Otago Spotlight Series
Cancer Research

Genomic health for personalised cancer care and prevention

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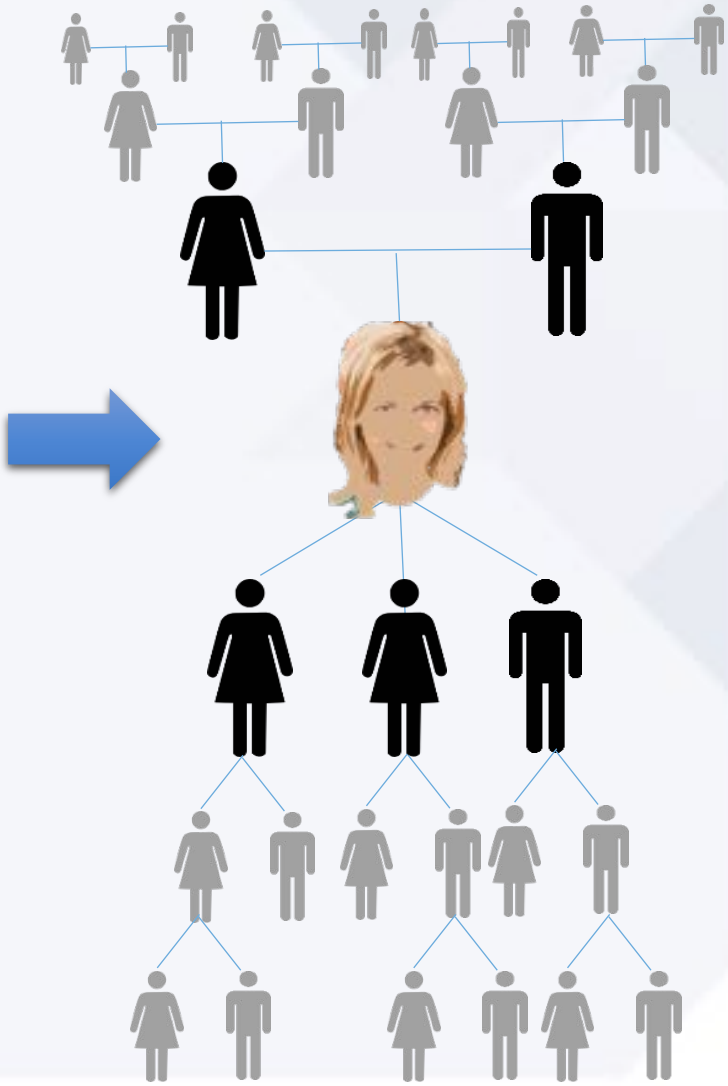
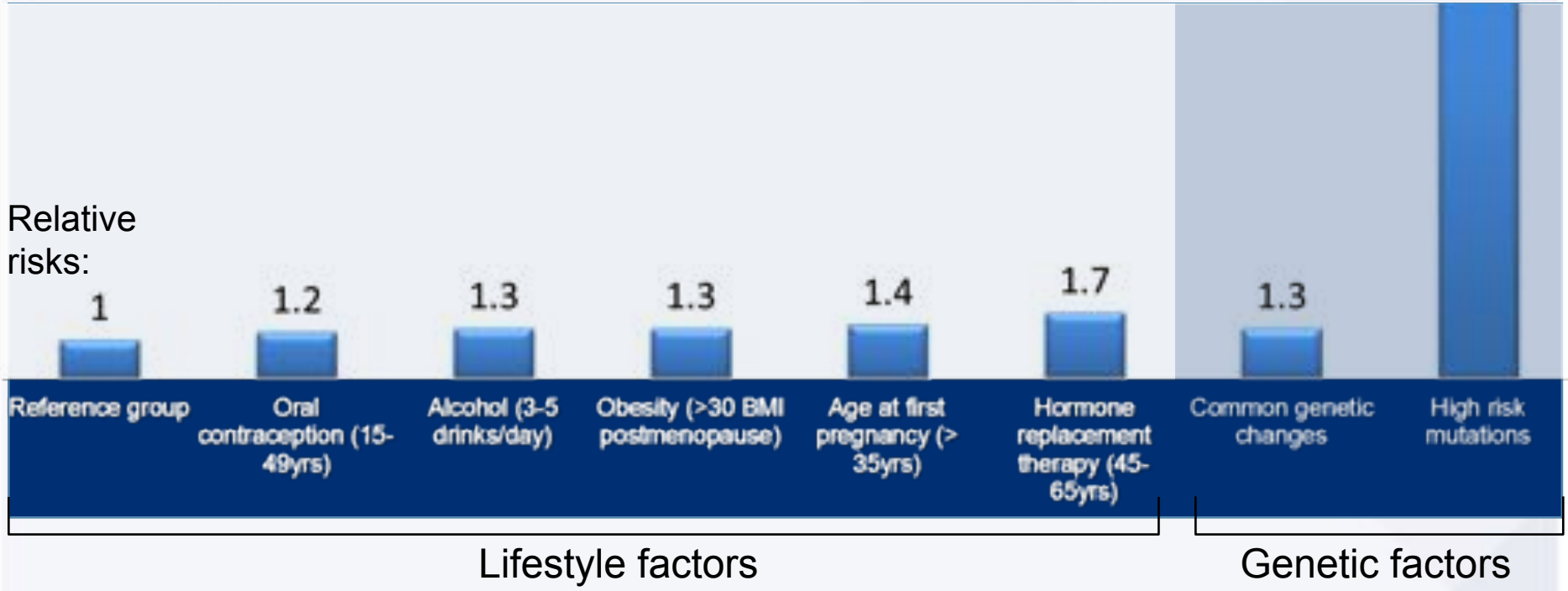
Who are most vulnerable to breast cancer?



Breast cancer risk factors



Breast cancer is not caused by

- wearing underwire bras
- implants
- deodorants/antiperspirants
- mammograms
- caffeine
- microwaves
- cell phones

Breast cancer statistics in NZ

Population statistics

~3000 women develop breast cancer in NZ each year

How many affected women carry a high-risk mutation?

Genetic screening statistics

300-350 women undergo genetic testing each year

<20% tests positive

~5-10% tests unclear

Future of genetic screening

Whole gene sequencing

Gene panel screening

Greater number of individuals screened

Greater number of reported unclassified variants

BRCA Challenge Project

Standardise data collection, variant interpretation and clinical genetic databases

Classifying genetic variants

Reported variant

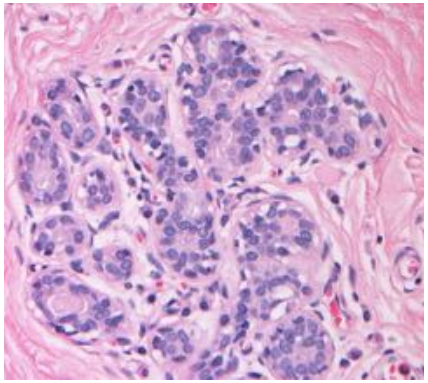
↓

ENIGMA

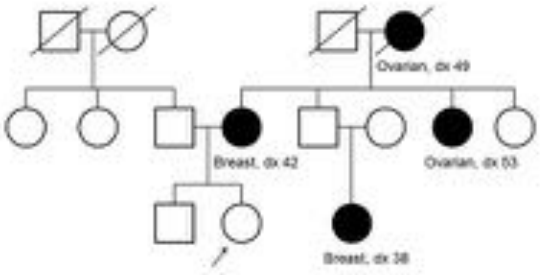
(Evidence-based Network for the Interpretation of Germline Mutant Alleles)

↓

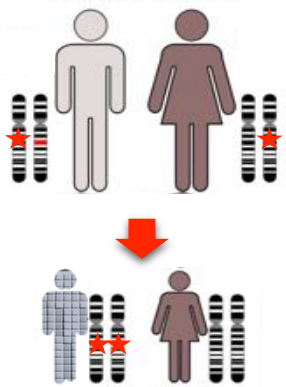
Multifactorial analysis



Tumour type



Family history and segregation



Co-occurrence

Molecular biology

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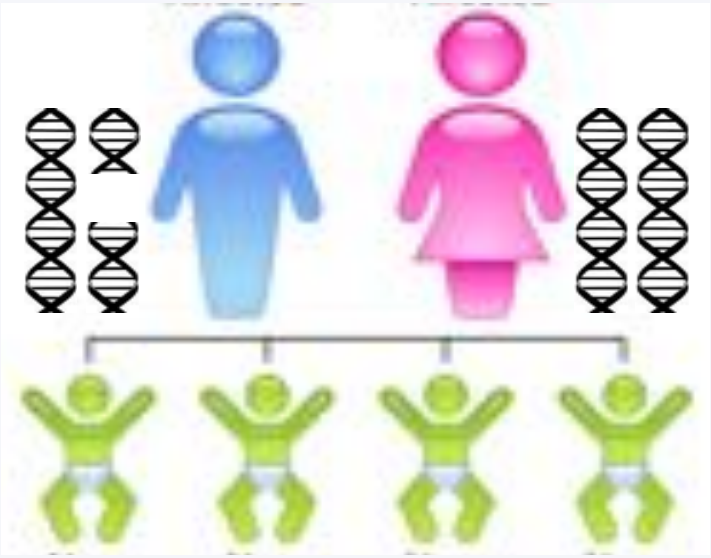
Not pathogenic or pathogenic

The Angelina Jolie effect

- "*My doctors estimated that I had an 87 percent risk of breast cancer and a 50 percent risk of ovarian cancer, although the risk is different in the case of each woman*."

- Why do *BRCA1* and *BRCA2* mutation carriers vary in risk?

Genetic modifiers of risk



LETTERS

nature genetics

A locus on 19p13 modifies risk of breast cancer in *BRCA1* mutation carriers and is associated with hormone receptor–negative breast cancer in the general population

Genetic data from 2500 *BRCA1* mutation carriers

Genome-wide association study

$$L = \prod_{i=1}^{m} P(g_i|y_i(t_i)) = \prod_{i=1}^{m} \frac{P(g_i)P(y_i(t_i)|g_i)}{P(y_i(t_i))}$$
$$= \prod_{i=1}^{m} \frac{P(g_i)P(y_i(t_i)|g_i)}{\sum_k P(g_i = k)P(y_i(t_i)|g_i = k)}$$
$$= \prod_{i=1}^{m} \frac{\tau_{g_i} \exp[-\Lambda_0(t_i)\, exp(\beta g_i) + O_i \beta g_i]}{\sum_k \tau_k \exp[-\Lambda_0(t_i)\, exp(\beta k) + O_i \beta k]}$$

$$U = \frac{\partial \log L}{\partial \beta}\Big|_{\beta=0}$$
$$= \sum_{i=1}^{m} (g_i - \bar{g})[O_i - \Lambda_0(t_i)]$$

New findings:
Breast Cancer
GeneX
Ovarian Cancer
GeneY

Validation

>20,000 *BRCA1* mutation carriers (CIMBA Consortium)

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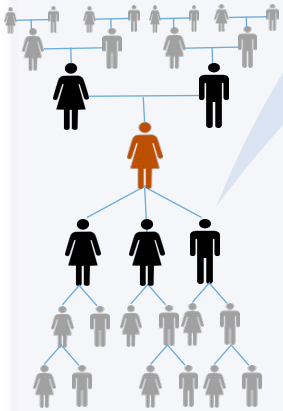
Genomic medicine

21st Century Health Care

Advancing knowledge for health professionals



Unpack genetic data

Utilise international resources

Implement advanced diagnostics

Reduce the impact of disease

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Michael Parsons
Louise Marquart

ENIGMA consortium
>100 research scientists/clinicians from >20 countries

CIMBA consortium
>100 research scientists/clinicians from >30 countries

kConFab (Peter MacCallum Cancer Centre)
Heather Thorne
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