

Vaccine effectiveness in pregnancy: the evidence

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Disclosure Statement

- I have no affiliation (financial or otherwise) with a pharmaceutical, medical device or communications organization.

Which vaccines?

- Recommended by NACI in every pregnancy:
 - Influenza
 - Pertussis
- Coverage of both vaccines is very low
 - About 1 in 3 pregnant women in Canada get influenza vaccination each year
- New vaccines in the pipeline:
 - Respiratory syncytial virus (RSV)
 - Group B streptococcus (GBS)

What does vaccine effectiveness (VE) mean in relation to vaccination during pregnancy?

- 1. Direct protection of the mother** during pregnancy (this also protects fetus during pregnancy)
- 2. Passive protection of infant** in early months of life before their routine immunization is fully protective
Level of antibody transferred depends on timing of immunization during pregnancy
- 3. Indirect protection of infant** in early months through reducing risk of transmission from mother to child

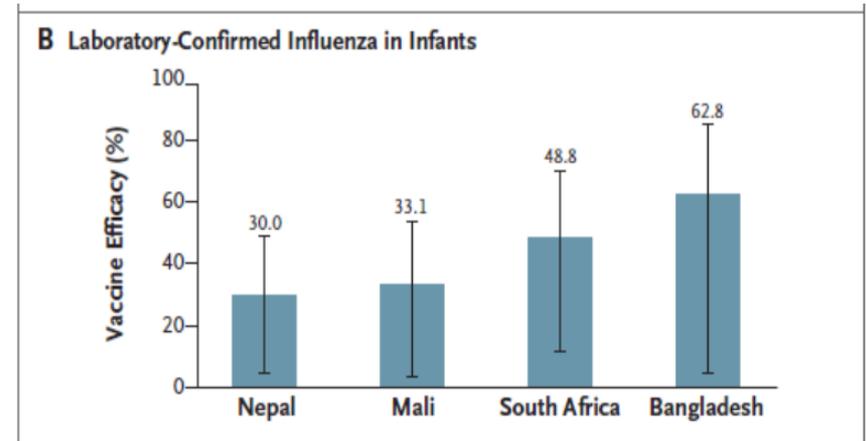
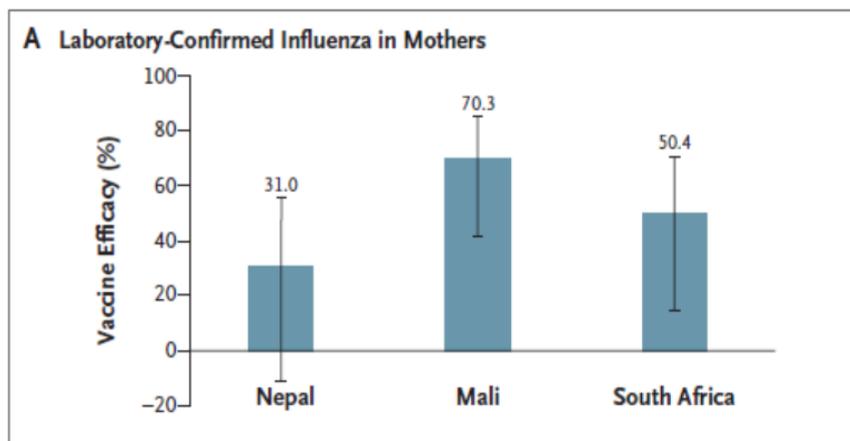
Influenza immunization during pregnancy



<https://www.thecut.com/2018/03/kate-middleton-pregnant-third-baby.html>

Vaccine efficacy against influenza

- Four RCTs of influenza vaccination during pregnancy - Bangladesh: Zaman et al., NEJM 2008; South Africa: Madhi et al., NEJM 2014; Mali: Tapia et al., Lancet ID 2016; Nepal: Steinhoff et al., Lancet ID 2017
- Vaccine efficacy against **lab-confirmed infections**:
 - 31-50% in mothers
 - 30-63% in infants



Vaccine effectiveness (VE) in pregnant women

- USA two seasons 2010-12: VE 48% and 51% against acute respiratory illness associated with PCR-confirmed influenza (1).
- Norway 2009-10: Pandemic influenza vaccines reduced risk of clinical diagnosis of influenza by 70% (2).
- Australia 2012-13: VE 81% (95%CI: 31, 95) reduction in emergency department visits and VE 65% (95%CI: 3, 87%) reduction in inpatient hospital admissions (3).
- Multi-centre Australia, Canada, Israel, USA 2010-16: VE 40% (95%CI: 12, 59) against PCR-confirmed influenza-associated hospitalization (4)

(1) Thompson MG et al Clin Infect Dis. 2013 (2) Haberg SE et al. N Engl J Med. 2013 (3) Regan AK et al Vaccine 2016 (4) Thompson et al CID 2018

Passive protection of infant

- Pooled analysis of three RCTs yielded an overall vaccine efficacy of 20% (95%CI: 1, 34) against all-cause LRTI (1).
- Four observational studies of influenza vaccination during pregnancy in preventing infant laboratory-confirmed influenza hospitalizations: pooled VE 72% (95%CI: 39, 87) (2).

(1) Omer SB et al. Pediatr Infect Dis J. 2018.

(2) Nunes MC et al. Human vaccines & immunotherapeutics. 2017:0.

Pertussis vaccination in pregnancy



<https://www.hellomagazine.com/royalty/gallery/2019042472350/prince-harry-meghan-markle-royal-baby-what-you-need-to-know/1/>

National Advisory Committee on Immunization (NACI) and Society of Obstetricians and Gynaecologists of Canada (SOGC) recommendations

NACI: Pertussis immunization in every pregnancy ideally administered between 27 and 32 weeks of gestation but evidence also supports providing maternal Tdap over a wider range of gestational ages, from 13 weeks up to the time of delivery, in view of programmatic and unique patient considerations.

SOGC: All pregnant women should be offered the diphtheria and tetanus toxoids and acellular pertussis vaccine during the second or third trimester, preferably between 21 and 32 weeks gestation, during every pregnancy, irrespective of their immunization history.

Source: NACI: Update on immunization in pregnancy with tetanus toxoid, reduced diphtheria toxoid and reduced acellular pertussis toxoid (Tdap) vaccine, 2018 and SOGC: [https://www.jogc.com/article/S1701-2163\(17\)31114-3/abstract](https://www.jogc.com/article/S1701-2163(17)31114-3/abstract)

Effectiveness of maternal Tdap vs infant disease

Study	Summary
Amirthalingam Lancet 2014	Vaccine effectiveness (VE) in the first 2 months: <u>90%</u> (95% CI: 82–95%)
Amirthalingam CID 2016	VE <3 months: <u>91%</u> (95% CI: 88-94%)
Baxter Pediatrics 2017	VE in the first 2 months: <u>91%</u> (95% CI: 20–99%)
Winter CID 2017	Adjusted VE against hospitalization <u>58%</u> (95% CI: 15-80%). No deaths in infants of vaccinated mothers
Winter CID 2017	Tdap in pregnancy <u>85%</u> (95% CI 33%-98%) more effective than postpartum Tdap in infants <8 weeks
Skoff CID 2017	VE any pertussis infection: <u>77.7%</u> (95% CI: 48.3–90.4) VE hospitalized pertussis: <u>90.5%</u> (95% CI: 65.2–97.4)

Effectiveness of maternal Tdap for older infants

Study	Summary
Amirthalingam CID 2016	VE <3 months: 91% (95% CI: 88 to 94) VE after commencing infant primary series: After 1 infant dose: 82% (95% CI: 65 to 91) After 2 infant doses: 69% (95% CI: 8 to 90) After 3 infant doses: 29% (95% CI: -112 to 76)
Baxter Pediatrics 2017	VE in the first 2 months: 91.4% (95% CI: 19.5–99.1) VE <12 months: 69% (95% CI: 44 to 83)

Other considerations

- Timing matters:
 - Vaccination not effective if given within a week of birth or after the birth (Public Health England unpublished data)
 - PHE data suggests effectiveness greatest before 31 weeks
- Vaccine product may matter:
 - UK switched from dT5aP/IPV to dT3P/IPV
 - VE fell from 92% (88-95%) to 87% (84-91%)
 - Not a significant difference but suggestive of a vaccine product effect

<https://www.cdc.gov/vaccines/vpd/dtap-tdap-td/hcp/about-vaccine.html>

Infant immune responses: blunting

- Increased concentrations of pertussis antibodies have been shown to interfere with infant immune responses
 - Blunting effect resolved after booster dose at 12 months in small RCTs in the US (Munoz et al., 2014) and Vietnam (Maertens et al., 2016), but not in a larger Canadian RCT (Halperin et al., 2018)
- Clinical relevance unclear
 - There is no antibody correlate of protection for pertussis
 - The antibody interference does not seem to reduce the clinical effectiveness of vaccination, at least in early infancy

Bottom line

Vaccination in pregnancy is **greater than 90% effective**
at preventing severe
pertussis in infants

Vaccines on the horizon



RSV vaccines in development

Study	Description of phase 3 study
A Study to Determine the Safety and Efficacy of the RSV F Vaccine to Protect Infants Via Maternal Immunization (NCT02624947)	<ul style="list-style-type: none">▪ Enrolled 4,636 third-trimester pregnant women in the Northern and Southern hemispheres, for up to four consecutive RSV seasons in each hemisphere▪ Phase 3, randomized, observer-blind, placebo-controlled▪ 1° outcome: Incidence of RSV LRTI up to 90 days▪ 2° outcomes: RSV hypoxemia, hospitalization, death up to 90 days; health care for wheezing up to 1 year

BILL & MELINDA
GATES *foundation*

From www.clinicaltrials.gov , January 11, 2019



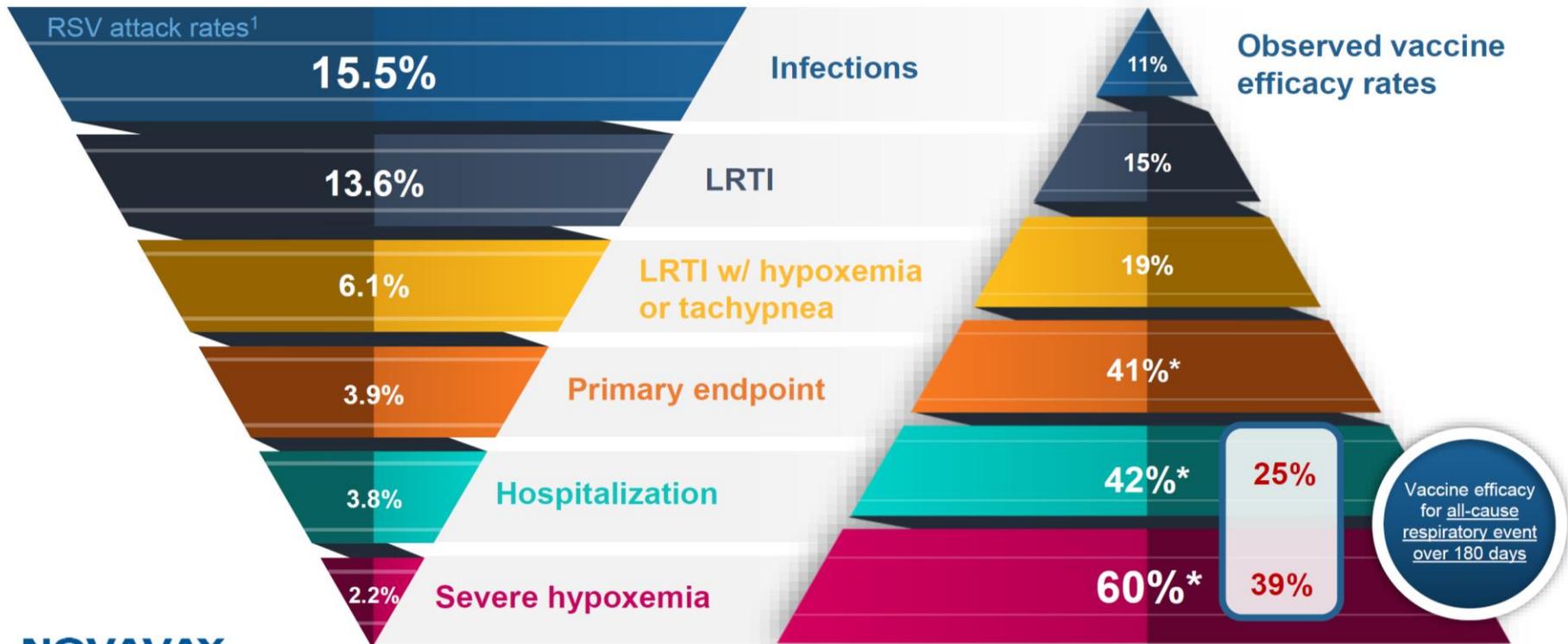
NOVAVAX

<https://clinicaltrials.gov/ct2/show/NCT02624947>;

http://www.novavax.com/download/files/presentations/NOVAVAX_WVC_RSV_2018APR3_FINAL.pdf

Novavax results

Vaccine impact on all-cause respiratory disease



NOVAVAX

<https://novavax.com/presentation.show>

1. Expanded data from sites and hospitalizations, through 90 days, * LB 95%CI >0

Group B Streptococcus (GBS) vaccines in development

- Current leading vaccine candidates are conjugated capsular polysaccharides (CPS) vaccines
- Phase I and II trials of a trivalent GBS vaccine (serotypes Ia, Ib and III) are underway or planned
- For example: 1 trial found vaccine efficacy of 36% (95% CI 1-58%) against first vaginal acquisition in healthy non-pregnant women (Hillier et al 2018)

Conclusions

- Strong evidence for benefits of influenza and pertussis vaccination in pregnancy
- New vaccines in pipeline indicate this is a growing area of research and practice
- Main challenge is implementation and low coverage



Thank you!
Any questions?



**Not Vaccinated?
No Kisses!**

Get the adult whooping cough vaccine.
www.VaccinateYourFamily.org