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Pandémie COVID19/SARS-CoV-2. Mesures de santé publique : qu'est-ce qui a finalement marché !?

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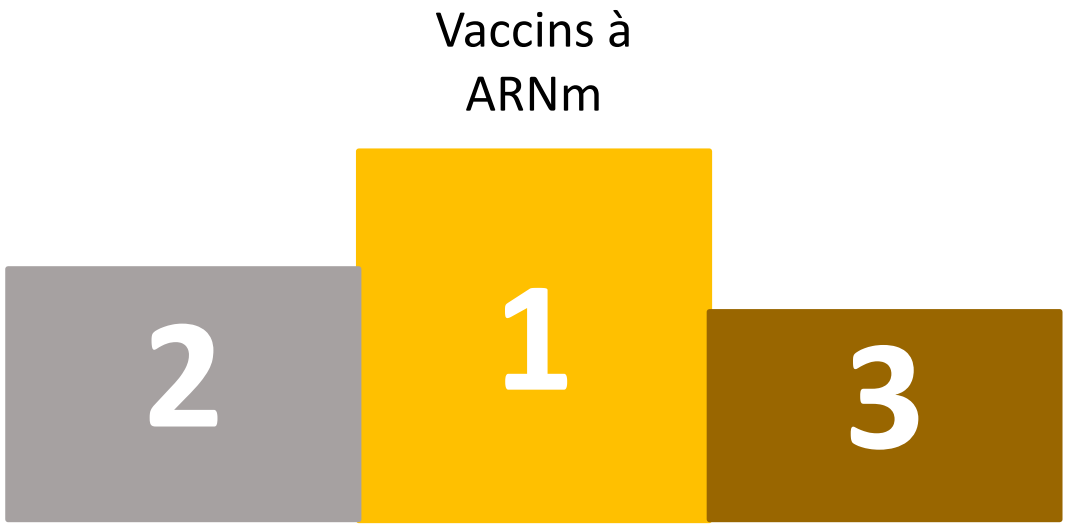
"Public health is the science and art of preventing disease, prolonging life and promoting health through organised efforts of society."

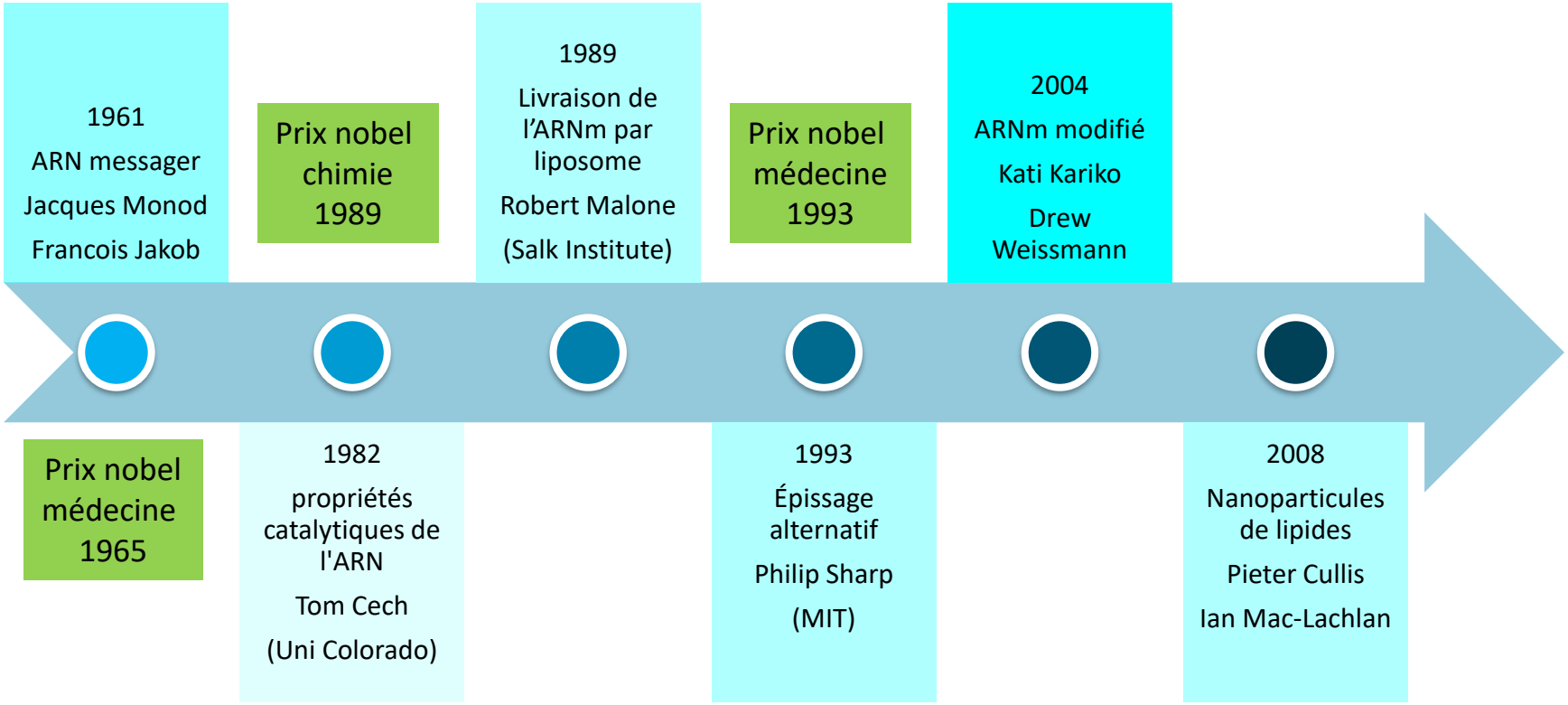
Sir Donald Acheson
Chief Medical Officer for England
1998

The science

And the winner is….



1960-1990: 30 ans de recherche fondamentale: ADN➔ ARN➔ protéines
1990-2020: 30 ans de recherches technologiques: vaccins à ARNm



Heidi-news. Les explorations, n11. septembre 2021

Une révolution médicale avec de multiples applications

- L'ARN messager modifié est une technologie vaccinale qui induit une réponse immunitaire à partir des protéines exprimées par des ARN messagers de synthèse transportés à l'aide de nanoparticules de lipides.
- 60 ans de recherches fondamentales et technologiques par des centaines de chercheurs ont été nécessaires pour aboutir à cette révolution médicale.
- Perspectives futures: thérapies basées sur l'ARN pour traiter les cancers, les maladies inflammatoires et certaines maladies rares.

Heidi-news. Les explorations, n11. septembre 2021

Quelques chiffres…

4.7 millions
nombre décès COVID-19 (22.09.2021)

4.7 milliards
de doses de vaccins contre le coronavirus

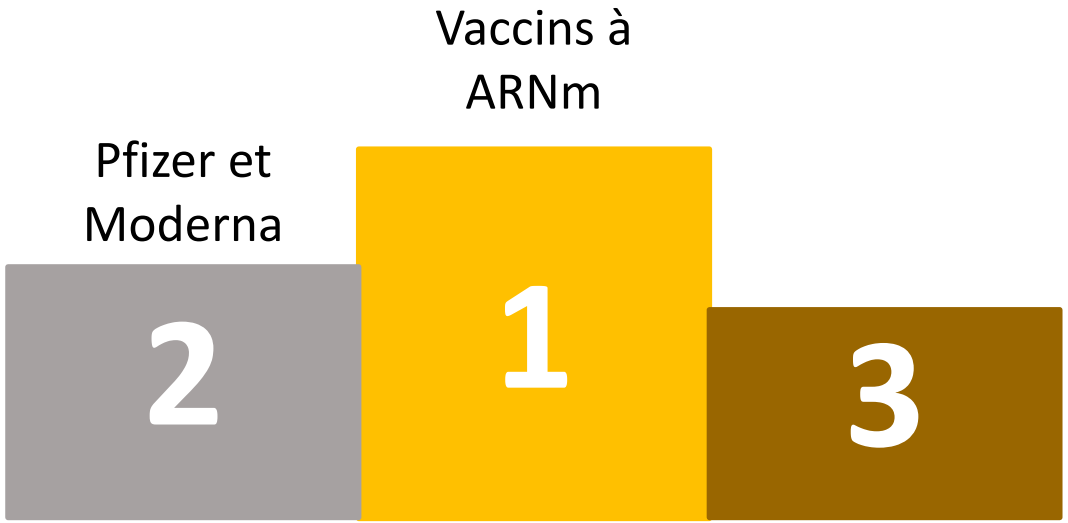
11 milliards de dollars de subventions du gouvernement américain (Warp Speed)

75 millions
Prix payé par BioNTech et Moderna pour la licence du brevet de l'ARN messager à U Pennsylvanie (recherches de Kati Kariko et Drew Weissmann)

56 milliards
de dollars de prévisions de vente de vaccins par Moderna et Pfizer en 2022

Heidi-news. Les explorations, n11. septembre 2021

And the winner is….



Pfizer and Moderna vaccines target the spike protein derived from SARS-CoV-2 isolated early in Wuhan, China

- Two of the vaccines currently in use worldwide, BNT162b2 (manufactured by Pfizer) and mRNA-1273 (manufactured by Moderna), are based on lipid nanoparticle delivery of mRNA encoding a prefusion stabilized form of spike protein derived from SARS-CoV-2 isolated early in the epidemic from Wuhan, China.
- Both of these vaccines demonstrated >94% efficacy at preventing COVID19 in phase III clinical studies performed in late 2020 in multiple countries (Polack et al., 2020; Badenet al., 2021).

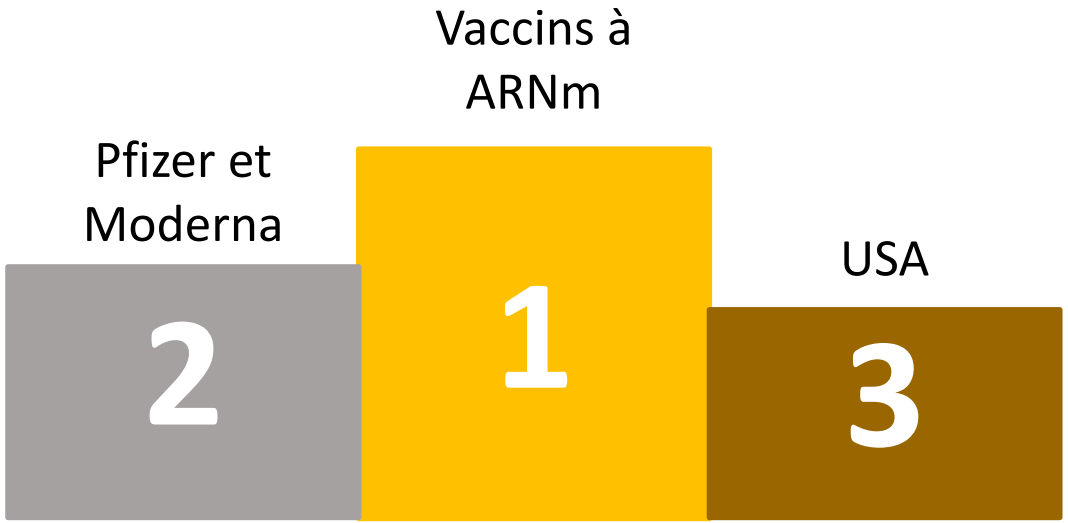
Garcia-Beltran et al., 2021, Cell 184, 2372–2383 April 29, 2021
Polack et al, N. Engl. J. Med., 383 (2020), pp. 2603-2615. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine.
Baden et al, N. Engl. J. Med., 384 (2021), pp. 403-416. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

Benefits of full vaccination against COVID-19 for transmission and implications for non-pharmaceutical interventions

- COVID-19 vaccines licensed in the EU/EEA highly effective in providing protection against symptomatic and severe COVID-19 in clinical trials.
- Evidence from real-life usage of COVID-19 vaccines has confirmed these clinical trial findings and also showed high vaccine effectiveness against PCR-confirmed SARS-CoV-2 infection.
- The risk of developing severe COVID-19 disease for a fully vaccinated individual is very low in people with no risk factors, and low in people with risk factors.
- The risk of developing severe COVID-19 disease for an unvaccinated individual who has been in contact with a fully vaccinated person exposed to SARS-CoV-2 infection is very low to low in people with no risk factors, and moderate in people with risk factors (limited evidence available so far).

https://www.ecdc.europa.eu/en/publications-data/interim-guidance-benefits-full-vaccination-against-covid-19-transmission

And the winner is….



Développement très rapide des vaccins à ARN messager contre la maladie COVID-19

Février 2020

Séquençage du SARS-CoV-2 (Autorités chinoises)

10 mois

Novembre 2020

Approbation des deux premiers vaccins à ARNm aux Etats-Unis

"Undoubtedly, the greatest success
during the pandemic response
was the rapid development of
vaccines and therapeutics,
including with innovative mRNA technologies."

Gostin, JAMA, September 15, 2021

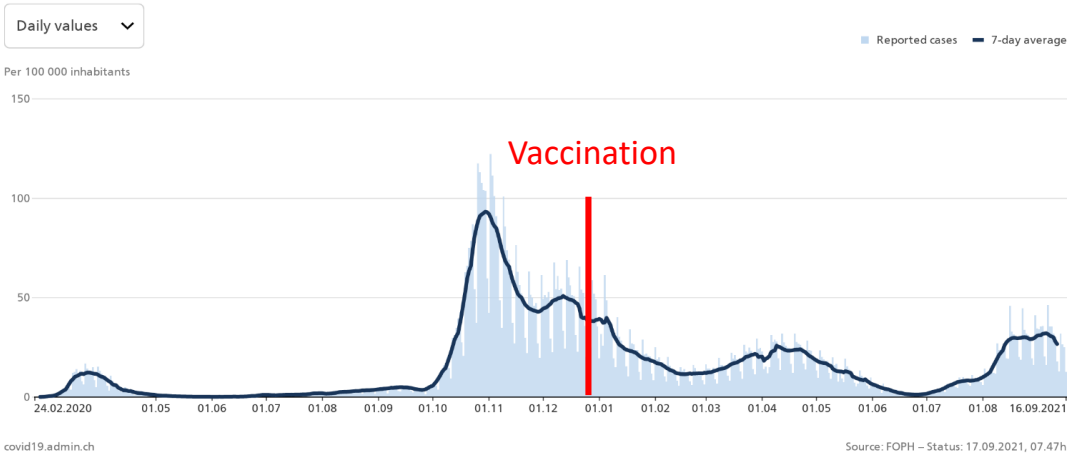
Development over time

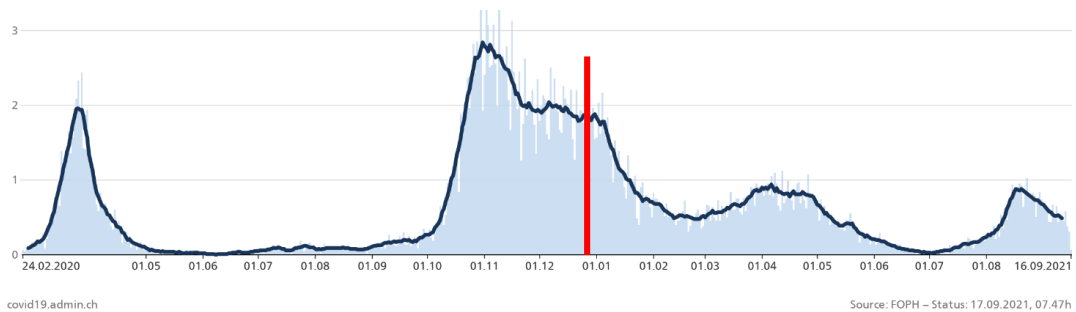
Laboratory-confirmed cases, Switzerland and Liechtenstein, 24.02.2020 to 16.09.2021, Per 100 000 inhabitants

The graph shows the development of laboratory-confirmed cases for the selected time frame.

Daily values: The line represents the 7-day rolling average (average of the previous 3 days to subsequent 3 days). 14-day values: The Line represents the sum of the last 14 days as the incidence (cases per 100 000 inhabitants) or as an absolute number. Total: The line represents the total of all cases for the selected time frame.

The published data is based on information submitted by laboratories, doctors and hospitals. It refers to the new reports we received and reviewed. The figures might therefore deviate from those communicated by the cantons.





Laboratory confirmed-cases per 100’000 inhabitatns

Laboratory confirmed-hospitalisations per 100’000 inhabitants

ne

Development over time

Vaccinated people, Switzerland and Liechtenstein, 21.12.2020 to 16.09.2021

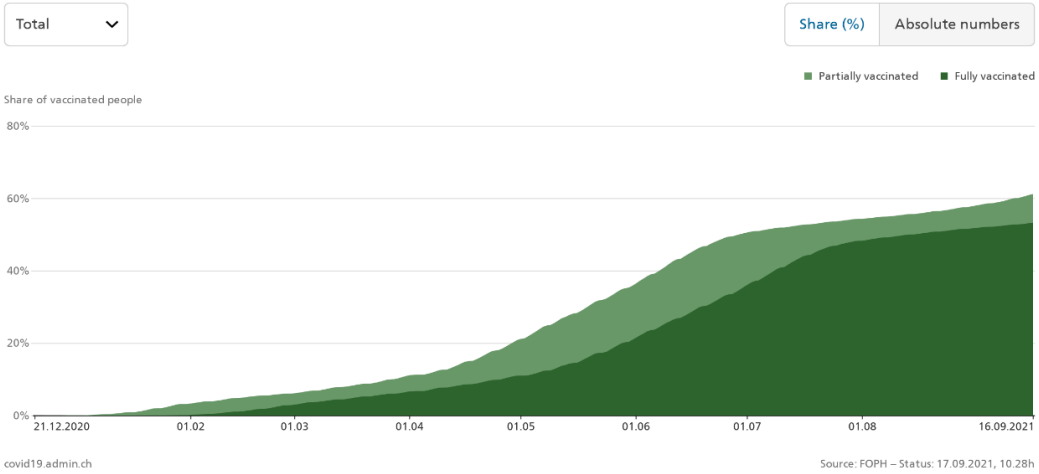
The graph shows the development of the number of vaccinated people.

Total: The areas represent the cumulative ratio up to the corresponding point in time. Daily values: People vaccinated on this day. The line represents the rolling 7-day average (average of the 3 days before and the three days after).

The data published here is based on information provided to us regularly by the cantons and the Principality of Liechtenstein. We publish the numbers on the following day. Therefore, they may differ from the numbers communicated by the cantons and Liechtenstein. The figures include vaccines from all suppliers.

Vaccinated people are assigned to the canton in which they live (canton of residence). People who have been vaccinated once and who have already recovered from COVID-19 are classified as «partially vaccinated», although they are considered to be fully vaccinated according to the FOPH/NITAG vaccination recommendation. The proportion of fully vaccinated people in the population is therefore slightly higher than shown here.

The cantons and the Principality of Liechtenstein provide us with the data via a secure electronic channel. They are sent in the form of anonymised individual data.



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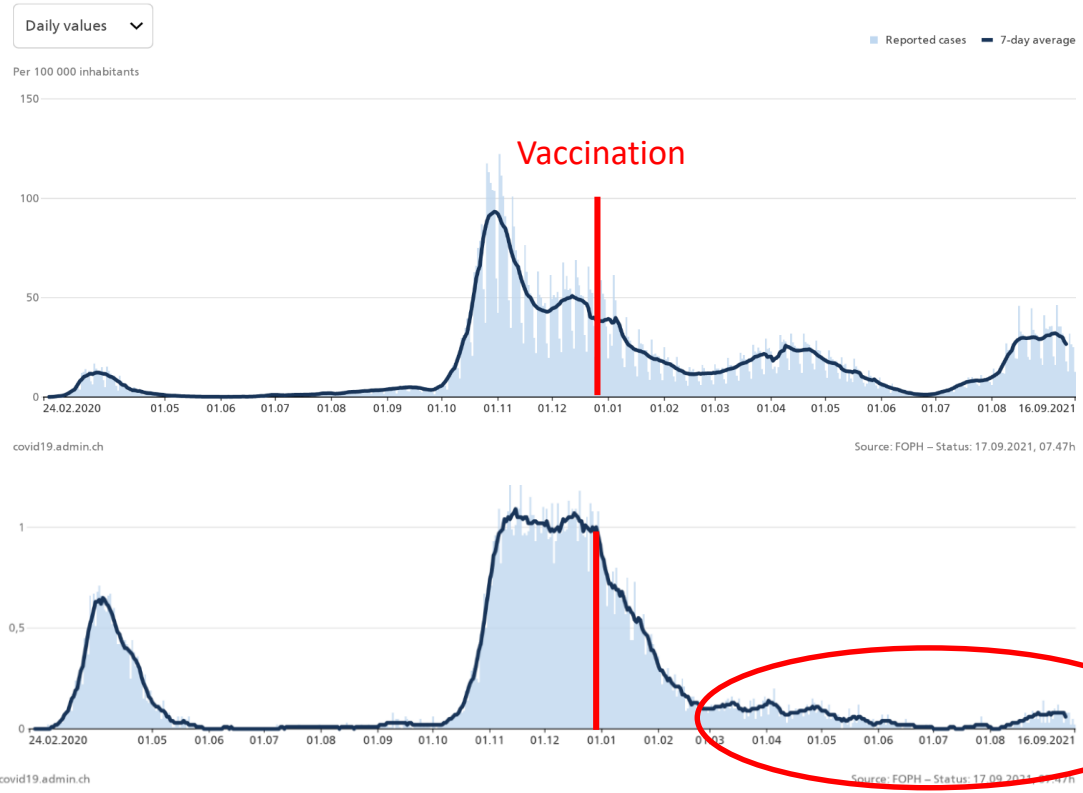
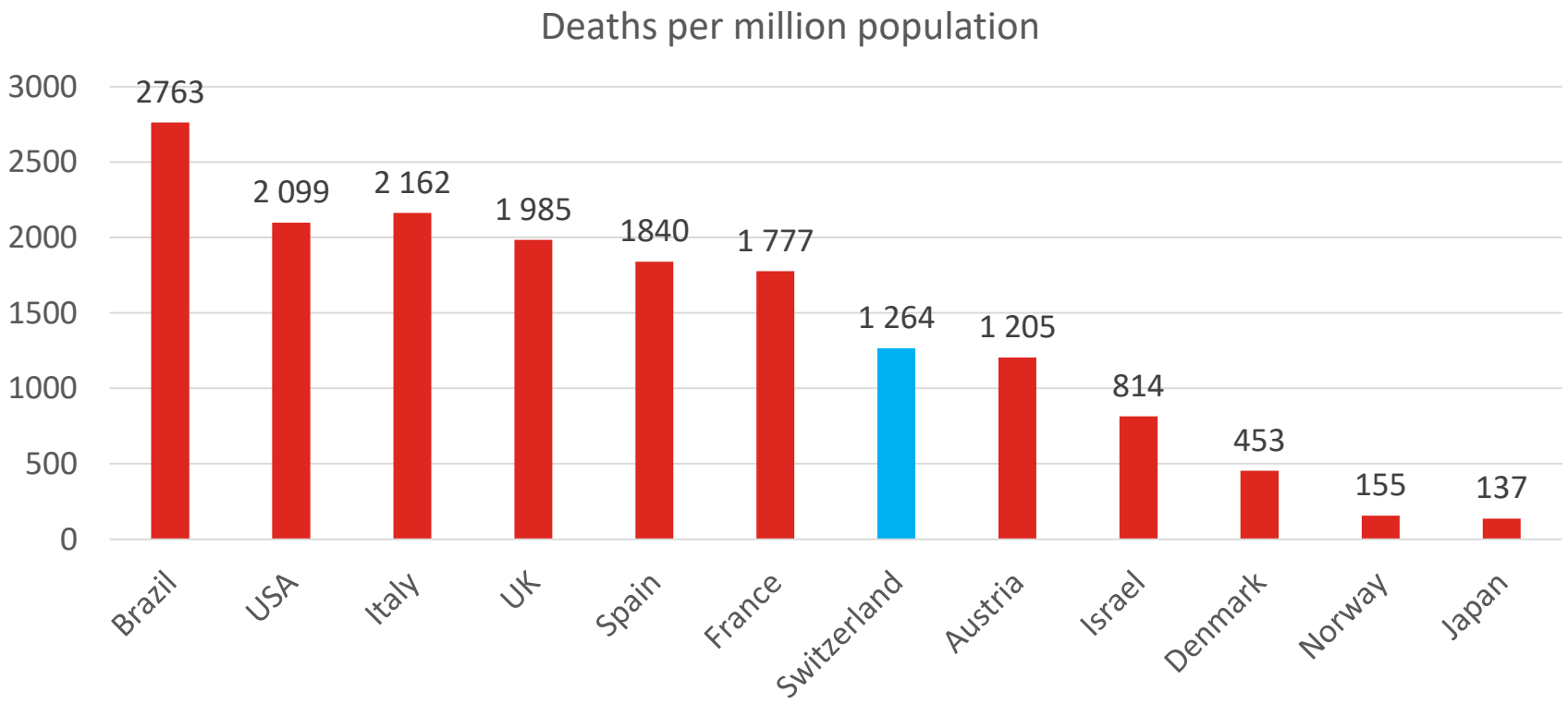


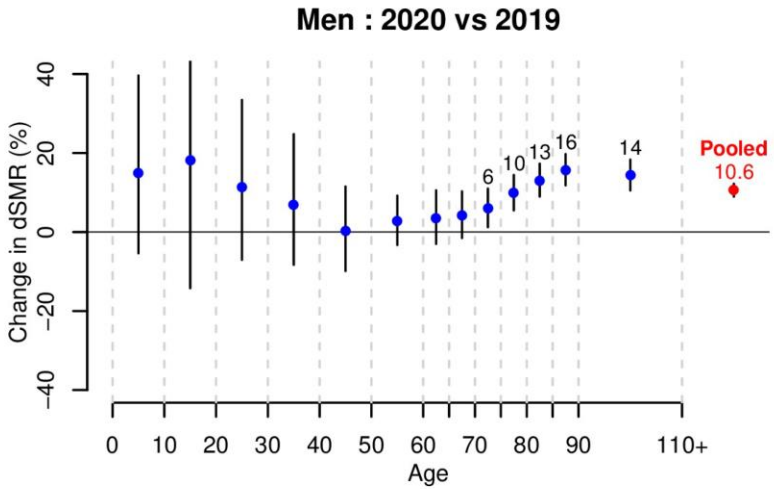
Laboratory confirmed-cases per 100’000 inhabitants

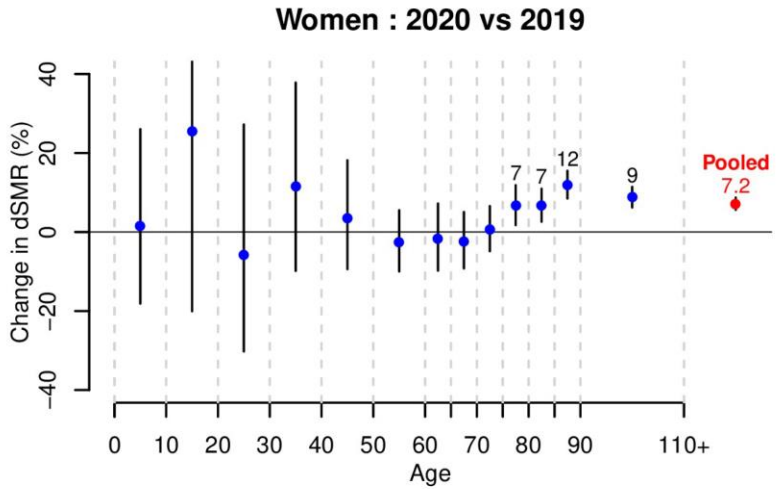
Laboratory confirmed- deaths per 100’000 inhabitants



Worldometer, 23.09.2021

Surmortalité en Suisse en 2020

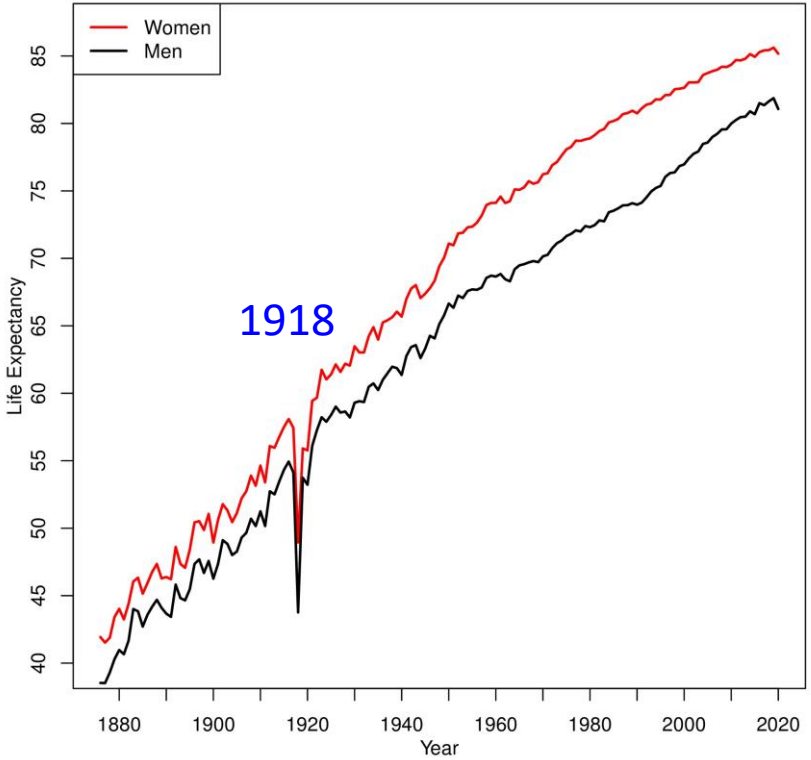




Aucune surmortalité en 2021 (6 premiers mois)

Locatelli & Rousson, PLos One 2021

Espérance de vie en Suisse entre 1880 et 2020



Loss of life expectancy in 2020
9.7 months for men
5.3 months for women

The art

Stratégie suisse: 3 pilliers

Vaccination

Tests

Mesures non-pharmaceutiques

Public health and social measures must be continuously adjusted to the intensity of transmission and the capacity of the health system in a country and at sub-national levels.

WHO, June 14, 2021; Considerations for implementing and adjusting public health and social measures in the context of COVID-19

Public health and social measures (PHSMs)

- personal protective measures (e.g. physical distancing, avoiding crowded settings, hand hygiene, respiratory etiquette, mask-wearing)
- environmental measures (e.g. cleaning, disinfection, ventilation)
- surveillance and response measures (e.g. testing, genetic sequencing, contact tracing, isolation, and quarantine)
- physical distancing measures (e.g. regulating the number and flow of people attending gatherings, maintaining distance in public or workplaces, domestic movement restrictions)

WHO, June 14, 2021; Considerations for implementing and adjusting public health and social measures in the context of COVID-19

An evidence review of face masks against COVID-19

Jeremy Howard[a,b,1], Austin Huang[c], Zhiyuan Li[d], Zeynep Tufekci[e], Vladimir Zdimal[f], Helene-Mari van der Westhuizen[g,h], Arne von Delft[h,i], Amy Price[j], Lex Fridman[k], Lei-Han Tang[l,m], Viola Tang[n], Gregory L. Watson[o], Christina E. Bax[p], Reshama Shaikh[q], Frederik Questier[r], Danny Hernandez[s], Larry F. Chu[j], Christina M. Ramirez[o], and Anne W. Rimoin[t]

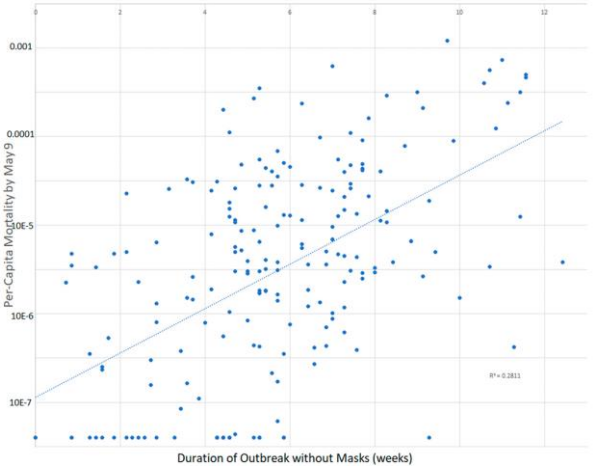
PNAS, January 11, 2021

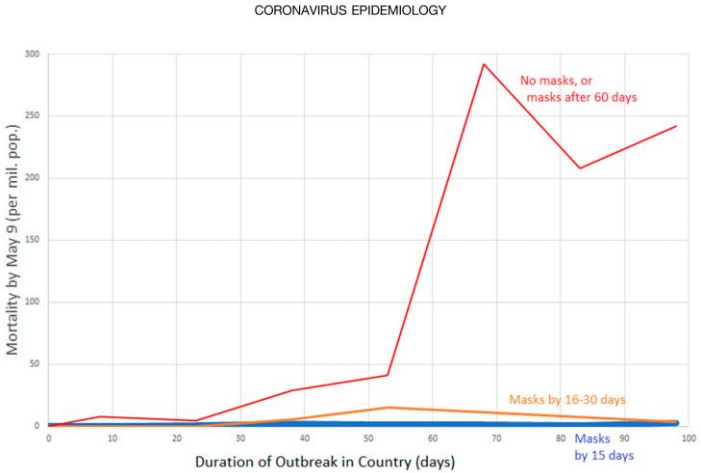
Edited by Lauren Ancel Meyers, The University of Texas at Austin, Austin, TX, and accepted by Editorial Board Member Nils C. Stenseth December 5, 2020 (received for review July 13, 2020)

- The preponderance of evidence indicates that mask wearing reduces transmissibility per contact by reducing transmission of infected respiratory particles in both laboratory and clinical contexts.
- Public mask wearing is most effective at reducing spread of the virus when compliance is high.
- This review of the literature offers evidence in favor of widespread mask use as source control to reduce community transmission.

Association of countrywide coronavirus mortality with demographics, testing, lockdowns, and public wearing of masks

200 countries by May 9, 2020





In a multivariable analysis of 196 countries, the duration of the outbreak in the country, and the proportion of the population aged 60 years or older were positively associated with per-capita mortality, whereas duration of mask-wearing by the public was negatively associated with mortality (all $P < 0.001$).

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Leffler, Am. J. Trop. Med. Hyg., 103(6), 2020, pp. 2400–2411

Effectiveness of public health measures to prevent the transmission of SARS-CoV-2 at mass gatherings: systematic review

- Systematic review (01.01.2020- 03.06.2021): 11 studies including 30’482 participants.
- implementing a range of measures may reduce the risk of SARS-CoV-2 transmission at mass gatherings .
- unlikely that the risk can be eliminated entirely
- all studies adopted a layered mitigation approach involving multiple measures.
- all included studies were only of ‘fair’ to ‘poor’ quality.

➔ There is currently limited evidence on the effectiveness of measures to prevent SARS-CoV-2 transmission at mass gatherings.

Walsh, Rev Med Virol. 2021 Aug 13.PMID: 34390056

Effectiveness of public health measures to prevent the transmission of SARS-CoV-2 at mass gatherings

TABLE 4 Overview of public health measures implemented in each included study

Public health measure	Revollo[30]	Fieldlab A[25]	Fieldlab B[24]	Fieldlab C[35]	Fieldlab D[36]	Hagemann[33]	Job[27]	Jokhdar[28], Ebrahim[23], Hashim[26]	Kim[29]	Moritz[31]	Schade[34,32]
Pre-event testing	✓	✓	✓	✓	✓	✓	-	✓	-	✓	N/A
Pre-event quarantine	-	-	-	-	-	✓	-	✓	-	-	N/A
Health screening	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A
Face masks	✓	✓	✓	P	P	✓	✓[a]	✓	✓	✓	✓
Ventilation	✓	✓	O	✓	O	-	✓	O	O	✓	✓
Excluded vulnerable populations	✓	✓	✓	✓	✓	-	✓[b]	✓	-	✓	N/A
Hand sanitiser	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A
Reduced numbers	✓	✓	✓	✓	✓	✓	-	✓	-	✓	N/A
Physical distancing	-	-	-	-	-	✓	✓	✓	✓	Va	N/A
Congestion control	✓	✓	✓	✓	✓	✓	✓	✓	-	Va	N/A
Cohorting	-	✓	✓	✓	-	✓	-	✓	-	Va	N/A
Contact tracing	✓	✓	✓	✓	✓	-	✓	✓	✓	✓	N/A
Post-event testing	✓	✓	✓	✓	✓	-	-	✓	✓	-	N/A
Restrict movements/ quarantine post event	-	✓	✓	✓	✓	-	-	✓	-	-	N/A

Note: Study trialled these measures to different intensities. ✓ = measure implemented. - = measure not implemented.

Abbreviations: N/A, not applicable as mechanistic study without human participants; O, outdoors; P, poor compliance; Va, varied.

[a]Provided to vulnerable people only.

[b]Advised not to attend, but was not enforced.

Walsh, Rev Med Virol. 2021 Aug 13.PMID: 34390056

Same-day SARS-CoV-2 antigen test screening in an indoor mass-gathering live music event: RCT

- Control group: did not attend the concert
- Intervention group: attended the concert.

- Participants could sing and dance in the concert hall room, and no physical distancing was recommended.

Evidence regarding the safety of indoor mass gathering events done during the COVID-19 outbreak based on a **comprehensive preventive intervention**, including same-day screening with Ag-RDT, compulsory facial mask-wearing, and adequate ventilation.

	Control group (n=495)	Experimental group (n=465)
Baseline screening		
Ag-RDT positive	0	0
TMA positive*	15 (3·0%)	13 (3%)
Cell culture positive	0	0
RT-PCR positive	1 (<1%)	1 (<1%)
Ct value	37	37
Follow-up assessment		
Ag-RDT positive	2 (0·4%)	0
TMA positive†	15 (3·0%)	12 (3%)
TMA positive at baseline	4	3
TMA negative at baseline	11	9
RT-PCR positive	2 (0·4%)	0
Ct value	26·3; 28·3	NA
Infected with SARS-CoV-2	2 (0·4%)	0

Ag-RDT=antigen-detecting rapid diagnostic tests. TMA=transcription-mediated amplification test. RT-PCR=real-time reverse transcriptase-polymerase chain reaction. Ct=cycle threshold. NA=not applicable. *Three TMA results in the control group were inconclusive. †One TMA result in the experimental group was inconclusive.

Table: **Virological assessment results for SARS-CoV-2 at baseline and day 8 after the event**

Revollo, Lancet Infect Dis 2021, May 27; S1473-3099(21)00268-1; PMID: 34051886

Holiday gatherings, mobility and SARS-CoV-2 transmission: results from 10 US states following Thanksgiving

While 47.2% had Thanksgiving at home with household members, 26.9% had guests and 25.9% traveled.

Those who had guests for Thanksgiving or traveled were only more likely to test positive for SARS-CoV-2 if they also had high activity (e.g., participated in > one non-essential activity/day in the prior 2 weeks)

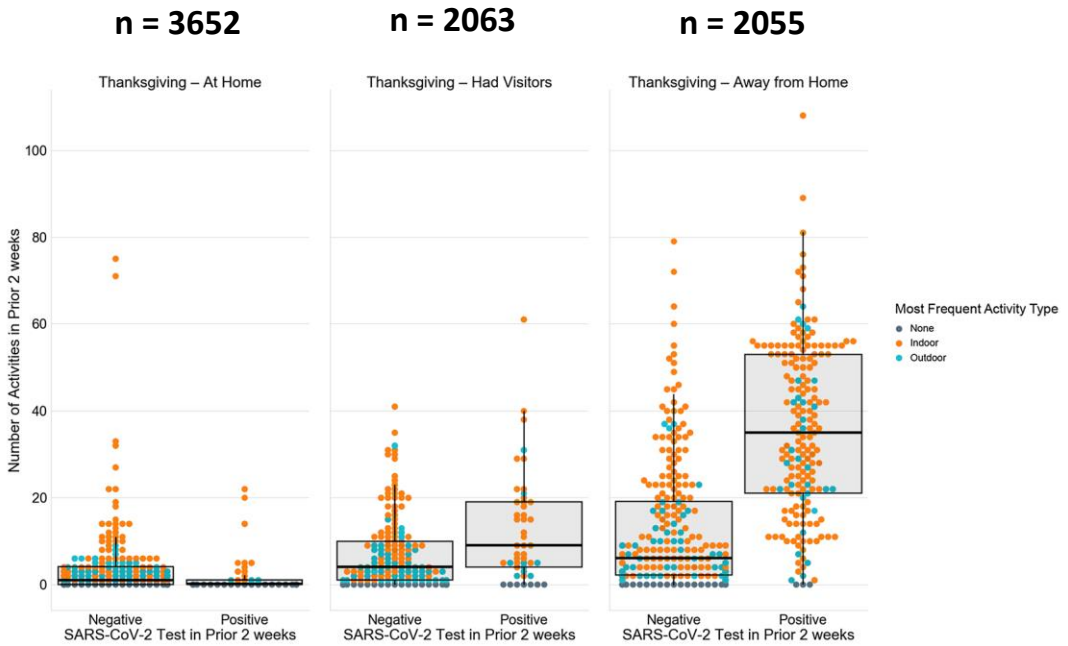

Figure 1. Summary of non-essential activities in the prior 2 weeks by Thanksgiving travel and SARS-CoV-2 test positivity in the prior 2 weeks.

Mehta .Sci Rep. 2021 Aug 30;11(1):17328.PMID: 34462499

Health care professionals advertising social media campain to stay at home for Thanksgiving and Christmas holidays (US)

- **Design**: RCT of the effect of a **Facebook advertising campaign** (videos recorded by doctors and nurses) to encourage users to stay at home for the Thanksgiving and Christmas holidays.
- **Interventions:** random assignment of counties to high intensity (n= 410 (386) at Thanksgiving (Christmas)) or low intensity (n= 410 (381)).
- **Primary outcomes**: holiday travel and fraction leaving home and COVID-19 infections.
- **Results**: **Average distance traveled** in high-intensity counties **decreased** for the 3 days before each holiday compared to low-intensity counties.
- **COVID-19 infections** (in the 2-week period starting 5 days after the holiday) **declined by 3.5%** (adjusted 95% CI: −6.2%, −0.7%; P = 0.013) in intervention compared to control zip codes.

This RCT shows the effects of travel reduction, which is a key non-clinical intervention whose effect had not been previously evaluated in a RCT.

Breza Nat Med. 2021, Aug 19.PMID: 34413518

Restart of the German Bundesliga during the pandemic

Measures taken:

- daily symptom monitoring
- PCR testing for SARS-CoV-2 RNA twice weekly,
- antibody tests (on two occasions—early during the phase in May 2020 and in the week of the last match)

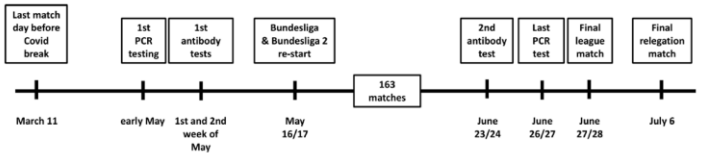

Figure 1 Time schedule from the interruption of the German professional football season 2019/20 until its successful termination. PCR, polymerase chain reaction.

After 165 matches played, no SARS-CoV-2 infection or seroconversion among players or officials

➔ professional outdoor football is feasible during the ongoing COVID-19 pandemic.

Meyer, Br J Sports Med. 2021 Jan;55(1):62-66. PMID: 32972979

Conclusions

- La gestion de la pandémie est complexe.
- Les vaccins (notamment ARNm) à disposition sont très efficaces
  ➔ la vaccination à ARN messager est une révolution médicale.
- L'efficacité des mesures non-pharmaceutiques de santé publique est difficile à démontrer
  ➔ Un ensemble de mesures est nécessaire et ces mesures doivent être adaptées au contexte local.