Week 7 – Thursday Session

Standardization

EPI202 – Epidemiologic Methods II

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So Far…
Exchangeability

- **Crude** assumes no confounding and no effect measure modification
- **If non-exchangeability**
  - Crude estimate is confounded
  - To attain exchangeability, stratify by levels of confounding factor(s) so that within strata, the exposed and unexposed are exchangeable
  - Assuming no residual confounding or other forms of bias, these stratified estimates are unbiased

So Far…
Typical Efficient Weighted Average Estimates

In the absence of true effect measure modification

- Assume all stratum-specific estimates arose from underlying distributions centered at the same true value of the population parameter

- Maximize efficiency by averaging across strata using MH weights (ratio measures) or MH-style weights (difference measures)

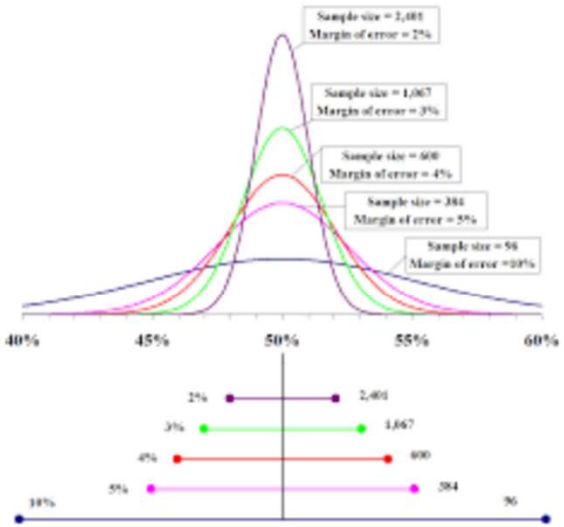
- Weights are driven by the data

So Far…
Effect Measure Modification

In the presence of true underlying effect measure modification

- Data-driven weights are inappropriate since summary measure does not reflect any particular population
  - e.g. beta-blockers and mortality
- Show stratum-specific estimates or… use standardization
- Standardization is an approach to creating weighted averages that reflect the distribution of stratification factor(s) in populations of interest
- Standardization does not assume homogeneity across strata

If there is no evidence of effect measure modification, standardization is the most statistically efficient method of calculating a summary measure.



- True
- False
- Do not know

Total Results: 0

Utility of Standardization

- A comparison of crude rates can be misleading because the comparison can be biased due to confounding, and difficult to interpret in the presence of effect measure modification
- While **stratum-specific** rate ratios provide information on stratum-specific associations, a summary measure is often helpful to estimate the expected average association in populations with a particular distribution of the stratification factor(s).
- In the presence of effect measure modification, an estimate weighted by the distribution of the data (e.g. Mantel-Haenszel) is not appropriate.
- Standardization can be used to control confounding, and still yield a meaningful summary estimate when effect measure modification is present
- The **standardized** rate ratio (or difference) is a weighted average of the stratum-specific rate ratios (or differences), with the weights taken from a **standard** distribution to allow estimation of the expected average association in a population with a particular distribution of the stratification factor(s).
- Standardization can also be used for other measures, such as cumulative incidence or odds

Data-driven Weighted Average vs. Standardization

	Data-driven (e.g. IRR_{MH})	Standardization (e.g. SMR)
Confounding	Controls for confounding	Controls for confounding
Effect Measure Modification	Assumes no effect measure modification across strata	Appropriate even in the presence of effect modification
Weights	Based on information in strata	Based on a standard population
Statistical Efficiency	Weights are statistically efficient but they are not explicit	Weights may be statistically inefficient but they are explicit
Generalizability	Results are comparable to other studies in the absence of effect measure modification (or with similar distribution of modifiers).	Results are comparable to other studies with a similar distribution of the modifiers as the chosen standard population. Thus, the result depends on the choice of standard (e.g. SMR vs. SRR).
If no effect measure modification, expected value of data-driven and standardized measures are the same		

Unified and Traditional Approaches

- Unified and traditional approaches are algebraically identical

- Unified Approach
  - Weighted average of stratum-specific measures of association
  - Analogous to Mantel-Haenszel approach, but applicable whether or not there is EMM

- Traditional Approach
  - Standardize the rate in the exposed and standardize the rate in the unexposed
  - Calculate the ratio or difference of the standardized rate in the exposed and the standardized rate in the unexposed

Choices for Standard Population

Distribution of the stratification factor(s) in the

- Unexposed (direct standardization)
- Exposed (indirect standardization)
- Total study population (sum of the study populations or groups)
- Artificial population (e.g. 1000 subjects per stratum)
- Population from which the study groups originate
  - e.g. The population of the state, province or country where the study is conducted
  - e.g. When comparing occupational groups in residents of a metropolitan area, total metropolitan area working population can serve as the standard
- External reference population (e.g. US census; World population)

Szklo & Nieto. Epidemiology. Jones & Bartlett Learning; 3 edition (October 24, 2012). p238-239

Direct vs. Indirect Standardization
Inference about Different Populations

- Weights are chosen to make inferences about the expected average associations in populations with a particular distribution of stratification factor(s)

- Typical choices of standards are often constructed to make inferences about a population with the distribution of the stratification factor(s) in
  - the **exposed** group in the study ("**indirect**" standardization)
  - the **unexposed** group in the study ("**direct**" standardization)
  - an external population of interest ("general population", e.g. US census, world population)

Choose all that are true:

The rate ratios produced by either direct or indirect standardization is hypothetical and describes a rate ratio that would have been obtained had the underlying structure been the same as that of the standard population.

Standardization can be used to control for effect measure modification but not confounding.

Total Results: 0

Indirectly Standardized Rate Ratio (1)
Unified Approach

To make inferences about a population with the distribution of the stratification factors in the **exposed** group, the weights are the percent of the **exposed** person-time in stratum i multiplied by the rate in the unexposed:

Weights for indirectly standardized rate ratios: $w_{1i} = \left(\frac{N_{1i}}{N_1} \right) I_{0i}$

Directly Standardized Rate Ratio (1)
Unified Approach

To make inferences about a population with the distribution of the stratification factors in the **unexposed** group, the weights are the percent of the **unexposed** person-time in stratum i multiplied by the rate in the unexposed:

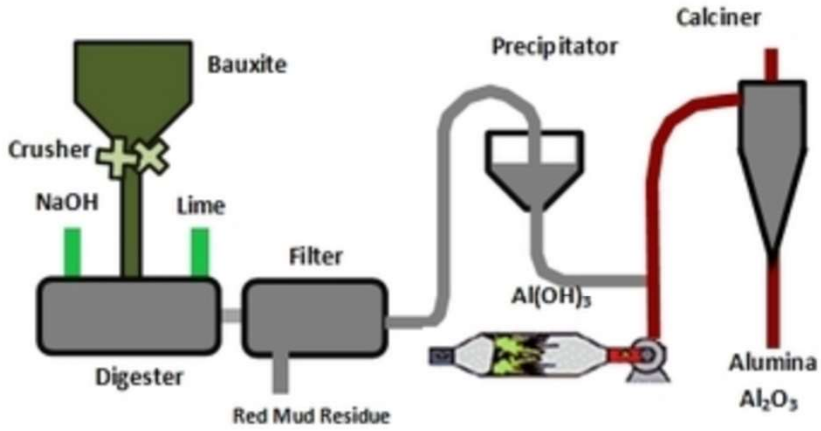
Weights for directly standardized rate ratios: $w_{0i} = \left(\frac{N_{0i}}{N_0} \right) I_{0i}$

Direct vs. Indirect Standardization
Advantages and Disadvantages

- **Direct (SRR)**
  - Requires subgroup-specific cumulative incidence/rate
  - Problematic when stratum-specific rate estimates are imprecise or unknown (e.g. company records only include total cases and person-time distribution)
  - Allows for comparison across study populations standardized to the same standard population

- **Indirect (SMR)**
  - Often used in occupational epidemiology
  - Particularly useful when
    - stratum-specific cumulative incidences/rates are missing in one of the groups under comparison
    - the study group(s) is (are) small so that the stratum-specific cumulative incidences/rates are unstable
  - Comparison of SMRs from different study populations is complicated by the fact that the weights used in obtaining SMRs are the stratum sizes of the exposed groups in the individual study populations rather than a common standard population

Directly standardized measures are comparable from study to study if the same standard population is used.



True

False

Do not know

Traditional Approach to Standardization

- In the traditional approach, standardization can be accomplished by first standardizing the ***rates*** in the exposed and standardizing the ***rates*** in the unexposed groups
- The standardized rate ratio can be calculated by dividing these standardized rates
- The standardized rate difference can be calculated by subtracting these standardized rates
- This approach is mathematically identical to taking a weighted average of stratum-specific measures of association or using the inverse probability weighting approach

Indirect Standardization
Advantages

- Only need information on
  - Total number of exposed cases
  - Distribution of the stratification factor(s) among the exposed (to calculate weights)
  - Stratum-specific rates in the unexposed (in occupational health studies, often taken from the general population)

- The variance of the indirectly standardized estimate is much smaller than the variance of the directly standardized estimate
  - SMR: numerator is total number of exposed cases
  - SRR: stratum specific rates must be estimated

- Conceptually similar to the counterfactual contrast to infer the effect of the exposure among the exposed

If the stratum-specific rates of a population are standardized to that population's distribution, then the standardized rate will be equal to the crude rate for that population.

True

False

Do not know

Total Results: 0

When effect measure modification of the rate ratio is present and there are some strata with only a few exposed cases, the most precise valid approach to estimation is to:

- Assume no effect measure modification and calculate a Mantel-Haenszel summary estimate
- Assume no confounding and report crude estimate
- Use direct standardization
- Use indirect standardization

HAVE A GOOD WEEK