

Case-control and Cross-sectional Studies

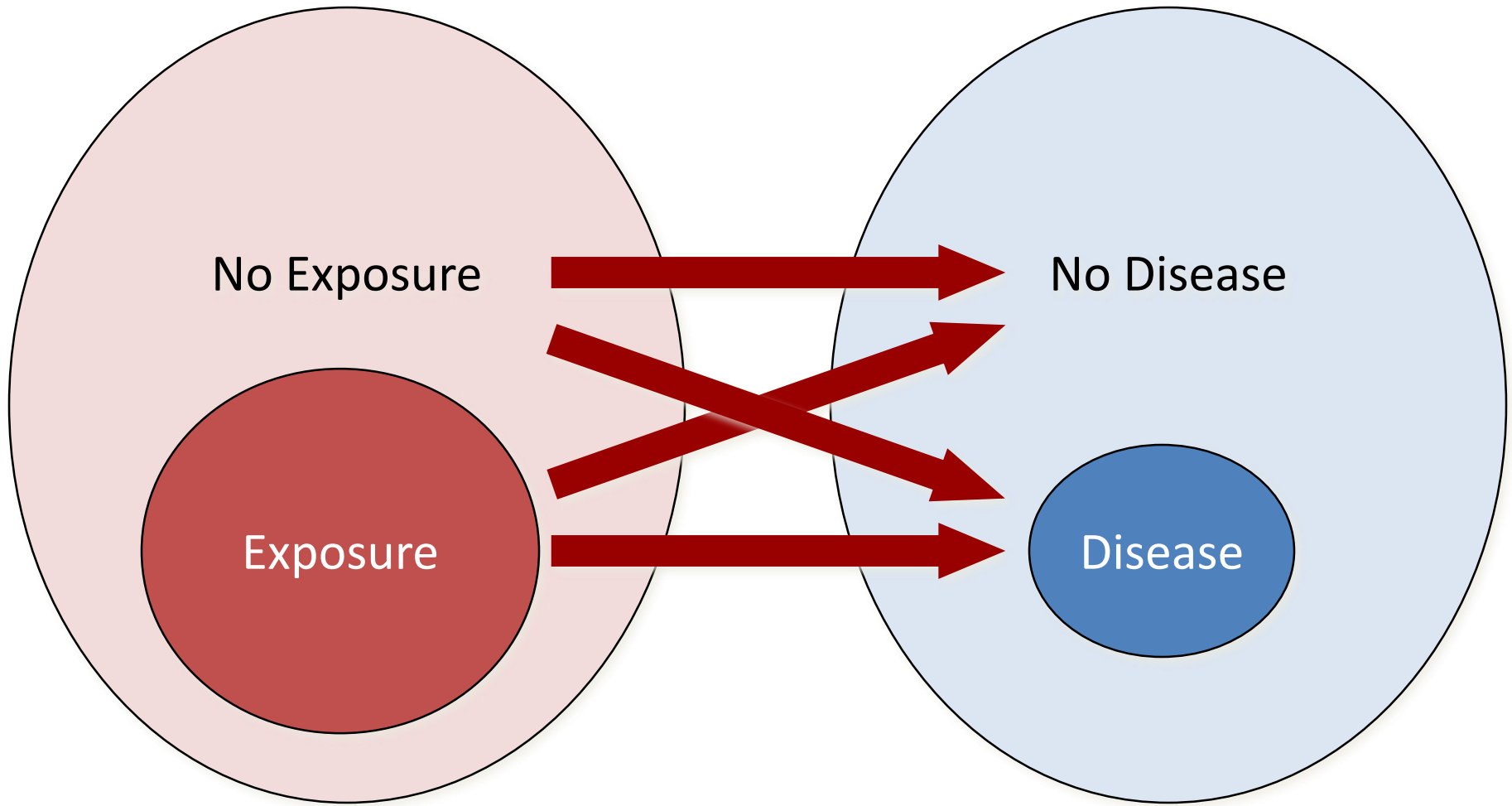
W. Ray Kim, MD
Professor and Chief
Gastroenterology and Hepatology
Stanford University
School of Medicine



Epidemiology: Study of Causation

Design	Metric	Statistics
Observational Studies		
Cohort	Time to event	Proportional hazards (Cox) regression
Case-control	Difference in proportion	Logistic regression
	Difference in distribution	Linear regression
Cross-sectional	Difference in proportion	Chi-square
	Difference in distribution	t-test, ANOVA Wilcoxon, Kruskal-Willis
	Incidence/Prevalence	Poisson regression
Interventional Studies (Trials)		

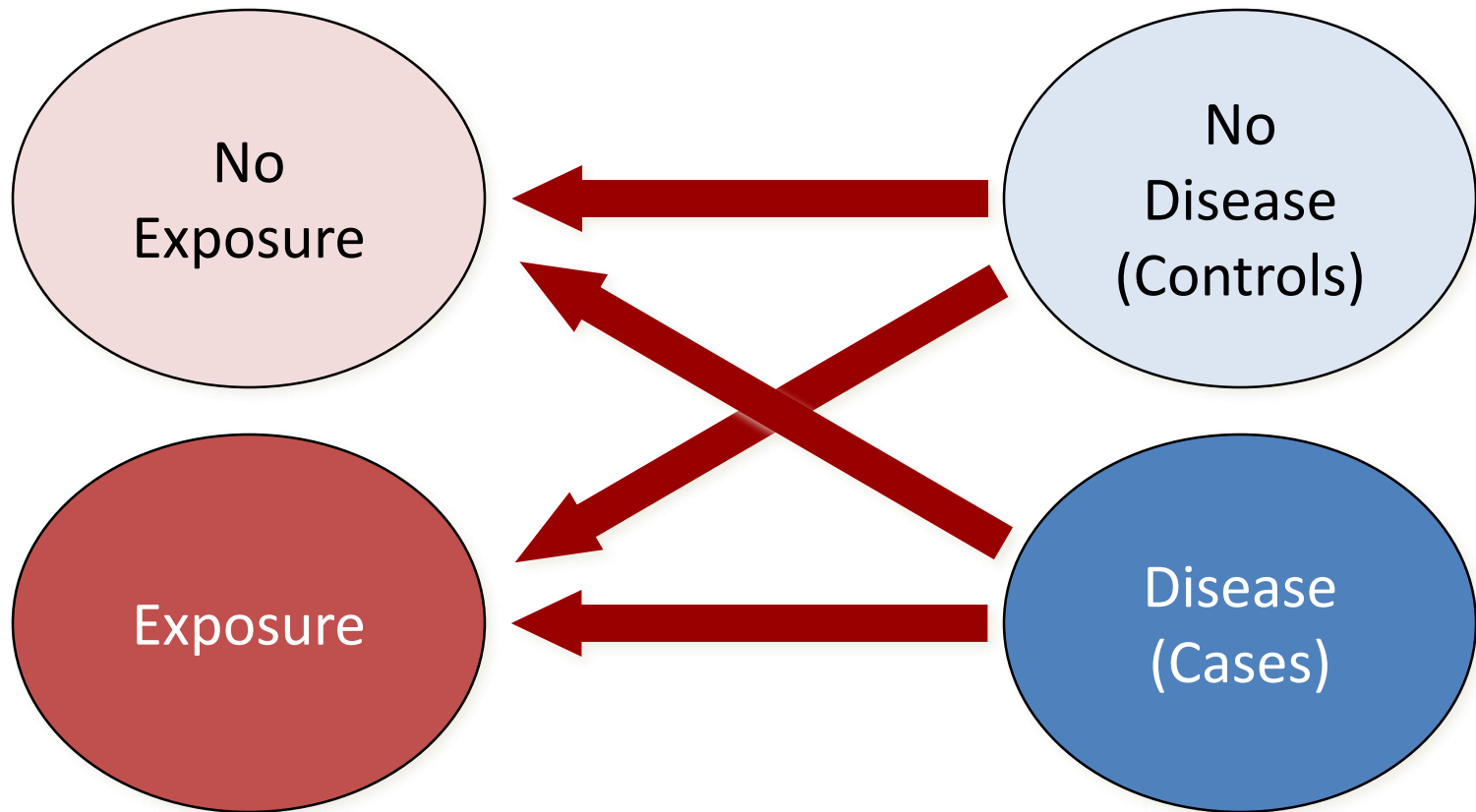
Cohort Study



Subject Selection

Assessment

Case-Control Study



Assessment

Patient Selection

Cohort Study

	Disease	No Disease	Total
Exposed	A	B	A+B
Not Exposed	C	D	C+D

- Incidence of disease among the exposed (I_E) = $A / (A+B)$
- Incidence of disease among the unexposed (I_U) = $C / (C+D)$
- Risk ratio = I_E / I_U
 $= \{A/(A+B)\} / \{C/(C+D)\}$
 $= A(C+D)/C(A+B)$

Case-control Study

	Disease (Cases)	No Disease (Controls)	Total
Exposed	a	b	a+b
Not Exposed	c	d	c+d

- Unlike a cohort study the ‘total’ column (a+b and c+d) has no meaning: incidence (and relative risk) may not be computed.
- Odds ratio = $a*d / b*c$
- The meaning of odds ratios is similar to that of relative risk.

Cohort Study Example

- Yang et al (NEJM 2002;347:168):
 - A cohort of 11,893 men from seven townships in Taiwan recruited 1991-92
 - Follow-up completed in 2001 (follow-up=7.8 years)

	HCC	No HCC	Total
HBsAg+	83	2278	2361
HBsAg-	29	9503	9532

- Incidence among HBsAg+: (I_E) = 83/2361
- Incidence among HBsAg-: (I_U) = 29/9532
- Risk ratio=11.7 (HBV increases risk of HCC by ~12 times)

Cohort versus Case-Control Study

If Yang chose to do a case-control study:

- Pick 100 cases (out of 112) and 100 controls (out of 11,781).
- If the selection is random, there would be
 - 100 HCC cases (74 HBsAg+, 26 HBsAg-)
 - 100 controls (19 HBsAg+, 81 HBsAg-)

Cohort Study		
	HCC	No HCC
HBsAg+	83 (74%)	2278 (19%)
HBsAg-	29 (26%)	9503 (81%)

Case-Control Study		
	HCC	No HCC
HBsAg+	74	19
HBsAg-	26	81

• R.R. = 11.7

• O.R. = 12.1

Case-control study will give the right answer only if selection of cases and controls are random with respect to exposure.

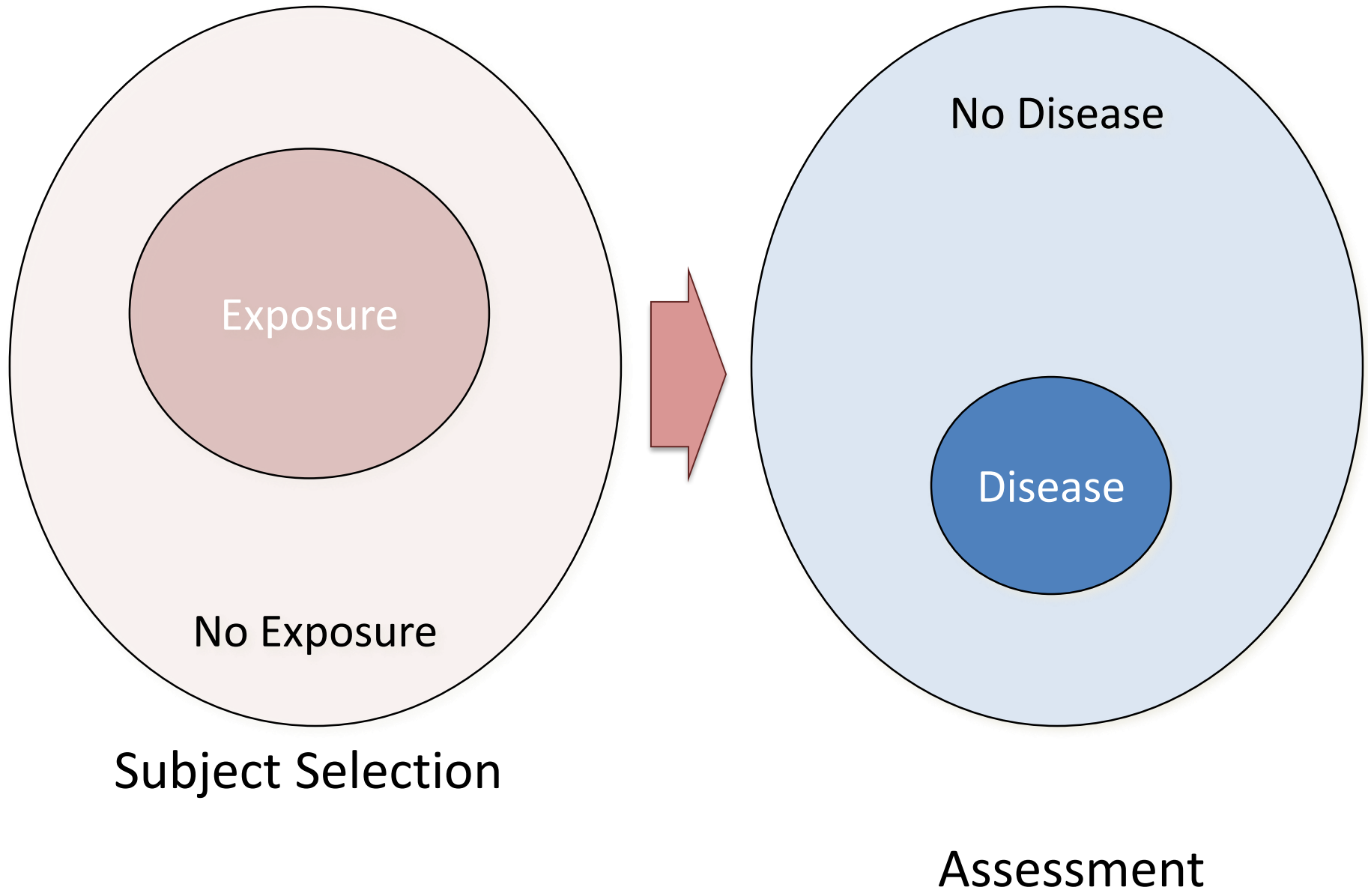
Caution: Case-Control Study

- For a case control study to be valid, exposure must be independent of (the probability for) selection for cases and controls.

Heavy Alcohol use	Cases (HCC in Liver Clinic)	Controls (Non-HCC in Addiction Clinic)
Yes	50	90
No	50	10

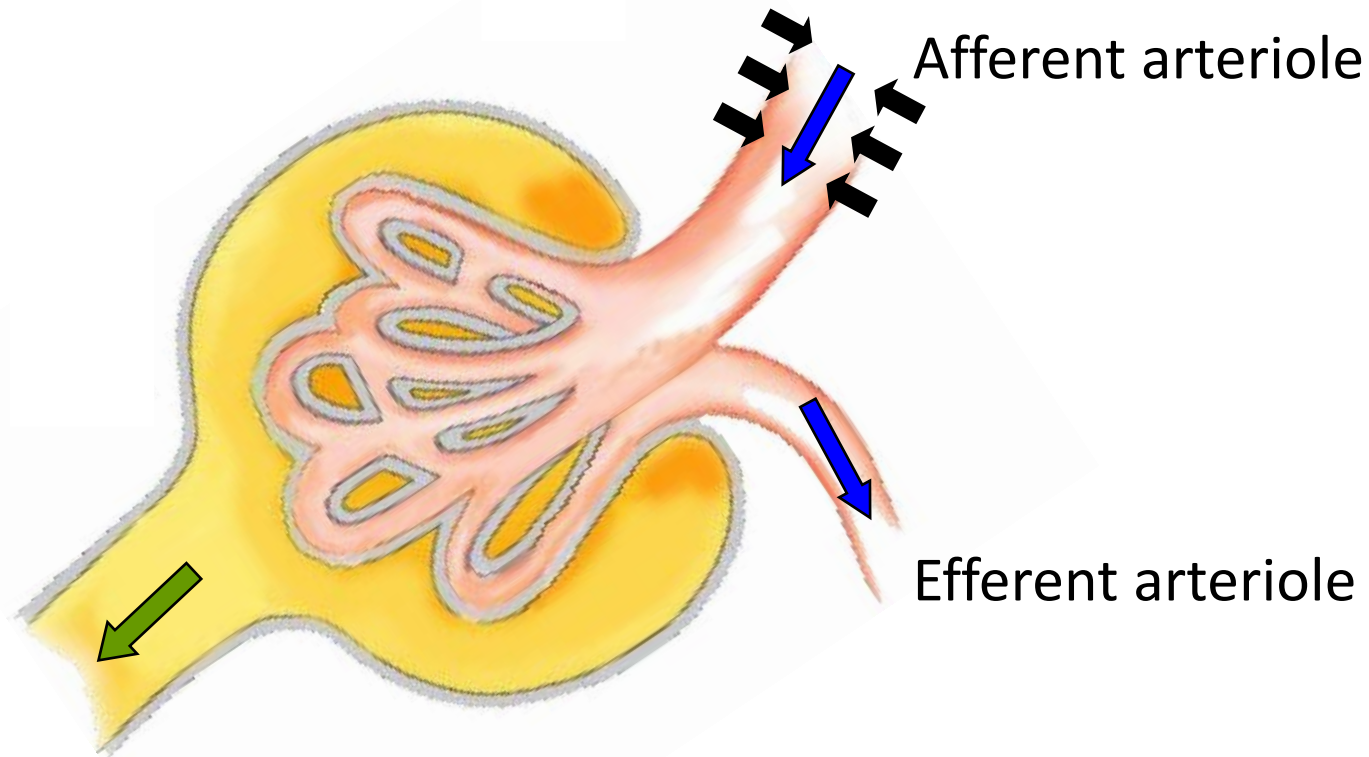
- $O.R. = (50 * 10) / (90 * 50) = 0.11$
 (Heavy alcohol use is associated with lower risk of HCC)
- Solution
 - Thoughtful selection of cases and controls
 - Avoid bias in measurement of exposure

Cross-sectional Study



Cross-sectional Study

- Genetic disposition to post-transplant chronic kidney disease



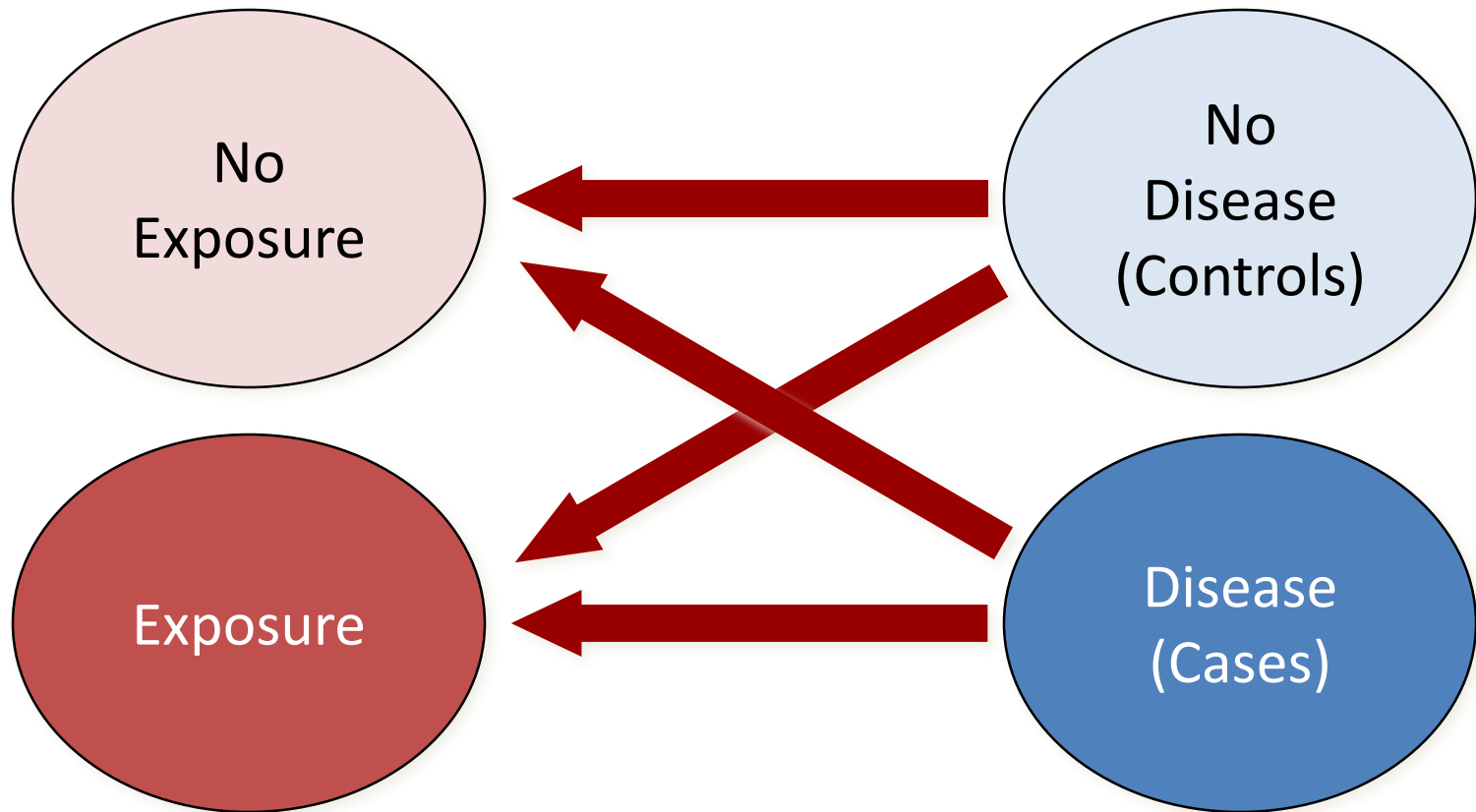
Genetic Polymorphisms affecting Vascular Physiology

- Candidate genes:
 - Angiotensin II receptor, type 1
 - Endothelin 1
 - Nitric oxide synthase (eNOS)
 - Adrenergic beta-2-receptor surface
 - Bradykinin receptor B1
 - Transforming growth factor beta-1

	CKD	No CKD	Total
eNOS Variant	19	15	34
eNOS Wild type	289	77	366

OR=2.9 (p=0.002 simple chi-square; p=0.05 multiple comparison)

Case-Control Study



Assessment

Patient Selection