

**Smoking and risk of breast cancer
in carriers of mutations in BRCA1
and BRCA2 aged less than 50.**

Environmental modifiers group

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BCFR, kCONFab, OCGN

Background

- Smoking and DNA damage
 - Carcinogenic polycyclic aromatic hydrocarbons, aromatic amines, *N*-nitroso compounds
 - DNA strand breaks, abasic sites, base adducts
- Smoking and estrogen exposure
 - earlier age at menopause
 - lower body weight

Smoking and risk of breast cancer in carriers of BRCA1 and BRCA2 mutations

- **Brunet et al JNCI 1998**
 - N=186/186
 - Smoking protective
 - OR=0.46 (95% CI: 0.3-0.8)
- **Ghaderian et al Int J Cancer**
 - N=1097/1097
 - No effect of smoking
 - OR=1.05 (95% CI: 0.9-1.2)
- **Baron and Haile JNCI 1998**
 - Prevalent cases
 - Convenience samples
 - Possible selection bias
 - Familial relationships
 - (testing: selection, methods)

Methods

- **Clinic and population based sites**
- **Recruitment of families**
- **Tested for BRCA1 and BRCA2 mutations**
 → **cases and controls**
- **Exposure to smoking**
 - **Standard questionnaire**
 - **Personal interview (all sites – Utah, Ontario)**
 - **Mailed questionnaire (Utah, Ontario)**
 - **Ever smoked, amount, age at start, total years**

Methods

- **Analysis**
- Non-Hispanic white subjects
- All subjects + those interviewed within 3 years of reference age
- Unconditional logistic regression
- Adjusted for site, alcohol use and family history
- Robust variance estimates (Whittemore and Halperin 2002)

Selected characteristics

	Cases (n=323)		Controls (n=481)	
	N	(%)	N	(%)
Source of data				
Clinic-based	196	(61)	442	(92)
Population based	127	(39)	39	(8)
Reference age (years)				
<30	33	(10)	114	(24)
30-39	149	(46)	167	(35)
40-49	141	(44)	200	(41)
Country of residence				
Australia	156	(48)	212	(44)
Canada	82	(25)	28	(6)
United States	64	(20)	124	(26)
Utah	21	(7)	117	(24)

Familial relationships

Cases/controls	0	1	2	3+	Total
0	0	153	39	23	215
1	210	60	10	10	290
2	10	2	1	2	15
3+	1	0	0	0	1
Total	221	215	50	35	523

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Smoking and breast cancer risk – BRCA1

	Cases (n=195)		Controls (n=302)		OR	95% CI
	N	(%)	N	(%)		
Smoking status						
Never	100	(52)	193	(67)	1.0	
Former	41	(21)	53	(18)	1.28	0.84-1.93
Current	52	(27)	44	(15)	1.78	1.14-2.77
Pack-years of smoking						
0	100	(53)	193	(67)	1.0	
1-4	27	(14)	48	(17)	0.93	0.56-1.56
≥5	62	(33)	46	(16)	2.13	1.42-3.18
Trend per Pack-year					1.06	<i>p</i> < 0.001

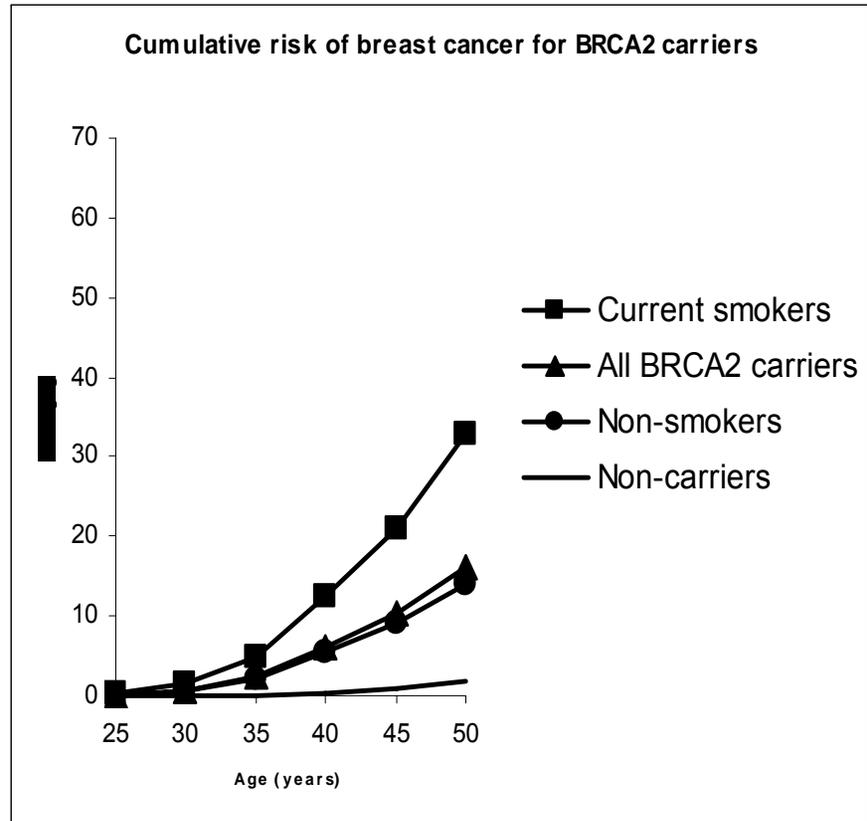
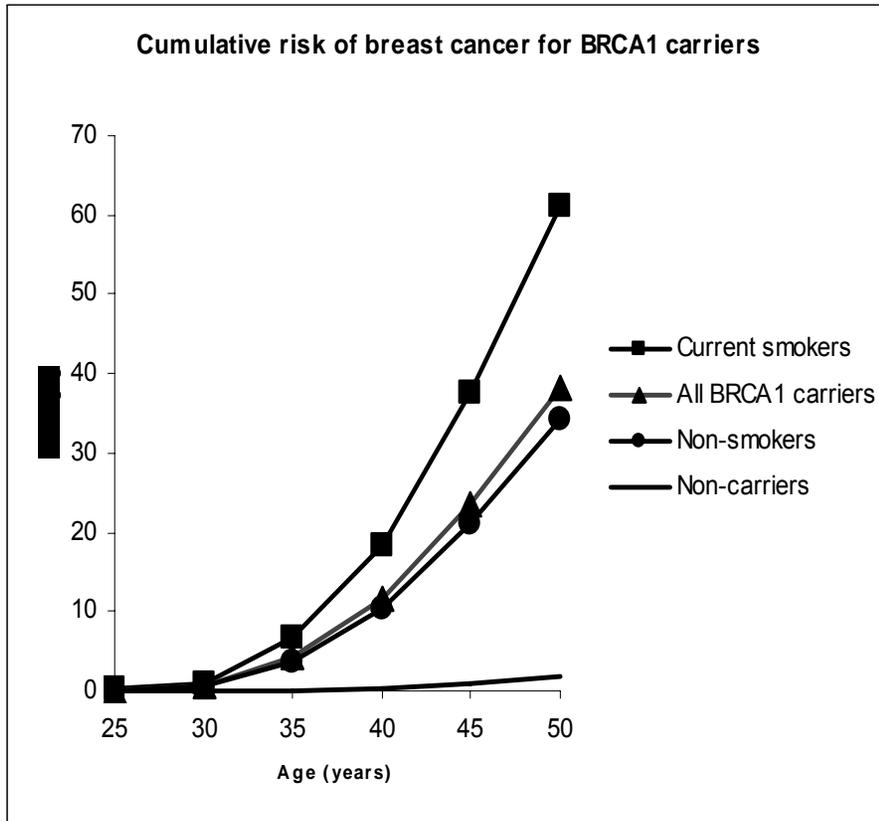
Smoking and breast cancer risk – BRCA2

	Cases (n=128)		Controls (n=179)		OR	95% CI
	N	(%)	N	(%)		
Smoking status						
Never	58	(46)	117	(66)	1.0	
Former	44	(35)	41	(23)	2.13	1.42-3.19
Current	24	(27)	20	(11)	2.33	1.24-4.37
Pack-years of smoking						
0	58	(46)	117	(66)	1.0	
1-4	27	(21)	31	(17)	1.80	1.06-3.07
≥5	41	(34)	30	(17)	2.59	1.73-3.87
Trend per Pack-year					1.06	<i>p</i> < 0.001

Smoking and breast cancer risk – combined

	Cases (n=323)		Controls (n=481)		OR	95% CI
	N	(%)	N	(%)		
Smoking status						
Never	158	(49)	310	(66)	1.0	
Former	85	(27)	94	(20)	1.60	1.19-2.14
Current	76	(24)	64	(14)	1.92	1.30-2.85
Pack-years of smoking						
0	158	(49)	310	(66)	1.0	
1-4	54	(18)	79	(18)	1.25	0.88-1.77
≥5	103	(33)	76	(16)	2.25	1.68-3.01
Trend per Pack-year					1.06	<i>p</i> < 0.001

Estimated cumulative incidence



Strengths and Limitations

- **Limitations**

- Prevalent cases
- Site specific protocols for selection for testing
- Site specific laboratory methods

- **Strengths**

- 82% interviewed within 3 years
- Standardized data collection
- No evidence of selection bias according to smoking habits
- Validation of laboratory methods
- Familial relationships taken into account in analysis

Conclusions

- Smoking is associated with an increased risk of breast cancer in carriers of mutations in BRCA1 and BRCA2 aged less than 50.
- Risk increased with increasing duration of smoking, but there was no evidence that age at start, or start before FFTP, influenced risk.
- Estimated cumulative incidence to age 50 is about 60% in BRCA1 carriers and 40% in BRCA2 carriers - double the rates for carriers who are non-smokers.

Authors

- **Stanford and LA**

- A Feldberg
- V McGuire
- A Whittemore
- R Haile

- **Northern California**

- E John

- **Fox Chase**

- M Daly
- A Godwin
- E Ross
- J Beck

- **New York and Boston**

- R Senie
- MB Terry

- A Miron

- **Australia**

- J Hopper
- G Giles
- M McCreadie
- R Milne
- M Southey
- M Jenkins
- G Trench

- **Ontario**

- NF Boyd
- I Andrulis
- J Knight

- **Utah**

- S Buys