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Background

Antibodies to measles, mumps, and rubella decline 3% per year on average. Individual variations and differences across antigens are not well understood.

Better understanding of vaccine induced antibody persistence after two doses of MMR vaccine (MMR2) is needed.

Objectives

- (1) Identify patterns of seropositivity and antibody persistence after MMR2
- (2) Compare antibody kinetic patterns across all three MMR antigens
- (3) Estimate the rate of decline in antibody titers over 12 years

Methods

Study Population:

Children vaccinated with MMR2 at 4-6 years of age were followed up to 12 years post-vaccination in Marshfield, WI (1994-2007).

Laboratory Methods:

Serum samples were collected prior to MMR2 (baseline) and at 1 month, 6 months, 2 years, and every 2-3 years post-vaccination until study completion.

Neutralizing antibody levels were evaluated by plaque-reduction neutralization (PRN).

**For the purposes of this study: a titer of >120 mIU/mL for measles, a titer of >10 for mumps, and a titer of ≥10 for rubella were considered seropositive.*

Analysis:

The rate of decline for each antigen among those with a declining trend was estimated using repeated measures linear mixed models.

Covariates examined:

- Sex
- Age at first dose of MMR (12-15 months vs.16-24 months)
- Level of MMR2 response (<2 fold, 2 to <4 fold, ≥4 fold)
- Log2-transformed baseline titers
- Time (months) between receipt of MMR1 and MMR2

Pattern and Trend Definitions

Seropositivity Patterns:

- (1) **Consistently Seropositive:** seropositive titer at every follow-up visit
- (2) **Seronegative Converters:** became and remained seronegative
- (3) **Inconsistent:** seronegative titer followed by a seropositive titer

Persistence Trends:

- (1) **Stable:** titers at or around baseline that did not decline during follow-up
- (2) **Declining:** majority of titers declining during follow-up
- (3) **Variable:** significant increases and decreases in titers during follow-up
- (4) **Other:** individuals who could not be classified

Results

Table 1. Comparison of Kinetic Patterns Across MMR Antigens

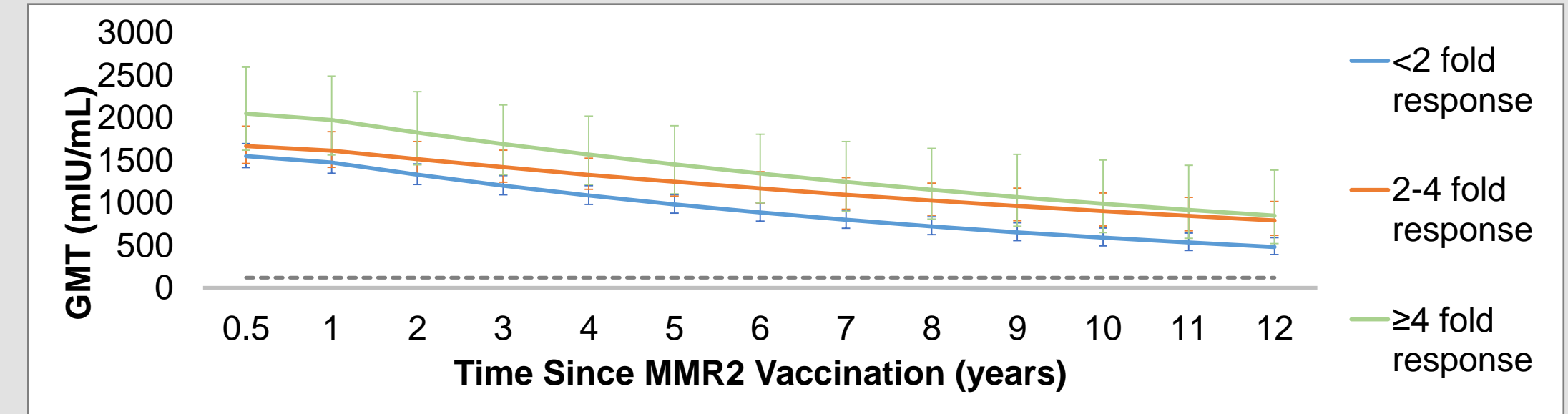
Patterns and Trends Across Time	Measles N=302	Mumps N=296	Rubella N=296	% With Same Pattern for all 3 Antigens, N= 291
Seropositivity Patterns				
Consistently Seropositive	291 (96)	260 (88)	235 (79)	212 (73)
Seronegative Converters	5 (2)	20 (7)	11 (4)	0
Inconsistent	6 (2)	16 (5)	50 (16)	0
Persistence Trends				
Stable	38 (13)	63 (2)	31 (11)	2 (1)
Declining	169 (56)	29 (10)	110 (37)	18 (6)
Variable	50 (17)	96 (32)	98 (33)	17 (6)
Other	45 (15)	108 (37)	57 (19)	4 (1)

14% of subjects had the same persistence trends for all antigens.

Model Results

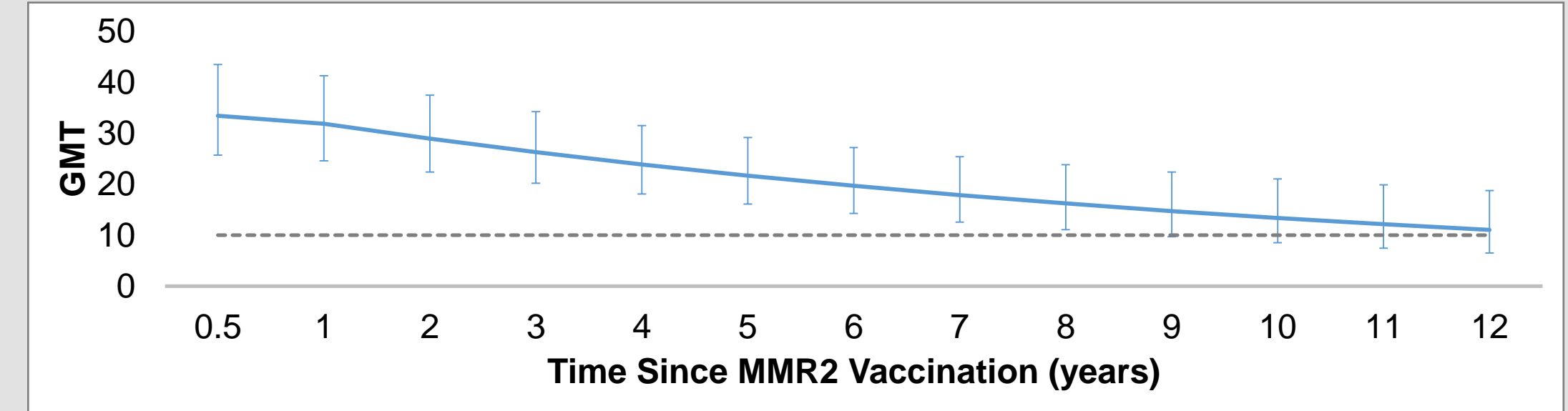
- Measles: MMR2 response and baseline titer were associated with decline
- Mumps: no factors were associated with decline
- Rubella: age at first dose of MMR (MMR1) was associated with decline

Figure 1. Measles Antibody Decline by MMR2 Response



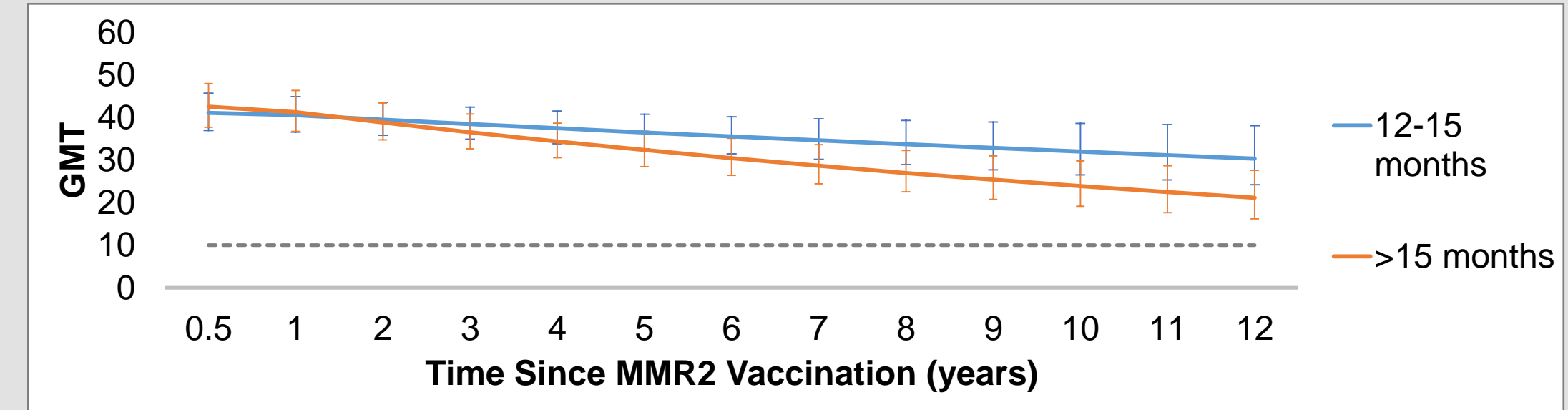
Measles rate of decline per year: 9.7% among individuals with <2 fold response, 6.3% among 2-4 fold response, and 7.4% among those with ≥4 fold response.

Figure 2. Mumps Antibody Decline



Mumps rate of decline per year: 9.2%.

Figure 3. Rubella Antibody Decline by Age at Receipt of MMR1



Rubella rate of decline per year: 2.6% among individuals vaccinated 12-15 months, 5.9% among those vaccinated >15 months.

Conclusions

The rate of antibody decay varied substantially across individuals and antigens.

A fast rate of decline coupled with high variation was observed for mumps, yet no predictors were identified.

Future research should focus on better understanding waning titers to mumps and its impacts on community protection, in light of recent outbreaks.