Estimation of overweight-attributable deaths

Katherine M. Flegal, Ph.D.

Centers for Disease Control and Prevention
National Center for Health Statistics

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Allison et al, 1999

- Allison, JAMA 1999 calculated deaths attributable to overweight and obesity in 1991,
  - using relative risks from six cohort studies
  - combined with overweight and obesity prevalence from NHANES III
  - and with mortality statistics for 1991.

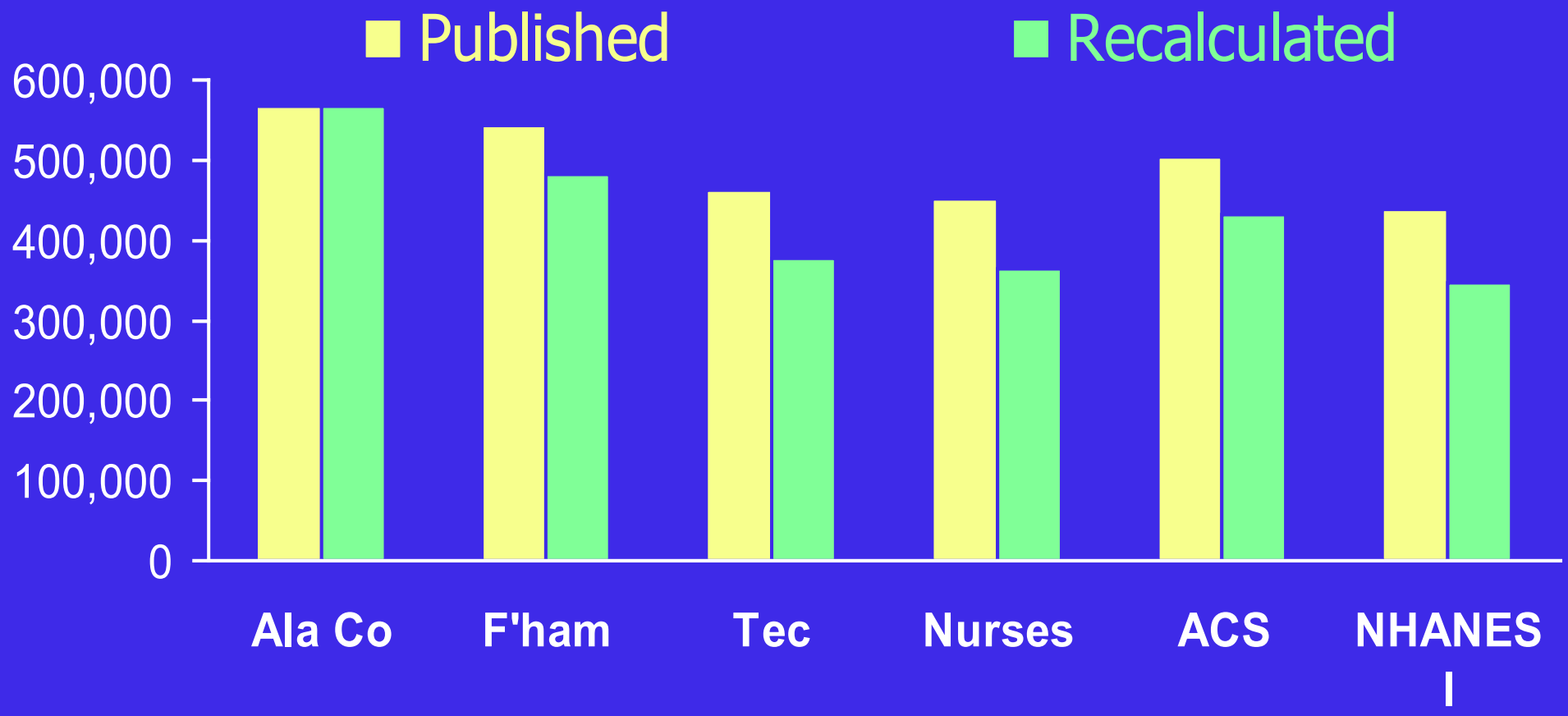
Actual causes of death paper, 2004

- Actual causes of death, JAMA 2004 calculated deaths attributable to overweight and obesity in 2000
  - using the same relative risks from the same six cohort studies as Allison
  - combined with overweight and obesity prevalence from NHANES 1999-2000
  - and with mortality statistics for 2000.

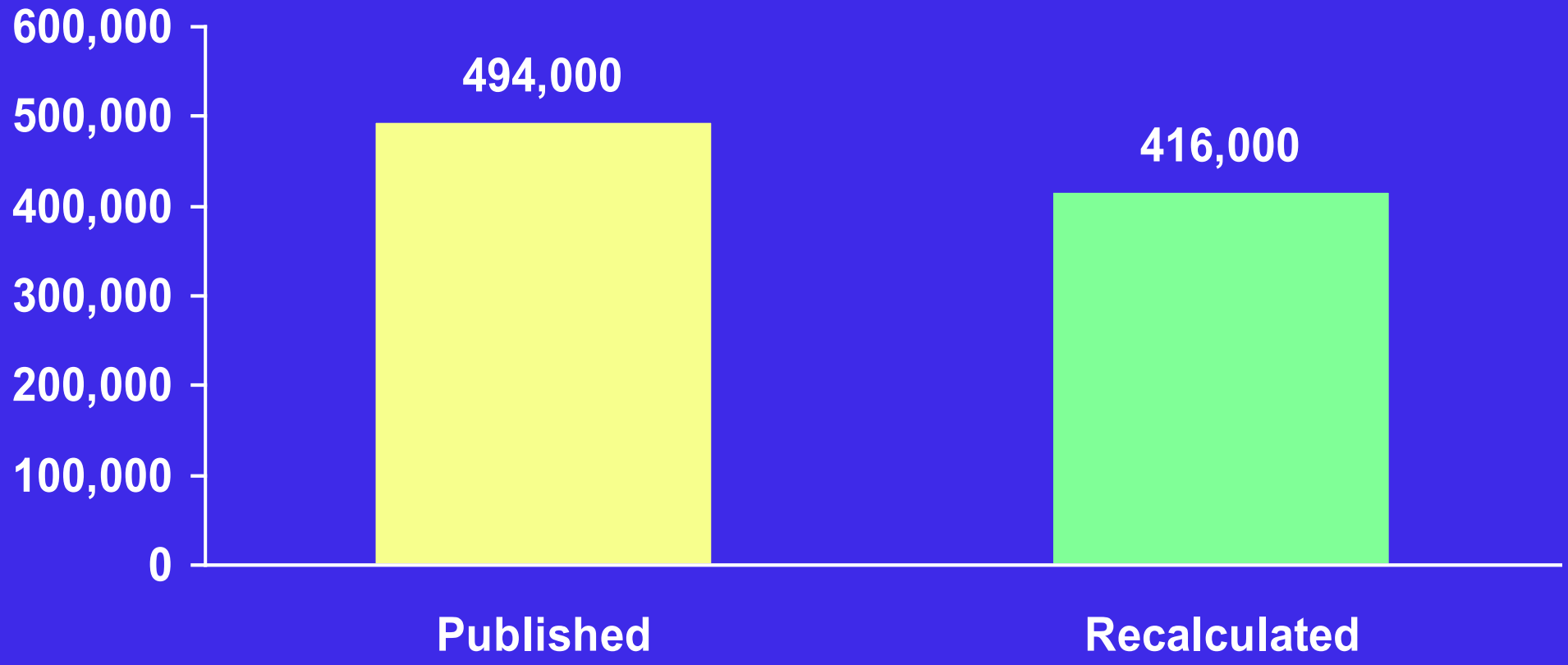
Calculation errors in Actual Causes of Death paper

- For five of the six cohorts, the number of deaths in 1991 was used instead of the number of deaths in 2000
- For five of the six cohorts, the prevalence of BMI < 25 was taken from NHANES III but the prevalence of higher BMI categories was taken from NHANES 99-00

Published and recalculated numbers of overweight-attributable deaths

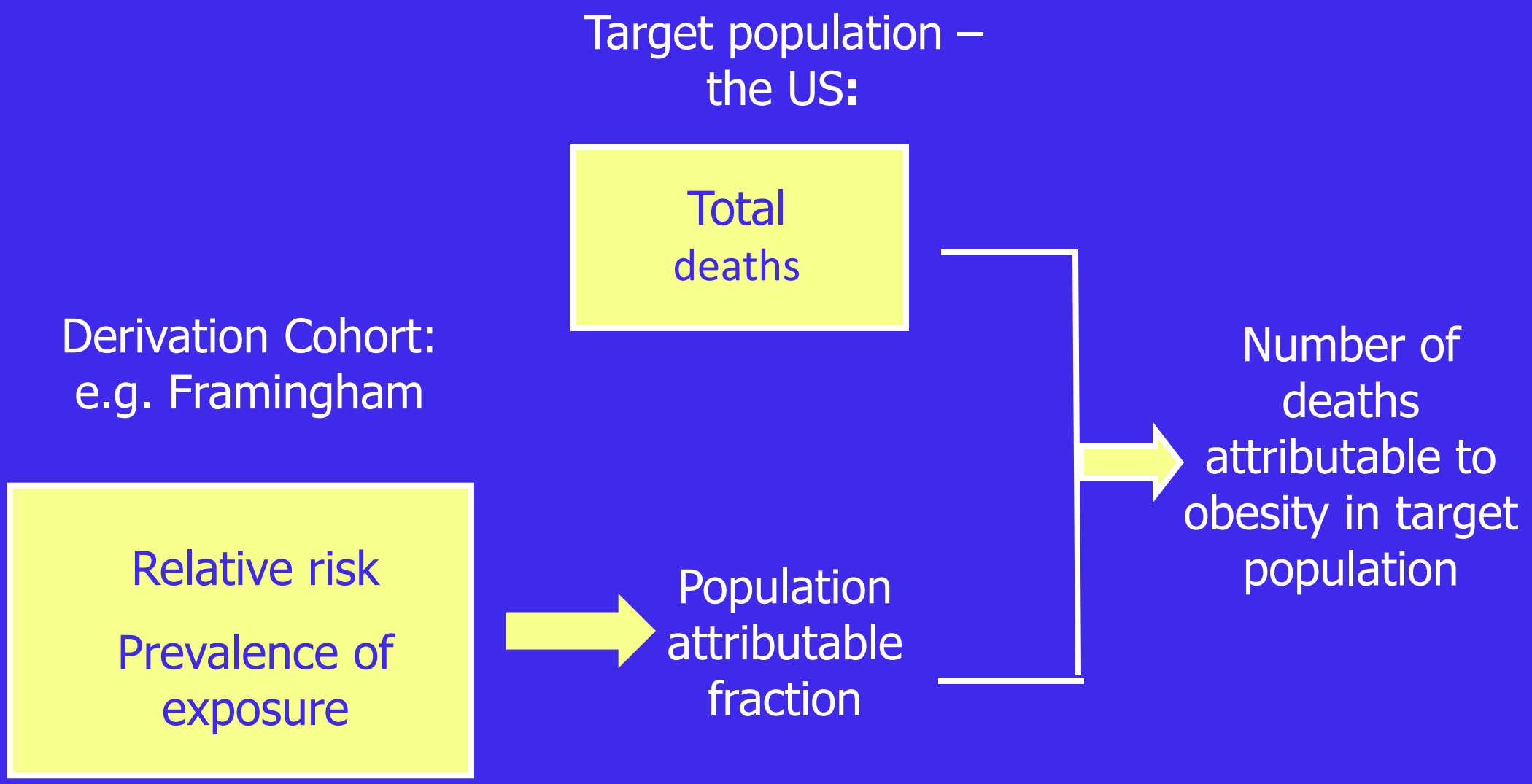


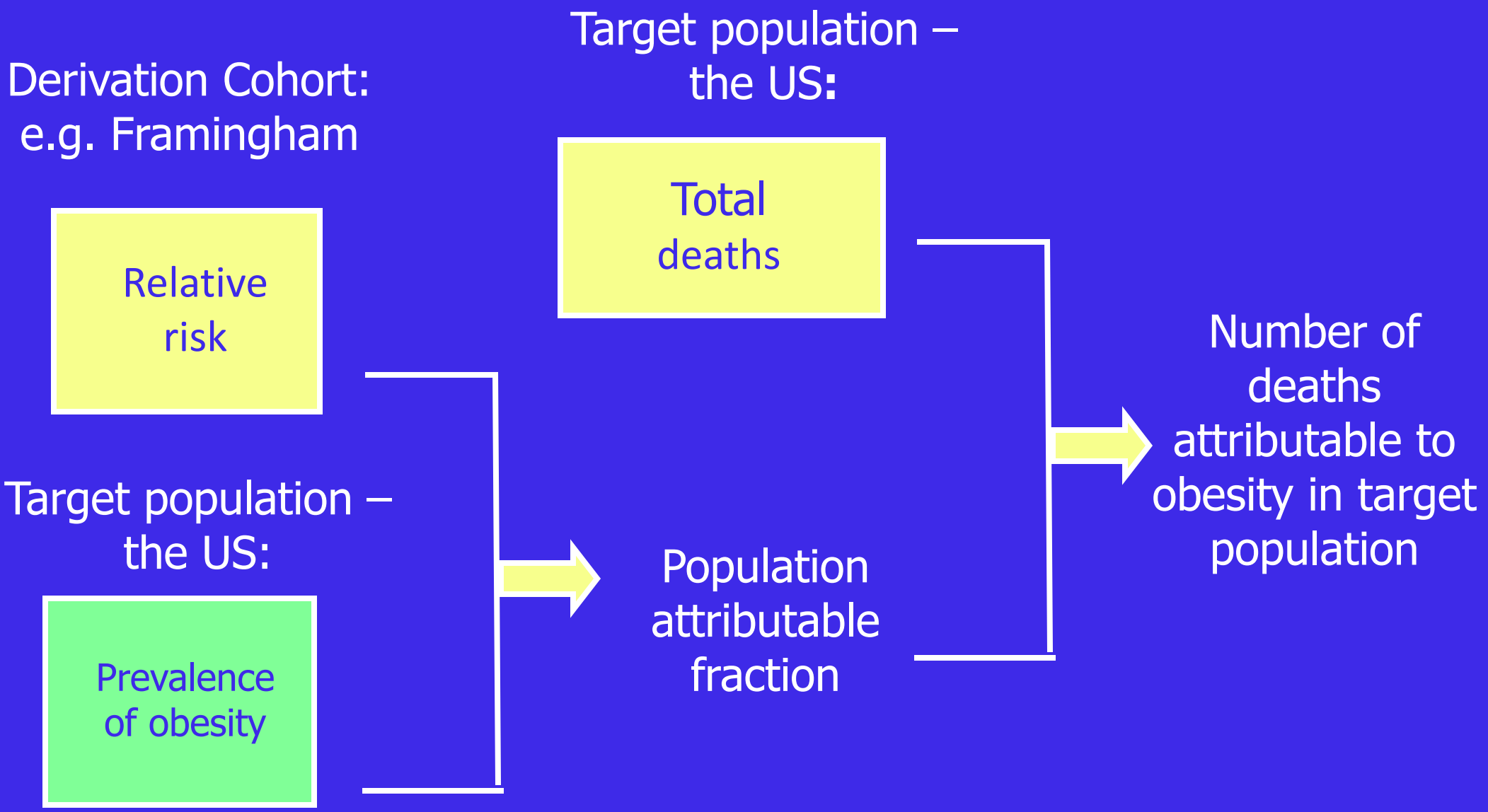
Mean overweight-attributable deaths over six cohorts



Issues - 2

- Allison 1999 used a method of calculating attributable fractions – the "partially adjusted" method - that does not fully account for confounding or effect modification


Target population – the US:
Total deaths
Derivation Cohort: e.g. Framingham
Relative risk
Prevalence of exposure
Population attributable fraction
Number of deaths attributable to obesity in target population


Derivation Cohort:
e.g. Framingham
Relative risk
Target population – the US:
Prevalence of obesity
Target population – the US:
Total deaths
Population attributable fraction
Number of deaths attributable to obesity in target population

Population Attributable Fraction (PAF)

$$PAF = \frac{P(E) * (RR-1)}{1 + (P(E) * (RR-1))}$$

P(E) = prevalence of obesity

RR = unadjusted relative risk of mortality associated with obesity

Calculating PAF when there is confounding of the exposure-outcome relation

- Weighted sum method
- "Partially-adjusted" method

Weighted sum method

Group	N	P(E)	RR	No. of deaths	PAF	Excess deaths
A	1000	.5	2	150	.333	50
B	500	.1	2	165	.0909	15
Sum						65

"Partially adjusted" method

Group	N	P(E)	RR	No. of deaths	PAF	Excess deaths
A	1000	.5	2	150	.333	50
B	500	.1	2	165	.0909	15
Sum						65
Total	1500	.37	2	315	.2683	84.5

Rockhill et al, 1998

- 1998, Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions, Am J Pub Hlth

"..Errors in estimation are common. Probably the most common error is the use of adjusted relative risks in formula 3 [formula for unadjusted RR]. The magnitude of the bias resulting from this error will depend on the degree of confounding." P. 16

"Partially-adjusted" method

- Annual deaths attributable to obesity in the United States. JAMA. 1999; 282:1530-8.
- A simple estimate of mortality attributable to excess weight in the European Union. Eur J Clin Nutr. 2003;57:201-8.
- Actual causes of death in the United States, 2000. JAMA. 2004;291:1238-45
- Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med. 2003;348:1625-38.

Benichou, 2001

- 2001, Benichou J, , A review of adjusted estimators of attributable risk, Stat Med

"Another natural approach based on using equation (2) [formula for unadjusted RR] and plugging in a common adjusted relative risk estimate…has been advocated but it too has been shown to yield inconsistent estimates. and accordingly, severe bias was exhibited in simulations…" p. 200

"Partially-adjusted" method

- Calculate adjusted relative risks
- Use a PAF formula appropriate only for unadjusted relative risks
- Treat the population as a single group (no stratification)
- In general, when there is confounding, gives biased results, but degree of bias not often quantified

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Methods of Calculating Deaths Attributable to Obesity

Katherine M. Flegal[1,2], Barry I. Graubard[3], and David F. Williamson[4]

[1] National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD.
[2] Center for Weight and Health, University of California at Berkeley, Berkeley, CA.
[3] National Cancer Institute, National Institutes of Health, Bethesda, MD.
[4] Division of Diabetes Translation, Centers for Disease Control and Prevention, Atlanta, GA.

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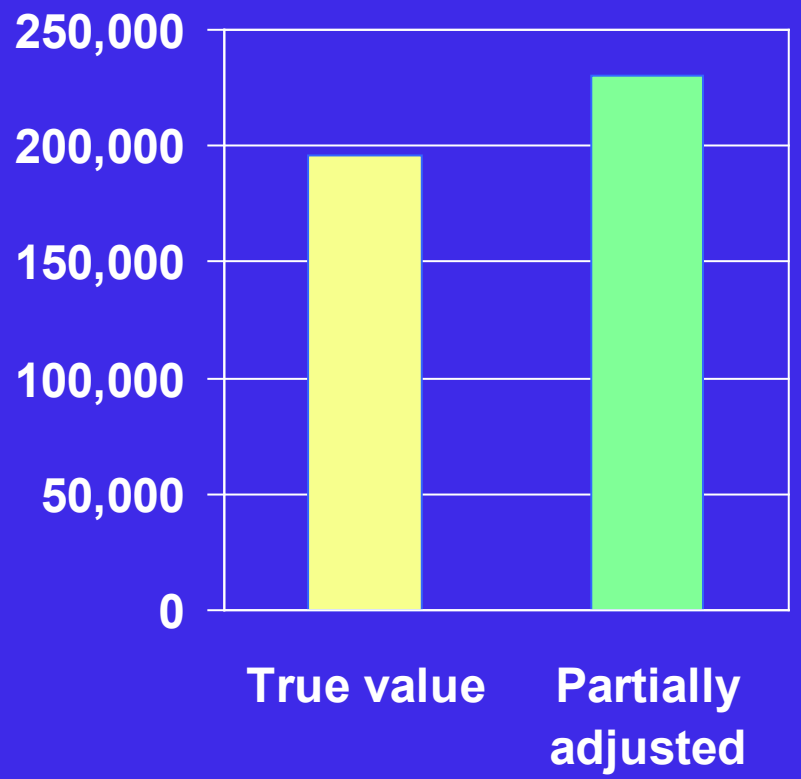
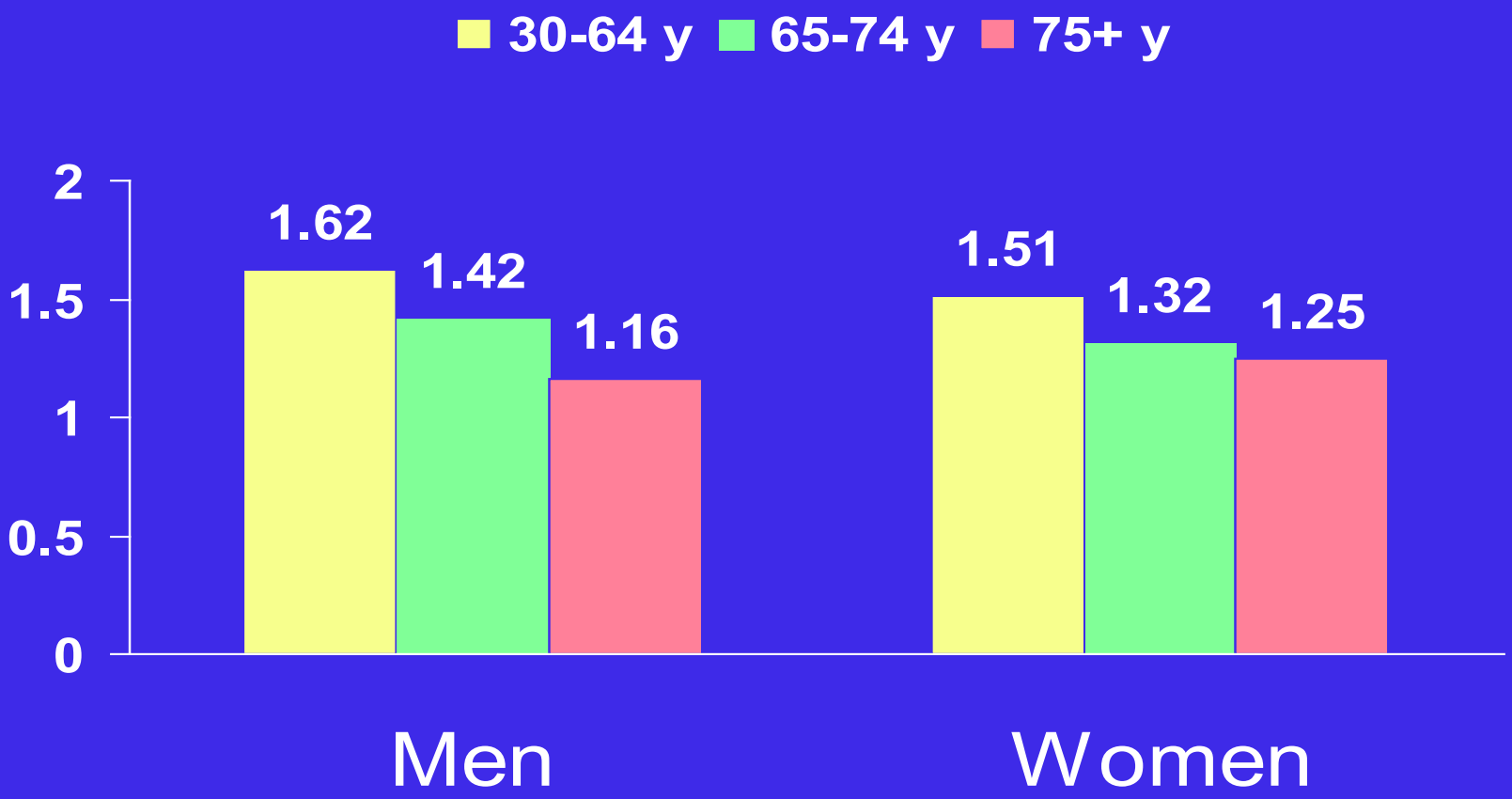
Bias arising from ignoring confounding by age and sex

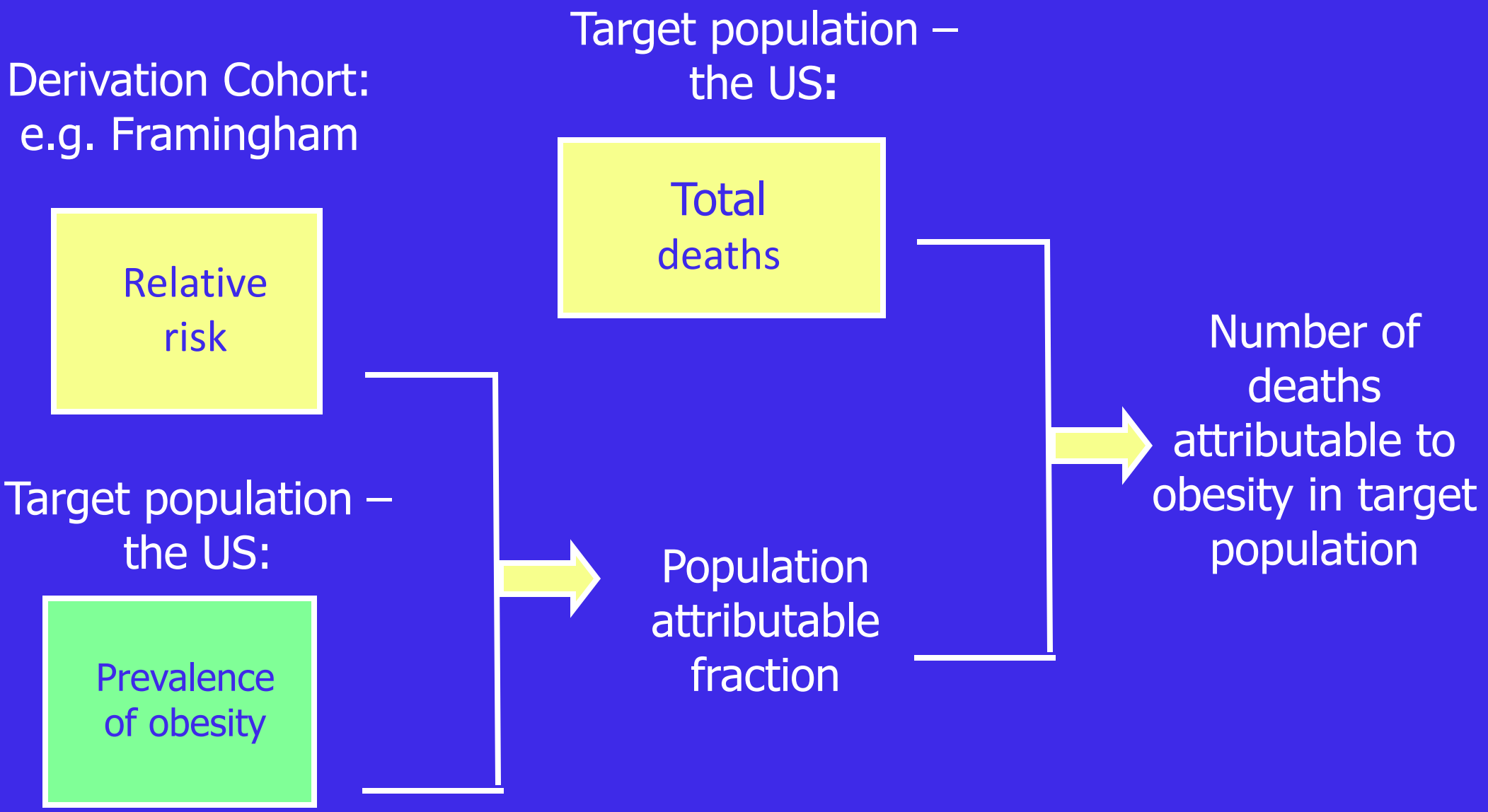
- Partially adjusted method overestimated excess deaths due to obesity by 17% in this hypothetical example using published relative risks, NHANES III prevalence estimates and 1991 mortality data



Relative risks of mortality associated with obesity decrease with age

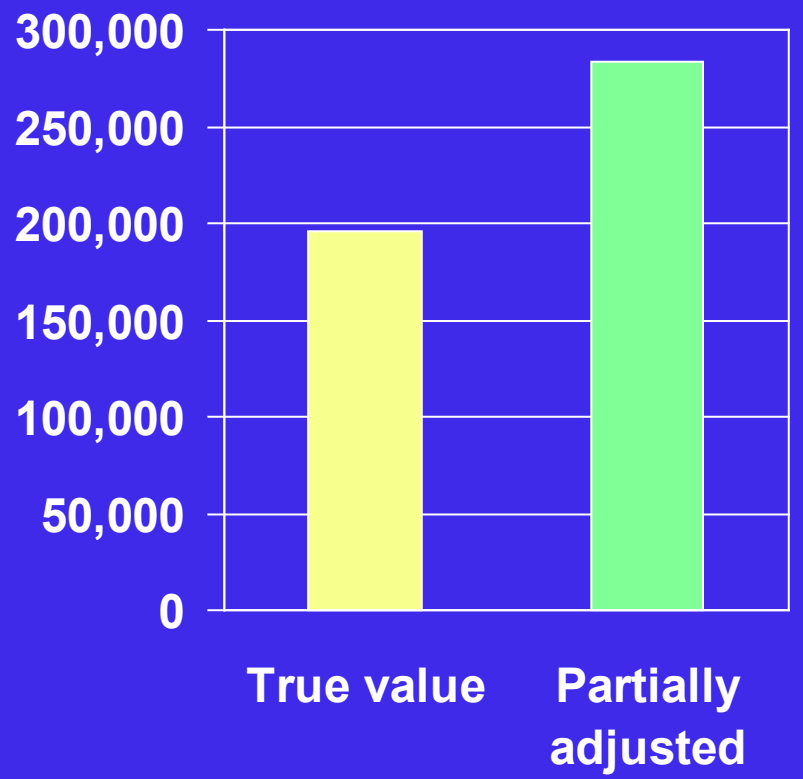


Source: Calle et al NEJM, 1999


Derivation Cohort:
e.g. Framingham
Relative risk
Target population – the US:
Prevalence of obesity
Target population – the US:
Total deaths
Population attributable fraction
Number of deaths attributable to obesity in target population

Bias arising from ignoring confounding and effect modification

- Partially adjusted method overestimated excess deaths by 42% in this example when the derivation cohort had 0.4% elderly (80+ y) and the target population had 3.4% elderly



Derivation cohort and the target population

- If there is effect modification, additional bias may result from using the 'partially adjusted method' when the derivation cohort differs from the target population in:
  - Relative proportion of subgroups
  - Probability of mortality in the non-obese
  - Prevalence of obesity

The "partially adjusted" method

- Commonly used and intuitively appealing
- Statistical literature has already documented that the partially adjusted method gives rise to bias
- Our hypothetical examples suggest bias upwards for deaths associated with obesity
- Even when this method shows little bias in a derivation cohort, the results may be biased when applied to a different population

Why not just use the weighted sum method?

- Age and sex are not the only confounders.
- The weighted sum method requires information on the number of deaths within each subgroup – information not generally available.
- An alternative PAF approach when there is confounding would require knowledge of the proportion of decedents who were obese – also information not generally available

The "partially adjusted" method

- Attempts to solve the problem of having relative risks from one cohort combined with exposure data from a different source
- This method has already been shown in the statistical literature to lead to bias
- A different approach is needed to account for confounding and for effect modification