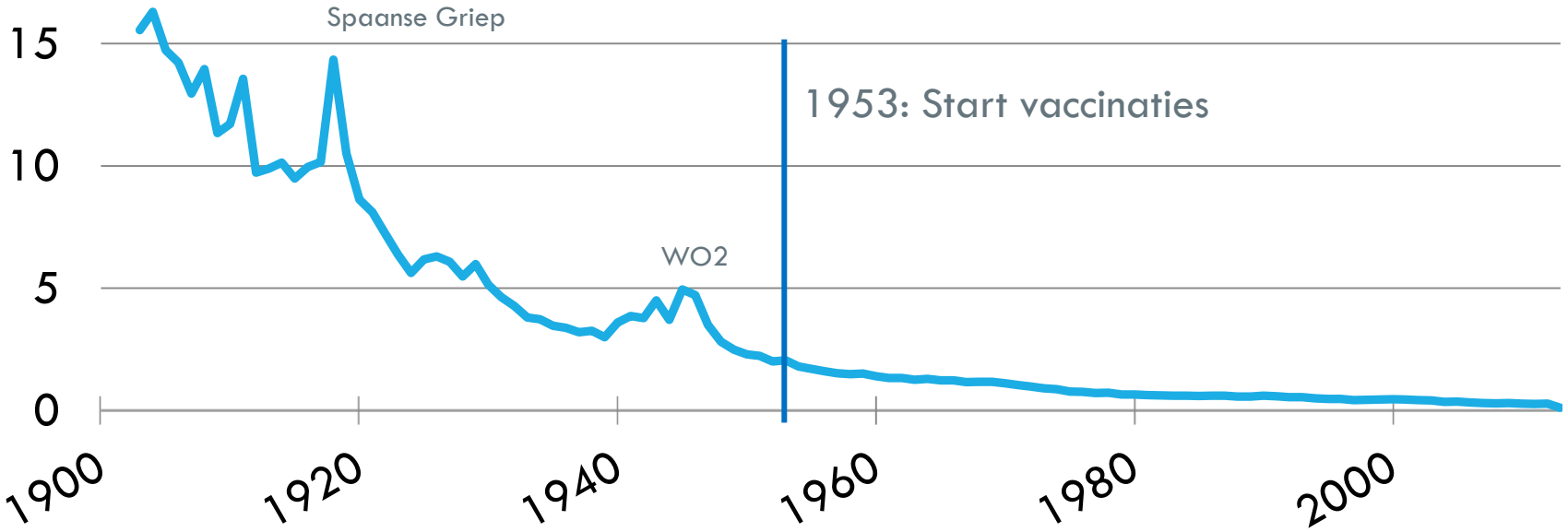
Voorkomen is slimmer dan genezen – symposium 18-01-2019

Een blik terug –
De effecten van meer dan een halve eeuw vaccineren

Maarten van Wijhe, PhD
Roskilde Universiteit – Denemarken

Centrum voor Infectieziektebestrijding (Cib, RIVM) – Jacco Wallinga
Rijksuniversiteit Groningen- Maarten Postma

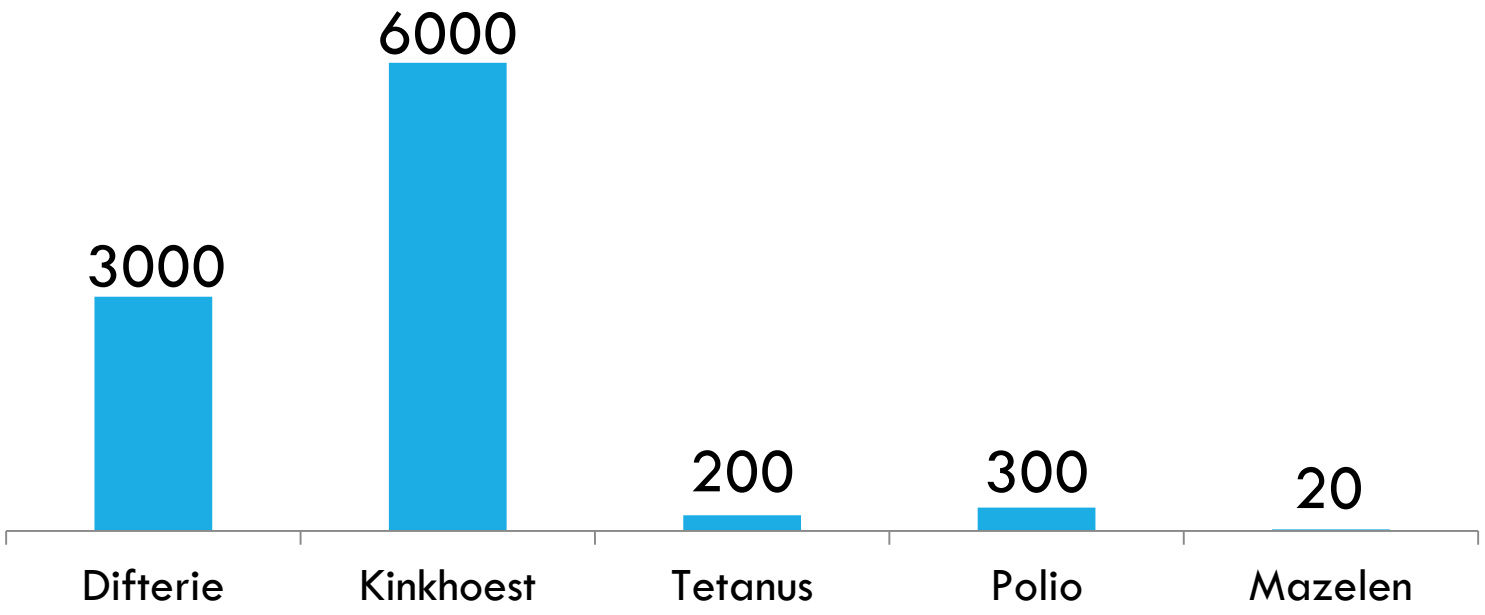
KINDERSTERFTE DOOR DE JAREN HEEN



Sterfte per 1000 kinderen onder de 20 jaar.

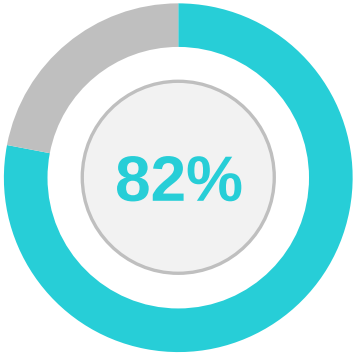
Bron: CBS

DUIZENDEN STERFGEVALLEN VOORKOMEN

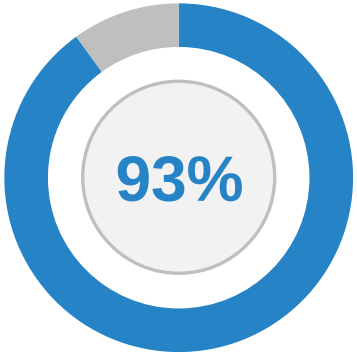


Van Wijhe et al, Lancet Infectious Diseases 2016

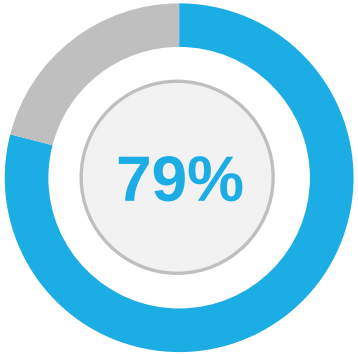
ZIEKTE VOORKOMEN



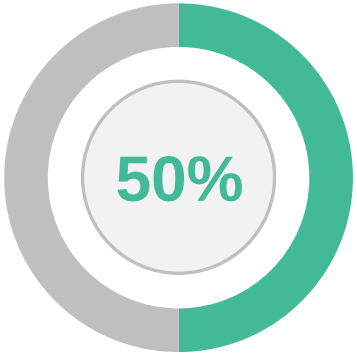
Difterie
20 duizend



Polio
5 duizend



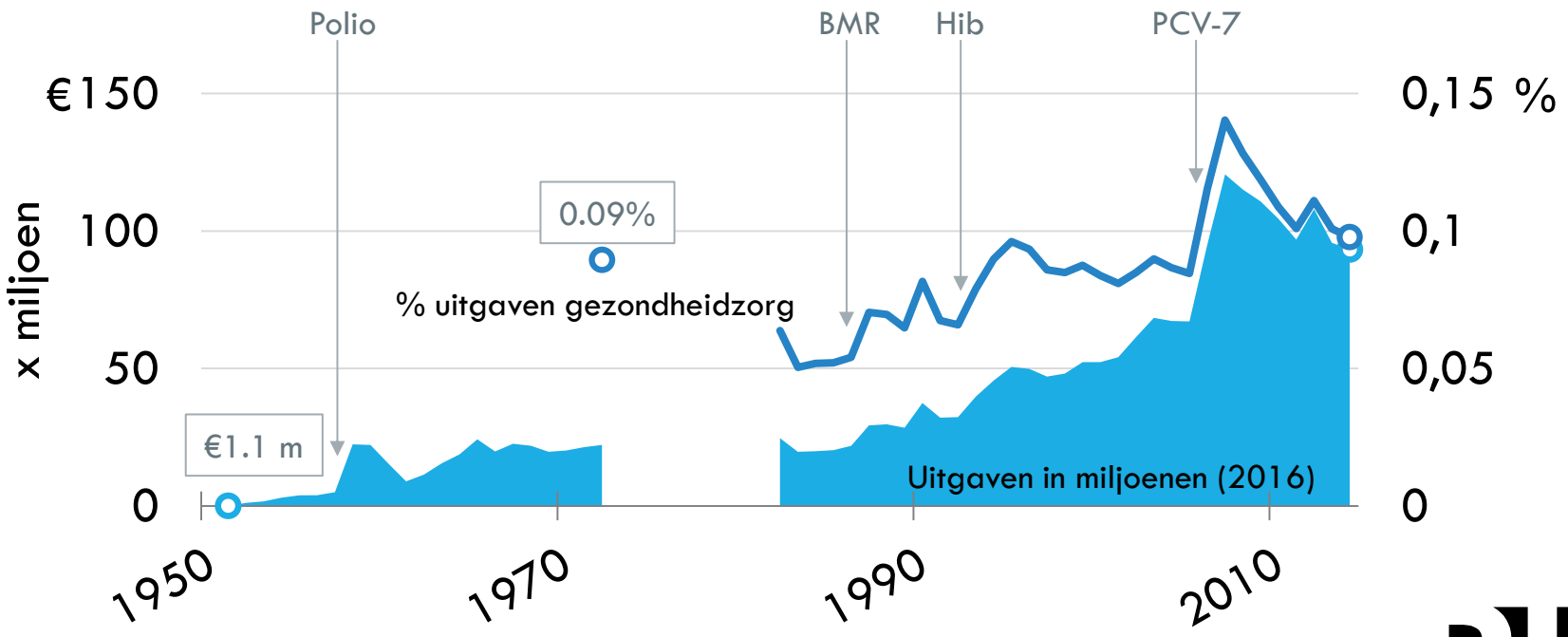
Bof
2 duizend



Rodehond
14 duizend

Van Wijhe et al, Epidemiology & Infection 2018

WAT BETREFT DE KOSTEN



KOSTEN IN 2014

Per persoon	Per geboorte	% van kosten gezondheidzorg	Totaal
€5,5	€530	0,10%	€93 m

KOSTEN PER PERSOON

Nederland

2014

€5,5

Duitsland

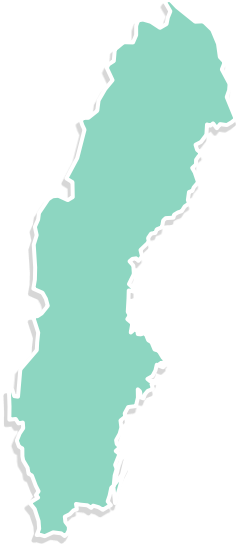
2016

€16

Frankrijk

2015

€8



Zweden

2015

€21

Bron: Ethgen et al, Human Vaccines & Immunotherapeutics, 2018

TOT SLOT

- Veel sterfte voorkomen
- Veel ziekte voorkomen
- Relatief goedkoop

Maar...

- Steeds duurder voor mogelijk minder winst
- Het blijft belangrijk om huidige en toekomstige programma's kritisch te evalueren

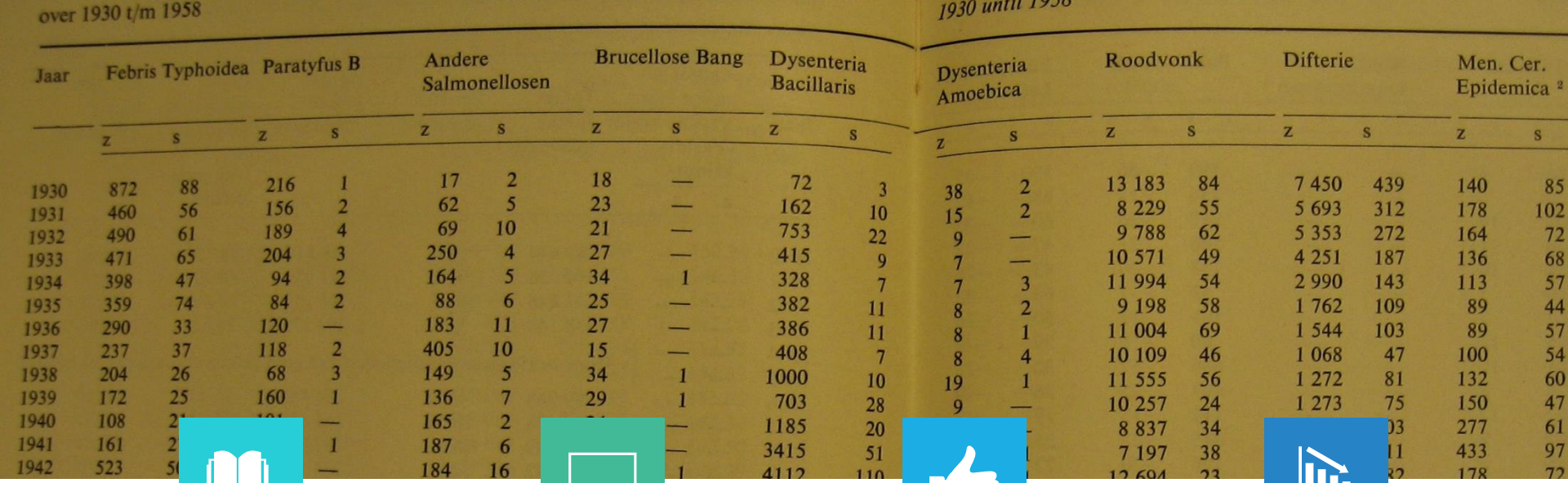
Per voorkomen sterfgeval

€89.000

Voor DKTP, BMR

Met dank aan:

Maarten Postma
Jacco Wallinga
Hester de Melker
Hester Korthals Altes
Scott McDonald
Lola Tulen
Pieter de Boer
Herman de Jong
Liselotte van Asten
Wim van der Hoek
Hans van Vliet



over 1930 t/m 1958 — 1930 until 1958

Jaar	Febris Typhoidea z	Febris Typhoidea s	Paratyfus B z	Paratyfus B s	Andere Salmonellosen z	Andere Salmonellosen s	Brucellose Bang z	Brucellose Bang s	Dysenteria Bacillaris z	Dysenteria Bacillaris s	Dysenteria Amoebica z	Dysenteria Amoebica s	Roodvonk z	Roodvonk s	Difterie z	Difterie s	Men. Cer. Epidemica [2] z	Men. Cer. Epidemica [2] s
1930	872	88	216	1	17	2	18	—	72	3	38	2	13 183	84	7 450	439	140	85
1931	460	56	156	2	62	5	23	—	162	10	15	2	8 229	55	5 693	312	178	102
1932	490	61	189	4	69	10	21	—	753	22	9	—	9 788	62	5 353	272	164	72
1933	471	65	204	3	250	4	27	—	415	9	7	—	10 571	49	4 251	187	136	68
1934	398	47	94	2	164	5	34	1	328	7	7	3	11 994	54	2 990	143	113	57
1935	359	74	84	2	88	6	25	—	382	11	8	2	9 198	58	1 762	109	89	44
1936	290	33	120	—	183	11	27	—	386	11	8	1	11 004	69	1 544	103	89	57
1937	237	37	118	2	405	10	15	—	408	7	8	4	10 109	46	1 068	47	100	54
1938	204	26	68	3	149	5	34	1	1000	10	19	1	11 555	56	1 272	81	132	60
1939	172	25	160	1	136	7	29	1	703	28	9	—	10 257	24	1 273	75	150	47
1940	108	[illegible]	[illegible]	—	165	2	[illegible]	—	1185	20	[illegible]	[illegible]	8 837	34	[illegible]	[illegible]	277	61
1941	161	[illegible]	[illegible]	1	187	6	[illegible]	—	3415	51	[illegible]	[illegible]	7 197	38	[illegible]	[illegible]	433	97
1942	523	[illegible]	[illegible]	—	184	16	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	178	72

Find old data in libraries and repositories

Often these data are in paper reports, or scanned books online (pdf).

Digitize relevant data

Using excel and other programs we digitize any data that may be relevant for the topic.

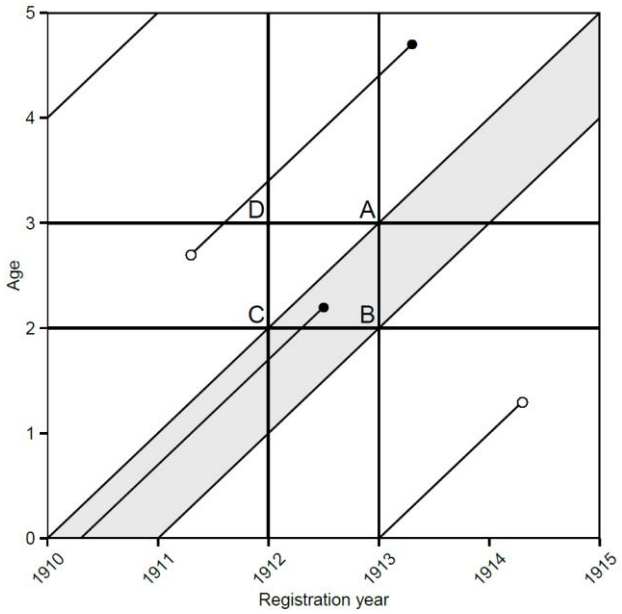
Curation and management

Data is cleaned of errors and readied for formal analysis. This included database construction.

Data analysis

Using mathematical and statistical tools from epidemiology and demographics.

BIRTH COHORT RECONSTRUCTION



We only have yearly deaths and need to obtain deaths by birth cohort.

We used Lexis triangles to assign a birth cohort to each death at random, taking into account relative birth cohort size.

We did this for each death between 0 and 20 years of age from 1903-2012; assigning them to birth cohorts 1903-1992.

ANALYSIS: CAUSE-SPECIFIC MORTALITY BURDEN

Mortality rate at age a for causes $i = 1, \ldots, k$

$$\mu(a) = \sum_i \mu^i(a)$$

Probability at birth of surviving past age x

$${}_xp_0 = e^{\left(-\int_0^x \mu(a)da\right)}$$

Life expectancy at birth

$${}_xe_0 = \int_0^x {}_ap_0 da$$

Probability at birth of dying from cause i before age x, i.e. the cause i cumulative incidence (CI)

$${}_xq_0^i = \int_0^x {}_ap_0 \mu^i(a) da$$

It follows that

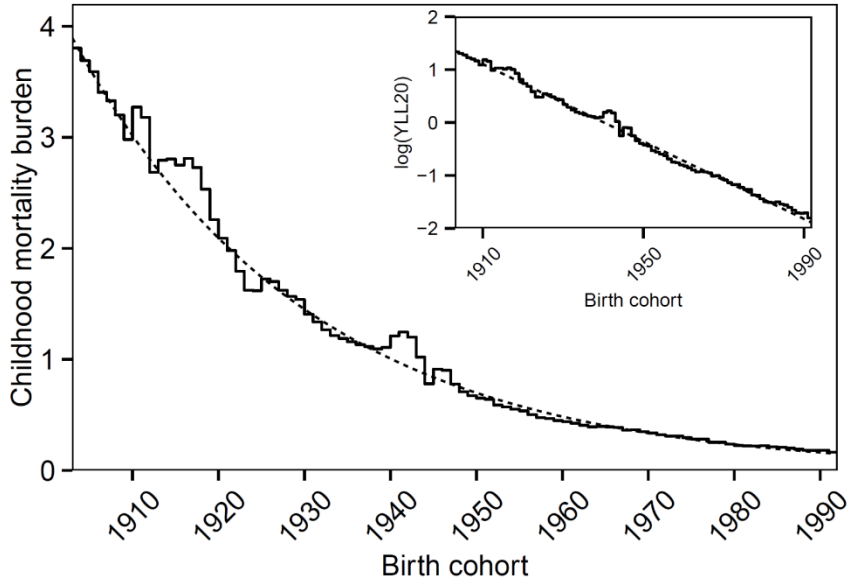
$${}_xp_0 + \sum_i {}_xq_0^i = 1 \qquad {}_ae_0 + \sum_i \int_0^a {}_xq_0^i dx = a$$

Expected yll before age a due to cause i

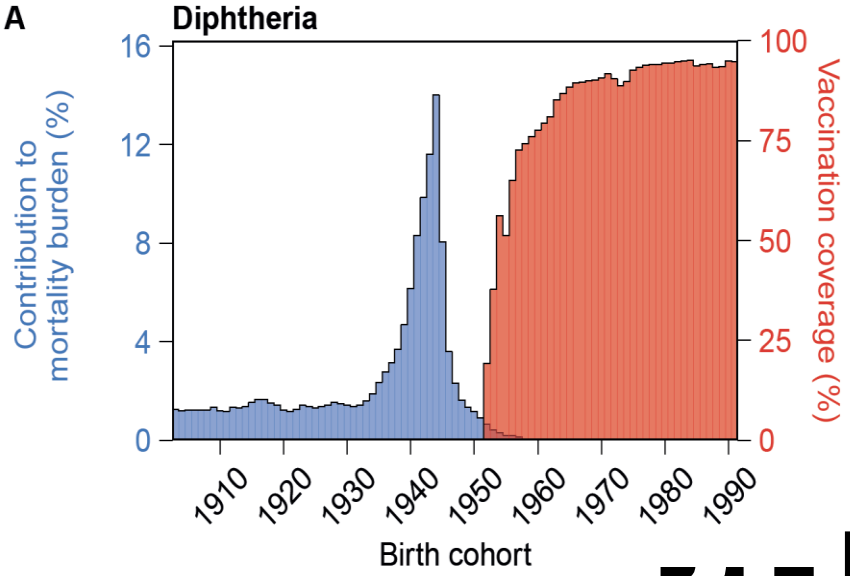
$${}_x\lambda_0^i = \int_0^a {}_xq_0^i dx$$

WHAT DOES THIS LOOK LIKE (2)?

All-cause mortality burden



Relative contribution of diphtheria



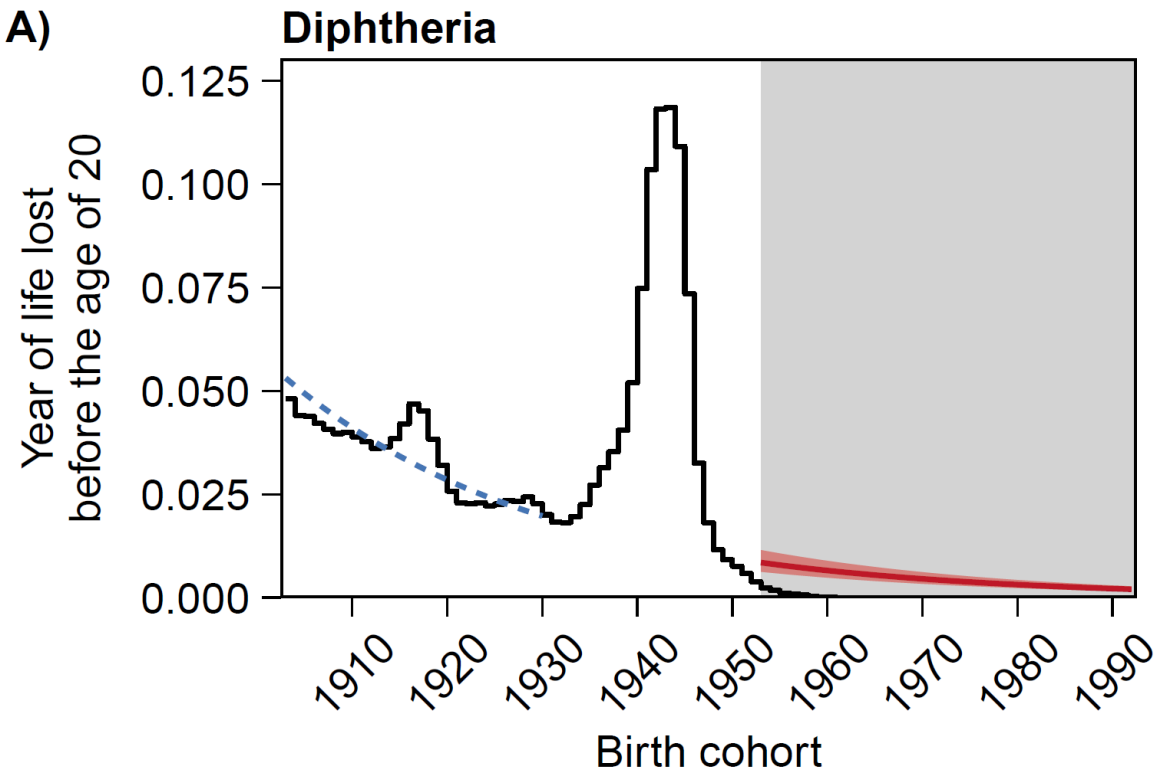
Source: van Wijhe et al, Lancet Infect Dis, 2016

THE COUNTERFACTUAL

What if a vaccination programme was not implemented?

$$\text{Averted} = \text{Expected} - \text{Observed}$$
$$\text{Averted} = p_i y_0 e^{-rt} - \text{Observed}$$

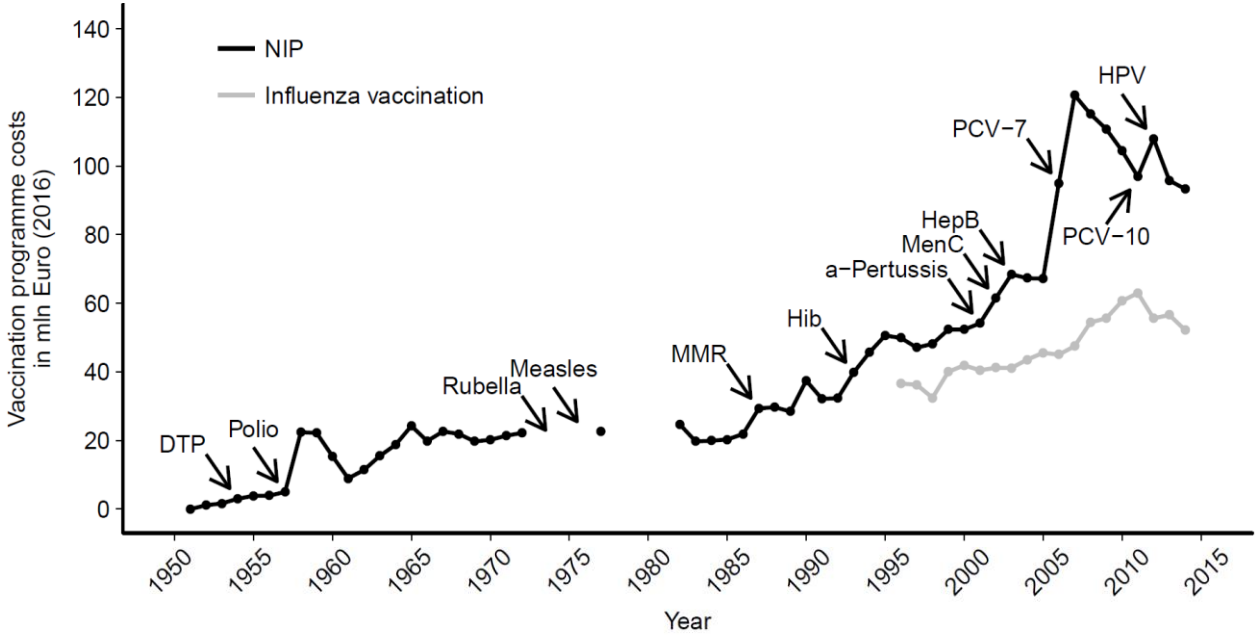
Averted deaths: 3000 (95% CI: 2000-4000)



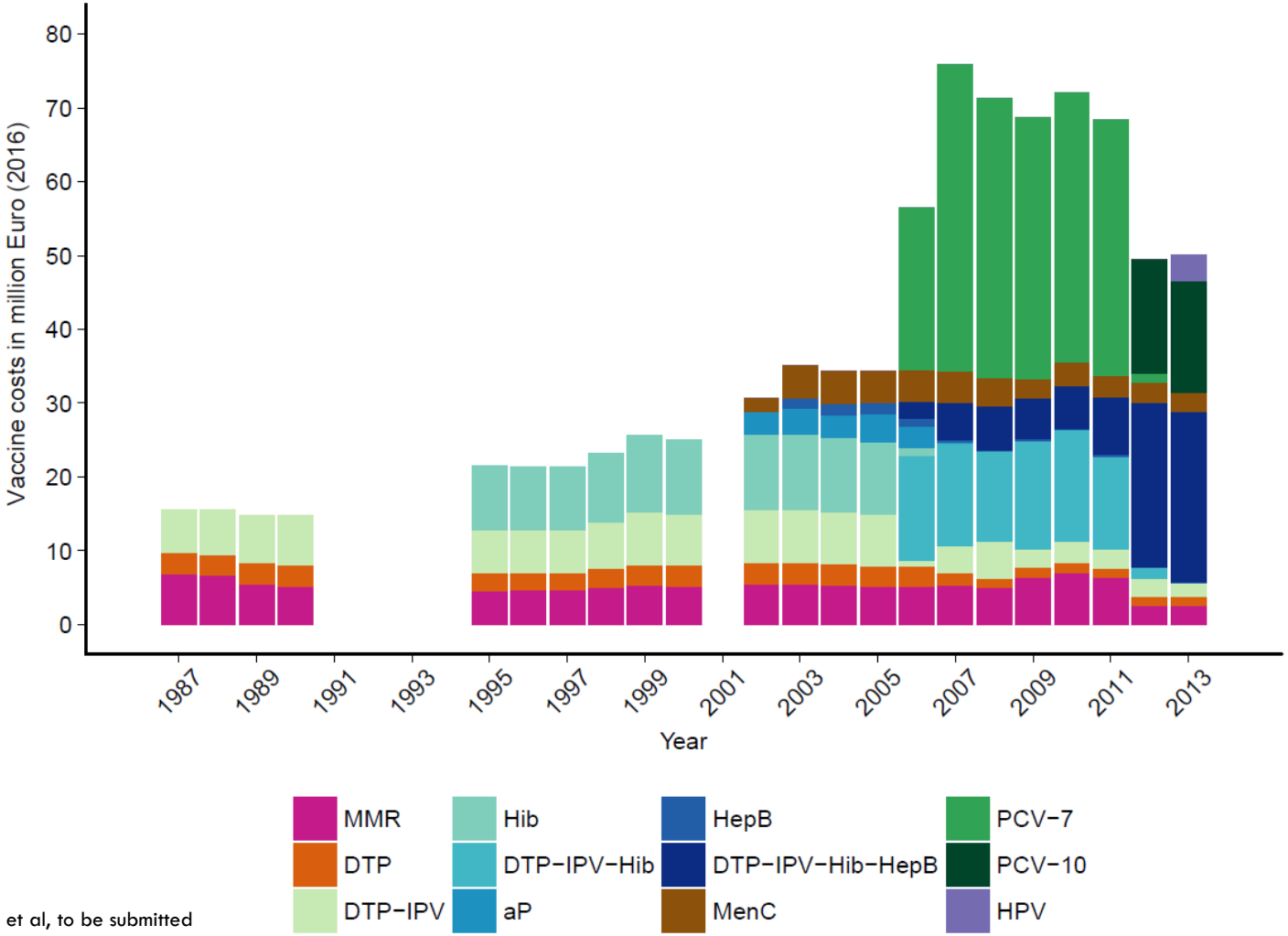
GOVERNMENT EXPENDITURE

Reported expenditure on vaccinations

Slow increase followed by a remarkable rise in costs with the inclusion of more expensive vaccines (PVC-7)



Source: van Wijhe et al, to be submitted

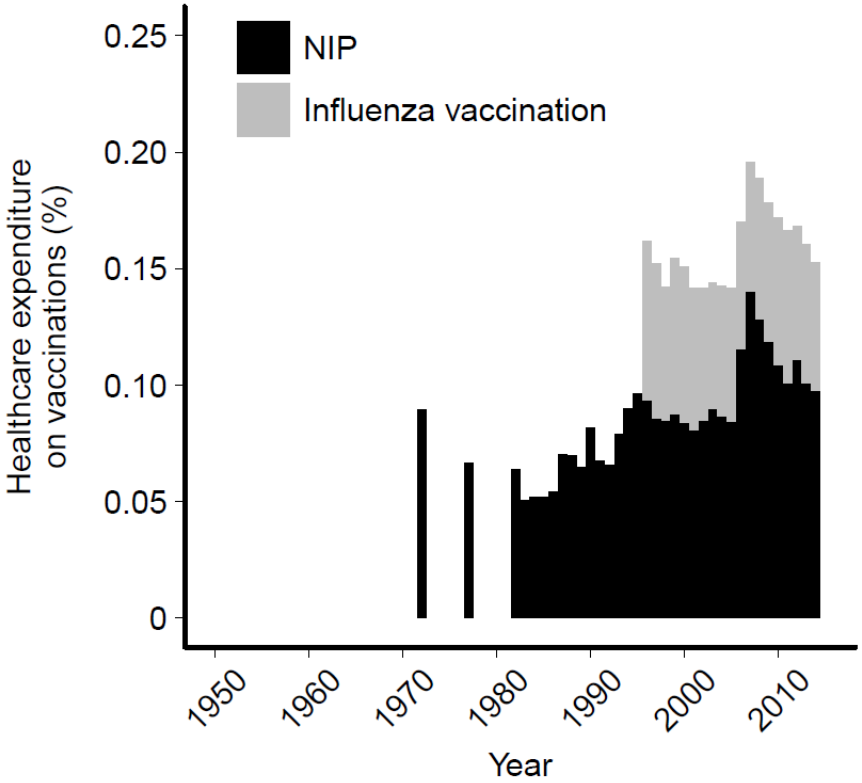


Source: van Wijhe et al, to be submitted

RELATIVE EXPENDITURE

Vaccine expenditure to healthcare expenditure

Vaccines only account for 0.15% of healthcare expenditure in 2014



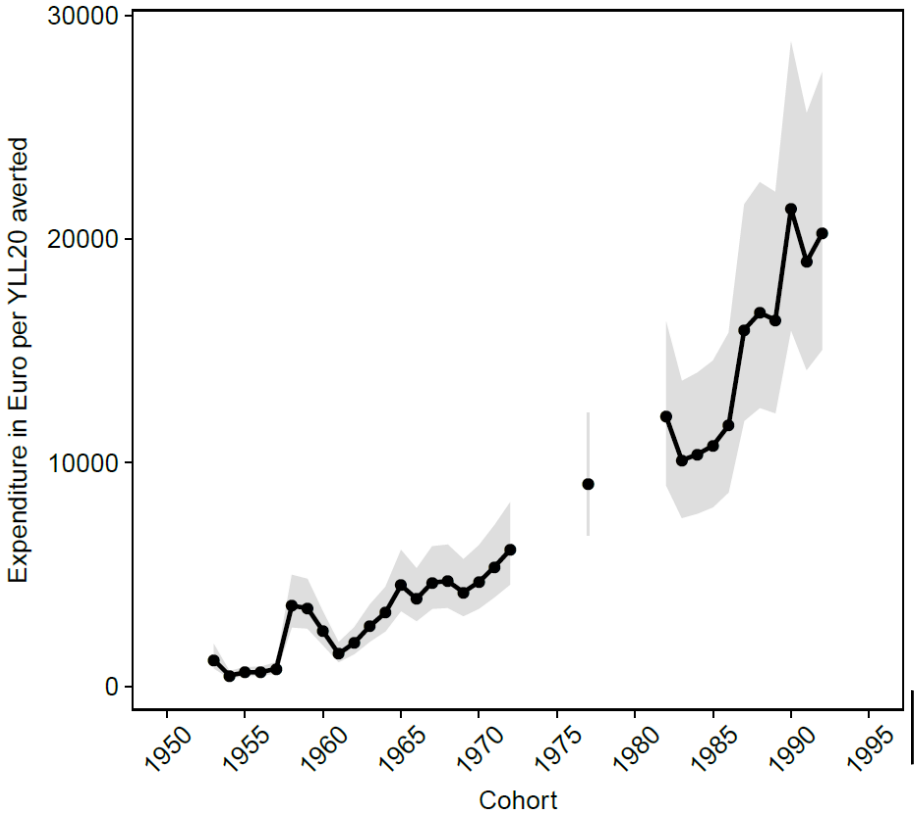
Source: van Wijhe et al, to be submitted

COST-EFFECTIVENESS?

We know the costs, we know the averted mortality burden

€ 5000 / YLL20

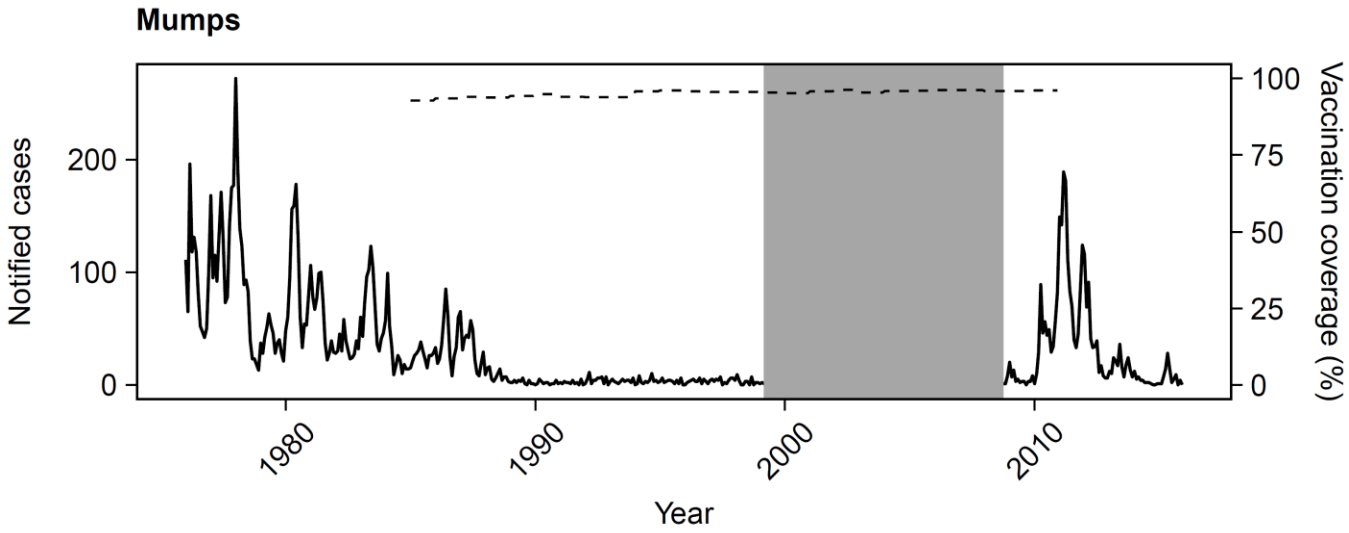
€ 89000 / death averted



WE PICK ANOTHER DISEASE: MUMPS

Reported cases of mumps

Again a decline before vaccination.
Regular outbreaks.
After vaccination nearly no cases….
Resurgence in 2008.



Source: van Wijhe et al, E&I, 2018

REGRESSION ANALYSIS

Latent process Poisson regression model

$$\log(\mu_t) = \log(p_t) + \beta_0 + \beta_1 t + \underbrace{\sum_{j=1}^{k}\left[\alpha_j \sin\left(\frac{2\pi t}{12\tau_j}\right) + \gamma_j \cos\left(\frac{2\pi t}{12\tau_j}\right)\right]}_{\text{Seasonal and multi-year cycles}} + x_t$$

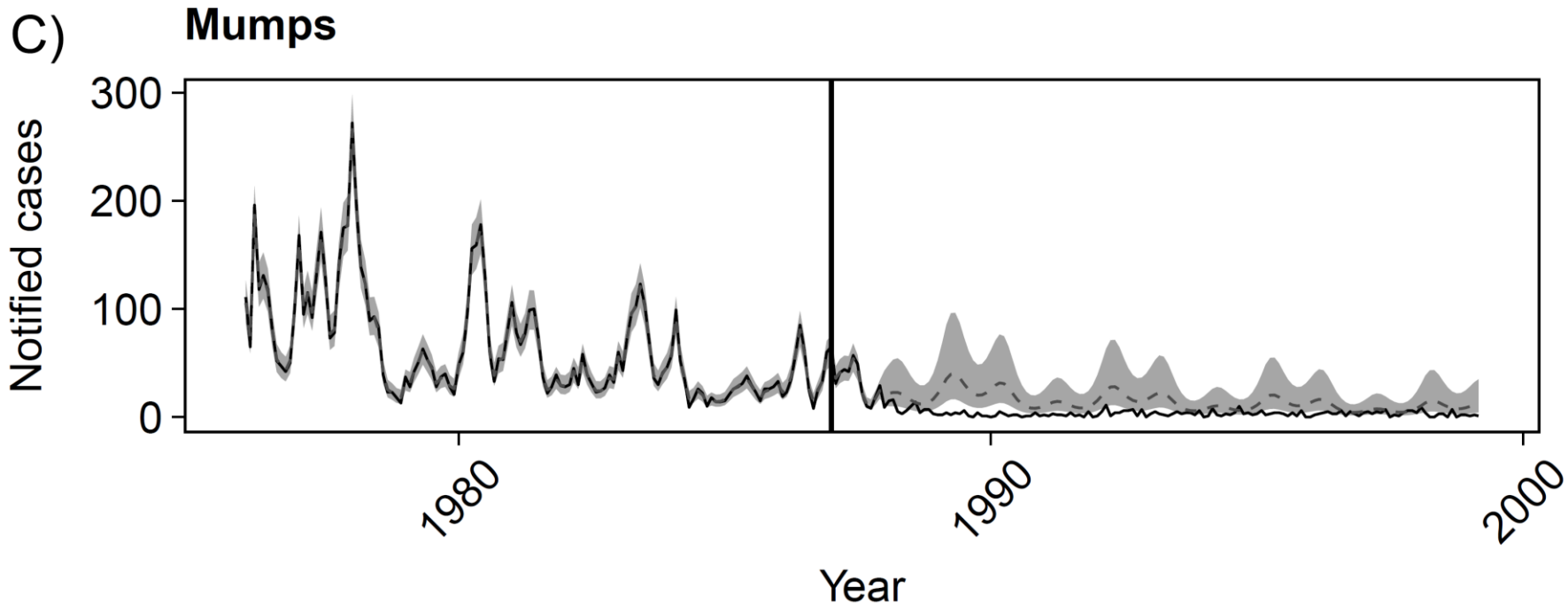
$Y_t \sim \text{Poisson}(\mu_t)$

β_0 is an intercept term

p_t is the general population of 0 to 20 year-olds at time t

β_1 is the coefficient of the secular trend

x_t is the latent autocorrelation process
(log incidence rate of infection, unobservable)



Regression model fit and counterfactual
Counterfactual constructed by drawing from posterior distributions.

Source: van Wijhe et al, E&I 2016