

Influenza Immunization in Patients with Heart Disease

AHA Representative

G. Marshall Lyon, MD
 Director of Transplant Infectious Disease
 Emory Transplant Center

Cause of Mortality: USA

Cause of death (based on ICD-10, 2004) and year	All ages ¹	55-64 years	65-74 years	75-84 years	85 years and over	Age-adjusted rate ³
All causes						
2009	793.8	871.9	1,928.8	4,774.4	13,021.2	741.1
2008	813.0	879.2	1,995.6	5,017.7	13,015.1	758.3
2007	803.6	877.7	2,011.3	5,011.6	12,946.5	760.2
2006	810.4	890.9	2,062.1	5,115.0	13,253.1	776.5
2005	825.9	906.9	2,137.1	5,260.0	13,798.6	798.8
2004	816.5	910.3	2,164.6	5,275.1	13,823.5	800.8
2003	841.9	940.9	2,255.0	5,463.1	14,593.3	832.7
2002	847.3	952.4	2,314.7	5,556.9	14,828.3	845.3
2001	848.5	964.6	2,353.3	5,582.4	15,112.8	854.5
2000	854.0	992.2	2,399.1	5,666.5	15,524.4	869.0
1999	857.0	1,005.0	2,457.3	5,714.5	15,554.6	875.6
Diseases of heart (I00-I09,I11,I13,I20-I51)						
2009	195.2	193.4	431.7	1,199.3	4,115.0	180.1
2008	202.9	198.0	449.8	1,276.7	4,175.7	186.5
2007	204.3	200.3	462.9	1,315.0	4,267.7	190.9
2006	211.0	207.3	490.3	1,383.1	4,480.8	200.2
2005	220.0	214.8	518.9	1,460.8	4,778.4	211.1
2004	222.2	218.8	541.6	1,506.3	4,895.9	217.0
2003	235.6	233.2	585.0	1,611.1	5,278.4	232.3
2002	241.7	241.5	615.9	1,677.2	5,466.8	240.8
2001	245.8	246.9	635.1	1,725.7	5,664.2	247.8
2000	252.6	261.2	665.6	1,780.3	5,926.1	257.6
1999	259.9	269.9	701.7	1,849.9	6,063.0	266.5

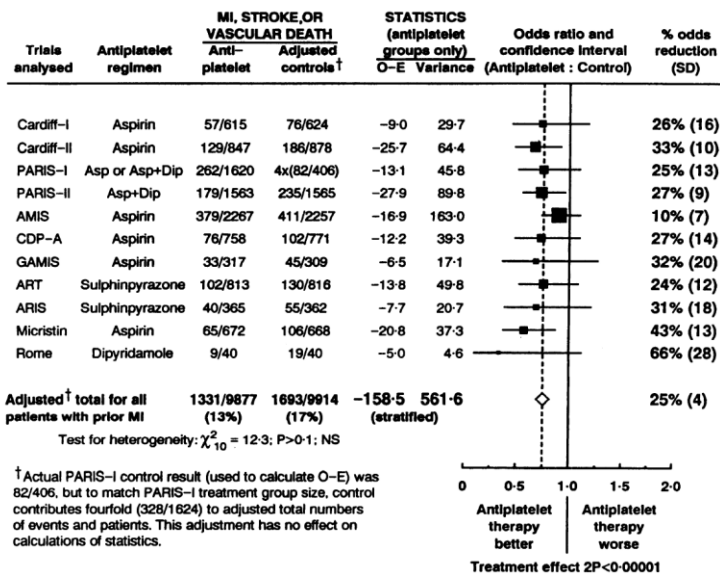
Cause of Mortality: USA

Cause of death (based on ICD-10, 2004) and year	All ages ¹	55-64 years	65-74 years	75-84 years	85 years and over	Age-adjusted rate ³
All causes						
2009	793.8	871.9	1,928.8	4,774.4	13,021.2	741.1
2008	813.0	879.2	1,995.6	5,017.7	13,015.1	758.3
2007	803.6	877.7	2,011.3	5,011.6	12,946.5	760.2
2006	810.4	890.9	2,062.1	5,115.0	13,253.1	776.5
2005	825.9	906.9	2,137.1	5,260.0	13,798.6	798.8
2004	816.5	910.3	2,164.6	5,275.1	13,823.5	800.8
2003	841.9	940.9	2,255.0	5,463.1	14,593.3	832.7
2002	847.3	952.4	2,314.7	5,556.9	14,828.3	845.3
2001	848.5	964.6	2,353.3	5,582.4	15,112.8	854.5
2000	854.0	992.2	2,399.1	5,666.5	15,524.4	869.0
1999	857.0	1,005.0	2,457.3	5,714.5	15,554.6	875.6
Diseases of heart (I00-I09,I11,I12,I20-I51)						
2009	195.2	193.4	431.7	1,199.3	4,115.0	180.1
2008	202.0	196.0	449.6	1,270.7	4,175.7	186.5
2007	204.3	200.3	462.9	1,315.0	4,267.7	190.9
2006	211.0	207.3	490.3	1,383.1	4,480.8	200.2
2005	220.0	214.8	518.9	1,460.8	4,778.4	211.1
2004	222.2	218.8	541.6	1,506.3	4,895.9	217.0
2003	235.6	233.2	585.0	1,611.1	5,278.4	232.3
2002	241.7	241.5	615.9	1,677.2	5,466.8	240.8
2001	245.8	246.9	635.1	1,725.7	5,664.2	247.8
2000	252.6	261.2	665.6	1,780.3	5,926.1	257.6
1999	259.9	269.9	701.7	1,849.9	6,063.0	266.5

Influenza Mortality: USA

○ CV Mortality = 195 crude / 180 age adj.

Cause of death (based on ICD-10, 2004) and year	All ages ¹	55-64 years	65-74 years	75-84 years	85 years and over	Age-adjusted rate ³
Influenza and pneumonia (J09-J18)						
2009 ⁴	17.5	11.9	30.1	105.9	413.5	16.2
2008	18.5	11.1	31.1	119.1	463.2	16.9
2007	17.5	9.6	28.7	114.1	463.2	16.2
2006	18.8	10.0	32.0	127.8	502.5	17.8
2005	21.3	11.3	35.5	142.2	593.9	20.3
2004	20.3	10.8	34.6	139.3	582.6	19.8
2003	22.4	11.2	37.3	151.1	666.1	22.0
2002	22.8	11.2	37.5	156.9	696.6	22.6
2001	21.8	10.7	36.3	148.5	685.6	22.0
2000	23.2	11.9	39.1	160.3	744.1	23.7
1999	22.8	11.0	37.2	157.0	751.8	23.5



BMJ, Jan 8, 1994

Effect of Flu or Pneumococcal Vaccination in Heart Disease

CDC Case-Control Study: 2006

- 750 cases with MI and 1735 controls from Group Health Cooperative in Seattle, WA
 - Controls matched on sex, age category, year, HTN
- Reviewed medical records of identified subjects

Heffelfinger et al., Hum Vacc, 2006

- In univariate analysis vaccination status not different between cases and controls.

Table 1 Characteristics of controls and cases

Characteristic	Controls (n = 1735)	MI Cases (n = 750)	P-value
Median age (years) ←	72.9	73.7	0.008
Males (%)	32.2	34.7	0.22
African-American race (%)	3.3	2.5	0.32
Median number of visits to Group Health Cooperative in last year ←	5	6	<0.001
Median duration of enrollment in Group Health Cooperative (years) ←	20.7	20.1	0.03
Treated hypertension (%)	65.7	67.7	0.33
Median systolic blood pressure (mm mercury)	140	140	0.33
Median cholesterol level (mg/dL) ←	226	235	<0.001
Diabetes mellitus (%) ←	10.4	23.1	<0.001
Treated hyperlipidemia (%)	7.1	8.8	0.14
Preexisting cardiovascular disease (%) ←	16.8	31.1	<0.001
Chronic obstructive pulmonary disease/asthma (%) ←	12.6	16.9	0.004
Current smoker (%) ←	10	16.3	<0.001
Past smoker (%)	38.9	41.9	0.14
Receipt of annual influenza vaccine prior to index date (%)	66	65.9	0.95
Past receipt of pneumococcal vaccine (%)	29.5	26.8	0.17

- No apparent protection when multivariable analysis performed (season)

FLUCAD & FLUVACS

○ FLUCAD

- Single center, randomized study at Polish MC in a single flu season, 2004-05
- Only enrolled atherosclerotic heart disease, not CHF

○ FLUVACS

- Randomized to receive flu vaccine
- Stratified into MI or undergoing PCI
- 301 patients overall

FLUCAD

Table 2 Primary and secondary study endpoints

Vaccine (n = 325)		Placebo (n = 333)		Hazard ratio (95% CI)	P-value
Number of events	Estimated 12-month cumulative event rate	Number of events	Estimated 12-month cumulative event rate		
Primary endpoint: cardiovascular death					
2	0.63%	2	0.76%	1.06 (0.15–7.56)	0.95
Secondary endpoints					
MACE					
9	3.00%	17	5.87%	0.54 (0.24–1.21)	0.13
Cardiovascular death					
2	0.63%	2	0.76%	1.06 (0.15–7.56)	0.95
Myocardial infarction (STEMI/NSTEMI)					
6	2.07%	9	3.23%	0.67 (0.24–1.88)	0.45
Coronary revascularization (PCI/CABG)					
1	0.32%	6	1.98%	0.17 (0.02–1.41)	0.10
Coronary ischaemic event					
16	6.02%	30	9.97%	0.54 (0.29–0.99)	0.047
MACE					
9	3.00%	17	5.87%	0.54 (0.24–1.21)	0.13
Hospitalization for myocardial ischaemia					
7	3.12%	13	4.35%	0.55 (0.22–1.37)	0.20

MACE, major adverse cardiac event.

FLUVACS

Table 1 Primary end-point rate at 12 months follow-up

	Group A (n=145) No. (%)	Group B (n=147) No. (%)	RR	P value
Cardiovascular death	9 (6)	26 (17)	0.34 (0.17–0.71)	0.002
Double end-point ^a	14 (10)	24 (16)	0.59 (0.32–1.10)	0.09
Triple end-point ^b	32 (22)	54 (37)	0.59 (0.4–0.86)	0.004

Table 2 Primary end-point Rates at 12 months follow-up for myocardial infarction patients

	Group A (n=96) No. (%)	Group B (n=97) No. (%)	RR	P value
Cardiovascular death	4 (4)	21 (21)	0.19 (0.07–0.53)	0.0002
Myocardial infarction	6 (6)	6 (6)	1.01 (0.34–3.02)	0.98
Re-hospitalization	8 (8)	14 (14)	0.58 (0.25–1.31)	0.18
Double end-point ^a	10 (10)	27 (28)	0.37 (0.19–0.72)	0.002
Triple end-point ^b	18 (19)	41 (42)	0.44 (0.27–0.71)	0.0003

Combined Flu/Pneumococcal Vaccination of Elderly: Hong Kong

- Enrolled >64yo patients; Observational
- Over 36K patients in 4 groups
 - TIV = Trivalent Influenza Vaccine
 - PPV = Polyvalent Pneumococcal Vaccine
 - TIV/PPV = Flu + Pneumococcal
 - Placebo

Hung et al, Clin Infect Dis, 2010

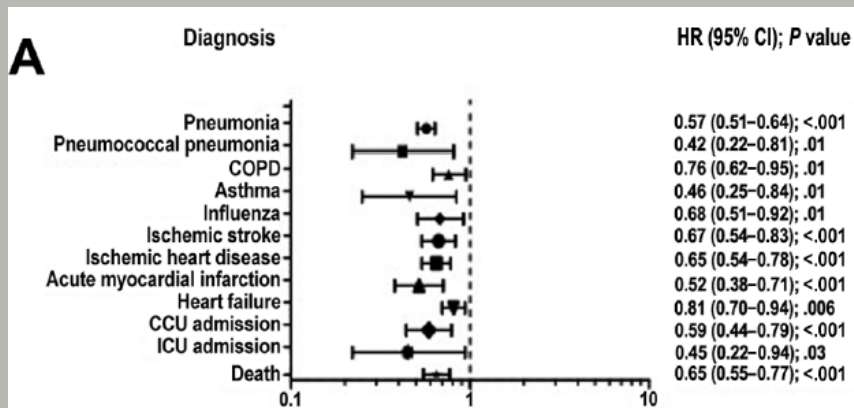
Combined Flu/Pneumococcal Vaccination of Elderly: Hong Kong

Characteristic	Unvaccinated persons (n = 25,393)	PPV-TIV group (n = 7292)	TIV-alone group (n = 2076)	PPV-alone group (n = 1875)	P
Age, median years (range)	75 (70–80)	77 (71–83)	75 (70–80)	75(71–80)	.81
→ Male sex	47	40	45	45	<.001
→ Asthma	2.2	2.2	2.2	2.8	.42
→ COPD	2.0	4.4	4.6	3.9	<.001
Ischemic heart disease	7.8	7.6	7.2	7.3	.64
Myocardial infarction	1.2	1.4	1.3	1.0	.33
Heart failure	7.9	7.6	7.9	8.7	.40
Hypertension	60.7	60.5	60.6	59.8	.91
Diabetes mellitus	24.1	25.5	24.6	24.5	.10
Ischemic stroke	7.1	7.8	7.5	7.4	.33
Chronic liver disease	0.3	0.2	0.1	0.3	.55
Chronic renal disease	2.3	2.4	2.5	2.6	.85
Cancer	5.9	5.2	6.7	5.4	.10
Smoker	13.5	14.2	13.8	14.8	.21

Hung et al, Clin Infect Dis, 2010

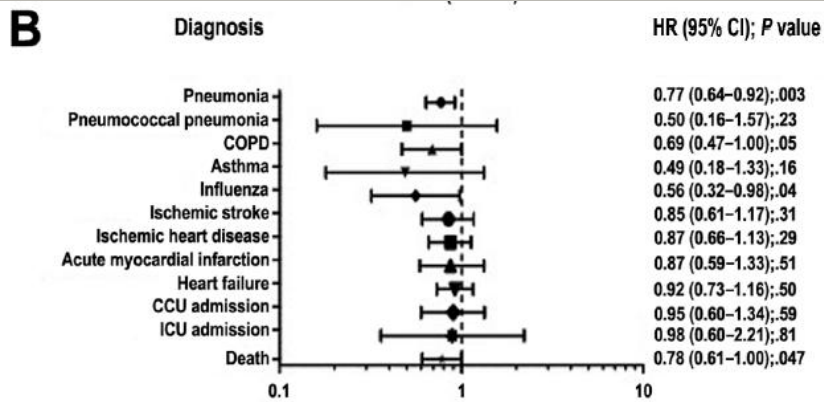
Results of Flu/Pneumococcal Vaccination in Elderly

TIV+PPV vs. unvaccinated



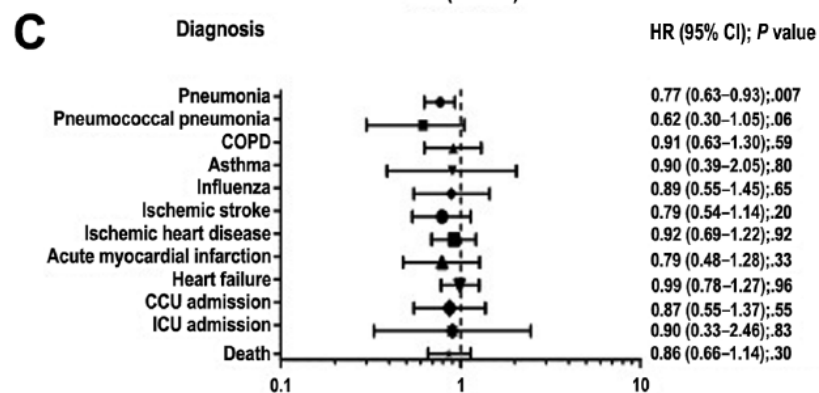
Results of Flu/Pneumococcal Vaccination in Elderly

Flu vaccine alone vs. unvaccinated

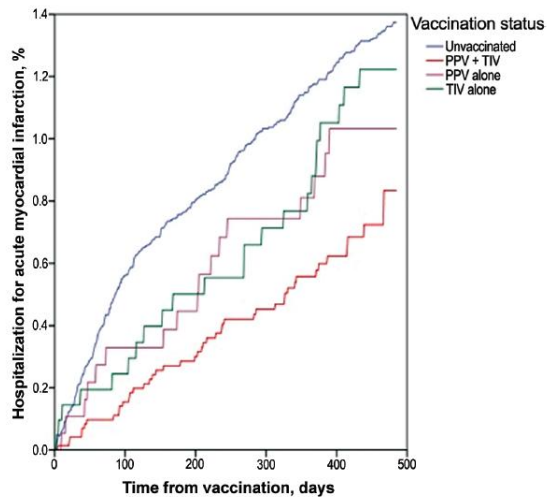


Results of Flu/Pneumococcal Vaccination in Elderly

Pneumococcal vaccine alone vs. unvaccinated



Hong Kong TIV+PPV Study



Thai Flu Vaccine Study in ACS: 2011

- Randomized, blinded study of flu vaccine in ACS patients in Thailand
- Slight imbalance in randomization
- Outcomes:
 - Major acute cardiovascular events
 - Mortality
 - Hospitalization

Eur Heart J: 2011

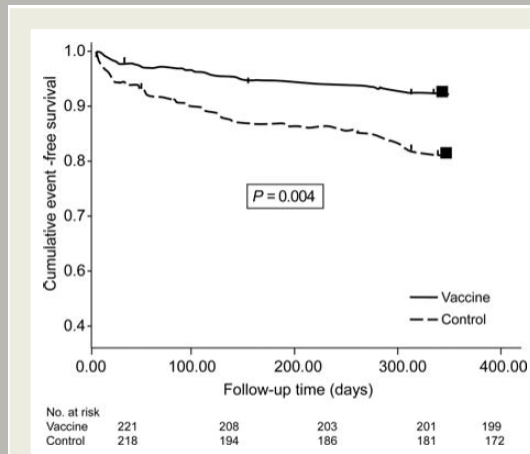
	Vaccine (n = 221)	Control (n = 218)	P-value
Age (years)	65 ± 9	67 ± 9	0.67
Male	135 (61)	114 (52)	0.07
HT	135 (63.1)	130 (61.6)	0.59
DM	64 (29.0)	70 (32.1)	0.53
Dyslipidemia	98 (44.3)	108 (49.5)	0.36
Chronic obstructive pulmonary disease	5 (2.4)	8 (3.9)	0.41
Smoking	28 (13.7)	20 (10.3)	0.36
Prior MI	10 (5.0)	8 (4.2)	0.81
CKD	10 (5.0)	10 (5.2)	0.59
Serum creatinine (mg/dL)	1.2 ± 0.4	1.2 ± 0.4	0.47
Type of ACS (%)			
STEMI	83 (37)	76 (35)	0.84
NSTEMI	102 (46)	104 (48)	
UA	36 (16)	38 (17)	
Reperfusion Rx in STEMI (n = 159)			
Primary PCI	30 (36.1)	23 (30.2)	0.21
Fibrinolytic Rx	36 (43.4)	33 (43.4)	
No reperfusion Rx	17 (20.5)	20 (26.3)	
Revascularization in NSTEMI/UA (n = 280)			
In admission	52 (37.7)	41 (28.2)	0.08
Delayed revascularization	21 (15.2)	23 (16.2)	
None	59 (42.8)	78 (54.9)	
LV EF (%)	46.4 (13.9)	46.1 (13.9)	0.93
Medication			
Aspirin	216 (97.7)	211 (96.8)	0.57
β-Blocker	168 (76.0)	157 (72.0)	0.38
ACE-I/ARB	142 (64.3)	115 (52.8)	0.02
Statin	192 (86.9)	177 (81.4)	0.19

Thai Flu Vaccine Study: Outcomes

Table 2 Effects of the influenza vaccine on major adverse cardiovascular events

Endpoints	Vaccine (n = 221)	Control (n = 218)	Unadjusted HR (95% CI)	P-value (unadjusted HR)	Adjusted HR (95% CI)	P-value (adjusted HR)
MACE, n (%)	21 (9.5)	42 (19.3)	0.70 (0.57–0.86)	0.004	0.67(0.51–0.86)	0.005
Death, n (%)	6 (2.7)	12 (5.5)	0.73 (0.50–1.03)	0.156	0.62 (0.34–1.12)	0.113
Hospitalization for ACS, n (%)	10 (4.5)	23 (10.6)	0.73 (0.55–0.91)	0.032	0.68 (0.47–0.98)	0.039
Hospitalization for HF, n (%)	4 (1.8)	10 (4.6)	0.69 (0.49–1.01)	0.111	0.62 (0.19–2.04)	0.136
Hospitalization for stroke, n (%)	1 (0.5)	0	—	1.0	—	—

Eur Heart J: 2011



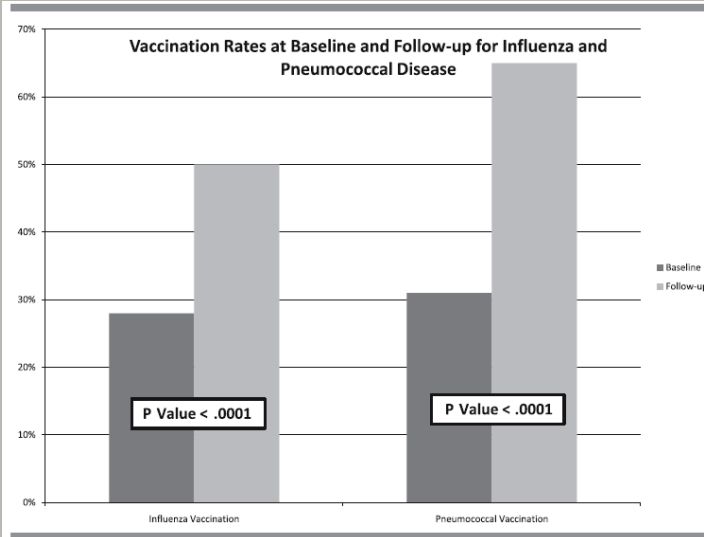
Eur Heart J: 2011

Increasing Vaccination Rates

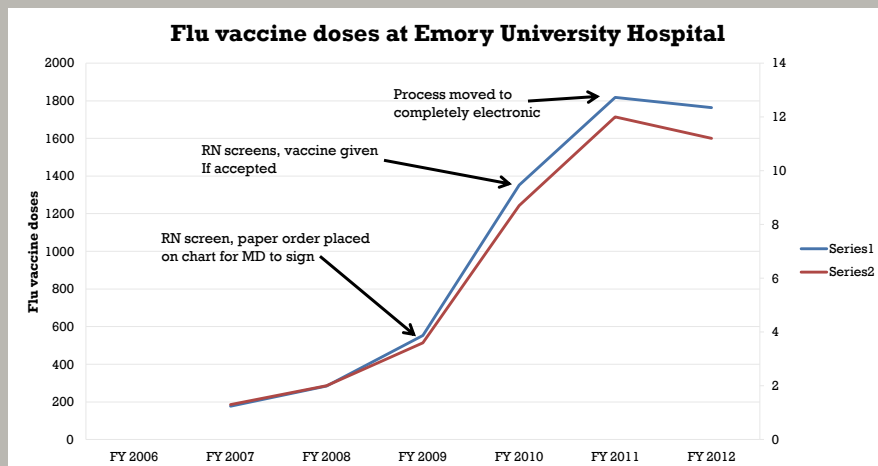
Prevalence of Flu or Pneumococcal Vaccination in Heart Failure

- **Single Center study in Miami**
 - Enrolled 549 patients with heart failure
 - Adopted a standard approach to vaccination with Flu and Pneumococcal
 - Front page check box
 - 18% refusal rate – primarily over concerns vaccine would give them disease
 - No association with demographic factors

Prevalence of Flu/Pna Vaccine in CHF



Emory Experience



Courtesy of Nathan Spell, EUH Quality Officer

Questions
