University of Otago
ŌTĀKOU WHAKAIHU WAKA

Measles
– do we need to do something about waning immunity?
- how would we do it?

Peter McIntyre
Professor
Department of Paediatrics and Child Health
Faculty of Medicine – Dunedin



BACKGROUND

Aerosol delivery of live attenuated measles vaccine – not a new idea

1980s



Albert Sabin

1990s

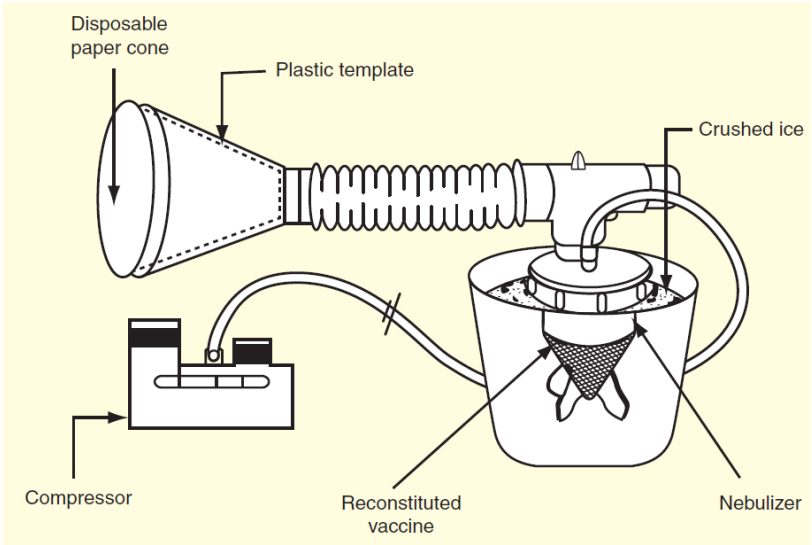


Figure 1. Diagram of the classical Mexican device used to aerosolize liquid measles virus vaccine.



Benett JV et al Bulletin of WHO 2002; 80:806-12



Dilraj A et al Lancet. 2000; 355:798-803

2002 WHO Measles Aerosol Va

" Aerosol measles vaccine appears to be
No increase in adverse side effects of
In 2002 WHO initiated the Measles Ae
achieve licensure of a device and

2015

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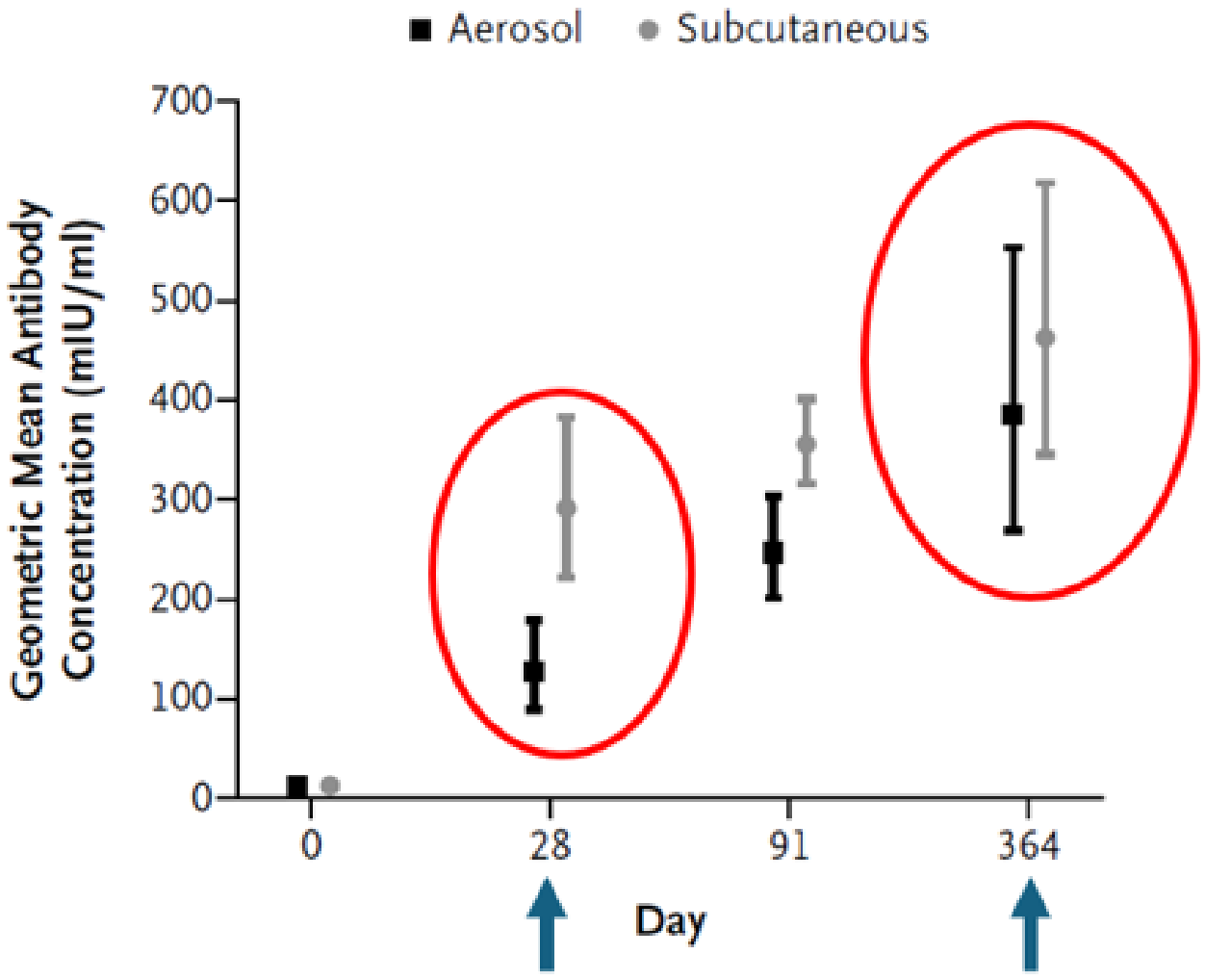


Figure 3. Geometric Mean Concentrations of Antibodies against Measles, According to Vaccine Group.

Mucosal vaccination route matters

News & views

Vaccine boosters

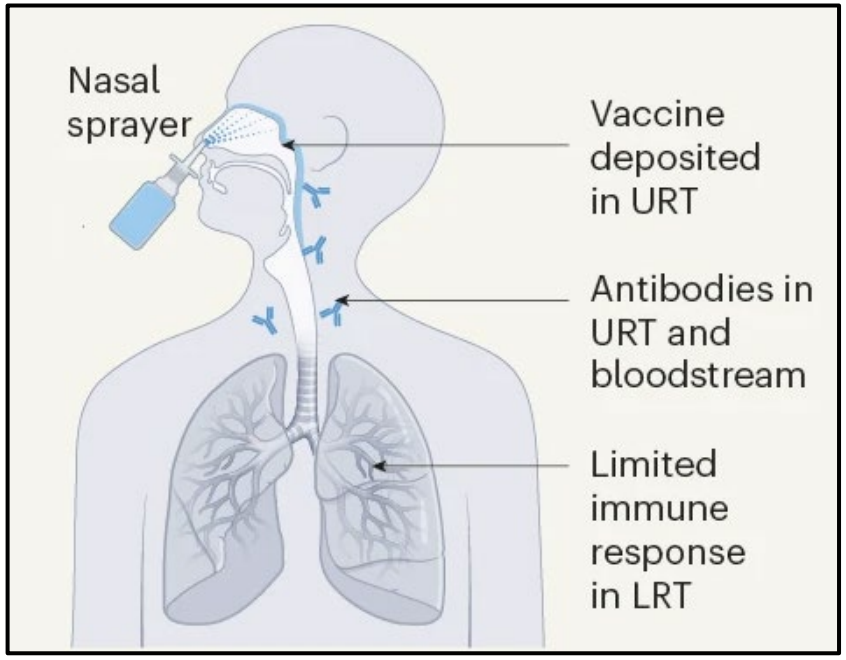
https://doi.org/10.1038/s41590-024-01950-6

The delivery device of SARS-CoV-2 mucosal vaccine matters

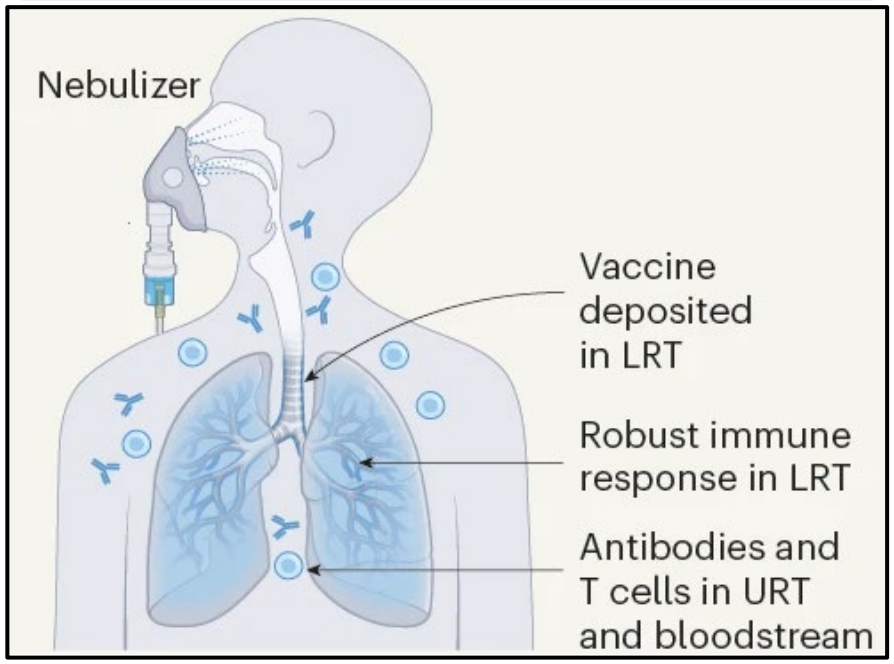
Fanchong Jian & Yunlong Cao

Published online: 03 September 2024

Intranasal



Inhaled aerosol







Technology Platform :: Vaxxas

Vaxxas

MAXXED TRIAL

MAXXED STUDY

PLOS ONE

Aerosol, intradermal, and intramuscular measles-mumps-rubella vaccine delivery in vaccinated young adults

PLOS ONE | https://doi.org/10.1371/journal.pone.0318893 March 21, 2025



Randomised Controlled Trial (RCT)

- **Low measles and/or mumps Ab randomised to:**
- **Aerosol** OR **Intradermal** OR **Intramuscular**











Challenge study

- **Measles and mumps above threshold**
- **Aerosol**

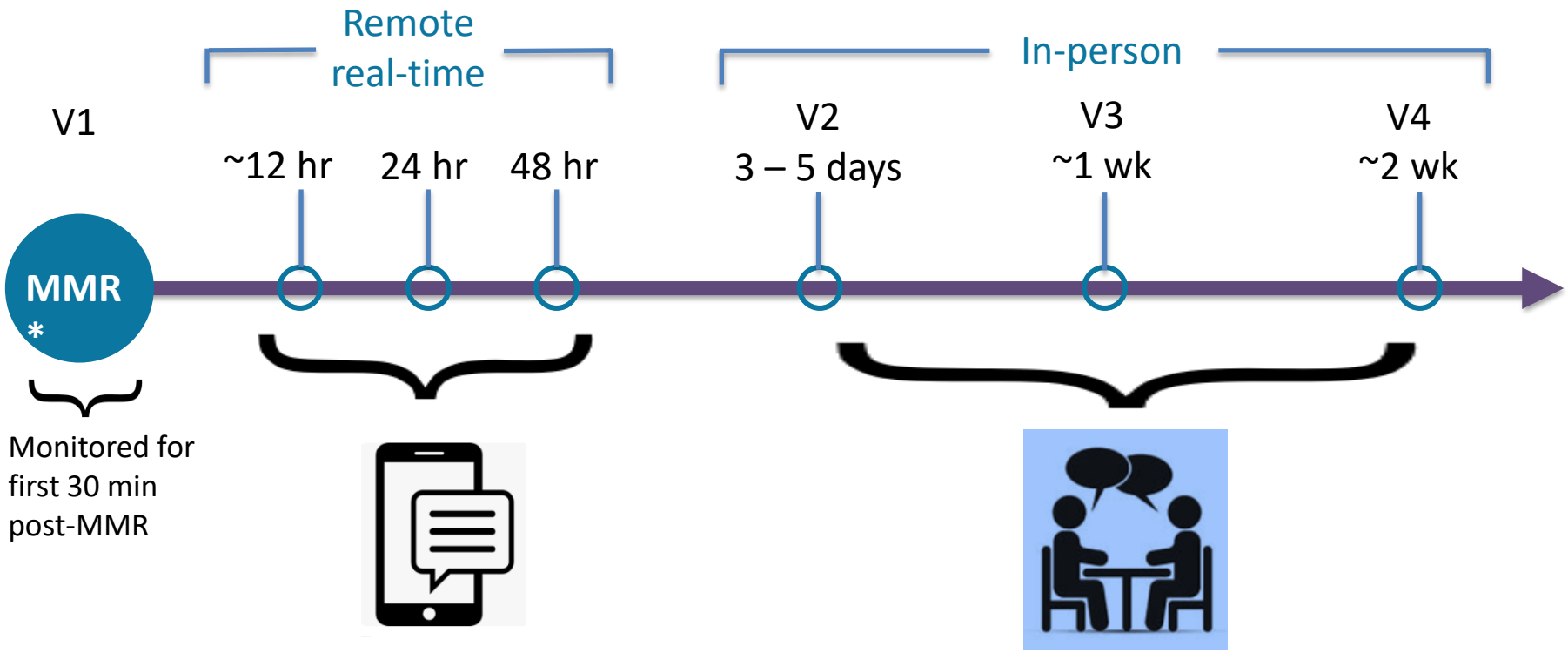


Aims, recruitment and vaccination overview

	• **Randomised controlled trial (RCT)**	• **Challenge study**
Aims	Immunogenicity and safety of MMR delivered by intradermal injection or inhaled aerosol vs. IM	"Challenge" with Aerosol MMR
Recruitment (based on local Diasorin assay results)	**Seronegative** (or equivocal) *measles and/or mumps*	**Seropositive to** *measles <u>and</u> mumps*
Participants	N = 190	N = 114

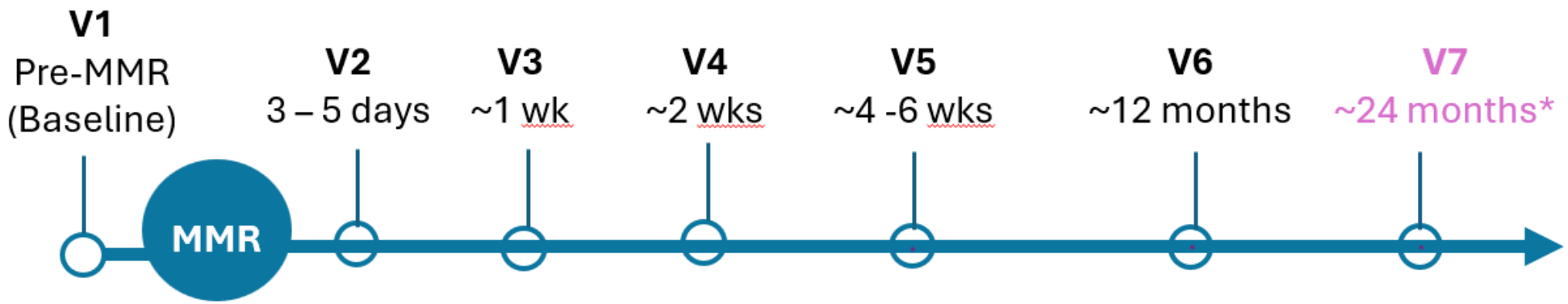
+ 46 who did not elect to be in RCT but provided paired baseline and '4 – 6 week' serum

MAXXED study symptom reporting



Exclusion criteria for study participation: NZ Immunisation Handbook contraindications
Limited to significant immunocompromise

Sample Collection Timeline

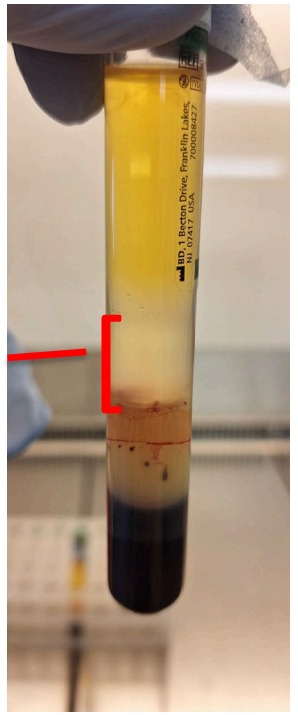


	V1	V2	V3	V4	V5	V6	V7
Serum: Local labs (Me+ Mum Abs)	✓				✓		
Serum: RIVM Netherlands: MIA (Me, Mu, Rub Abs)	✓	✓	✓	✓	✓	✓	✓
Oral fluid (gingival crevicular fluid)		✓	✓	✓			

T cell and mucosal immunology: PhD sub-cohort N = 57

	Baseline	3 – 5 days	~1 wk	~2 wks	4 – 6 wks	12 mths
	V1	V2	V3	V4	V5	V6
Lymphocytes (peripheral blood mononuclear cells)	✓				✓	✓
Nasal lining fluid	✓				✓	✓
Plasma	✓				✓	✓
Serum: Local labs (Me+ Mum Abs)	✓				✓	
Serum: RIVM Lab Netherlands: MIA (Me, Mu, Rub Abs)	✓		✓	✓	✓	✓
Oral fluid (gingival crevicular fluid)	✓	✓	✓	✓	✓	✓

PBMCs





Nasal lining fluid swab

RESULTS
– RCT IMMUNOGENICITY @ 12 MONTHS
- BY ROUTE IM V ID V AER

Measles antibody response @ 12 months: pre-MMR Ab in lowest third N = 40

Route	Pre-MMR[a]		Post-MMR @ 12 months			
	Min, max	GMT (95% CI)	Min, max	GMT (95% CI)	Post/pre GMT ratio	Ratio of post/pre GMT ratio
IM n=13	130, 490	282.3 (221.7, 359.4)	241, 2190	848.3 (571.5, 1259.3)	3.0 (1.9, 4.7)	Ref
ID n=14	70, 520	288.1 (208.2, 398.7)	260, 1220	533.5 (404.5, 703.6)	1.9 (1.2, 2.8)	0.6 (0.3, 1.1)
AE n=13	80, 320	199.3 (154.5, 257.0)	327, 3530	1384.3 (871.7, 2198.5)	6.9 (4.2, 11.5)	2.3 (1.2, 4.4)

[a]Using pre-MMR tertile cut-off for respective vaccine delivery route

Measles antibody response @ 12 months: Tertile 2 N = 39

Route	Pre-MMR[a]		Post-MMR @ 12 months			
	Min, max	GMT (95% CI)	Min, max	GMT (95% CI)	Post/pre GMT ratio	Ratio of post/pre GMT ratio
IM n=13	500, 970	757.6 663.9, 864.6	534, 1550	1014.6 (816.6, 1260.6)	1.4 (1.1, 1.7)	Ref
ID n=13	560, 970	707.1 640.1, 781.0	370, 1000	738.3 (616.1, 884.7)	1.0 (0.9, 1.3)	0.8 (0.6, 1.1)
AE n=13	350, 690	482.8 416.8, 559.2	454, 350	957.8 (672.5, 1364.1)	2.0 (1.4, 2.9)	1.5 (1.0, 2.3)

[a]Using pre-MMR tertile cut-off for respective vaccine delivery route

Measles antibody response: Tertile 3 N = 38

Route	Pre-MMR[a]		Post-MMR @ 12 months			
	Min, max	GMT (95% CI)	Min, max	GMT (95% CI)	Post/pre GMT ratio	Ratio of post/pre GMT ratio
IM n=12	1080, 5310	1904.705 1365.228 2657.359	780 4268	1631.1 (1161.7, 2290.2)	0.9 (0.5, 1.3)	Ref
ID n=13	1030, 6760	2392.18 1731.292 3305.349	1080 4994	2351.8 (1722.5, 3211.0)	1.0 (0.6, 1.5)	1.1 (0.6, 2.1)
AE n=13	700, 4640	1262.391 906.8445 1757.337	390 2270	1029.7 (765.0, 1386.0)	0.8 (0.5, 1.2)	1.0 (0.5, 1.7)

RESULTS

– AEROSOL RECIPIENTS @ 4-6 WEEKS

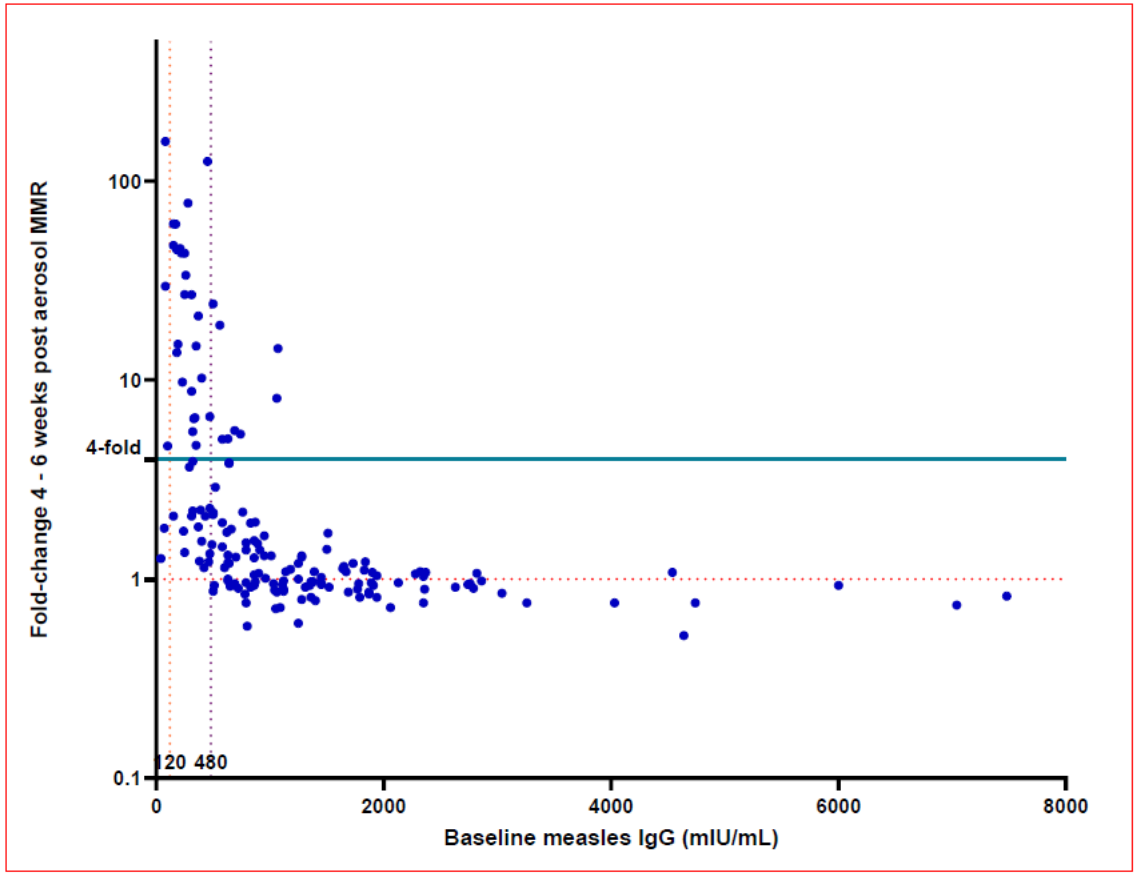
*** SAFETY SIGNAL – COUGH/CHEST TIGHTNESS**

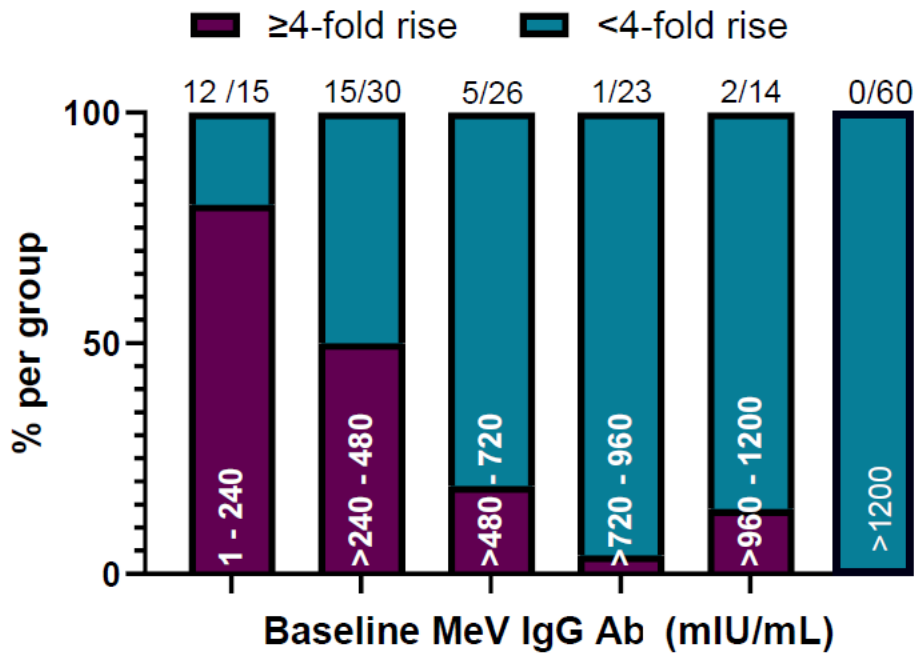
~ 20%

~ 80% PREFER AEROSOL EVEN IF EXPERIENCED COUGH

Measles

MAXXED study





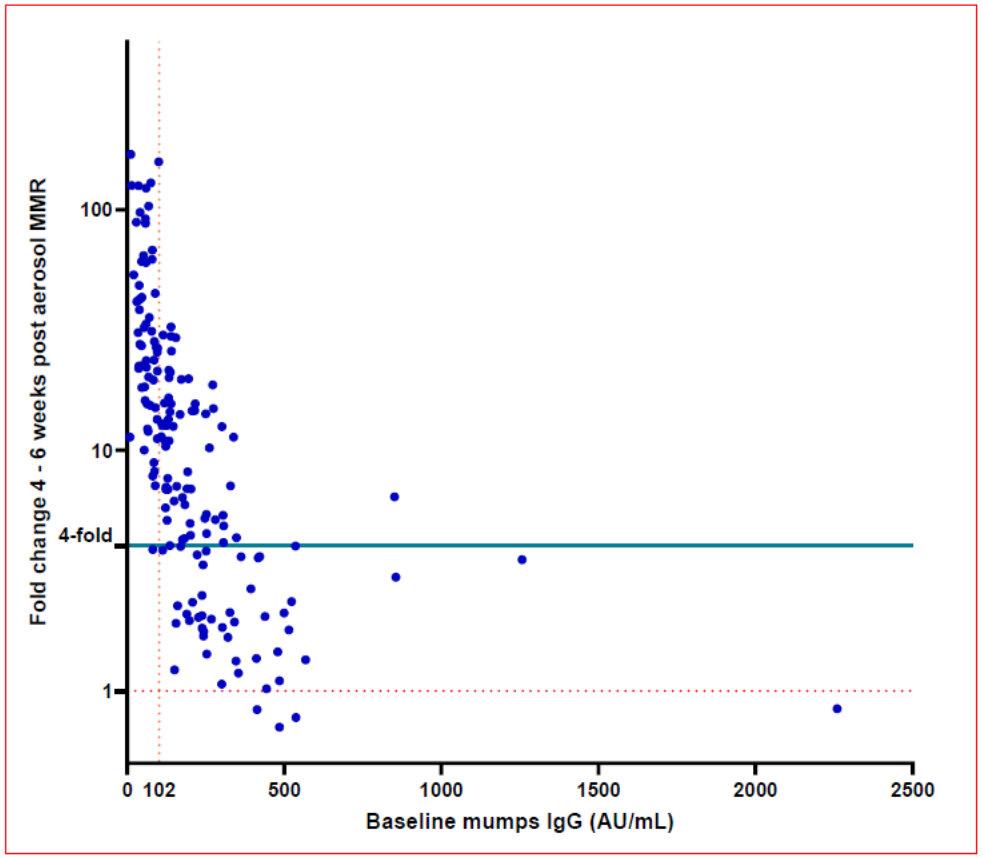
Baseline Measles virus (MV) IgG

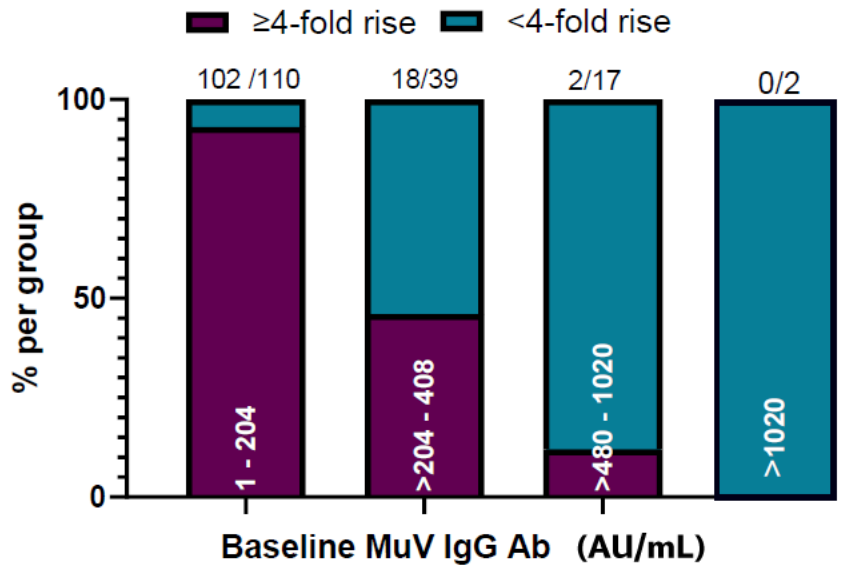
- 3% < 120 mIU/mL
- 27% < 480 mIU/mL

- 21% of participants had a 4-fold rises in measles IgG @ 4- 6 wks
- No ≥4-fold rises if MeV Ab >1071 mIU/mL
- Consistent with data from real-world studies

Mumps

MAXXED study





Baseline Mumps IgG Ab, arbitrary RIVM units/mL

- **61/168 (36%) <102 AU/mL**

- 4-fold rises in mumps IgG @ 4 – 6 wks seen in 73% of participants up to baseline level ~851 AU/mL

WILL ELIMINATION COUNTRIES NEED “BOOSTING”FOR MEASLES AND/OR MUMPS?

IF THERE WAS AN MMR 3 HOW WOULD YOU DO IT?



