Addressing Pediatric Vaccine Hesitancy

Part 2: Specific Vaccine Concerns

Jab Gab: Childhood and Adolescent Vaccination Updates for Health Professionals

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Disclosures

- Nothing to disclose

Part 1 Recap… (12/3/24)

Drs. Braddock and Wilson

- Vaccine hesitancy is not a new phenomenon
- Vaccine hesitancy is complex and multifactorial
  - Safety, importance, religious concerns, uncertainty, etc.
- Misinformation / disinformation is rampant
  - Social media
  - Post-Covid effect
- Policy, community, clinic interventions
- How to talk to patients/parents

Objectives

- Address specific concerns surrounding vaccine hesitancy
  - Efficacy
  - Side effects
  - Allergies to vaccine ingredients
  - Trending vaccine topics and misinformation
- Resources for clinicians

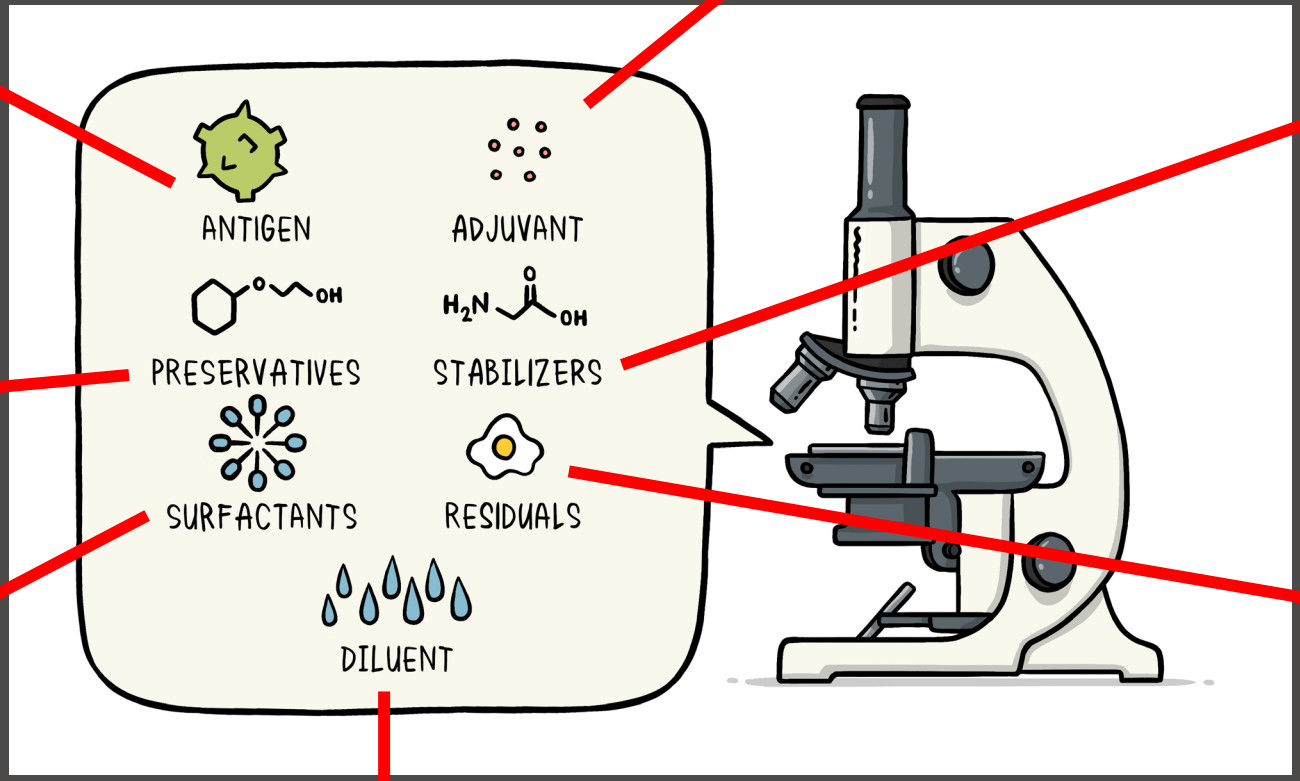
Anatomy of a Vaccine

Full or partial microbe component, generates immune response; live or killed

Increases immune response to vaccine, e.g. keeping vaccine at site longer or stimulating local immune cells [aluminum]

Prevents vaccines in multi-dose vials from being contaminated; not present in single dose vials [Thimerosal]

Prevent clumping or settling of ingredients



Prevent chemical reactions from occurring within the vaccine and keep the vaccine components from sticking to the vaccine vial [Gelatin, lactose, glycine]

Tiny residual amounts of substances used in manufacturing [egg proteins, yeast]

Added just before injection to bring vaccine to correct concentration [usually sterile water]

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https://www.who.int/news-room/feature-stories/detail/how-are-vaccines-developed

Vaccine Efficacy

And how to discuss it

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Vaccine Efficacy

- WHO: Expanded Programme on Immunization (EPI)
- Globally from 1974 – 2024
  - 154 million deaths avoided
  - 9 billion years of life saved
  - 10.2 billion years of full health gained

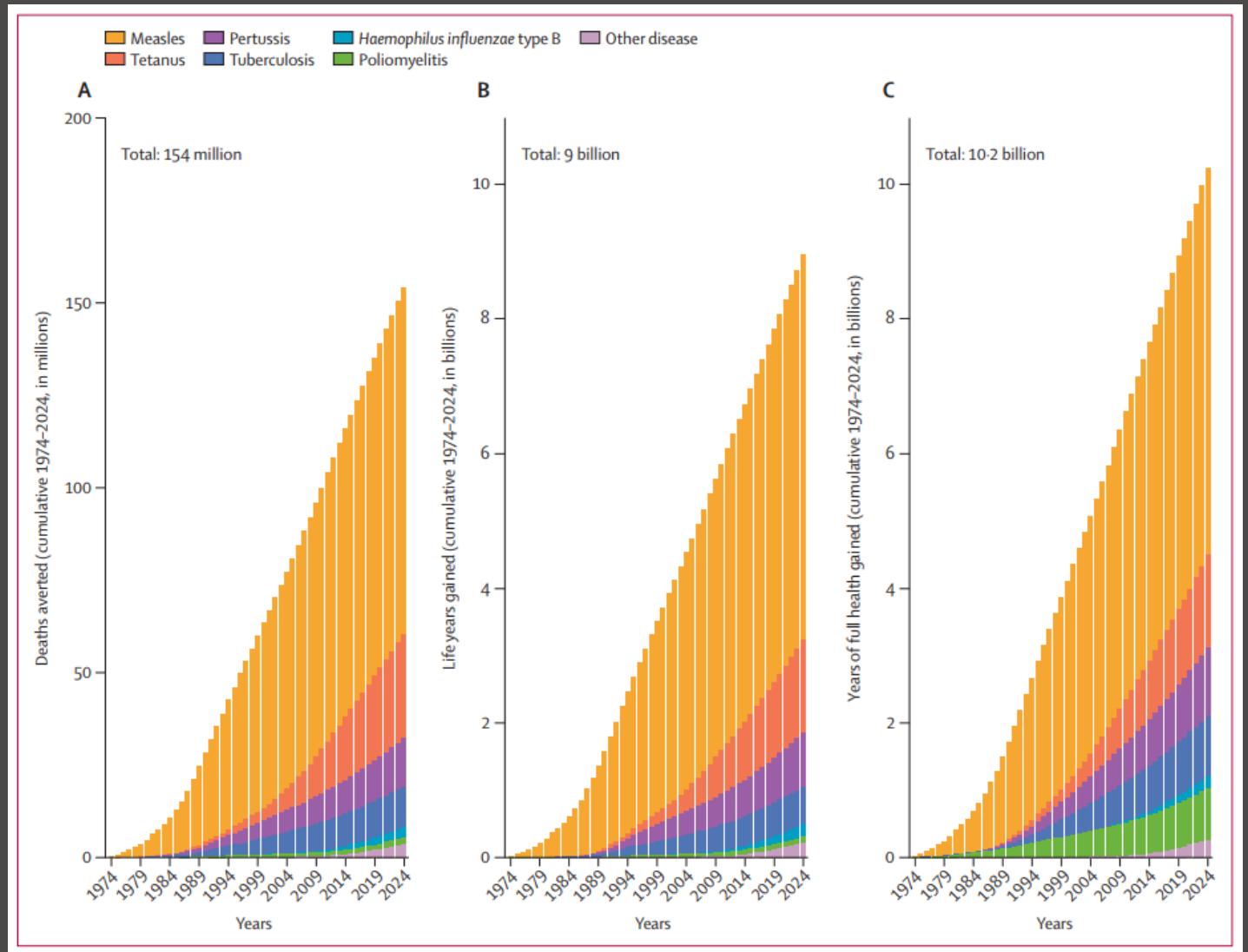

Figure 1: **Deaths averted, years of life saved, and years of full health gained due to vaccination**
Data are cumulative 1974–2024. Measles: deaths averted: 93·7 million; years of life saved: 5·7 billion; years of full health gained: 5·8 billion. Tetanus: deaths averted: 27·9 million; years of life saved: 1·4 billion; years of full health gained: 1·4 billion. Pertussis: deaths averted: 13·2 million; years of life saved: 0·8 billion; years of full health gained: 1 billion. Tuberculosis: deaths averted: 10·9 million; years of life saved: 0·6 billion; years of full health gained: 0·9 billion. Haemophilus influenzae type B: deaths averted: 2·8 million; years of life saved: 0·2 billion; years of full health gained: 0·2 billion. Poliomyelitis: deaths averted: 1·6 million; years of life saved: 0·1 billion; years of full health gained: 0·8 billion. Other diseases: deaths averted: 3·8 million; years of life saved: 0·2 billion; years of full health gained: 0·3 billion.

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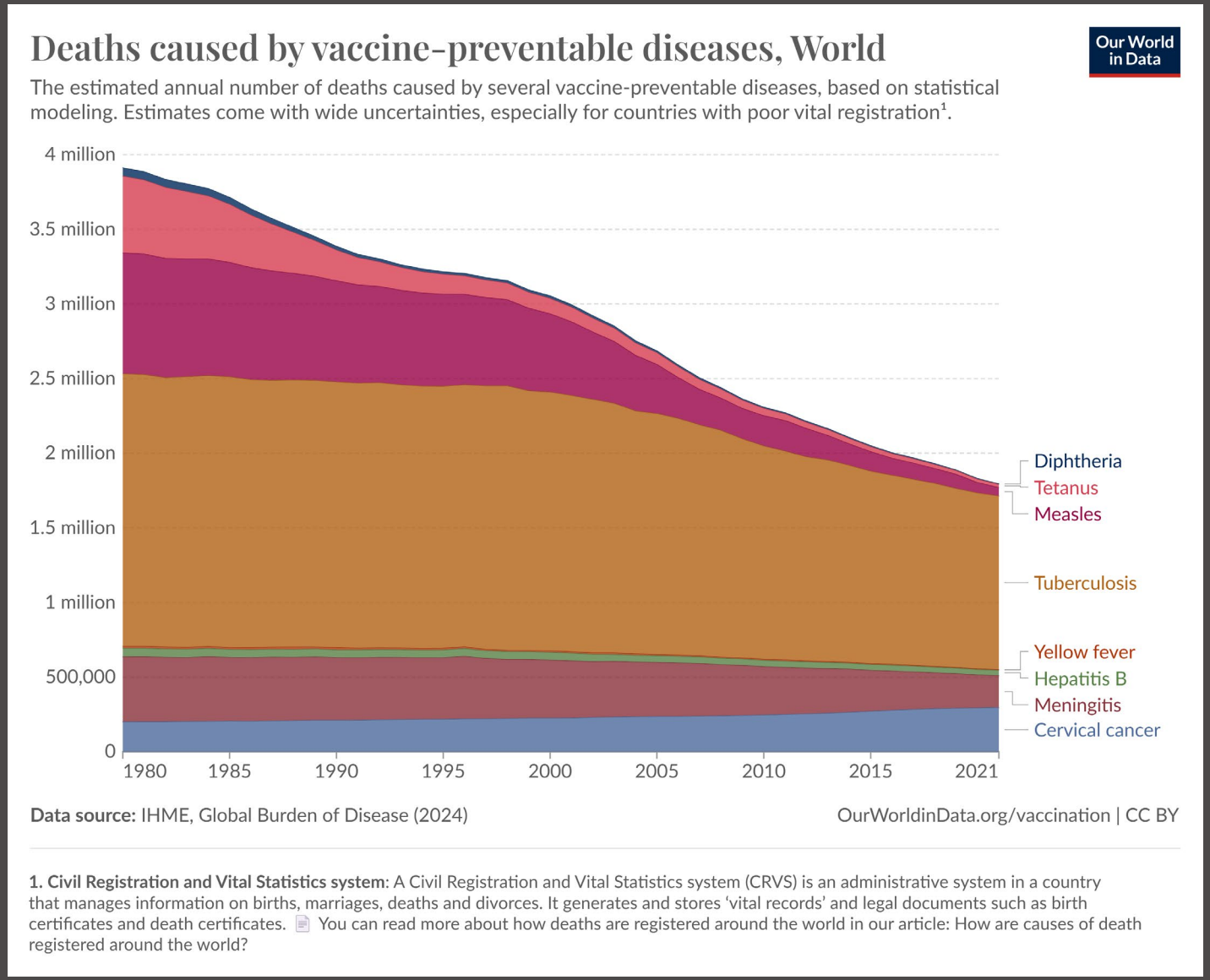
Contribution of vaccination to improved survival and health: modelling 50 years of the Expanded Programme on Immunization.
Shattock, Andrew J et al. The Lancet, Volume 403, Issue 10441, 2307 - 2316

Vaccine Efficacy

- One child is saved every 10 seconds due to immunization
- Vaccines have reduced infant mortality by 40%
- Despite significant progress, there is more work to be done



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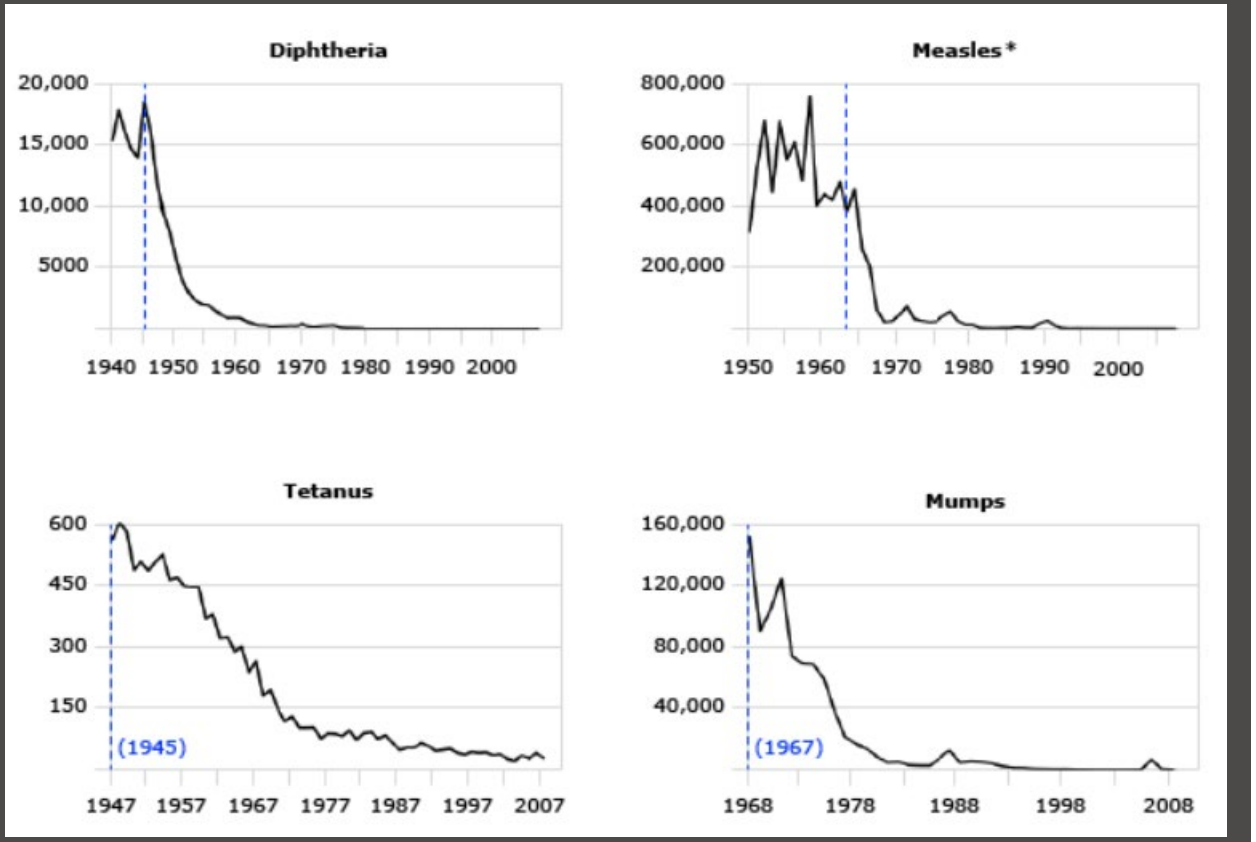
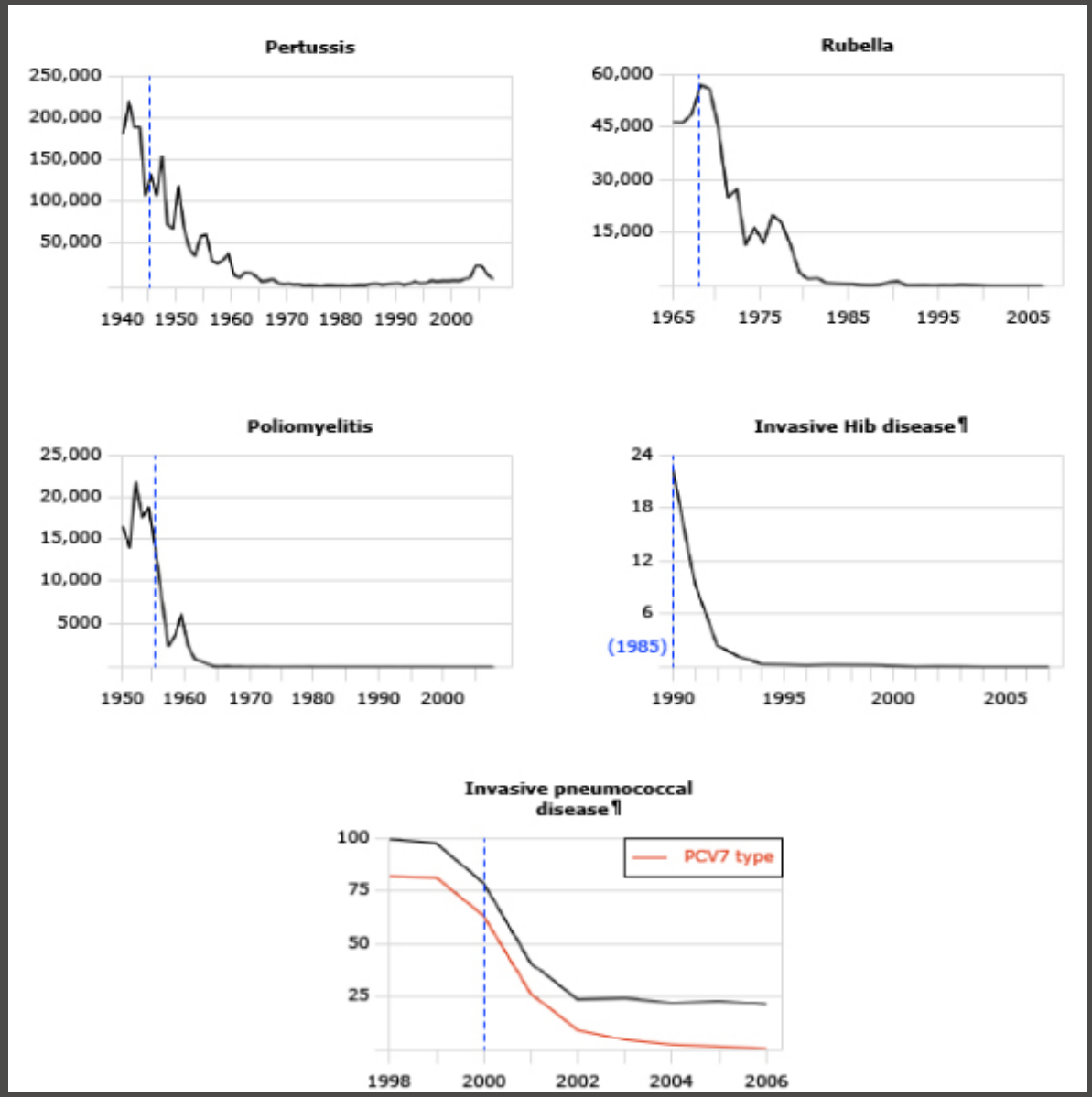
Hannah Ritchie (2024) - "Vaccines have saved 150 million children over the last 50 years" Published online at OurWorldinData.org. Retrieved from: 'https://ourworldindata.org/vaccines-children-saved'

Vaccine Efficacy – Zooming In

Vaccine Efficacy





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Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine-Preventable Diseases, 11th ed, Atkinson W, Wolfe S, Hamborsky J, McIntyre L (Eds), Public Health Foundation, Washington DC 2009.

Vaccine Efficacy

Vaccines Work!

CDC statistics demonstrate dramatic declines in vaccine-preventable diseases when compared with the pre-vaccine era

DISEASE	PRE-VACCINE ERA ESTIMATED ANNUAL MORBIDITY[1]	MOST RECENT REPORTS OR ESTIMATES OF U.S. CASES	PERCENT DECREASE
Diphtheria	21,053	2[2]	>99%
H. influenzae serotype B (invasive, <5 years of age)	20,000	18[2]	>99%
Hepatitis A	117,333	(est) 37,700[3]	68%
Hepatitis B (acute)	66,232	(est) 20,700[3]	69%
Measles	530,217	1,275[2]	>99%
Meningococcal disease (all serotypes)	2,886[4]	371[2]	87%
Mumps	162,344	3,780[2]	98%
Pertussis	200,752	18,617[2]	91%
Pneumococcal disease (invasive, <5 years of age)	16,069	1,700[5]	89%
Polio (paralytic)	16,316	0[2]	100%
Rotavirus (hospitalizations, <3 years of age)	62,500[6]	30,625[7]	51%
Rubella	47,745	6[2]	>99%
Congenital Rubella Syndrome	152	1[2]	>99%
Smallpox	29,005	0[2]	100%
Tetanus	580	26[2]	96%
Varicella	4,085,120	8,297[8]	>99%

Up to 2022

1. CDC. *JAMA* November 14, 2007; 298(18): 2155–63.
2. CDC. National Notifiable Infectious Diseases and Conditions, United States: Annual Tables 2019. Accessed August 2, 2022.
3. CDC. Viral Hepatitis Surveillance – United States, 2019. Published May 2021. Estimated total cases account for under-reporting.
4. CDC. *MMWR* October 6, 1995; 43(53):1–98.
5. CDC. Active Bacterial Core Surveillance (ABCs) Report; Emerging Infections Program Network *Streptococcus pneumoniae*, 2019.
6. CDC. *MMWR*, February 6, 2009; 58(RR-2): 1–25.
7. CDC. New Vaccine Surveillance Network, 2017 data (unpublished); U.S. rotavirus disease now has a biennial pattern.
8. CDC. Varicella Program, 2017 data (unpublished)

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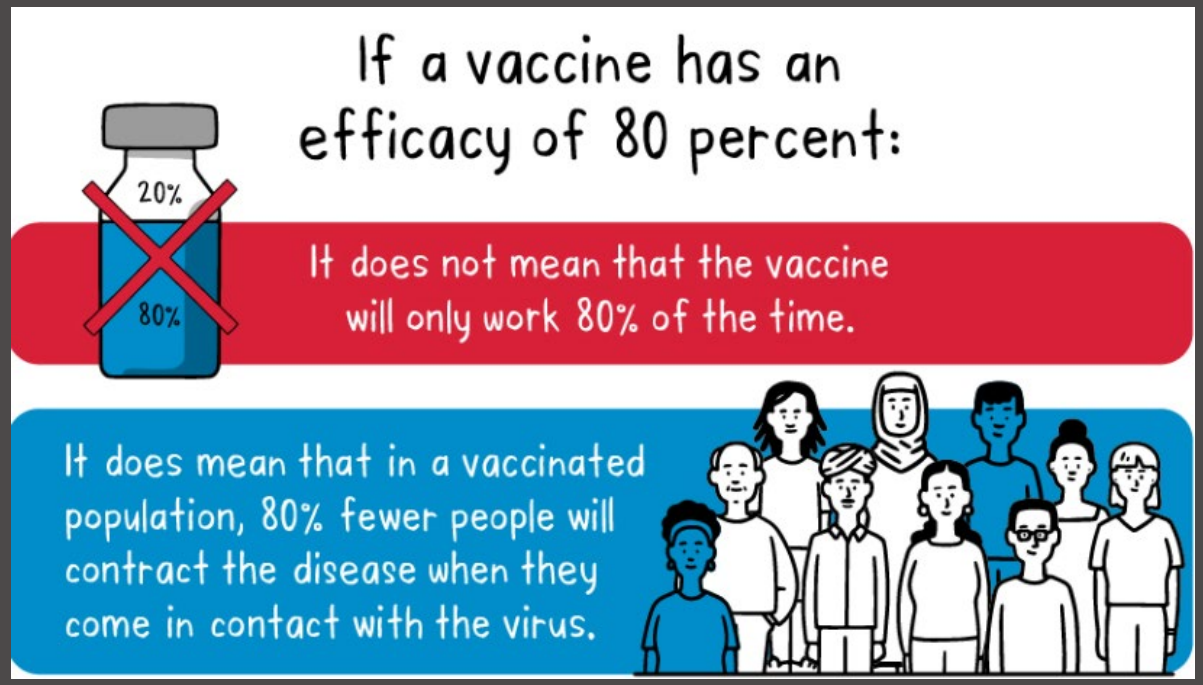
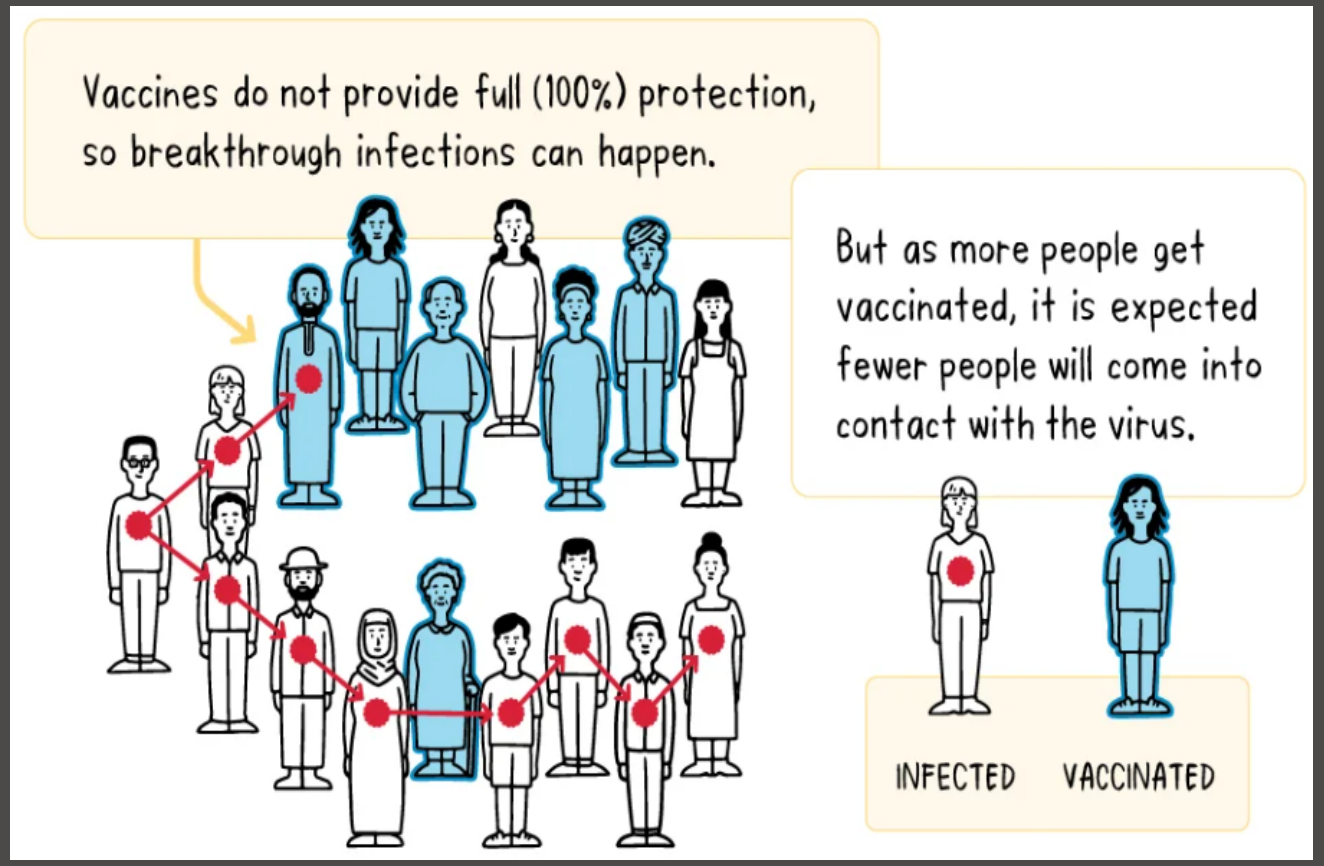
Vaccine Efficacy – Zooming In

Vaccine Efficacy

- Setting expectations
  - 50%+ efficacy is reasonable, depending on disease





- Take a “we’re all in this together” view

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https://www.who.int/news-room/feature-stories/detail/vaccine-efficacy-effectiveness-and-protection

Vaccine Efficacy Talking Points

- We know that vaccines are effective
  - Both individual and population
- Efficacy does not mean perfection
  - Reduced incidence and/or reduced severity is the goal
- We have the tools and knowledge to save millions of lives
- Vaccinating older children protects younger children, grandparents, immunocompromised people
- We want our family and community to be safe
  - We all work together towards this goal

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Vaccine Safety

And how to alleviate fears

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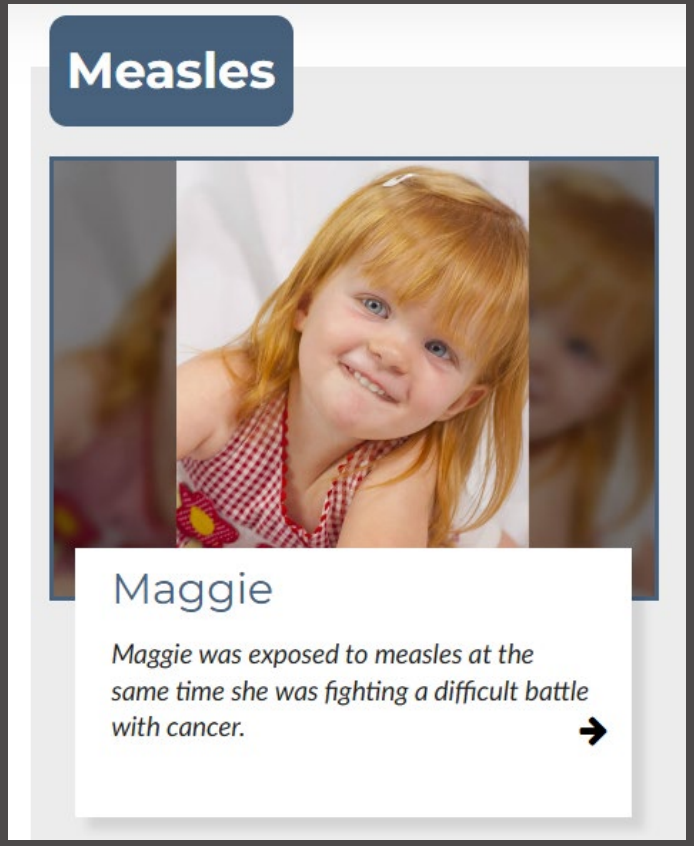
Vaccine Safety

- Risk of natural infection
  - Vaccination has been so successful, the risks of natural infection may be poorly understood
  - Caregivers may be unaware of individual and community risks
  - Potential risks of vaccination may seem more important than benefits in this context

Vaccine Safety

- Consider sharing stories of vaccine-preventable diseases
  - A more “close to home” problem
- https://www.immunize.org/clinical/vaccine-confidence/unprotected-people/
  - Resources for many sites sharing patient stores
  - Could even be available to read / watch in clinic waiting room – more enlightening, less “preachy”



https://vaccinateyourfamily.org/why-vaccinate/personal-stories/

Vaccine Safety

- Transparency / Validate concerns about vaccine risks
  - E.g. Rotavirus vaccine → intussusception risk
  - E.g. Covid vaccines → myocarditis
  - E.g. Influenza vaccine → Guillain-Barre
  - Discuss the real but very small risk of these
- Many safety concerns lack scientific proof
  - But account for 60-70% of vaccine exemption requests
  - Social media or news media – misinformation / disinformation
  - Stories from family / friends

Clin Infect Dis. 2019 Aug 1;69(4):726-731. doi: 10.1093/cid/ciz135.

Principal Controversies in Vaccine Safety in the United States

Frank DeStefano [1], Heather Monk Bodenstab [2], Paul A Offit [3]

Issue	Allegation
MMR vaccine and autism	MMR vaccine causes autism
Thimerosal	Thimerosal, a mercury-based preservative in some vaccines, increases risk of autism and other neuro-developmental disabilities
GBS	Influenza vaccines can cause GBS
Autoimmunity	Vaccines can cause chronic diseases of autoimmune etiology
Safety of HPV vaccine	HPV vaccines may increase risk of autoimmune and other disorders
Aluminum	Aluminum in vaccines can cause autoimmune diseases and a variety of other disorders, including MMF
Too many too soon	Too many vaccines given early in life might overwhelm the immune system and predispose to health and developmental problems

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Frank DeStefano, Heather Monk Bodenstab, Paul A Offit, Principal Controversies in Vaccine Safety in the United States, Clinical Infectious Diseases, Volume 69, Issue 4, 15 August 2019, Pages 726–731

Vaccine Safety

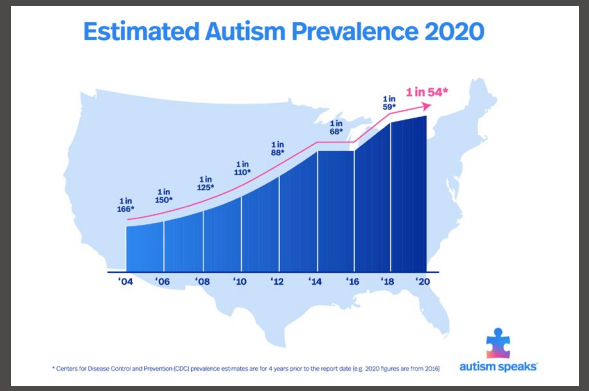
- The question of MMR and autism
  - Disproven many times
  - Initial report (1998) retracted – bad science, conflicts of interest $$
  - Autism has a strong genetic component beginning in utero, thus MMR vaccine at 12 months would not cause autism
  - Exposure to > 10,000 vaccine antigens in the first 24 months of life (1047 children) was not associated with adverse neuropsychological outcomes
  - Many (>25) studies show no association
    - Even in high risk (younger siblings of kids with autism) MMR does not cause autism

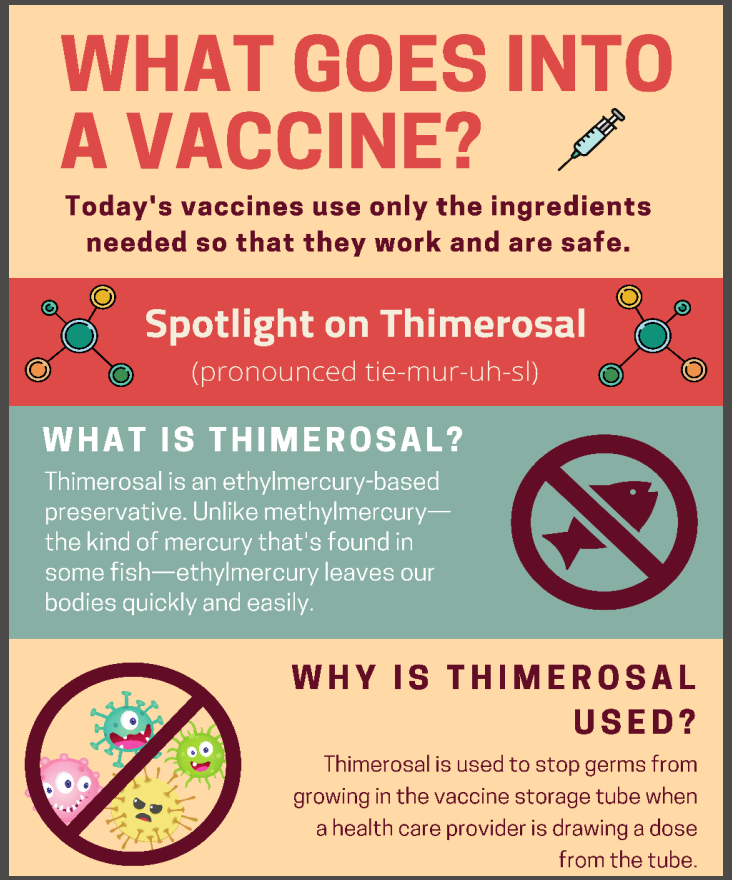
Iqbal S, Barile JP, Thompson WW, DeStefano F. Number of antigens in early childhood vaccines and neuropsychological outcomes at age 7-10 years. Pharmacoepidemiol Drug Saf. 2013 Dec;22(12):1263-70.

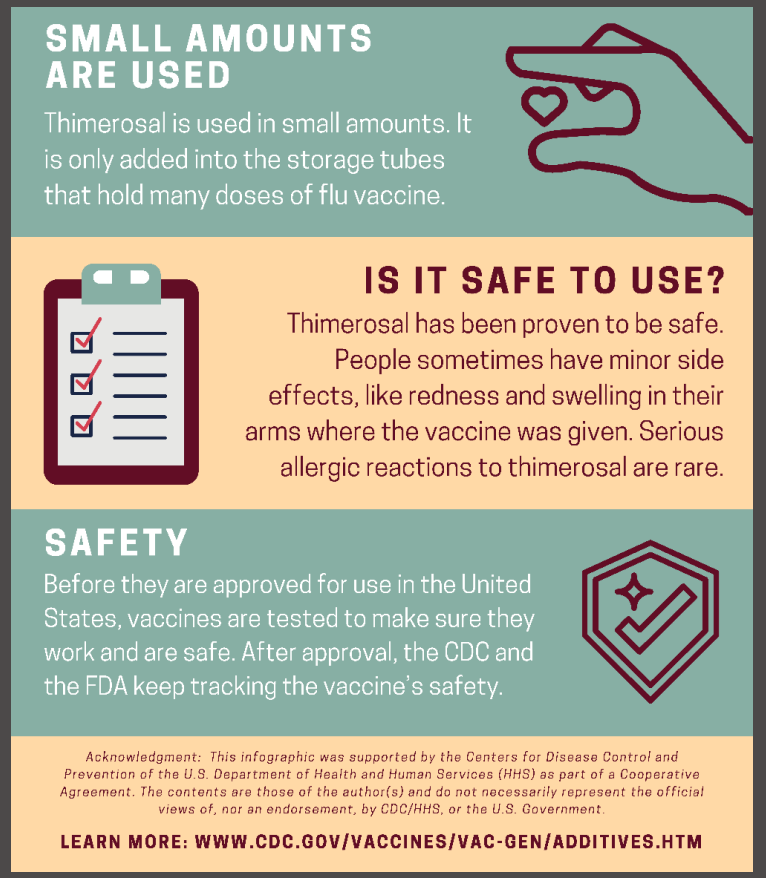
Vaccine Safety

- Thimerosal and neurodevelopmental disorders (autism)

- Multiple large studies – no correlation
- All thimerosal containing vaccines in the US (besides multidose flu) expired in 2003
  - Autism rates continued to rise







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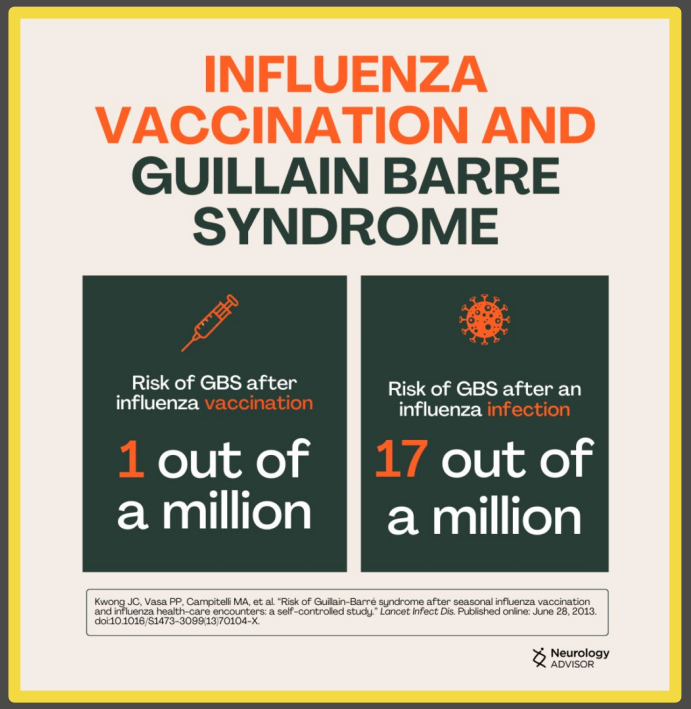
https://www.immunizationmanagers.org/resources/infographic-what-goes-into-a-vaccine-thimerosal-spotlight/

Vaccine Safety

- Guillain-Barre syndrome (GBS)
  - Possible risk with swine flu vaccine in 1976 (1 in 100,000)
  - Variable findings since
    - Seasons with slightly increased risk: 2-3 cases/1 million vaccines
  - Influenza infection itself leads to higher GBS risk – so vaccination actually decreases absolute GBS cases
  - MMR, HPV, Men ACWY, polio, pneumococcal, varicella, Hib, rabies, tetanus, diphtheria, hep A, and hep B – do not increase GBS risk
  - GBS + influenza vaccine – small and inconsistent GBS risk, less than risk with influenza infection



Frank DeStefano, Heather Monk Bodenstab, Paul A Offit, Principal Controversies in Vaccine Safety in the United States, Clinical Infectious Diseases, Volume 69, Issue 4, 15 August 2019, Pages 726–731

https://www.neurologyadvisor.com/features/investigating-guillain-barre-syndrome-and-vaccines-is-there-a-link/

Vaccine Safety

- Vaccines and autoimmune disease
  - Autoimmunity = antibodies against self-antigens; mechanisms to develop these are present at birth
  - No physiologic mechanism would explain a causal relationship
  - Multiple studies have shown no correlation
    - MMR, BCG, smallpox, pertussis vaccines do not cause type I diabetes
    - Hep B, tetanus, influenza vaccines do not exacerbate MS

Frank DeStefano, Heather Monk Bodenstab, Paul A Offit, Principal Controversies in Vaccine Safety in the United States, Clinical Infectious Diseases, Volume 69, Issue 4, 15 August 2019, Pages 726–731

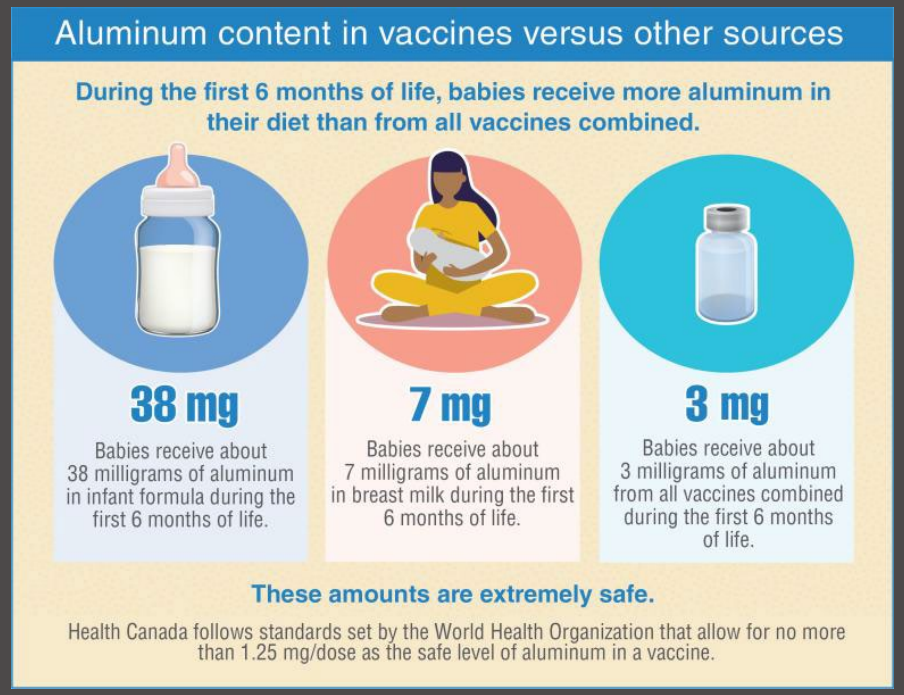
Vaccine Safety

- HPV vaccine safety concerns
  - Negative media attention raising concern
  - Large studies show no correlation w/ autoimmune diseases
    - Denmark/Sweden: > 696,000 doses, no link between HPV + autoimmune disease or neurologic complications
    - France: case-control study → no increased risk of ITP, central demyelination, GBS, connective tissue disorders, T1DM, or autoimmune thyroiditis
    - Denmark/Sweden: 800,000 women who received HPV vaccine = no increased risk of MS or other demyelinating diseases
  - No evidence of HPV vaccine causing premature ovarian insufficiency, complex regional pain syndrome, POTS

Frank DeStefano, Heather Monk Bodenstab, Paul A Offit, Principal Controversies in Vaccine Safety in the United States, Clinical Infectious Diseases, Volume 69, Issue 4, 15 August 2019, Pages 726–731

Vaccine Safety

- Aluminum



https://immunizebc.ca/vaccine-safety/ingredients

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Vaccine Safety

- Aluminum
  - Currently used in hep A, hep B, diphtheria-tetanus vaccines, Hib, and pneumococcal vaccines,
  - Not used in the live viral vaccines (MMR, varicella, rotavirus)
  - Serum levels in kids after vaccination are well below toxic range
    - One study showed no correlation between infant blood / hair aluminum concentrations and vaccine history or between blood aluminum and overall developmental status

Frank DeStefano, Heather Monk Bodenstab, Paul A Offit, Principal Controversies in Vaccine Safety in the United States, Clinical Infectious Diseases, Volume 69, Issue 4, 15 August 2019, Pages 726–731

Vaccine Safety

- “Autoimmune inflammatory syndrome induced by adjuvants”
  - A proposed condition, but not well-defined or proven
  - One study looked at incidence of autoimmune disease in >18 000 patients who received allergen-specific immunotherapy containing large quantities of injected aluminum adjuvants
    - Patients receiving injected aluminum had a lower incidence of autoimmune disease compared with controls

Frank DeStefano, Heather Monk Bodenstab, Paul A Offit, Principal Controversies in Vaccine Safety in the United States, Clinical Infectious Diseases, Volume 69, Issue 4, 15 August 2019, Pages 726–731

Vaccine Safety

- Do multiple vaccines in short succession affect immunity?
  - Given the number of antibody-generating B cells, the number of vaccine-specific antigens infants are exposed to, and the # of antibodies necessary to react to each antigen, it has been estimated that infants have the theoretical capacity to respond to at least 10,000 vaccines at one time
- No study has found an increased risk of disease according to the number of vaccines/vaccine antigens received in childhood
- Multiple studies say no adverse effect on immunity
  - Non-vaccine preventable infections, autoimmune disease, or neurologic disorders

Glanz JM, Newcomer SR, Daley MF, DeStefano F, Groom HC, Jackson ML, Lewin BJ, McCarthy NL, McClure DL, Narwaney KJ, Nordin JD, Zerbo O. Association Between Estimated Cumulative Vaccine Antigen Exposure Through the First 23 Months of Life and Non-Vaccine-Targeted Infections From 24 Through 47 Months of Age. JAMA. 2018 Mar 6;319(9):906-913.

Frank DeStefano, Heather Monk Bodenstab, Paul A Offit, Principal Controversies in Vaccine Safety in the United States, Clinical Infectious Diseases, Volume 69, Issue 4, 15 August 2019, Pages 726–731

Vaccine Safety Talking Points

- Vaccines undergo rigorous testing before going on the market
- Safety is monitored closely (VAERS & others)
- Nothing is “zero” risk, but the benefits of vaccines far outweigh the small risk of side effects
- Acknowledge fears and remain transparent
- Child’s capacity for immunogenicity is amazing
- Ask parents/caregivers what specific concerns they may have and be prepared to discuss it with them

Vaccine Component Allergies

And what to know about them

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Vaccine Component Allergies

- Resources:
- https://www.vaccinesafety.edu/components-allergens/
  - Institute for Vaccine Safety maintains updated list of potential allergens including adjuvants, preservatives, coloring agents
- https://www.fda.gov/vaccines-blood-biologics/vaccines/vaccines-licensed-use-united-states
  - Package inserts for US-licensed vaccinations available through FDA

Vaccine Component Allergies

- Gelatin

Vaccine (United States brand name and manufacturer)	Gelatin content in milligrams per dose
Influenza (Flumist, Medimmune)	2 mg per 0.2 mL dose
Measles, mumps, rubella (M-M-R-II, Merck)	14.5 mg per 0.5 mL dose
Measles, mumps, rubella, varicella (ProQuad, Merck)	11 mg per 0.5 mL dose
Rabies (RabAvert, Bavarian Nordic)	12 mg per 1 mL dose
Typhoid Vaccine Live Oral Ty21a (VIVOTIF, Bavarian Nordic)	Capsule
Varicella (VARIVAX, Merck)	12 mg per 0.5 mL dose
Yellow fever (YF-Vax, Sanofi Pasteur)	7.5 mg per 0.5 mL dose¶

Gelatin content for vaccines available in the United States Note that there are gelatin-free alternatives available, including injectable influenza vaccine, PRIORIX measles/mumps/rubella vaccine, Imovax rabies vaccine, and injectable typhoid vaccine in the US and other countries and VARILRIX varicella vaccine and STAMARIL yellow fever vaccine outside the US.

Vaccine Component Allergies

- Gelatin
  - Added to several vaccines as a stabilizer
  - The most common identifiable cause of anaphylaxis to vaccine
  - 1-2 cases in 2 million doses
  - Alpha-gal may predispose to vaccine gelatin allergy
- Take a history of any allergy to gelatin-containing foods (e.g. marshmallows, gummy candies)
  - If yes, skin testing → if positive, gelatin-free vaccine; if neg skin testing, monitor for 30 min after vaccine administration

Food allergy to gelatin in children with systemic immediate-type reactions, including anaphylaxis, to vaccines. Sakaguchi, Masahiro et al. Journal of Allergy and Clinical Immunology, Volume 98, Issue 6, 1058 - 1061

Vaccine Component Allergies

- Hen's Egg

Egg content of vaccines (subject to change - check package inserts)

Vaccine	Grown in	Egg protein content	Approach in egg-allergic patient
Measles and mumps	Chick embryo fibroblast cell cultures	Picograms to nanograms	Administer in usual manner
Purified chick embryo rabies	Chick embryo fibroblast cell cultures	Picograms to nanograms	Administer in usual manner
Influenza (killed injected and live attenuated nasal)	Chick extra-embryonic allantoic fluid	<1 microgram	Administer in usual manner; refer to UpToDate topic on influenza vaccination in persons with egg allergy
Yellow fever	Chick embryos	Micrograms	Administer in usual manner but observe for 30 minutes

Vaccine Component Allergies

- Hen's Egg
  - No need to inquire about egg allergy for MMR, influenza, rabies
  - Yellow fever: package insert recommends those with egg allergy undergo skin testing; if negative, give vaccine; if positive, give in graded doses
  - Clinically based on very low risk – egg allergic patients can be given YF vaccine in full dose, without skin testing, and monitored after for 30 min

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https://www.allergy.org.au/hp/papers/vaccination-of-the-egg-allergic-individual

Vaccine Component Allergies

- Cow's Milk
  - Casein – allergenic protein in cow's milk
  - Very small number of children severely allergic to milk may have had anaphylaxis to Tdap or DTaP
  - Vaccines are prepared in a medium derived from cow's milk proteins, tiny amount of casein can be detected
  - Vast majority, even if severely allergy to cow's milk, don't have allergy to these vaccines

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Anaphylaxis to diphtheria, tetanus, and pertussis vaccines among children with cow's milk allergy. Kattan, Jacob D. et al. Journal of Allergy and Clinical Immunology, Volume 128, Issue 1, 215 - 218

Vaccine Component Allergies

- Latex
  - “Rubber” vial stoppers can contain latex
  - 28 cases of possible reactions in > 160,000 vaccine doses (VAERS)
  - Only 1 case of anaphylaxis attributed to a latex rubber stopper
- Patients with latex allergy can safely receive vaccines regardless of vial stopper, exceedingly low risk

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Russell M, Pool V, Kelso JM, Tomazic-Jezic VJ. Vaccination of persons allergic to latex: a review of safety data in the Vaccine Adverse Event Reporting System (VAERS). Vaccine. 2004 Dec 16;23(5):664-7

Vaccine Component Allergies

- Polyethylene glycol (PEG)
  - Stabilizer in mRNA Covid vaccines
  - Less allergenic PEG than other products with PEG
  - Multiple studies have shown Covid vaccines can be given safely to those with confirmed or suspected PEG allergy

  - Novavax contains polysorbate, structurally similar to PEG
    - Allergy to polysorbate remains a contraindication per manufacturer label

Trending Vaccine Topics

Keeping up with the times

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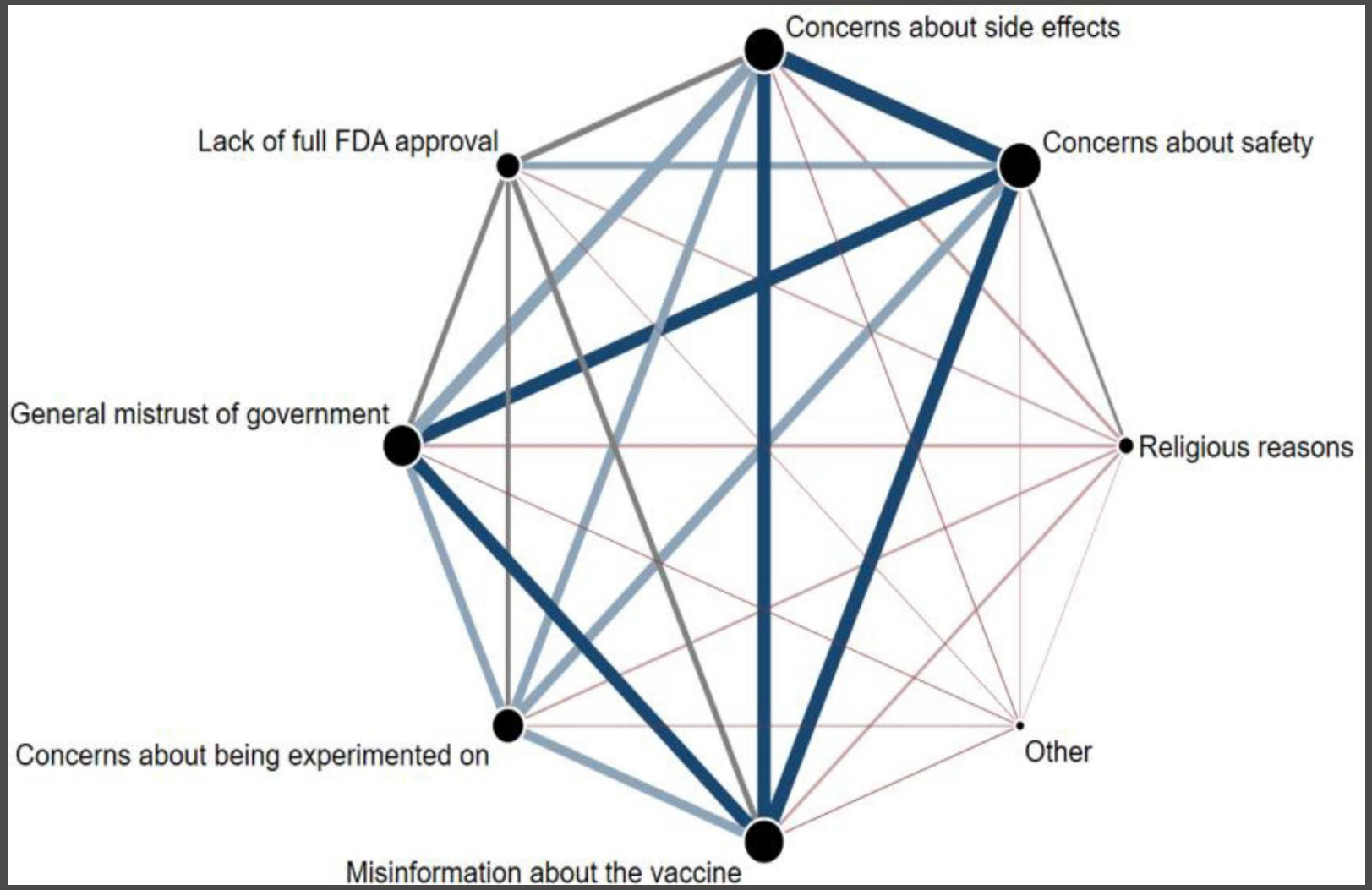
Disclaimer

- Acknowledging that vaccination has been a hot topic in recent years and in the current political atmosphere, some information references political parties as they related to vaccine sentiments
- This is not intended to be a politically based or biased talk, but to increase awareness that vaccine beliefs may fall along political lines
- This information may help us better serve all our patients regardless of political party or belief
- We must be aware of misinformation and misconceptions to combat them

Fig. 1. Physician-reported reasons their patients were hesitant to be vaccinated. Each node represents a distinct patient concern. Node size indicates how often a reason was reported. Ties between nodes represent co-selection of concerns by at least one physician. Edge thickness indicates how often two reasons were co-reported.



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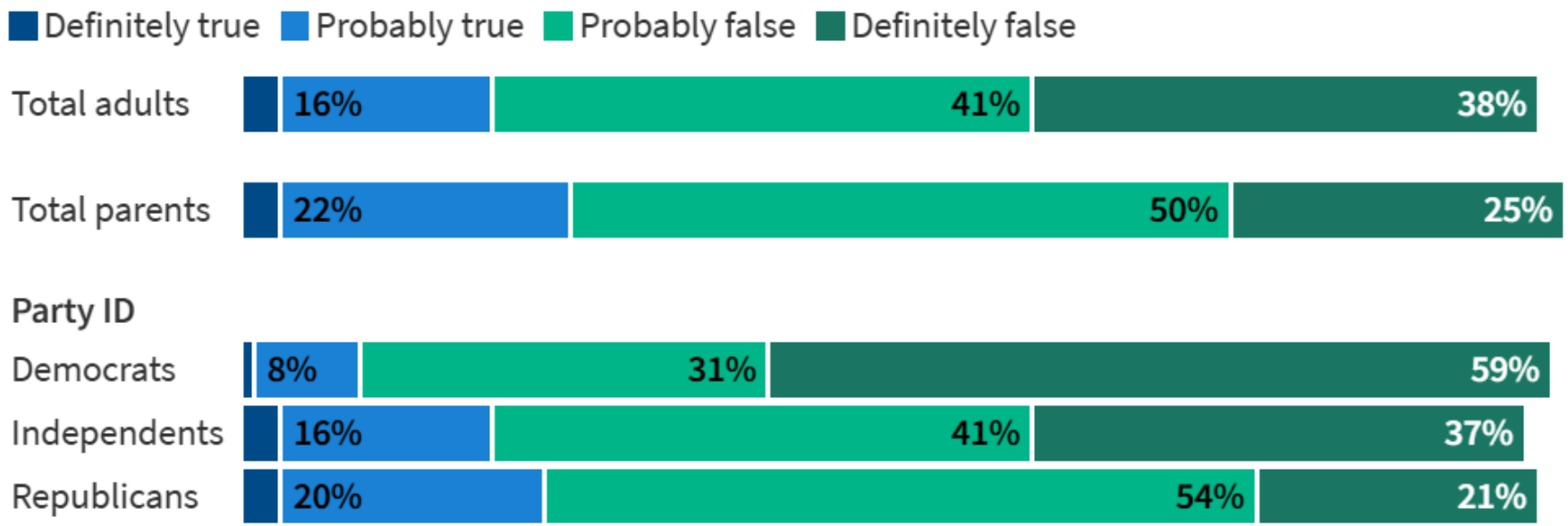
Joy Melnikow, Andrew Padovani, Jingwen Zhang, Marykate Miller, Melissa Gosdin, Sabrina Loureiro, Brock Daniels. Patient concerns and physician strategies for addressing COVID-19 vaccine hesitancy. Vaccine, Volume 42, Issue 14, 2024, Pages 3300-3306, ISSN 0264-410X

Figure 1

While Most Adults Say It Is False That Getting the Measles Vaccine Is More Dangerous Than a Measles Infection, Fewer Parents and Republicans Are Certain

Do you think that it is ... that getting the measles vaccine is more dangerous than becoming infected with measles?



Note: Parents are parents or guardians of a child under the age of 18 living in their household. See topline for full question wording.

Source: KFF Health Misinformation Tracking Poll (Feb. 20-28, 2024) • Get the data • Download PNG

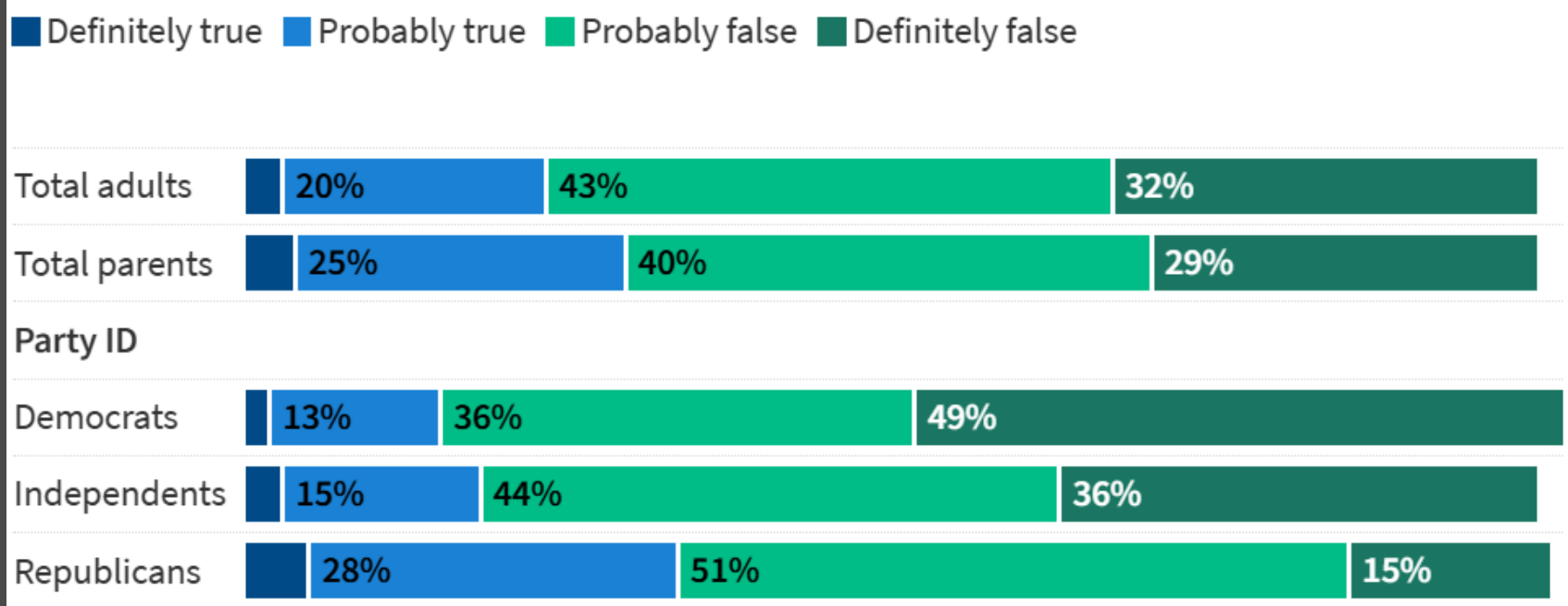
KFF

25% of parents believe that measles infection is safer than the MMR vaccine

Figure 2

Most Adults - Including Most Parents - Are Uncertain Whether the False Claim that MMR Vaccines Have Been Proven To Cause Autism in Children is Definitely True Or Definitely False

Do you think that it is...that the measles, mumps, rubella vaccines, also known as the MMR vaccines, have been proven to cause autism in children?



Note: Parents are parents or guardians of a child under the age of 18 living in their household. See topline for full question wording.

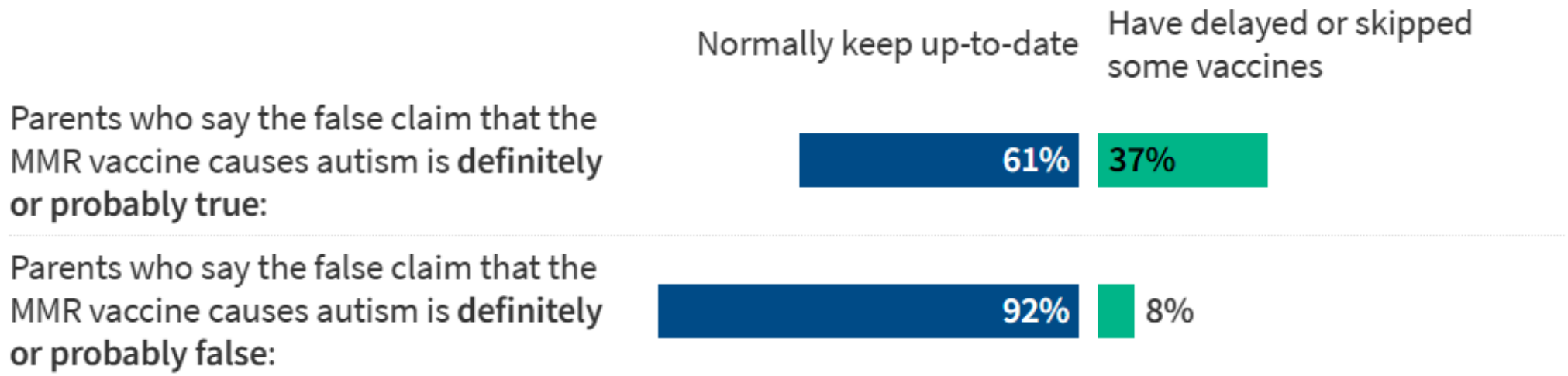
Source: KFF Health Misinformation Tracking Poll Pilot (May 23-June 12, 2023) • Get the data • Download PNG

KFF

Only 29% of parents believe that MMR causing autism has been definitively disproven

Parents Who Believe False Claim About MMR Vaccines Causing Autism Are More Likely To Have Skipped Some Routine Vaccines for Their Child

Do you normally keep your children up-to-date with recommended childhood vaccines such as the MMR vaccine, or have you ever delayed or skipped some childhood vaccines for your children?



Note: Among parents or guardians of a child under the age of 18 living in their household. See topline for full question wording.

Source: KFF Tracking Poll on Health Information and Trust (Jan. 7-14, 2025) • Get the data • Download PNG

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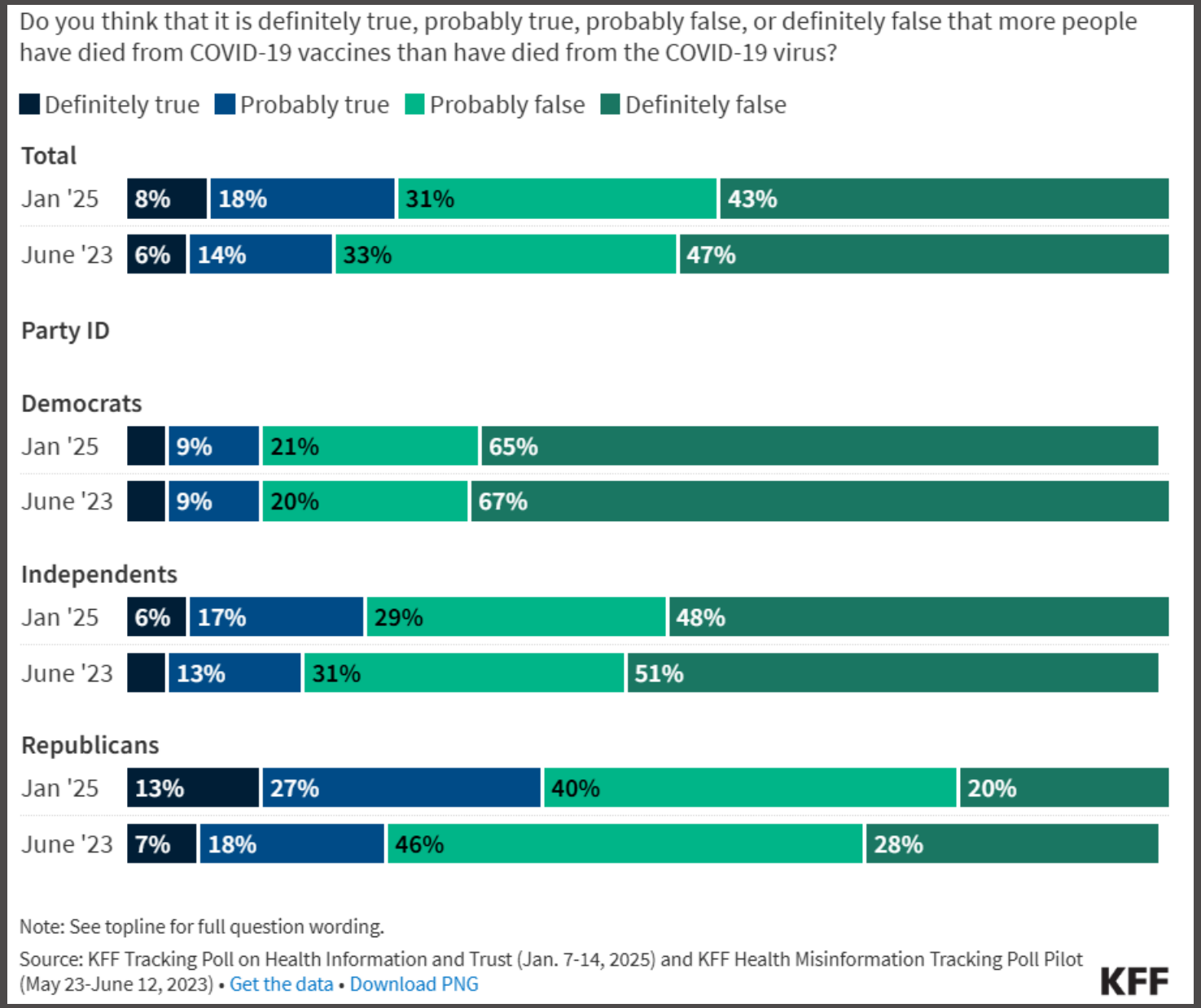
Emphasizes importance of continued follow up with skeptical parents

MU Health Care

https://www.kff.org/
Independent source for health policy research, polling, and news



<50% of adults are certain that Covid infection killed more people than the Covid vaccines

https://www.kff.org/
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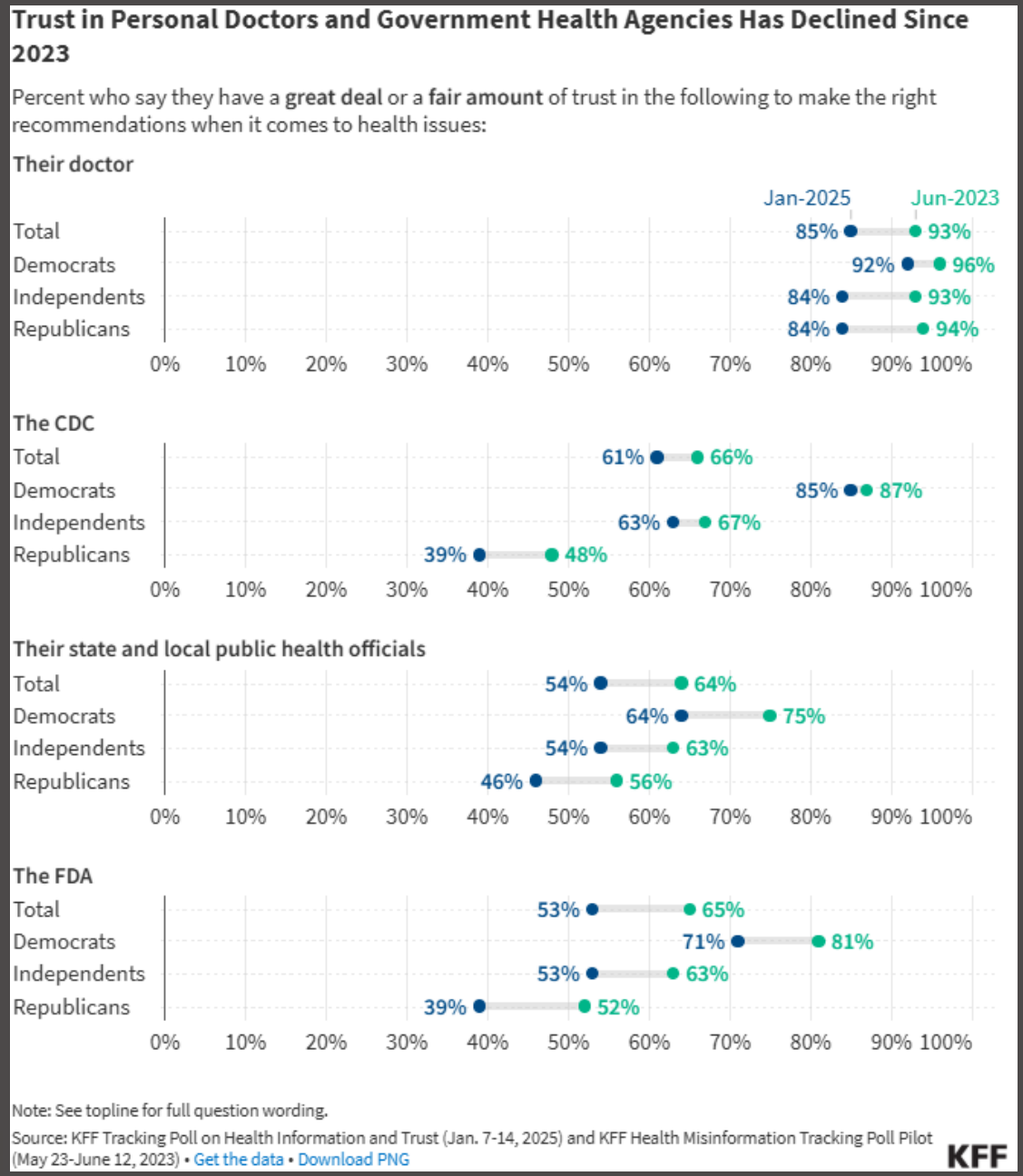

Significant decline in trust in just 18 months in all categories

Health Care

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Other common vaccine misconceptions

- Natural immunity is better than vaccine-induced immunity
- Vaccines are only for infants/young children
- Vaccine-preventable diseases are rare, vaccines aren’t necessary
- Vaccines don’t work because people who got vaccinated went on to get the infection
- Vaccines cause the disease they are supposed to prevent
- Choosing not to vaccinate only affects that child/person

https://www.rush.edu/news/8-myths-about-vaccines-and-kids
https://www.sunshinecoast.health.qld.gov.au/about-us/news/trending/eight-common-vaccine-misconceptions
https://www.ankurahospitals.com/breaking-down-vaccine-myths-key-facts-every-parent-should-know-in-2025/
https://www.who.int/news-room/questions-and-answers/item/vaccines-and-immunization-myths-and-misconceptions

Resources for Clinicians

- https://www.immunize.org/
  - https://www.immunize.org/clinical/external/apps/
- https://www.cdc.gov/vaccines/hcp/conversations/your-practice.html
- https://health.mo.gov/living/wellness/immunizations/
- https://vaccinateyourfamily.org/
- https://www.who.int/news-room/questions-and-answers/item/vaccines-and-immunization-myths-and-misconceptions
- https://www.vaccinesafety.edu/

Thank you!

- Questions, comments?

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Health Care