E2041 – Introduction to Epidemiology and Environmental Health
Seminar, 14.11.2024

Comparison of cohort studies and randomized trials

Randomized trials are very expensive to conduct so they are often preceded by years of observational research. In some instances, the results of RCTs confirm the findings from observational studies, in others they show something different. In one notable case, hormone replacement therapy for women after menopause, while long-term follow-up of cohort studies suggested protective benefits of supplemental estrogen on heart disease, RCTs seemed to indicate harm. One trial or at least one of its arms to test the effects of estrogen plus progestin hormone replacement on women's health, the Women's Health Initiative, was stopped because of indications of excess harm to women. It is important to compare the observational and experimental evidence to understand the potential grounds for these discrepancies.

Using the following publications, compare the evidence on hormone replacement and coronary heart disease risk. Complete the table below and answer the questions that follow.

WHI Working Group. Risks and benefits of estrogen plus progestin in healthy postmenopausal women. *JAMA* 2001; 288: 321-333.

Stampfer MJ et al. Postmenopausal estrogen therapy and cardiovascular disease, ten-year follow-up from the Nurses' Health Study. *NEJM* 1991; 325: 756-62.

Detailed study analysis – following the CONSORT Clinical Trial Reporting Checklist

Study design feature	Stampfer et al, 1991	WHI Working Group, 2001
What is the specific hypothesis for the study?		
Setting & location where the data were collected		
Eligibility criteria for study participation		
Intervention – for the trial, describe the intervention in each study arm		

Randomization – describe how women were randomized to study arm		
Blinding – describe how blinding was done in the trial and whether blinding/masking was done in the cohort study		
Outcomes – name the outcomes and describe how they were measured as well as how often		
Sample size – for the trial, how was this calculated? For the cohort study, what is the sample size on which reporting is based (find in text or tables)		
Statistical analyses: what kinds of models were conducted and what confounders/covariates were taken into account when analyzing the study data?		
Length of follow-up: how long were the women followed to observe the outcomes?		
Loss to follow-up: how many women were lost to follow-up or left the trial or cohort study? For the trial, did the loss to follow-up differ by study arm? What were characteristics of people lost to follow-up, if discussed?		

What were the characteristics of the women in the study? For the trial, did the study arms differ or were they similar on basic characteristics?		
For the study outcome, what were the results in relation to hormone replacement therapy exposure/use? Provide RR/OR/HR as well as 95% confidence interval. Interpret the main findings.		
Limitations: what were the stated limitations of the study?		
Generalizability: to what population groups can the results be generalized?		

Questions

1. What do you see as the main differences between the study populations?
2. Are there important differences in how the outcomes were assessed and the length of follow-up? What are they?