

https://www.theasm.org.au/covid19

COVID-19 Vaccine: Safety, Efficacy and Acceptability

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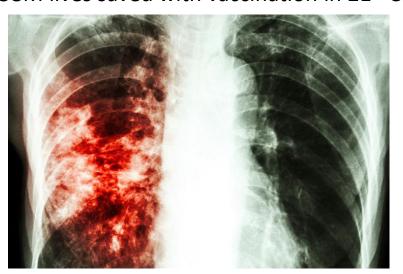
Disclosure

I have NO financial disclosure or conflicts of interest with the presented material in this presentation.

Smallpox: Estimated 300M deaths in 20th C. Globally eradicated by vaccination in 1980 ¹



Tuberculosis: 1.5M deaths in 2018. 58M lives saved with vaccination in 21st C.³



Measles: eliminated in USA in 2000.

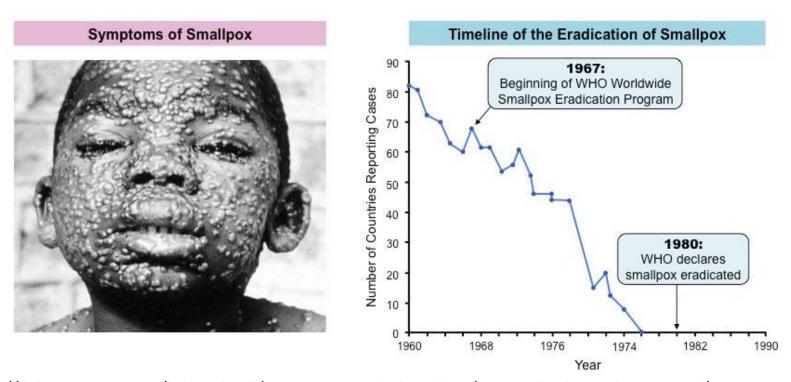
Resurgence in USA and Europe since 2010.



Polio: 350,000 paralysis cases in 1988. Vaccination reduced cases to 38 in 2018.



- 1 https://globalbiodefense.com/2019/09/30/why-do-we-need-a-new-smallpox-vaccine/
- 2 https://patch.com/georgia/atlanta/measles-georgia-add-highest-rate-disease-eradication
- 3 https://www.who.int/teams/global-tuberculosis-programme/global-report-2019
- 4 https://blog.forumias.com/polio-in-india/ 5 https://ourworldindata.org/polio



https://ib.bioninja.com.au/higher-level/topic-11-animal-physiology/111-antibody-production-and/vaccination.html

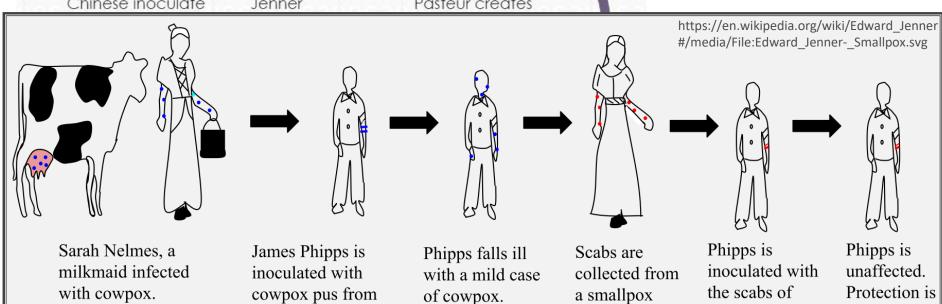


https://ed.ted.com/lessons/how-we-conquered-the-deadly-smallpox-virus-simona-zompi



Chinese inoculate Pasteur creates Jenner

Nelmes.



smallpox.

patient.

complete.

Vaccine Safety

Benefit vs. Risk

Variolation – 1% mortality (cf. 30% for wild type smallpox) Modern vaccines – 0.00001% mortality (typically 1 per Million)

(Elaine R. Miller, Pedro L. Moro, Maria Cano, and Tom Shimabukuroa. Deaths following vaccination: What does the evidence show? Vaccine. 2015 Jun 26; 33(29): 3288–3292)

When things go wrong - polio vaccine

The Cutter Incident (1953)

- 40,000 polio infections
- 200 paralytic cases
- 10 deaths



When things go wrong - unethical human experimentation on black and Caribbean study populations

Tuskegee, AL Syphilis Study (U.S. Public Health Service 1932 - 1972)

- 600 persons enrolled without informed consent
- diagnosis of syphilis withheld
- medication for syphilis withheld



Presidential Apology: https://www.cdc.gov/tuskegee/clintonp.htm

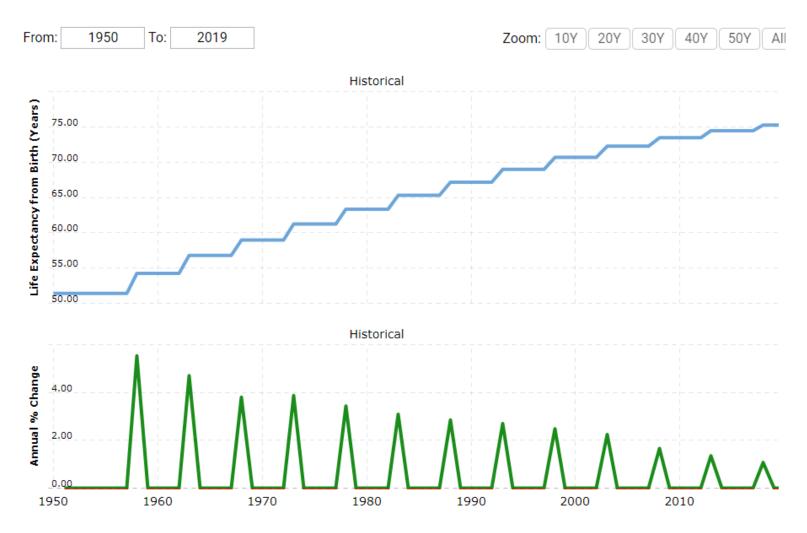
Guatemala STD Study (U.S. Public Health Service, NIH 1946 - 1948)

- 1308 persons deliberately infected with STDs
- 83 deaths



Presidential Apology: https://www.bloomberg.com/news/articles/2 010-10-01/obama-apologizes-to-guatemalafor-infecting-prisoners-with-stds-in-1940s

Life expectancy in the age of vaccination: Latin America and Caribbean



https://www.macrotrends.net/countries/LCR/latin-america-and-the-caribbean/life-expectancy#:~:text=The%20life%20expectancy%20for%20Latin,a%200%25%20increase%20from%202016.

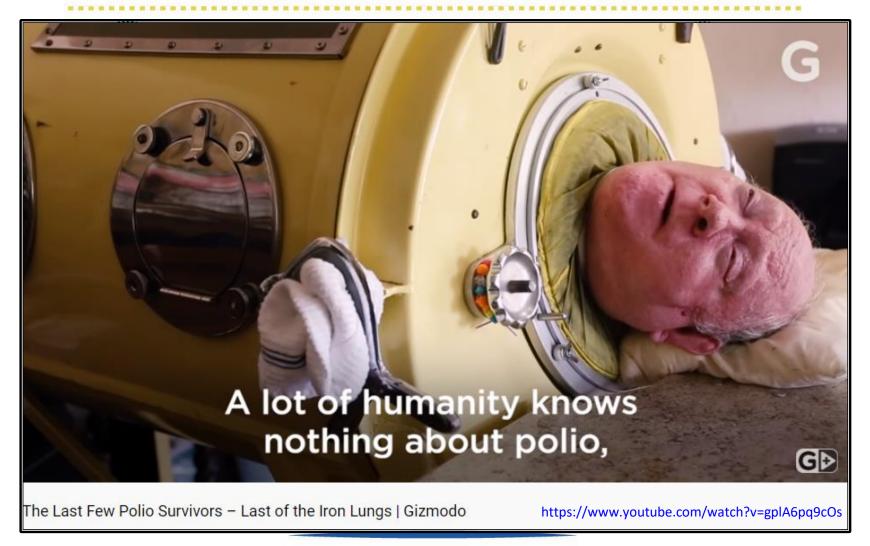
Impact of Vaccines in the Americas

Disease

Before Vaccines

After Vaccines

Achievements



#GetVax www.paho.org/vwa



HOW A NEW VACCINE IS DEVELOPED, APPROVED AND MANUFACTURED

Food and Drug Administration (FDA) sets rules for the three phases of clinical trials to ensure the safety of the volunteers. Researchers test vaccines with adults first.



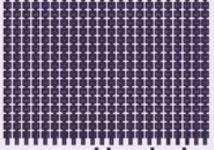
Is this vaccine safe?

Does this vaccine seem to work?

Are there any serious side effects?

How is the size of the dose related to side effects?

PHASE 2

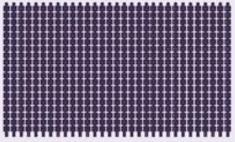


several hundred VOLUNTEERS

What are the most common short-term side effects?

How are the volunteers' immune systems responding to the vaccine?

PHASE 3



HUNDREDS or THOUSANDS of VOLUNTEERS

How do people who get the vaccine and people who do not get the vaccine compare?

Is the vaccine safe?

Is the vaccine effective?

What are the most common side effects?

FDA licenses the vaccine only if:

- It's safe and effective
- · Benefits outweigh risks



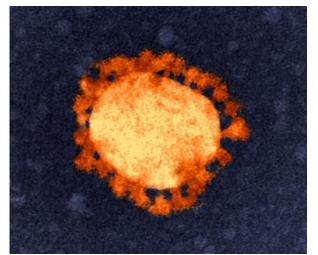


Vaccines are made in batches called lots. Manufacturers must test all lots to make sure they are safe,

pure and potent. The lots can only be released once FDA reviews their safety and quality.

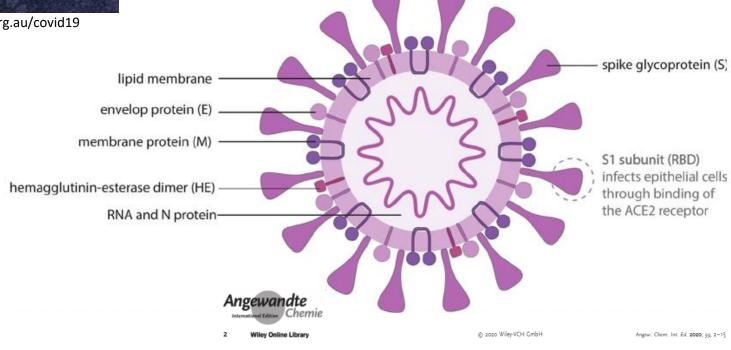


The FDA inspects manufacturing facilities regularly to ensure quality and safety.



COVID-19 Vaccine Development

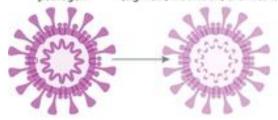
https://www.theasm.org.au/covid19



Tingting Ye Dr. Zifu Zhong Prof. Dr. Adolfo García-Sastre Prof. Dr. Michael Schotsaert Prof. Bruno G. De Geest. Current Status of COVID-19 (Pre)Clinical Vaccine Development. Angew. Chem. Int. Ed. 2020, 59, 2-15.

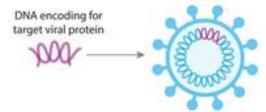
inactivated virus vaccine

target viral pathogen inactivation step (e.g. heat, irradiation, chemical treatment)



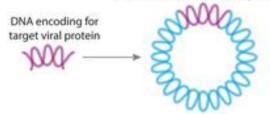
viral vector vaccine

integration into viral vector (e.g. adenovirus)



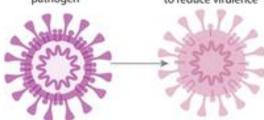
DNA vaccine

integration in expression vector plasmid administration with electroporation



live attenuated virus vaccine

target viral pathogen transformation step to reduce virulence

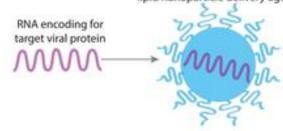


protein subunit vaccine

target viral selected protein epitopes formulation with (molecular) adjuvants

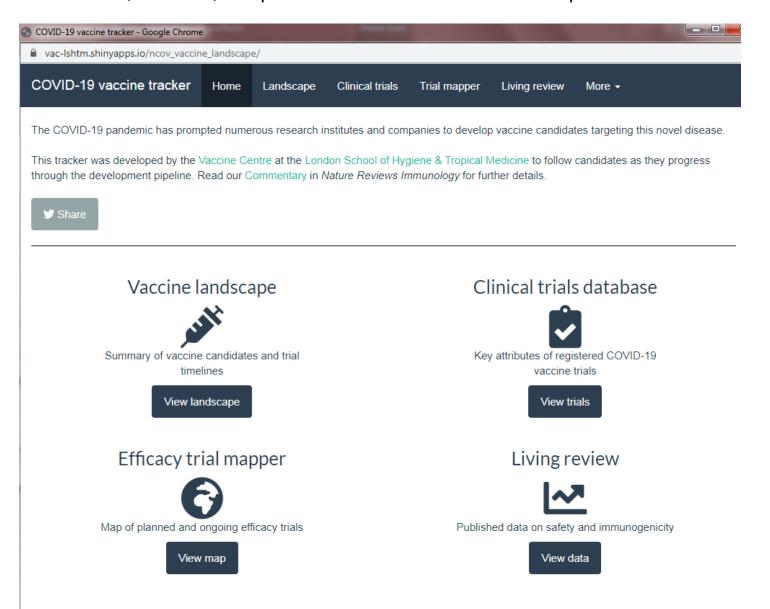
RNA vaccine

formulation into lipid nanoparticle delivery agent

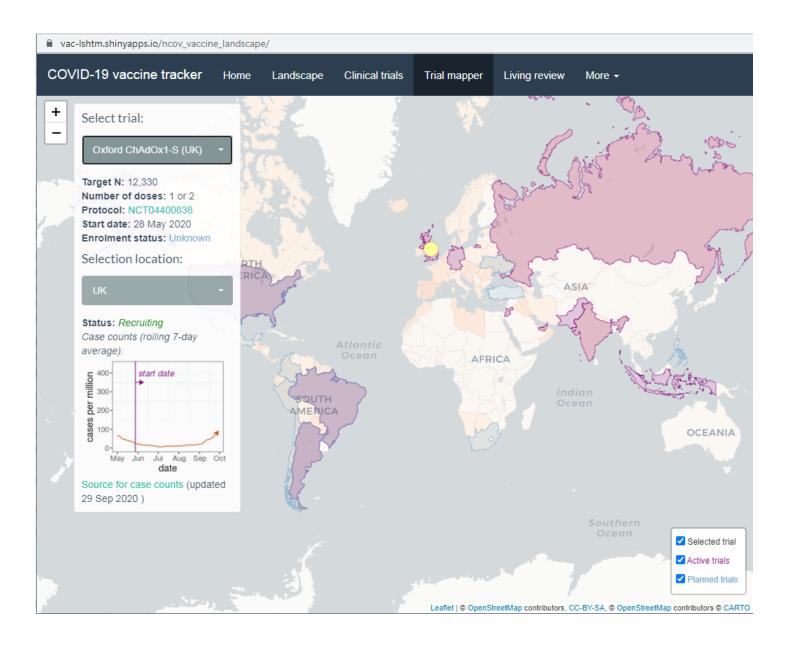


Keeping track of the SARS-CoV-2 vaccine pipeline

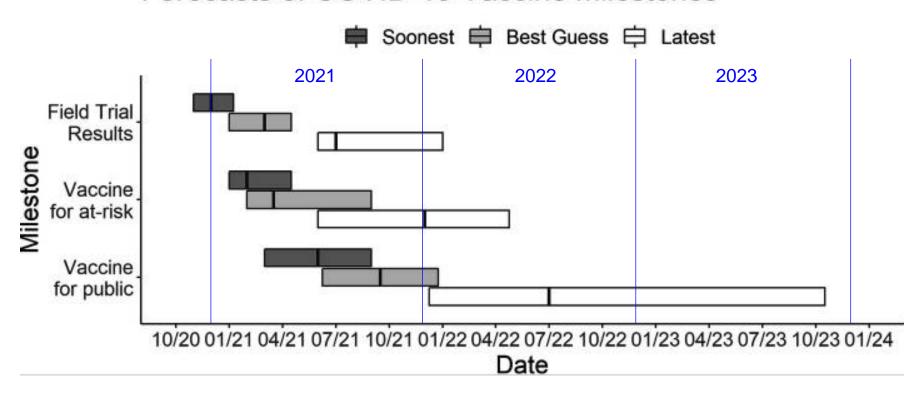
Parker EPK, Shrotri M, Kampmann B. Nat Rev Immunol. 2020 Sep 28:1.



https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape



Soonest, Best Guess and Latest Forecasts of COVID-19 Vaccine Milestones



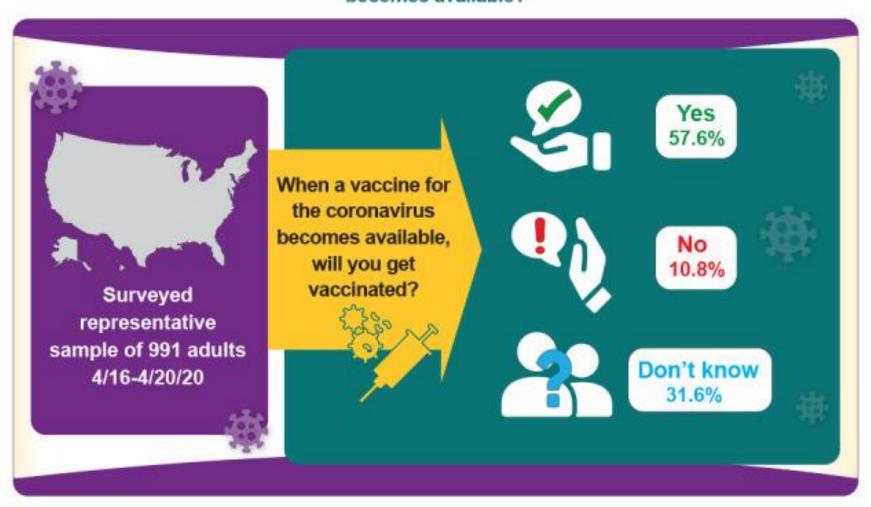
Kane PB, Moyer H, MacPherson A, Papenburg J, Ward BJ, Broomell SB, Kimmelman J. Expert Forecasts of COVID-19 Vaccine Development Timelines. J Gen Intern Med. 2020 Sep 28:1-3. Chem. Int. Ed. 2020, 59, 2 – 15.

COVID-19 Vaccine Acceptability



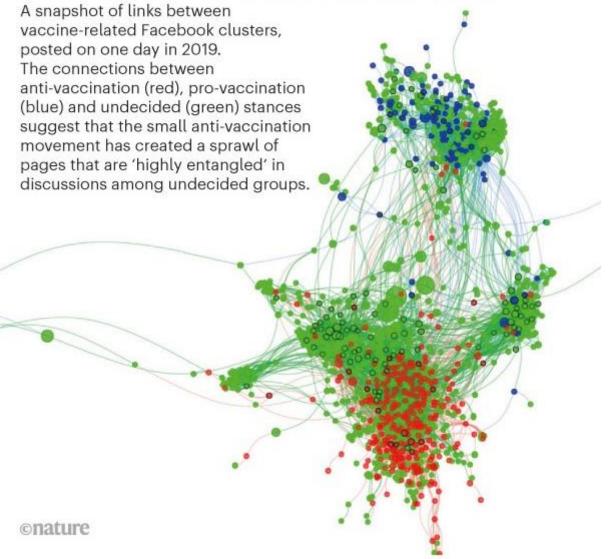
https://hub.jhu.edu/magazine/2018/winter/vaccines-mistrust-and-misinformation/

Do adults residing in the US intend to receive COVID-19 vaccination when it becomes available?





ONLINE COMPETITION BETWEEN VACCINE VIEWS



Johnson, N. F. et al. Nature https://doi.org/10.1038/s41586-020-2281-1 (2020)





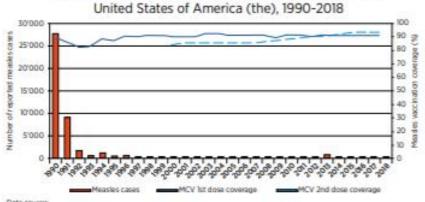
Lancet. 1998 Feb 28;351(9103):637-41. doi: 10.1016/s0140-6736(97)11096-0.

Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

A J Wakefield ¹, S H Murch, A Anthony, J Linnell, D M Casson, M Malik, M Berelowitz, A P Dhillon, M A Thomson, P Harvey, A Valentine, S E Davies, J A Walker-Smith

"The UK lost its measles-free status and the US is soon to follow"

"



Measeles cases - Reported by National Authorities to WHO annually: Measels Containing Vaccines (MCV) vaccination

WHO/I INICEE immunization goverage estimates 1990; 2018 (Data as of 1 July 2019).

Supplementary Imumnization (Activities (SIA): WHO/EPI database (Data as of 1 July 2019).

https://www.who.int/entity/immunization/monitoring_surveillance/data/Summary_Measeles_SIAs.xls.

Source: www.who.int (29 Aug 2019)

(Activities (SIA): WHO/EPI database (Data as of 1 July 2019).

coverage (Date as of 1 July 2019);

Reported measles cases and MCV vaccination coverage,

20000 ## 50

Reported measles cases and MCV vaccination coverage,

United Kingdom of Great Britain and Northern Ireland (the), 1990-2018

Data source:

30'000

25'000

Measles cases - Reported by National Authorites to WHO annually. Measeles Containing vaccines (MCV) vaccination coverage (Date as of 1 July 2019);

WHO I MICEE immunistration mayage actimates 1990; 2019 (flata as of 1 July 2019). (Activities (SIA): WHO/EPI database (Data as of 1 July 2019).

Supplementary Immunization Activities (SIA) WHO/EPI database (Data as of 1 July 2019). https://www.who.int/entity/immunization/monitoring_surveillance/data/Summary_Measeles_SIAs.xls

Wakefield tells GMC he was motivated by concern for autistic children. Dyer O. BMJ. 2008 Apr 5; 336(7647):738

Wakefield admits fabricating events when he took

children's blood 336(7649):850

Wakefield was MMR research 29;340:c593

Lancet retracts Dyer C. BMJ. 2

Wakefield is st ranging finding BMJ. 2010 Ma

Wakefield's art was fraudulent BMJ. 2011 Jan

Assuring reseating Opel DJ, Dieke BMJ. 2011 Jan

Wakefield sues Dyer C. BMJ. 2

Texas court dis Andrew Wakef 2014 Oct 6;349 The MMR Vaccine and Autism. Frank DeStefano, Tom T. Shimabukuro. Annu Rev Virol. 2019 Sep 29; 6(1): 585–600.

Wakefield is struck off for the "serious and wide-ranging findings against him" BMJ 2010;340:c2803

Andrew Wakefield, the British gastroenterologist who sparked a worldwide scare over the measles, mumps, and rubella (MMR) vaccine, has been found guilty of <u>serious professional misconduct</u> and struck off the medical register by the General Medical Council.

In January Dr Wakefield was found guilty of dishonesty and irresponsibility by the GMC, the UK's regulatory body. The fitness to practise panel held that Dr Wakefield abused his position, subjected children to intrusive procedures such as lumbar puncture and colonoscopy that were not clinically indicated, carried out research that flouted the conditions of ethics committee approval, and brought the medical profession into disrepute (BMJ 29 January 2010, ;340:c593)

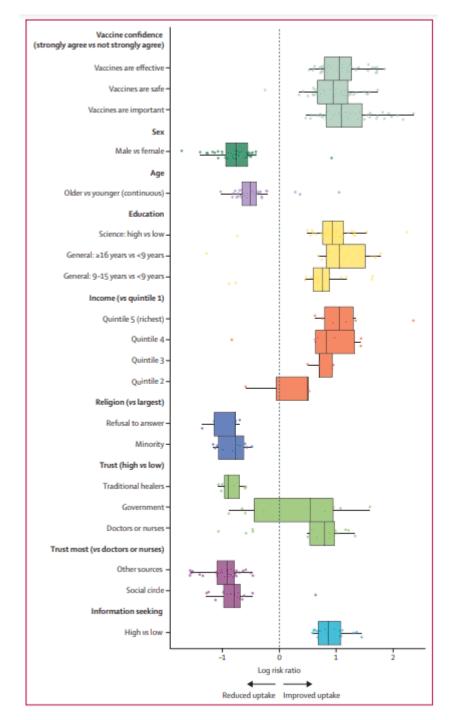
During the two and half year case, the longest in GMC history, Dr Wakefield was found to have failed to show that he had received funding from the legal aid board through a solicitor who hoped to mount a legal action against the vaccine manufacturer and that he had filed a patent for a new vaccine when he submitted the paper to the *Lancet*.

Unvaccinated "Wakefield cohorts" blamed for 5000 cases of mumps in England last year. Kmietowicz Z. BMJ. 2020 Feb 14;368:m619.

Andrew Wakefield calls Trump "on our side" over vaccines after meeting. Dyer O. BMJ. 2016 Dec 5;355:i6545







Mapping global trends in vaccine confidence and investigating barriers to vaccine uptake: a large-scale retrospective temporal modelling study.

de Figueiredo A, Simas C, Karafillakis E, Paterson P, Larson HJ

Lancet. 2020 Sep 26;396(10255):898-908

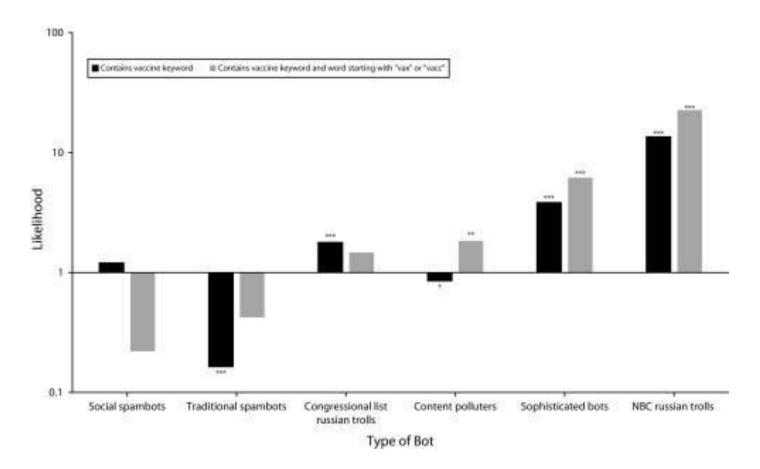


Figure 4: Univariate determinants of vaccine uptake within the Wellcome Global Monitor dataset
Global trends in univariate associations between vaccine uptake and confidence in vaccines, demographics
and socioeconomic status, sources of trust, and information-seeking behaviours. Each point represents a
significant association (95% HPD interval excludes zero) between a variable and uptake in a given country.
Boxplots show the median log risk ratio and IQR. All variables (except age, which is continuous) are categorical
and baseline groups are specified by each category (eg, high vs low denotes low as the baseline group; see the
table for definitions). HPD-highest posterior density.

Weaponized Health Communication: Twitter Bots and Russian Trolls Amplify the Vaccine Debate

David A. Broniatowski, Amelia M. Jamison, SiHua Qi, Lulwah AlKulaib, Tao Chen, Adrian Benton, Sandra C. Quinn, Mark Dredze

Am J Public Health. 2018 Oct; 108(10): 1378–1384.

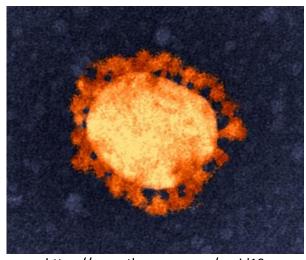


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Antivaccine theme	Example tweet	Provaccine theme	Example tweet
Freedom of	VaccinateUS mandatory #vaccines infringe on constitutionally protected	Vaccines work	#VaccinateUS #vaccines save 2.5 million children from preventable diseases
choice/antimandatory	religious freedoms		every year
vaccines		Vaccines should be	Your kids are not your property! You have to #vaccinate them to protect them
Can't trust government on	Did you know there was a secret government database of #vaccine-damaged	mandatory	and all the others! #VaccinateUS
vaccines	children? #VaccinateUS	People who don't	#VaccinateUS You can't fix stupidity. Let them die from measles, and I'm for
Pharmaceutical companies	Pharmacy companies want to develop #vaccines to cash, not to prevent deaths	vaccinate are stupid	#vaccination!
want vaccine profits	#VaccinateUS	Vaccination protects herd	#VaccinateUS #vaccines protect community immunity
Vaccines cause bad side	#VaccinateUS #vaccines can cause serious and sometimes fatal side effects	immunity	
effects		People who don't	#VaccinateUS My freedom ends where another person's begins. Then children
Natural immunity is better	#VaccinateUS natural infection almost always causes better immunity than #vaccines	vaccinate put me/my kids	should be #vaccinated if disease is dangerous for OTHER children
		at risk	
General vaccine conspiracy theories	Dont get #vaccines. Iluminati are behind it. #VaccinateUS	Vaccines don't cause	#vaccines cause autism—Bye, you are not my friend anymore. And try to think
		autism	with your brain next #VaccinateUS
Vaccines cause autism	Did you know #vaccines caused autism? #VaccinateUS	You deserve bad things if	#vaccines are a parent's choice. Choice of a color of a little coffin
Vaccine ingredients are	·	you don't vaccinate	#VaccinateUS
dangerous	#VaccinateUS #vaccines contain mercury! Deadly poison!	Alternative medicine	Do you still treat your kids with leaves? No? And why don't you #vaccinate
_	HTT: in a TIO at discuss that H is a task of the H	doesn't work	them? Its medicine! #VaccinateUS
Diseases aren't so	#VaccinateUS most diseases that #vaccines target are relatively harmless in	People died without	Most parents in Victorian times lost children regularly to preventable illnesses.
dangerous	many cases, thus making #vaccines unnecessary	vaccines	#vaccines can solve this problem #VaccinateUS

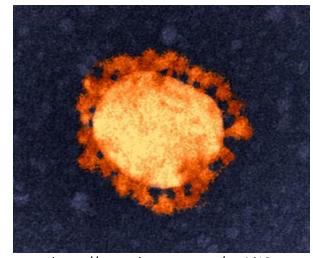


https://www.theasm.org.au/covid19

COVID-19 Vaccine: Conclusions

- 1. The scale of vaccine development against COVID-19 is unprecedented
- 2. There is broad consensus that an effective vaccine will be discovered
- 3. Vaccine safety is paramount: regulatory agencies must not yield to political pressures in the approval and licensing process
- 4. Licensing of a safe and effective COVID-19 vaccine is likely in 2021
- 5. The scientific community must engage more actively in communicating the public-health benefits of vaccination
- 6. Grassroots anti-vaccine communities should be acknowledged and engaged respectfully; knowledge-seeking should be encouraged
- 7. Synthetic anti-vaccine social media content must be exposed

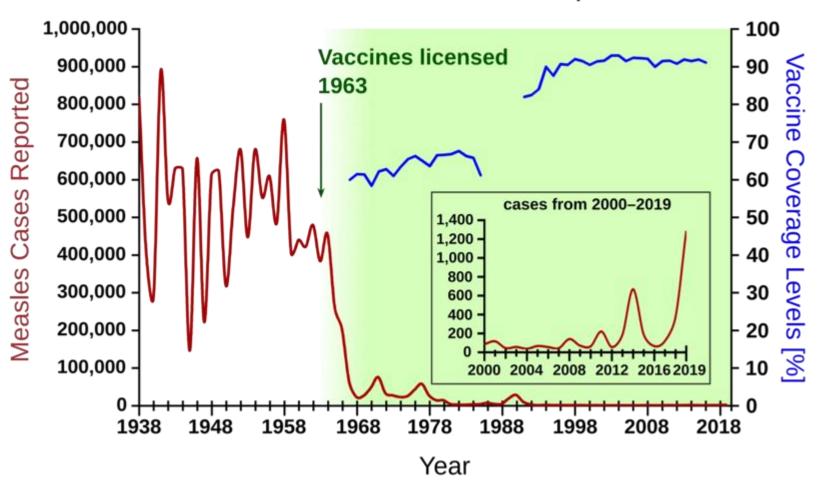




https://www.theasm.org.au/covid19

Thank You

Measles cases in the United States, 1938–2019

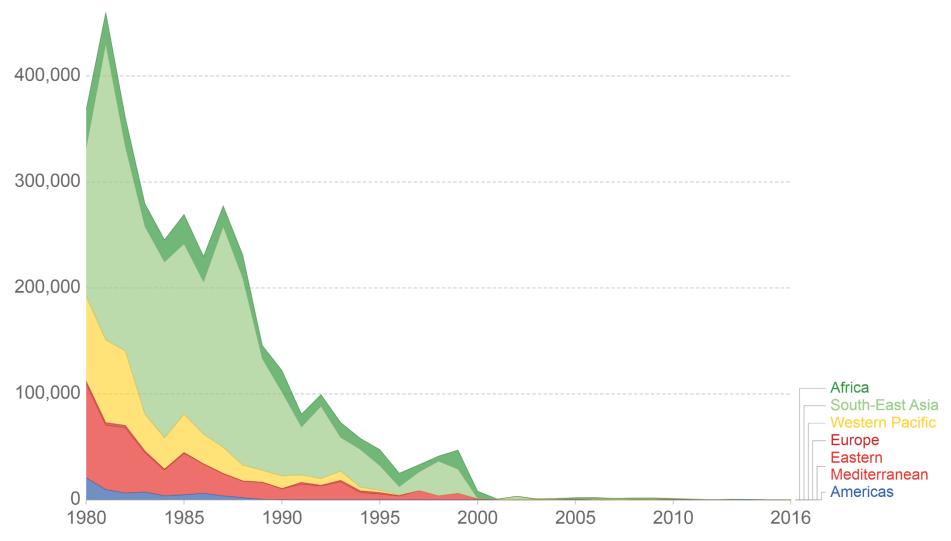


https://commons.wikimedia.org/wiki/File:Measles_US_1938-2019.png

Polio cases by world region, 1980 to 2016



Shown is the estimate of the total number of paralytic polio cases.



Source: WHO (2018) and Tebbens et al. (2011)

OurWorldInData.org/polio/ • CC BY

Note: These estimates are based on a model by Tebbens et al. (2011) that multiplies the reported number of cases with a correction factor based on the quality of each country's surveillance system. After a country is certified polio-free, however, the reported polio cases are used.

Maximum and current reported cases of vaccinepreventable diseases and adverse events, USA

Prevaccine era* (year)	1997†	% change			
206 939 (1921)	5	-99.99			
894 134 (1941)	135	-99.98			
152 209 (1968)	612	-99.60			
265 269 (1934)	5519	-97.92			
21 269 (1952)	0	-100.00			
57 686 (1969)	161	-99.72			
20 000 (1964-5)+	4	-99.98			
rubella syndrome					
1560 (1948)†	43	-97.24			
20 000 (1984)+	165	-99.18			
1639 066‡	6644	-99.59			
0	11 365	+++			
	(year) 206 939 (1921) 894 134 (1941) 152 209 (1968) 265 269 (1934) 21 269 (1952) 57 686 (1969) 20 000 (1964–5)† ne 1560 (1948)† 20 000 (1984)† 1639 066‡	(year) 206 939 (1921) 5 894 134 (1941) 135 152 209 (1968) 612 265 269 (1934) 5519 21 269 (1952) 0 57 686 (1969) 161 20 000 (1964–5)† 4 ne 1560 (1948)† 43 20 000 (1984)† 165 1639 066† 6644			

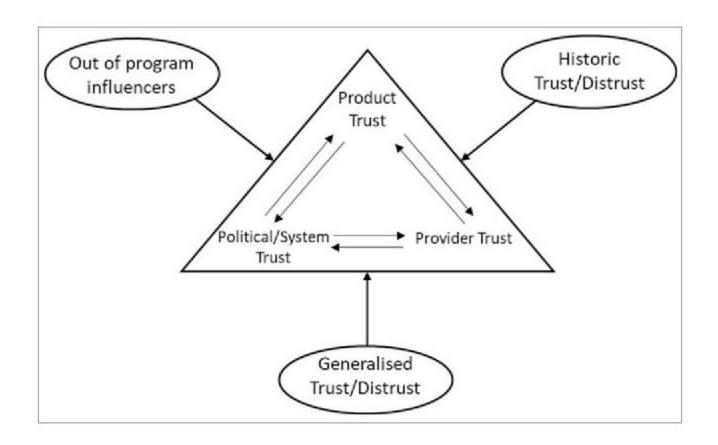
^{*}Maximum cases reported in prevaccine era and year. †Provisional. †Estimated because no national reporting existed in the prevaccine era.

Vaccine adverse events: causal or coincidental?

Robert T. Chen, Frank DeStefano

Lancet 351(103): 611-612. (1998)

Hib = Haemophilus influenzae b



A visulisation of the trust relationship related to vaccination.

Measuring trust in vaccination: A systematic review.

Larson HJ, Clarke RM, Jarrett C, Eckersberger E, Levine Z, Schulz WS, Paterson P.

Hum Vaccin Immunother. 2018 Jul 3;14(7):1599-1609.