Cancer Model of care for Population Genetic Testing

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TheAHSNNetwork NHS England
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Research Funding

GCaPPS
Genetic Cancer Prediction through Population Screening

the eve appeal
fighting women's cancers
Registered charity numbers 1091708 & SC040932

TheAHSNNetwork NHS England
NHS Innovation Accelerator

The movement for REFORM JUDAISM

Boots

JEWISH CARE

NORWOOD
CHILDREN & FAMILIES FIRST

ovacome
the ovarian cancer support network

THE ACADEMIC STUDY GROUP ISRAEL AND THE MIDDLE EAST

Indian Jewish Association UK

liberal judaism

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Barts Health NHS
NHS Trust

BACKGROUND

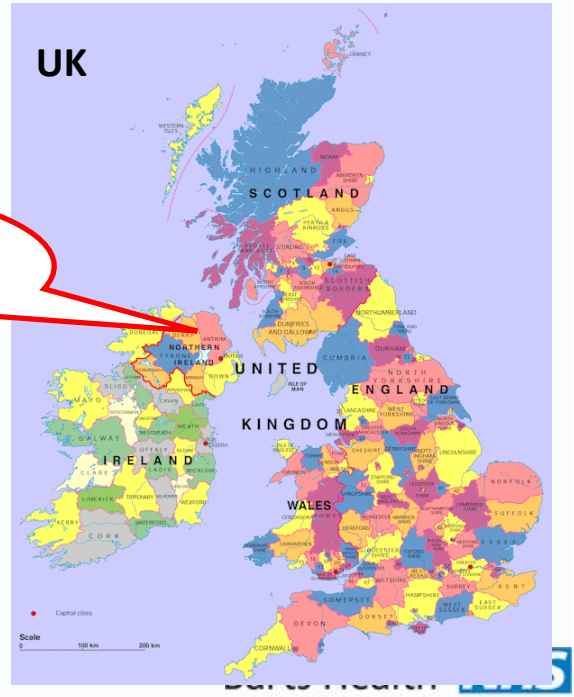
Predicted Rise in Cancer Cases by 2040

USA

BC– 26%
OC– 31%

BC 47%
OC 47%

UK

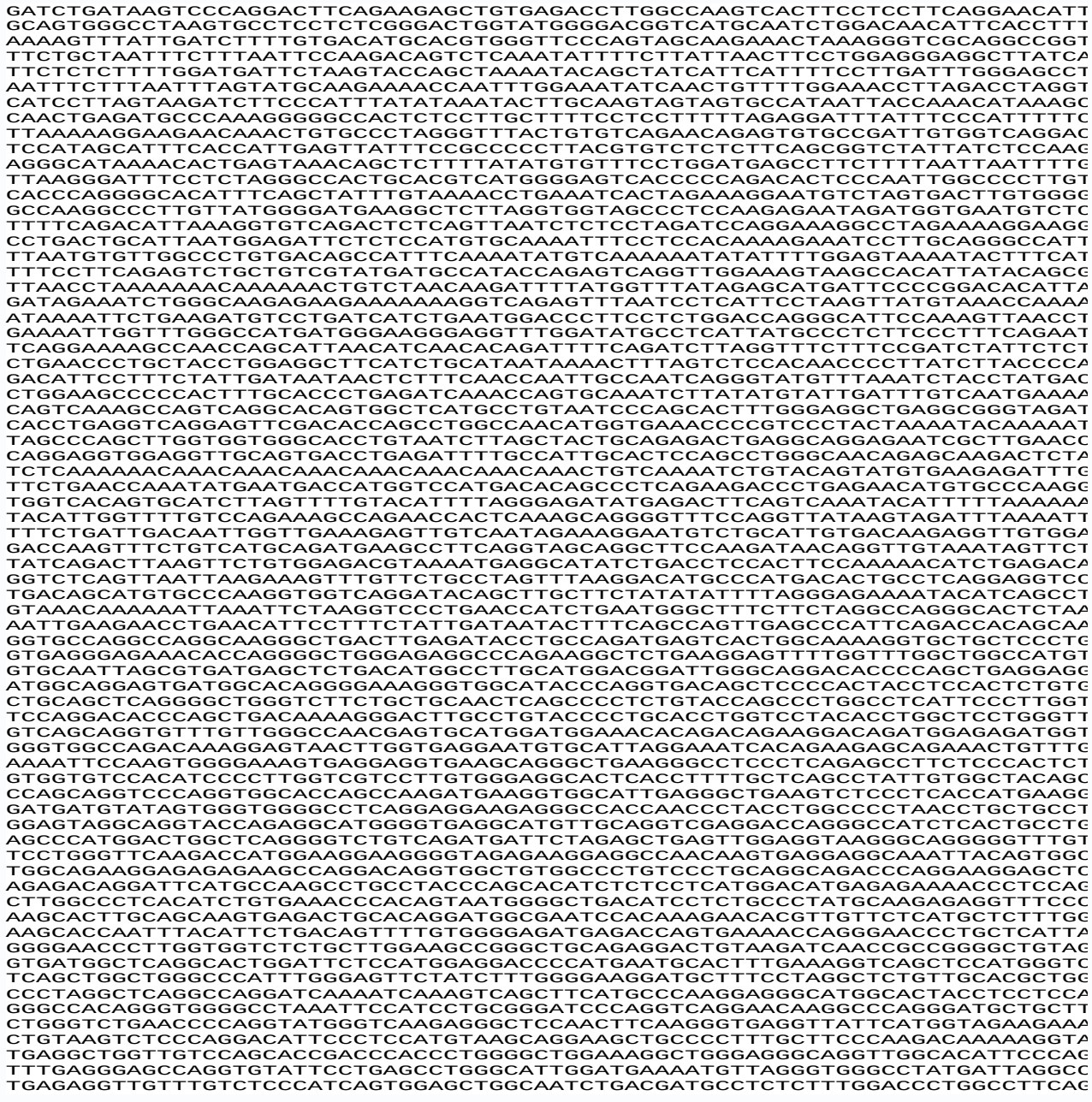


BC 20%
OC 26%

BC- Breast Cancer
OC- Ovarian Cancer

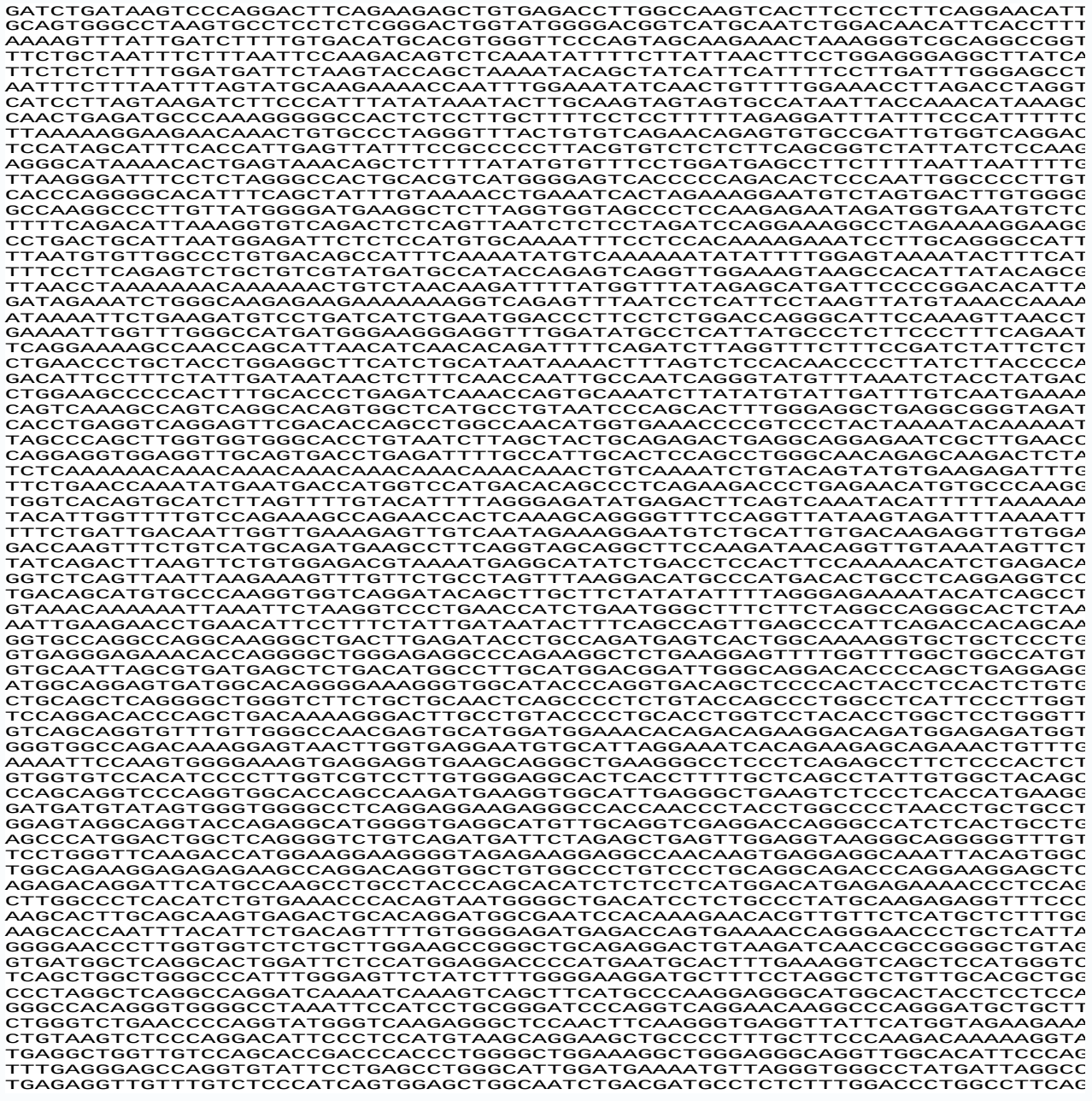
Page 1

A typical gene looks a bit like this…

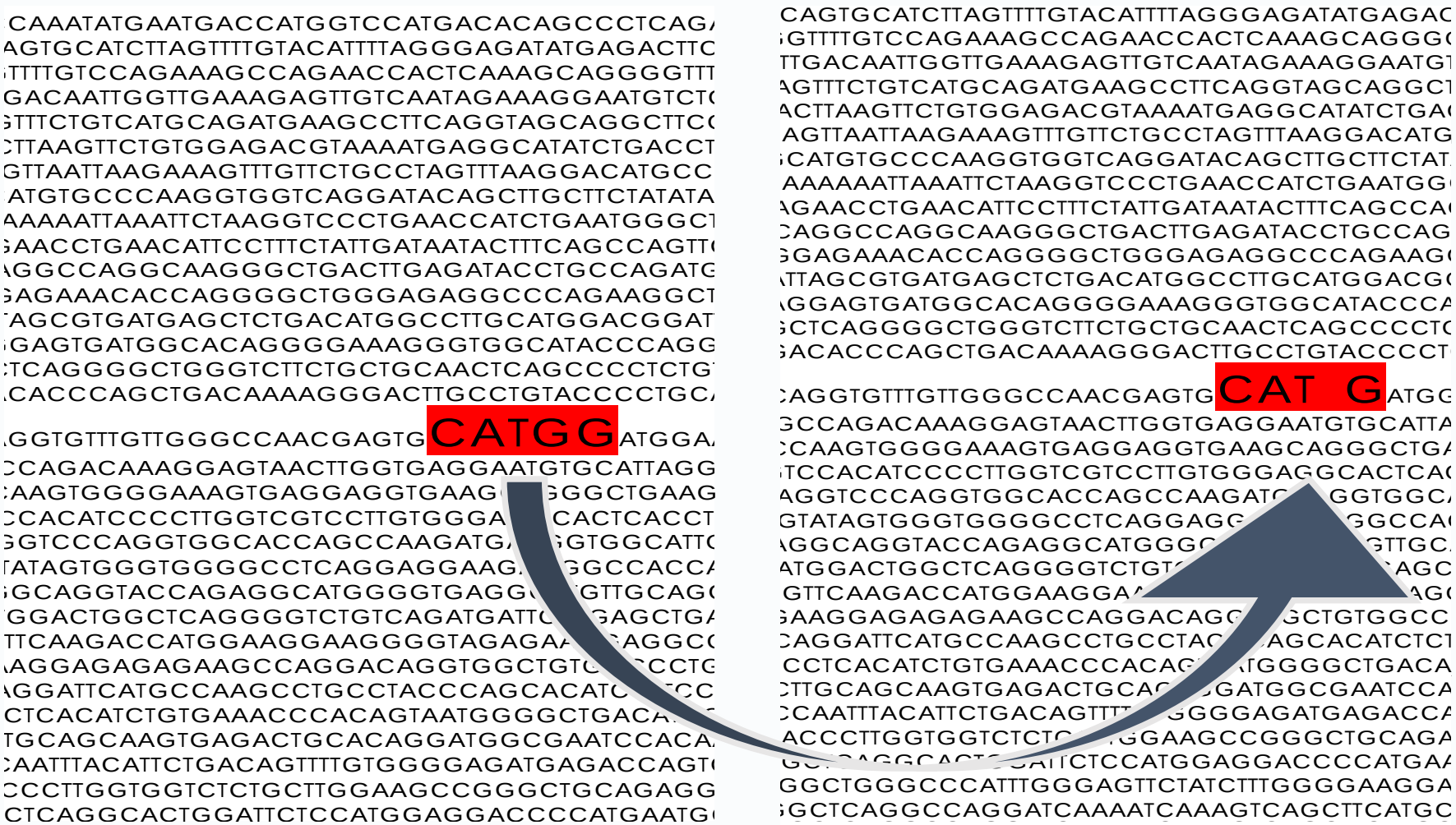


Page 200

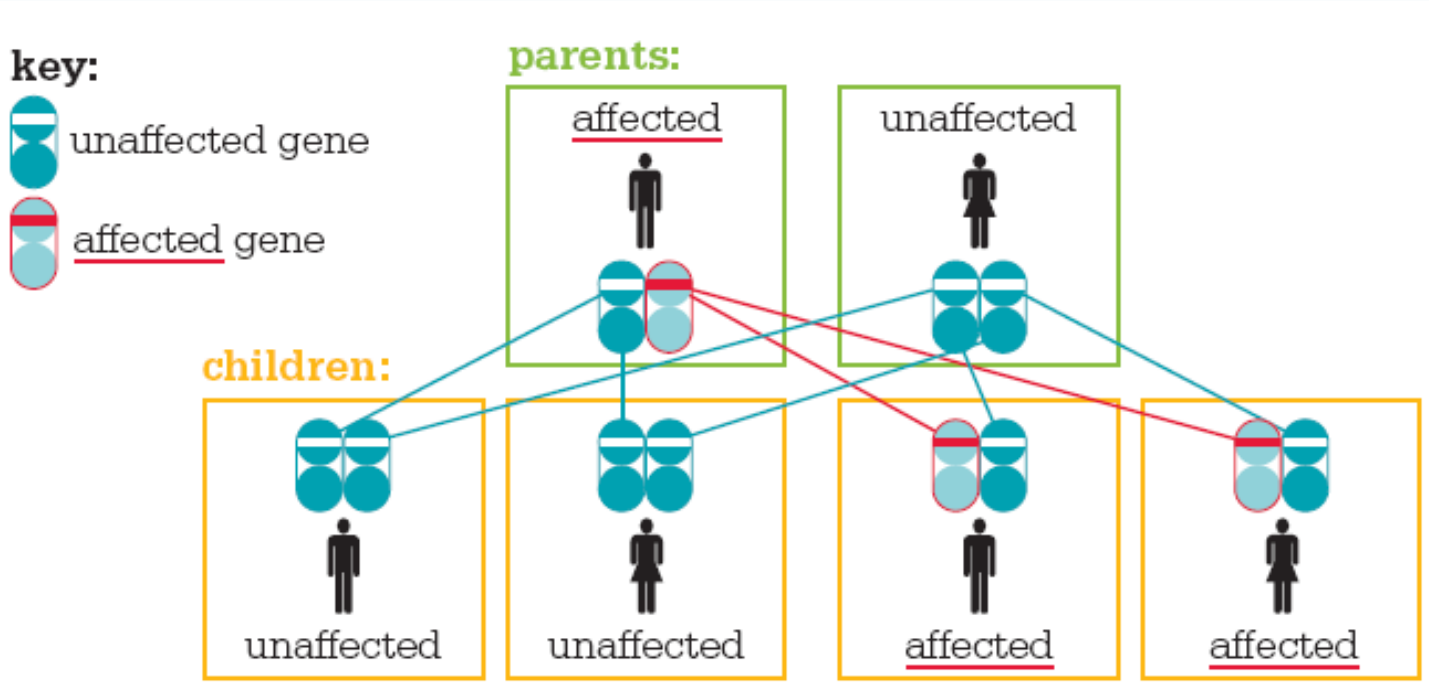
And so on till Page 200….



Gene alterations (mutations) are usually small

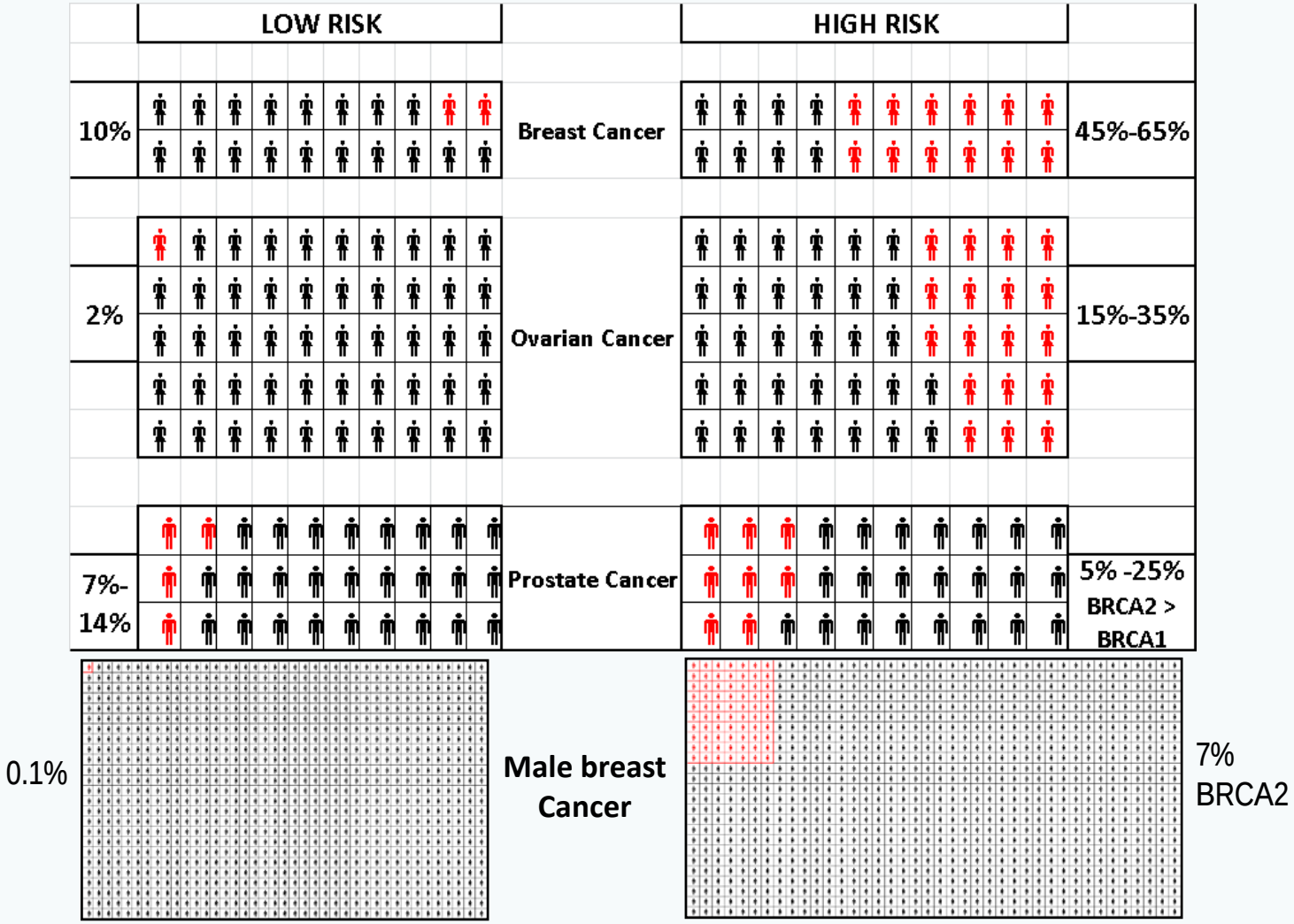


And can occur anywhere within a gene

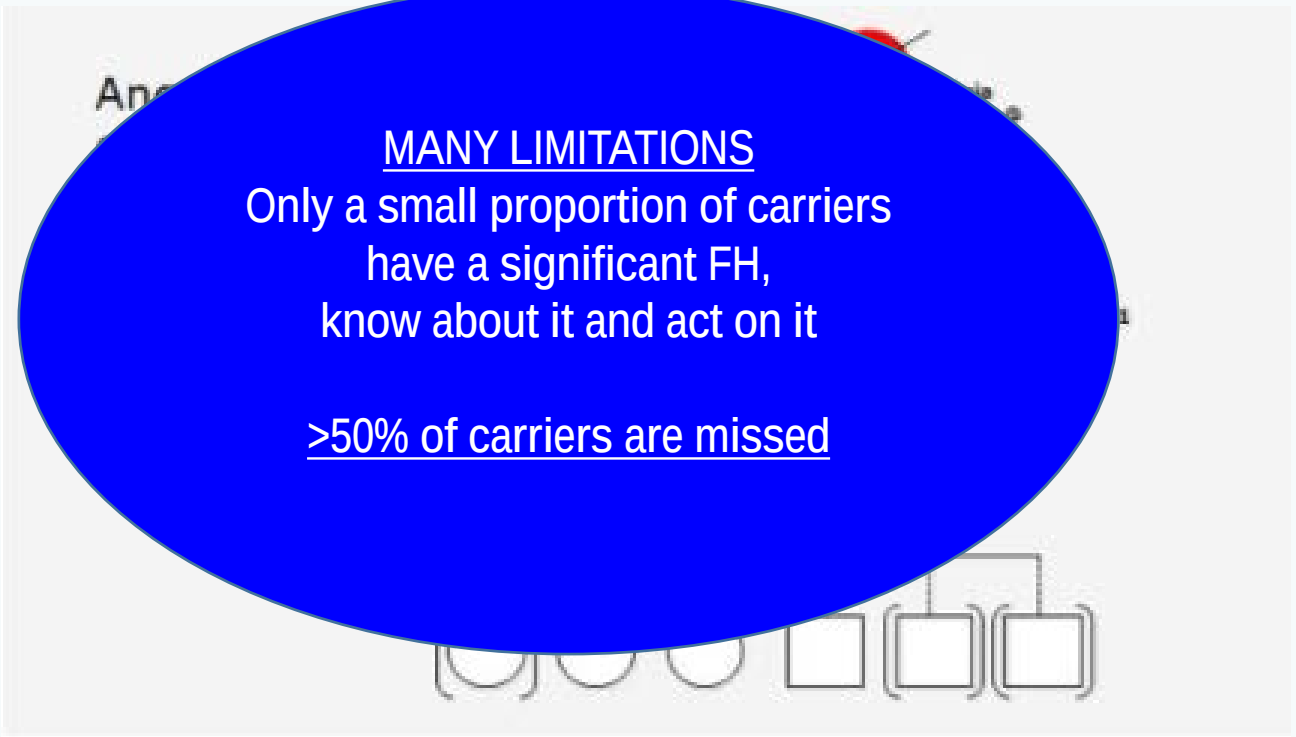


50% or 1 in 2 chance of inheriting faulty gene

50% or 1 in 2 chance of inheriting normal gene


LOW RISK
HIGH RISK
10%
Breast Cancer
45%-65%
2%
Ovarian Cancer
15%-35%
7%-14%
Prostate Cancer
5% -25%
BRCA2 > BRCA1
0.1%
Male breast Cancer
7%
BRCA2

Conventional Clinical Criteria/ FH-based approach: 10% BRCA probability



MANY LIMITATIONS
Only a small proportion of carriers
have a significant FH,
know about it and act on it

>50% of carriers are missed

Advantages of BRCA Carrier Identification

Time Magazine, December 24, 2012

Reduce your Risk of Cancer

- REPRODUCTIVE / LIFE STYLE CHOICES → Contraceptive Pill; PGD; Breast Feeding Planning
- SCREENING → MRI, Mammograms
- PREVENTION Chemo/ Surgical
- New Drugs/ Therapies (PARP Inhibitors) Clinical Trials

NGS – The Revolution

MiSeq

150,000,000 bases

20% of genome

An exome >20,000 genes

HiSeq

20,000,000,000 bases

6 genomes

80 exomes

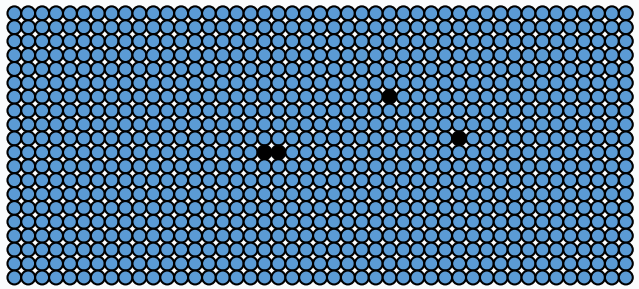

STRATEGY
POPULATION TESTING
BETTER IDENTIFICATON OF HIGH RISK GROUPS
BETTER TARGETED PREVENTION
REDUCED CANCER INCIDENCE & MORTALITY

WHY DO WE NEED TO WAIT FOR PEOPLE TO GET CANCER TO IDENTIFY PEOPLE IN WHOM WE CAN PREVENT CANCER??

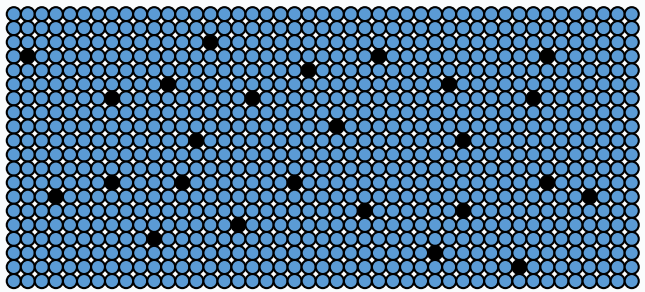
CAN WE TEST POPULATIONS?

- Increased Carrier identification?
- Risk/ Penetrance?
- Psychological / QoL Impact?
- Acceptable?
- Cost effective?
- New approaches for delivery?

Populations in the world which have frequent BRCA mutations (Founder Mutations)



1 in 200



1 in 40- AJ population

5 x More Common

National Estimates of Genetic Testing in Women With a History of Breast or Ovarian Cancer

Christopher P. Childers, Kimberly K. Childers, Melinda Maggard-Gibbons, and James Macinko

JOURNAL OF CLINICAL ONCOLOGY

2017

Conclusion

Fewer than one in five individuals with a history of BC or OC meeting select National Cancer Comprehensive Network criteria have undergone genetic testing. Most have never discussed testing with a health care provider. Large national efforts are warranted to address this unmet need.

Current detection rates and time-to-detection of all identifiable *BRCA* carriers in the Greater London population

J Med Genet 2018

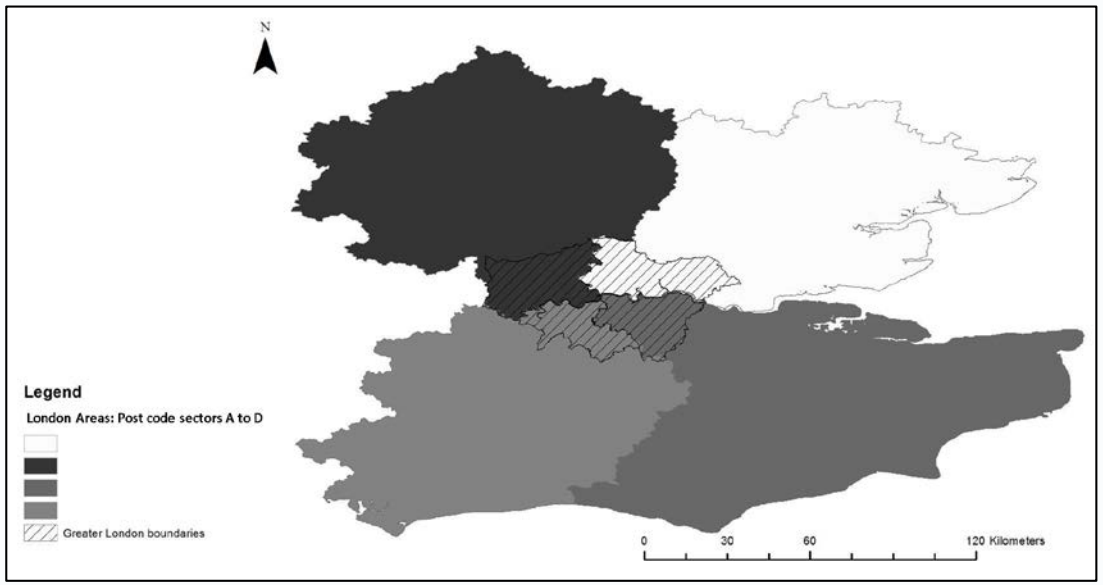
Ranjit Manchanda,[1,2,3] Oleg Blyuss,[4,5] Faiza Gaba,[1,2] Vladimir Sergeevich Gordeev,[6] Chris Jacobs,[7,8] Matthew Burnell,[4] Carmen Gan,[2] Rohan Taylor,[9] Clare Turnbull,[1] Rosa Legood,[10] Alexey Zaikin,[4] Antonis C Antoniou,[11] Usha Menon,[3] Ian Jacobs[12]

AJ = 0.0261 **1:40**

Gen Pop = 0.00677 **1:200**

Gen pop BRCA – 3%
AJ Pop – 10%

Vast majority are unidentified



Map of London coverage areas (A, B, C, D)

based on postcode sectors covered by NHS Genetics Services

1995 – 2014, 16 Million pop

All BRCA carriers detected

Mapped for London Post Code

THE RESEARCH

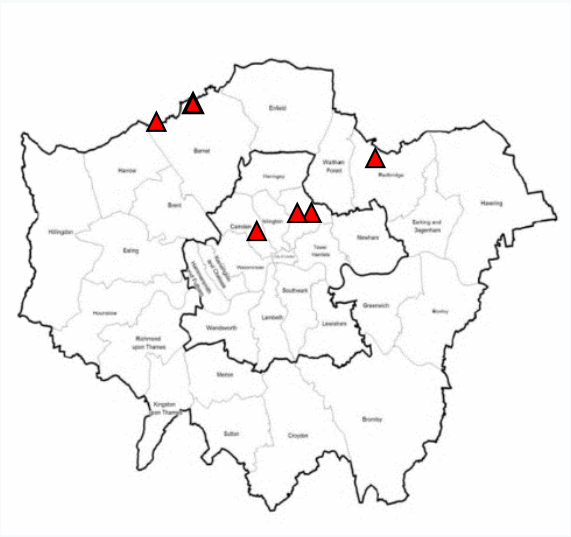
Barts Cancer Institute
Queen Mary University of London

TheAHSNNetwork NHS England
NHS Innovation Accelerator

Queen Mary University of London

THE AJ MODEL

GCaPPS Genetic Cancer Prediction through Population Screening



AJ (>18 yr) Genetic Counselling

- Population Screening (Everyone)
- Testing on FH

Outcomes
- Psychological health
- Quality of Life
- Impact of Genetic Test Result
- BRCA carriers identified
- Health Economics

J Med Genet 2016

Cluster-randomised non-inferiority trial comparing DVD-assisted and traditional genetic counselling in systematic population testing for BRCA1/2 mutations

Ranjit Manchanda,[1,2,3] Matthew Burnell,[1] Kelly Loggenberg,[1] Rakshit Desai,[1] Jane Wardle,[4] Saskia C Sanderson,[5] Sue Gessler,[1] Lucy Side,[1] Nyala Balogun,[1] Ajith Kumar,[6] Huw Dorkins,[7] Yvonne Wallis,[8] Cyril Chapman,[9] Ian Tomlinson,[10] Rohan Taylor,[11] Chris Jacobs,[12] Rosa Legood,[13] Maria Raikou,[14] Alistair McGuire,[14] Uziel Beller,[15] Usha Menon,[1] Ian Jacobs[1,16]

JNCI 2015

OXFORD

JNCI J Natl Cancer Inst, 2015, 1–11

RTICLE

opulation Testing for Cancer Predisposing RCA1/BRCA2 Mutations in the Ashkenazi-Jewish ommunity: A Randomized Controlled Trial

anjit Manchanda, Kelly Loggenberg, Saskia Sanderson, Matthew Burnell, ne Wardle, Sue Gessler, Lucy Side, Nyala Balogun, Rakshit Desai, Ajith Kumar, uw Dorkins, Yvonne Wallis, Cyril Chapman, Rohan Taylor, Chris Jacobs, n Tomlinson, Alistair McGuire, Uziel Beller, Usha Menon, Ian Jacobs

JNCI 2015

JNCI J Natl Cancer Inst, 2015, 1–14

t-effectiveness of Population Screening for BRCA ations in Ashkenazi Jewish Women Compared h Family History–Based Testing

Manchanda, Rosa Legood, Matthew Burnell, Alistair McGuire, Raikou, Kelly Loggenberg, Jane Wardle, Saskia Sanderson, Sue Gessler, Side, Nyala Balogun, Rakshit Desai, Ajith Kumar, Huw Dorkins, ne Wallis, Cyril Chapman, Rohan Taylor, Chris Jacobs, omlinson, Uziel Beller, Usha Menon, Ian Jacobs

AJOG 2017

Cost-effectiveness of population based *BRCA* testing with varying Ashkenazi Jewish ancestry

Ranjit Manchanda, MRCOG, PhD; Shreeya Patel, MSc; Antonis C. Antoniou, PhD; Ephrat Levy-Lahad, PhD; Clare Turnbull, PhD; D. Gareth Evans, PhD; John L. Hopper, PhD; Robert J. Macinnis, PhD; Usha Menon, MD; FRCOG; Ian Jacobs, MD, FRCOG; Rosa Legood, PhD

BJOG 2019

Attitude towards and factors affecting uptake of population-based *BRCA* testing in the Ashkenazi Jewish population: a cohort study

R Manchanda,[a,b] M Burnell,[c] F Gaba,[a,b] S Sanderson,[d] K Loggenberg,[e] S Gessler,[c] J Wardle,[d,f] L Side,[f] R Desai,[c] AF Brady,[g] H Dorkins,[h] Y Wallis,[i] C Chapman,[j] C Jacobs,[k,l] I Tomlinson,[m] U Beller,[n] U Menon,[c] I Jacobs[o]

NHS Trust

BJOG An International Journal of Obstetrics and Gynaecology

Attitude towards and factors affecting uptake of population-based *BRCA* testing in the Ashkenazi Jewish population: a cohort study

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2019

96% interest
60% intention
88% uptake

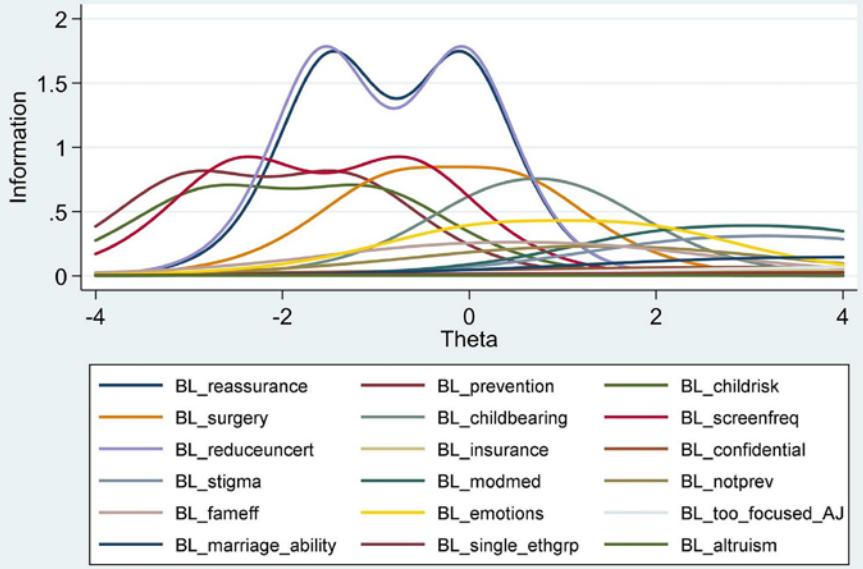
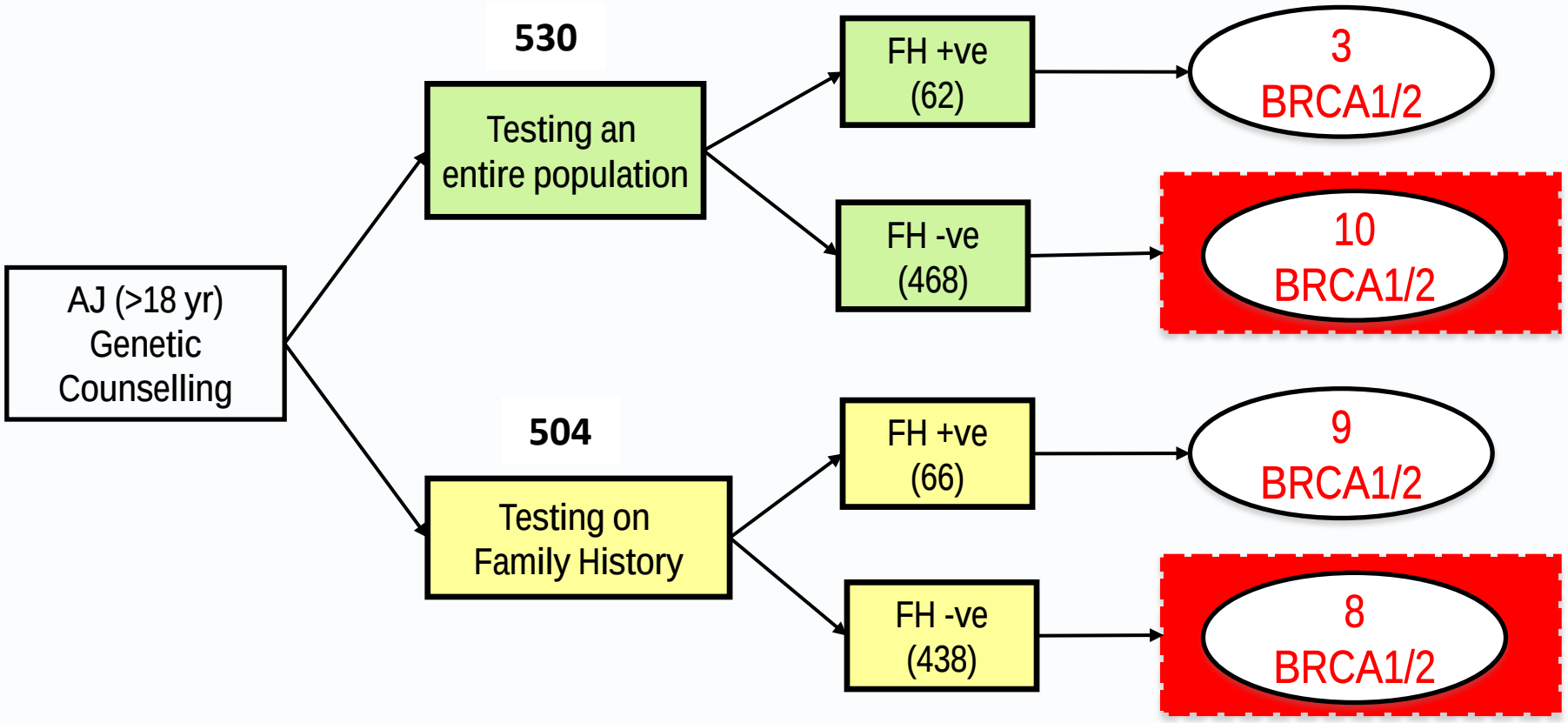


Figure S1. Item Information Functions

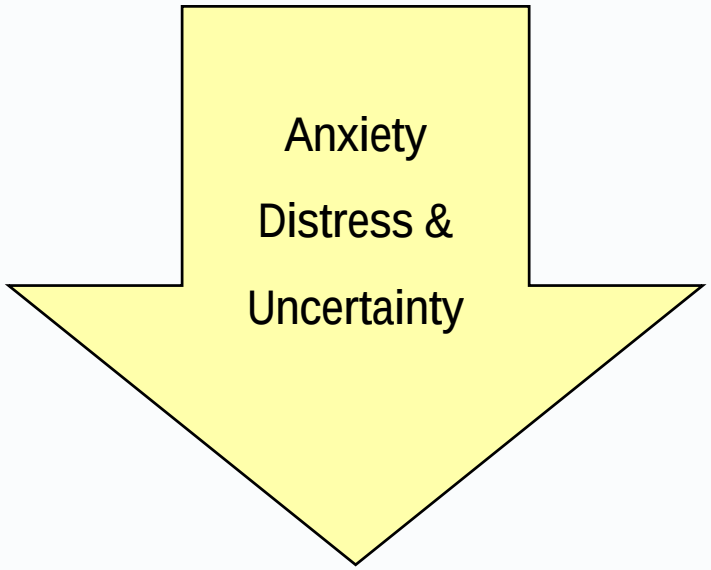
Reassurance
Reducing Uncertainty
Married/Cohabiting – 4x

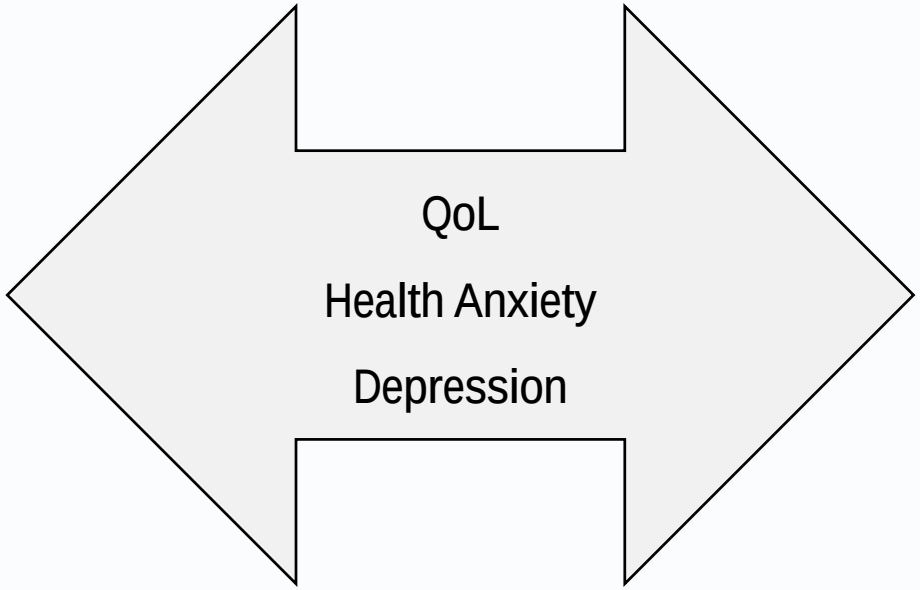


60% (18/30) BRCA carriers are identified by Population Testing Only

Manchanda et al.
JNCI J Natl Cancer Inst, 2015, 1–11

Effect of Time





The Current model of FH based testing has a number of limitations

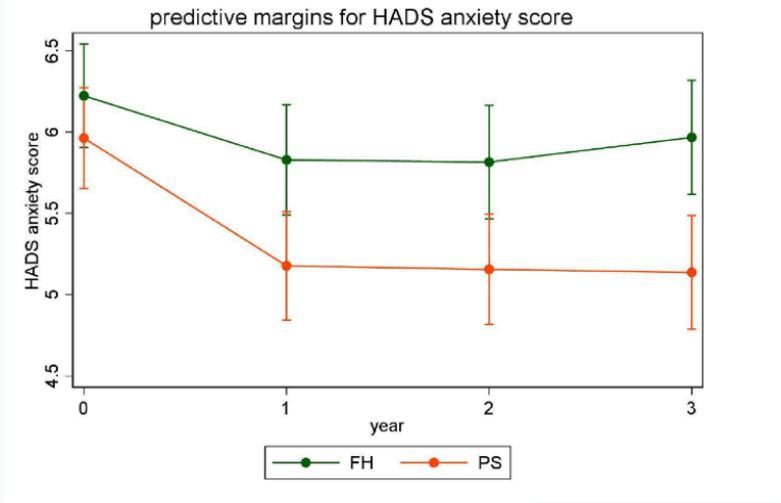
60% carriers do NOT have a strong FH & are identified by Population Testing Only

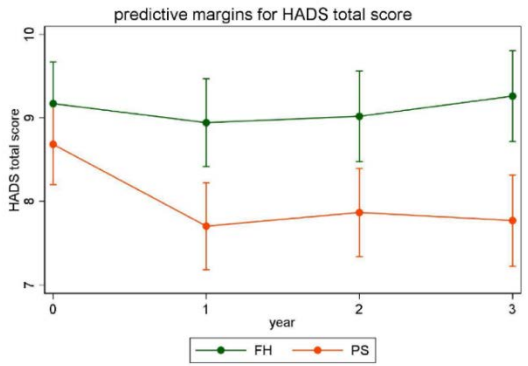
Population Testing is feasible and acceptable in AJ

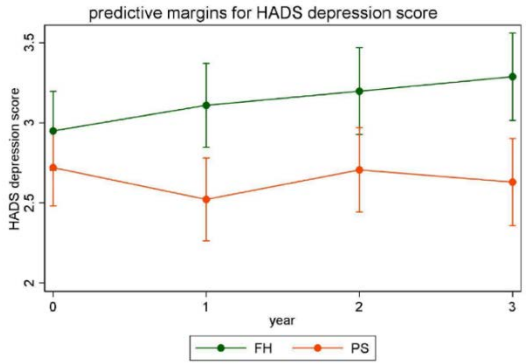
High Satisfaction

It is possible to provide pre-test counselling and testing effectively in more time efficient ways in a community setting

RESULTS: LONG TERM





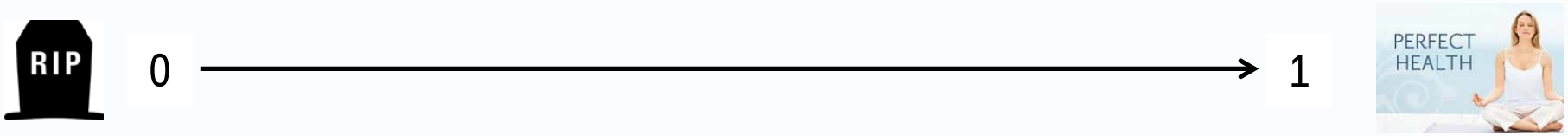


Decrease in anxiety following testing

Reduction was significantly greater with population screening compared to clinical criteria/ FH testing.

No Difference in
QOL
Health Anxiety
Uncertainty
Distress

QALY = (Survival) x (Utility score)



Utility Score

- Way of capturing Quality of Life in Cost Effectiveness Analysis
- Measured on a scale of 0 to 1
- 1 = Perfect Health
- 0 = Death
- Can be applied across all disease areas and variety of health states

HEALTH ECONOMICS (HE)

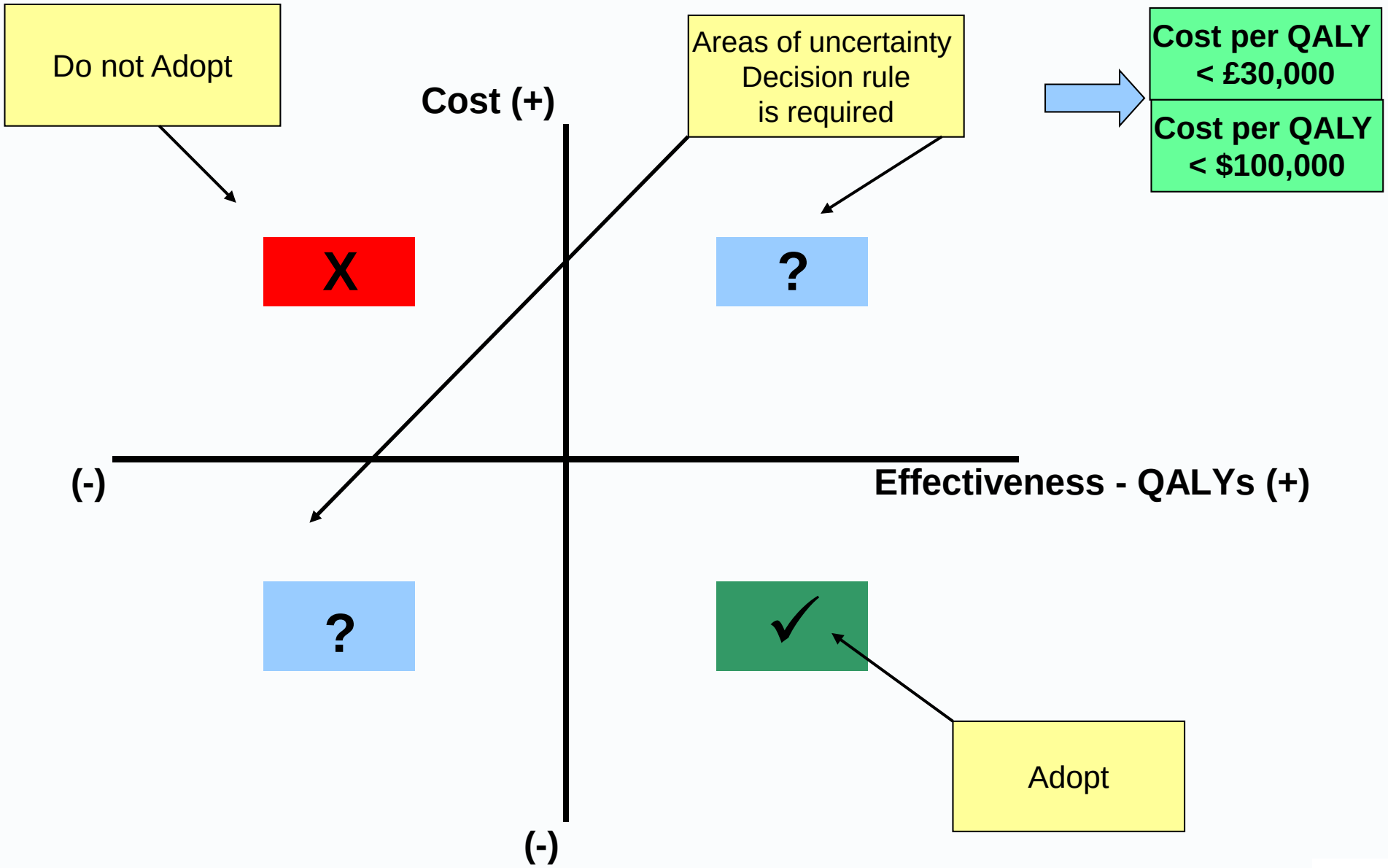
ICER: Incremental Cost effectiveness Ratio

$$\frac{(\text{Total Costs A}) - (\text{Total Costs B})}{(\text{Total QALYs A}) - (\text{Total QALYs B})}$$

A= Pop Testing
B= FH/Clinical Criteria Testing

HEALTH ECONOMICS (HE)

Should the NHS / Health Service adopt a new intervention?



Pop screening is cost saving and is highly cost-effective in Jewish women

Incremental cost-**effectiveness ratio (ICER) = — £2079/QALY**

Can be cost saving for the NHS by £3.7 million

Reduces Ovarian and Breast Cancer incidence by 0.34% & 0.62%

Can reduce number of Ovarian cancers by 276

Can reduce number of Breast cancers by 508

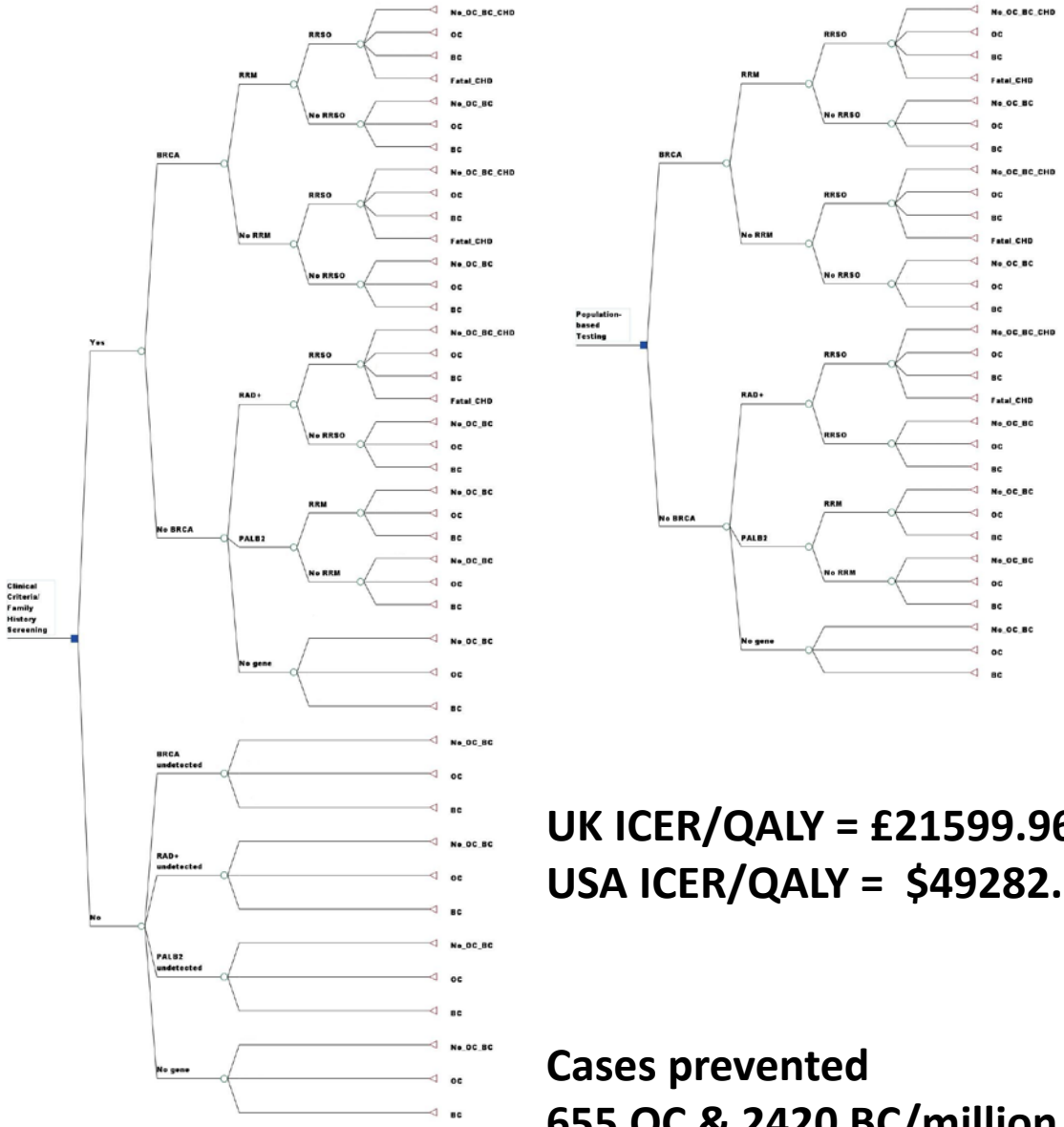
Do we prevent more cancers through population testing?	YES
Do we identify more people at risk through population testing?	YES
Are we causing psychological/QOL harm?	NO
Is there high satisfaction?	YES
Is it feasible and acceptable?	YES
Can we do it outside a hospital setting?	YES
Is it cost-effective?	YES

BEYOND THE AJ POPULATION

POPULATION PANEL TESTING OC/BC MUTATIONS

Queen Mary University of London

NHS Innovation Accelerator



UK ICER/QALY = £21599.96

USA ICER/QALY = $49282.19

Cases prevented

655 OC & 2420 BC/million

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JNCI J Natl Cancer Inst (2018) 110(7): djx265

doi: 10.1093/jnci/djx265

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Article

Cost-effectiveness of Population-Based BRCA1, BRCA2, RAD51C, RAD51D, BRIP1, PALB2 Mutation Testing in Unselected General Population Women

Ranjit Manchanda, Shreeya Patel, Vladimir S. Gordeev, Antonis C. Antoniou, Shantel Smith, Andrew Lee, John L. Hopper, Robert J. MacInnis, Clare Turnbull, Susan J. Ramus, Simon A. Gayther, Paul D. P. Pharoah, Usha Menon, Ian Jacobs, Rosa Legood

All women over 30 should be tested for fault gene, researchers say

Barts Cancer Institute research estimates around 83,000 cancers could be prevented if all women over 30 were screened.

All women over 30 should be screened for the faulty gene that can cause cancer

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Health

Angelina Jolie gene testing for all?

By James Gallagher
Health and science correspondent, BBC News

18 January 2018 | 109 | Share

IMPACT!

64493	BC prevented	237610
17505	OC prevented	65221

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MODEL OF CARE FOR PREVENTING CHRONIC DISEASE

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THE UK SHOULD BE THE FIRST HEALTH SYSTEM WORLD WIDE TO IMPLEMENT POPULATION GENOMICS FOR PREVENTING CANCER AND CHRONIC DISEASE

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Barts Health NHS
NHS Trust

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Katherine Duerden
Gemma Byrne
Fiona MacDonald
Louise Bayne
Ruth Payne
Michelle Ferris

Robert Liston
Vijay Devineni
Andy Ryan
Jack Cuzick
Michael Baum
Boots Pharmacy
Norwood
Jewish Care
Ovacome
Agudas Israel Housing Association
Academic Study group on Israel and the Middle East
Liberal Judaism
Movement for Reform Judaism
Indian Jewish Association
Stamford Hill Group Practice
Lane End Medical Centre

Thank you