VITAMIN D

Vitamin D receptor (VDR) polymorphisms and severe RSV bronchiolitis: a systematic review and meta-analysis

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PMID: 24019226 DOI: 10.1002/ppul.22877

Abstract

Background: A number of small studies have suggested a relationship between vitamin D status and severe acute lower respiratory tract infection (ALRI), including RSV-bronchiolitis. The objective of this study was to evaluate the relationship between vitamin D receptor (VDR) polymorphism and severe RSV-bronchiolitis through a systemic literature review and meta-analysis.

Methods: A comprehensive electronic literature search was conducted to identify all studies published before January 2013. Two reviewers independently screened all abstracts, followed by the full text of potential articles to evaluate eligibility. Study methodological quality was evaluated using the Newcastle Ottawa scale and individual component analysis. Meta-analysis evaluated associations at the allele and genotype levels.

Results: Of 803 studies identified from our literature search, three met eligibility criteria. Two VDR polymorphisms were included in more than one study: TaqI (rs731236) and FokI (rs2228570). All three reported a positive relationship between the FokI minor allele and disease with random effects meta-analyses demonstrating a statistically significant relationship (OR 1.52, CI: 1.12, 2.05). Genotype analysis was highly suggestive of a dominant or incomplete dominance model with combined odds ratios for fF (OR 1.73, CI: 0.92-3.36) and ff (OR 2.24, CI: 0.98-5.14) compared to the FF genotype. No association between TaqI and severe RSV-bronchiolitis was evident at the allele or genotype level.

Conclusions: Available literature supports an association between the FokI polymorphism and severe RSV disease. Determination of VDR receptor polymorphism status could help predict high-risk infants who might benefit from preventive measures.

Vitamin D and neonatal immune function

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PMID: 23131172 DOI: 10.3109/14767058.2012.746304

Abstract

Vitamin D deficiency is widespread in the neonatal and paediatric population of northern latitudes, particularly in children of African, Middle Eastern and Asian ethnicity. This is associated with diminished immune function and increases the risk of Th1 autoimmune diseases like type 1 diabetes. Epidemiological studies

have also shown a link between vitamin D deficiency in children and a more severe course of illness with lower respiratory tract infection or Respiratory Syncitial Virus (RSV) bronchiolitis. The mechanism by which vitamin D enhances immunity is complex. It acts through the innate immune system by inducing antimicrobial peptides in epithelial cells, neutrophils and macrophages. The role of Vitamin D in neonatal and paediatric immunomodulation requires further study.

Better newborn vitamin D status lowers RSV-associated bronchiolitis in infants

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• PMID: 22946854 DOI: 10.1111/j.1753-4887.2012.00517.x

Abstract
Each year 1.5 million children under the age of 5 years die from pneumonia. In the United States, respiratory syncytial virus (RSV) is the number one cause of bronchiolitis and pneumonia in children under 1 year of age. Low serum 25(OH)D is associated with an increased risk of lower respiratory tract infections (LRTI). Two recent studies have provided important information concerning the association between cord blood 25(OH)D and subsequent risk of developing respiratory infection in very young children. These findings support the need in future studies to determine the extent to which an intervention to change the vitamin D status of mothers during pregnancy can reduce the risk of RSV-associated LRTI in their offspring. An answer to this question would have significant worldwide public health importance given the high prevalence of low vitamin D status worldwide and the high mortality burden accompanying infectious lung diseases in young children.

Serum Vitamin D Levels and Life-Threatening Respiratory Syncytial Virus Infection in Previously Healthy Infants

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• PMID: 35106574 DOI: 10.1093/infdis/jiac033

Abstract
Background: 25-hydroxyvitamin D (VD) effects on lung function and immune-modulation might affect respiratory syncytial virus (RSV) infection outcomes. We aimed to assess VD levels on admission and their association with life-threatening RSV disease (LTD).
Methods: A prospective cohort study was conducted during 2017-2019. Previously healthy infants aged <12 months, hospitalized with a first episode of RSV infection, were enrolled. LTD was defined by need for intensive care and ventilatory support. Serum VD levels <20 ng/mL were categorized as deficient, and 20-29.9 ng/mL as insufficient.

Results: Of 125 patients studied, 73 (58%) were male. Median age was 4 months. Twenty-two patients developed LTD. No differences in viral load were seen between cases with LTD and controls (P = .94). Patients who developed LTD had significantly lower VD levels: median 18.4 ng/mL (IQR, 15.1-26.9 ng/mL) versus 31.7 ng/mL (IQR, 23.6-42.0 ng/mL), P < .001; 59% of infants with LTD had VD deficiency compared with 12% in those with better outcome. Multivariable regression analysis confirmed VD deficiency as a risk factor (odds ratio, 11.83; 95% confidence interval, 3.89-35.9; P < .001).
Conclusions: These findings provide additional evidence for the development of strategies to prevent severe RSV infections.

Vitamin D in respiratory viral infections: a key immune modulator?

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- PMID: 34470511 DOI: 10.1080/10408398.2021.1972407

Abstract
Respiratory viral infections are common respiratory diseases. Influenza viruses, RSV and SARS-COV2 have the potential to cause severe respiratory infections. Numerous studies have shown that unregulated immune response to these viruses can cause excessive inflammation and tissue damage. Therefore, regulating the antiviral immune response in the respiratory tract is of importance. In this regard, recent years studies have emphasized the importance of vitamin D in respiratory viral infections. Although, the most well-known role of vitamin D is to regulate the metabolism of phosphorus and calcium, it has been shown that this vitamin has other important functions. One of these functions is immune regulation. Vitamin D can regulate the antiviral immune response in the respiratory tract in order to provide an effective defense against respiratory viral infections and prevention from excessive inflammatory response and tissue damage. In addition, this vitamin has preventive effects against respiratory viral infections. Some studies during the COVID-19 pandemic have shown that vitamin D deficiency may be associated with a higher risk of mortality and sever disease in patients with COVID-19. Since, more attention has recently been focused on vitamin D. In this article, after a brief overview of the antiviral immune response in the respiratory system, we will review the role of vitamin D in regulating the antiviral immune response comprehensively. Then we will discuss the importance of this vitamin in influenza, RSV, and COVID-19.

Vitamin D3 protects against respiratory syncytial virus-induced barrier dysfunction in airway epithelial cells via PKA signaling pathway

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- PMID: 37354621 DOI: 10.1016/j.ejcb.2023.151336

Free article

Abstract
Respiratory syncytial virus (RSV) is the leading cause of acute lower respiratory tract infection in infants and young children globally and is responsible for hospitalization and mortality in the elderly population. Virus-induced airway epithelial barrier damage is a critical step during RSV infection, and emerging studies suggest that RSV disrupts the tight junctions (TJs) and adherens junctions (AJs) between epithelial cells, increasing the permeability of the airway epithelial barrier. The lack of commercially available vaccines and effective antiviral drugs for RSV emphasizes the need for new management strategies. Vitamin D3 is a promising intervention for viral infection due to its critical role in modulating innate immune responses. However, there is limited evidence on the effect of vitamin D3 on RSV pathogenies. Here, we investigated the impact of vitamin D3 on RSV-induced epithelial barrier dysfunction and the underlying mechanisms. We found that pre-incubation with 1,25(OH)2D3, the active form of vitamin D3, alleviated RSV-induced epithelial barrier disruption in a dose-dependent manner without affecting viability in 16HBE cells. 1,25(OH)2D3 induced minor changes in the protein expression level of TJ/AJ proteins in RSV-infected cells. We observed increased CREB phosphorylation at Ser133 during 1,25(OH)2D3 exposure, indicating that vitamin D3 triggered protein kinase A (PKA) activity in 16HBE. PKA inhibitors modified the restoration of barrier function by 1,25(OH)2D3 in RSV-infected cells, implying that PKA signaling is responsible for the protective effects of vitamin D3 against RSV-induced barrier dysfunction in airway epithelial cells. Our findings suggest vitamin D3 as a prophylactic intervention to protect the respiratory epithelium during RSV infections.

Vitamin D-binding protein haplotype is associated with hospitalization for RSV bronchiolitis

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- PMID: 24447085 PMCID: PMC5062603 DOI: 10.1111/cea.12247

Free PMC article

Abstract
Background: Between 75 000 and 125 000 U.S. infants are hospitalized for respiratory syncytial virus (RSV) bronchiolitis every year. Up to half will be diagnosed with asthma in later childhood. Vitamin D deficiency has been associated with susceptibility to asthma and respiratory infections. Measured vitamin D is largely bound to vitamin D-binding protein (VDBP); VDBP levels are influenced by its gene (GC) haplotype.
Objective: We assessed the relationship between polymorphisms rs7041 and rs4588, which define haplotypes GC1s, GC1f, and GC2, and RSV bronchiolitis susceptibility and subsequent asthma.
Methods: We retrospectively recruited 198 otherwise healthy children (93% White) hospitalized for severe RSV bronchiolitis in Boston and 333 parents into a follow-up study to assess asthma diagnosis. Data were analysed using family-

based genetic association tests. We independently validated our results in 465 White children hospitalized with RSV bronchiolitis and 930 White population controls from the Netherlands.
Results: The rs7041_C allele (denoting haplotype GC1s) was overtransmitted (P = 0.02, additive model) in the entire Boston cohort, in Whites (P = 0.03), and especially in children subsequently diagnosed with asthma (P = 0.006). The GC1f haplotype was undertransmitted in the asthma subgroups (all races and White, both P < 0.05). The rs7041_C allele was also more frequent in the RSV bronchiolitis group compared with controls (OR 1.12, 95% CI 1.02, 1.4, P = 0.03) in the Netherlands, especially in mechanically ventilated patients (P = 0.009).
Conclusion and clinical relevance: GC1s haplotype carriage may increase the risk of RSV bronchiolitis in infancy and subsequent asthma development. The GC1s haplotype is associated with higher VDBP levels, resulting in less freely available vitamin D.

Effects of Maternal Vitamin D Supplementation During Pregnancy and Lactation on Infant Acute Respiratory Infections: Follow-up of a Randomized Trial in Bangladesh

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PMID: 34213544 PMCID: PMC8557369 DOI: 10.1093/jpids/piab032
Free PMC article

Abstract
Background: We examined the effect of maternal vitamin D supplementation during pregnancy and lactation on risk of acute respiratory infection (ARI) in infants up to 6 months of age in Bangladesh.
Methods: This study was nested in a randomized, double-blind, placebo-controlled, 5-arm dose-ranging trial of prenatal and postpartum vitamin D supplementation. One group of women received 0 IU vitamin D per week during pregnancy and for 26 weeks post delivery ("placebo" group), one group received high-dose prenatal vitamin D supplementation of 28 000 IU per week and 26 weeks post delivery, and there were 3 additional dose-ranging groups receiving vitamin D supplementation during pregnancy only (4200, 16 800, and 28 000 IU per week, respectively). Episodes of ARI were identified by active and passive surveillance. The primary outcome was microbiologically confirmed ARI, and the primary analysis compared the high-dose prenatal plus postpartum vitamin D vs placebo groups.
Results: In total, 1174 mother-infant pairs were included. Among infants born to mothers in the placebo group, 98% had a venous umbilical cord 25(OH)D level below 30 nmol/L compared with none in the high-dose prenatal plus postdelivery vitamin D group. Incidence of microbiologically confirmed ARI in the high-dose

prenatal plus postpartum vitamin D (1.21 episodes per 6 person-months; N = 235) and placebo groups (1.07 episodes per 6 person-months; N = 234) was not significantly different (hazard ratio of 1.12 [95% confidence intervals: 0.90-1.40]). There were no differences in the incidence of microbiologically confirmed or clinical ARI, upper, lower, or hospitalized lower respiratory tract infection between high-dose prenatal plus postpartum vitamin D and placebo groups.
Conclusions: Despite a high prevalence of maternal baseline vitamin D deficiency and significant effects of maternal vitamin D supplementation on infant vitamin D status, the intervention did not reduce the risk of microbiologically confirmed ARI in infants up to 6 months of age.

Bernadette's note: the high-dose prenatal group were given 28,000 iu of Vit D per week, which is 4,000 iu per day, and likely too low to raise cord blood levels to optimal range, which is above 75 nmol/L. The supplemental data gives two ranges for cord blood found at study end <30 nmol/L and <50 nmol/L. So it appears supplementation did not bring any of cord blood to optimal range. See the below study on cord blood.

Association between umbilical cord vitamin D levels and adverse neonatal outcomes

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We investigated the associations between cord blood concentration of 25-hydroxyvitamin D [25(OH)D], neonatal outcomes, and the risk of hospitalization during the first year of life.
Methods
A total of 402 newborn infants and their mothers were prospectively enrolled and divided in four groups according to season of the year. We determined 25(OH)D serum concentrations from maternal–neonatal pairs at delivery by electrochemiluminescence immunoassay. Cut-offs at 25, 50, and 75 nmol/L defined vitamin D status, corresponding to deficiency, insufficiency, and sufficiency, respectively. Crude odds ratio (cOR) and 95% confidence intervals (CI) were estimated using logistic regression.
Results
Vitamin D severe deficiency (i.e., <25 nmol/L) was present in 18% of newborns. Cord blood severe deficiency was associated with an increased risk of preterm birth (cOR 3.6, 95% CI: 1.1–12.2), neonatal respiratory distress syndrome (cOR 5.9, 95% CI: 1.1–33.2), and increased risk of hospitalization during the first year of life because of acute respiratory infection (cOR 3.9, 95% CI: 1.4–10.6) or acute gastroenterocolitis (cOR 5.2, 95% CI: 1.4–19.1).
Conclusion
Cord blood vitamin D deficiency is associated with increased risk of preterm birth, neonatal respiratory distress syndrome, and hospitalization during the first year of life.

Table 2.

Distribution of vitamin D concentrations in maternal and cord blood by season [n (%)].

Vitamin D	Sep 2013n = 101 (%)		Dec 2013n = 100 (%)		Mar 2014n = 101 (%)		Jun 2014n = 100 (%)	
	Mother	Child	Mother	Child	Mother	Child	Mother	Child
<25 nmol/L (severely deficient)	10 (10)	6 (6)	42 (42)	18 (18)	43 (42)	39 (39)	9 (9)	11 (11)
25–50 nmol/L (deficient)	38 (38)	20 (20)	40 (40)	33 (33)	47 (47)	33 (33)	35 (35)	32 (32)
50–75 nmol/L (insufficient)	38 (38)	28 (28)	16 (16)	27 (27)	10 (10)	23 (23)	35 (35)	30 (30)
>75 nmol/L (optimal)	15 (15)	47 (47)	2 (2)	22 (22)	1 (1)	6 (6)	21 (21)	27 (27)

Vitamin D decreases respiratory syncytial virus induction of NF-kappaB-linked chemokines and cytokines in airway epithelium while maintaining the antiviral state

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Free PMC article

Abstract

Epidemiological studies suggest that low vitamin D levels may increase the risk or severity of respiratory viral infections. In this study, we examined the effect of vitamin D on respiratory syncytial virus (RSV)-infected human airway epithelial cells. Airway epithelium converts 25-hydroxyvitamin D3 (storage form) to 1,25-dihydroxyvitamin D3 (active form). Active vitamin D, generated locally in tissues, is important for the nonskeletal actions of vitamin D, including its effects on immune responses. We found that vitamin D induces IkappaBalpha, an NF-kappaB inhibitor, in airway epithelium and decreases RSV induction of NF-kappaB-driven genes such as IFN-beta and CXCL10. We also found that exposing airway epithelial cells to vitamin D reduced induction of IFN-stimulated proteins with important antiviral activity (e.g., myxovirus resistance A and IFN-stimulated protein of 15 kDa). In contrast to RSV-induced gene expression, vitamin D had no effect on IFN signaling, and isolated IFN induced gene expression. Inhibiting NF-kappaB with an adenovirus vector that expressed a nondegradable form of IkappaBalpha mimicked the effects of vitamin D. When the vitamin D receptor was silenced with small interfering RNA, the vitamin D effects were abolished. Most importantly we found that, despite inducing IkappaBalpha and dampening chemokines and IFN-beta, there was no increase in viral mRNA or protein or in viral replication. We conclude that vitamin D decreases the inflammatory response to viral infections in airway epithelium without jeopardizing viral clearance. This suggests that adequate vitamin D levels

would contribute to reduced inflammation and less severe disease in RSV-infected individuals.

IODINE

In Vitro Bactericidal and Virucidal Efficacy of Povidone-Iodine Gargle/Mouthwash Against Respiratory and Oral Tract Pathogens https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5986684/

> "PVP-I gargle/mouthwash diluted 1:30 (equivalent to a concentration of 0.23% PVP-I) showed effective bactericidal activity against Klebsiella pneumoniae and Streptococcus pneumoniae and rapidly inactivated SARS-CoV, MERS-CoV, influenza virus A (H1N1) and rotavirus after 15 s of exposure."

Iodine: the Forgotten Weapon Against Influenza Viruses http://simplymimi.net/wp-content/uploads/2020/03/WebPage.pdf

> "Iodine is the most effective broad-spectrum antiseptic with low toxicity.[21] Iodine has very high germicidal activity, and no organism develops resistance to iodine. [12]
>
> Iodine has been used in various forms as an antiseptic for the skin, wounds, and mucous surfaces of the body. It has also been used to sterilize the air and inanimate objects such as catgut and surgical instruments. Moreover, it has been used as a prophylactic and therapeutic agent in diseases caused by bacteria, viruses, and fungi, and to sanitize eating utensils.[7,12] Iodine kills bacteria, virus-es, fungi, protozoa, and even spores of bacteria and fungi, including anthrax spores. Iodine was used successfully against influenza, herpes, small pox, and chicken pox viruses.[7]
>
> When iodine was suspended in a solution, viral inactivation occurred at dilutions of 1/1,000,000. Aerosols inactivated many viruses within 30 seconds or less. [7,8,12] Watery solutions such as Lugol's are the superior germicides.[12]"
>
> "**Current Iodine Doses and Doses Needed to Prevent Invasion**
> Our current recommended iodine intake by the WHO is 150 to 200 micrograms daily. This dose first started by David Marine in 1920 has success- fully prevented goiters, cretinism, and mental retardation.[21] If the daily iodine dose is above 3 mg for over 2 weeks, the thyroid gland becomes saturated and no longer takes up much iodine.[25]
>
> Then, dietary iodine goes to other sites named above and is excreted into the upper respiratory and gastrointestinal tract mucus.[16] It seems logical that air borne viruses become stuck in mucus and killed by free iodine.

Dietary iodine found in iodized salt is below the amounts needed to fill mucus defense roles. To protect themselves, people wishing to boost their defense against infections should supplement their diets with iodine in the form of Lugol's. Most people will probably be protected by an amount of Lugol's that provides the average amount of iodine ingested by Japanese populations for centuries. This amount is about 12 mg daily. Two drops of Lugol's daily in the liquid of their choice will provide 13 mg.

Potential Effects of Iodine Supplementation on Inflammatory Processes and Toxin Removal Following COVID-19 Vaccination https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8552616/

"Iodine has shown virucidal activities against SARS-CoV-2. A few publications are available on the quick deactivating action of povidone-iodine (PVP-1) on COVID-19. Povidone-iodine has been observed to have rapid and efficient antiviral activity. This activity is believed to be sufficient as a preventive measure against COVID-19."

Povidone Iodine (PVP-I) Oro-Nasal Spray: An Effective Shield for COVID-19 Protection for Health Care Worker (HCW), for all
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8026810/

Mostafa Kamal Arefin
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Abstract
SARS- CoV-2 or novel coronavirus enters in human body through nose and mouth, stays there for a while. Then binds with ACE2 receptor, enters inside cell, multiply there and manifests. Again, Polyvinyl Pyrrolidone or Povidone Iodine (PVP-I) is a strong microbicidal agent having 99.99% virucidal efficacy in its only 0.23% concentration, irrespective of all known viruses, even in SARS- CoV-2 (in vitro). An oro-nasal spray is designed to apply the PVP-I in nose and oral cavity to gain a protective layer or coating over nasal and oral mucosa, so that SARS-CoV-2 can't bind with the ACE-2 receptor and prevent their entry inside. So, it will be effective for prevention of COVID-19. Moreover, as PVP-I has the ability for destruction of SARS-CoV-2, transmission of SARS- CoV-2 from patient will be reduced also. Thus PVP-I oro-nasal spray can act as an effective shield for COVID-19 protection for healthcare workers, for all.

June 18, 2020* | *Courtney Chandler, UConn Health *https://today.uconn.edu/2020/06/uconn-health-researchers-find-simple-oral-rinse-can-inactivate-covid-19-virus/#*

UConn Health Researchers Find a Simple Oral Rinse Can Inactivate the COVID-19 Virus

Faculty from UConn Health have proven that a simple method of rinsing with a diluted version of over-the-counter Povidone-Iodine (PVP-I) oral rinse can kill viruses like the SARS CoV-2 coronavirus and prevent transmission in as little as 15 seconds. The COVID-19 pandemic has posed a severe threat to the safety of dental and medical professionals […]

Can povidone iodine gargle/mouthrinse inactivate SARS-CoV-2 and decrease the risk of nosocomial and community transmission during the COVID-19 pandemic? An evidence-based update https://pubmed.ncbi.nlm.nih.gov/33747261/

Abstract
The Coronavirus disease in 2019 (COVID-19), also referred to as the novel 'CoV19 (nCov19)' is caused by a new coronavirus strain similar to Severe Acute Respiratory Syndrome (SARS-CoV-2). SARS-CoV-2 spreads via respiratory droplets, saliva, or direct contact. Therefore it is important to control the viral load in the saliva and respiratory secretions. One of the most simple and cost-effective measures that can be adopted by the public and healthcare professionals to prevent cross-contamination and community transmission, is the implementation of effective oral and throat hygiene. Recent evidence has confirmed that 0.5% povidone iodine (PVP-I) mouthrinse/gargle for 30 s can reduce SARS-CoV-2 virus infectivity to below detectable levels. PVP-I can even interrupt SARS-CoV-2 attachment to oral and nasopharyngeal tissues and lower the viral particles in the saliva and respiratory droplets. Thus, the use of PVP-I mouthrinse as a prophylactic measure has been advocated across the globe to reduce disease transmission. Although the efficacy of PVP-I against SARS-CoV-2 is proven, no review articles have yet discussed the evidence and mechanisms of PVP-I against the SARS-CoV-2. Thus, this paper highlights the rationale, safety, recommendations, and dosage of PVP-I gargle/mouthrinse as an effective method to decrease the viral loads during the pressing times of COVID-19.

RSV Vaccines & AstraZeneca's monoclonal antibody

Defender article: https://childrenshealthdefense.org/defender/rsv-vaccine-babies-pregnant-women/

'Risky Strategy': CDC Signs Off on Pfizer RSV Vaccine for Pregnant Women to Protect Newborns

Key concerns (paraphrased & partial quotes) about Pfizer's Abrysvo from the article:

- Safety signal of preterm deliveries and low birth weight babies
- Potential provocation of fever, a common determinant of preterm labor and in some cases fetal loss or premature delivery
- GSK dropped their vaccine candidate that was almost identical due to such concerns
- the clinical trial for Abrysvo reported 18 peripartum fetal deaths — the FDA stated that these deaths were "unlikely" to be related to the shot
- 37.1% of infants whose mothers received the experimental Pfizer vaccine experienced adverse events within one month of birth — with 15.5% classified as "serious," 4.5% as "severe" and 1% as "life-threatening
- According to this CDC study that spanned 12 years https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8562311/ there were 1,001 death certificates that listed RSV on them in the entire United States — so less than 100 people dying with an RSV-associated death per year - only 17 babies per year are thought to be due to RSV
- Ineffective within 6 months

Medical student shows that the full trial data do not support either safety or effectiveness of the RSV vaccine for pregnant women at the FDA's VRBPAC. https://t.co/DwyitEjKJW

FDA's September 12, 2023 Summary Basis for Regulatory Action - ABRYSVO (STN 125768)

> Phase 1/2 trials were designed with participants exposed to non-adjuvanted RSV vaccine, adjuvanted RSV vaccine, flu vaccines, Tdap, or "placebo", in rotation, with no true control group. Flu and Tdap are not inert or without known risks.
>
> Phase 3 Clinical trials did not use inert saline placebo.
> - "The placebo group is administered a matching volume containing excipients reconstituted in sterile water for injection, containing no RSVpreF antigens." https://classic.clinicaltrials.gov/ProvidedDocs/08/NCT05096208/Prot_000.pdf
> - Placebo: Lyophile match, containing excipients matched to those in the RSVpreF vaccine formulation, without the active ingredients. The physical appearance of the reconstituted RSVpreF and placebo are similar. Lots: DC8153 (19-005013), DE0469 (19-005014). (from the Summary Basis)

> "RSV infection does not confer lasting immunity and re-infections occur throughout an individual's lifespan. There is currently no immune marker widely accepted as predictive of protection against RSV. The durability of naturally acquired immunity after RSV infection is also not well understood."

Original Antigenic Sin and Respiratory Syncytial Virus Vaccines
Ralph A. Tripp1,* and Ultan F. Power2
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> "OAS is fundamentally important in vaccine development because a vaccine strategy that stimulates immune diversification could change the VE upon the appearance of a variant strain. As noted, RSV causes repeat infections which implies that RSV does not induce durable and robust immunity, and the humoral and cellular immune responses to RSV are known to be insufficient [42,43,44]. Repeat RSV infections may be analogous to suboptimal vaccination, and in the context of OAS, levels of restricted immunity may modify the immune repertoire and RSV memory response. Age and host genetics affect the balance of immune responses, and studies examining RSV infection of the young infant have shown that the age at initial infection has a role in determining the severity of disease [46,47]. How OAS affects the original response to the infecting strain and subsequent infections needs to be better understood, particularly in RSV vaccine development."

The continuing need for therapeutic agents for respiratory syncytial virus infection

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10424541/

> "Even if an RSV vaccine is licensed and widely used, it should be expected that many in the population will not respond adequately to the vaccine and/or will suffer severe enough re-infections that the availability of effective therapeutic anti-RSV agents will be required to fully address the challenges by RSV. Thus, effective therapeutic agents for RSV are likely to be needed, especially for high-risk populations, even after effective vaccine development. Limited immune function at the extremes of life (infancy and old age), and with immunosuppression due to disease or its therapy, combined with RSV effects on the recall immune response, make a continued search for effective anti-RSV antiviral agents an important partner to vaccine development."

FDA Approves New Drug to Prevent RSV in Babies and Toddlers - Press Release of Fast Track Approval and links to the clinical trials https://www.fda.gov/news-events/press-announcements/fda-approves-new-drug-prevent-rsv-babies-and-toddlers

- Relative Risk Reductions ranged between 70 - 75% compared to placebo — which calculates to Absolute Risk Reduction ranging between 3.8 and 6.9%
- "Beyfortus comes with warnings and precautions about serious hypersensitivity reactions, including anaphylaxis, which have been observed with other human IgG1 monoclonal antibodies. Beyfortus should be given with caution to infants and children with clinically significant bleeding disorders."

Despite 12 Deaths During Clinical Trials, CDC Signs Off on RSV Shots for Newborns Defender article: https://childrenshealthdefense.org/defender/cdc-beyfortus-nirsevimab-rsv-shots-newborns/

BEYFORTUS (nirsevimab-alip) injection FDA product insert: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761328s000lbl.pdf

> "The safety of BEYFORTUS was evaluated in Trial 05, a randomized, double-blind, palivizumab-controlled multicenter trial in infants at high risk for severe RSV disease."

FDA insert for SYNAGIS® (palivizumab) https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/103770s5185lbl.pdf

> "The safety and efficacy of Synagis have not been established for treatment of RSV disease."
>
> "Palivizumab may interfere with immunological-based RSV diagnostic tests such as some antigen detection-based assays."