy, including to immunoglobulin products, or history of allergic reaction.
- Receipt of palivizumab or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination.
- Receipt of any monoclonal or polyclonal antibody (e.g., hepatitis B immune globulin, intravenous

HARMONIE – open label bias?

270 All-cause LRTI hospitalizations occurred in 45 (1.1%) infants in the nirsevimab group
271 (4 per 1,000 person-months) and 98 (2.4%) infants in the no intervention group (10
272 per 1,000 person-months) through the RSV season, corresponding to an efficacy of
273 58.0% (nominal 95% CI, 39.7 to 71.2) for nirsevimab.

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HARMONIE – 61% because of 2022/2023 season?

318 been randomized. Of note, HARMONIE also confirms that RSV contributes to a

319 sizable burden of all-cause LRTI hospitalizations as demonstrated in the no

320 intervention group (61%; 60/98). In addition, HARMONIE built on the existing data

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HARMONIE

The HARMONIE study was designed to be event driven. It was initially planned to enrol 28,860 participants based on a number of factors, including country-specific epidemiological data from previous RSV seasons, using conservative estimates for the incidence (1.1%), and efficacy to ensure sufficient power for the primary hospitalization endpoint at country level.[22-24] The attack rate during the study (2022/2023 RSV season), after relaxation of non-pharmaceutical interventions imposed by the COVID-19 pandemic, was higher than assumed. Together with the

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NIRSE-GAL

Effectiveness and impact of universal prophylaxis with nirsevimab in infants against hospitalisation for respiratory syncytial virus in Galicia, Spain: initial results of a population-based longitudinal study

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Summary

Background Galicia (Spain) was one of the first regions worldwide to incorporate nirsevimab for universal respiratory syncytial virus (RSV) prophylaxis in infants into its immunisation programme. The NIRSE-GAL longitudinal population-based study aimed to assess nirsevimab effectiveness in preventing hospitalisations (ie, admittance to hospital).

Methods The 2023–24 immunisation campaign with nirsevimab in Galicia began on Sept 25, 2023, and concluded on March 31, 2024. The campaign targeted three groups: infants born during the campaign (seasonal group), infants younger than 6 months at the start of the campaign (catch-up group), and infants aged 6–24 months with high-risk factors at the start of the campaign (high-risk group). Infants in the seasonal group were offered immunisation on the first day of life before discharge from hospital. Infants in the catch-up and high-risk groups received electronic appointments to attend a public hospital or health-care centre for nirsevimab administration. For this interim analysis, we used data collected from Sept 25 to Dec 31, 2023, from children born up to Dec 15, 2023. Data were retrieved from public health registries. Nirsevimab effectiveness in preventing RSV-associated lower respiratory tract infection (LRTI) hospitalisations; severe RSV-related LRTI requiring intensive care unit admission, mechanical ventilation, or oxygen support; all-cause LRTI hospitalisations; and all-cause hospitalisations was estimated using adjusted Poisson regression models. Data from five past RSV seasons (2016–17, 2017–18, 2018–19, 2019–20, and 2022–23), excluding the COVID-19 pandemic period, were used to estimate the number of RSV-related LRTI hospitalisations averted along with its IQR. The number needed to immunise to avoid one case in the 2023–24 season was then estimated from the averted cases. Nirsevimab safety was routinely monitored. The NIRSE-GAL study protocol was registered on ClinicalTrials.gov (NCT06180993), and follow-up of participants is ongoing.

Findings 9408 (91·7%) of 10 259 eligible infants in the seasonal and catch-up groups received nirsevimab, including 6220 (89·9%) of 6919 in the catch-up group and 3188 (95·4%) of 3340 in the seasonal group. 360 in the high-risk group were offered nirsevimab, 348 (97%) of whom received it. Only infants in the seasonal and catch-up groups were included in analyses to estimate nirsevimab effectiveness and impact because there were too few events in the high-risk group. In the catch-up and seasonal groups combined, 30 (0·3%) of 9408 infants who received nirsevimab and 16 (1·9%) of 851 who did not receive nirsevimab were hospitalised for RSV-related LRTI, corresponding to an effectiveness of 82·0% (95% CI 65·6–90·2). Effectiveness was 86·9% (69·1–94·2) against severe RSV-related LRTI requiring oxygen support, 69·2% (55·9–78·0) against all-cause LRTI hospitalisations, and 66·2% (56·0–73·7) against all-cause hospitalisations. Nirsevimab effectiveness against other endpoints of severe RSV-related LRTI could not be estimated because of too few events. RSV-related LRTI hospitalisations were reduced by 89·8% (IQR 87·5–90·3), and the number needed to immunise to avoid one RSV-related LRTI hospitalisation was 25 (IQR 24–32). No severe adverse events related to nirsevimab were registered.

Interpretation Nirsevimab substantially reduced infant hospitalisations for RSV-associated LRTI, severe RSV-associated LRTI requiring oxygen, and all-cause LRTI when given in real-world conditions. These findings offer policy makers and health authorities robust, real-world, population-based evidence to guide the development of strategies for RSV prevention.

NIRSE-GAL

	Overall (N=10 259)	Nirsevimab recipients (n=9408)	Nirsevimab non-recipients (n=851)	p value
Age, months				
Mean (SD)	4·22 (2·44)	4·14 (2·44)	5·05 (2·29)	<0·001*
Median (Q1–Q3)	4·00 (2·00–6·00)	4·00 (2·00–6·00)	5·00 (3·00–7·00)	<0·001†
Age categories, months	..	..	..	<0·001‡
≤3	4279 (41·7%)	4064 (43·2%)	215 (25·3%)	..
>3 to 6	3677 (35·8%)	3311 (35·2%)	366 (43·0%)	..
>6	2303 (22·4%)	2033 (21·6%)	270 (31·7%)	..
Sex	..	..	..	0·245‡
Female	5060 (49·3%)	4657 (49·5%)	403 (47·4%)	..
Male	5199 (50·7%)	4751 (50·5%)	448 (52·6%)	..
Enrolment group	..	..	..	<0·001‡
Catch-up§	6919 (67·4%)	6220 (66·1%)	699 (82·1%)	..
Seasonal¶	3340 (32·6%)	3188 (33·9%)	152 (17·9%)	..
Weight at birth, grams				
Mean (SD)	3230 (520)	3220 (519)	3270 (530)	0·015*
Median (Q1–Q3)	3260 (2940–3560)	3250 (2940–3560)	3290 (3000–3590)	0·016†
Data missing (%)	309 (3·0%)	216 (2·3%)	93 (10·9%)	..
Gestational age at birth, weeks				
Mean (SD)	39·0 (1·74)	39·0 (1·75)	39·1 (1·68)	0·270*
Median (Q1–Q3)	39·0 (38·0–40·0)	39·0 (38·0–40·0)	39·0 (38·0–40·0)	0·623†
Data missing (%)	323 (3·1%)	227 (2·4%)	96 (11·3%)	..
Preterm	..	..	..	0·154‡
No (≥37 weeks)	9280 (90·5%)	8565 (91·0%)	715 (84·0%)	..
Yes (<37 weeks)	656 (6·4%)	616 (6·5%)	40 (4·7%)	..
Data missing	323 (3·1%)	227 (2·4%)	96 (11·3%)	..
Healthy Child programme visits	..	..	..	<0·001‡
≥1	9527 (92·9%)	8810 (93·6%)	717 (84·3%)	..
0	732 (7·1%)	598 (6·4%)	134 (15·7%)	..
Residential area	..	..	..	0·207‡
North	5954 (58·0%)	5478 (58·2%)	476 (55·9%)	..
South	4305 (42·0%)	3930 (41·8%)	375 (44·1%)	..

Data are n (%) unless otherwise stated. *p value from Student's t-test. †p value from Wilcoxon rank sum test. ‡p value from χ^2 test. §Birth dates between April 1 and Sept 24, 2023. ¶Birth dates between Sept 25 and Dec 15, 2023.

Table 1: **Demographic characteristics of infants born between April 1 and Dec 15, 2023, who were eligible for immunisation with nirsevimab**

NIRSE-GAL

Title:

Too good to be true: when effectiveness exceeds efficacy

Severe infection with respiratory syncytial virus (RSV) is a leading cause of pediatric hospitalization.[1] Randomized clinical trials have shown that passive prophylaxis with the monoclonal antibody nirsevimab has a protective efficacy of 70% to 80% against RSV hospitalization, which is promising.[2]

However, a recent observational study published in The Lancet Infectious Disease found that the effectiveness of nirsevimab exceeded the efficacy observed in trials, which is unusual.[3] Additionally, non-specific protective effects against all-cause respiratory infections and even all-cause hospitalization were observed.[3] Given the well-known healthy-and-wealthy-vaccinee bias,[4] caution is warranted regarding such potentially too-good-to-be-true signals.

Scrutinizing Table 1 reveals clear differences between nirsevimab recipients and non-recipients: high proportions of missing data on severe RSV risk factors such as birth weight, gestational age, and preterm birth, and a high proportion of zero Healthy Child program visits in the nirsevimab non-recipient group.

Bias is an inherent challenge in observational studies, especially when studying vaccine effects. While emulated trial designs can mitigate bias risk,[5] residual confounding may still be present. The healthy-and-wealthy-vaccinee bias arises from systematic differences between vaccine recipients and non-recipients, with the former typically having better health and wealth. This bias can significantly inflate estimates of protective vaccine effects, leading to seemingly miraculous findings, such as the observed protective effect of nirsevimab against all-cause hospitalization. However, I believe such findings are likely explained by the healthy-and-wealthy-vaccinee bias.

References

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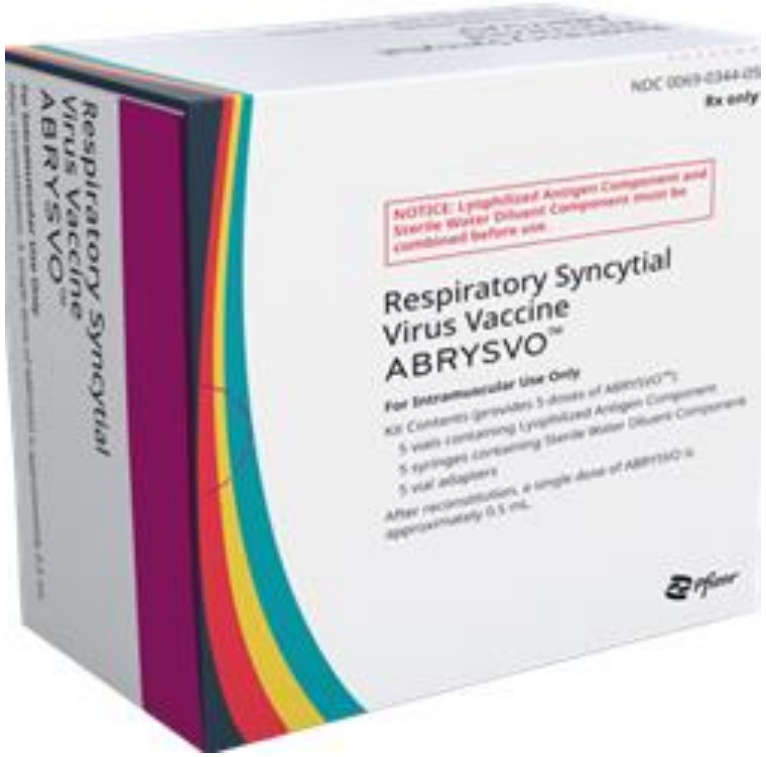
3. Ares-Gomez S, Mallah N, Santiago-Perez MI, et al. Effectiveness and impact of universal prophylaxis with nirsevimab in infants against hospitalisation for respiratory syncytial virus in Galicia, Spain: initial results of a population-based longitudinal study. *Lancet Infect Dis* 2024.
4. Remschmidt C, Wichmann O, Harder T. Frequency and impact of confounding by indication and healthy vaccinee bias in observational studies assessing influenza vaccine effectiveness: a systematic review. *BMC Infect Dis* 2015; **15**: 429.
5. Kildegaard H, Lund LC, Pottegard A, Stensballe LG. Effectiveness of the quadrivalent live attenuated influenza vaccine against influenza-related hospitalisations and morbidity among children aged 2 to 6 years in Denmark: a nationwide cohort study emulating a target trial. *Lancet Child Adolesc Health* 2023; **7**(12): 852-62.

Nirsevimab summary

- Forvent beskyttende effekt
- Forvent mindre beskyttende effekt end fundet i RCT og observationelt
  - 60 (-70%) hos i øvrigt raske danske børn
  - (30-) 50% hos risikobørn (som for palivizumab)
- Number needed to vaccinate (HARMONIE)
  - Jo lavere forekomst des højere NNT
  - ARR = Placebo event rate – Nirsevimab event rate = 0.015 – 0.003 = 0.012
  - NNT = 1/ARR = 83 dvs. ≈ 100+ raske børn og ≈50 for højrisikobørn

Maternal RSV-vaccine (Abrysvo/RSVPreF3-Mat)



Maternal RSV-neutralising antibodies

PMID: 19150677 (2009)

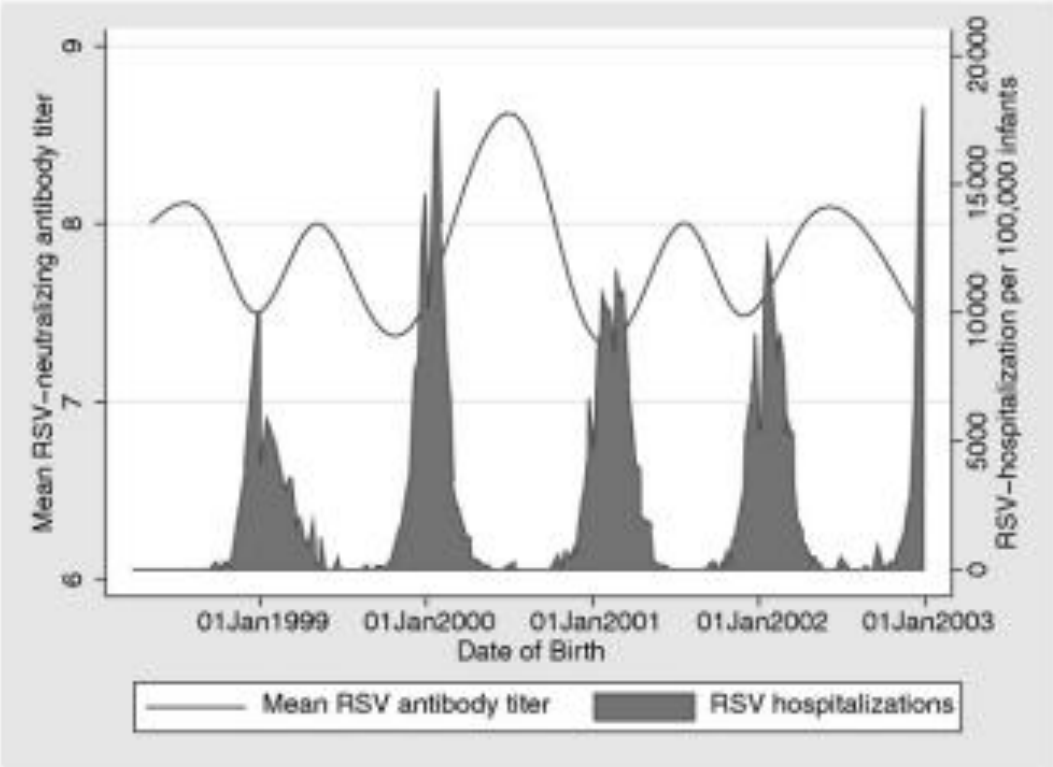


Figure. The titer of maternally derived RSV-neutralizing antibody in 457 cord blood samples from Danish infants born 1998-2003 and incidence of RSV hospitalization per 100 000 Danish infants younger than 6 months of age 1998-2003. Note: The mean RSV antibody titer expressed to the log base 2 is presented by use of the cubic spline technique and based on 58 infants born in 1998, 92 infants in 1999, 112 infants in 2000, 110 infants in 2001, and 85 in 2002.

Study design, number of participants and year	Primary effect results	Secondary effect results	Safety	Funds	Designation and PMID, N=
RCT 1:1, DOB-90-120-150-180 dage, 3682 og 3676 mødre	90 dage: Medically attended *severe* RSV-associated lower respiratory tract illness 6/3495 (0.17%) vs. 33/3480 (0.95%)= efficacy 81.8% NNT 128 180 dage 69.4%	90 dage: RSV hospitalization 10/3495(0.3) vs. 31/3480 (0.9)=67.7% NNT 167 180 dage: RSV hospitalization 56.8% NNT 125	Prematurity 5.6% vs. 4.7%	Pfizer	MATISSE PMID: 37018474
RCT 2:1, 5328 mødre, DOB-6 mdr-12mdr	6 måneder, severe RSV 8/3426 14/1711 69% Medically attended RSV-associated lower respiratory tract illness 16/3426 24/1711 Efficacy 65.6%		Prematurity 6.8% vs 4.9%	GlaxoSmith Cline	PMID: 38477988

MATISSE exclusion criteria

Inkluderer raske, normale gravide uden IVF eller risikofaktorer herunder for preterm fødsel

Eligibility Criteria

Healthy participants, as determined by medical history, physical examination, and clinical judgment, were eligible for inclusion in the study. Participants were receiving prenatal standard of care based on country requirements; had a fetal anomaly ultrasound examination performed at ≥18 weeks of pregnancy with no significant abnormalities observed; and had a documented negative HIV antibody test, syphilis test, and hepatitis B virus surface antigen test during the current pregnancy and before randomization.

Participants were excluded if they had bleeding diathesis or a condition associated with prolonged bleeding; a history of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the product or any related vaccine; or a major illness of the maternal participant or conditions of the fetus that, in the investigator's judgment, would substantially increase the risk associated with the maternal or infant participant's participation in and completion of the study or could preclude the evaluation of the maternal participant's response (includes positive serologic testing for regional endemic conditions assessed during routine maternal care, as per local standards of care and obstetric recommendations).

Exclusion criteria related to the current pregnancy included in vitro fertilization; pregnancy complications or abnormalities at the time of consent that would increase the risk associated with participation in and completion of the study (including but not limited to preeclampsia, eclampsia, or uncontrolled gestational hypertension; placental abnormality; polyhydramnios or oligohydramnios; significant bleeding or a blood clotting disorder; endocrine disorders, including untreated hyperthyroidism or untreated hypothyroidism or disorders of glucose intolerance antedating pregnancy or occurring during pregnancy if uncontrolled at the time of consent; any signs of premature labor with the pregnancy or having ongoing intervention [medical/surgical] to prevent preterm birth).

Exclusion criteria related to prior pregnancies included those that would increase the risk associated with the participation in and completion of the study (including but not limited to prior preterm delivery at ≤34 weeks' gestation; prior stillbirth or neonatal death; previous infant with a known genetic disorder or significant congenital anomaly).

Other exclusion criteria for maternal participants were congenital or acquired immunodeficiency disorder, or rheumatologic disorder or other illness requiring chronic treatment with known immunosuppressant medications, including monoclonal antibodies, within the year before enrolment or other acute or chronic medical or psychiatric condition including recent (within the past year) or active suicidal ideation or behavior or laboratory abnormality that may have increased the risk

associated with study participation or investigational product administration or with the interpretation of study results.

Maternal participants were also excluded if they received the following prior or concomitant therapies: investigational drug(s) within 28 days before consent and/or during study participation; monoclonal antibodies within the year before enrolment or systemic corticosteroids for >14 days within 28 days before study enrolment (participants could receive SARS-CoV-2 monoclonal antibodies, prednisone doses of <20 mg/day for ≤14 days and inhaled/nebulized, intra-articular, intrabursal, or topical corticosteroids). Other exclusion criteria included alcohol abuse or illicit drug use and receipt of blood or plasma products or immunoglobulin, from 60 days before investigational product administration, or planned receipt through delivery (except Rho[D] immune globulin). Participants could not have received any licensed or investigational RSV vaccine or planned receipt during study participation.

Gestation at injection — wk			
Mean	30.8±3.5		31.3 (24.0–36.9)
Median (range)	31.3 (24.0–36.6)	31.3 (24.0–36.9)	
Race or ethnic group — no./total no. (%)†			
White	2383/3682 (64.7)	2365/3675 (64.4)	4748/7357 (64.5)
Black	720/3682 (19.6)	723/3675 (19.7)	1443/7357 (19.6)
Asian	454/3682 (12.3)	464/3675 (12.6)	918/7357 (12.5)
Multiracial	30/3682 (0.8)	21/3675 (0.6)	51/7357 (0.7)
Race not reported	41/3682 (1.1)	45/3675 (1.2)	86/7357 (1.2)
Race unknown	7/3682 (0.2)	8/3675 (0.2)	15/7357 (0.2)
Hispanic or Latinx	1049/3682 (28.5)	1075/3675 (29.3)	2124/7357 (28.9)
Not Hispanic or Latinx	2603/3682 (70.7)	2567/3675 (69.8)	5170/7357 (70.3)
American Indian or Alaska Native	38/3682 (1.0)	37/3675 (1.0)	75/7357 (1.0)
Native Hawaiian or other Pacific Islander	9/3682 (0.2)	12/3675 (0.3)	21/7357 (0.3)
Ethnic group not reported or unknown	30/3682 (0.8)	33/3675 (0.9)	63/7357 (0.9)
Infant participants			
Sex — no./total no. (%)			
Male	1816/3568 (50.9)	1793/3558 (50.4)	3609/7126 (50.6)
Female	1752/3568 (49.1)	1765/3558 (49.6)	3517/7126 (49.4)
Gestational age at birth — no./total no. (%)			
24 to <28 wk	1/3568 (<0.1)	1/3558 (<0.1)	2/7126 (<0.1)
28 to <34 wk	20/3568 (0.6)	11/3558 (0.3)	31/7126 (0.4)
34 to <37 wk	180/3568 (5.0)	157/3558 (4.4)	337/7126 (4.7)
37 to <42 wk	3343/3568 (93.7)	3356/3558 (94.3)	6699/7126 (94.0)
≥42 wk	21/3568 (0.6)	30/3558 (0.8)	51/7126 (0.7)
Apgar score, 5 min			
	8/3528 (0.2)	5/3517 (0.1)	13/7045 (0.2)

201/169 = 5,6 4,7

Maternal RSV-vaccine

- Forvent beskyttende effekt

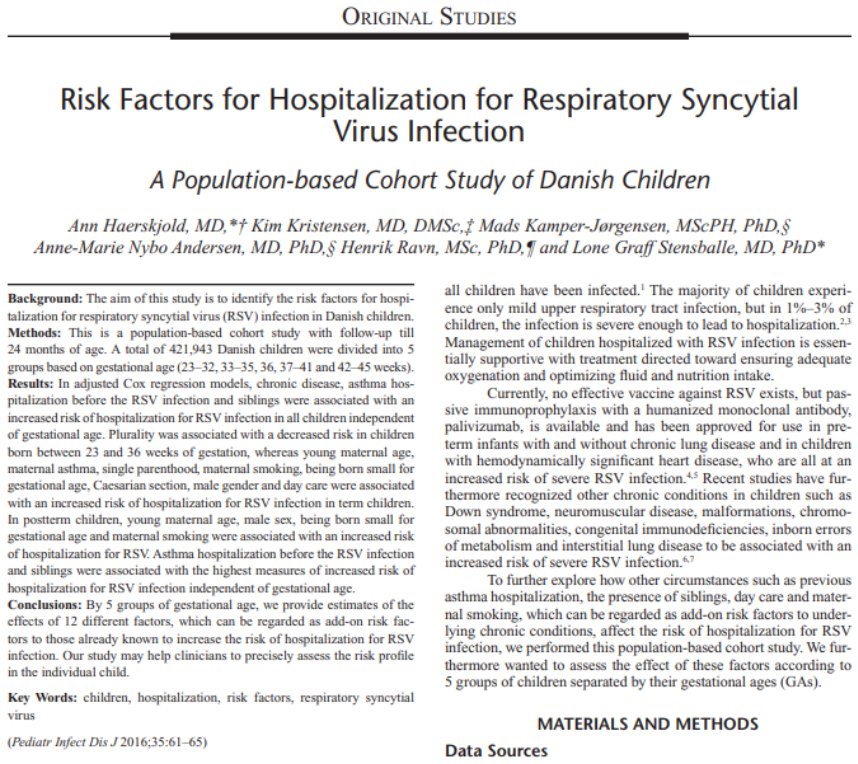
- Forvent mindre beskyttende effekt end fundet i RCT
  - 60 (-70%) hos i øvrigt raske danske børn
  - (30-) 50% hos risikobørn (som for palivizumab)

- Number needed to vaccinate
  - ≈ 100+ raske børn og ≈50 for højrisikobørn

- Safety signal: Preterm birth

RSV DK historik

1997-2003 2.9% < 2 år indlagt med RSV



ORIGINAL STUDIES

Risk Factors for Hospitalization for Respiratory Syncytial Virus Infection

A Population-based Cohort Study of Danish Children

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Background: The aim of this study is to identify the risk factors for hospitalization for respiratory syncytial virus (RSV) infection in Danish children.
Methods: This is a population-based cohort study with follow-up till 24 months of age. A total of 421,943 Danish children were divided into 5 groups based on gestational age (23–32, 33–35, 36, 37–41 and 42–45 weeks).
Results: In adjusted Cox regression models, chronic disease, asthma hospitalization before the RSV infection and siblings were associated with an increased risk of hospitalization for RSV infection in all children independent of gestational age. Plurality was associated with a decreased risk in children born between 23 and 36 weeks of gestation, whereas young maternal age, maternal asthma, single parenthood, maternal smoking, being born small for gestational age, Caesarian section, male gender and day care were associated with an increased risk of hospitalization for RSV infection in term children. In postterm children, young maternal age, male sex, being born small for gestational age and maternal smoking were associated with an increased risk of hospitalization for RSV. Asthma hospitalization before the RSV infection and siblings were associated with the highest measures of increased risk of hospitalization for RSV infection independent of gestational age.
Conclusions: By 5 groups of gestational age, we provide estimates of the effects of 12 different factors, which can be regarded as add-on risk factors to those already known to increase the risk of hospitalization for RSV infection. Our study may help clinicians to precisely assess the risk profile in the individual child.

Key Words: children, hospitalization, risk factors, respiratory syncytial virus

(*Pediatr Infect Dis J* 2016;35:61–65)

all children have been infected.[1] The majority of children experience only mild upper respiratory tract infection, but in 1%–3% of children, the infection is severe enough to lead to hospitalization.[2,3] Management of children hospitalized with RSV infection is essentially supportive with treatment directed toward ensuring adequate oxygenation and optimizing fluid and nutrition intake.

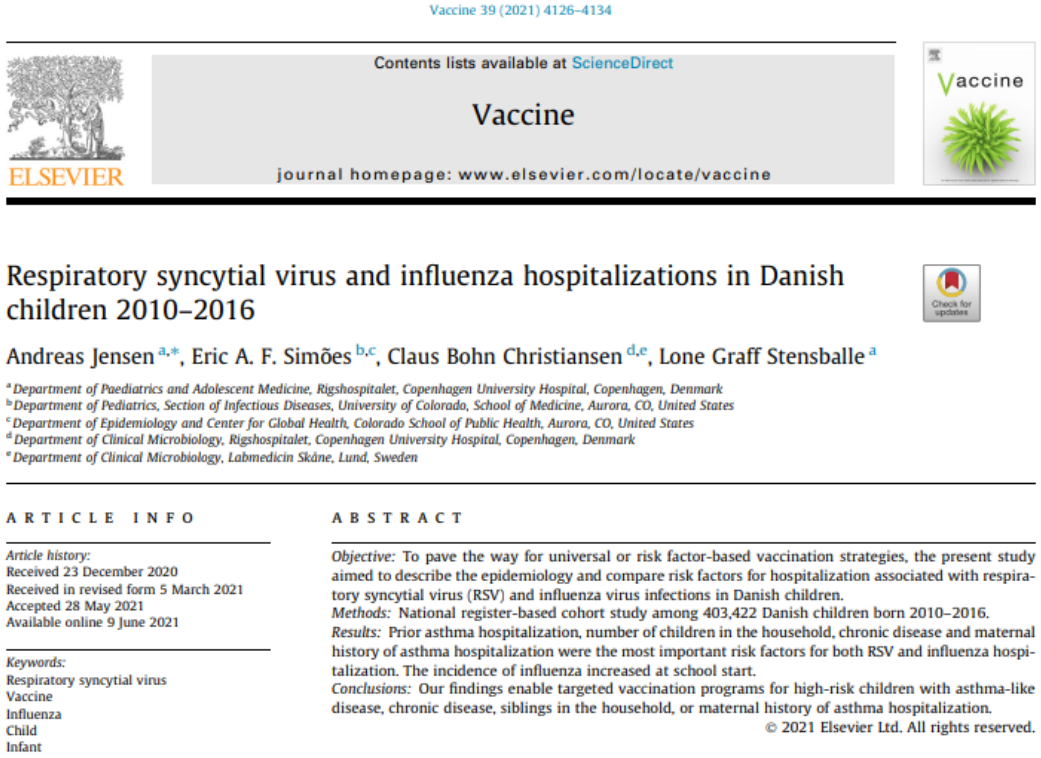
Currently, no effective vaccine against RSV exists, but passive immunoprophylaxis with a humanized monoclonal antibody, palivizumab, is available and has been approved for use in preterm infants with and without chronic lung disease and in children with hemodynamically significant heart disease, who are all at an increased risk of severe RSV infection.[4,5] Recent studies have furthermore recognized other chronic conditions in children such as Down syndrome, neuromuscular disease, malformations, chromosomal abnormalities, congenital immunodeficiencies, inborn errors of metabolism and interstitial lung disease to be associated with an increased risk of severe RSV infection.[6,7]

To further explore how other circumstances such as previous asthma hospitalization, the presence of siblings, day care and maternal smoking, which can be regarded as add-on risk factors to underlying chronic conditions, affect the risk of hospitalization for RSV infection, we performed this population-based cohort study. We furthermore wanted to assess the effect of these factors according to 5 groups of children separated by their gestational ages (GAs).

MATERIALS AND METHODS

Data Sources

2010-2016 2.6% < 6 år indlagt med RSV



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Respiratory syncytial virus and influenza hospitalizations in Danish children 2010–2016

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ABSTRACT

Objective: To pave the way for universal or risk factor-based vaccination strategies, the present study aimed to describe the epidemiology and compare risk factors for hospitalization associated with respiratory syncytial virus (RSV) and influenza virus infections in Danish children.
Methods: National register-based cohort study among 403,422 Danish children born 2010–2016.
Results: Prior asthma hospitalization, number of children in the household, chronic disease and maternal history of asthma hospitalization were the most important risk factors for both RSV and influenza hospitalization. The incidence of influenza increased at school start.
Conclusions: Our findings enable targeted vaccination programs for high-risk children with asthma-like disease, chronic disease, siblings in the household, or maternal history of asthma hospitalization.

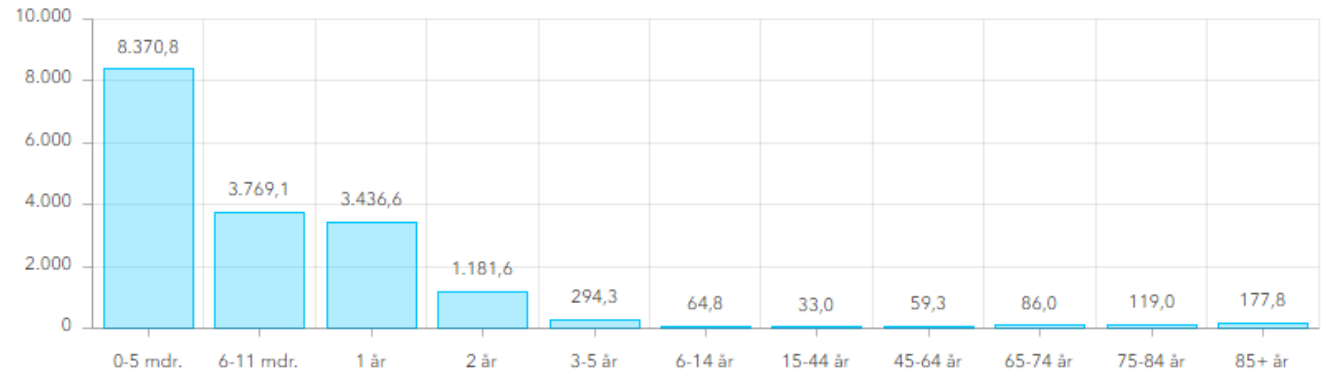
Opdateret den 21. maj. 2024

Hele sæsonen (sæson 2023/2024)

Antal tests	Bekræftede tilfælde	Incidens	Nye indlæggelse	Dødsfald
162.700	10.114	169,9	3.251	109

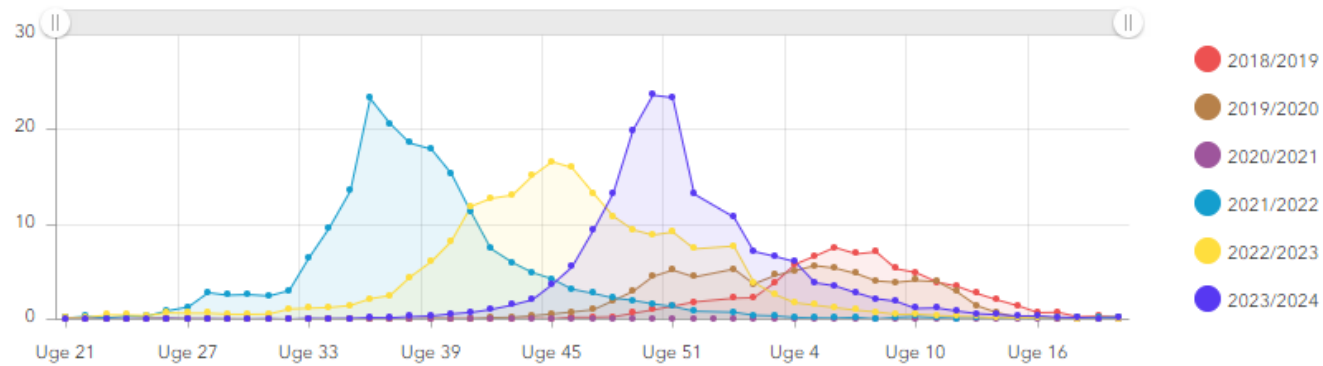
Incidens for de seneste 7 dage

Incidens pr. aldersgruppe (hele sæsonen)



Incidens pr. aldersgruppe

Incidens pr. sæson pr. uge



Incidens pr. sæson pr. uge

Vi maxer ud på test

- Vi er blevet mere forsigtige
- OBS: Overbehandling
- OBS: Spild af ressourcer
- OBS: Bivirkninger

DK 2019-2022: Vi maxer ud på indlæggelser

- Vi er blevet mere forsigtige
- OBS: Overbehandling
- OBS: Spild af ressourcer
- OBS: Bivirkninger

2022-2023-sæsonerne skilte sig ud

- Immunologisk gæld efter corona-restriktionerne medførte mange indlæggelseskrævende infektioner

2012 – 2022: RSV-mortalitet er heldigvis lav i Danmark (≈ 5/10.000)

Hold øje med de større børn:

0 år: 6 døde ud af 18,836 (3 per 10,000)

1 år: 7 døde ud af 7,904 (9 per 10,000)

2-17 år: 6 døde ud af 5,589 (11 per 10,000)

(mortalitet målt som død *af alle årsager* indenfor 30 dage efter positiv RSV-test)

DK 2010-2022 Lav GA giver høj risiko

- Nirsevimab er velegnet til for tidligt fødte

Take home message

- Watch out for hypes and overtreatment
- Nirsevimab protects against RSV-hospitalisation
- Maternal RSV-vaccine protects against RSV-hospitalisation, but may increase preterm birth

- Watchfull waiting offering maternal RSV vaccine and using nirsevimab for high-risk infants?