Lamerato et al. Impact of Childhood Vaccination on Short and Long-Term Chronic Health Outcomes in Children: A Birth Cohort Study. Unpublished Henry Ford Study

High-quality systematic reviews and meta-analyses (SMRAs) have asked, and re-asked, the question of whether routine childhood vaccines are associated with autism/autism spectrum disorder (ASD). The answer to this question has been a consistent "*no*". One of the key studies was done by Taylor et al and published in 2014. These authors pooled cohort and case–control studies and concluded there is no evidence of a link (association) between MMR vaccine or thimerosal-containing vaccines and ASD.[1] A similar result of *"no association/link"* was reported by Di Pietrantonj et al in a 2020 Cochrane SRMA.[2] Both of these studies involved more than a million children.

The broader vaccine safety literature has been repeatedly synthesized with rigorous inclusion criteria (active surveillance, analytic designs, and confounder control), reinforcing overall safety while identifying rare, known adverse events.[3],[4]

Because concerns sometimes focus on adjuvants, a recent nationwide Danish cohort (n > 1.2 million children) used detailed registry linkage and dose-response modelling to examine cumulative aluminum exposure from vaccines. Adjusted hazard ratios per additional mg of aluminum showed no increased risk for ASD (HR 0.93 [95% CI 0.89 to 0.97]), ADHD, autoimmune, atopic, or neurologic outcomes through follow-up, with extensive sensitivity analyses for healthcare utilization, socioeconomic status (SES), and other confounders.[5]

The bottom line from the best available evidence on childhood vaccines is that the potential benefits generally outweigh the potential harms in most children. Specifically, vaccines prevent serious infectious diseases and are not associated with autism/ASD.

Clinical Question: Is exposure to any childhood vaccination vs no vaccination associated with the subsequent development of chronic health conditions?

PECOT

- **Population:** Consecutive birth cohort of children born 2000–2016, enrolled for ≥ 60 days in the Health Alliance Plan with Henry Ford Health System (HFHS).
    - **Exclusions**: Children with chromosomal abnormalities, cerebral palsy, cystic fibrosis, spina bifida, congenital heart disease, or brain/neurological/other congenital conditions present or discovered after birth.
- **Exposure:** Receipt of any vaccine on the US Centers for Disease Control and Prevention (CDC) childhood schedule; exposure status classified before onset of each outcome (exposed vs unexposed) using HFHS electronic records plus the Michigan state immunization registry. (n=16,511 vaccinated**)**
- **Comparison:** No vaccine exposure during plan enrollment. (n=1,957 unvaccinated)
- **Outcome:**
    - **Primary Outcome:** A composite of *"chronic health condition"* (diabetes, asthma, food allergy, cancer, brain dysfunction, atopic disease, autoimmune disease, and neurological, neurodevelopmental, seizure, and mental health disorders) based on ICD-9/10 codes.
    - **Secondary Outcomes:** Not part of the composite: asthma attack/bronchospasm, anaphylaxis, eczema (acute/chronic), ear infection (acute/chronic), and peanut allergy.
- **Type of Study:** Retrospective birth cohort (observational) study.

Authors' Conclusions: *"This study found that exposure to vaccination was independently associated with an overall 2.5-fold increase in the likelihood of developing a chronic health condition, when compared to children unexposed to vaccination. This association was primarily driven by asthma, atopic disease, eczema, autoimmune disease and neurodevelopmental disorders. This suggests that in certain children, exposure to vaccination may increase the likelihood of developing a chronic health condition, particularly for one of these conditions."*

Quality Checklist for Observational Studies:

1. **Clearly focused issue? Yes.** Exposure (any vaccine) vs no exposure (no vaccine) with a prespecified composite outcome.
2. **Appropriate method? Yes** (for associations). A retrospective cohort can determine associations but should not conclude causality.
3. **Cohort recruited acceptably? Yes.** Consecutive birth cohort within a defined insured population.
4. **Exposure measured accurately? Yes.** Ascertainment from EHR plus state registry; Michigan mandates reporting to the registry within 72 hours.
5. **Outcome measured accurately? Unsure.** Reliance on ICD codes, plus large differences in healthcare utilization, raises ascertainment bias concerns.
6. **Important confounders identified/handled? No.** Limited baseline adjustment (sex, race, birthweight, prematurity, birth trauma, and respiratory distress) with no SES variables and only sensitivity checks for utilization. This means substantial residual confounding is likely.
7. **Follow-up complete enough? No.** Marked differential follow-up (median 970 days vaccinated vs 461 unvaccinated) despite sensitivity analyses.
8. **Precision of results? Unsure.** The composite Hazard Ratio (HR) is precise (HR 2.54 [95% CI 2.16 to 2.97]), but many components are sparse/unstable with zero events in some of the unexposed group (ex: diabetes, ADHD and learning disabilities).
9. **Do you believe the results? No.** Direction and magnitude are plausibly explained by residual confounding and detection/ascertainment bias.
10. **Applicability to the local population? Unsure.** A single integrated Health Maintenance Organization (HMO) in Detroit may not have external validity to other health systems and countries.
11. **Fit with other evidence? No** for the broad *"chronic disease"* signal. The large positive associations reported for several chronic categories conflict with higher-quality evidence and recent nationwide Danish data. However, the study's null result for autism aligns with multiple SRMAs.
12. **Who funded the study?** No external funding declared.
13. **Conflicts of interest declared? Unsure.** A specific conflict-of-interest statement was not found in the manuscript provided.

Results: A total of 18,468 children met eligibility (1,957 unvaccinated and 16,511 vaccinated). The median doses of vaccines in the exposed group were 18. Compared with unvaccinated children, the vaccinated group had longer follow-up (median 970 vs 461 days) and a higher prevalence of female sex, African American race, low birth weight, prematurity, and respiratory distress/trauma at birth.

Key Result: After multivariable adjustment, any vaccination was associated with a higher hazard of the composite chronic health condition (HR 2.54 [95% CI 2.16 to 2.97]).

- **Primary Outcome:** Vaccination was associated with a higher incidence by Poisson and a higher hazard by Cox models for the composite outcome of chronic health conditions. The 10-year *"free of chronic condition"* probability is 43% vaccinated vs 83% unvaccinated.
- **Secondary Outcomes:**
    - Higher hazards were reported for ear infection (HR 7.00), chronic ear infection (HR 7.89), asthma attack/bronchospasm (HR 5.82), anaphylaxis (HR 5.64), and eczema (HR 1.31)
    - No significant associations were reported for chronic eczema or peanut allergy.
    - Multiple outcomes yielded no calculable HRs due to zero events in the unvaccinated group.
    - Note, autism showed no association (adjusted HR 0.62 [95% CI 0.10 to 3.69]).

Five Key Threats to Validity:

1) Ascertainment Bias: Vaccinated children had ~7 encounters/year, unvaccinated ~2 (rising to ~5 only if they had a chronic diagnosis). Diagnoses that depend on clinical contact, like asthma & speech delay, will be detected more often in kids who see clinicians more often. The authors acknowledge this and perform sensitivity analyses restricted to children with ≥ 1 encounter, but large utilization imbalances remain an inherent bias source in HER-based cohorts comparing *"any vaccination"* to *"none"*. This is a classic observational pitfall emphasized in quality tools (comparability domain; confounders and follow-up adequacy).

2) Residual Confounding: The model adjusts for sex, race, birthweight, prematurity, birth trauma, and respiratory distress, but not SES, parental education, environmental exposures, parental health-seeking behaviour, or daycare attendance. These are all linked to both vaccination decisions and the likelihood of diagnosis. The authors explicitly note no SES data. This leaves large, directionally plausible confounding that can inflate associations between "*any vaccination*" and outcomes that rely on healthcare contact. The Newcastle-Ottawa comparability standards highlight this risk.

3) Follow-Up: Median follow-up was roughly half as long in the unvaccinated group (461 vs 970 days). Even with time-to-event methods and sensitivity analyses (1 to 5-year enrollment subsets), censoring patterns that differ by exposure can distort hazards, particularly when many outcomes are diagnosed later in childhood (neurodevelopmental and mental health disorders were only assessed from age ≥ 2 years).

4) Crude Exposure & Heterogeneous Composite Endpoint: *"Any vaccine"* collapses timing, product, dose, and schedule into a binary exposure. That makes the assessment of temporality, dose–response, or specific attributions more difficult. At the same time, the primary outcome bundles disparate conditions (from asthma to autoimmune disease to speech disorder). Composite outcomes can be useful, but they risk misleading signals when component conditions vary dramatically in baseline incidence, detection thresholds, and clinical importance. This is especially true in the presence of detection bias. The paper itself notes it did not evaluate temporal relationships or the number/type of vaccines.

5) Few Events & Unstable Estimates: For several outcomes, the unvaccinated group had zero events, precluding HR estimation (ADHD, diabetes and learning disability). Where HRs were estimable, several had very wide CIs (anaphylaxis), consistent with instability. Such sparsity, combined with differential follow-up, undermines confidence in the size and even the direction of reported associations.

How does this fit with the existing evidence on vaccines and autism?

On the autism question, this study is consistent with the large prior body of evidence reporting no association between vaccination and autism/ASD. That aligns with multiple SRMAs concluding no link between MMR or thimerosal-containing vaccines and autism and with modern, high-quality registry studies assessing adjuvant-related dose–response (Danish aluminum analysis) that found no increased ASD risk despite excellent control for healthcare use and SES.

However, the paper's broad claim of a 2.5-fold increased risk for a composite of chronic conditions diverges from the better-controlled literature. For example, the Danish nationwide cohort, which was an order of magnitude larger in size with careful adjustment and sensitivity analyses, found no increased hazards for neurodevelopmental, autoimmune, atopic, or neurologic outcomes as aluminum exposure increased. Given the Henry Ford study's design limitations (ascertainment bias, residual confounding, differential follow-up, and crude exposure), the balance of evidence still supports vaccine safety and no causal association with autism.

SGEM Bottom Line: This unpublished single-system retrospective birth-cohort reports an association between "*any vaccination*" and a heterogeneous composite of chronic diseases. The results are inconsistent with the strongest evidence showing no association between childhood vaccines & chronic conditions. We should be skeptical of these findings due to substantial risks of ascertainment bias, residual confounding, and differential follow-up in the Lamerato et al. study.

---

[1] Taylor LE, Swerdfeger AL, Eslick GD. Vaccines are not associated with autism: an evidence-based meta-analysis of case-control and cohort studies. Vaccine. 2014 Jun 17;32(29):3623-9. doi: 10.1016/j.vaccine.2014.04.085. Epub 2014 May 9. PMID: 24814559.

[2] Di Pietrantonj C, Rivetti A, Marchione P, Debalini MG, Demicheli V. Vaccines for measles, mumps, rubella, and varicella in children. Cochrane Database Syst Rev. 2020 Apr 20;4(4):CD004407. doi: 10.1002/14651858.CD004407.pub4. Update in: Cochrane Database Syst Rev. 2021 Nov 22;11:CD004407. doi: 10.1002/14651858.CD004407.pub5. PMID: 32309885; PMCID: PMC7169657.

[3] Maglione MA, Das L, Raaen L, Smith A, Chari R, Newberry S, Shanman R, Perry T, Goetz MB, Gidengil C. Safety of vaccines used for routine immunization of U.S. children: a systematic review. Pediatrics. 2014 Aug;134(2):325-37. doi: 10.1542/peds.2014-1079. Epub 2014 Jul 1. PMID: 25086160.

[4] Gidengil C, Goetz MB, Newberry S, Maglione M, Hall O, Larkin J, Motala A, Hempel S. Safety of vaccines used for routine immunization in the United States: An updated systematic review and meta-analysis. Vaccine. 2021 Jun 23;39(28):3696-3716. doi: 10.1016/j.vaccine.2021.03.079. Epub 2021 May 25. PMID: 34049735.

[5] Andersson NW, Bech Svalgaard I, Hoffmann SS, Hviid A. Aluminum-Adsorbed Vaccines and Chronic Diseases in Childhood : A Nationwide Cohort Study. Ann Intern Med. 2025 Jul 15. doi: 10.7326/ANNALS-25-00997. Epub ahead of print. Erratum in: Ann Intern Med. 2025 Jul 17. doi: 10.7326/ANNALS-25-03233. PMID: 40658954.