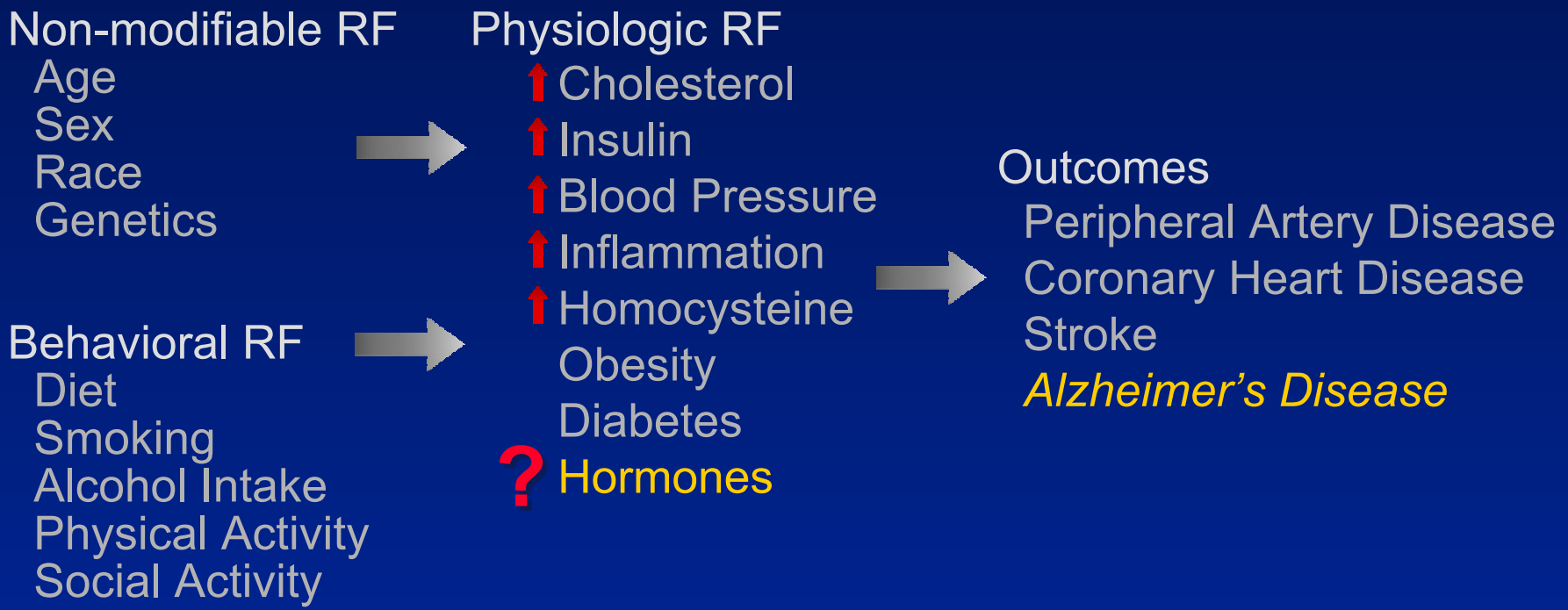
Endogenous levels of sex hormones and the risk for brain aging in population-based studies

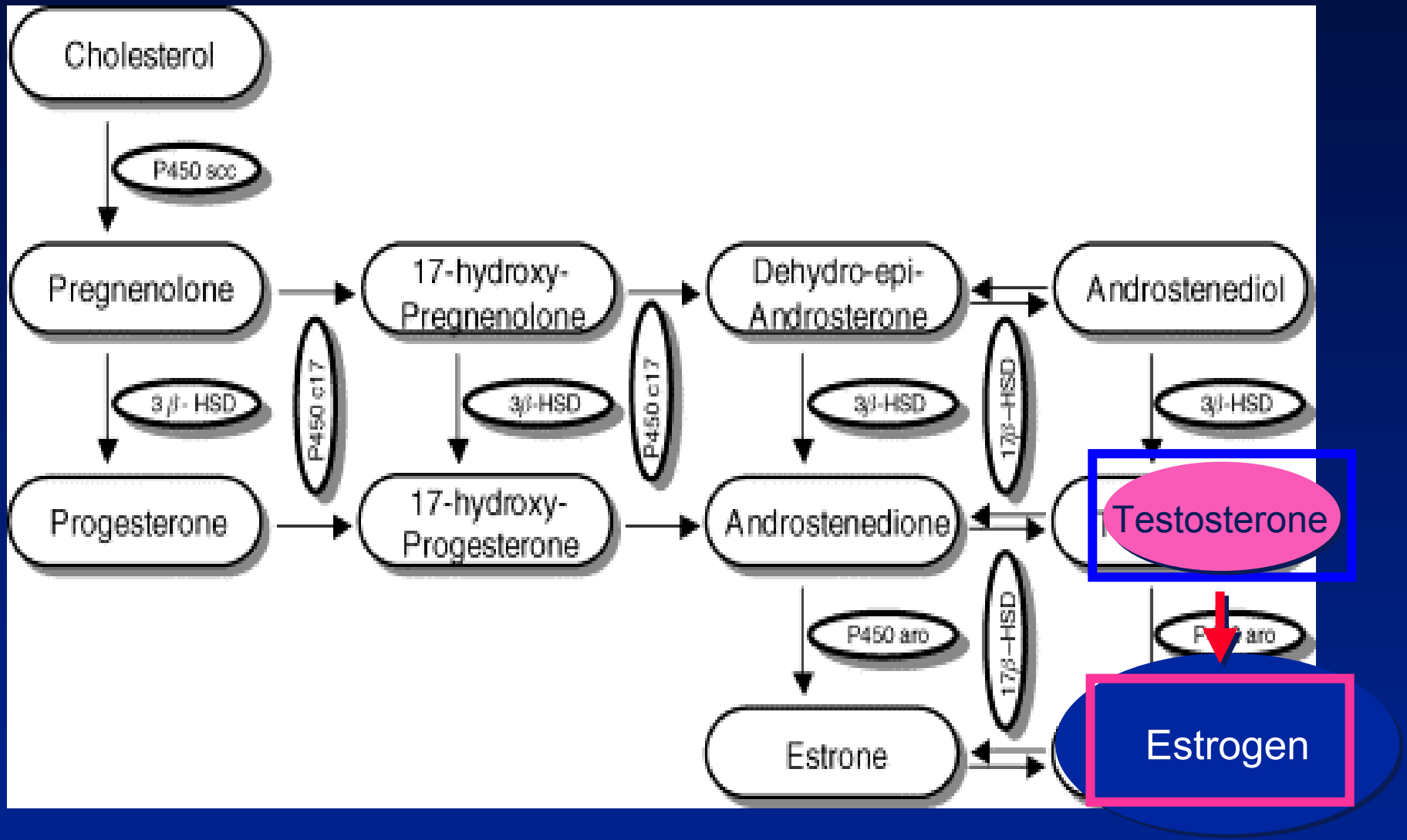
Lenore J. Launer

Laboratory of Epidemiology, Demography Biometry

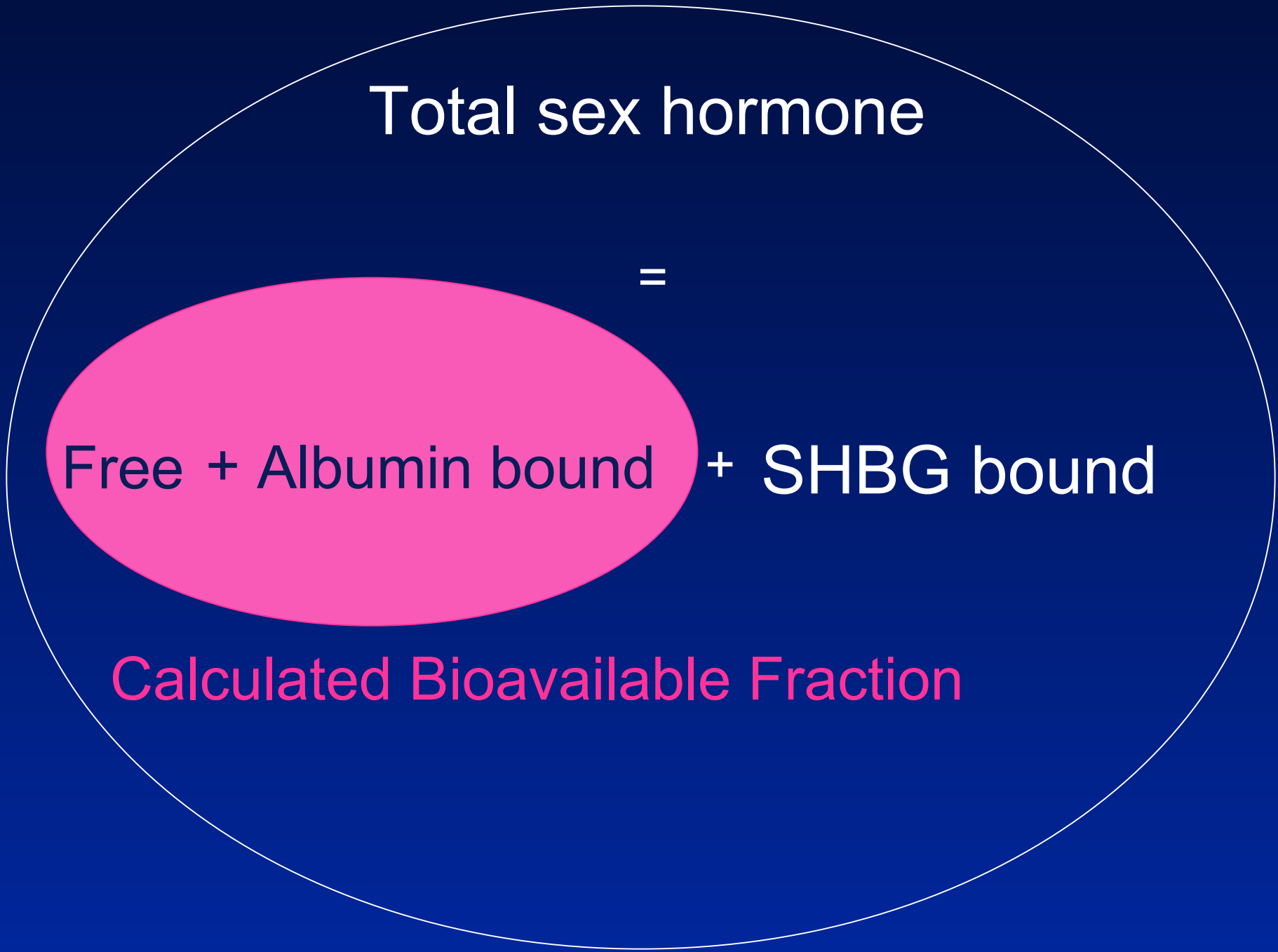
National Institute on Aging

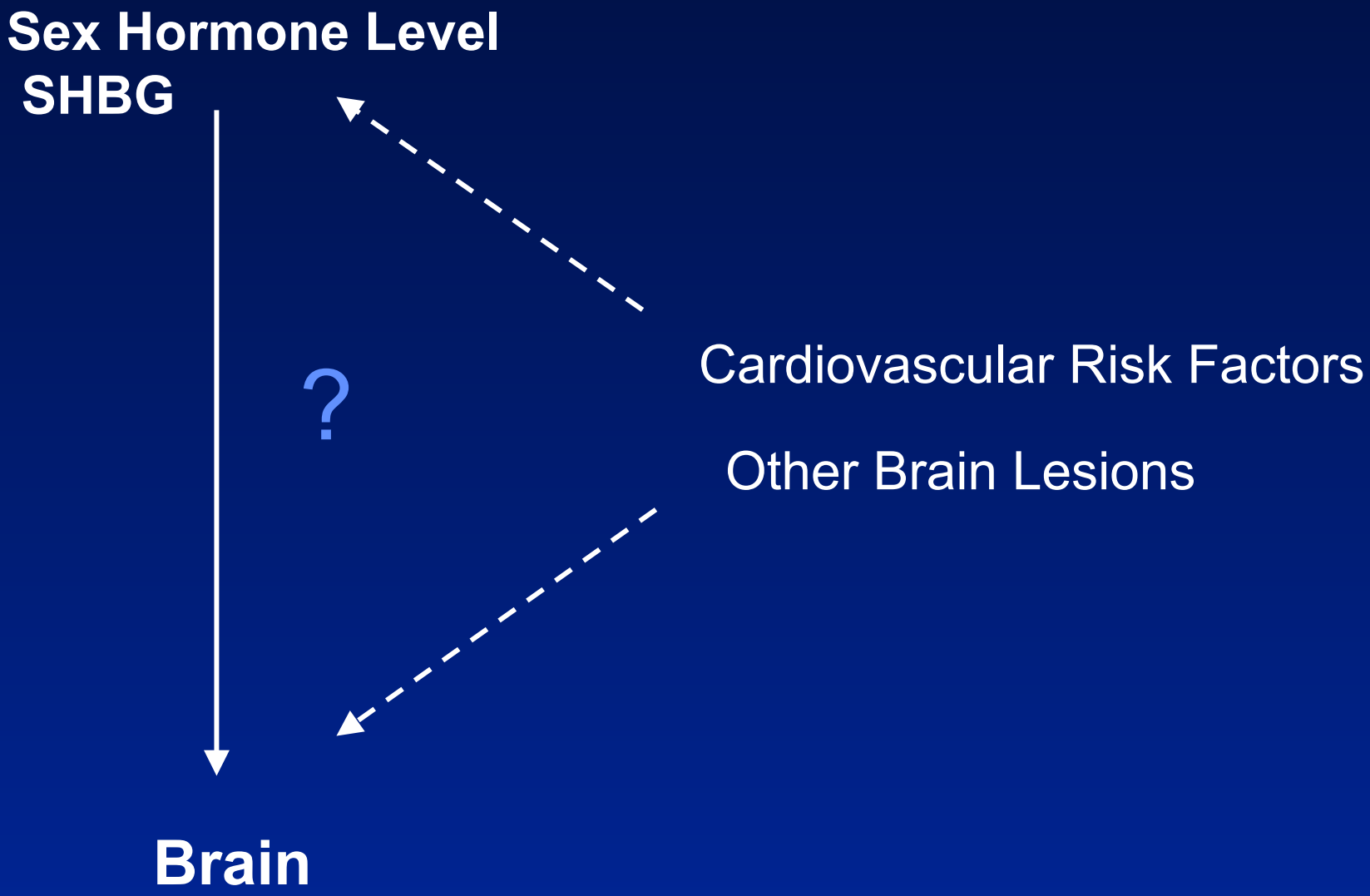
Risk Factors and Outcome: Dementia





(Retrieved from Garcia-Segura LM, 2003)


Total sex hormone
=
Free + Albumin bound
+ SHBG bound
Calculated Bioavailable Fraction


Sex Hormone Level
SHBG
?
Cardiovascular Risk Factors
Other Brain Lesions
Brain

Population based Studies

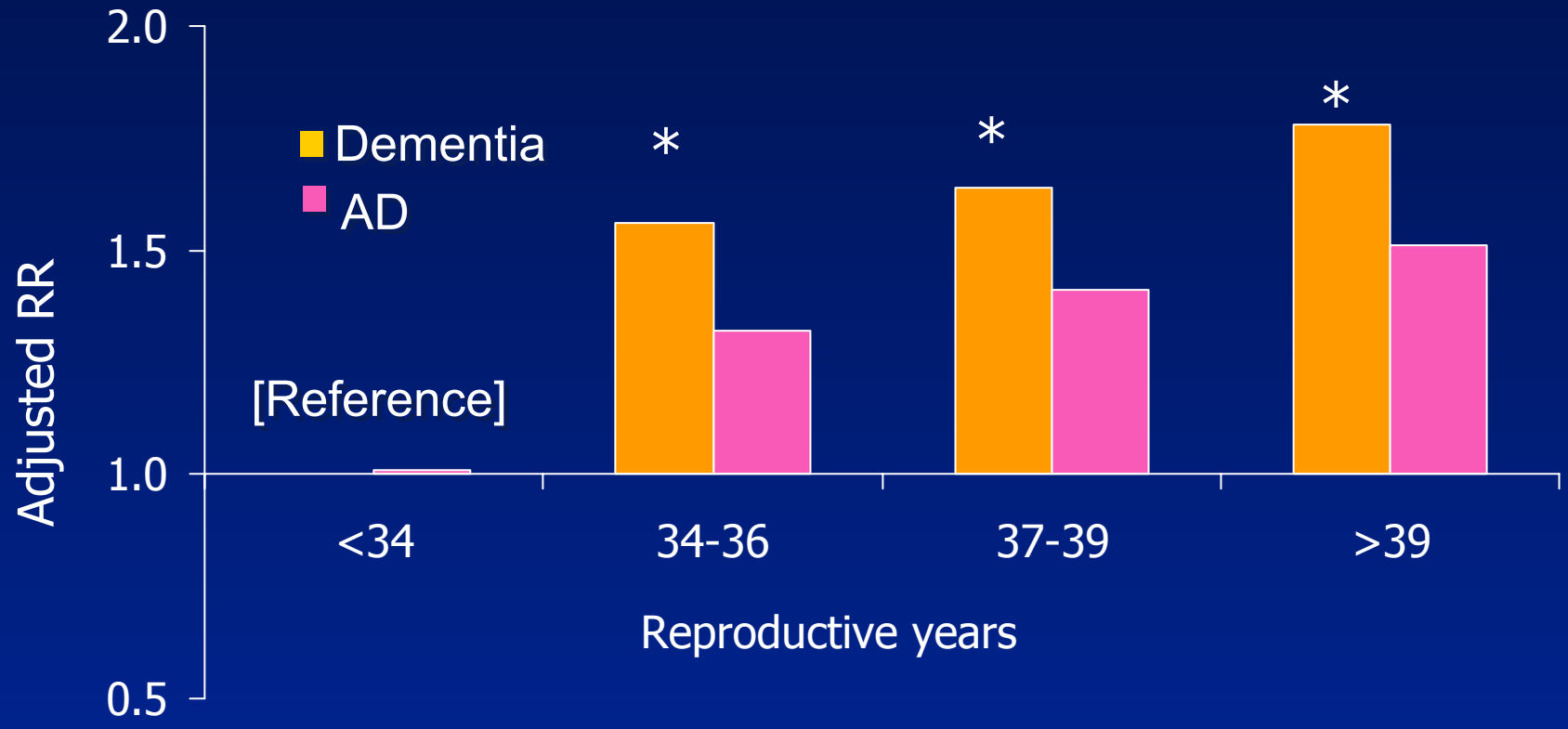
Rotterdam Study Women

- 1991 – on-going
- Incident dementia
- MRI – medial temporal structures
- Researchers: Geerlings, Breteler, Pols

Sample characteristics: Rotterdam Study

	Sample			
	Clinical		MRI	
	Men (n=438)	Women (n=508)	Men (n=210)	Women (n=202)
Age (yrs)	68.7	71.0	69	70
BMI	25.7	26.7	26.1	26.8

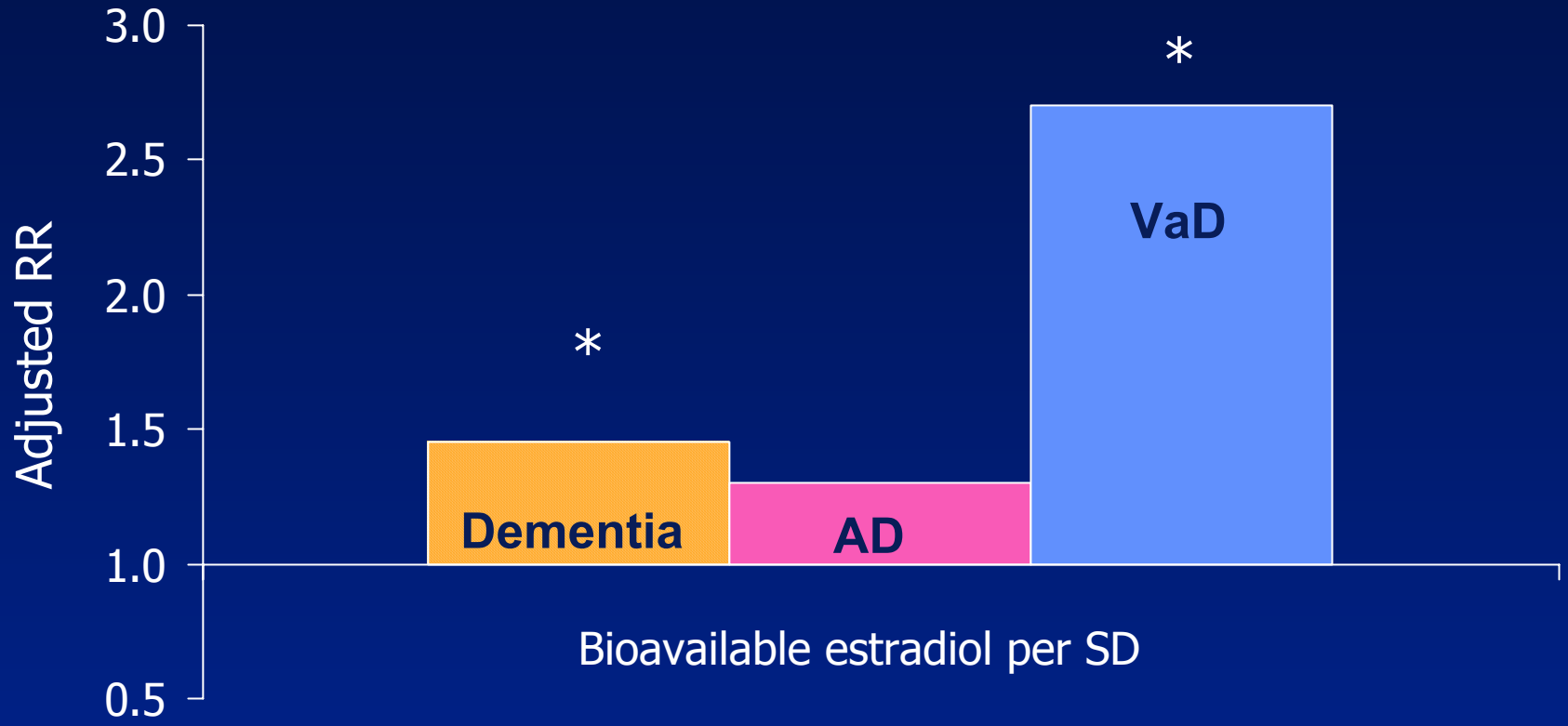
reproductive yrs and dementia: Rotterdam Study



* Different from reference <34 yrs ($p<0.05$); Adjusted for demographic and cardiovascular factors

Geerlings et al, JAMA; 2001

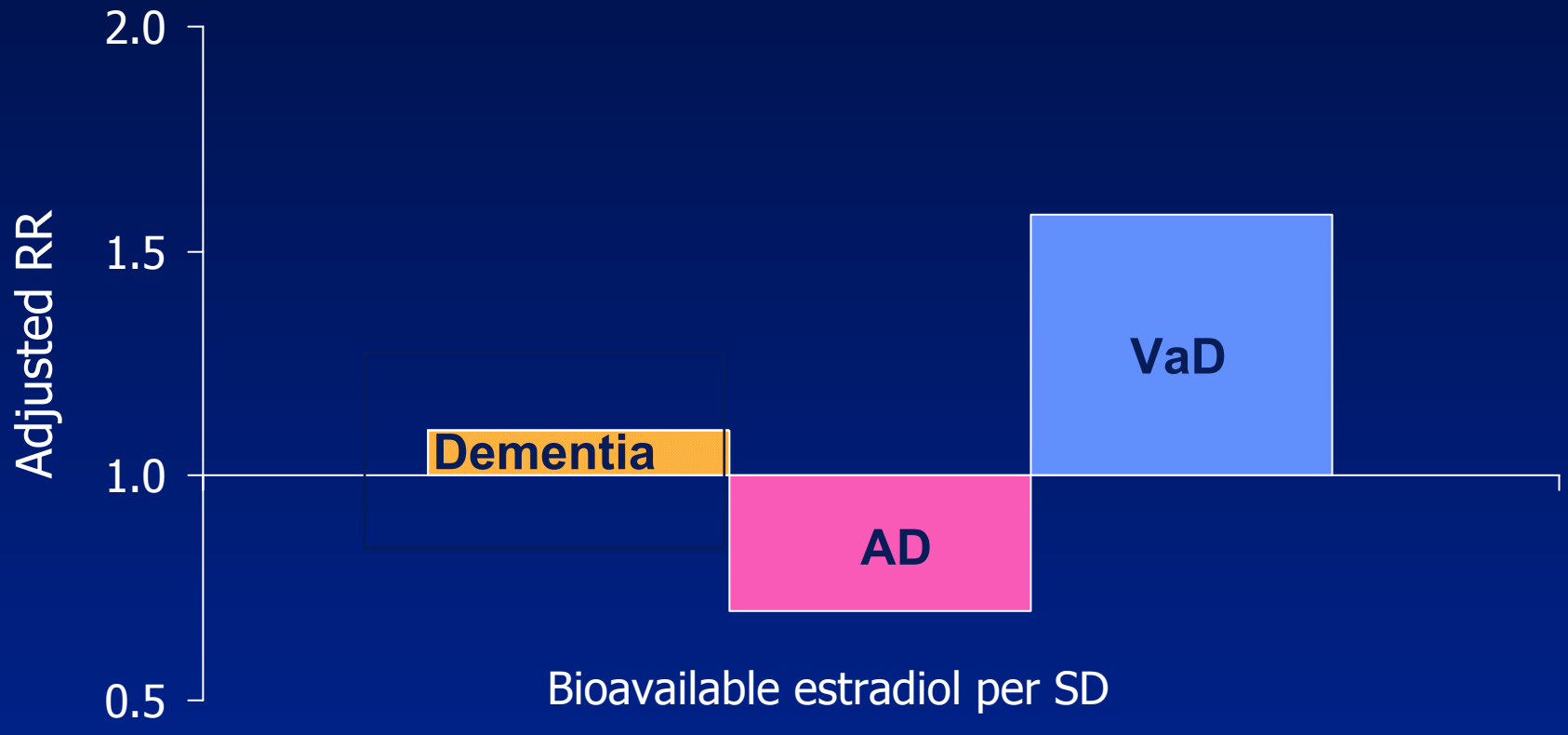
Bioavailable estradiol and dementia: Rotterdam Study Women



* Different (p<0.05) from reference not demented ; Adjusted for demographic and cardiovascular risk factors

Geerlings et al, Ann Neurol; 2003

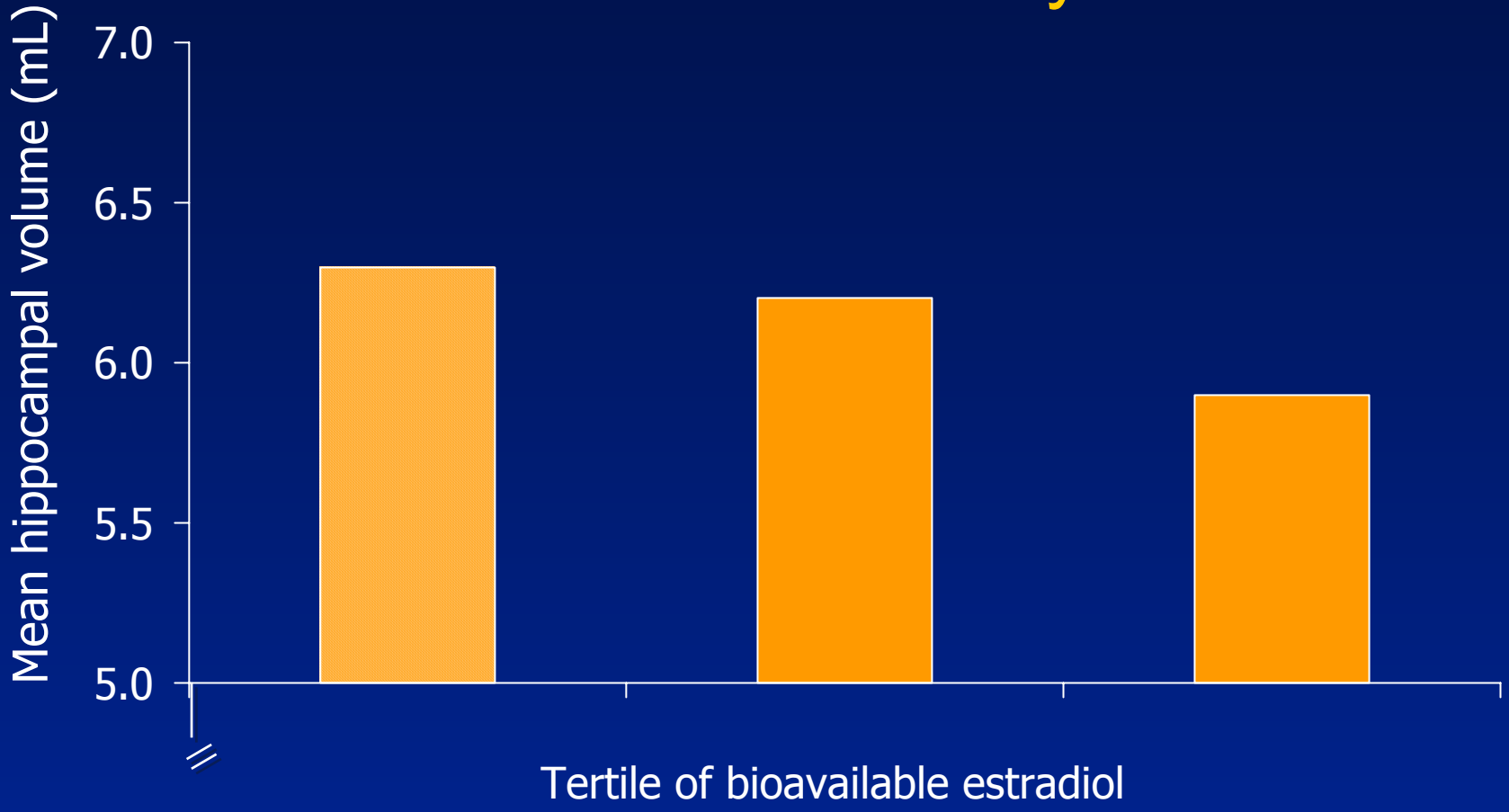
Bioavailable estradiol and dementia: Rotterdam Study Men



Adjusted for demographic and cardiovascular risk factors

Geerlings et al, Ann Neurol; 2003

Bioavailable estradiol and hippocampal volume: Rotterdam Study Women



Adjusted for demographic and cardiovascular risk factors

Den Heijer, Arch Neurol 2003

Summary- Rotterdam Study

With increasing estradiol levels, women:

- were at higher risk for dementia, particularly vascular dementia
- Hippocampal volume decreased

Population based Studies

Honolulu Asia Aging Study Men

- 1965 – ongoing
- Incident dementia
- MRI – atrophy and ischemic lesions
- Autopsy
- Researchers: Strozyk, Irie, White, Masaki, Remaley

Sample characteristics: HAAS

	Sample	
	Clinical (n=2300)	MRI (n=452)
Age (yrs)	76.9	81.6
BMI	23.7	23.4

Summary- HAAS (data are not published)

- Compared to normals, prevalent dementia cases have a higher mean estradiol and a lower mean testosterone
- Testosterone levels decrease with age; estradiol levels don't change; sex hormone binding globulin increases with age
- Higher levels of estradiol are associated with an increased risk for dementia and lacunae on MRI
- No association of testosterone to dementia, but an association of increased testosterone with ventricular enlargement measured on MRI

Conclusion

- If we add therapeutic levels of hormones, we should understand better the role of physiologic levels of the hormones and how these hormones change with age
- Cardiovascular risk factors need to be taken into account as possible confounders or mediators of the associations of hormone levels and brain.