Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Association Between Hospitalization for Pneumonia and Subsequent Risk of Cardiovascular Disease

Vicente F. Corrales-Medina, MD, MSc; Karina N. Alvarez, MS; Lisa A. Weissfeld, PhD; Derek C. Angus, MD, MPH; Julio A. Chirinos, MD, PhD; Chung-Chou H. Chang, PhD; Anne Newman, MD, MPH; Laura Loehr, MD, PhD; Aaron R. Folsom, MD, MPH; Mitchell S. Elkind, MD; Mary F. Lyles, MD; Richard A. Kronmal, PhD; Sachin Yende, MD, MS

IMPORTANCE The risk of cardiovascular disease (CVD) after infection is poorly understood.

OBJECTIVE To determine whether hospitalization for pneumonia is associated with an increased short-term and long-term risk of CVD.

DESIGN, SETTINGS, AND PARTICIPANTS We examined 2 community-based cohorts: the Cardiovascular Health Study (CHS, n = 5888; enrollment age, ≥65 years; enrollment period, 1989–1994) and the Atherosclerosis Risk in Communities study (ARIC, n = 15 792; enrollment age, 45-64 years; enrollment period, 1987–1989). Participants were followed up through December 31, 2010. We matched each participant hospitalized with pneumonia to 2 controls. Pneumonia cases and controls were followed for occurrence of CVD over 10 years after matching. We estimated hazard ratios (HRs) for CVD at different time intervals, adjusting for demographics, CVD risk factors, subclinical CVD, comorbidities, and functional status.

EXPOSURES Hospitalization for pneumonia.

MAIN OUTCOMES AND MEASURES Incident CVD (myocardial infarction, stroke, and fatal coronary heart disease).

RESULTS Of 591 pneumonia cases in CHS, 206 had CVD events over 10 years after pneumonia hospitalization. Compared with controls, CVD risk among pneumonia cases was highest during the first year after hospitalization and remained significantly higher than among controls through 10 years. In ARIC, of 680 pneumonia cases, 112 had CVD events over 10 years after hospitalization. After the second year, CVD risk among pneumonia cases was not significantly higher than among controls.

	Pneumonia Cases	Controls	HR (95% CI)
CHS			
No. of participants	591	1182	
CVD events			
0-30 d	54	6	4.07 (2.86-5.27)
31-90 d	11	9	2.94 (2.18-3.70)
91 d-1 y	22	55	2.10 (1.59-2.60)
9-10 y	4	12	1.86 (1.18-2.55)
ARIC			
No. of participants	680	1360	
CVD events			
0-30 d	4	3	2.38 (1.12-3.63)
31-90 d	4	0	2.40 (1.23-3.47)
91 d-1 y	11	8	2.19 (1.20-3.19)
1-2 y	8	7	1.88 (1.10-2.66)

CONCLUSIONS AND RELEVANCE Hospitalization for pneumonia was associated with increased short-term and long-term risk of CVD, suggesting that pneumonia may be a risk factor for CVD.

JAMA. 2015;313(3):264-274. doi:10.1001/jama.2014.18229

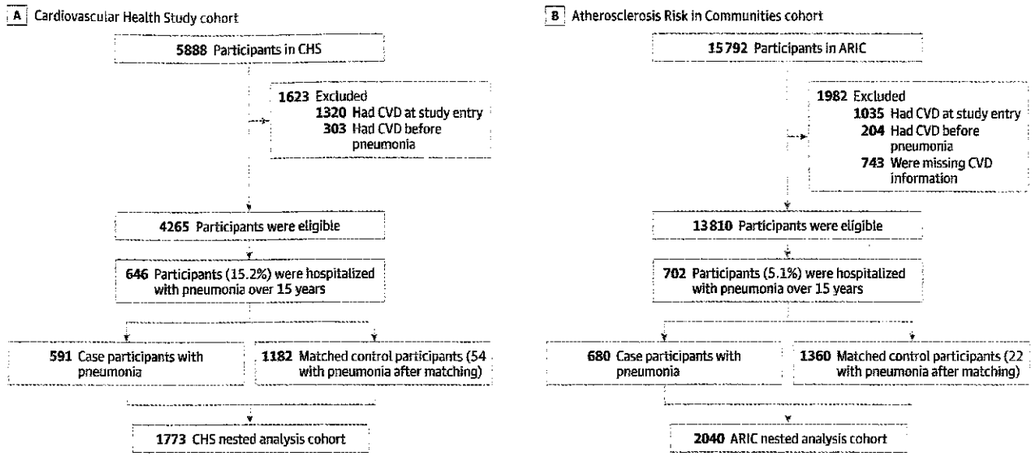
Supplemental content at jama.com

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Sachin Yende, MD, MS, The Clinical Research, Investigation, and Systems Modeling of Acute Illness (CRISMA) Center, Department of Critical Care Medicine, University of Pittsburgh, 606D Scaife Hall, 3550 Terrace St, Pittsburgh, PA 15261 (yendes@upmc.edu).

Section Editor: Derek C. Angus, MD, MPH, Associate Editor, *JAMA* (angusdc@upmc.edu).

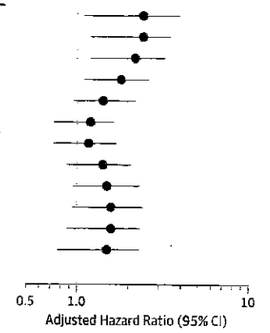
Figure 1. Selection of the Nested Analysis Cohorts From the Cardiovascular Health Study and the Atherosclerosis Risk in Communities Study



ARIC indicates Atherosclerosis Risk in Communities study; CHS, Cardiovascular Health Study; CVD, cardiovascular disease. We used an incidence density approach to match pneumonia cases to controls. Controls were not hospitalized with pneumonia when matched or prior to matching but could develop pneumonia at a later time during follow-up; thus, 54 controls in CHS and 22 controls in ARIC developed pneumonia after matching.

Figure 4. Risk of Cardiovascular Disease (CVD) Events After Hospitalization for All Pneumonia in the Atherosclerosis Risk in Communities Study

Time Intervals After Pneumonia	Pneumonia Cases: No. of CVD Events/ No. at Risk (%)	Controls: No. of CVD Events/ No. at Risk (%)	Hazard Ratio (95% CI): Unadjusted	Hazard Ratio (95% CI): Adjusted
0-30 d	4/426 (0.9)	3/917 (0.3)	3.30 (1.97-4.62)	2.38 (1.12-3.63)
31-90 d	4/380 (1.1)	0/913 (0)	3.23 (2.03-4.43)	2.40 (1.23-3.47)
91 d-1 y	11/360 (3.1)	8/912 (0.9)	3.01 (1.98-4.05)	2.19 (1.20-3.19)
1-2 y	8/311 (2.6)	7/896 (0.8)	2.59 (1.78-3.39)	1.88 (1.10-2.66)
2-3 y	8/285 (2.8)	14/879 (1.6)	2.06 (1.46-2.67)	1.52 (0.92-2.11)
3-4 y	5/261 (1.9)	19/859 (2.2)	1.74 (1.24-2.23)	1.26 (0.77-1.74)
4-5 y	2/243 (0.8)	15/827 (1.8)	1.64 (1.17-2.10)	1.23 (0.76-1.70)
5-6 y	5/229 (2.2)	6/795 (0.8)	1.86 (1.31-2.40)	1.45 (0.89-2.01)
6-7 y	7/213 (3.3)	11/758 (1.5)	1.91 (1.32-2.51)	1.59 (0.93-2.24)
7-8 y	6/190 (3.2)	9/699 (1.3)	1.87 (1.24-2.50)	1.66 (0.93-2.39)
8-9 y	6/165 (3.6)	7/630 (1.1)	1.82 (1.16-2.48)	1.67 (0.88-2.47)
9-10 y	3/136 (2.2)	12/529 (2.3)	1.75 (1.05-2.45)	1.54 (0.74-2.34)



The analysis included 2040 participants (680 pneumonia cases and 1360 controls). The number of participants at risk and those who developed an event over each time interval were estimated using a complete case approach and participants with missing data for covariates were excluded. The estimates were adjusted for age, sex, race, hypertension, diabetes mellitus, plasma total, high-density lipoprotein and low-density lipoprotein cholesterol, smoking, alcohol abuse,[26] atrial fibrillation, chronic kidney disease,[27] presence of diagnostic Q waves in electrocardiogram, peripheral arterial disease (defined by ankle brachial index <0.9), carotid artery wall thickness, presence of carotid atherosclerotic plaque by ultrasound, and percentage of predicted forced expiratory volume in first second of expiration (FEV_1) measured by spirometry. Adjusted hazard ratios were calculated using baseline (at study entry) covariates measurements.