

Risk-benefit Analysis of Vaccinating Lactating Women and Children Below 1 year of Age with rVSVΔG-ZEBOV-GP

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Background: vaccine

- rVSVΔG-ZEBOV-GP is a live, attenuated replication-competent, viral vector expressing EBOV glycoprotein
- Lack of clinical data and potential safety concerns associated with VSV vaccines in subgroups
 - Potential shedding of vaccine virus in breastmilk and risk to neonate
 - immature immune system in children <1 year
- Compassionate use protocol in DRC excludes lactating women (LW) and children <1 year

Background: Lactating women and children <1 year

- Estimated 1.7 million women of reproductive age (15-49 years) in North Kivu
- Estimated 35% of women of reproductive age are breastfeeding in DRC
 - Inadequate data to quantify the number of lactating women at risk
 - Lactation status not routinely collected
- Estimated 250,000 breastfeeding infants in North Kivu
 - High case-fatality rates observed in children <1 year

Objectives

- Compare the risk of vaccination in lactating women with rVSVΔG-ZEBOV-GP with the risk of acquiring EVD
- Compare the risk of vaccination in children <1 with rVSVΔG-ZEBOV-GP with the risk of acquiring EVD

Methods

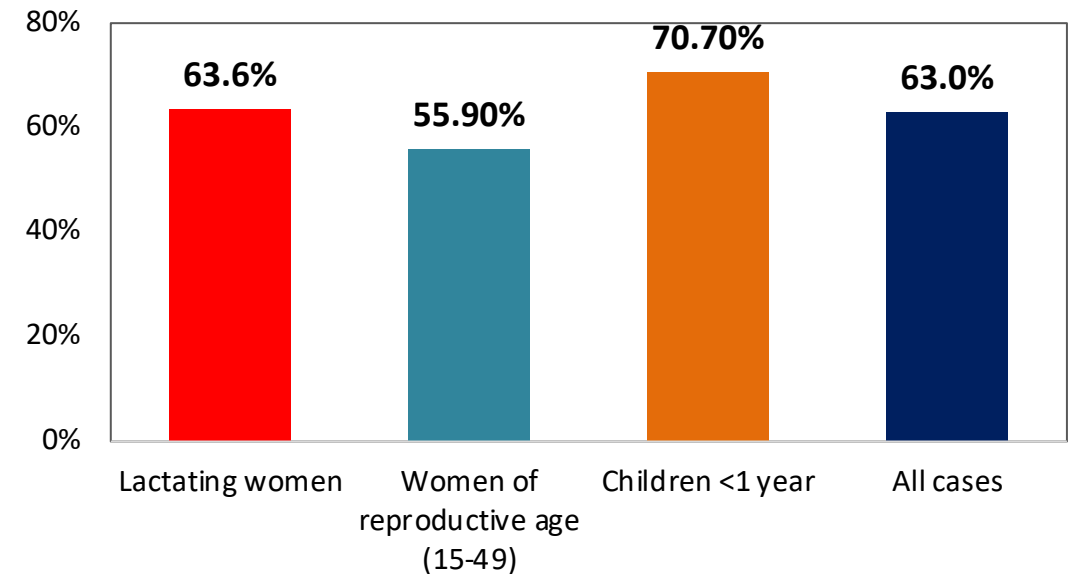
- Review published and grey literature
- Published and unpublished epidemiologic data from recent outbreaks in DRC and in West Africa
- Reviewed current recommendations for other live attenuated vaccines (LAV) used in lactating women and children <1 year
- Reviewed safety evidence in lactating women and very young infants
 - Vesicular stomatitis virus (VSV) vector vaccines
 - VSV survival of vaccine virus in the environment

EVD in lactating women and children <1, North Kivu, DRC

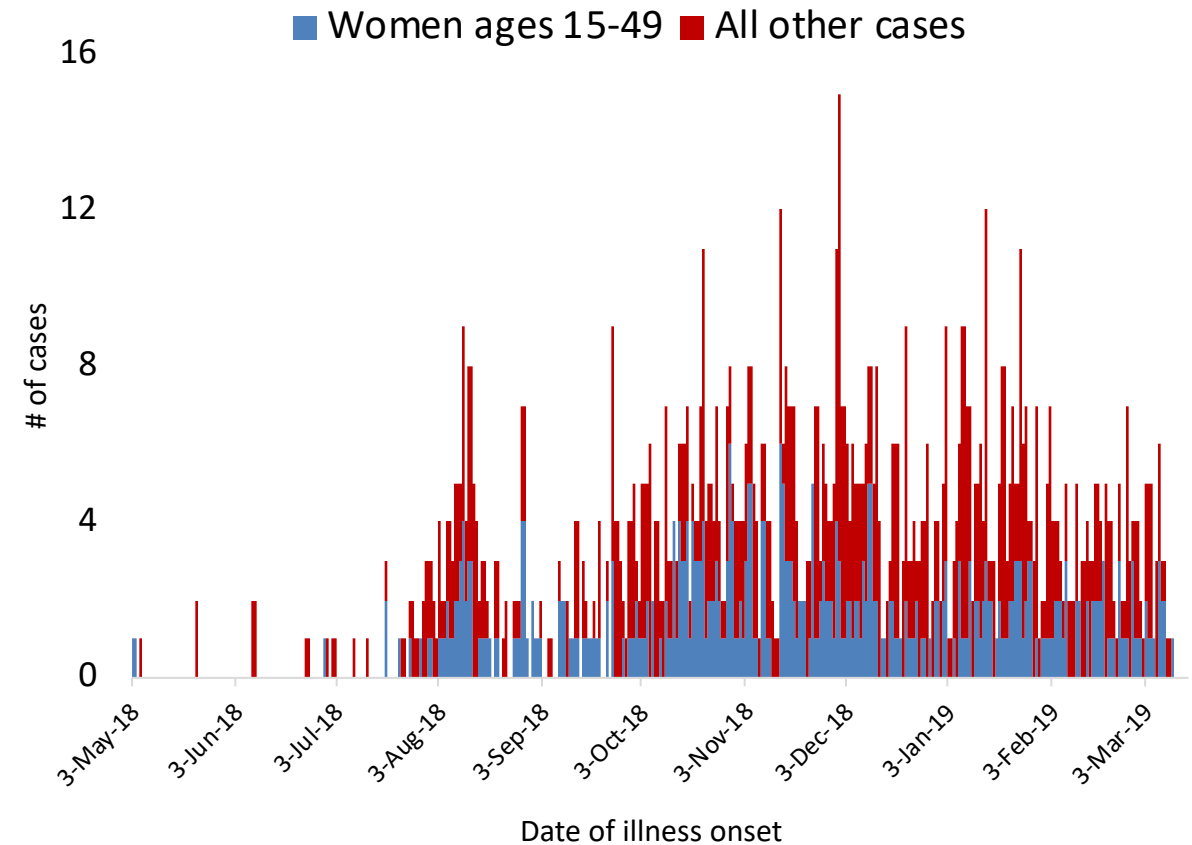
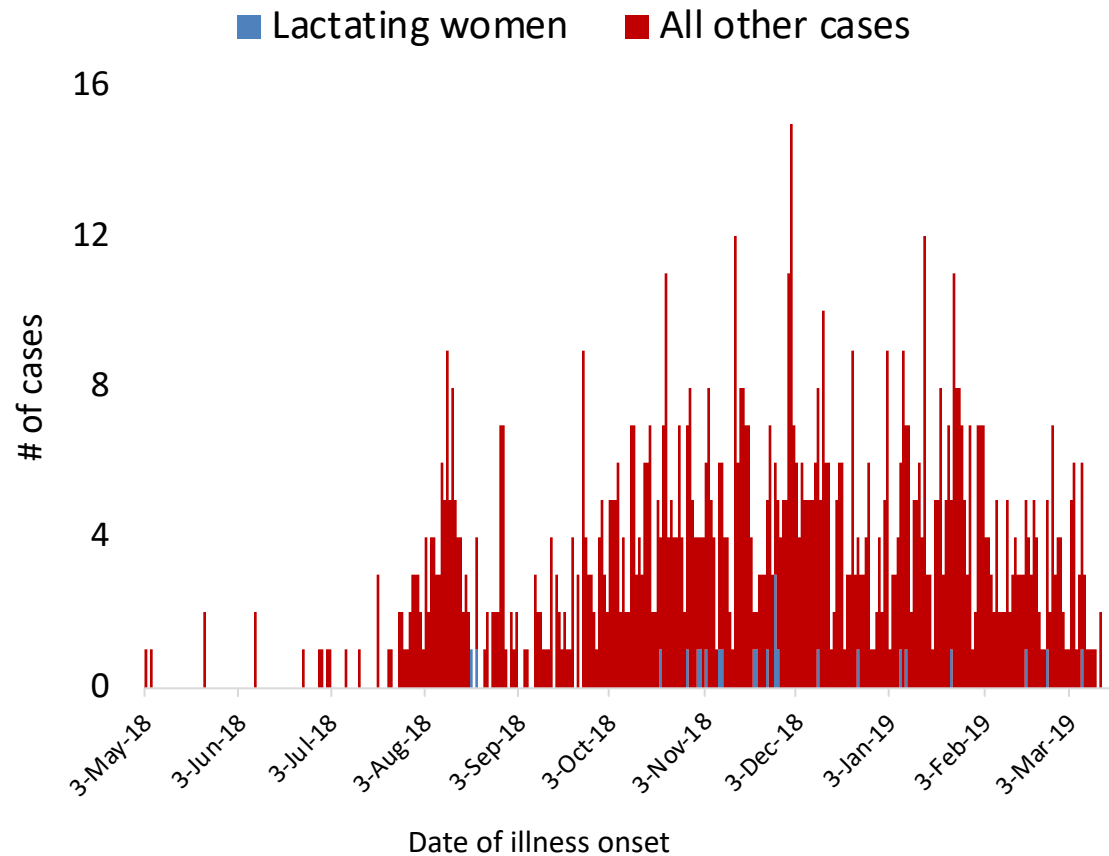
	Cases (n)	Deaths (n)	% proportion of total cases	Attack rate (per 100,000)
Lactating women (reported)	22	14	2.0%	1.3 cases
Women of Reproductive age (15-49)	401	224	36.8%	23.5 cases (repro age)
Children <1 year	75	53	6.9%	30 cases (<1 year)

Data as of April 2, 2019

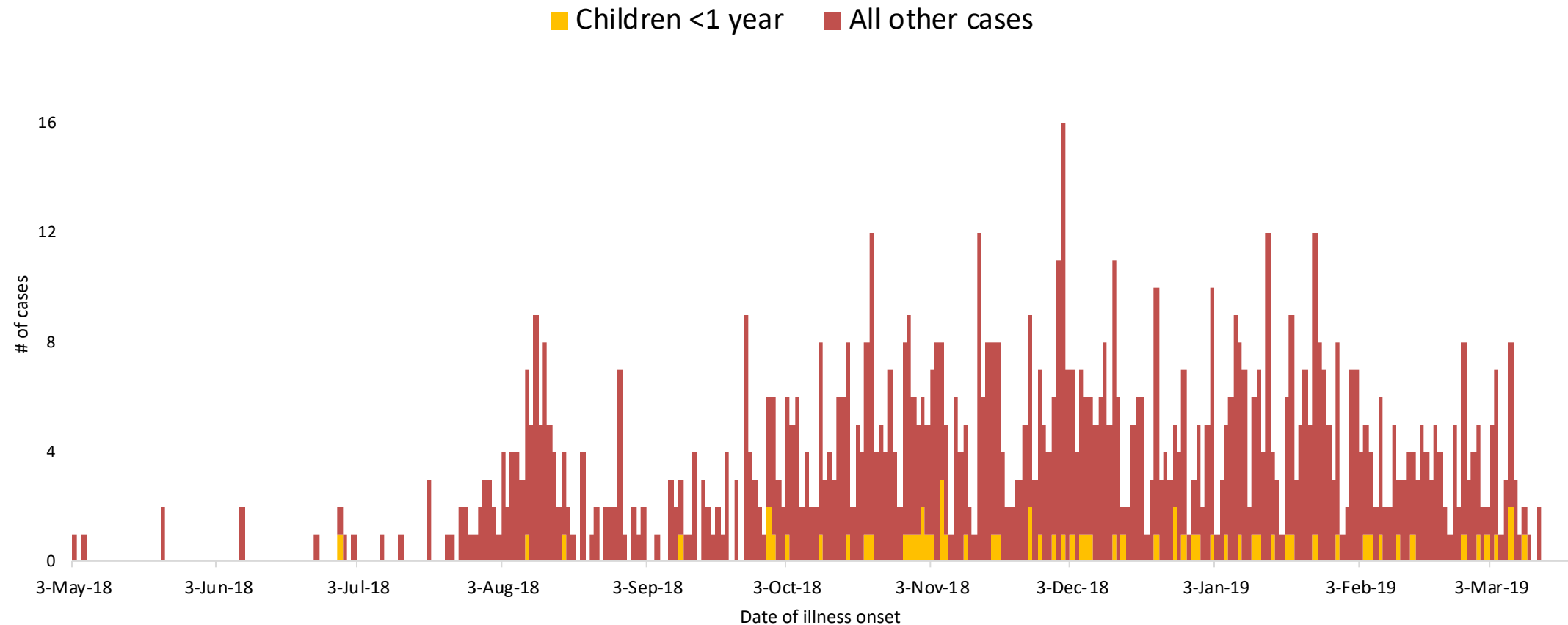
Case-Fatality rates by subgroup



EVD in women, North Kivu, DRC, 2018-19



EVD in children <1 year, North Kivu, DRC, 2018-19



Risk of EVD: absence of vaccination

























Outbreak	Total cases (n)	Children <1 year			Women of reproductive age (15-49 years)			
		Cases (n)	Proportion of all cases% (95% CI)	Case-fatality Rate (%)	Cases among women aged 15-49 (n)	Proportion of female cases aged 15-49 % (95% CI)	Proportion of female cases lactating* % (95% CI)	Case Fatality Rate (%)
Boende 2014	68	1	1.5 (0-4.3)	100	22	32.4 (11.7-21.2)	11.7 (4.0-19.3)	81.8
Mweka 2008	32	1	3.1 (0-9.2)	100	5	15.6 (3.0-28.2)	5.6 (3.0-28.2)	60.0
Mweka 2007	264	-	-	-	55	20.8 (15.9-25.7)	7.5 (15.9-25.7)	67.3
Kikwit 1995	317	4	1.3 (0.0-2.5)	100	80	25.2 (30.7-57.7)	9.1 (20.5-30.0)	75.0
Yambuku 1976	318	24	7.5 (4.6-10.5)	NA	105	33.0 (27.9-38.2)	11.9 (27.9-38.2)	93.3

*Assumes 35% of women of reproductive age are lactating

Risk of EVD: presence of vaccination

- The risk of EVD was low in vaccinated rings at coverage levels of 50% or more (Ca Suffit, 2015)
 - 0 EVD cases among excluded lactating women in both immediate (n=11) and delayed vaccination arms (n=14)
- Most of the cases in lactating women were likely not vaccine-preventable (North Kivu)
 - Vaccine coverage for listed contacts in rings is high (90%+)
 - Only 2 cases were found in are locations where rings had been conducted

Recommendations for other LAV

Vaccine	Lactating women	Children less than 1 year
<i>Adenovirus</i>		
<i>Influenza (LAIV)</i>		
<i>Polio</i>		
<i>Measles</i>		
<i>Mumps</i>		
<i>Rubella</i>		
<i>Varicella</i>		
<i>Japanese Encephalitis</i>		
<i>Rotavirus</i>		
<i>Yellow Fever</i>	 Except in outbreak	
<i>Smallpox</i>		
<i>Zoster</i>		

 Recommended

 Not indicated

 Not recommended

Vesicular Stomatitis Virus (wild type VSV)

- Leads to asymptomatic or mild flu-like symptoms (usually without vesicle formation)
 - 2 cases of VSV-induced encephalitis recorded
- Transmission may occur through contact with vesicular lesions
- Disease potential in children appears the same as for adults
- wtVSV is rarely shed in faeces, urine or milk
 - Detected occasionally in the faeces of symptomatic, experimentally infected swine
 - Potential to pass virus to infants through contaminated vesicle material
 - Nursing opossums remained asymptomatic, although their wtVSV infected mother had lesions

rVSV-ZEBOV vaccine candidate studies

- Animal studies
 - No clinical illness in most animal species tested (mice, rats, guinea pigs, hamsters, ferrets and NHP), young pigs developed clinical illness resembling wtVSV symptoms
 - Shedding of viral RNA in urine
- Clinical studies
 - Viremia and shedding is largely restricted to the first 1–3 days
 - Level of vaccine virus in excretions/secretions appears to be low (<1000 copies/mL, which corresponds to <10 plaque forming units/mL)
 - RNA detected in saliva and urine in <10% of adult subjects and 80% of adolescent saliva
 - Transient vesicular or purpuric skin lesions have been noted in small numbers of vaccinated individuals 7-9 days after vaccination
 - Vaccine virus has been identified in synovial fluid and skin in a small number of subjects by qRT-PCR, but infectious virus was rarely present

Summary

- Number of lactating cases (2% of all cases) is potentially underestimated
- Children <1 year represent 7% of EVD cases
- Risk of infection for unvaccinated individuals in rings is low when vaccine coverage in rings is high
- Other LAV vaccines are given to both groups, recommendations depend on context
- Limited safety evidence in VSV candidate vaccines for lactating women or children <1 year
- Based on animals studies the vaccine virus may shed in body fluids, unlikely in breastmilk
- Uncertain if VSV vaccines are safe to be used in children under 1-year and lactating women

Thank you



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