Epidemiology of Breast Cancer Selected Highlights

Jack Cuzick, Ph.D
Cancer Research UK
London

Major Factors

- Family history
- Reproductive/ Hormonal
- Benign Pathology
- Mammographic Density

Family History

BRCA 1/2

Accounts for <5% of breast cancer. Important in some populations with founder mutations.

Askenazi Jews
Penetrance 50-80%

- Low penetrance genes specific genes unknown
 - Age at onset
 - Multiple family members
 - Bilaterality

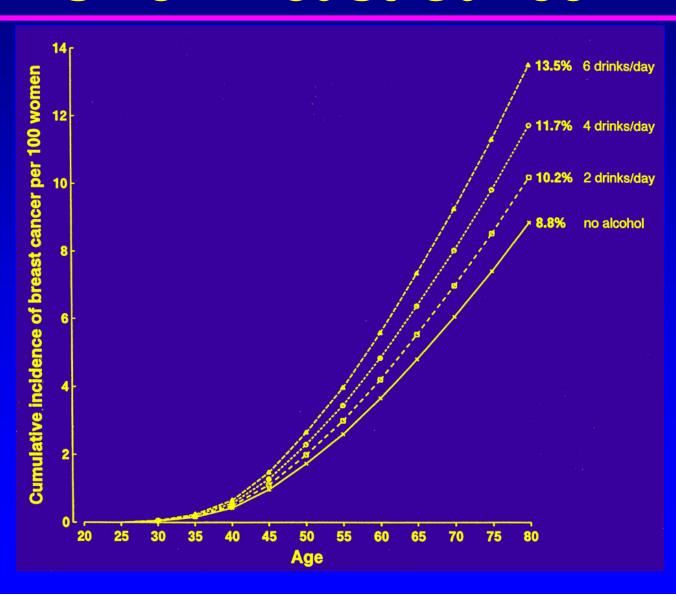
Number of Relatives with Breast Cancer

Number of first-degree relatives with breast cancer	Cases (n=58 209)	Controls (n=101 986)	Risk ratio
None	50 713	94 548	1.00
1	6810	6998	1.80
2	603	404	2.93
3 or more	83	36	3.90

Age at Diagnosis - Relative Risk

Woman's age (years)	Relative's age at diagnosis of breast cancer					
	<40 years	40-49 years	50-59 years	>60 years		
<40	5.7	2.9	2.8	2.0		
40-49	3.0	2.0	2.3	1.7		
50-59	2.0	2.2	1.6	1.6		
>60	1.4	1.4	1.5	1.4		

Alcohol – Cumulative Risk of Breast Cancer



Reproductive/ Childbirth

Age 1st childbirth –

Nulliparous \cong First birth age = 30 years RR \cong 3% / year

Parity

 $RR \simeq -7\%$ / birth

Breast Feeding ≅ - 4.3% / year

Reproductive-Menstrual Factors

Age at Menopause

~ 3% / year

Age at Menarche

~ - 4% / year

- Oral Contraceptives24% increase in current users only
- Hormonal Replacement Therapy
 2.3% / year in current users only
 oestrogen + progestin twice as high

~ 5% /year.

Other Hormonal

Weight – postmenopausal

1% increase / kg

Height

1% increase / cm

Alcohol

~ 7% per drink (10g) / day

Benign Breast Disease

Lobular Carcinoma-in-situ

~ 10-fold risk

Atypical Hyperplasia

4-fold risk

Proliferative lesion without atypia.

2-fold risk

Mammographic Density

Quantitative Effect

	None	<10%	10-25	25-50	50-75	>75
Rel. Risk	1.0	1.2	2.2	2.4	3.4	5.3
% of Controls	4.9	12.7	19.5	27.0	22.2	13.7

High Attributable Risk

> 50% density PAR = 33%

> 75% density PAR = 15%

(Boyd, et al. 1995)

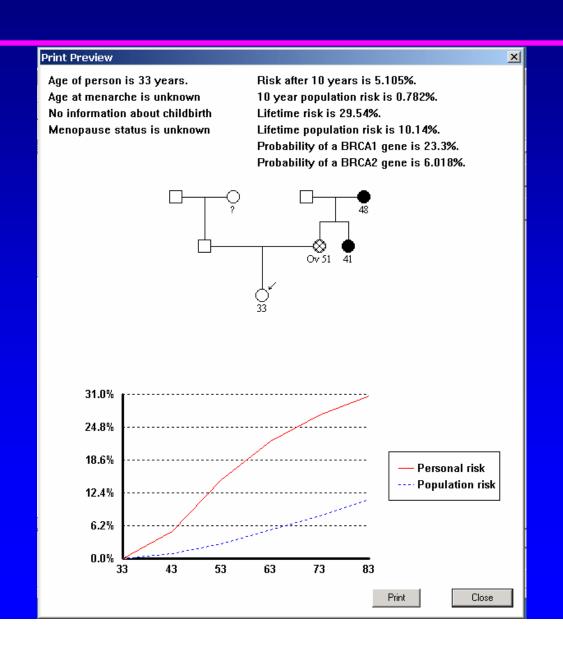
Estimating risks for individuals

The risk calculator program	_ I X
Woman's 33 Menarche: ? Height ? Weight ? [kg]: Nulliparous: O Age First Child: ? Premenopausal: O Age at menopause: Postmenopausal: O Age at menopause: Postmenopausal: O No information: O No	Measurements Metric: Imperial: HRT use Length of use (years): 5 or more years ago: Less than 5 years ago:
Ovarian: Paternal Status: Age: Ovarian: Affected Status: Age: Ovarian: Ovarian: Maternal Status: Age: Ovarian: Ovarian	Current user:
status: Mother: Affected	Ovarian:

Displaying the predictions



Summary output



Which factors involve Hormonal Regulation?

- Age at Menarche & Menopause
- Childbirth
- Weight
- Mammographic Density ?
 - At least partially
- Benign Breast Disease ?
 - Maybe
- Family History ?
 - Unclear

Which factors are associated with ER+ Cancers?

- Age at Menarche & Menopause ?
- Childbirth ?
- Weight ?
- Mammographic Density ?
- Benign Breast Disease ?
- Family History ?