


Public Health Importance of Vaccination:

Protection beyond the Vaccinee.

Prof. Ab Osterhaus DVM, PhD

Director Research Center for Emerging Infections and Zoonoss (RIZ)

University of Veterinary Medicine Hannover (D)

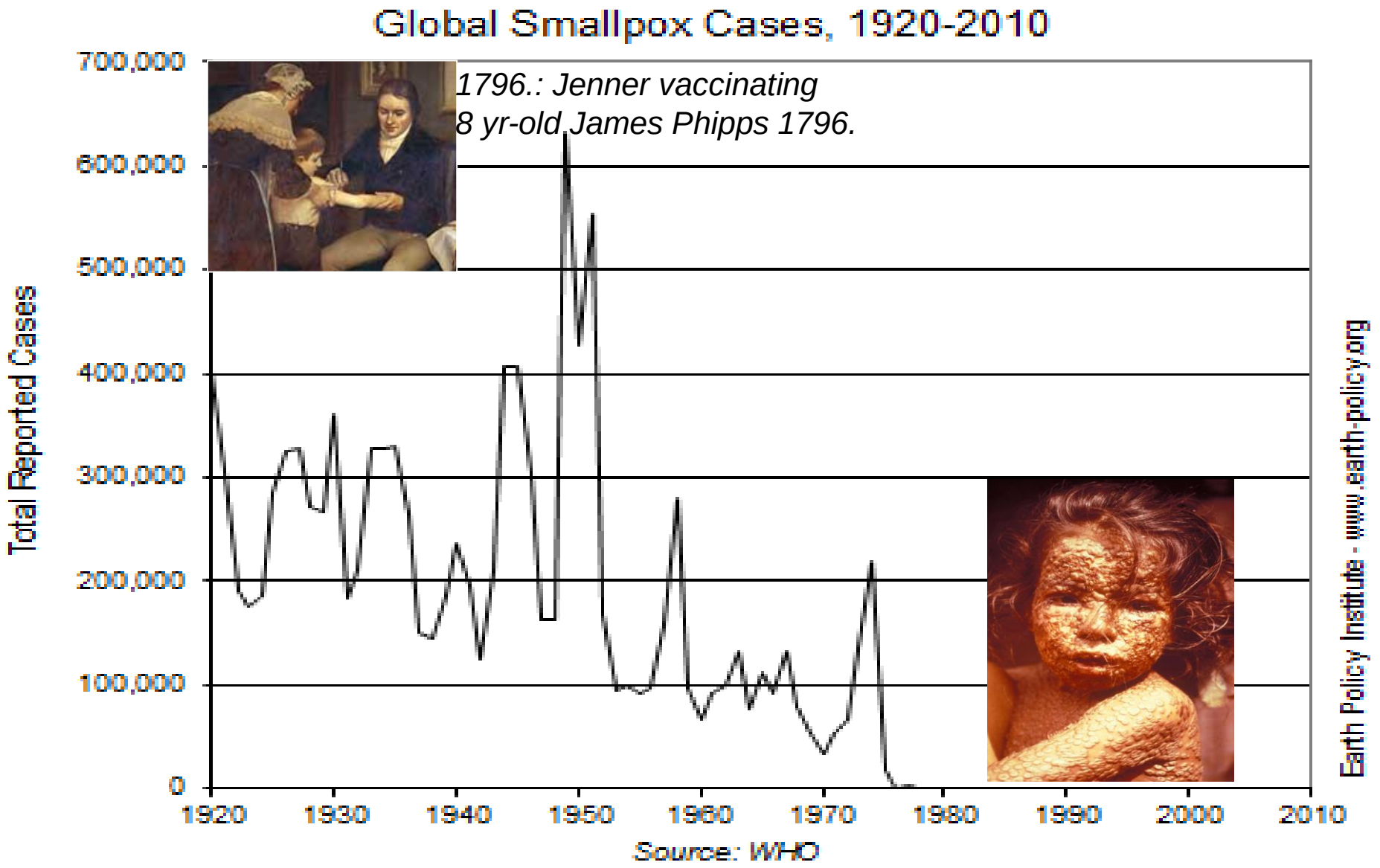
CSO Viroclinics-Biosciences BV (NL)

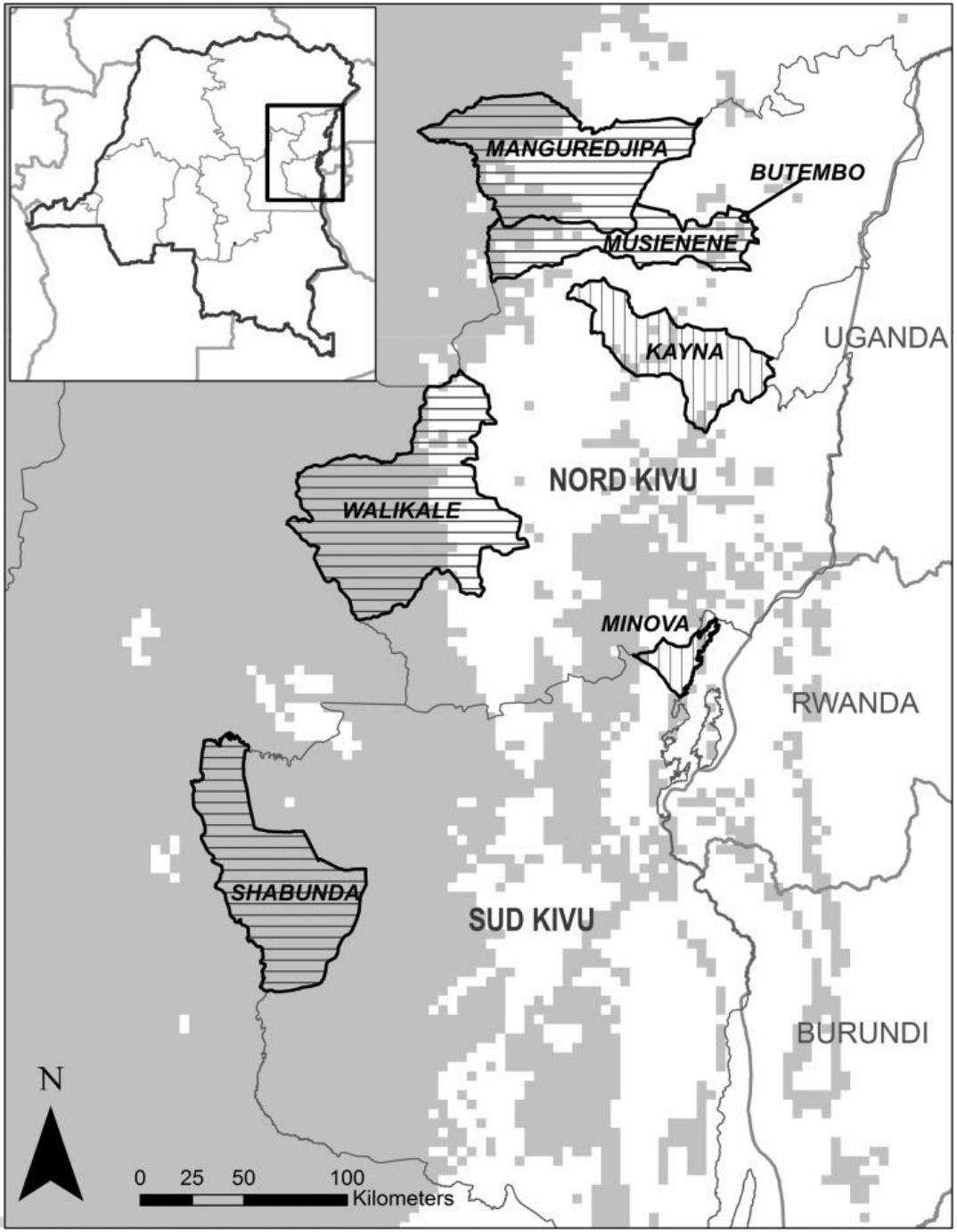
Chair One Health Platform

Chair ESWI

Les Pensieres December 5th 2017

Vaccines Success Stories: Smallpox





Human Monkeypox in the Kivus, a Conflict Region of the Democratic Republic of the Congo.
McCollum AM., *et al., AM J Trop Med Hyg*. *2015 Oct;93(4):718-21.*

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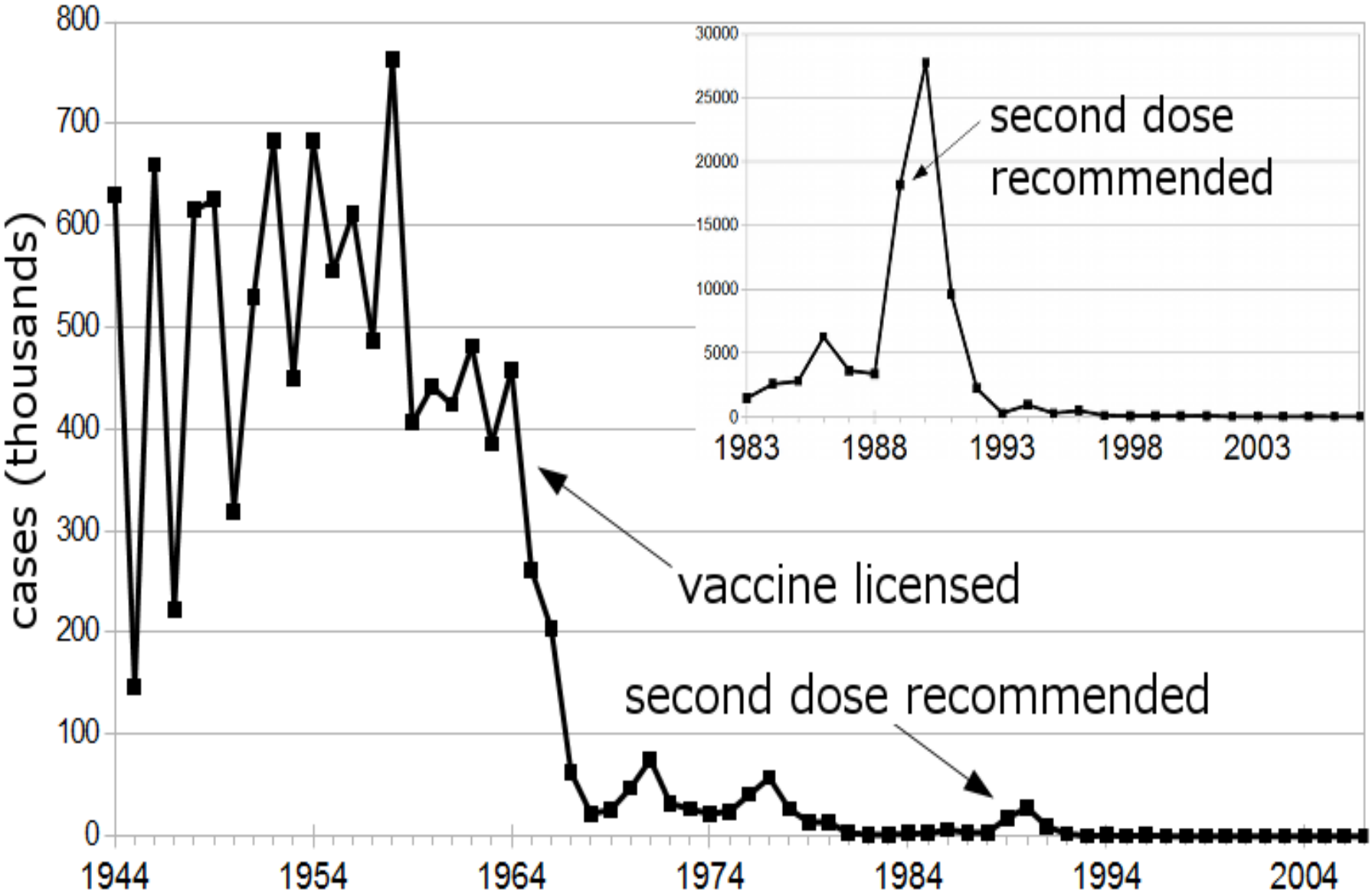
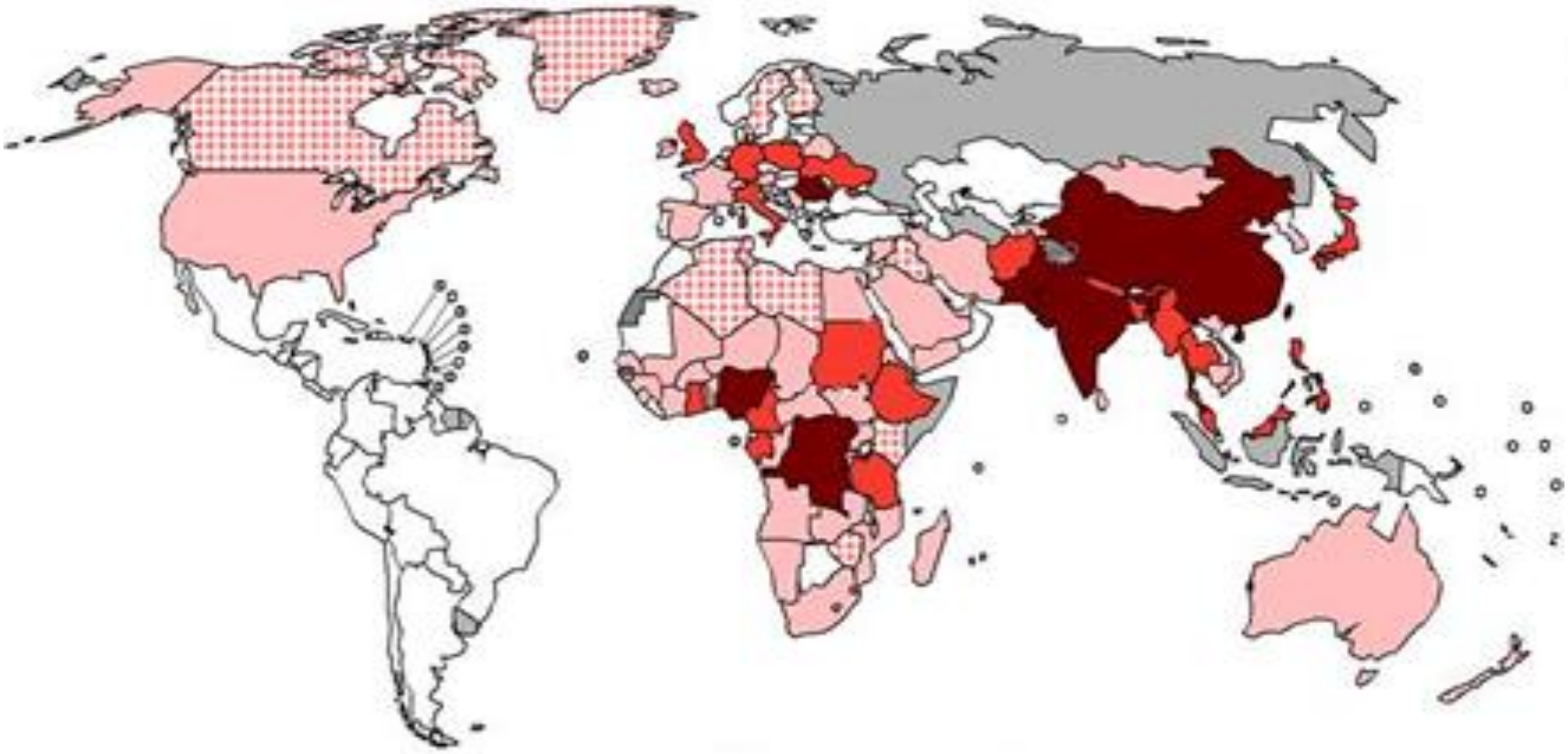
Measles cases in the United States, 1944-2007



Source: ://www.infectionlandscapes.org/

Figure 1. Measles cases reported worldwide in the 6-month period from August 2016 to January 2017

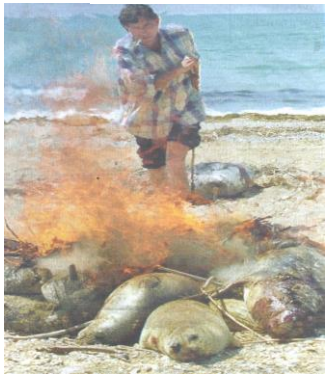


Source: WHO

Morbilliviruses crossing species barriers
A pandemic risk after measles eradication?

PDV in European Harbour seals
Nature 1988 / Science 2002

CDV in Baikal seals
Nature 1988

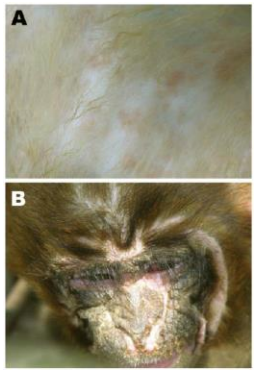


CDV in Caspian seals
EID 2000

DMV
Fin Whale Denmark 2016
(submitted)

DMV
Med. monk seals
Nature 1997

CDV in Serengeti lions
Vaccine 1994



CDV in macaques
China, EID 2011

Should we continue measles vaccination for ever?

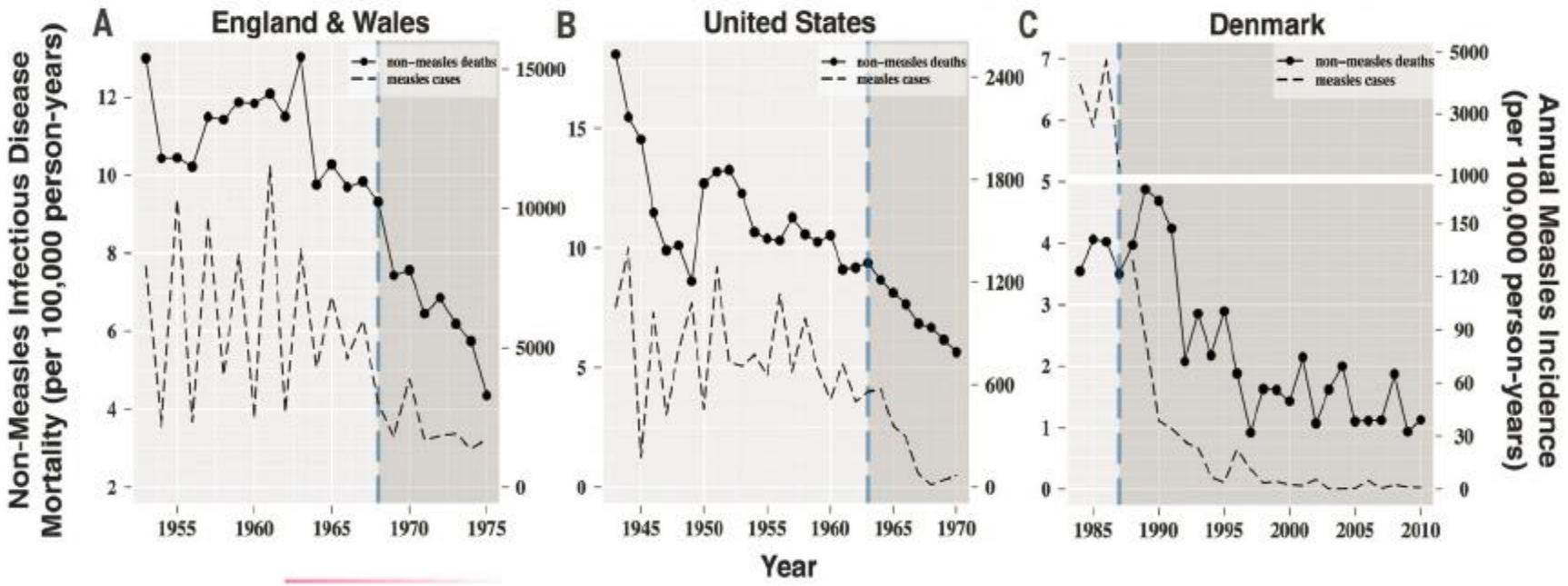
REPORT

SCIENCE sciencemag.org

VACCINES

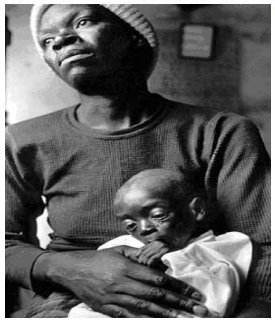
Long-term measles-induced immunomodulation increases overall childhood infectious disease mortality

Michael J. Mina,[1,2]* C. Jessica E. Metcalf,[1,3] Rik L. de Swart,[4] A. D. M. E. Osterhaus,[4] Bryan T. Grenfell[1,3]



Measles immune suppression; lessons from the macque model.
de Vries RD, et al., PLoS Pathog. 2012

CD45RA(-) memory T-lymphocytes and follicular B-lymphocytes killed



STIFTUNG TIERÄRZTLICHE HOCHSCHULE HANNOVER
17 78

HIV/AIDS
Ebola-Reston
Hanta HPS
Hendra
H5N1
Nipah
West Nile
SARS
Monkeypox
H1N1 pd
H3N2v
MERS
H7N9
Ebola
ZIKA

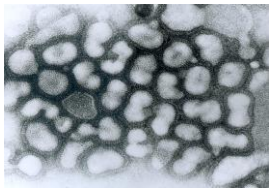
1980
1990
2000
2010

Lyme
E. Coli O157:H7
BSE
vCJD
EHEC O104:H4

Reperant LA, Cornaglia G, Osterhaus AD Curr Top Microbiol Immunol.2013

The importance of understanding the human-animal interface: from early hominins to global citizens

Human influenza:



three appearances

Seasonal influenza

(A: H3N2, H1N1; B)

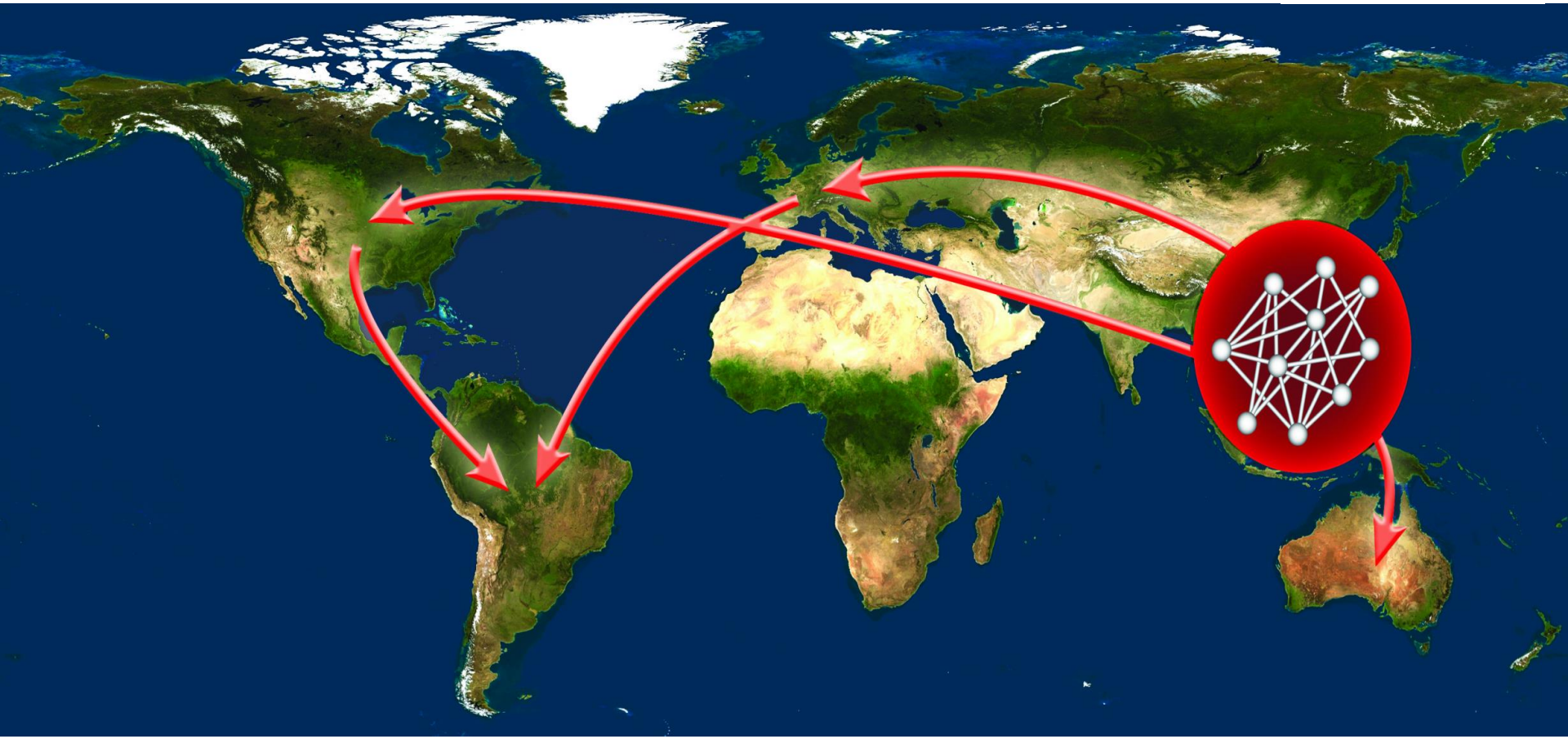
Avian influenza A:

H5, H6, H7, H9, H10…

Pandemic influenza

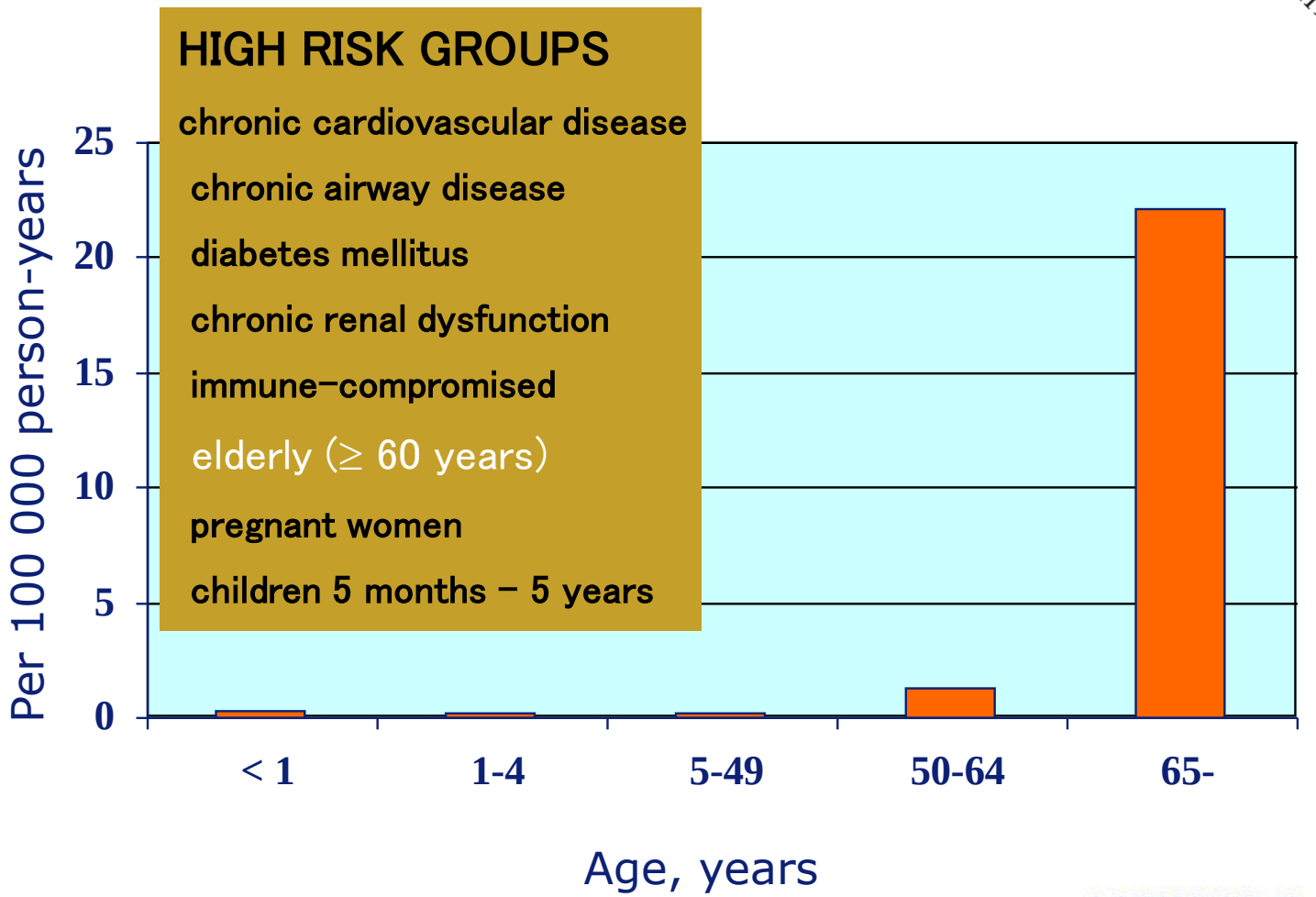
(A: H1N1, H2N2, H3N2, H1N1…?)

Global Circulation of Seasonal Influenza A (H3N2) Viruses



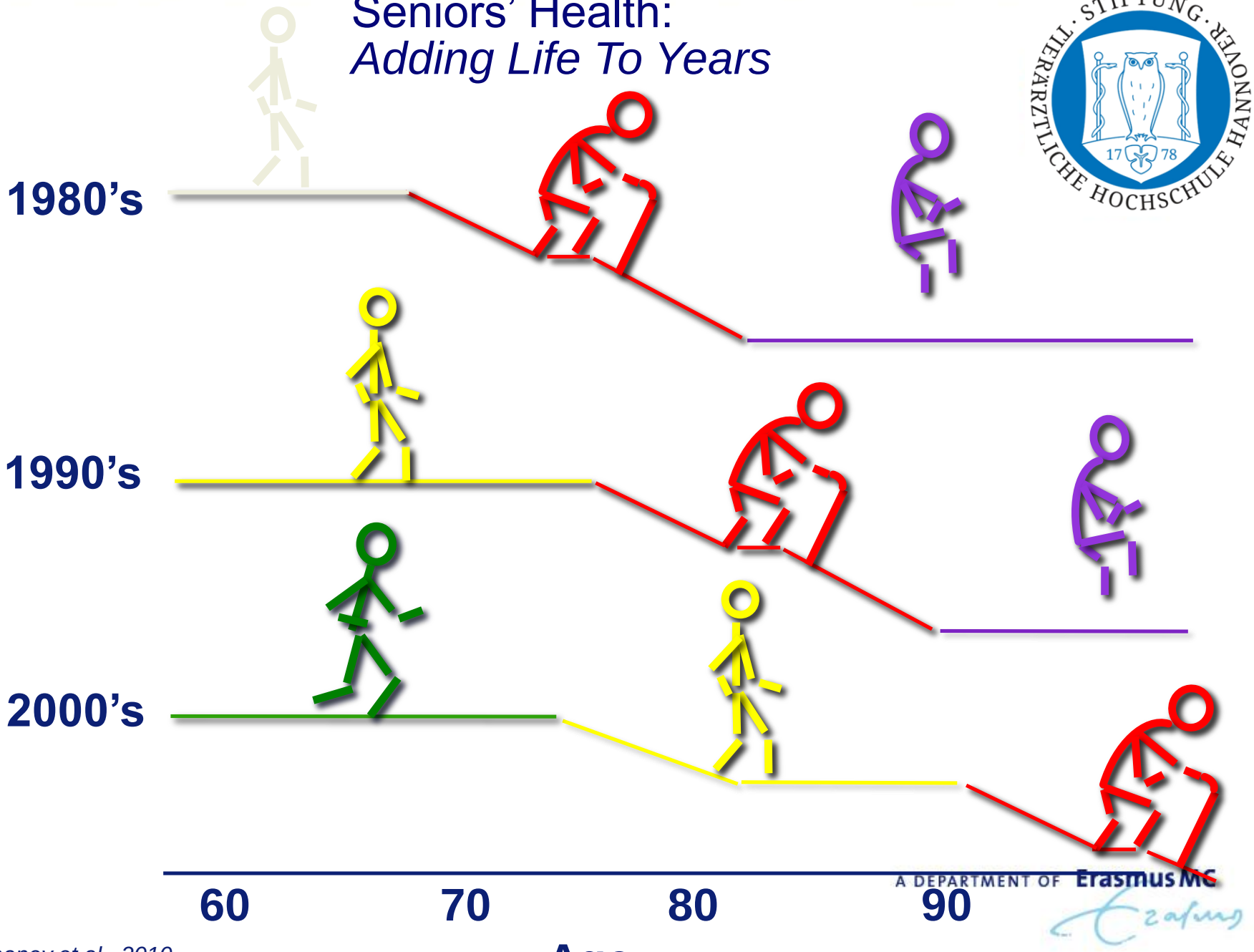
Asia is the epicenter for both influenza A/H1N1 and /H3N2 subtypes.
Russel et al. Science, 2008
But not for influenza B viruses. ***van der Vries et al., submitted***

Annual influenza-associated mortality rates



Thompson et al., JAMA 2003

Seniors' Health:
Adding Life To Years



McElhaney et al., 2010

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Association Between Influenza Vaccination and Reduced Risk of Brain Infarction

Philippa Lavallée, MD; Véronique Perchaud, MD; Marion Gautier-Bertrand; David Grabli, MD; Pierre Amarenco, MD

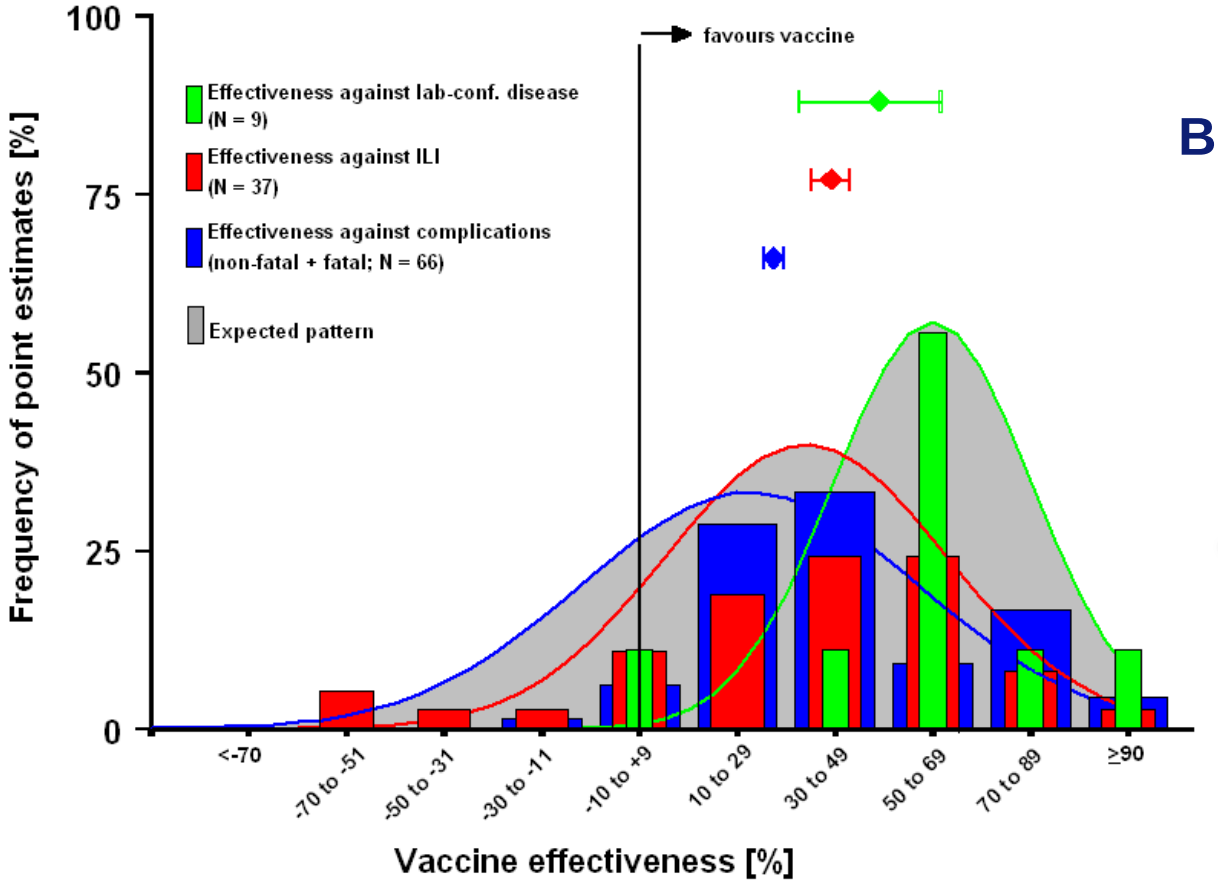
TABLE 2. Influence of Influenza Vaccination on Brain Infarction

				Cases and Matched Controls Free of Cardiovascular and Cerebrovascular History	
	Vaccinated, % (n)	OR (95% CI)*	OR (95% CI)†	% (n)	OR (95% CI)†
Vaccinated during last vaccination season					
Controls	59.4 (107/180), P=0.047	0.55 (0.32–0.96), P=0.036	0.45 (0.24–0.84), P=0.012 0.50 (0.26–0.94), P=0.033‡	58.5 (62/106)	0.37 (0.15–0.87), P=0.024
Cases	46.7 (42/90)			42.4 (25/59)	
Vaccinated in last 5 years					
Controls	56.1 (101/180), P=0.020	0.51 (0.30–0.89), P=0.017	0.37 (0.19–0.70), P=0.002 0.42 (0.21–0.81), P=0.009‡	54.7 (58/106)	0.32 (0.13–0.75), P=0.009
Cases	41.1 (37/90)			35.6 (21/59)	

OR indicates odds ratio.
*Adjusted for age and sex.
†Adjusted for age, sex, diabetes, hypertension, body mass index, current smoking, and cholesterol.
‡Adjusted for the same variables plus use of antibiotics in the last 3 months.

Stroke. 2002; 33:513-518

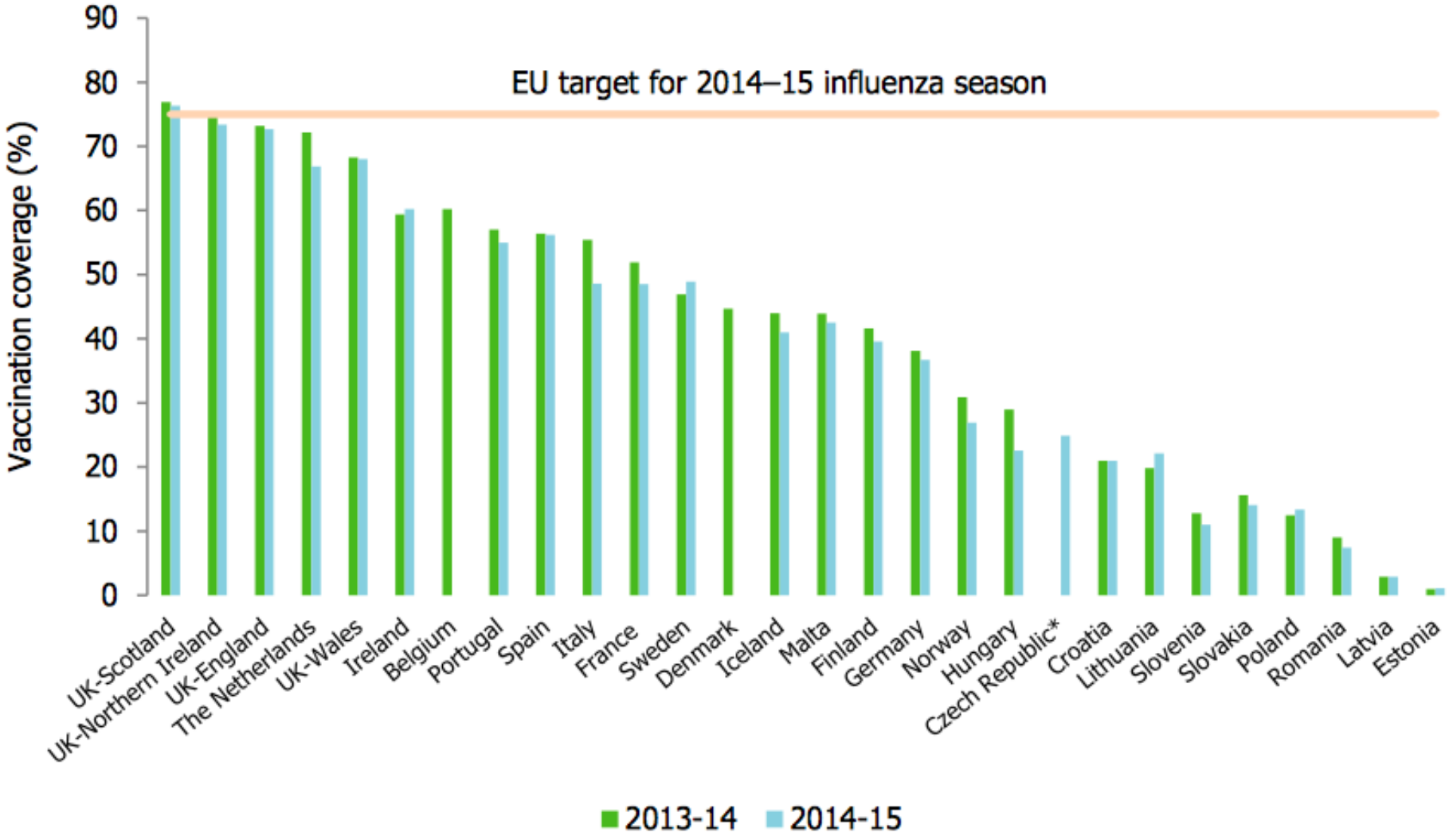
Distribution of VE point estimates according to alternative outcome definitions.



Beyer *et al.*, 2013 Vaccine:

'Cochrane revisited'

Figure 4. Seasonal influenza vaccination coverage rates in older age groups, 25 EU/EEA Member States, 2013–14 and 2014–15 influenza seasons



Source: National seasonal influenza vaccination survey, December 2015

SOURCE: ECDC

Vaccines don't protect, vaccination does!!!

Influenza Vaccination in the Prevention of Acute Otitis Media in Children

Terho Heikkinen, MD; Olli Ruuskanen, MD; Matti Waris, MSc; et al

» Author Affiliations

Am J Dis Child. 1991;145(4):445-448. doi:10.1001/archpedi.1991.02160040103017

Influenza A Vaccine Decreases the Incidence of Otitis Media in 6- to 30-Month-Old Children in Day Care

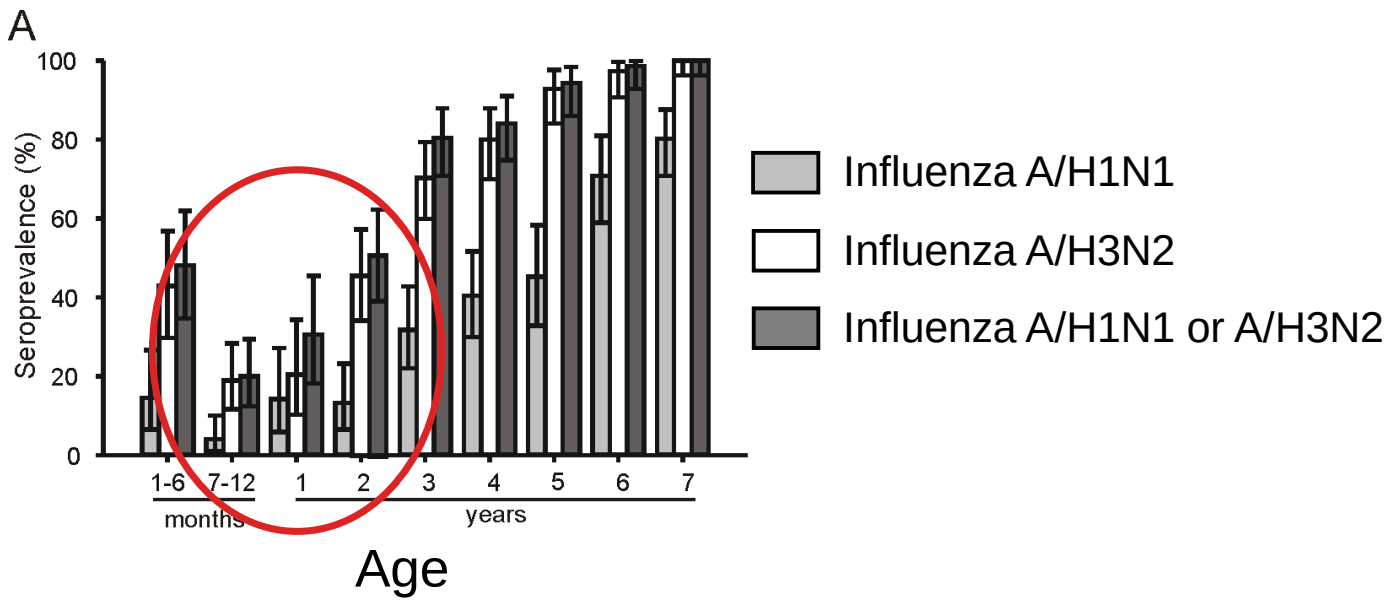
Dennis A. Clements, MD, PhD; Lori Langdon; Christina Bland, RN; et al

» Author Affiliations

Arch Pediatr Adolesc Med. 1995;149(10):1113-1117. doi:10.1001/archpedi.1995.02170230067009

Possible decrease of antibiotics usage

Seroprevalence of antibodies against seasonal influenza A and B viruses in children in the Netherlands

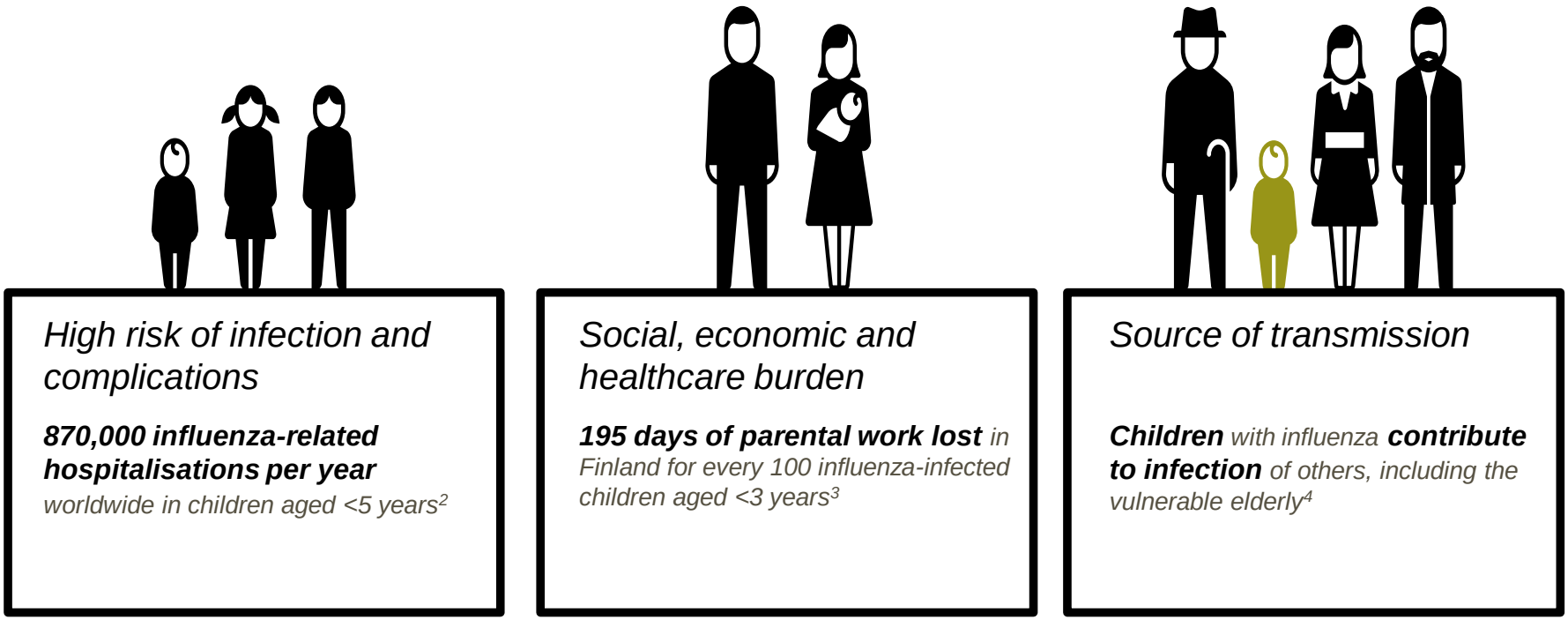


Proportion of children lack HSI

Bodewes et al., 2011, Clin. Vac. Immunol. 18(3):469-76

Influenza has a sizeable burden on children and their families

- Influenza occurs globally, with an annual attack rate estimated at **5–10% in adults and 20–30% in children**[1]
- Young children are at **high risk** of influenza infection and complications
- Young children **excrete more virus** and longer



High risk of infection and complications

870,000 influenza-related hospitalisations per year *worldwide in children aged <5 years*[2]

Social, economic and healthcare burden

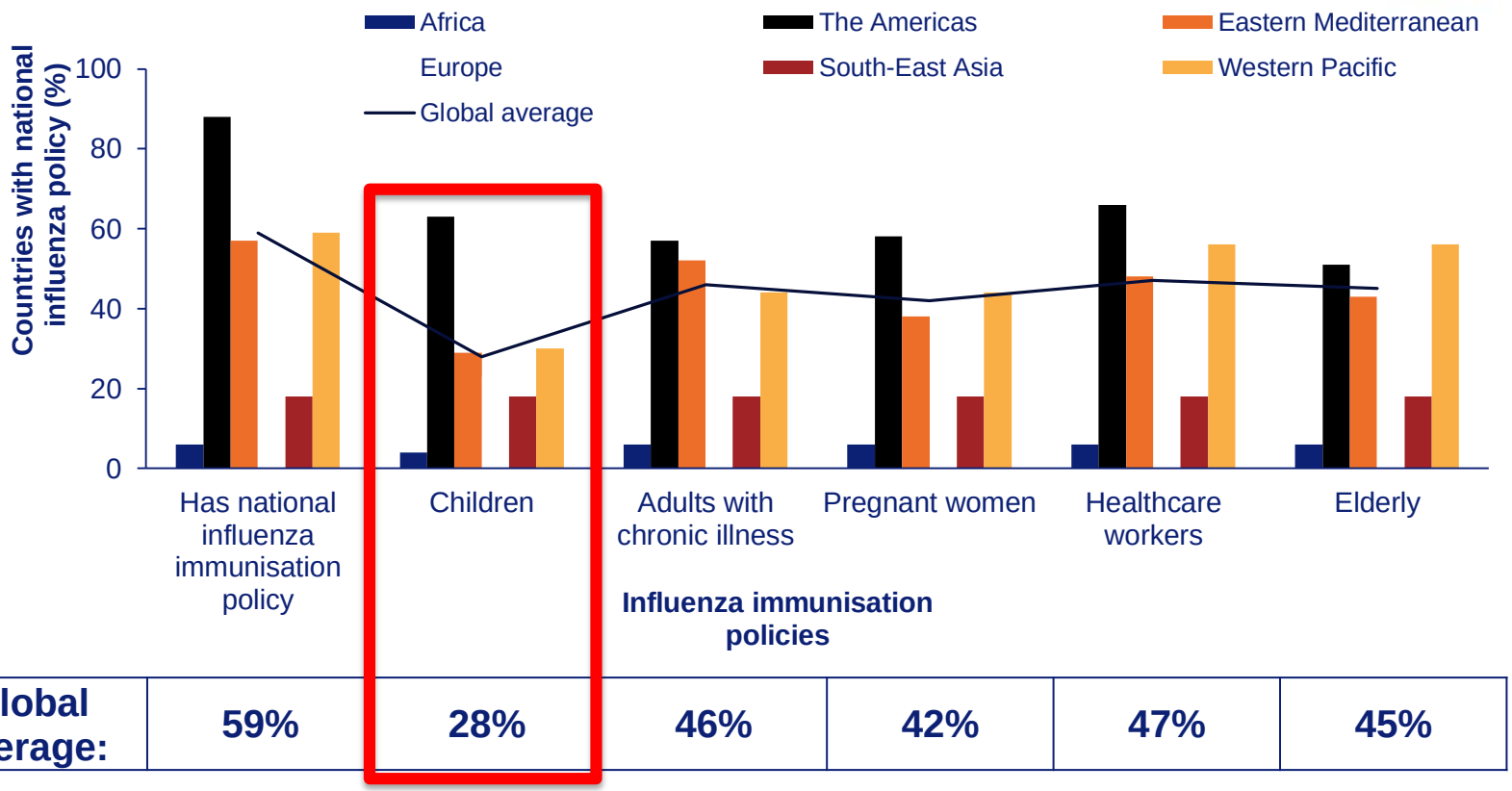
195 days of parental work lost *in Finland for every 100 influenza-infected children aged <3 years*[3]

Source of transmission

Children *with influenza* ***contribute to infection*** *of others, including the vulnerable elderly*[4]

1. World Health Organization (WHO). *Wkly Epidemiol Rec* 2012;87:461–76; 2. Lafond KE *et al*. *PLoS Med* 2016;13:e100197; 3. Heikkinen T *et al*. *J Infect Dis* 2004;90:1369–1373; 4. Heikkinen T *et al*. *Pediatr Infect Dis J* 2013;32:881–888

Globally, less than a third of countries have recommendations for national influenza childhood vaccination



Global average:	**59%**	**28%**	**46%**	**42%**	**47%**	**45%**

There is still room for improvement – only 28% of countries have a childhood recommendation

Ortiz JR *et al. Vaccine* 2016;34:5400–5405

Vaccine 35 (2017) 5242–5248

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Pneumococcal vaccination: Direct and herd effect on carriage of vaccine types and antibiotic resistance in Icelandic children

Samuel Sigurdsson [a], Helga Erlendsdóttir [a,b], Sigríður Júlía Quirk [a,b], Júlíus Kristjánsson [a], Kristján Hauksson [a], Birta Dögg Ingudóttir Andrésdóttir [a], Arnar Jan Jónsson [a], Kolbeinn Hans Halldórsson [a], Árni Sæmundsson [a], Óli Hilmar Ólason [a], Birgir Hrafnkelsson [c], Karl G. Kristinsson [a,b], Ásgeir Haraldsson [a,d,*]

European Journal of Clinical Microbiology & Infectious Diseases

November 2017, Volume 36, Issue 11, pp 2109–2116 | Cite as

Streptococcus pneumoniae antimicrobial resistance decreased in the Helsinki Metropolitan Area after routine 10-valent pneumococcal conjugate vaccination of infants in Finland

Authors Authors and affiliations

R. Sihvonen, L. Siira, M. Toropainen, P. Kuusela, A. Pätäri-Sampo

Ann Clin Microbiol Antimicrob. 2017; 16: 23. PMCID: PMC5381081

Published online 2017 Apr 4. doi: 10.1186/s12941-017-0200-6

Molecular characterization of penicillin non-susceptible *Streptococcus pneumoniae* isolated before and after pneumococcal conjugate vaccine implementation in Casablanca, Morocco

Idrissa Diawara,[1,2] Abouddihaj Barguigua,[3] Khalid Katfy,[1,2] Kaotar Nayme,[1,4] Houria Belabbes,[1,2] Mohammed Timinouni,[4] Khalid Zerouali,[1,2] and Naima Elmdaghri[1,2]

Exploratory objective, Total vaccinated cohort (TVC)

*Among children with confirmed **moderate-to-severe influenza**, compared with controls, D-QIV:*

Reduced use of antibiotics

Reduction **69%**

(0.8% vs 2.6% use)

Reduced risk of GP visits

RRR **65%**

RR: 0.35
(95% CI: 0.27–0.46)

Reduced risk of ER visits

RRR **80%**

RR: 0.20
(95% CI: 0.06–0.69)

CI, confidence interval; ER, emergency room; GP, general practitioner; RR, relative risk; RRR, relative risk reduction

CI, confidence interval; ER, emergency room; GP, general practitioner; RR, relative risk; RRR, relative risk reduction

Presented ESPID 2017 http://espid2017.kenes.com/scientific-information/interactive-programme#.WTbbX_IzUid
Study 115345. 2017. Available at: www.gsk-clinicalstudyregister.com/

Most recent pandemics

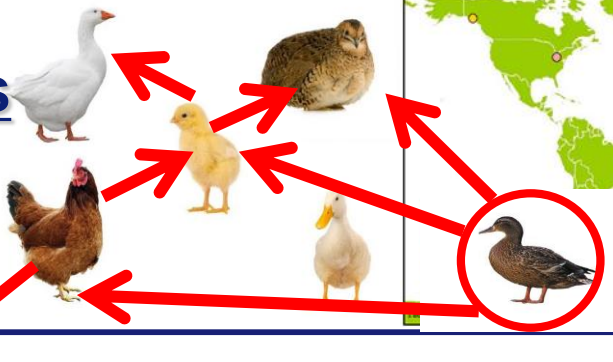
Year	*Subtype*	Name	Estimated deaths
1918	*H1N1*	Spanish Flu	$20\text{-}40 \times 10^6$
1957	*H2N2*	Asian Flu	1×10^6
1968	*H3N2*	Hong Kong Flu	7×10^5
2009	*H1N1*	Mexican Flu	$2 \times 10^4 – 3 \times 10^5$

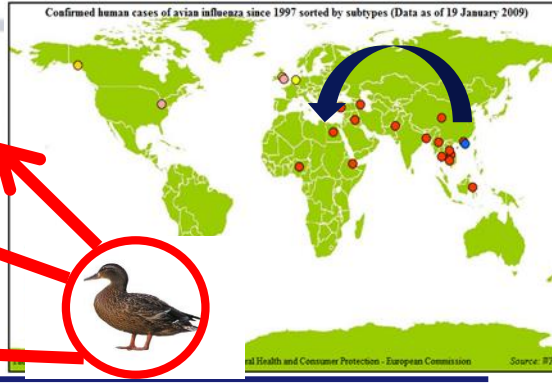
Spanish Flu 1918


How to avoid Influenza
Gargle Daily

Avian Influenza: Asia

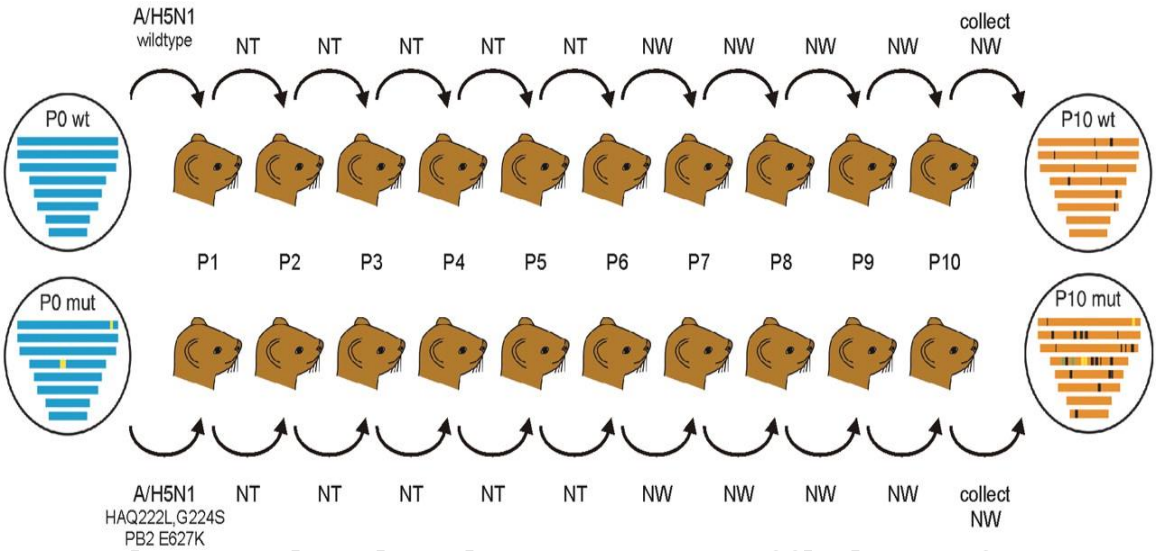
Recent zoonotic transmissions from birds -confirmed human cases-

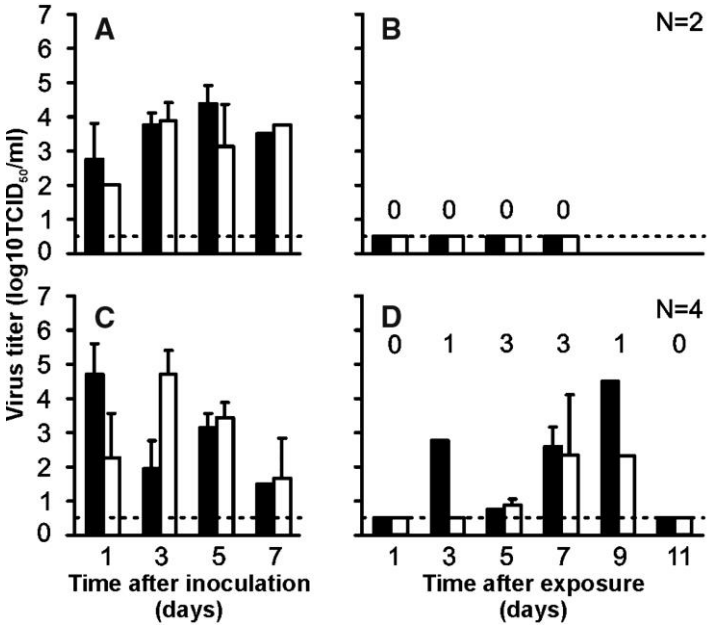




Subtype	Country	Year	# Cases	# Deaths
H7N7	UK	1996	1	0
H5N1	Hong Kong	1997	18	6
H9N2	SE-Asia	1999	>2	0
H5N1	Hong Kong	2003	2?	1
H7N7	Netherlands	2003	89	1
H7N2	USA	2003	1	0
H7N3	Canada	2004	2	0
H5N1	SE-Asia/M-East/ Europe/W-Africa	2003-17*	>850 *CFR ~ 55%	>450 (increasing)
H7N9	PR China	2013	>1500	>600
H9, H10, H6..	Asia…	ongoing	<5	<5

HPAI H5N1 virus passaging in ferrets
- toward transmissibility -





Five substitutions are sufficient for airborne transmission between ferrets

Munster et al., Science 2009
Herfst et al., Science 2012
Russel et al., Science 2012
Linster et al., Cell 2014

Published by AAAS

Heterosubtypic immunity
- animal models -

JOURNAL OF BACTERIOLOGY, Jan., 1965
Copyright © 1965 American Society for Microbiology
Vol. 89, No. 1
Printed in U.S.A.

Induction of Partial Specific Heterotypic Immunity in Mice by a Single Infection with Influenza A Virus

JEROME L. SCHULMAN AND EDWIN D. KILBOURNE

Journal of General Virology (2000), **81**, 2689–2696. Printed in Great Britain

Heterologous protection against lethal A/HongKong/156/97 (H5N1) influenza virus infection in C57BL/6 mice

Eduardo O'Neill,[1] Scott L. Krauss,[1] Janice M. Riberdy,[2] Robert G. Webster[1] and David L. Woodland[2]†

INFECTION AND IMMUNITY, Aug. 1980, p. 650–653
0019-9567/80/08-0650/04$02.00/0

Heterotypic Immunity to Influenza in Ferrets

ROBERT A. YETTER, W. HENRY BARBER, AND PARKER A. SMALL, JR.*

Journal of General Virology (2001), **82**, 2697–2707. Printed in Great Britain

Respiratory and systemic humoral and cellular immune responses of pigs to a heterosubtypic influenza A virus infection

Paul P. Heinen, Els A. de Boer-Luijtze and Andre T. J. Bianchi

The Journal of Immunology, 1997, 158: 1222–1230.

Mechanisms of Heterosubtypic Immunity to Lethal Influenza A Virus Infection in Fully Immunocompetent, T Cell-Depleted, β_2-Microglobulin-Deficient, and J Chain-Deficient Mice

Suzanne L. Epstein,[1]* Chia-Yun Lo,* Julia A. Misplon,* Cassandra M. Lawson,[2]†
Barbara A. Hendrickson,‡ Edward E. Max,§ and Kanta Subbarao[3]†

Available online at www.sciencedirect.com
ScienceDirect
Vaccine 25 (2007) 612–620
Vaccine
www.elsevier.com/locate/vaccine

Primary influenza A virus infection induces cross-protective immunity against a lethal infection with a heterosubtypic virus strain in mice

J.H.C.M. Kreijtz, R. Bodewes, G. van Amerongen, T. Kuiken, R.A.M. Fouchier, A.D.M.E. Osterhaus, G.F. Rimmelzwaan*

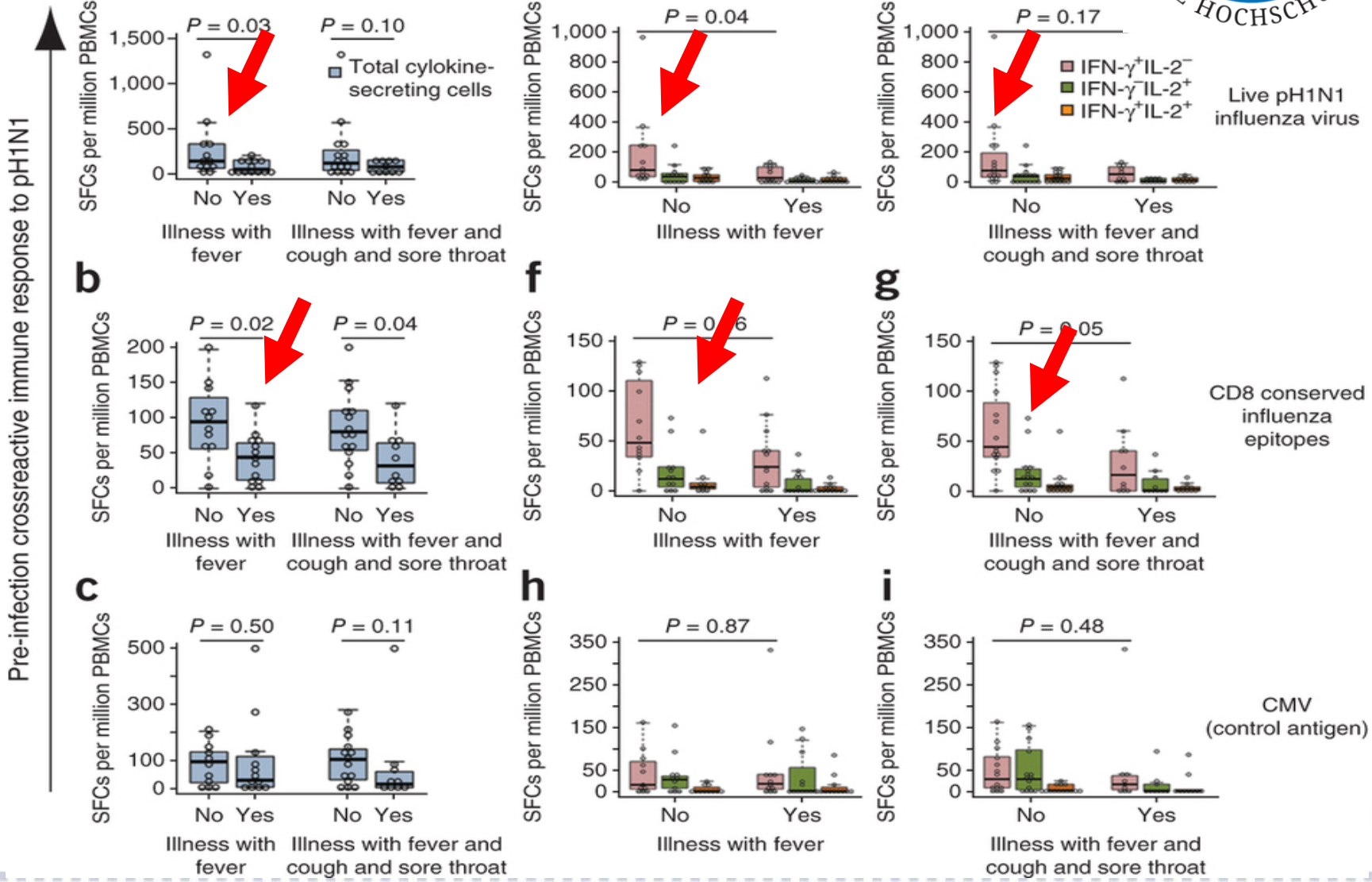
JOURNAL OF VIROLOGY, Mar. 2001, p. 2516–2525
0022-538X/01/$04.00+0 DOI: 10.1128/JVI.75.6.2516–2525.2001
Vol. 75, No. 6

Cross-Reactive, Cell-Mediated Immunity and Protection of Chickens from Lethal H5N1 Influenza Virus Infection in Hong Kong Poultry Markets

SANG HEUI SEO AND ROBERT G. WEBSTER*

The frequencies of pre-existing cross-reactive T cells are inversely associated with illness severity in infected individuals.

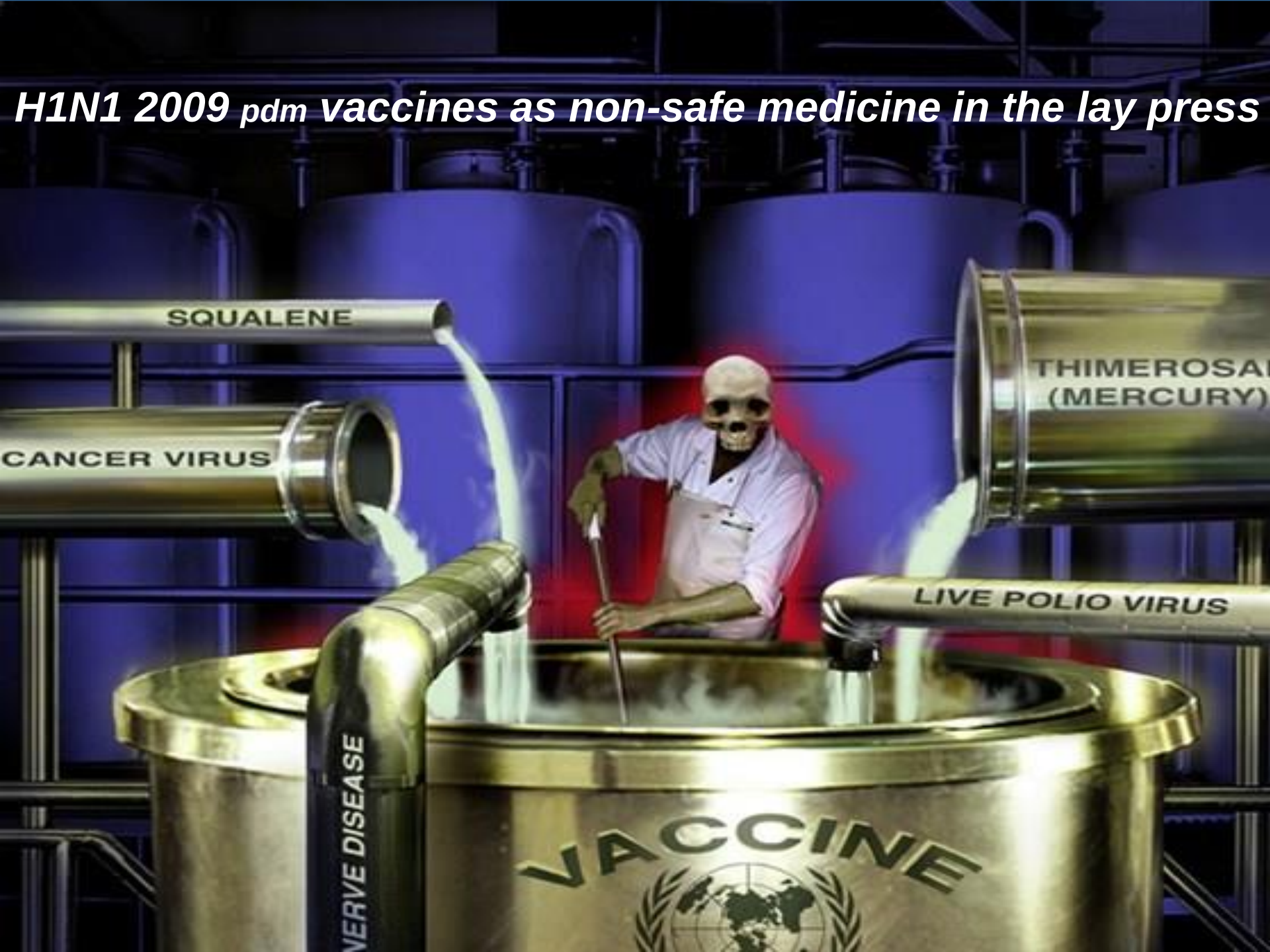
- Sridhar et al., *Nature Med 2013 19:1305–1312* -



PREVENTION AT THE SOURCE?

MERS VACCINATION ***(HAAGMANS ET AL., SCIENCE 2016)***

H1N1 2009 pdm vaccines as non-safe medicine in the lay press




Edward Jenner
“father of vaccination”

CONCLUSIONS

Vaccination benefits beyond vaccinees:

Prevention of:

- **Immune suppression** (measles)
  - *Protection from virus spreading allowing eradication*
  - *Protection from previously conquered infectious disease (spreading)*
- **Spreading into vulnerable** / at-risk
  - *E.g. inluenza in the elderly*
- **AMR development**
  - *Directly and indirectly (e.g. influenza) by reducing antimicrobial usage*
  - *Veterinary vaccines (cattle, pigs, camels, chickens…)*
- **Infection with related pathogens?**
  - *Hetero-subtypic / avian / pandemic influenza*
  - *E.g. pox- and morbilliviruses*

One Health Platform activities

- Programme reflects One Health Agenda:
- Theme: One Health in underprivileged communities
- Co-organizer: University of Saskatchewan
- One Health Fellowship Fund
- www.onehealthcongress.com