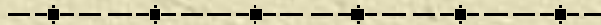


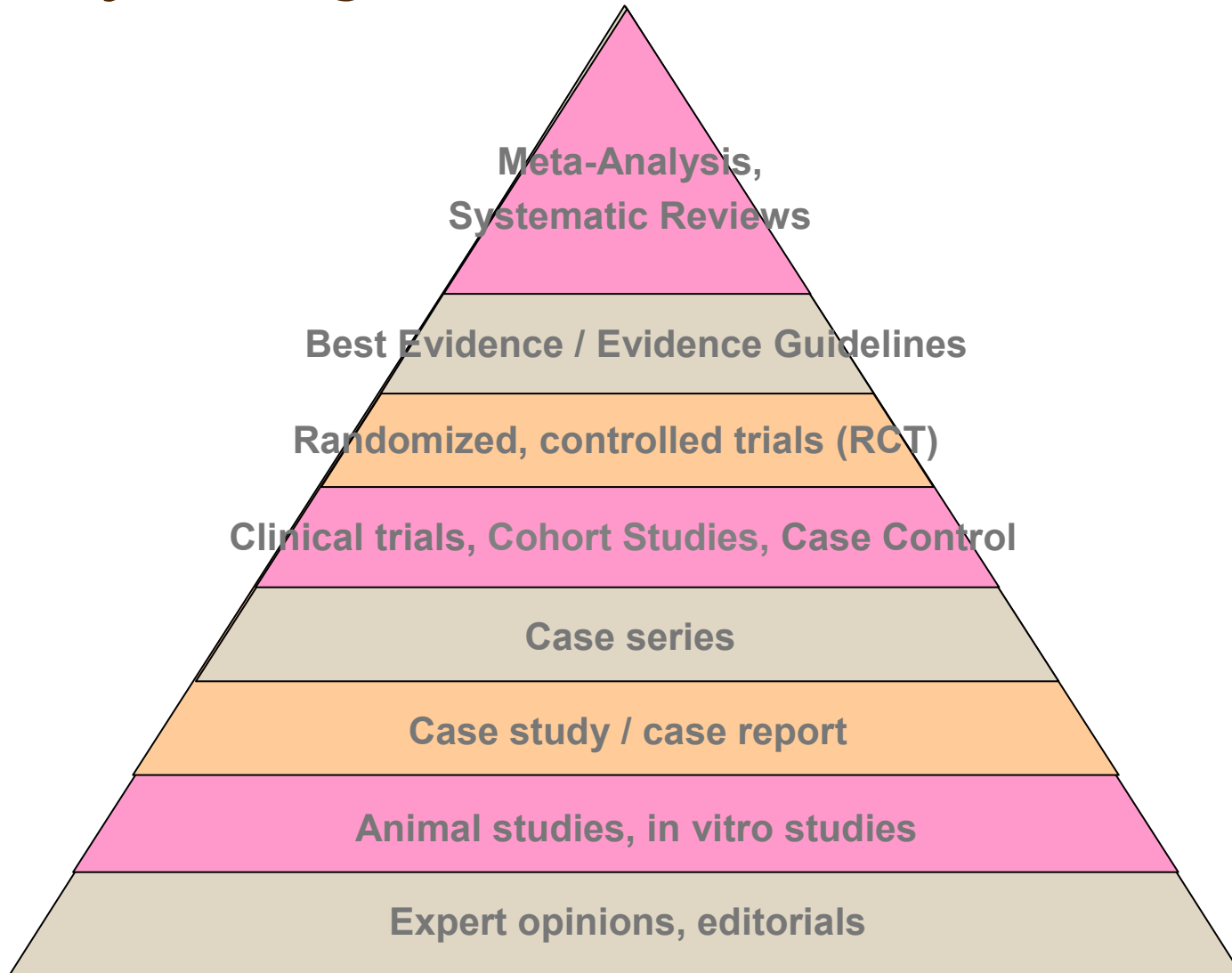


STUDY DESIGN
(continued)

Thomas Grieve, DC
Department of Research



Study designs



We already discussed analytical study designs

- ✦ Experimental studies
 - Clinical trials
- ✦ Observational studies
 - Cohort studies
 - Case control studies

*But there are also
DESCRIPTIVE study designs!*

✦ Analytical

1. Experimental
2. Observational

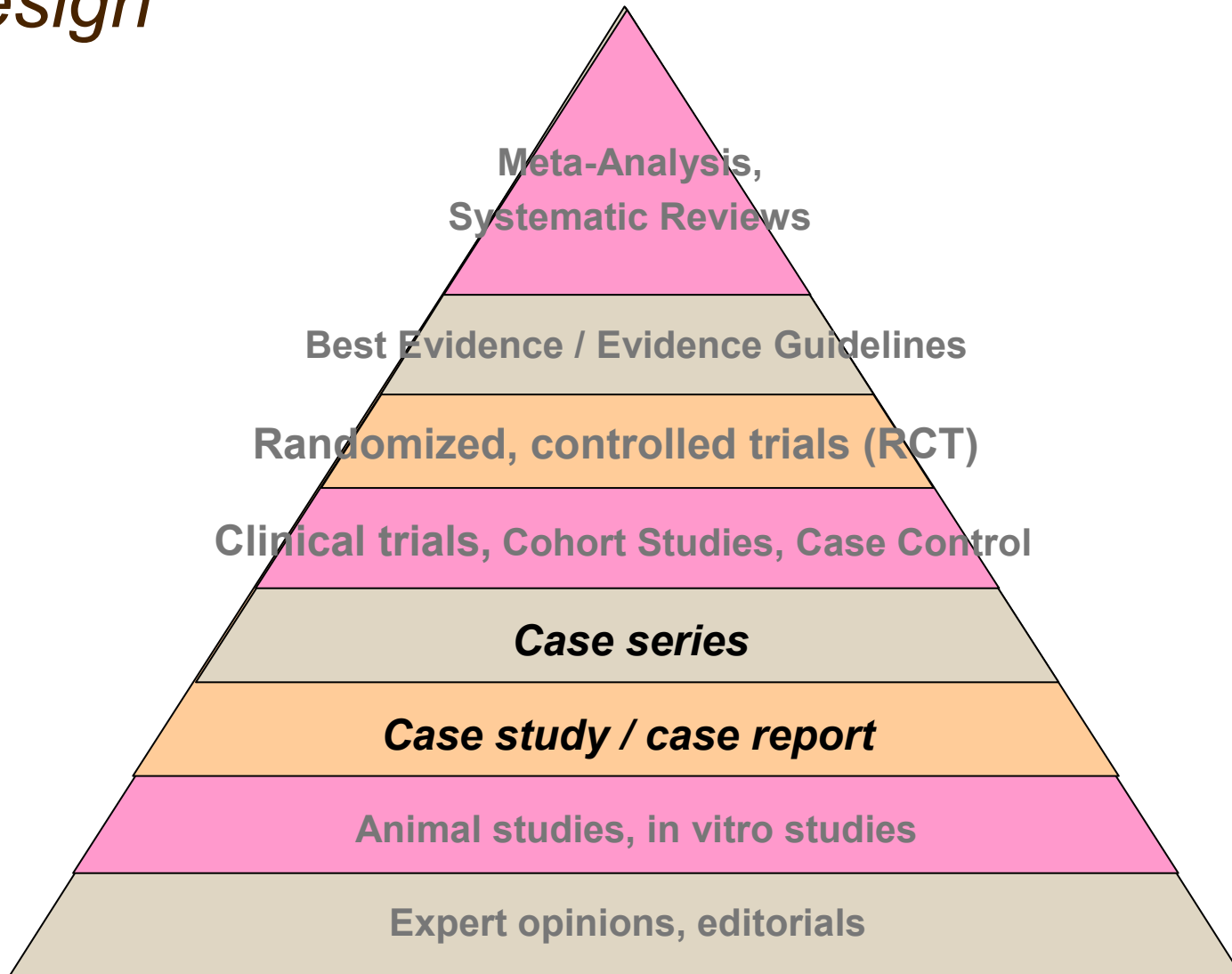
✦ Descriptive

1. Case study
2. Cross sectional: Descriptive survey
3. Qualitative study: Interview

1. *Case study (Descriptive)*

- ✦ A case study (case report) is a method of descriptive research that documents a practitioner's experiences, thoughts, or observations related to the care of a single client.
- ✦ A case series combines the observations from a group of similar clients

Hierarchy of Evidence: strength of study design



Case studies usually feature:

- ✦ New disease or condition
- ✦ Rare or sparsely reported condition
- ✦ Unusual presentation of a common disease
- ✦ Impact of one disease process on another
- ✦ Unexpected event in the course of observing or treating a patient
- ✦ Impact of a treatment regime of one condition on another condition
- ✦ Unexpected complication of treatment or procedure
- ✦ New and unique treatment

Case study example

✦ Four previously healthy homosexual men contracted pneumocystis carinii pneumonia, extensive mucosal candidiasis, and multiple viral infections. In three of the patients these infections followed prolonged fevers of unknown origin. In all four cytomegalovirus (CMV) was recovered from secretions. Kaposi's sarcoma developed in one patient eight months after he presented with esophageal candidiasis.... The inversion of the T/ helper to suppressor/cytotoxic ratio suggested that CMV infection was an important factor in the pathogenesis of the immunodeficient state. A high level of exposure of male homosexuals to CMV-infected secretions may account for the occurrence of this immune deficiency.

Gottlieb MB, et al. N Engl J Med 1981;38805(24):1425-31.

Benefits of case studies

- ✦ Convey detailed information that might be lost in a clinical trial through documentation of actual events and interventions in clinical practice
- ✦ Are faster and less expensive to complete than clinical trials
- ✦ Provide a rationale for further investigation

Vertebral osteomyelitis: a **case report** of a patient presenting with acute low back pain

✦ Ursprung WM, Kettner NW, Boesch R. J Manipulative Physiol Ther. 2005;28(9):713-8.

OBJECTIVE: To report and discuss a case of vertebral osteomyelitis presenting to a chiropractic clinic. CLINICAL FEATURES: **A 65-year-old man presented to a chiropractic clinic with acute low back pain...** CONCLUSIONS: This case report presents a typical clinical presentation of vertebral osteomyelitis and reviews the diagnostic imaging, pathophysiology of spontaneous vertebral osteomyelitis, and treatment options in the management of this condition.

2. Cross sectional study (Descriptive)

- ✦ A survey with questions used to describe a population
 - Do you take vitamins?
 - What vitamins do you take?
 - When do you take them?

Hartvigsen J, Christensen K. Pain in the back and neck are with us until the end: a nationwide interview-based survey of Danish 100-year-olds. Spine. 2008 Apr 15;33(8):909-13.

STUDY DESIGN: Nationwide interview survey. OBJECTIVES: To determine the 1-month prevalence and impact of back and neck pain among centenarians and to investigate associations between back and neck pain and other health measures such as physical function, depression, comorbidity, and self-rated health.

SUMMARY OF BACKGROUND DATA: To our knowledge prevalence and impact of back and neck pain has never been studied among the oldest old. METHODS:

Information on the 1-month prevalence of back and neck pain and bothersomeness of back and neck pain was collected using face-to-face interviews in a nationwide survey of Danish centenarians. In addition, information on physical and mental functional abilities, self-rated health, and comorbidities were collected. RESULTS:

Two hundred fifty-six persons completed the interview (response rate, 56%).

Twenty-nine percent of women and 17% of men had experienced back pain, and 23% of women and 19% of men had experienced neck pain during the past month.

This was comparable to another nationwide Danish survey of younger seniors.

Twenty-one percent had been bothered by back pain either when moving, resting, or sleeping. Poor overall physical function, bad self-rated health, and higher depression score were associated with higher prevalence of back and neck pain.

CONCLUSION: Back pain and neck pain continue to be common and bothersome complaints even into extreme old age. Thus, back pain and neck pain are not limited to working populations.

Sometimes cross sectional studies are observational...

- ✦ A cross sectional study might include questions that can be related in the form of a hypothesis.
- ✦ Survey might include the questions:
 - Do you take vitamins?
 - Do you have diabetes?
- ✦ Hypothesis:
 - People who take vitamins are less likely to have diabetes.

McGill CR, Fulgoni VL 3rd, DiRienzo D, Huth PJ, Kurilich AC, Miller GD. Contribution of dairy products to dietary potassium intake in the United States population. J Am Coll Nutr. 2008 Feb;27(1):44-50.

✱ OBJECTIVE: Adequate dietary potassium intake is associated with a reduced risk of cardiovascular and other chronic diseases. The Dietary Guidelines for Americans 2005 identifies milk and milk products as a major contributor of dietary potassium and lists dairy products, along with fruits and vegetables, as food groups to encourage. This paper further examines the impact of dairy consumption on the potassium intake of the United States (US) population. METHODS: Using data from the National Health and Nutrition Examination Survey (NHANES) 1999-2002 we determined potassium intakes for various age groups of individuals who met the recommended number of dairy servings compared to those who did not. We also examined the impact of dairy servings consumed on mean and median potassium intakes and compared intakes to the age-appropriate Adequate Intakes (AI). RESULTS: For all age groups, mean and median potassium intakes did not meet the respective AI. Mean potassium intakes were significantly greater in those subjects who met dairy intake recommendations compared to those who did not for all age groups. Mean and median potassium intakes increased with increasing dairy intake but were below current intake recommendations for all age groups analyzed. For adults age 19 to 50, 16.1% consumed the recommended number of dairy servings per day. For those 51 and older, 10.7% met current dairy intake recommendations. CONCLUSIONS: Consumption of dairy products is below current recommendations which contributes in part to suboptimal dietary potassium intakes among a large proportion of the US population. Since adequate potassium intake is associated with decreased risk of chronic disease, consumption of a variety of potassium-rich foods, including fruits, vegetables and low-fat and fat free dairy products, should continue to be encouraged.

3. Qualitative study (Descriptive)

- ✦ An interview with one or more people asking open-ended question. Subjects are asked to describe the QUALITY of a situation
 - How does low back pain affect you in your daily life?
- ✦ Interview is sometimes called a Focus Group
- ✦ Subjects are allowed to take discussion in any direction. Researcher looks for common themes in responses.

Granich J, Rosenberg M, Knuiman M, Timperio A. Understanding children's sedentary behaviour: a qualitative study of the family home environment. Health Educ Res. 2008 May 22.

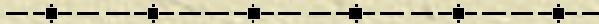
- ✦ Electronic media (EM) (television, electronic games and computer) use has been associated with overweight and obesity among children. Little is known about the time spent in sedentary behaviour (SB) among children within the family context. The aim of this study was to explore how the family home environment may influence children's electronic-based SB. Focus groups and family interviews were conducted with 11- to 12-year old children (n = 54) and their parents (n = 38) using a semi-structured discussion guide. Transcripts were analysed using a thematic content approach. A brief self-completed questionnaire was also used to measure leisure behaviour and electronic devices at home. Children incorporated both sedentary and physical activities into their weekly routine. Factors influencing children's EM use included parent and sibling modelling and reinforcement, personal cognitions, the physical home environment and household EM use rules and restrictions. Participants were not concerned about the excessive time children spent with EM. This under-recognition emerged as a personal influencing factor and was viewed as a major barrier to modifying children's electronic-based SB. Efforts to reduce SB in children should focus on the influencing factors that reciprocally interact within the family home. An emphasis on increasing awareness about the risks associated with spending excessive time in screen-based activities should be a priority when developing intervention strategies aimed at modifying the time children spend in SB.

Hill-Sakurai LE, Muller J, Thom DH. Complementary and alternative medicine for menopause: a qualitative analysis of women's decision making. J Gen Intern Med. 2008 May;23(5):619-22.

✦ **BACKGROUND:** While almost half of women use complementary and alternative medicine (CAM) during their menopause, almost no literature explores why women choose CAM for menopausal symptoms. Clinician-patient conversations about CAM can be unsatisfactory, and exploration of women's choices may benefit communication. **OBJECTIVE:** The objective of this study was to describe women's choices to use CAM for menopausal health issues. **DESIGN:** This is a qualitative study utilizing semi-structured interviews. **PARTICIPANTS:** Convenience sample of 44 menopausal women ages 45 to 60 recruited in two primary care clinics. Both users and non-users of CAM were included. **APPROACH:** Transcripts of semi-structured interviews were analyzed for themes that were refined through comparison of labeled text. **MAIN RESULTS:** Four themes emerged in decisions to use CAM: (1) valuing CAM as "natural", although the meaning of "natural" varied greatly, (2) perceiving menopause as marking a change in life stage, (3) seeking information about menopause generated from personal intuition and other women's experiences, and (4) describing experiences before menopause of using CAM and allopathic medication in patterns similar to current use (patterned responses). **CONCLUSION:** Women's decisions about using CAM during menopause can be understood through their perspectives on menopause and overall health. Increased clinician awareness of these themes may promote supportive discussions about CAM during counseling for menopause.



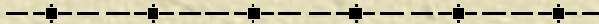
Let's go back to the big picture and re-assess



Study designs that you need to know

- ✦ Randomized clinical trial
- ✦ Cohort study (prospective and historical)
- ✦ Case control study
- ✦ Case study
- ✦ Cross sectional study
- ✦ Qualitative study

*Comparison of two
studies: Cohort vs.
clinical trial*



Cohort study

- ✦ Grodstein F, Manson JE, Colditz GA, Willett WC, Speizer FE, Stampfer MJ. **A prospective, observational study of postmenopausal hormone therapy and primary prevention of cardiovascular disease.** *Ann Intern Med.* 2000 Dec 19;133(12):933-41.

Nurses Health Study Cohort

✦ “The Nurses’ Health Study began in 1976 when 121,700 female nurses 30 to 55 years of age completed a mailed questionnaire about their postmenopausal hormone use and medical history, including cardiovascular disease and its risk factors. We update information with biennial follow-up questionnaires. Dietary and physical activity questionnaires were added in 1980. Cohort follow-up is greater than 90%.”

Subjects

✦ n= 70,533

✦ Inclusion: postmenopausal female nurses

✦ Exclusion: stroke, myocardial infarction, angina, coronary revascularization, or previous cancer

Exposure status

✦ “In 1976, women were asked about use and duration of hormone therapy after menopause. Beginning in 1978, we collected information on type of hormones taken, and starting in 1980, we asked about the dose of oral conjugated estrogen. All information is updated biennially.”

Treatment groups

✦ Treatment groups:

- Estrogen alone (different doses)
- Estrogen + progesterone
- No hormones

✦ Treatment group was determined by the subject and their physician, no randomization occurred.

Baseline differences?

- ✦ Authors state no differences, but no list of characteristics in each group
- ✦ Because there was no randomization, we cannot be sure that the groups were equal.
- ✦ There may have been a bias based on some other factor that led women to use or not use hormonal therapies.

Results

- ✦ Short term and current use of HRT is protective for coronary heart disease.
- ✦ Stroke increased with higher than 0.625 mg/day of estrogen

Table 2: Risk for major coronary heart disease among current postmenopausal hormone users and nonusers, Nurses' Health Study, 1976-1996

Hormone Use	Person-Years of Follow-up	Cases, n	Age-Adjusted Relative Risk (95% CI)	Multivariate-Adjusted Relative Risk (95% CI)*
Never	358 125	662	1.0 (referent)	1.0 (referent)
Past	185 497	337	0.88 (0.77–1.00)	0.82 (0.72–0.94)
Current	265 203	259	0.54 (0.46–0.62)	0.61 (0.52–0.71)
<1 yt	20 091	9	0.30 (0.16–0.58)	0.40 (0.21–0.77)
1–1.9 yt	19 155	9	0.32 (0.16–0.61)	0.41 (0.21–0.80)
2–4.9 yt	78 928	60	0.47 (0.36–0.61)	0.53 (0.41–0.70)
5–9.9 yt	77 435	74	0.51 (0.40–0.65)	0.58 (0.45–0.74)
≥10 yt	69 594	107	0.69 (0.56–0.85)	0.74 (0.59–0.91)

* Adjusted for age, body mass index, history of diabetes, hypertension, high cholesterol level, age at menopause, cigarette smoking, and parental history of premature heart disease.

† Duration of use is underestimated by an average of 1 year, since duration during each 2-year follow-up period was established at the start of each period.

*Table 3: **Risk for stroke** among postmenopausal current users of hormone therapy and nonusers **by duration** of therapy, Nurses' Health Study, 1976-1996*

Hormone Use	Person-Years of Follow-up	All Stroke		
		Cases, <i>n</i>	Age-Adjusted Relative Risk (95% CI)	Multivariate-Adjusted Relative Risk (95% CI)*
Never	358 125	312	1.0 (referent)	
Past	185 497	217	1.11 (0.93–1.33)	1.02 (0.85–1.24)
Current	265 203	238	1.03 (0.87–1.22)	1.13 (0.94–1.35)
<1 yt	20 091	13	1.05 (0.60–1.85)	1.32 (0.76–2.32)
1–1.9 yt	19 155	10	0.85 (0.45–1.60)	1.04 (0.55–1.97)
2–4.9 yt	78 928	61	1.08 (0.82–1.43)	1.14 (0.86–1.52)
5–9.9 yt	77 435	63	0.94 (0.71–1.23)	1.05 (0.79–1.38)
≥10 yt	69 594	91	1.09 (0.85–1.39)	1.17 (0.91–1.49)

Table 4: **Risk for stroke** among postmenopausal current users of hormone therapy and nonusers **by dose** of oral conjugated estrogen, Nurses' Health Study, 1980-1996

Hormone Use	Person-Years of Follow-up	All Stroke		
		Cases, n	Age-Adjusted Relative Risk (95% CI)	Multivariate-Adjusted Relative Risk (95% CI)*
Never	313 661	290	1.0 (referent)	
0.3 mg	19 964	9	0.43 (0.22–0.83)	0.54 (0.28–1.06)
0.625 mg	116 150	124	1.11 (0.90–1.37)	1.35 (1.08–1.68)
≥1.25 mg	39 026	46	1.58 (1.16–2.15)	1.63 (1.18–2.26)

Clinical trial

- ✦ Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, Jackson RD, Beresford SA, Howard BV, Johnson KC, Kotchen JM, Ockene J; Writing Group for the Women's Health Initiative Investigators. **Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial.** *JAMA* 2002 Jul 17;288(3):321-33.

Subjects

✦ n= 16,608

✦ Inclusion: ages 50-79, postmenopausal, 3 year residence, written informed consent

✦ Exclusion: competing health risks, safety issues, issues with medical compliance

Treatment groups

- ✦ Treatment groups:
 - Estrogen + progesterone combined
 - Placebo
- ✦ This was a randomized trial so women were randomized to one group or the other. Unlike the cohort study, the women and their physicians did not self-select their treatment.

Baseline differences?

- ✦ No substantive differences were found between the treatment groups (Table 1)
- ✦ This is common for clinical trials, but not as common for cohort studies.

Results- STOP THE STUDY!

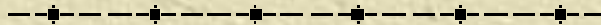
- ✦ The DSMB recommended early stopping of the estrogen plus progestin component of the trial.
- ✦ Evidence for breast cancer harm and some **increase in CHD**, stroke, and PE outweighed the evidence of benefit for fractures and possible benefit for colon cancer.

Results: Coronary heart disease

- ✦ Hazard ratio (similar to relative risk) for coronary heart disease in HRT users versus non-users was 1.29, meaning the hormone users had a **GREATER** risk of heart disease than the non-users.
- ✦ These results differed from the cohort studies.



Comparison of the studies



Slight study differences

1. Choice of reference group
2. Blinding to treatment
3. Treatment modification
4. Frequency of data collection
5. Specific outcome measures
6. Diagnostic criteria
7. Determination of cause of death

Major difference: Baseline characteristics

- ✦ NHS (cohort): Women who chose to take estrogens had
 - more favorable lifestyles
 - fewer heart disease risk factors
 - less diabetes than untreated women
 - higher compliance in seeing physician and taking meds, which might be a surrogate for otherwise not easily measurable factors such as better adherence to diet and exercise

- ✦ WHI (RCT): Women were randomized to treatment, so baseline characteristics were more balanced!

Bottom line

- ✦ HRT was considered cardio-protective until the WHI was complete
- ✦ Results of WHI were a surprise to the medical community
- ✦ Methods of treatment with HRT changed significantly!!

RECENT UPDATE

- ✦ When the WHI findings were released in 2001, there was a 50% reduction in the use of HRT.
- ✦ This, in turn, led to a 6.7% drop in breast cancer diagnoses* between 2002 and 2003! We continue to see the rates of breast cancer drop.

*The absolute risk of breast cancer in women who take HRT is 8 in 100,000.

Any questions?

