

## WEB MATERIAL

### **Associations of High-Sensitivity Cardiac Troponin and Natriuretic Peptide With Subsequent Risk of Infection in Persons Without Cardiovascular Disease: The Atherosclerosis Risk in Communities Study**

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**Web Table 1. List of ICD-9 codes and corresponding diagnosis**

<b>ICD-9</b>	<b>Referred disease description</b>
001–139	Infectious and parasitic diseases
254.1	Abscess of thymus
320–326	Diseases of the nervous system
331.81	Rye's syndrome
372–372.39	Conjunctivitis
373.0–373.2	Inflammation of eyelids (Blepharitis, Chalazion)
382–382.4	Suppurative and unspecified otitis media
383	Mastoiditis
386.33	Suppurative labyrinthitis
386.35	Viral labyrinthitis
388.6	Otorrhea
390–393	Rheumatic Fever
421–421.1	Acute and subacute endocarditis
422	Acute myocarditis
422.91–422.93	Acute myocarditis, idiopathic
460–466	Acute respiratory infections
472–474.0	Chronic pharyngitis and nasopharyngitis
475–476.1	Peritonsillar abscess
478.21–478.24	Other diseases of upper respiratory tract
478.29	Other diseases of upper respiratory tract
480–486	Pneumonia
490	Bronchitis, not specified as acute or chronic
491.1	Mucopurulent chronic bronchitis
494	Bronchiectasis
510	Empyema
511	Pleurisy
513	Abscess of lung and mediastinum
518.6	Allergic bronchopulmonary aspergillosis
519.01	Infection of tracheostomy stoma
522.5	Periapical abscess without sinus
522.7	Periapical abscess with sinus
527.3	Abscess of salivary gland
528.3	Cellulitis and abscess of oral soft tissues
540–542	Appendicitis
566–567.9	Abscess of anal and rectal regions
569.5	Abscess of intestine
572–572.1	Liver abscess and sequelae of chronic liver disease
573.1–573.3	Hepatitis, toxic
575–575.12	Other disorders of gallbladder
590–590.9	Infections of kidney
595–595.4	Cystitis
597–597.89	Urethritis, not sexually transmitted, and urethral syndrome
598	Stricture, urethral, unspecified infection
599	Urinary tract infection, unspecified/pyuria
601–601.9	Inflammatory diseases of prostate
604–604.9	Orchitis and epididymitis
607.1	Balanitis

607.2	Other inflammatory disorders of penis
608	Seminal vesiculitis
608.4	Other inflammatory disorders of male genital organs
611	Inflammatory disease of breast
614–616.1	Inflammatory disease of ovary fallopian tube pelvic cellular tissue and peritoneum
616.3–616.4	Abscess of Bartholin's gland, Other abscess of vulva
616.8	Other specified inflammatory diseases of cervix vagina and vulva
670	Major puerperal infection
680–686.9	Infections of skin and subcutaneous tissue
706	Acne varioliformis
711–711.9	Arthropathy associated with infections
730–730.3	Osteomyelitis, periostitis, and other infections involving bone
730.8–730.9	Osteomyelitis, periostitis, and other infections involving bone
790.7	Bacteremia (not septicemia)
790.8	Viremia, unspecified
996.60–996.69	Infection and inflammatory reaction due to internal prosthetic device implant and graft
997.62	Infection of amputation stump, unspecified extremity
998.5	Postoperative infection not elsewhere classified
999.3.	Other infection due to medical care not elsewhere classified

\*The definitions of infection-related ICD-9 codes were based on the analytical methods used in United States Renal Data System (USRDS). Details are available at the USRDS website ([http://www.usrds.org/2014/view/v2\\_00\\_appx.aspx](http://www.usrds.org/2014/view/v2_00_appx.aspx).)

**Web Table 2. Adjusted hazard ratios of hospitalization with infection accounting for incident CVD among participants without prevalent CVD**

	Adjusted hazard ratio (95%CI)		
	Censored for incident CVD	Sub-hazard model with incident CVD as a competing risk	Adjusted for incident CVD as a time-varying variable
<b>hs-cTnT (ng/L)</b>			
Categorical			
< 3	1 [Reference]	1 [Reference]	1 [Reference]
4-5	1.08 (0.97, 1.20)	1.09 (0.98, 1.21)	1.10 (1.00, 1.22)
6-8	1.13 (1.01, 1.26)	1.12 (1.01, 1.26)	1.13 (1.02, 1.25)
9-13	1.31 (1.15, 1.49)	1.26 (1.11, 1.44)	1.23 (1.09, 1.39)
≥ 14	1.47 (1.24, 1.75)	1.32 (1.10, 1.59)	1.39 (1.19, 1.62)
Continuous			
Per log(hs-cTnT)	1.23 (1.14, 1.32)	1.16 (1.07, 1.25)	1.17 (1.10, 1.26)
<b>NTproBNP (pg/mL)</b>			
Categorical			
< 48.1	1 [Reference]	1 [Reference]	1 [Reference]
48.1-80.1	1.07 (0.97, 1.19)	1.07 (0.96, 1.19)	1.01 (0.91, 1.12)
80.2-137.2	1.19 (1.07, 1.33)	1.15 (1.03, 1.28)	1.08 (0.98, 1.19)
137.2-248.0	1.20 (1.05, 1.36)	1.12 (0.98, 1.28)	1.10 (0.97, 1.24)
≥ 248.1	1.59 (1.35, 1.87)	1.26 (1.06, 1.51)	1.37 (1.18, 1.59)
Continuous			
Per log(NTproBNP)	1.09 (1.05, 1.14)	1.04 (1.00, 1.08)	1.04 (1.01, 1.08)

Abbreviations: CVD, cardiovascular disease, hs-cTnT, high sensitivity cardiac troponin T; NTproBNP, N-terminal pro B-type natriuretic peptide.

**Web Table 3. Crude incidence rates and adjusted hazard ratios for hospitalization with infection using a cut-off for hs-cTnT of <5 ng/L**

hs-cTnT category (ng/L)	n	Events, n	Incidence rate per 1,000 person-y (95% CI)	Adjusted hazard ratio (95% CI)
< 5	4302	1442	24.8 (23.5, 26.1)	1 [Reference]
5-8	2503	1002	31.8 (29.9, 33.8)	1.13 (1.04, 1.24)
9-13	1028	480	40.3 (36.9, 44.1)	1.27 (1.13, 1.42)
≥ 14	504	263	52.8 (46.8, 59.6)	1.46 (1.26, 1.70)

Abbreviations: CVD, cardiovascular disease, hs-cTnT, high sensitivity cardiac troponin T; NTproBNP, N-terminal pro B-type natriuretic peptide.

**Web Table 4. Crude incidence rates and adjusted hazard ratios for hospitalization with infection restricting to 1,664 cases of primary diagnosis of infection**

	n	Events, n	Incidence rate per 1,000 person-y (95% CI)	Adjusted hazard ratio (95% CI)
Overall sample				
Without prevalent CVD at baseline	8,337	1398	12.0 (11.4, 12.6)	1 [Reference]
Prevalent CVD at baseline	1,066	266	21.3 (18.9, 24.1)	1.28 (1.11, 1.49)
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Without prevalent CVD at baseline				
hs-cTnT (ng/L)				
Categorical				
< 3	3,401	460	9.2 (8.4, 10.1)	1 [Reference]
4-5	1,717	252	10.2 (9.0, 11.5)	1.01 (0.86, 1.18)
6-8	1,687	328	14.2 (12.8, 15.9)	1.33 (1.14, 1.54)
9-13	1,028	225	16.9 (14.9, 19.3)	1.37 (1.15, 1.63)
≥ 14	504	133	23.3 (19.7, 27.7)	1.69 (1.35, 2.12)
Continuous				
Per log(hs-cTnT)				1.30 (1.17, 1.44)
NTproBNP (pg/mL)				
Categorical				
< 48.1	3,378	479	9.8 (8.9, 10.7)	1 [Reference]
48.1-80.1	1,712	266	10.9 (9.7, 12.3)	1.07 (0.92, 1.24)
80.2-137.1	1,691	301	12.8 (11.4, 14.3)	1.23 (1.06, 1.43)
137.2-248.0	1,034	214	15.5 (13.5, 17.7)	1.38 (1.16, 1.64)
≥ 248.1	522	138	22.4 (19.0, 26.5)	1.74 (1.41, 2.14)
Continuous				
Per log(NTproBNP)				1.14 (1.08, 1.20)

Abbreviations: CVD, cardiovascular disease, hs-cTnT, high sensitivity cardiac troponin T; NTproBNP, N-terminal pro B-type natriuretic peptide.

**Web Table 5. Adjusted hazard ratios of hospitalization with infection in subgroups by age, sex, race, and status of diabetes and CKD**

Subgroup		No. of subjects	Participants without prevalent CVD at baseline (n=8,435)			
			hs-cTnT per log(hs-cTnT) HR (95% CI)	p-interaction	NTproBNP per log(NTproBNP) HR (95% CI)	p-interaction
Age, y	<65	5,325	1.29 (1.18, 1.42)	0.32	1.11 (1.06, 1.16)	0.14
	≥65	3,012	1.34 (1.22, 1.47)		1.18 (1.12, 1.25)	
Sex	Male	3,445	1.35 (1.23, 1.47)	0.87	1.11 (1.06, 1.17)	0.15
	Female	4,892	1.29 (1.17, 1.41)		1.17 (1.11, 1.24)	
Race	White	6,483	1.28 (1.19, 1.38)	0.33	1.17 (1.12, 1.22)	0.12
	African-American	1,854	1.39 (1.21, 1.60)		1.06 (0.99, 1.13)	
Diabetes	No	7,144	1.31 (1.22, 1.42)	0.14	1.13 (1.09, 1.18)	0.90
	Yes	1,193	1.30 (1.14, 1.47)		1.15 (1.06, 1.24)	
CKD	No	7,443	1.28 (1.18, 1.38)	0.31	1.13 (1.09, 1.18)	0.87
	Yes	894	1.41 (1.23, 1.63)		1.14 (1.05, 1.25)	

\*CKD was defined as estimated glomerular filtration <60 ml/min/1.73m<sup>2</sup> or urinary albumin-to-creatinine ratio ≥30 mg/g.

Abbreviations: CKD, chronic kidney disease; CVD, cardiovascular disease, hs-cTnT, high sensitivity cardiac troponin T; NTproBNP, N-terminal pro B-type natriuretic peptide.

**Web Table 6. Crude mortality rate and adjusted hazard ratios of infection-related deaths**

	n	Events, n	Mortality rate per 1,000 person-y (95% CI)	Adjusted hazard ratio (95% CI)
Overall sample				
Without prevalent CVD at baseline	8,337	523	4.2 (3.9, 4.6)	1 [Reference]
Prevalent CVD at baseline	1,066	143	10.6 (9.0, 12.5)	1.57 (1.27, 1.93)
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Without prevalent CVD at baseline				
hs-cTnT (ng/L)				
Categorical				
< 3	3,401	132	2.5 (2.1, 3.0)	1 [Reference]
4-5	1,717	95	3.7 (3.0, 4.5)	1.17 (0.89, 1.53)
6-8	1,687	133	5.4 (4.6, 6.4)	1.53 (1.19, 1.98)
9-13	1,028	96	6.7 (5.5, 8.2)	1.46 (1.09, 1.95)
≥ 14	504	67	10.6 (8.4, 13.5)	1.91 (1.34, 2.71)
Continuous				
Per log(hs-cTnT)				1.38 (1.18, 1.61)
NTproBNP (pg/mL)				
Categorical				
< 48.1	3,378	160	3.1 (2.7, 3.6)	1 [Reference]
48.1-80.1	1,712	95	3.7 (3.0, 4.6)	1.14 (0.88, 1.48)
80.2-137.1	1,691	116	4.7 (3.9, 5.6)	1.38 (1.07, 1.77)
137.2-248.0	1,034	82	5.6 (4.5, 6.9)	1.42 (1.07, 1.89)
≥ 248.1	522	70	10.4 (8.2, 13.1)	2.14 (1.55, 2.94)
Continuous				
Per log(NTproBNP)				1.23 (1.13, 1.35)

\*The model was adjusted for age, sex, race, body mass index, smoking status, alcohol consumption, years of education, physical inability, high sensitivity C-reactive protein, status of CKD, medication use of aspirin, anticoagulant, and statin, and medical history of hypertension, diabetes, cancer, and chronic obstructive pulmonary disease.

Abbreviations: CVD, cardiovascular disease, hs-cTnT, high sensitivity cardiac troponin T; NTproBNP, N-terminal pro B-type natriuretic peptide.



**Web Figure 1. Estimates for the cumulative incidence of hospitalization with infection accounting for death as a competing risk event stratified by (A) hs-cTnT and (B) NTproBNP categories: The ARIC Study, 1996-2013**

