Informing menopausal hormone therapy use: do the strengths of association with breast and colorectal cancers depend on familial risk?

Robert MacInnis

Cancer Epidemiology Division,
Cancer Council Victoria, Australia

25 September 2024
(I have no conflicts of interest to disclose)

WORLD CONGRESS OF EPIDEMIOLOGY 2024

Background

Associations with Menopause Hormone Therapy (MHT) use:

- increased risk of breast cancer
- decreased risk of colorectal cancer

But studies had a small proportion of women with family history

MHT choice: “**Should I take it if I have a family history of cancer?**”

Data Sources

Prospective Family Study Cohort (ProF-SC) - Aust, Can, USA; 1992-2011
Colon Cancer Family Registry Cohort (CCFRC) - Aust, Can, USA; 1997-2012
Melbourne Collaborative Cohort Study (MCCS) - Aust; 2003-2007

24,488 women aged 45+ years at baseline

Exclusions:
Existing diagnosis of any cancer
Pathogenic variants in *BRCA1*, *BRCA2*, *MLH1, MSH2, MSH6, PMS2*
Missing data on MHT use or missing covariates

Statistical Analyses

Want better measure of family history than yes/no

Compute 5-year risk based on detailed family history and current age of consultee

Breast cancer: BOADICEA risk model, Colorectal cancer: CRISP risk model

Familial Risk Score: $\log\left(\frac{\text{5-year risk based on age, family history}}{\text{5-year risk based on age}}\right)$

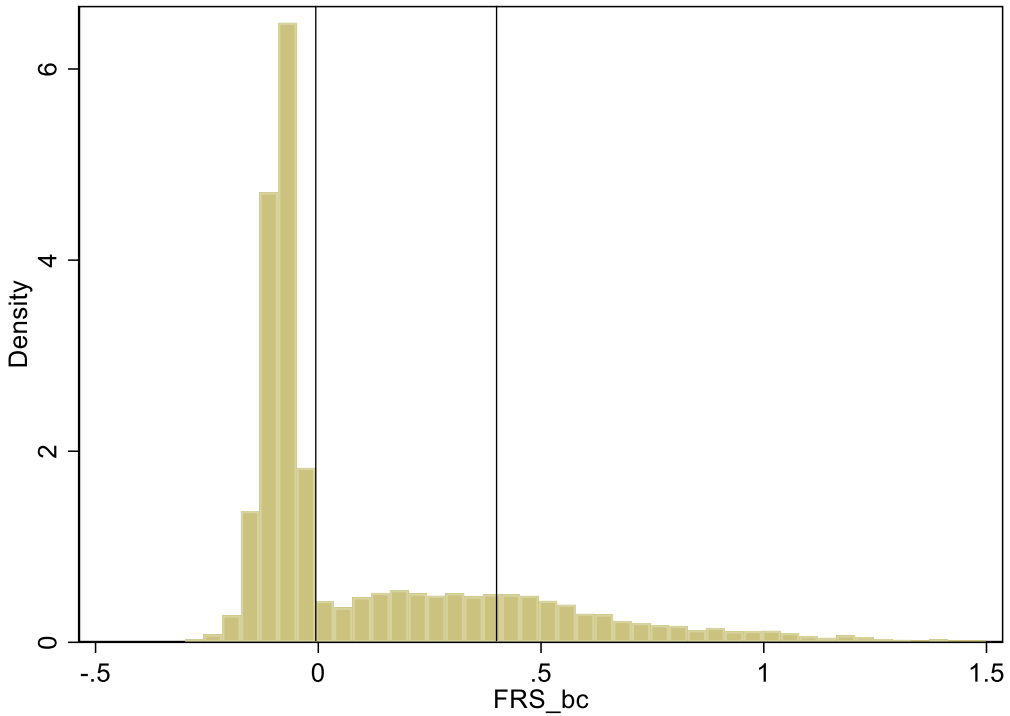
Cox regression

- age as time scale
- stratified by study
- adjusted for BMI, parity, education, alcohol, smoking status, OC use, country

Familial Risk Score

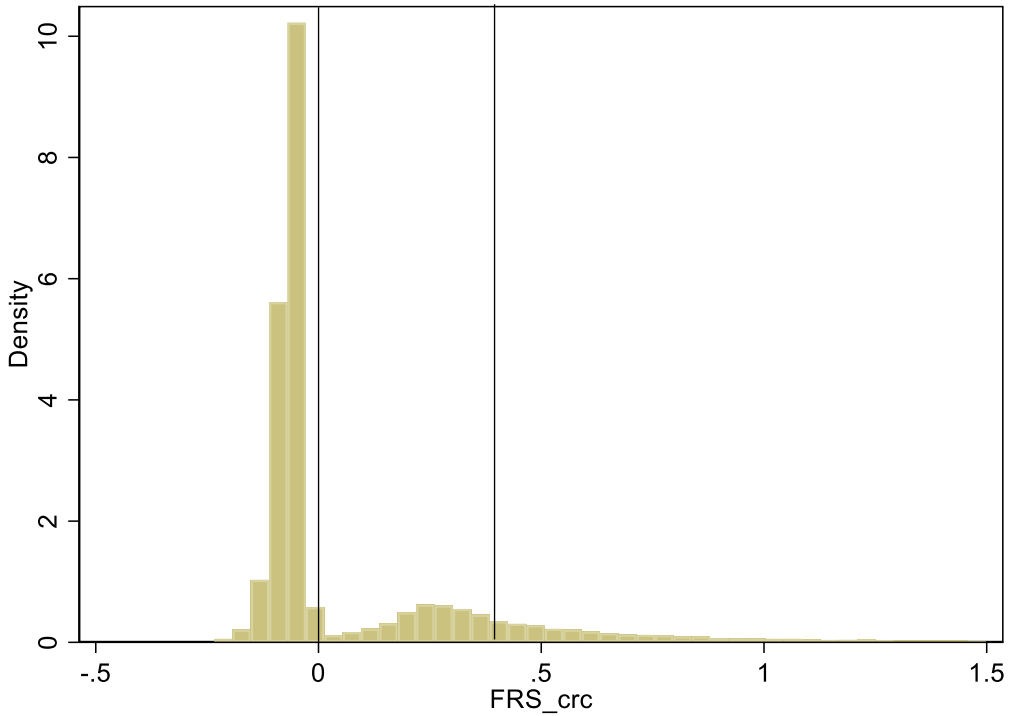
Breast Cancer

Family history: No Weak **Moderate/Strong**



Colorectal Cancer

No Weak **Moderate/Strong**



FRS 0.4 -> 50-year-old woman with one parent diagnosed with either cancer before age 55 years

MHT Cox Regression Results

MHT use: 55% never, 45% ever
Average follow-up time: 12.6 years
Mean age at attendance: 58 (ProF-SC), 58 (CCFRC), 63 (MCCS)

Breast cancer cases = 1243

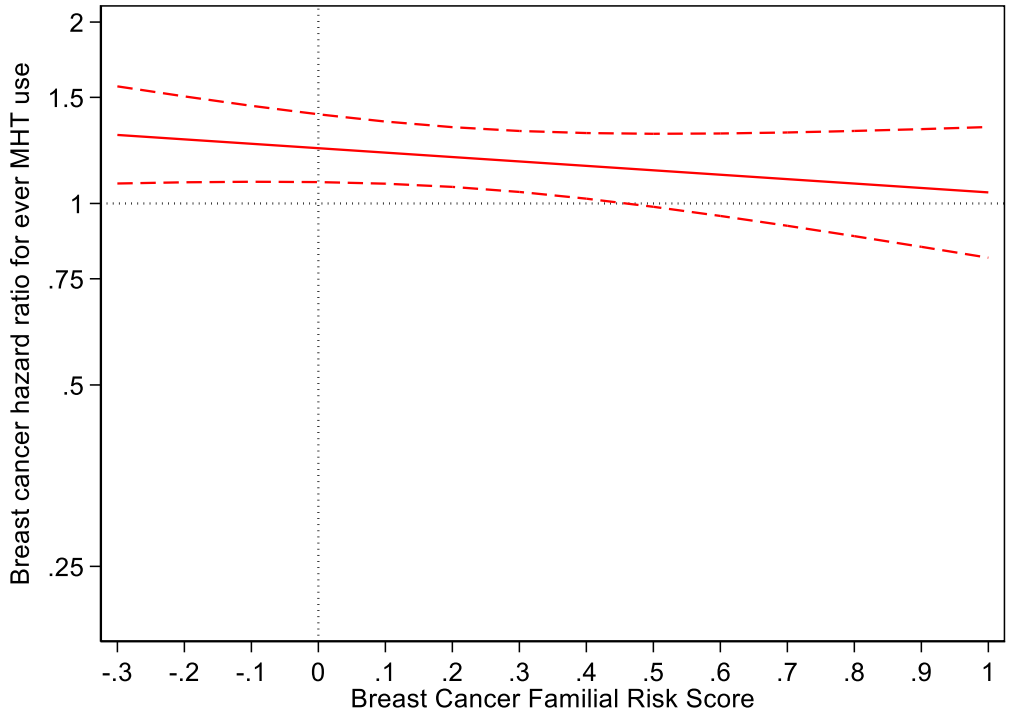
Variable	HR (95% CI)	P-value
MHT use	1.20 (1.07-1.34)	0.001

Colorectal cancer cases = 405

Variable	HR (95% CI)	P-value
MHT use	0.73 (0.59-0.90)	0.003

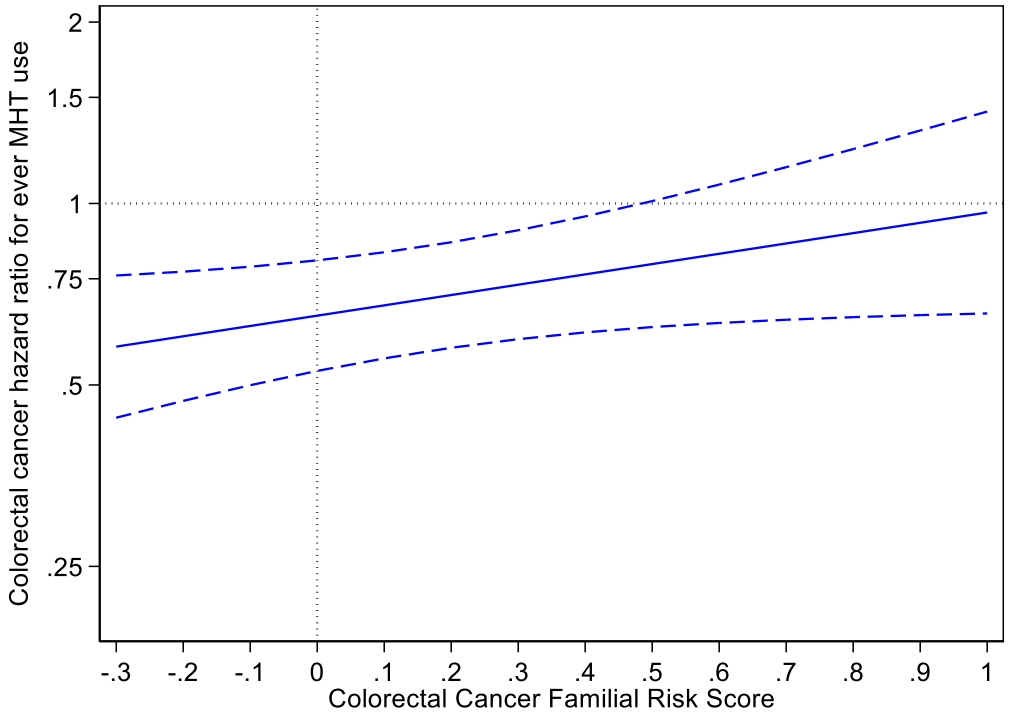
MHT Results By FRS

Breast Cancer



P-interaction MHT and BC_FRS = 0.25

Colorectal Cancer



P-interaction MHT and CRC_FRS = 0.10

Cox Regression Results

Breast cancer

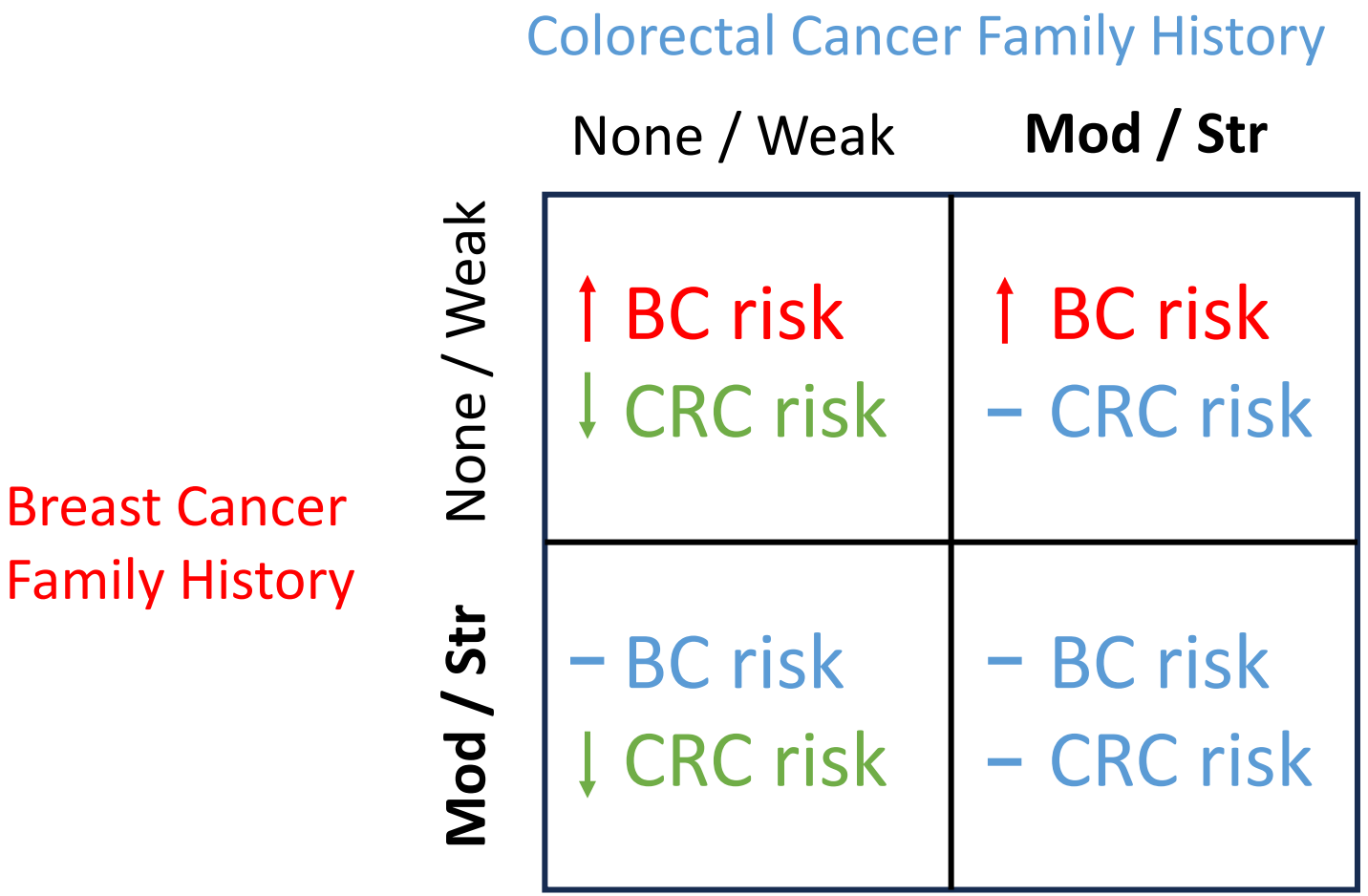
Variable	HR (95% CI)	P-difference
MHT use – no BC FH	1.30 (1.11-1.53)	
MHT use – weak BC FH	1.22 (0.96-1.56)	0.65
MHT use – mod/str BC FH	1.03 (0.83-1.27)	0.07

Colorectal cancer

Variable	HR (95% CI)	P-difference
MHT use – no CRC FH	0.65 (0.50-0.83)	
MHT use – weak CRC FH	0.74 (0.45-1.23)	0.63
MHT use – mod/str CRC FH	1.21 (0.74-1.98)	0.03

Adjusted for BMI parity, education, smoking status, OC use; stratified by country; age as time variable

Summary


Colorectal Cancer Family History
None / Weak
Mod / Str
Breast Cancer Family History
None / Weak
Mod / Str
↑ BC risk
↓ CRC risk
↑ BC risk
– CRC risk
– BC risk
↓ CRC risk
– BC risk
– CRC risk

Thank you!

Participants and Investigators from the three cohorts

ProF-SC

Mary Beth Terry

John Hopper

Esther John

Mary Daly

Irene Andrulis

Sarah Colonna

Kelly Phillips

MCCS

Roger Milne

Graham Giles

Melissa Southey

CCFRC

Mark Jenkins

Loic Le Marchand

Polly Newcomb

Amanda Phipps

Stephanie Schmidt

Finlay Macrae

Dan Buchanan

Steve Gallinger

Rish Pai

Niloy Samadder

AEA Australasian Epidemiological Association