Loren Regier BSP, BA
www.sdh.sk.ca/RxFiles – Sept 2002

HRT in Light of the WHI – Data in Perspective

THE RISK OF BREAST CANCER IN PERSPECTIVE Adapted from JOGC Dec-2001

Factor	Baseline breast cancers per 1000 women 20 yrs	Additional cancers per 1000 women 20 yrs	Total cancers per 1000 women 20 yrs
No HRT use (baseline)	**45**	**0**	**45**
5 years HRT use RCT-Level 1 Evidence		4 †	49
10 years HRT use		6	51
15 years HRT use		12	57
Late menopause (10yr delay)		13	58
Body mass index (10kg/m^2 ↑)		14	59
Alcohol: 2drinks/day		27	72
Lack regular exercise (<4hr/week)		27	72
Weight gain after menopause		45	90

⇨ **(WHI; 5.2yrs)** Estimate prior to WHI was 2 additional cases per 1000 women

Baseline or basic risk applies to all women and is due to factors that cannot be controlled (such as aging and gender). From Reid RL Progestins in hormone replacement therapy: impact on endometrial and breast cancer. J Soc Obstet Gynaecol Can 2000;22:679.

† Subgroup analysis: women reporting prior postmenopausal hormone use had increased risk compared to "HRT never users"

THE WHI - DIFFERENT WAYS TO LOOK AT THE DATA JAMA 2002;288 (3): 21-333.

- 16,608 healthy postmenopausal women with an intact uterus; mean age at recruitment 63 years (5,522 subjects aged 50-59)
- conjugated equine estrogen 0.625mg/day + medroxyprogesterone 2.5mg/day (e.g. PREMPRO/PREMPLUS)
- trial stopped after a mean of 5.2 years due to risks exceeding benefits
- for every 10,000 women taking this combination of HRT for 1 year there were:

	for 5.2years:
- 8 more cases of invasive breast cancer	- **42** more cases
- 7 more coronary heart disease events	- **36** more cases
- 8 more strokes	- **42** more cases
- 8 more pulmonary embolisms	- **42** more cases

- the absolute increase in risk of getting invasive breast cancer **per year** was 0.08%
  - Treat **1,250** women with HRT for one year to see 1 extra breast cancer compared to placebo WHI **extrapolation**

- the absolute increase in risk of getting breast cancer **per 5.2 years** was 0.42%
  - Treat **238** women with HRT for 5.2 years to see 1 extra breast cancer compared to placebo (WHI **ACTUAL data**)

Medical Letter comment (Sept 2, 2002):
- "assuming that no women had more than one event, taking the 2 drugs for 5 years would have a **1.5%** chance of developing one of these events (CHD, strokes, pulmonary emboli, invasive breast cancers) because of the drugs"
- (Interpretation in NNH: **for every 66 women treated for 5.2 years, there was one extra major adverse event**)

TIPS IN INTERPRETING DATA:

Relative Versus Absolute Numbers:
- Relative numbers are often used to make an effect sound impressive (better or worse than it actually is).
- Absolute numbers give a better picture of how likely a patient is to experience an event. Since they do not sound as impressive or significant, absolute numbers can downplay adverse event rates if compared to relative numbers used to magnify the benefits.

Modification Of The Time To See A Given Benefit/Risk
- Benefits of preventative therapies are often expressed in terms of effect over several years; adverse effects for the same therapies are often given as events per year. This enhances the perception of benefit and minimizes the perception of risk.

Contextualization Of Trial Evidence
- Since a trial is conducted in a controlled environment, applying the results to practice requires an assessment of whether the conditions are transferable to a given practice setting. For the WHI, limitations include the age of recruitment: mean 63years.

For the WHI trial, data is often being discussed as events per year or as events per 10,000 patients per year. This may be more appropriate when discussing the risk/benefit of short-term therapy but less useful in discussing the risk/benefit of long-term therapy. For an individual woman, risks should be individually assessed and weighed against the potential benefits.

Update Feb, 2009:

- Further analysis of the WHI breast cancer data finds ↑ risk for combination (estrogen + progestagen) especially in older ♀ with family hx & high risk factors Gail model {NNH= 50-238/5.2yrs}. Incidence of breast cancer was up to 2x greater in hormone treated groups of women.
- Breast cancer risk diminishes to normal within 2 years of discontinuation of HRT
- If HRT chosen for menopausal symptom management, consider lowest dose for the shortest time.