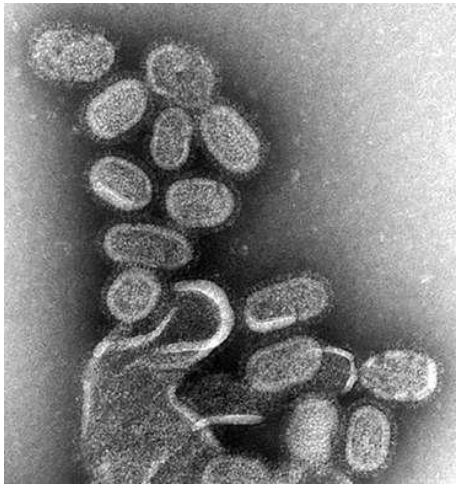
Der Dominoeffekt der Influenzaimpfung

Eine neue Bewertung der Nutzen/Risiko Abwägung

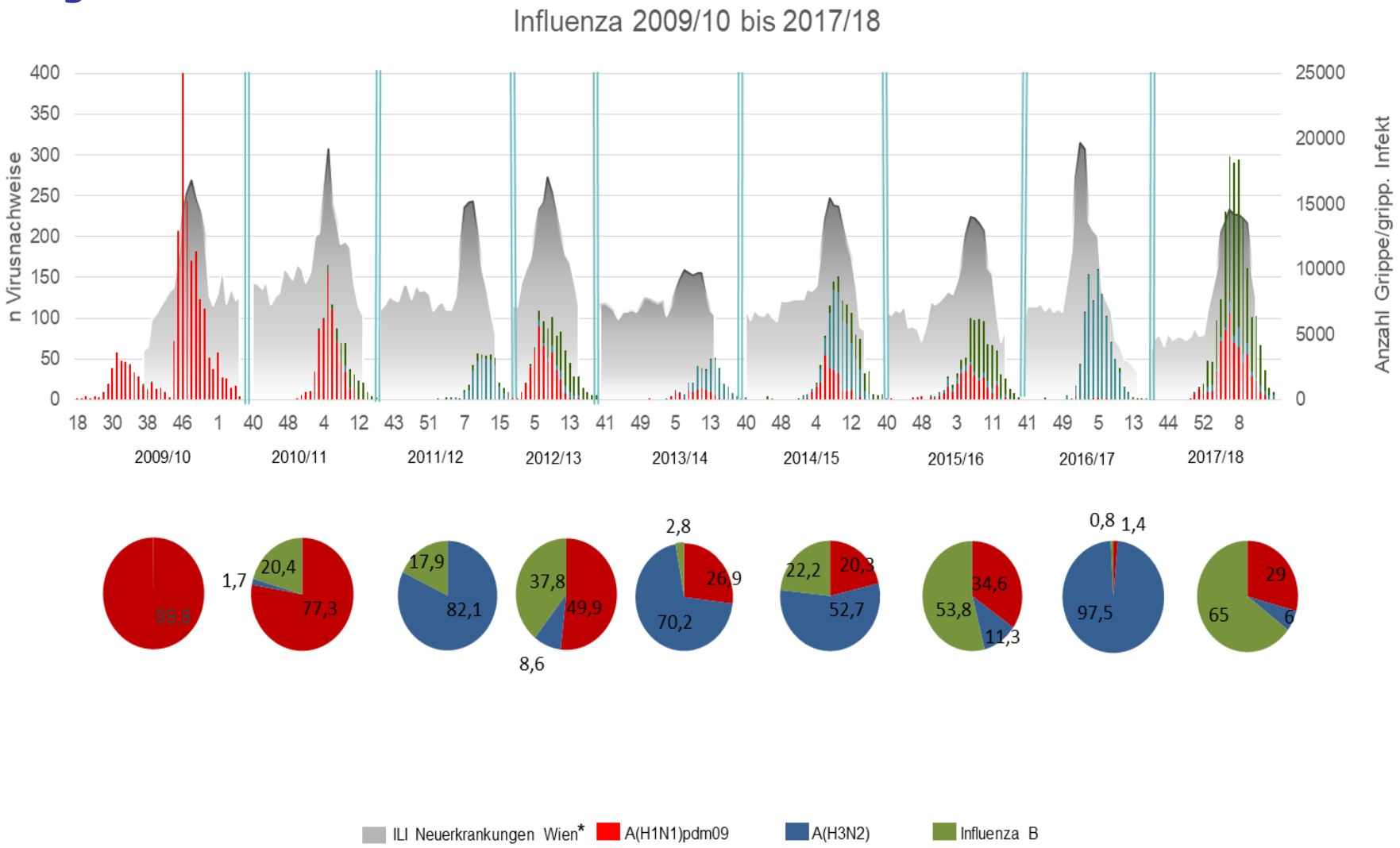
Dr. Christoph Wenisch,
Kaiser Franz Josef Hospital, Vienna

Agenda



- Epidemiologie Österreich
- Influenza Klinik
- Effekte der Influenza-Impfung
- Empfehlungen

Influenzawellen 2009/10 bis 2017/18 im Vergleich



* Daten MA 15

Mit freundlicher Genehmigung von Fr. Dr. Redlberger-Fritz

Klinische Symptomatik

- plötzlicher Krankheitsbeginn, Fieber, Husten oder Halsschmerzen sowie Muskel- und/oder Kopfschmerzen
- weiters allgemeine Schwäche, Schweißausbrüche, Rhinorrhö, auch Übelkeit/Erbrechen und Durchfall

Nicht alle Influenza-Infizierten erkranken:

- 1/3 fieberhaften Verlauf,
- 1/3 leichterer, unspez. Verlauf
- 1/3 asymptomatischen Verlauf.
- Die Krankheitsdauer : 5 bis 7 Tage, bei Komplikationen und Risikofaktoren (Immunsuppression etc.) jedoch auch deutlich länger

Seltener schwere Verläufe, v.a. pulmonale Komplikationen :

- primäre Influenzapneumonie durch das Virus selbst
- bakterielle Pneumonie nach Superinfektion (u.a. durch Pneumokokken, Staphylokokken, *Haemophilus influenzae*)
- die Beteiligung weiterer Organe kann zu Myositis und Rhabdomyolyse, Enzephalitis oder Myokarditis führen
- Typisch ist auch die Verschlechterung bereits bestehender Grundkrankheiten (Bsp. Herzinsuffizienz bzw. COPD Exazerbation)

Influenza Klinik

- **Aufnahme im Krankenhaus**
  - **Bei Kardiovaskulär/Stroke, COPD, Asthma**
- **Hausärztin/Hausarzt**
- **Kein ÄrztInnenkontakt**
- Asymptomatische Infektion
- Nicht infiziert

Kein Schulbesuch,
Krankenstand,
Lebensqualität,
Kosten Gesundheit

Influenza im Krankenhaus

- Studie 2017/2018
- KFJ Spital, Grippestation nach PCR-POCT in der Notfallaufnahme
- Ergebnis: Influenza-Plus

DOI:10.1111/irv.12398
www.influenzajournal.com

Systematic Review

The frequency of influenza and bacterial coinfection: a systematic review and meta-analysis

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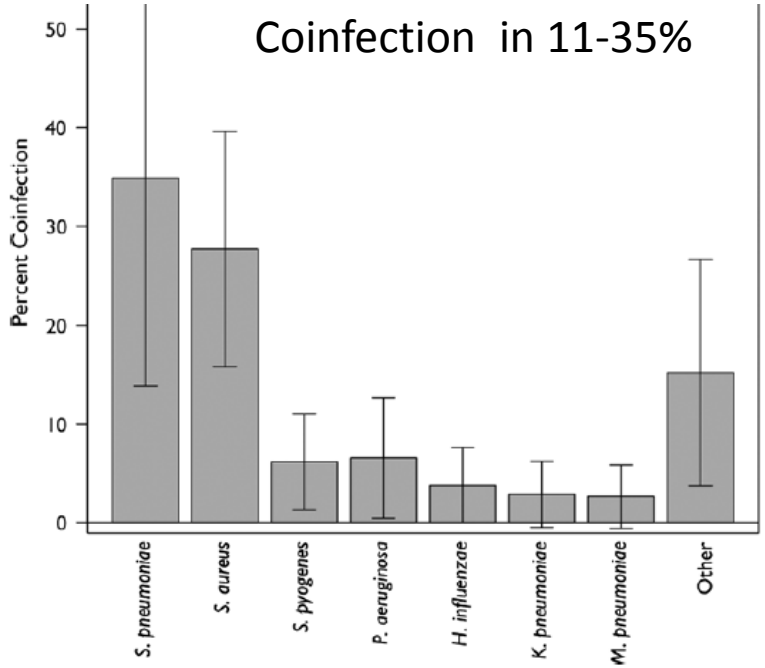
Accepted 14 May 2016.

Coinfection in 11-35%



THE LANCET
Respiratory Medicine

Log in R

ARTICLES | VOLUME 6, ISSUE 10, P782-792, OCTOBER 01, 2018

Purchase Su

Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study

Alexander F A D Schauwvlieghe, MD † • Bart J A Rijnders, PhD † • Nele Philips, MSc • Rosanne Verwijs, MSc • Lore Vanderbeke, MD • Carla Van Tienen, PhD • Prof Katrien Lagrou • Prof Paul E Verweij, PhD • Frank L Van de Veerdonk, PhD • Prof Diederik Gommers, PhD • Peter Spronk, PhD • Dennis C J J Bergmans, PhD • Astrid Hoedemaekers, PhD • Eleni-Rosalina Andrinopoulou, PhD • Charlotte H S B van den Berg, PhD • Prof Nicole P Juffermans, PhD • Casper J Hodiamont, PhD • Alieke G Vonk, PhD • Prof Pieter Depuydt, PhD • Prof Jerina Boelens, PhD • Prof Joost Wauters, PhD on behalf of the Dutch-Belgian Mycosis study group • Show less

Show footnotes

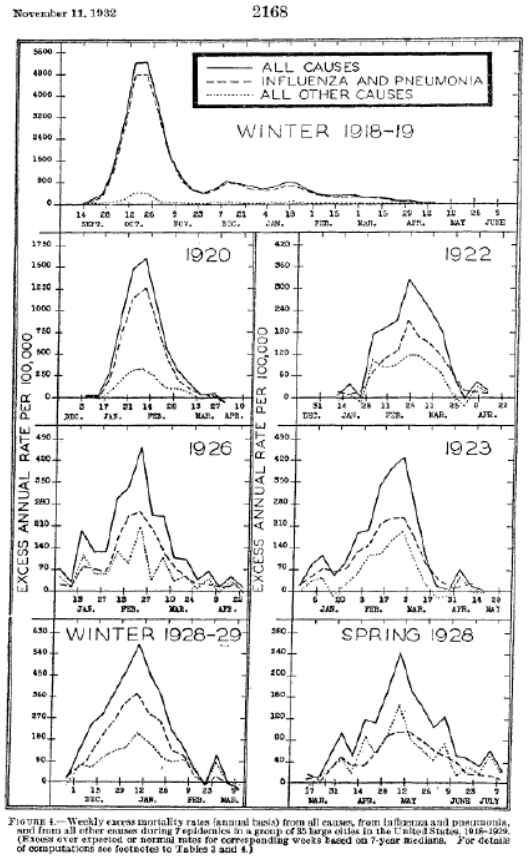
Published: July 31, 2018 • DOI: https://doi.org/10.1016/S2213-2600(18)30274-1 • Check for updates

- 83 **(19%) of 432 patients**

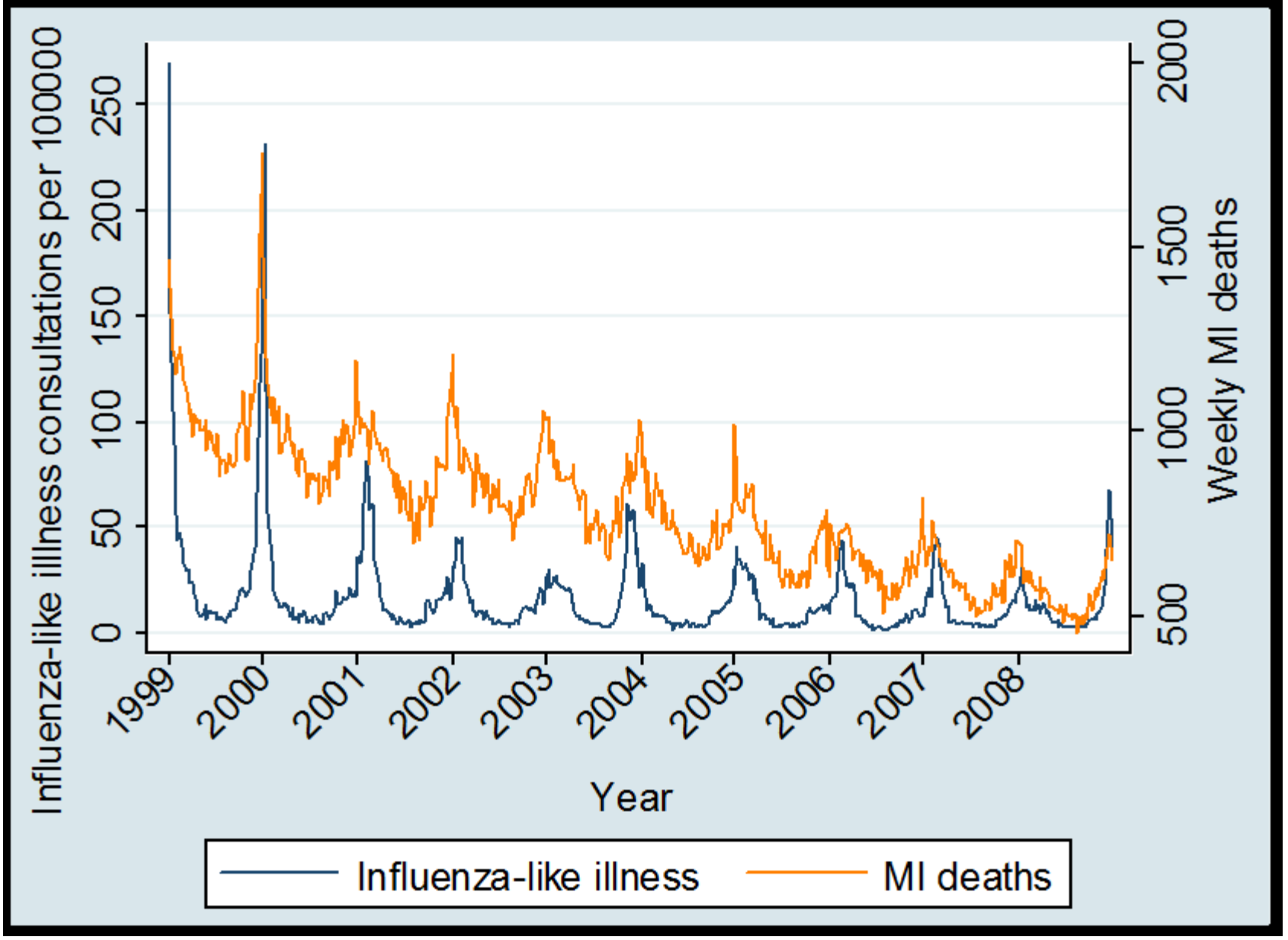
Interpretation
Influenza was identified as an independent risk factor for invasive pulmonary aspergillosis and is associated with high mortality.

Early ecological studies measured deaths due to CVD during influenza epidemics

- Population level studies have been used for decades to investigate cause-specific mortality during influenza epidemics.
- "Organic heart disease" accounted for a 14.7% excess in expected mortality during the influenza epidemic of 1918-19 and 1920 compared to other time periods.

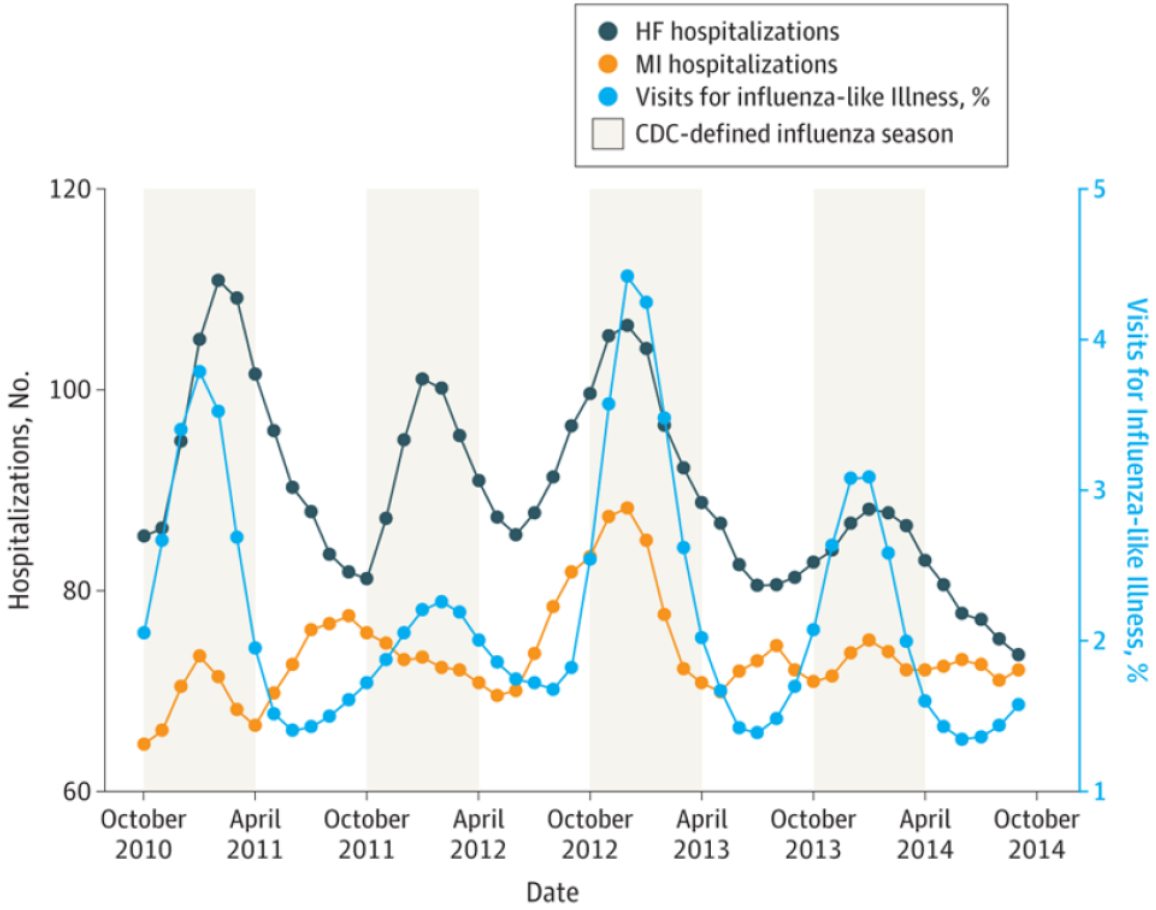


Collins et al. *Public Health Rep*. 1932; 47: 2159-79



Warren-Gash et al. *J Infect Dis* 2011; 203 (12): 1710-8.

CVD hospitalisations, especially due to heart failure, are associated with monthly ILI activity



Kytomaa S et al. *JAMA Cardiol.*
Published online March 27 2019

Kardiovaskuläre Erkrankungen

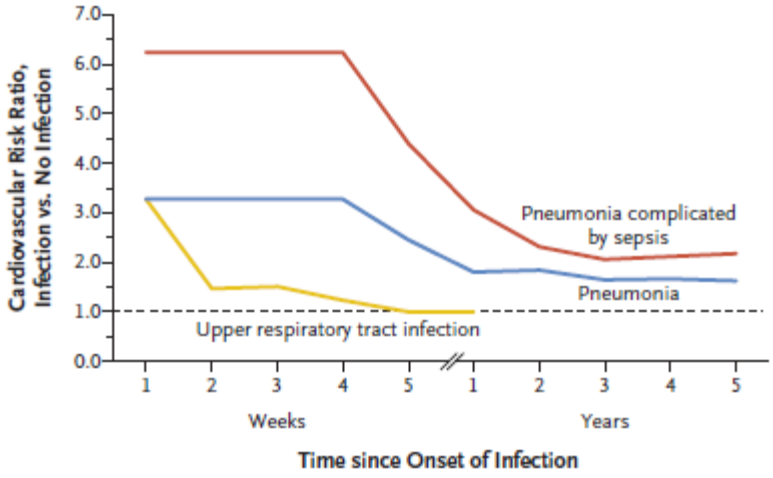


Figure 1. Temporal Pattern of Cardiovascular Risk after the Onset of Acute Infection.

The risk of a cardiovascular event is several times higher after the onset of respiratory infection than in the absence of infection. The risk of a cardiovascular event is proportional to the severity of the infection. The risk returns to baseline over a period of weeks after an upper respiratory tract infection. However, the time required for the risk to return to baseline is prolonged after a severe infection, such as pneumonia. Data are pooled from Smeeth et al.,[2] Kwong et al.,[5] Corrales-Medina et al.,[12] Warren-Gash et al.,[14] and Warren-Gash et al.[15]

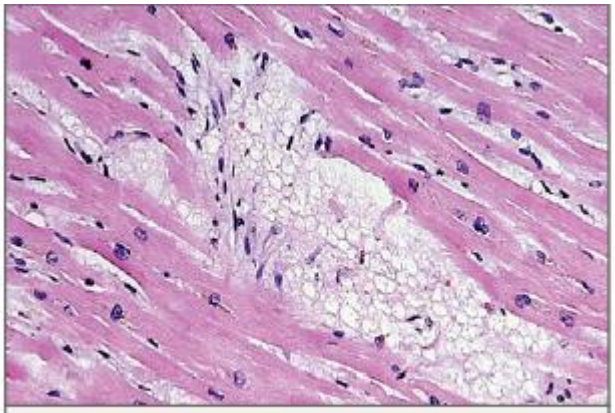
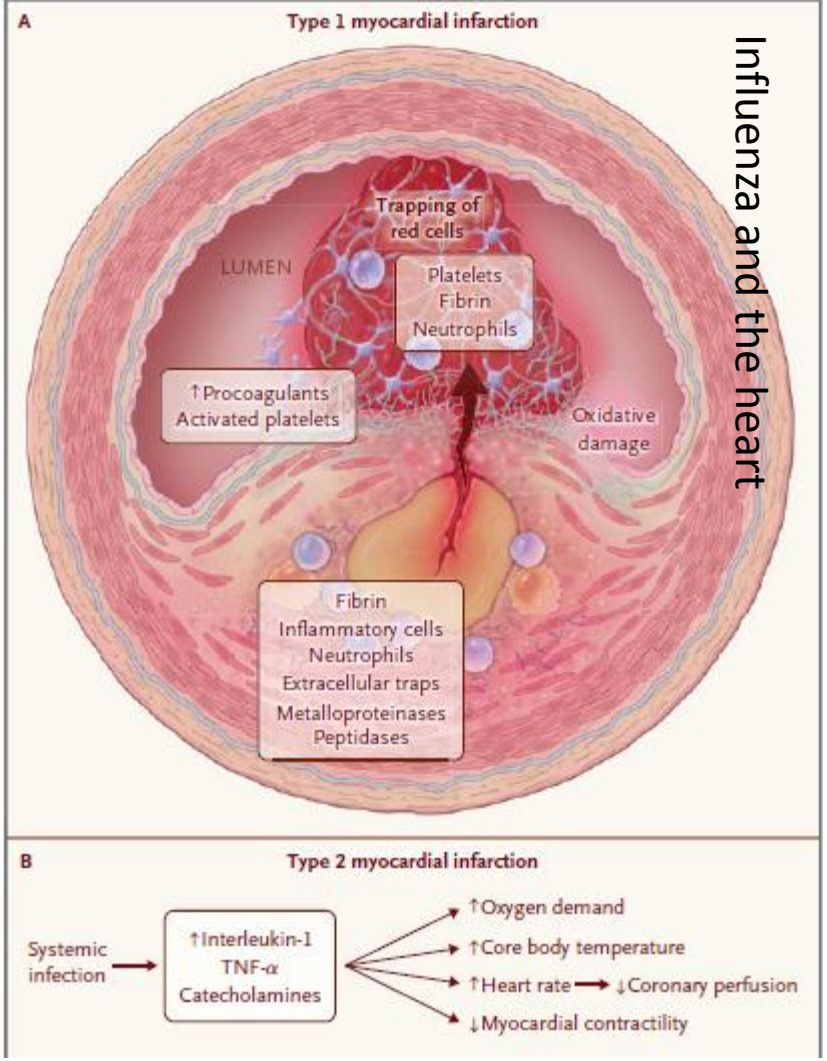


Figure 4. Features Present after Cardiac Involvement in Acute Infection.



Influenza and the heart

- Influenza = 6x increased risk for myocardial infarction

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection

Jeffrey C. Kwong, M.D., Kevin L. Schwartz, M.D., Michael A. Campitelli, M.P.H.,

N Engl J Med 2018

Retrospektive Analyse von 364 Patienten mit MCI innerhalb eines Jahres vor oder nach einer bestätigten Influenzainfektion

Table 2. Incidence Ratios for Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection.*

Variable	Incidence Ratio (95% CI)
Primary analysis: risk interval, days 1–7	6.05 (3.86–9.50)
Days 1–3	6.30 (3.25–12.22)
Days 4–7	5.78 (3.17–10.53)
Days 8–14	0.60 (0.15–2.41)
Days 15–28	0.75 (0.31–1.81)

Acute respiratory infections and MI/ stroke

Time period after infection (days)	Age-adjusted incidence ratio (95% C.I.) for MI	Age-adjusted incidence ratio (95% C.I.) for stroke
1-3	4.95 (4.43-5.53)	3.19 (2.81-3.62)
4-7	3.20 (2.84-3.60)	2.23 (2.05-2.66)
8-14	2.81 (2.54-3.09)	2.09 (1.89-2.32)
15-28	1.95 (1.79-2.12)	1.68 (1.54-1.82)
29-91	1.40 (1.33-1.48)	1.33 (1.26-1.40)
Baseline	1.00	1.00

- In a self-controlled case series study of 20,921 MI patients and 22,400 stroke patients, there was a transient increase in risk of MI and stroke after acute 'systemic' respiratory infection based on GP diagnosis

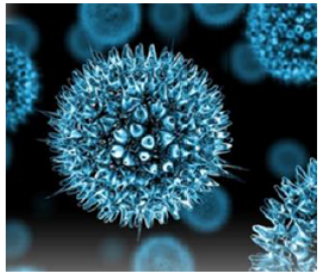
Smeeth L et al. *NEJM* 2004; 351(25):2611-8

Lab-confirmed infections and MI/ stroke

Time period after sample (days)	Adjusted incidence ratio for *S.pneumoniae*	P value	Adjusted incidence ratio for respiratory viruses	P value
Outcome: Non-fatal MI				
Day 1-3	5.41 (2.02-14.5)	0.001	6.20 (1.97-19.6)	0.002
Day 4-7	3.13 (1.01-9.75)	0.049	3.25 (0.80-13.1)	0.10
Day 8-14	1.78 (0.57-5.56)	0.32	1.06 (0.15-7.53)	0.96
Day 15-28	2.19 (1.04-4.62)	0.04	2.23 (0.83-5.98)	0.11
Baseline	1.00		1.00	
Outcome: Stroke				
Day 1-3	9.87 (3.67-26.5)	<0.001	3.97 (0.55-28.5)	0.17
Day 4-7	7.60 (2.83-20.4)	<0.001	3.15 (0.44-22.6)	0.25
Day 8-14	5.34 (2.20-13.0)	<0.001	5.74 (1.82-18.1)	0.003
Day 15-28	3.90 (1.84-8.27)	<0.001	3.70 (1.35-10.1)	0.01
Baseline	1.00		1.00	

Warren-Gash et al. *Eur Resp J*. 2018, 51(3):1701794

Potential mechanisms for an association



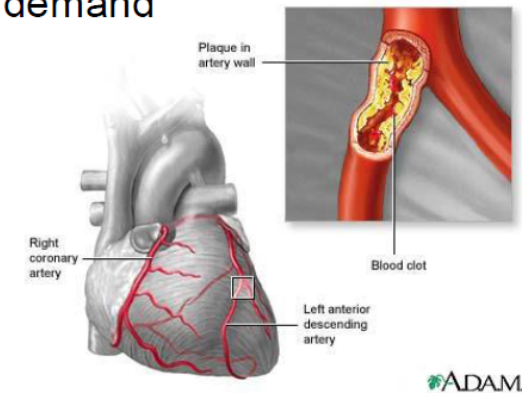
Systemic inflammation

Haemostatic effects
- ↑ platelet reactivity
- ↑ platelet aggregation
- ↑ fibrinogen
- ↑ plasma viscosity

Haemodynamic effects
- coronary vasoconstriction
- peripheral vasodilatation
- increased metabolic demand
- hypoxaemia

Localised vascular inflammation
- focal inflammatory effects within atherosclerotic plaques and coronary vessels

Plaque rupture and thrombosis



Randomised controlled trials of the effect of influenza vaccination for prevention of coronary heart disease

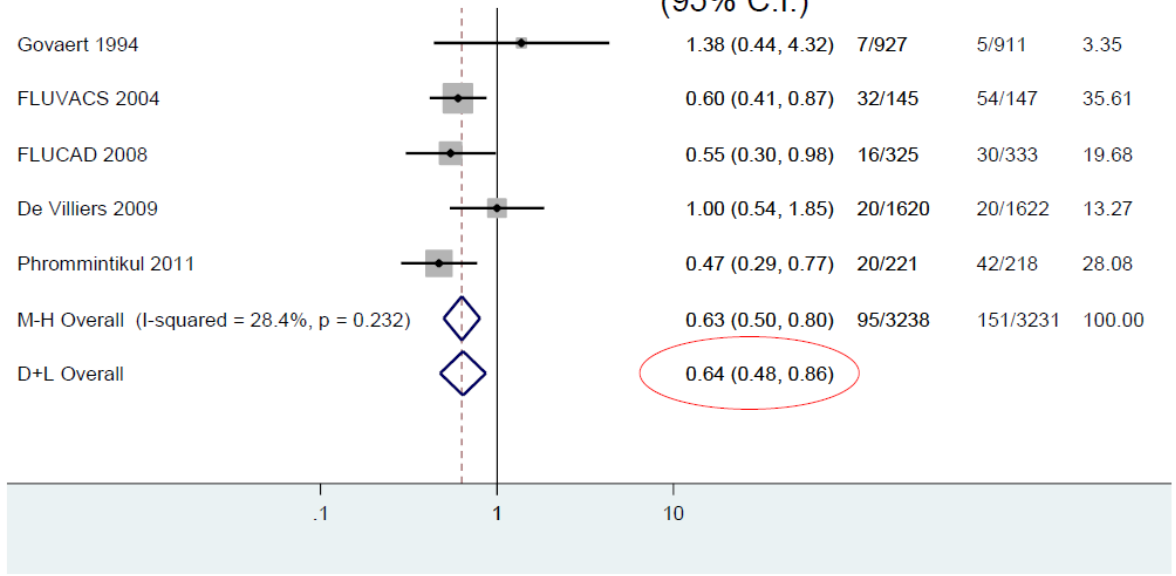
	Study population	Number allocated to intervention or control groups	Outcomes	Hazard ratio (95% CI)	p value
FLUVACS (2004)[55]	200 patients with acute myocardial infarction and 101 patients that received elective percutaneous coronary intervention (no history of acute myocardial infarction, unstable angina, coronary artery bypass graft, or percutaneous coronary intervention)	151 intervention, 150 control	Death caused by cardiovascular disease	0·34 (0·17–0·71)*	0·002
			Acute myocardial infarction or death caused by cardiovascular disease	0·59 (0·32–1·10)*	0·09
			Acute myocardial infarction or recurrent ischaemia leading to admission to hospital or death caused by cardiovascular disease	0·59 (0·40–0·86)*	0·004
FLUCAD (2008)[51]	658 patients with angiographically-confirmed coronary artery disease	325 intervention, 333 placebo	Death caused by cardiovascular disease	1·06 (0·15–7·56)	0·95
			MACE	0·54 (0·24–1·21)	0·13
			Coronary ischaemic event†	0·54 (0·29–0·99)	0·047

MACE=major adverse cardiac event (cardiovascular death, acute myocardial infarction, or coronary revascularisation).
* Hazard ratios for results of follow-up at 1 year (combined for acute myocardial infarction and elective patients receiving percutaneous coronary intervention).
† MACE or hospitalisation for myocardial ischaemia.

Warren-Ghash et al.- Lancet ID 2009

Does influenza vaccine reduce cardiovascular risk?

A meta-analysis showed a protective effect of influenza vaccine against major adverse CVD events across five small RCTs: RR 0.64 (95% C.I. 0.48-0.86)

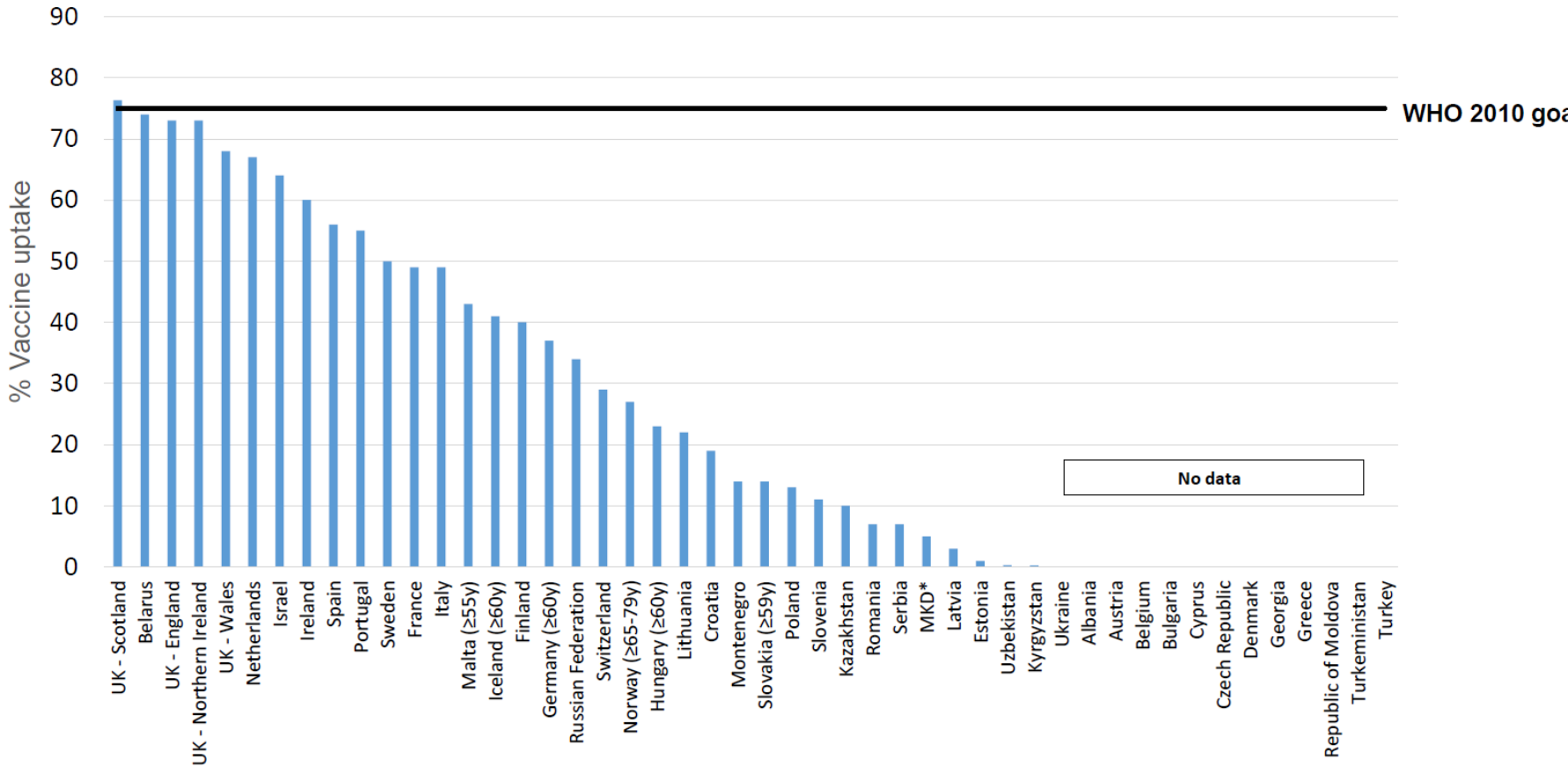


Udell J et al. *JAMA* 2013; 310(16):1711-20

Influenza vaccination is effective for secondary prevention of CVD

- All of these trials took place among participants with existing CVD
- Cardio-protection was higher among patients with recent acute coronary syndrome: RR 0.45 (95% C.I. 0.32-0.63) compared to those with stable coronary artery disease: RR 0.94 (95% C.I. 0.55-1.61)
- Annual influenza vaccine is recommended for patients with established CVD by WHO, ECDC, the US CDC, and is also recommended for cardiovascular disease prevention (2016 European Guidelines on cardiovascular disease prevention in clinical practice) and stroke prevention (2014 AHA-ASA guidelines for primary prevention of stroke)

Influenza vaccine uptake in Europe: over 65s



Herzinsuffizienz

Circulation

ORIGINAL RESEARCH ARTICLE

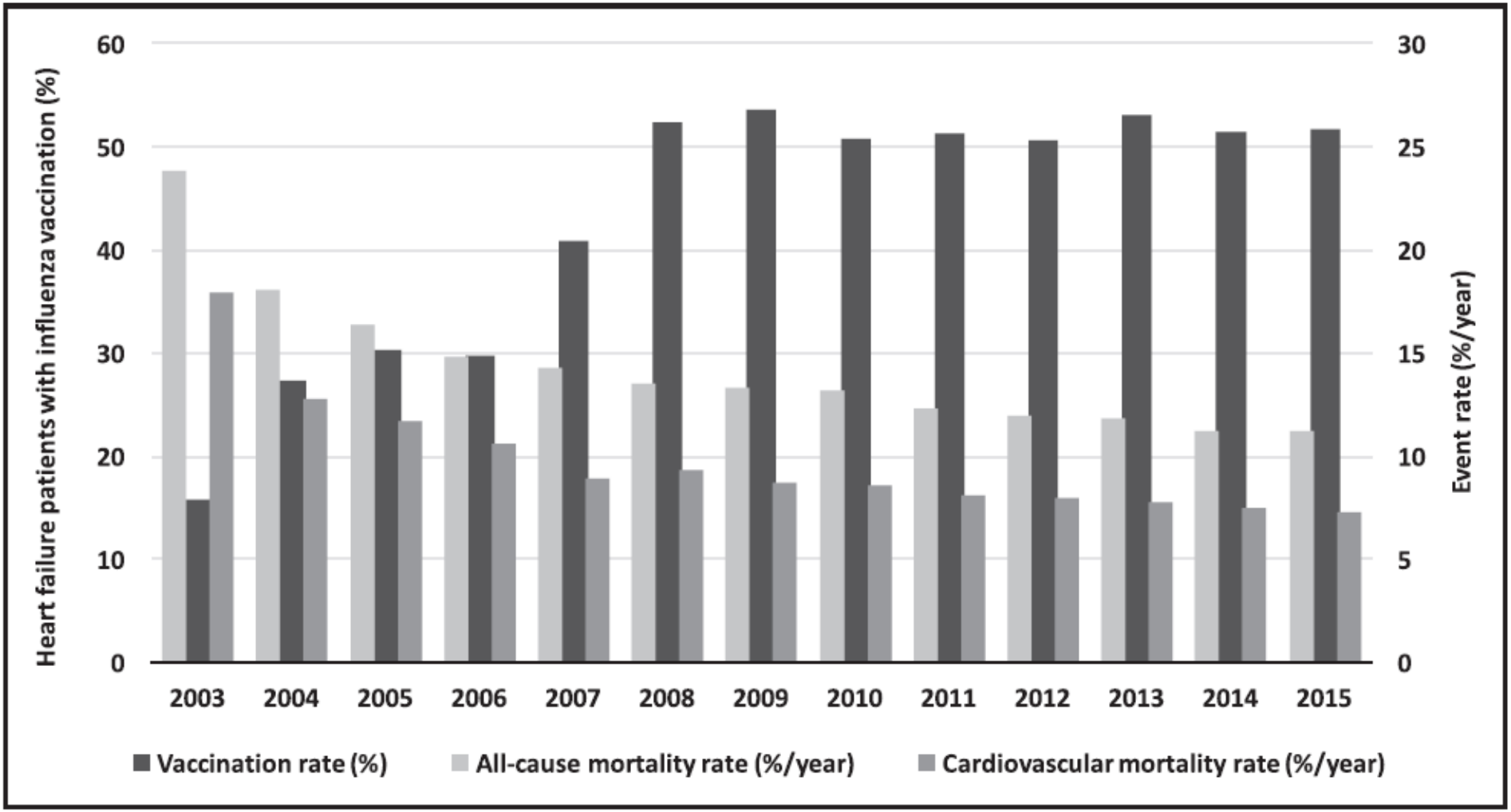
Influenza Vaccine in Heart Failure

Cumulative Number of Vaccinations, Frequency, Timing, and Survival: A Danish Nationwide Cohort Study

Circulation. 2018;139:00–00. DOI: 10.1161/CIRCULATIONAHA.118.036788

METHODS: We performed a nationwide cohort study including all patients who were >18 years of age and diagnosed with HF in Denmark in the period of January 1, 2003, to June 1, 2015 (n=134 048). We collected linked data using nationwide registries. Vaccination status, number, and frequency during follow-up were treated as time-varying covariates in time-dependent Cox regression.

RESULTS: Follow-up was 99.8% with a median follow-up time of 3.7 years (interquartile range, 1.7–6.8 years). The vaccination coverage of the study cohort ranged from 16% to 54% during the study period. In unadjusted analysis, receiving ≥1 vaccinations during follow-up was associated with a higher risk of death. After adjustment for inclusion date, comorbidities, medications, household income, and education level, receiving ≥1 vaccinations was associated with an 18% reduced risk of death (all-cause: hazard ratio, 0.82; 95% CI, 0.81–0.84; $P<0.001$; cardiovascular causes: hazard ratio, 0.82; 95% CI, 0.81–0.84; $P<0.001$). Annual vaccination, vaccination early in the year (September to October), and greater cumulative number of vaccinations were associated with larger reductions in the risk of death compared with intermittent vaccination.


Heart failure patients with influenza vaccination (%)
Event rate (%/year)
60
50
40
30
20
10
0
30
25
20
15
10
5
0
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
Vaccination rate (%)
All-cause mortality rate (%/year)
Cardiovascular mortality rate (%/year)

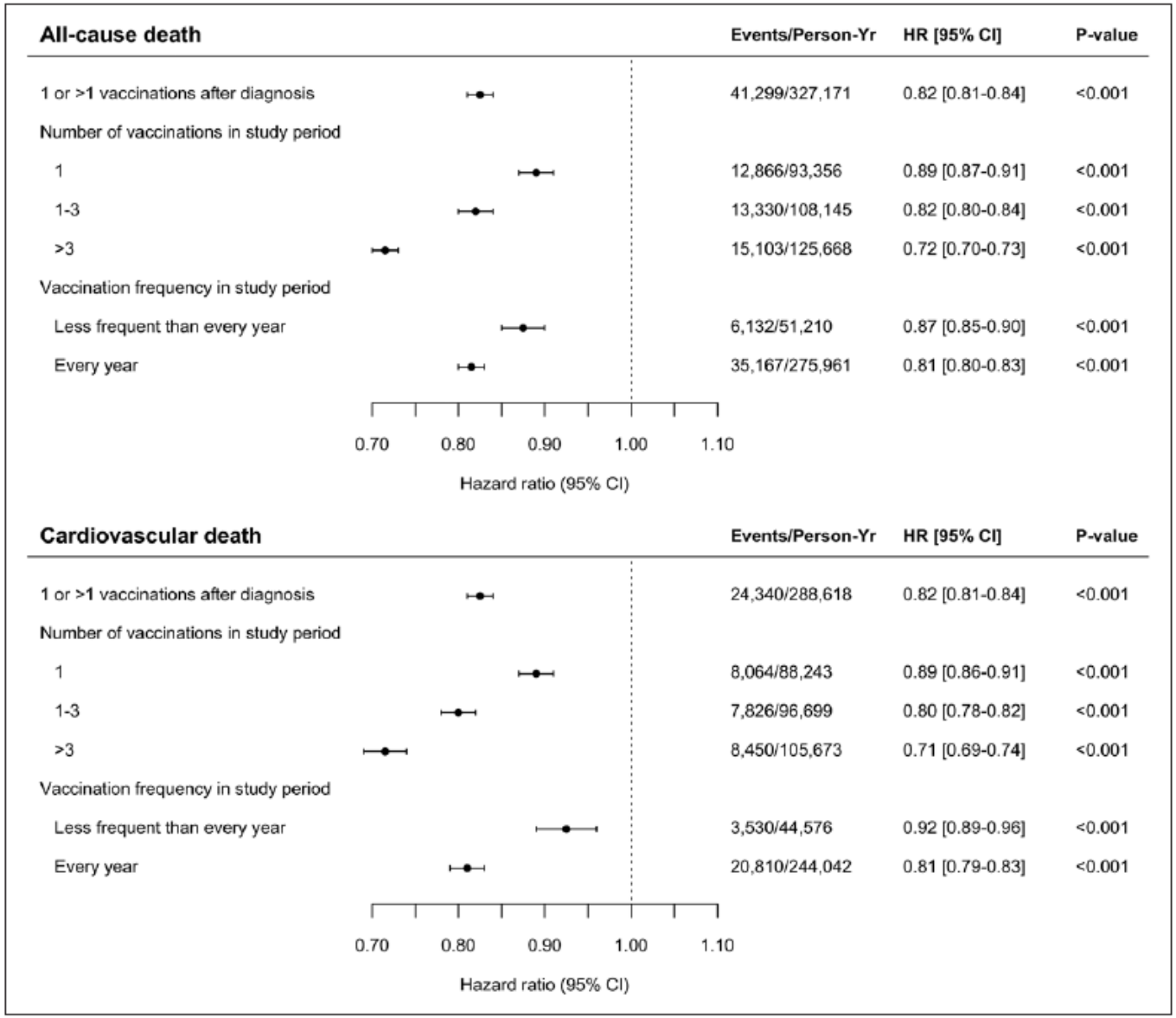


Figure 2. Vaccination and outcome.

Forest plots of the association between vaccination after heart failure diagnosis (≥1), the cumulative number of vaccinations received after diagnosis, and the vaccination frequency after diagnosis and the risk of death. Error bars represent 95% CIs. Vaccination parameters and age were entered as time-varying covariates in a time-dependent Cox regressions model adjusted for all variables displayed in Table 1 with the addition of inclusion year. HR indicates hazard ratio.

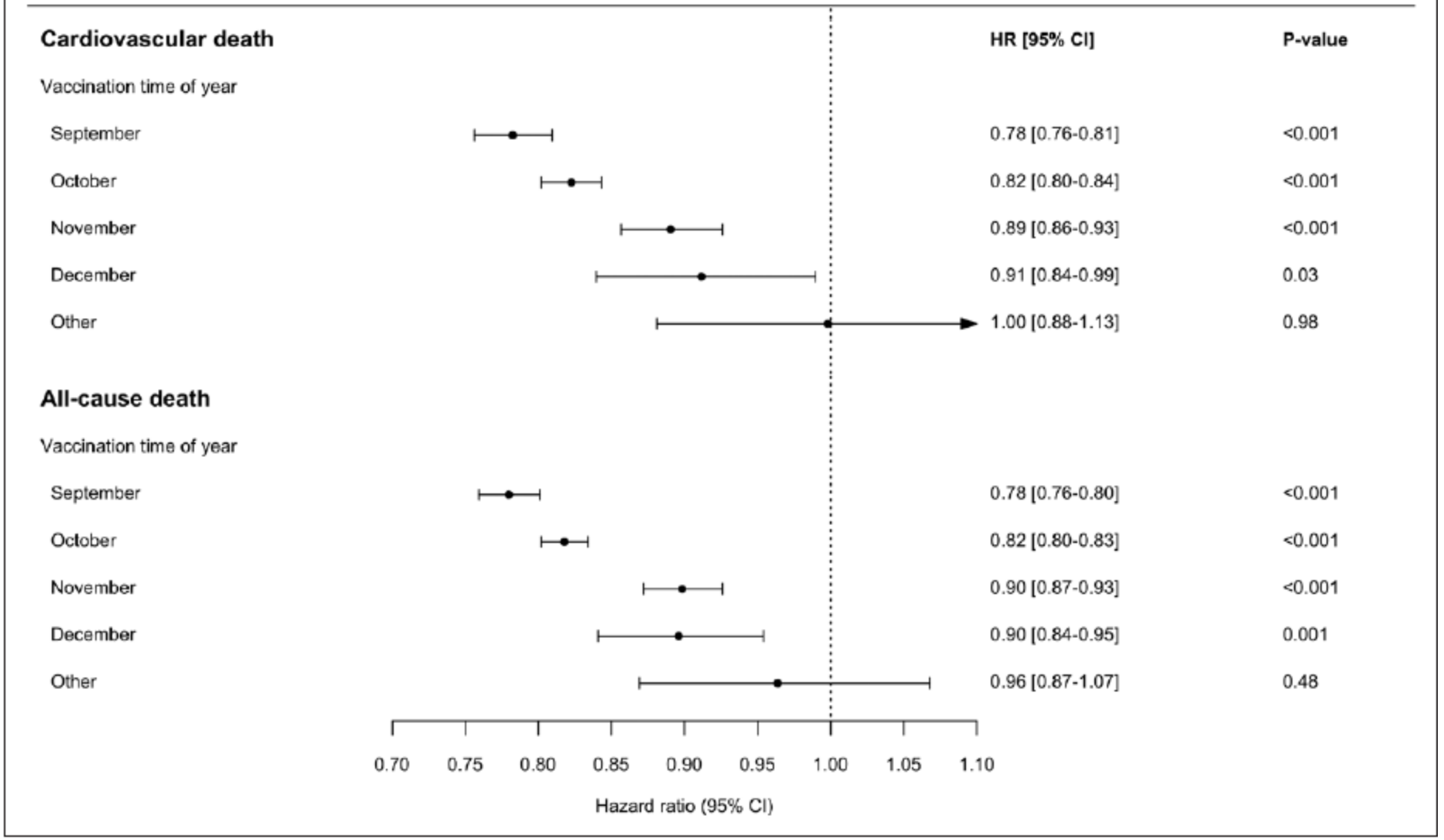


Figure 3. Vaccination time of year and outcome.
Association between the vaccination time of year and the risk of death. The reference was no vaccination. Error bars represent 95% CIs. Vaccination time of year was entered as a time-varying covariate in a time-dependent Cox regression model adjusted for all variables in Table 1 with the addition of inclusion year. HR indicates hazard ratio.

Table 2. Landmark Analyses Assessing the Association Between Influenza Vaccination and All-Cause and Cardiovascular Mortality in Each Influenza Season Included in the Study Period

All-Cause Death					Cardiovascular Death				
Season	Patients, n	Events, n	HR (95% CI)	*P* Value	Season	Patients, n	Events, n	HR (95% CI)	*P* Value
2003–2004	7765	851	0.69 (0.56–0.85)	<0.001	2003–2004	7765	620	0.65 (0.51–0.84)	0.001
2004–2005	17726	1663	0.76 (0.66–0.87)	<0.001	2004–2005	17726	1177	0.76 (0.65–0.89)	0.001
2005–2006	25565	2092	0.83 (0.73–0.95)	0.007	2005–2006	25565	1467	0.87 (0.75–1.02)	0.09
2006–2007	32337	2577	0.81 (0.70–0.93)	0.003	2006–2007	32337	1663	0.76 (0.64–0.91)	0.003
2007–2008*	37867	2826	0.88 (0.78–0.99)	0.03	2007–2008*	37867	1760	0.88 (0.76–1.02)	0.09
2008–2009	42598	3187	0.84 (0.75–0.95)	0.004	2008–2009	42598	2121	0.83 (0.72–0.96)	0.01
2009–2010	47044	3339	0.80 (0.71–0.90)	<0.001	2009–2010	47044	2180	0.78 (0.67–0.91)	0.001
2010–2011	51159	3525	0.79 (0.69–0.90)	<0.001	2010–2011	51159	2307	0.80 (0.68–0.94)	0.007
2011–2012	54917	3657	0.75 (0.66–0.85)	<0.001	2011–2012	54917	2455	0.80 (0.68–0.93)	0.003
2012–2013	58252	3926	0.80 (0.71–0.91)	<0.001	2012–2013	58252	2604	0.73 (0.63–0.85)	<0.001
2013–2014	61275	3762	0.71 (0.62–0.81)	<0.001	2013–2014	61275	2508	0.76 (0.65–0.89)	0.001
2014–2015	64336	4087	0.87 (0.77–0.98)	0.02	2014–2015	64336	2713	0.87 (0.75–1.01)	0.07
2015–2016*	64556	3907	0.88 (0.76–1.01)	0.07	2015–2016*	64556	1399	0.91 (0.72–1.18)	0.52

For each season, follow-up was counted from September 1 to April 1 the next year, encompassing the influenza season in Denmark. Influenza vaccination was implemented as a time-varying covariate in time-dependent Cox regression, and patients were switched to the vaccinated group at the time of vaccination if they were vaccinated during the season. The Cox regression models were adjusted for all variables displayed in Table 1 with the addition of inclusion year and time since heart failure diagnosis. HR indicates hazard ratio.

*In these seasons, known mismatches between vaccine influenza strains and circulating strains occurred.

Heart Failure Reviews (2019) 24:109–114
https://doi.org/10.1007/s10741-018-9736-6

The effect of influenza vaccination on mortality and hospitalization in patients with heart failure: a systematic review and meta-analysis

Hidekatsu Fukuta[1] · Toshihiko Goto[2] · Kazuaki Wakami[2] · Takeshi Kamiya[3] · Nobuyuki Ohte[2]

Published online: 26 October 2018

Abstract

Influenza infection is associated with increased risk for mortality and hospitalization in heart failure patients. Although there are no published randomized controlled trials examining the effect of influenza vaccination on clinical outcomes in heart failure patients, the effect has been examined in observational cohort studies. Nevertheless, results are inconsistent due partly to limited power with small sample sizes and use of different definitions of outcomes. We therefore aimed to conduct a systematic review and meta-analysis of the effect of influenza vaccination on mortality and hospitalization in heart failure patients. The search of electronic databases identified 6 observational cohort studies with 22,486 patients examining the effect of influenza vaccination on mortality and hospitalization in heart failure patients. Pooled analysis of confounder-adjusted hazard ratio showed that influenza vaccination was associated with reduced risk of mortality during 1-year follow-up (risk ratio [95% CI] = 0.76 [0.63–0.92], $P_{fix} < 0.01$) and during long-term (up to 4 years) follow-up (0.80 [0.71–0.90], $P_{fix} < 0.001$). Furthermore, influenza vaccination was associated with reduced risk of mortality during influenza season (risk ratio [95% CI] = 0.52 [0.39–0.69], $P_{random} < 0.001$) and during non-influenza season (0.79 [0.69–0.90], $P_{fix} < 0.001$). Only a few studies reported the effect of influenza vaccination on hospitalization, which did not permit us to perform pooled analysis. In conclusion, our meta-analysis showed that influenza vaccination was associated with reduced risk of mortality in heart failure patients. Large-scale and adequately powered randomized controlled trials should be planned to confirm our observed potential survival benefit of influenza vaccination in these patients.

Keywords Heart failure · Influenza · Vaccine · Prognosis · Meta-analysis

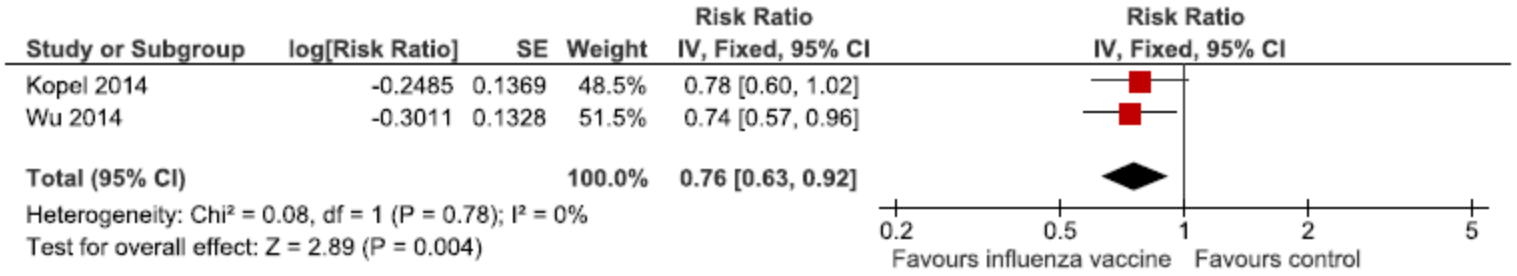


Fig. 2 Forest plot showing the effect of influenza vaccination on mortality during 1-year follow-up

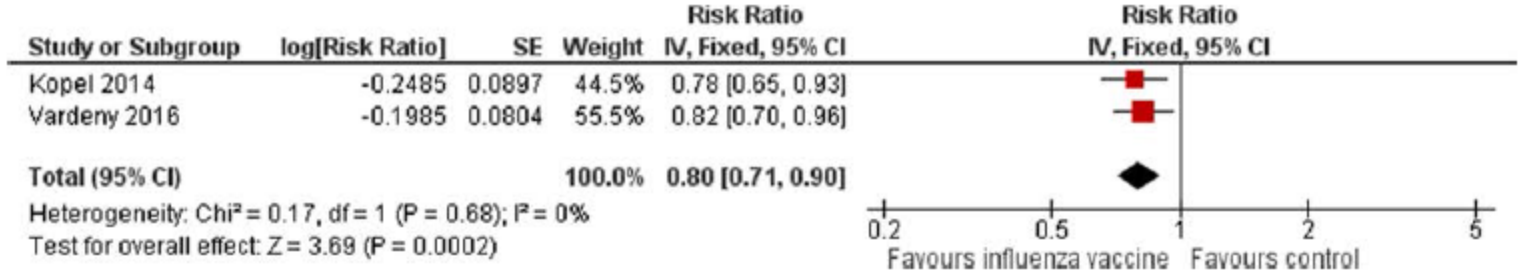


Fig. 3 Forest plot showing the effect of influenza vaccination on mortality during long-term follow-up

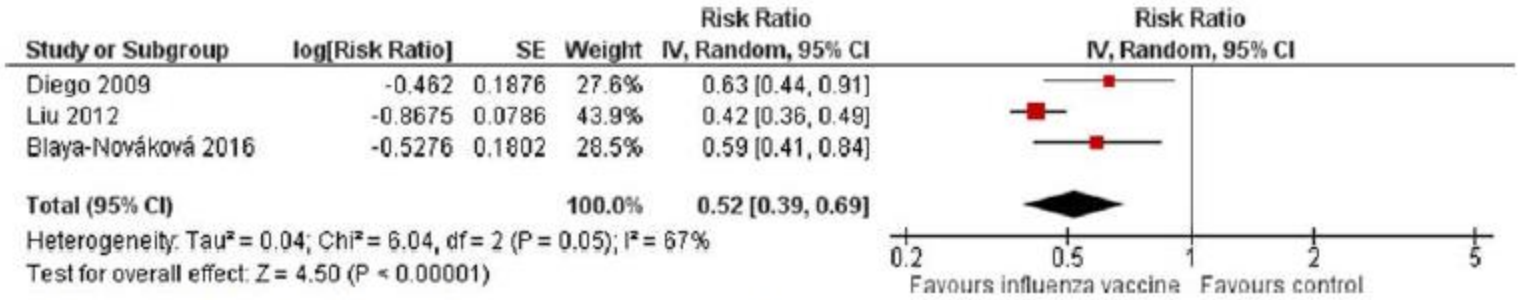


Fig. 4 Forest plot showing the effect of influenza vaccination on mortality during influenza season

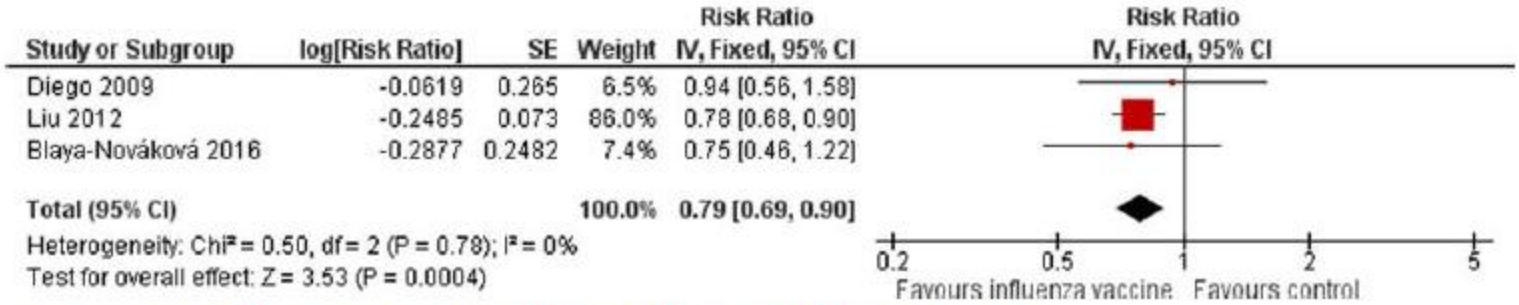


Fig. 5 Forest plot showing the effect of influenza vaccination on mortality during non-influenza season

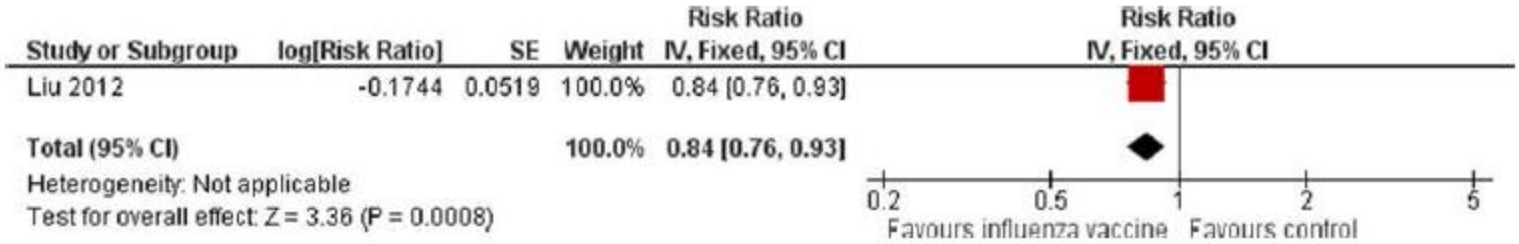


Fig. 6 Forest plot showing the effect of influenza vaccination on cardiovascular hospitalization during influenza season

Influenza vaccination is encouraged by cardiac societies but without evidence level or class of recommendation

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

ACCF/AHA PRACTICE GUIDELINE

2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the Heart Rhythm Society

Influenza vaccine in hypertension

The Flu Vaccine and Mortality in Hypertension. A Danish Nationwide Cohort Study

Unpublished 2019

Daniel Modin[1], MB; Brian Claggett[2], PhD; Mads Emil Jørgensen[1], MD; Lars Køber[3,4], MD, DMSci; Thomas Benfield[3,5], MD, DMSci; Morten Schou[1,3], MD, PhD; Jens Ulrik Stæhr Jensen[1,3], MD, PhD; Scott D. Solomon[2], MD; Ramona Trebbien[6], PhD; Michael Fralick[7], MD, SM; Orly Vardeny[8], PharmD, MS; Marc A. Pfeffer[2], MD, PhD; Christian Torp-Pedersen[1,3], MD, DMSci; Gunnar Gislason[1,3], MD, PhD; Tor Biering-Sørensen[1,9], MD, PhD, MPH

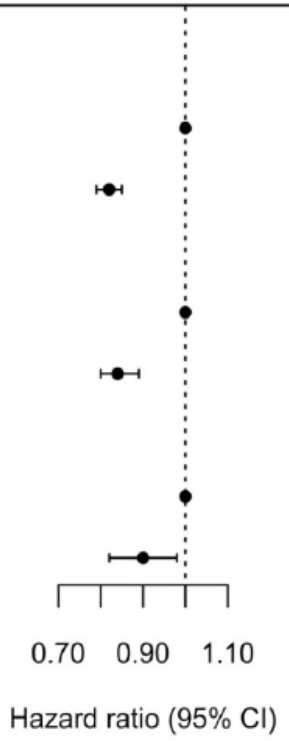
608,452 unique patients with hypertension (no IHD, HF, COPD, cancer, stroke)

Followed for a median of 5 seasons (interquartile-range: 2-8)

21,571 patients died of all-causes (3.5%), 12,270 patients died of cardiovascular causes (2.0%) and 3,846 patients died of AMI or stroke (0.6%)

Influenza vaccine in hypertension

	Events/PY	HR [95% CI]	P-value
All-cause death			
Not vaccinated (reference)	11,018/640,560	Reference	
Vaccinated	10,553/335,342	0.82 [0.79-0.85]	<0.001
Cardiovascular death			
Not vaccinated (reference)	6,178/640,560	Reference	
Vaccinated	6,092/335,342	0.84 [0.80-0.89]	<0.001
Stroke or AMI death			
Not vaccinated (reference)	1,858/640,560	Reference	
Vaccinated	1,988/335,342	0.90 [0.82-0.98]	0.017



Vaccination parameters and age were entered as time-varying covariates in a time-dependent Cox regressions model adjusted for all variables displayed in Table 1 with the addition of inclusion year.

Influenza vaccine in diabetes

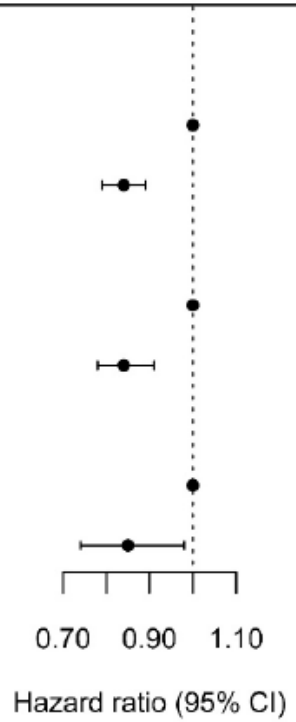
Preliminary analysis (March 2019)

268,881 unique patients with diabetes (no IHD, HF, COPD, cancer, stroke)

Followed for a median of 5 seasons (interquartile-range: 2-8)

8,207 patients died of all-causes (3.1%), 4,127 patients died of cardiovascular causes (1.5%) and 1,439 patients died of AMI or stroke (0.5%)

Diabetes Mellitus and influenza vaccination



	Events/PY	HR [95% CI]	P-value
All-cause death			
Not vaccinated (reference)	4,412/282,699	Reference	
Vaccinated	3,795/142,619	0.84 [0.79-0.89]	<0.001
Cardiovascular death			
Not vaccinated (reference)	2,111/282,699	Reference	
Vaccinated	2,016/142,619	0.84 [0.78-0.91]	<0.001
Stroke or AMI death			
Not vaccinated (reference)	727/282,699	Reference	
Vaccinated	712/142,619	0.85 [0.74-0.98]	0.027

ISSN: 2164-5515 (Print) 2164-554X (Online) Journal homepage: http://www.tandfonline.com/loi/khvi20

Immunogenicity, safety, and effectiveness of seasonal influenza vaccination in patients with diabetes mellitus: A systematic review

Gael Dos Santos, Halima Tahrat & Rafik Bekkat-Berkani

To cite this article: Gael Dos Santos, Halima Tahrat & Rafik Bekkat-Berkani (2018): Immunogenicity, safety, and effectiveness of seasonal influenza vaccination in patients with diabetes mellitus: A systematic review, Human Vaccines & Immunotherapeutics, DOI: 10.1080/21645515.2018.1446719

To link to this article: https://doi.org/10.1080/21645515.2018.1446719

- 15 Studien, 2000-17

Stroke

Protective effect of influenza vaccination on outcomes in geriatric stroke patients: A nationwide matched cohort study

Fai Lam[a,b,c,d], Ta-Liang Chen[b,c,d], Chun-Chuan Shih[e], Chao-Shun Lin[b,c,d], Chun-Chieh Yeh[f,g], Yuarn-Jang Lee[h], Chaur-Jong Hu[i], Hung-Yi Chiou[a,1], Chien-Chang Liao[b,c,d,j,k,*,1]

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[b] *Department of Anesthesiology, Taipei Medical University Hospital, Taipei, Taiwan*
[c] *Department of Anesthesiology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan*
[d] *Anesthesiology and Health Policy Research Center, Taipei Medical University Hospital, Taipei, Taiwan*
[e] *The School of Chinese Medicine for Post-Baccalaureate, I-Shou University, Kaohsiung, Taiwan*
[f] *Department of Surgery, China Medical University Hospital, Taichung, Taiwan*
[g] *Department of Surgery, University of Illinois, Chicago, IL, USA*
[h] *Division of Infectious Diseases, Department of Internal Medicine, Taipei Medical University Hospital, Taipei, Taiwan*
[i] *Department of Neurology, Shuan Ho Hospital, Taipei Medical University, New Taipei City, Taiwan*
[j] *Department of Anesthesiology, Shuan Ho Hospital, Taipei Medical University, New Taipei City, Taiwan*
[k] *School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan*

HIGHLIGHTS

- Stroke patients with influenza vaccination (IV) showed better outcome than non-vaccinated patients.
- IV was associated with reduced post-stroke outcomes in various subgroups.
- Less consumption of medical resources were also noted in stroke patients with IV.

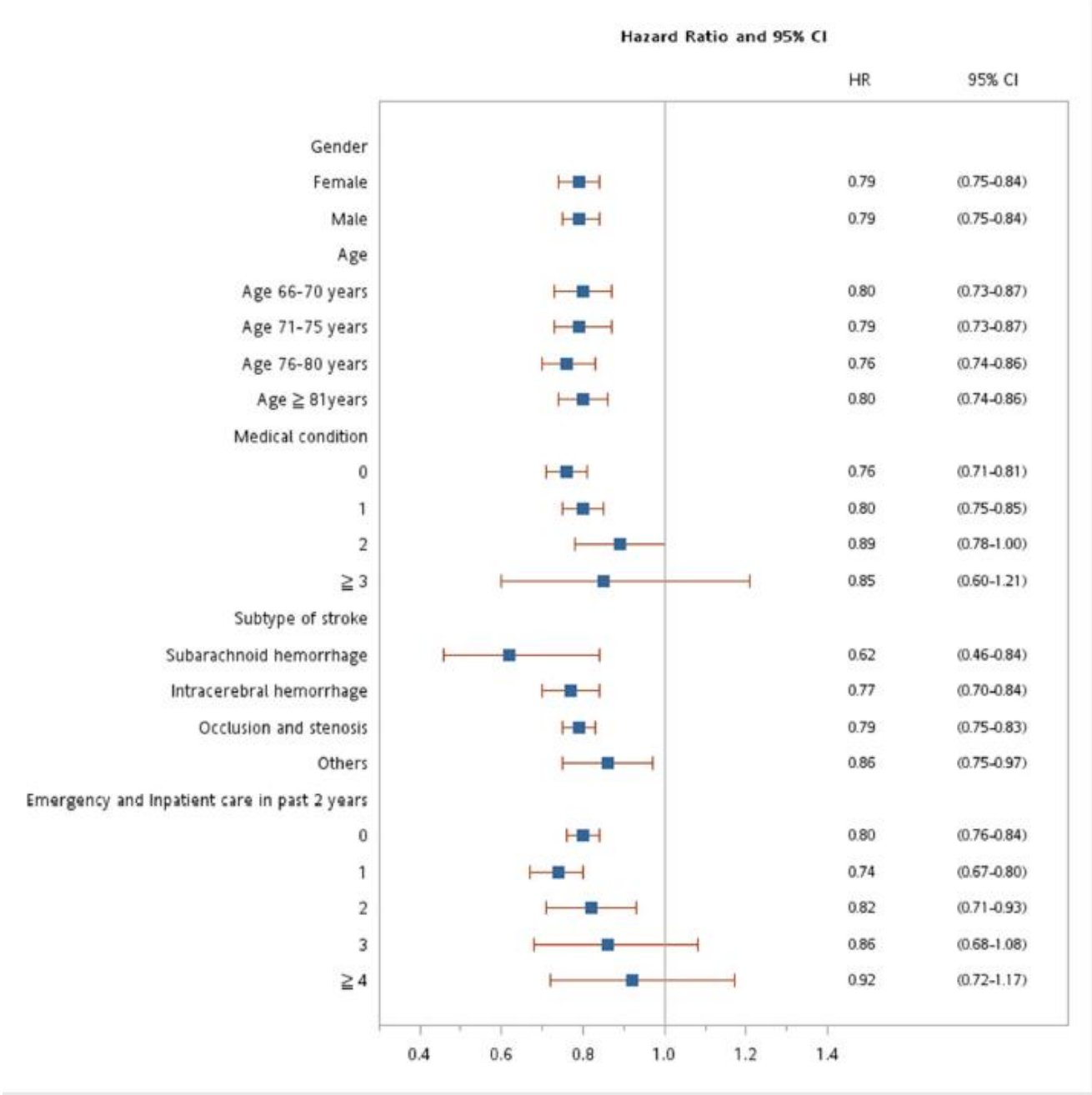


Fig. 1. The stratification analysis for influenza vaccination associated with post-stroke adverse events.

Effect of Influenza Vaccination on Risk of Stroke: A Systematic Review and Meta-Analysis

- Eleven studies fulfilled our inclusion criteria. In a random-effects model
- Vaccinated individuals had a decreased risk of stroke compared with unvaccinated individuals (OR 0.82; 95% CI 0.75-0.91; $p < 0.001$).
- The relationship between influenza vaccination and stroke risk remained robust in subgroup analyses.
- The significant effect of influenza vaccination was associated with ascertainment of vaccination status and stage of prevention

Lee et al. Neuroepidemiologie 2017 Jun 21;48(3-4):103-110.

COPD und Asthma

ORIGINAL ARTICLE

Prevalence of viral infection detected by PCR and RT-PCR in patients with acute exacerbation of COPD: A systematic review

ANANT MOHAN,[1] SUBHASH CHANDRA,[2] DIPTI AGARWAL,[2] RANDEEP GULERIA,[1] SHOBHA BROOR,[1] BHARTI GAUR[1] AND RAVINDRA MOHAN PANDEY[1]

[1]*All India Institute of Medical Sciences, New Delhi, India, and* [2]*Department of Medicine, Mayo Clinic, RoChester, New York, USA*

Results: **Eight studies met the inclusion criteria. The WMP of respiratory viral infection in AECOPD was 34.1% (95% CI: 23.9–44.4). picornavirus was the most commonly detected virus with WMP 17.3% (95% CI: 7.2–27.3), followed by influenza; 7.4% (95% CI: 2.9–12.0), respiratory syncytial virus; 5.3% (95% CI: 1.6–9.0), corona viruses; 3.1% (95% CI: 0.4–5.8), parainfluenza; 2.6% (95% CI: 0.4–4.8), adenovirus; 1.1% (95% CI: –1.1 to 3.3), and human metapneumovirus; 0.7% (95% CI: –0.3 to 1.8). Maximum WMP was observed in studies from Europe followed by the USA, Australia and Asia. Picorna was the most common virus detected in Western countries whereas influenza was most common in Asia.**

Respiratory Viruses and Treatment Failure in Children With Asthma Exacerbation

Joanna Merckx, MD,[a,b] Francine M. Ducharme, MD,[c,d] Christine Martineau, PhD,[e,f] Roger Zemek, MD,[g,h] Jocelyn Gravel, MD,[c] Dominic Chalut, MD,[i] Naveen Poonai, MD,[j] Caroline Quach, MD, MSc,[b,e,k] for the Pediatric Emergency Research Canada (PERC) DOORWAY team

RESULTS: Of 958 participants, 61.7% were positive for ≥1 pathogen (rhinovirus was the most prevalent [29.4%]) and 16.9% experienced treatment failure. The presence of any pathogen was not associated with higher baseline severity but with a higher risk of treatment failure (20.7% vs 12.5%; RD = 8.2% [95% confidence interval: 3.3% to 13.1%]) compared to the absence of a pathogen. Nonrhinovirus pathogens were associated with an increased absolute risk (RD) of treatment failure by 13.1% (95% confidence interval: 6.4% to 19.8%), specifically, by 8.8% for respiratory syncytial virus, 24.9% for influenza, and 34.1% for parainfluenza.

To cite: Merckx J, Ducharme FM, Martineau C, et al. Respiratory Viruses and Treatment Failure in Children With Asthma Exacerbation. *Pediatrics*. 2018;142(1):e20174105

Received: 29 August 2018 | Revised: 19 December 2018 | Accepted: 31 December 2018
DOI: 10.1111/irv.12633

ORIGINAL ARTICLE

WILEY

Impact of influenza on hospitalization rates in children with a range of chronic lung diseases

Nusrat Homaira[1,2] | Nancy Briggs[3] | Ju-Lee Oei[1,4] | Lisa Hilder[1,5] | Barbara Bajuk[6] | Tom Snelling[7,8,9,10] | Georgina M. Chambers[1,5,11] | Adam Jaffe[1,2]

Background: Data on burden of severe influenza in children with a range of chronic lung diseases (CLDs) remain limited.

Method: We performed a cohort study to estimate burden of influenza-associated hospitalization in children with CLDs using population-based linked data. The cohort comprised all children in New South Wales, Australia, born between 2001 and 2010 and was divided into five groups, children with: (a) severe asthma; (b) bronchopulmonary dysplasia (BPD); (c) cystic fibrosis (CF); (d) other congenital/chronic lung conditions; and (e) children without CLDs. Incidence rates and rate ratios for influenza-associated hospitalization were calculated for 2001-2011. Average cost/episode of hospitalization was estimated using public hospital cost weights.

Results: Our cohort comprised 888 157 children; 11 058 (1.2%) had one of the CLDs. The adjusted incidence/1000 child-years of influenza-associated hospitalization in children with CLDs was 3.9 (95% CI: 2.6-5.2) and 0.7 (95% CI: 0.5-0.9) for children without. The rate ratio was 5.4 in children with CLDs compared to children without. The adjusted incidence/1000 child-years (95% CI) in children with severe asthma was 1.1 (0.6-1.6), with BPD was 6.0 (3.7-8.3), with CF was 7.4 (2.6-12.1), and with other congenital/chronic lung conditions was 6.9 (4.9-8.9). The cost/episode (95% CI) of influenza-associated hospitalization was AUD 19 704 (95% CI: 11 715-27 693) for children with CLDs compared to 4557 (95% CI: 4129-4984) for children without.

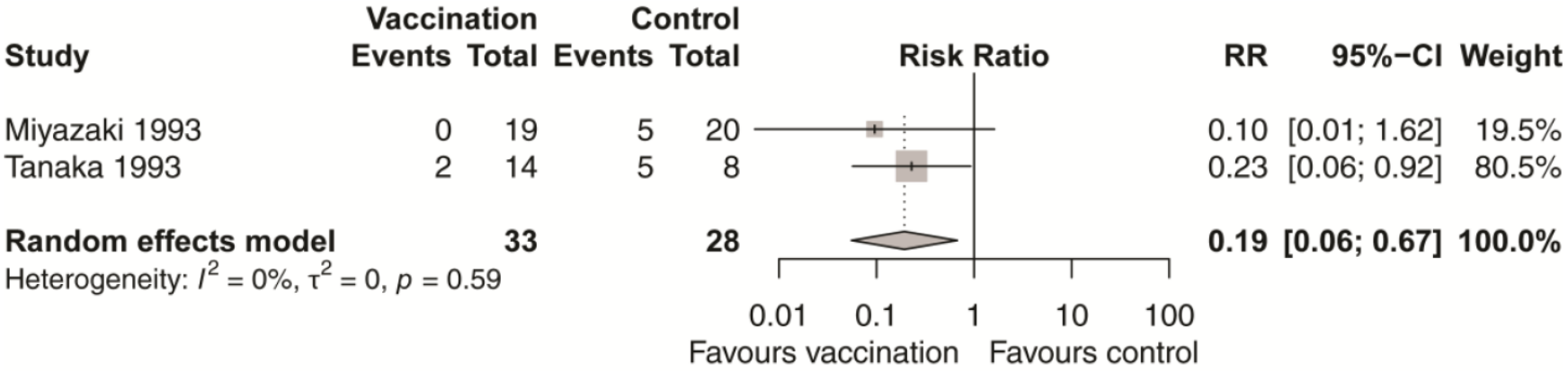
Effectiveness of influenza vaccines in asthma: a systematic review and meta-analysis

- Pooled vaccine effectiveness in 1,825 people with asthma from two test-negative design case-control studies was 45% (95% CI 31 to 56) for laboratory-confirmed influenza.
- Pooled efficacy of live vaccines in reducing influenza was 81% (95% CI 33 to 94).
- Influenza vaccine prevented 59-78% of asthma attacks leading to emergency visits and/or hospitalizations. For people with asthma influenza vaccination may be effective in both reducing influenza infection and asthma attacks.

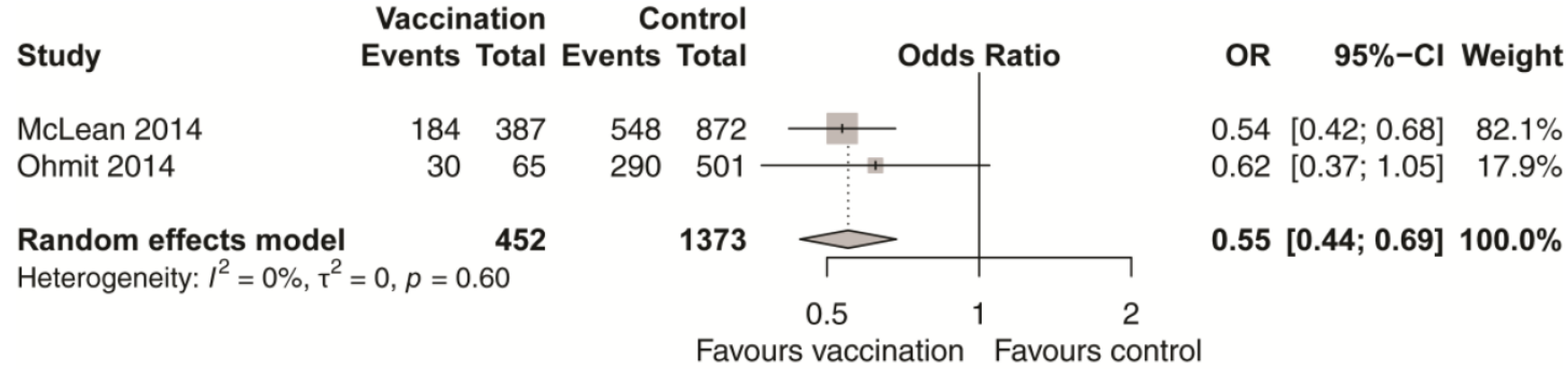
Vasileiou et al. Clin Infect Dis 2017, Jun 7th

IMPFEFFIZENZ bei ASTHMA-Patienten

Live attenuated vaccine



Seasonal influenza vaccine



Alter

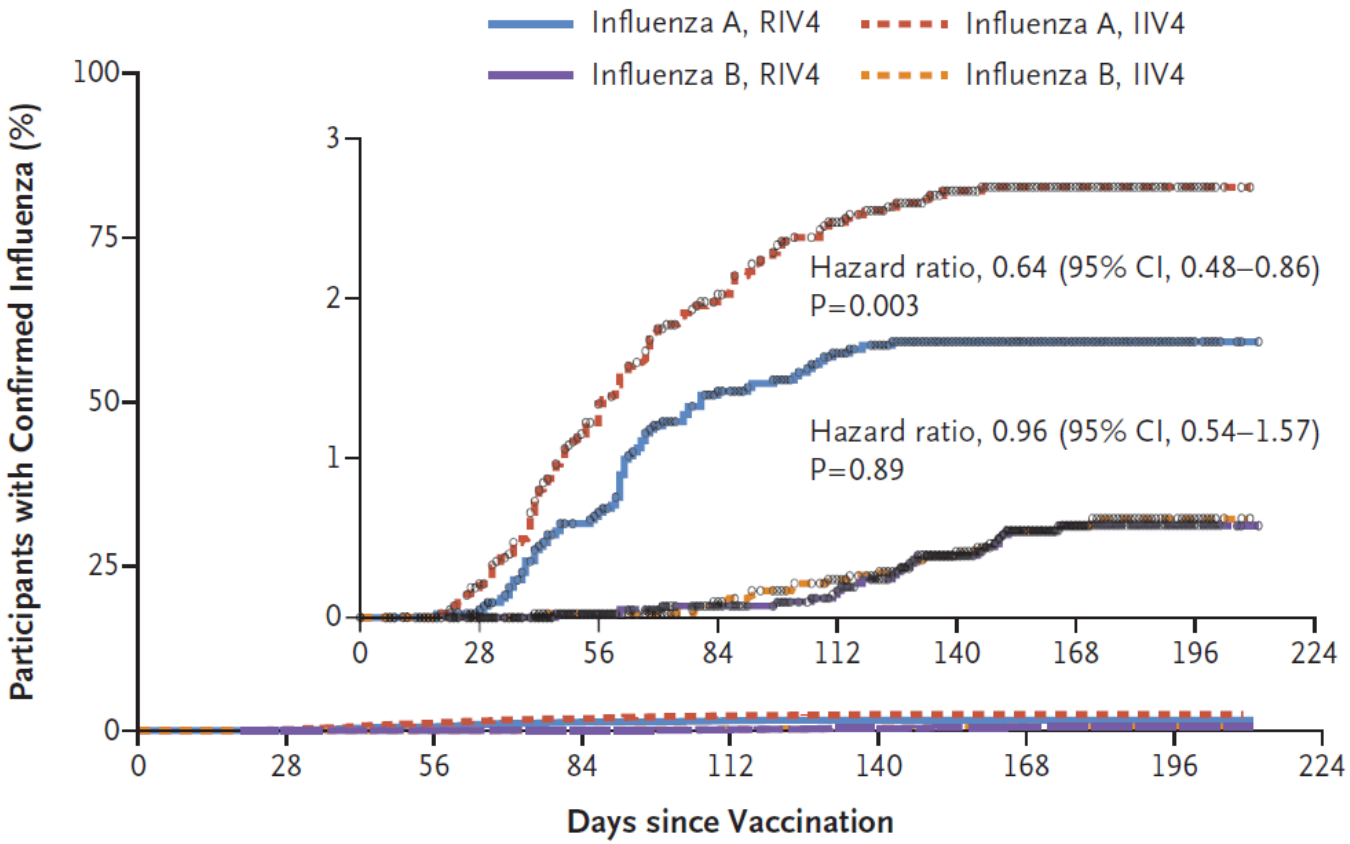
Efficacy of Recombinant Influenza Vaccine in Adults 50 Years of Age or Older

Lisa M. Dunkle, M.D., Ruvim Izikson, M.D., M.P.H., Peter Patriarca, M.D., Karen L. Goldenthal, M.D., Derek Muse, M.D., Janice Callahan, Ph.D., and Manon M.J. Cox, Ph.D., for the PSC12 Study Team*

We conducted a randomized, double-blind, multicenter trial of RIV4 (45 μg of recombinant hemagglutinin [HA] per strain, 180 μg of protein per dose) versus standard-dose IIV4 (15 μg of HA per strain, 60 μg of protein per dose) to compare the relative vaccine efficacy against reverse-transcriptase polymerase-chain-reaction (RT-PCR)–confirmed,

Dunkle et al. New Engl J Med, June 22nd 2017

B Type A or Type B Influenza



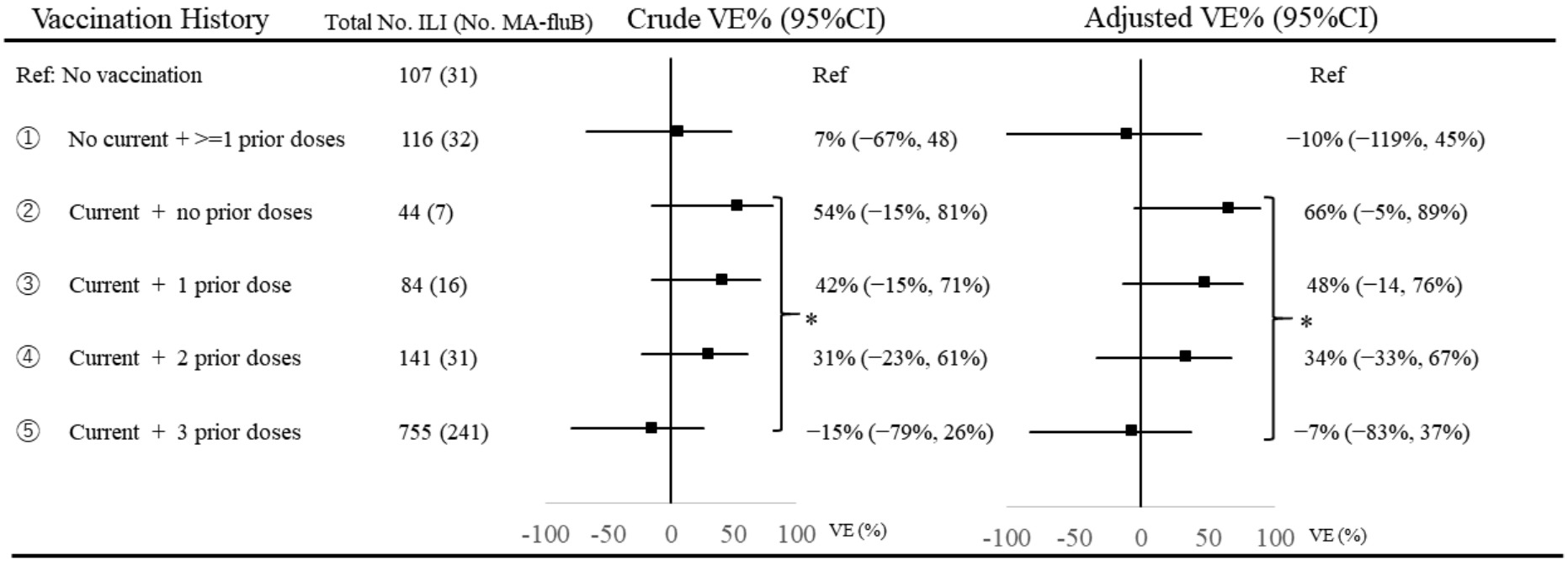
No. of Participants

Influenza A, RIV4	4303 (0)	4266 (2)	4201 (28)	4127 (60)	4081 (70)	3859 (73)	2339 (73)	15 (73)	0 (73)
Influenza A, IIV4	4301 (0)	4261 (9)	4177 (57)	4120 (27)	4073 (105)	3832 (113)	2336 (114)	14 (114)	0 (114)
Influenza B, RIV4	4303 (0)	4268 (0)	4228 (1)	4184 (3)	4144 (7)	3915 (16)	2371 (23)	16 (23)	0 (23)
Influenza B, IIV4	4301 (0)	4270 (0)	4232 (1)	4201 (1)	4167 (10)	3924 (17)	2395 (23)	14 (24)	0 (24)

Dunkle et al. New Engl J Med, June 22nd 2017

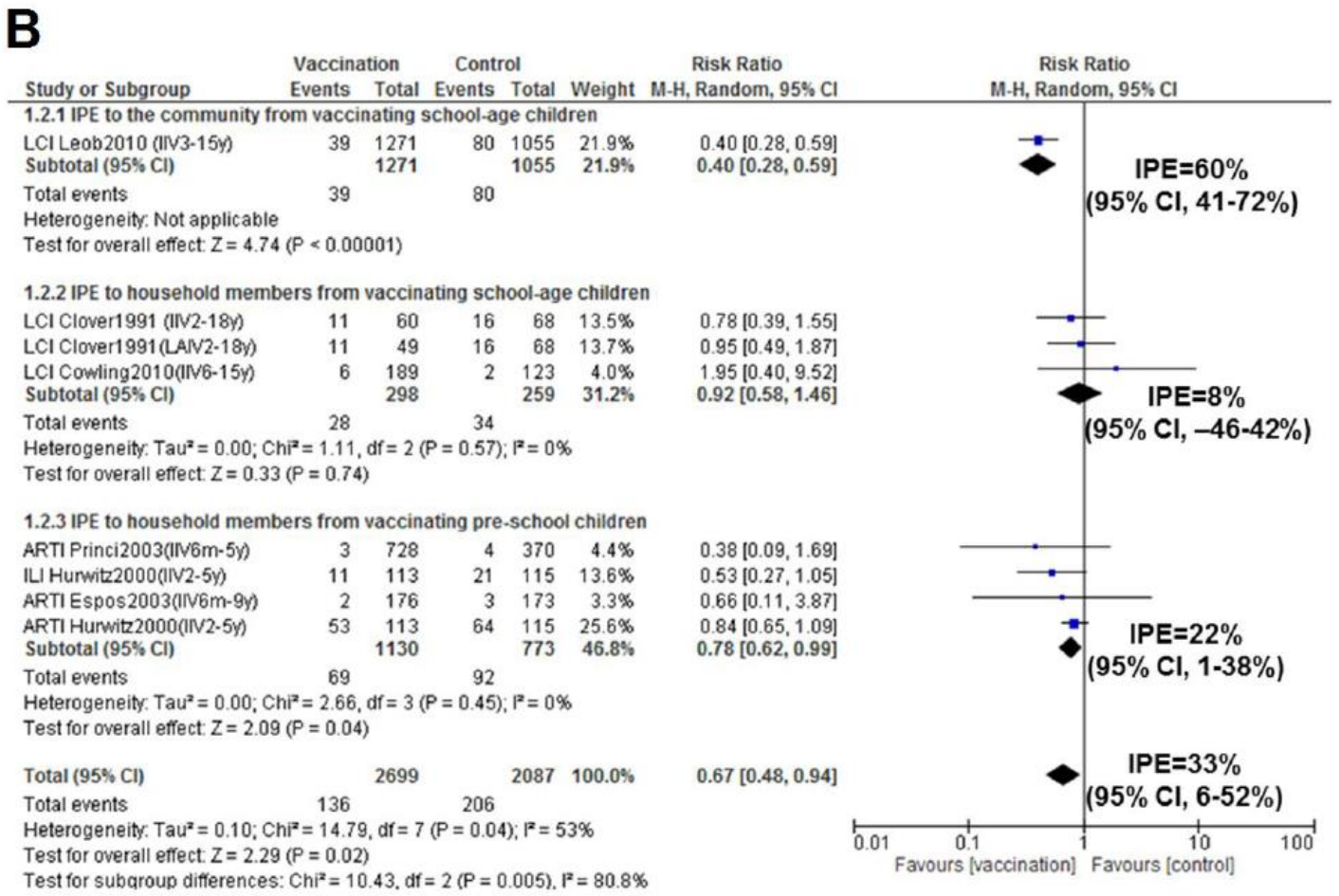
Effect of previous vaccination on vaccine efficacy in Influenza

Figure 4



Saito et al. Clin Infect Dis 2018

Systematic review and meta-analysis of indirect protection afforded by vaccinating children against seasonal influenza: implications for policy



Yin et al. CID 2017

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Systematic Review and Meta-analysis of Indirect Protection Afforded by Vaccinating Children Against Seasonal Influenza: Implications for Policy

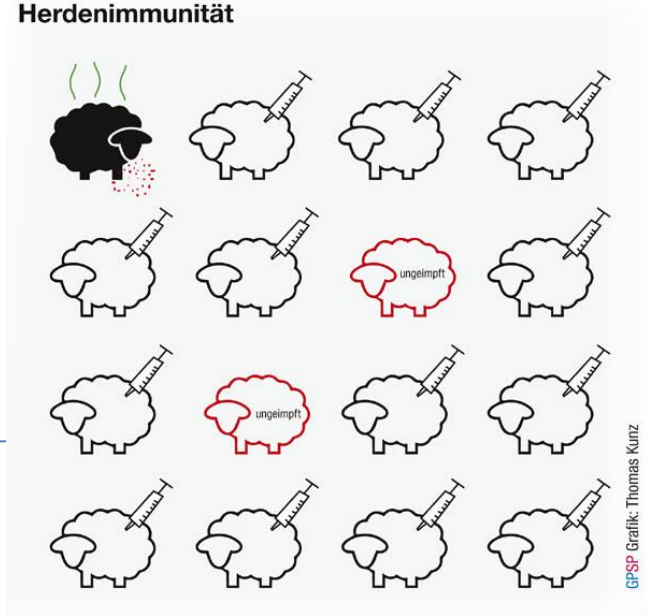
J. Kevin Yin,[1,2,3,a] Anita E. Heywood,[4] Melina Georgousakis,[1,2,3] Catherine King,[1,2,5] Clayton Chiu,[1,2,5] David Isaacs,[2,5] and Kristine K. Macartney[1,2,5]

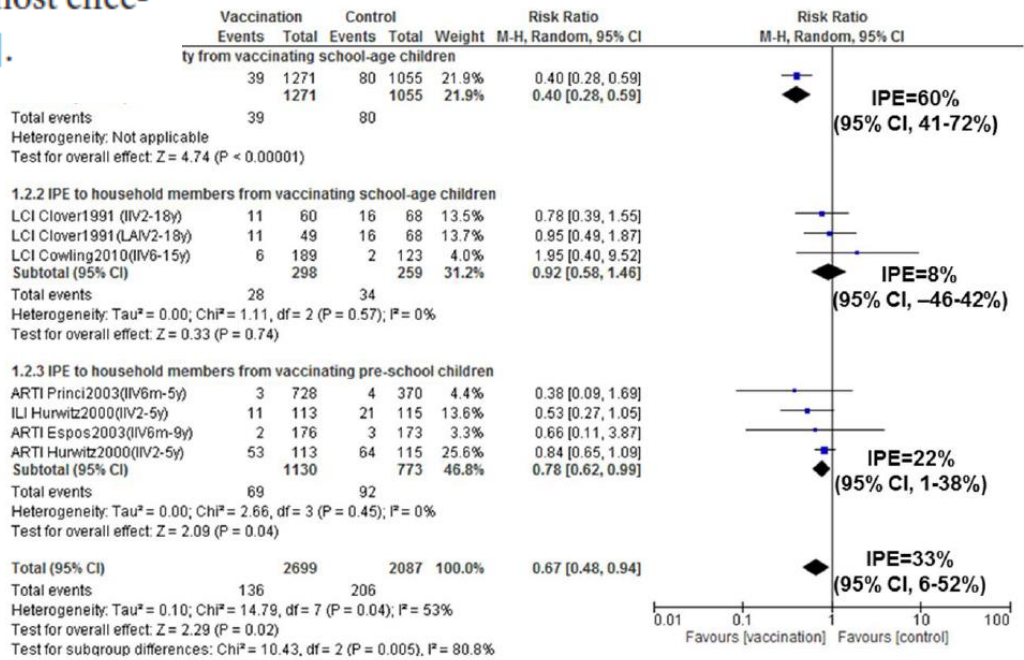
[1]National Centre for Immunisation Research and Surveillance, Westmead and [2]The Children's Hospital at Westmead, [3]Sydney School of Public Health, Faculty of Medicine, University of Sydney, [4]School of Public Health and Community Medicine, University of New South Wales, and [5]Discipline of Child and Adolescent Health, Faculty of Medicine, University of Sydney, New South Wales, Australia

In conclusion, our findings can inform decision making regarding the introduction and implementation of childhood influenza vaccination programs. However, unvaccinated contacts will still remain more susceptible than vaccinees; indirect protection cannot replace annual vaccination as the most effective way to prevent influenza at an individual level [1].

„Herdenschutz“

Herdenimmunität





Empfehlungen

- Impfplan 2019: Grundsätzlich ist die Influenza-Impfung für alle Personen ab dem vollendeten 6. Lebensmonat empfohlen, insbesondere für Ältere, chronisch Kranke, Personengruppen mit anderen Risikofaktoren und Personal im Gesundheitswesen.
- Herzversagen: 18% weniger Sterblichkeit
- Myokardinfarkt: 41-66% weniger Sterblichkeit, weniger Reinfarkt
- Asthma: 59-78% weniger im Spital
- Stroke: 18% weniger Stroke bei Risikopat.
- Hypertonie: 10% weniger Sterblichkeit (5 Saisonen)
- “herd immunity” durch Schulkinderimpfung

Danke Mr. Influenza