



Question: What is the relationship between sodium intake and risk of cardiovascular disease?

Table 1. Summary of studies examining the relationship between sodium and risk of cardiovascular disease (CVD)

Author, Year Study Design; Location (Trial or Cohort Name) Risk of Bias*	Sample Size (Gender; Age) Duration of Follow-up	Description of Sodium Assessment and Intake	Results	Summary of Findings
Cook, 2014 Prospective Cohort Study (PCS); US (Trials of Hypertension Prevention) Risk of Bias: 0/28	N=2,275 (31% female); Age ~43y 10-15y Cases: 193 cardiovascular events or deaths	24-hour urine collections (3-7 times) were used to calculate estimated mean sodium excretion. Mean sodium excretion was 3,630mg/d. Subjects were categorized as: <2,300mg 2,300-3,600mg 3,600-4,800mg (referent category) >4,800mg	There were no significant differences in CVD risk based on category of sodium intake (NS). When sodium was considered as a continuous term, there was a 17% increase in CVD risk per 1,000mg/d increase in sodium (P=0.054).	Higher sodium intake was associated with increased risk of CVD.
Joosten, 2014 PCS; The Netherlands (Prevention of Renal and Vascular End-stage Disease (PREVEND) Study) Risk of Bias: 4/28	N=7,543 (51% women; Age ~48y) 10.5y Cases: 452 coronary heart disease (CHD) events	24-hour urine collections (2 consecutive days) were used to estimate sodium excretion. Mean sodium excretion was 137mmol (~3,360mg). Subjects categorized as (women/men): <95/<122mmol (<2,185/<2,806mg) 95-121/122-154mmol (2,185-2,783/2,806-3,542mg) 122-151/155-190mmol (2,806-3,473/3,565-4,370mg) >151/>190mmol (>3,473/>4,370mg)	There were no significant associations between sodium excretion and CHD risk in the full sample (NS). Increased sodium excretion (as a continuous variable) was associated with increased CHD risk among hypertensives (per 1g/d increase, HR=1.14, 95% CI=1.01-1.28, P=0.03), but not in normotensives or when analyzed as a categorical variable. Increased sodium excretion (as a continuous variable) was associated with increased CHD risk in those with NT-proBNP among the sex-specific median (per 1g/d increase, HR=1.16, 95% CI=1.03-1.30, P=0.01), but not in those below the median.	Overall, there was no association between sodium excretion and risk of CHD. However, higher sodium excretion was associated with higher CHD risk among hypertensives and those with elevated NT-proBNP.
O'Donnell, 2014 PCS; Argentina, Bangladesh,	N=101,945 (58% women; Age ~51y)	A fasting morning urine sample was collected at baseline, and used to estimate 24-hour urinary sodium excretion (using the Kawasaki formula).	7g/d vs. 4-5.99 g/d Sodium Excretion 7g/d was associated with increased risks of:	An estimated sodium intake between 3-6g/d was associated with a lower risk of death and cardiovascular



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<p>Brazil, Canada, Chile, China, Colombia, India, Iran, Malaysia, Pakistan, Poland, South Africa, Sweden, Turkey, United Arab Emirates, Zimbabwe (Prospective Urban Rural Epidemiology Study)</p> <p>Risk of Bias: 12/26</p>	<p>3.7y</p> <p>Cases: 3,317 CVD events or death (650 CVD deaths, 857 myocardial infarctions, 872 strokes, 261 with heart failure)</p>	<p>Mean sodium excretion was 4.93g/d.</p> <p>Subject categorized as:</p> <p><3g/d 3-3.99g/d 4-5.99g/d (referent category) 6-6.99g/d >7g/d</p>	<ul style="list-style-type: none"> • <i>Primary composite CVD:</i> (OR=1.15; 95% CI: 1.02-1.30) • <i>Death, any cause:</i> (OR=1.25; 95% CI: 1.07-1.48) • <i>A major cardiovascular event:</i> (OR=1.16; 95% CI: 1.01-1.34) • <i>Death from CVD:</i> (OR=1.54; 95% CI: 1.21-1.95) • <i>Stroke (death or hospitalization):</i> (OR=1.29; 95% CI: 1.02-1.63) <p>The associations for composite CVD, major cardiovascular events, and stroke resulting in death or hospitalization were not significant after adjusting for blood pressure or prior hypertension, but death from any cause remained significant.</p> <p>3g/d vs. 4-5.99 g/d Sodium Excretion</p> <p>3g/d was associated with increased risks of:</p> <ul style="list-style-type: none"> • <i>Primary composite CVD:</i> (OR=1.27; 95% CI: 1.12-1.44) • <i>Death, any cause:</i> (OR=1.38; 95% CI: 1.15-1.66) • <i>A major cardiovascular event:</i> (OR=1.30; 95% CI: 1.13-1.50) • <i>Death from CVD:</i> (OR=1.77; 95% CI: 1.36-2.31) • <i>Stroke (death or hospitalization):</i> (OR=1.37; 95% CI: 1.07-1.76) <p>These associations remained significant after adjusting for blood pressure or prior hypertension.</p>	<p>events than was either a higher (>7g/d) or lower (3g/d) estimated level of intake.</p>
<p>Pfister, 2014</p>	<p>N=19,857</p>	<p>Casual urine specimen at baseline; formula</p>	<p>Risk of heart failure was highest in the lowest and</p>	<p>Risk of heart failure was</p>



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PCS; UK (European Prospective Investigation into Cancer and Nutrition EPIC- Norfolk) Risk of Bias: 6/26	(55% female); Age~58y 12.9y Cases: 1,210 (137 fatal, 1,073 non-fatal) incident cases of heart	(from the Japanese Society of Hypertension) was used to estimate 24-h urinary sodium excretion Median estimated 24-h urinary sodium excretion: 158mmol/d (~3,634mg) Subjects were categorized by quintiles of estimated 24-h urinary sodium excretion: 115mmol/d (~2,645mg) 145mmol/d (~3,335mg) (Referent category) 163mmol/d (~3,749mg) 182mmol/d (~4,186mg) 218mmol/d (~5,014mg)	highest quintiles of estimated urinary sodium excretion: <ul style="list-style-type: none"> • Q1: 115mmol/d (~2,645mg): HR=1.30 (95% CI=1.08-1.55) • Q2: 145mmol/d (~3,335mg): HR=1.00 (reference) • Q3: 163mmol/d (~3,749mg): HR=1.03 (95% CI=0.85-1.24) • Q4: 182mmol/d (~4,186mg): HR=0.99 (95% CI=0.82-1.19) • Q5: 218mmol/d (~5,014mg): HR=1.22 (95% CI=1.02-1.46) 	highest in the lowest (~2,645mg) and highest quintiles (~5,014mg) of estimated urinary sodium excretion, compared to the reference category (~3,335mg).