

Cancer Model of care for Population Genetic Testing

Dr Ranjit Manchanda MD, MRCOG, PhD

Clinical Senior Lecturer & Consultant Gynaecological Oncologist

NHS Innovation Accelerator (NIA) Fellow

Research Funding



BACKGROUND

Predicted Rise in Cancer Cases by 2040

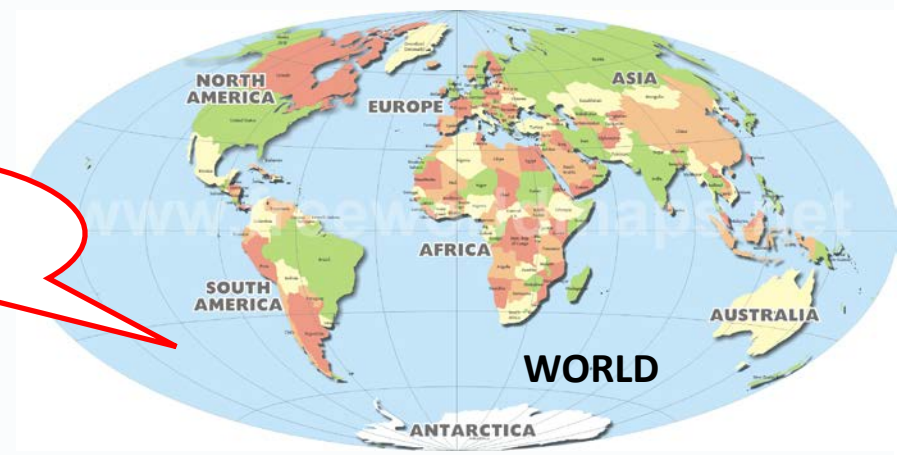
USA



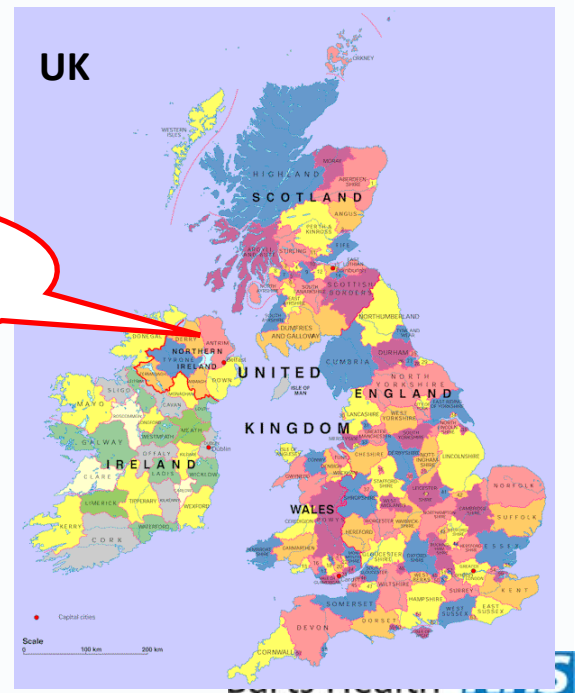
BC- 26%
OC- 31%

BC- Breast Cancer
OC- Ovarian Cancer

BC 47%
OC 47%



BC 20%
OC 26%



A typical gene looks a bit like this...

GATCTGATAAAGTCCCAGGACTTCAGAAGAGCTGTGAGACCTTGGCCAAGTCACTTCCCTCCTTCAGGAACATI
GCAGTGGGCTAAGTGCCTCCTCCTCGGGACTGGTATGGGGACGGTCAATCTGGACAACATTCACCTTI
AAAAGTTTTATTGATCTTTTTGTGACATGCACGTGGGTTCCAGTAGCAAGAAAATAAAGGGTCCGAGGCCGGI
TCTGTCAATTTCTTTAATTTCAAGACAGTCTCAAATATTTCTTTATTAACCTCCTGGAGGGAGGCTTATCA
TTCTCTCTTTTGGATGATTTCTAAGTACCAGCTAAAATACAGCTATCATTTCTTTCTGATTTGGGAGCCI
AATTTCTTTAATTTAGTATGCAAGAAAACCAATTTGGAAATATCAACTGTTTTGGAAAACCTTAGACCTAGGI
CATCCTTAGTAAGATCTTCCCATTTATATAAAATACTTGCAGTAGTAGTGCCATAAATTACCAAACATAAAGC
CAACTGAGATGCCCAAAGGGGGCCACTCCTCTGCTTTCTTCTCCTTTTAGAGGATTTATTTCCCATTTTTC
TTAAAAGGAAGAACAACAACTGTGCCCTAGGTTTACTGTGTCTCAGAACAGAGTGTGCCGATTGTGGTCAGGAC
TCCATAGCATTTCACCATTGAGTTATTTCCGCCCTTACGTGTCTCTCTTTCAGCGGTCTATTTATCTCCAAG
AGGGCATAAAAACACTGAGTAAAACAGCTCTTTTATATGTGTTCCTGGATGAGCCTTCTTTAATTAATTTTG
TTAAGGGATTTCTCTTAGGGCCACTGCACGTCTAGGGGAGTCAACCCAGACACTCCAATTTGGCCCTTGI
CACCCAGGGGCACATTTTACGTATTTGTA AACCTGAAATCACATAGAAAGGAATGTCTAGTACTTTGTGGG
GCCAAGGCCCTTGTATGGGGATGAAGGCTCTTAGTGGTAGCCCTCCAAGAGAATAGATGGTGAATGTCTC
TTTTCAGACATTAAGGTGTGACACTCTAGTCTAGTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCT
CCTGACTGCATTAATGGAGATTTCTCTCCATGTGCAAAAATTTCTTCCACAAAAGAAATCCTTTCAGGGCCATI
TTAATGTGTTTGGCCCTGTGACAGCCATTTCAAATAATGTCAAAAATATATTTTGGAGTAAAATACTTTCAI
TTTCTTTCAGAGTCTGTCTGTATGATGCCATAACCAGAGTCAAGTTGGAAAAGTAAGCCACATTATACAGCC
TTAACCTAAAAACA AAAAATCTGTCTAACAAAGATTTTATGTTTTATAGAGCATGATTTCCCGGACACATTA
GATAGAAATCTGGGCAAGAGAAGAAAAGGTTAGAGTTTAACTCTCATTCCTAAGTTATGTA AACCCAAA
ATAAAATTTCTGAAGATGTCTGTATCATCTGAAATGGACCTTCTCTGACCAGGGCATTTCCAAAGTTAACCI
GAAAATTTGGTTTGGGCCATGATGGGAAGGGAGGTTTTGGATATGCTCATTTATGCCCTCTTCCCTTTTCAGAAI
TCAGGAAAAGCCAAACCAGCATTAACATCAACACAGATTTTTCAGATCTTAGGTTTTCTTTCCGATCTATTCTCI
CTGAACCCCTGCTACCTGGAGGCTTTCATCTGCATAATAAAAATTTAGTCTCCACAACCCCTTATCTTACCCCA
GACATTTCTTTCTATTGATAAATAACTCTTTCAACCAATTTGCCAATCAGGGTATGTTTTAAATCTACCTATGAC
CTGGAAGCCCCACTTTTGCACCCTGAGATCAAAACAGTGCAAAATCTTATATGTATTGATTTGTCAATGAAA
CAGTCAAAGCCAGTCAAGGCACAGTGGCTCATGCTGTAATCCCAGCACTTTGGGAGGCTGAGGCCGGGTAGAI
CACCTGAGGTGAGGATTCGACACCAGCCTGGCCAAACATGGTGAACCCCGTCCCTACTAAAATACAAAAA
TAGCCAGCTTTGGTGGTGGGCACCTGTAATCTTAGCTACTGACAGAGACTGAGGCAGGAGAATCGCTTGAAC
CAGGAGGTGGAGGTTGCAGTGCCTGAGATTTTGGCCATGCACTCCAGCCTGGGCAACAGAGCAAGACTCTA
TCTCAAAAACA AAAAACA AAAAACA AAAAACA AAAAACA AAAAACA AAAAACA AAAAACA AAAAACA AAAAACA
TTCTGAACCAAAATATGAATGACCATGGTCCATGACACAGCCCTCAGAAGACCCTGAGAACATGTGCCCAAAG
TGGTCAAGTGCATCTTAGTTTTGTACATTTTAGGGAGATATGAGACTCAGTCAAATACATTTTTAAAAA
TACATTTGGTTTTTGTCCAGAAAAGCCAGAACCACCTCAAAGACAGGGTTTTCCAGGTTATAAGTAGATTTAAAA
TTTCTGATTGACAAATGGTTGAAAGAGTTGTCAATAGAAAAGGAATGTCTGCATTTGTGACAAGAGGTTGTGG
GACCAAGTTTTCTGTCTATGCAGATGAAGCCTTCAGGTAGCAGGTTTCCAAGATAACAGGTTGTAATAAGTTCTI
TATCAGACTTAAGTTCTGTGGAGACGTAAAATGAGGCATATCTGACCTCCACTTCCAAAAACATCTGAGACA
GGTCTCAGTTAATTAAGAAAAGTTTTGTTCTGCCITAGTTTAAAGACATGCCCCATGACACTGCCTCAGGAGGTC
TGACAGCATGTGCCAAAGGTGGTTCAGGATACAGCTTGCTTCTATATATTTTAGGGAGAAAATACATCAGCCI
GTAAACAAAAAATTAATTTCTAAGTCCCTGAACCATCTGAAATGGGCTTCTTCTTAGGCCAGGGCACTCTA
AATTAAGAACCTGAACATTTCTTATTTGATAATACTTTTTCAGCCAGTTGAGCCCATTCAGACCACAGCA
GGTGCCAGGCCAGGCAAGGGCTGACTTGAGATACCTGCCAGATGAGTCACTGGCAAAGGTGCTGCTCCCTG
GTGAGGGAGAAAACACCAGGGGCTGGGAGAGGCCCAAAGGCTCTGAAAGGAGTTTTGGTTTTGGCTGGCCATGI
GTGCAATTAGCGTGTGATGAGCTCTGACATGGCCCTTGATGGACGGATTGGGCAAGGACACCCAGCTGAGGAG
ATGGCAGGAGTGTGACACAGGGGAAAGGGTGGCATACCCAGTGGACAGCTCCCACTACCTCCACTCTGTG
CTGCAGCTCAGGGGCTGGGTCTTCTGCTGCAACTCAGCCCTCTGTACCAGCCCTGGCCTCATTCCTTTGGI
TCCAGGACACCCAGCTGACAAAAGGGACTTGCCTGTACCCTGACCTGGTCTTACACTGGCTCCTGGGTI
GTCAGCAGGTGTTTTGTTGGGCCAACGAGTGCATGGATGGAAACACAGACAGAAGGACAGATGGAGAGATGGI
GGGTGGCCAGACAAAAGGAGTAACTTGGTGGAGAAATGTGCATTAGGAAATCACAGAAGAGCAGAAAACCTGTTG
AAAATTTCAAAGTGGGAAAGTGGGAGGTGAAGCAGGGCTGAAGGGCCCTCCCTCAGAGCCTTCTCCCACTCI
GTGGTGTCCACATCCCTTTGGTCTCTTGTGGGAGGCACCTCCTTTGCTCAGCCTATTGTGGCTACAGC
CCAGAGGTCCCAGGTGGCCACAGCCAAAGTGAAGTTGGGCTGAGGCTGAAGTCTCCCTCACCATGAAGG
GATGATGTATAGTGGGTGGGGCTCAGGAGGAAGAGGGCCAAACCTACCTGGCCCTAACCTGCTGCC
GGAGTAGGCAGGTACCAAGAGGCTGGGGTGAAGACTGTTGCAGGTCGAGGACCAGGGCCATCTCACTGCCTG
AGCCCATGGACTGGCTCAGGGGTCTGTGATGATTTCTAGAGCTGAGTTGGAGGTAAGGGCCAGGGGTTTTGI
TCTTGGGTTCAAGACCATGGAAGGAAGGGGTAGAGAAGGAGGCCAAACAAGTGAAGGAGGCAAAATTACAGTGGC
TGGCAGAAGGAGAGAGAAGCCAGGACAGGTGGCTGTGGCCCTGTCCCTGCAGGCAGACCAGGAAAGGAGCTC
AGAGACAGGATTCATGCCAAGCCTGCCATACCAGCAGCATCTCTCCTCATGGACATGAGAGAAAACCCCTCCAG
CTTGGCCCTCACATCTGTGAAAACCCACAGTAAATGGGGCTGACATCCTCTGCCCTATGCAAGAGAGGTTTTCCC
AAGCACTTGCAGCAAGTGAAGTGCACAGGATGGCGAATCCACAAGAACAACAGTTGTTCTCATGCTCTTTGG
AAGCACAATTTACATTTCTGACAGTTTTTGTGGGGAGATGAGACCAAGTGA AAAACACAGGGAACCCCTGCTCATT
GGGGAACCCCTTGGTGGTCTCTGCTTGGAAAGCCGGGCTGCAGAGGACTGTAAGATCAACCCCGGGGCTGTAG
GTGATGGCTCAGGCACCTGGATTCTCCATGGAGGACCCCATGAAATGCACTTTGAAAGGTGACCTCCATGGGTC
TCAGCTGGCTGGGCCCATTTGGGAGTTCTATCTTTGGGGAAGGATGCTTTCTTAGGCTCTGTGACAGCTGC
CCCTAGGCTCAGGCCAGGATCAAAAATCAAAGTCAAGTCAAGTCCCAAGGAGGCAATGGCACTACCTCCTCC
GGGCCACAGGGTGGGGCTAAAATTTCCATCTCGGGGATCCAGGTCAGGAACAAGGCCAGGGATGCTGCTI
CTGGGTCTGAACCCCAAGTATGGGTCAAGAGGGCTCCAATTCAGAGGTTAGGTTATTTCAATGGTGAAGAAA
CTGTAAGTCTCCCAAGCATTTCCCTCCATGTAAGCAGGAAAGCTGCCCTTTGCTTCCCAAGCAAAAAGGTA
TGAGGCTGGTTGCTCCAGCAGCCACCCCTCGGGGCTGGAAAGGCTGGGAGGGCAGGTTGGCCATTTCCAG
TTTGGGGAGGTCAGGTGATTTCTGAGCTGGGCTGGGATGGATGAAAATGTTAGGTTGGGCTATGATTTAGGCC
TGAGAGGTTGTTGTCTCCCATCAGTGGAGCTGGCAATCTGACGATGCCTCTCTTTGGACCCTGGCCTTCAG

And so on till
Page 200....

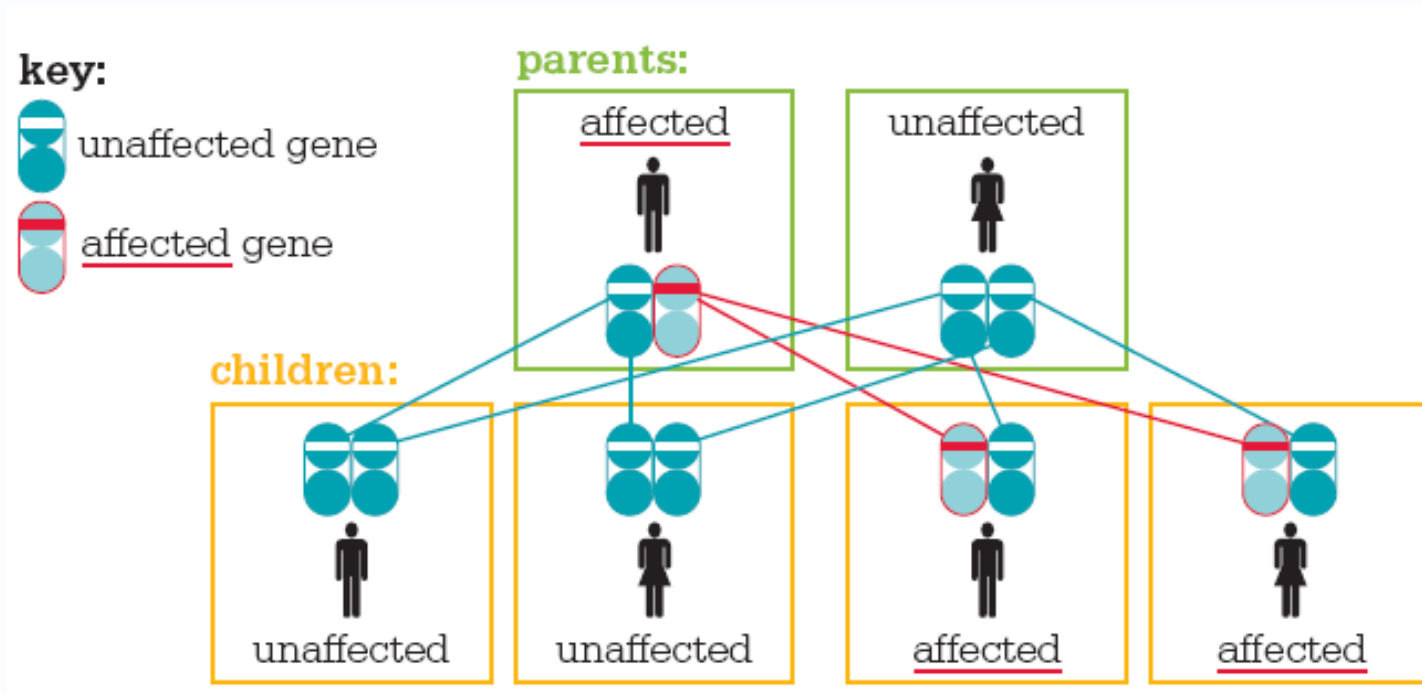
GATCTGATAAGTCCCAGGACTTCAGAAGAGCTGTGAGACCTTGGCCAAAGTCACTTCCTCCTTCAGGAACATI
GCAGTGGGCCCTAAGTGCCTCCTCTCGGGACTGGTATGGGGACGGTTCATGCAATCTGGACAACATTACACCTTI
AAAAGTTTATATGATCCTTTTGTGACATGCACGTGGGTTCCAGTAGCAAGAACTAAAGGGTCCGAGGCCGGI
TTCTGCTAATTTCTTTAATCCAAGACAGTCTCAAATATTTCTTATTAACCTTCCTGGAGGGAGGCTTATCA
TTCTCTCTTTTGGATGATTTCTAAGTACCAGCTAAAATACAGCTATCATTTCTTTTCTTGGATTTGGGAGCCI
AATTTCTTTAATTTAGTATGCAAGAAAACCAATTTGGAAATATCAACTGTTTTGGAAACCTTAGACCTAGGI
CATCCTTAGTAAGATCTTCCCATTTATATAAATACTTTGCAAGTAGTAGTGCCATAAATTACCAAACATAAAGC
CAACTGAGATGCCCAAAGGGGGCCACTCCTTGTCTTTTCTCCTTTTCTAGAGGATTTATTTCCCATTTTTC
TTAAAAGGAAGAACAACAACTGTGCCCTAGGGTTTTACTGTGTGCAACAGAGTGTGCCGATTGTGGTTCAGGAC
TCCATAGCATTTCCACCATTGAGTTATTTCCGCCCTTACGTGTCTCTTTCAGCGGTCTATTATCTCCAAG
AGGGCATAAAAACACTGAGTAAACAGCTCTTTTATATGTGTTCCTGGATGAGCCTTCTTTAATTAATTTTGG
TTAAGGGATTTCTCTAGGGCCACTGCACGTCTAGGGGAGTCAACCCAGACACTCCCAATTGGCCCCCTTGI
CACCCAGGGGCACATTTGAGCTATTTGTAAACACTGAAATCACTAGAAAGGAATGTCTAGTACTTGTGGG
GCCAAGGCCCTTGTATGGGGATGAAGGCTCTTAGGTTGGTAGCCCTCCAAGAGAATAGATGGTGAATGTCTC
TTTTCAGACATTAAGGTGTGAGACTCTCAGTCTAGTCTCTCCTAGATCCAGGAAAGGCCTAGAAAAGGAAGC
CCTGACTGCATTAATGGAGATTTCTCTCCATGTGCAAAAATTTCTCCACAAAAGAAATCCTTGCAGGGCCAT
TTAATGTGTGGCCCTGTGACAGCCATTTCAAAATATGTCAAAAATATATTTTTGGAGTAAAATACTTTCAI
TTTTCTCAGAGTCTGTCTGTCGTATGATGCTTCAATACCAGTCAAGTTGGAAAGTAAGCCACATTATACAGCC
TTAACCTAAAAAAACAAAAAAGTGTCTAAACAAGATTTATGGTTTATAGAGCATGATTTCCCGGACACATTA
GATAGAAATCTGGGCAAGAGAAGAAAAAAGGTCAGAGTTTAACTCTCATTCCTAAGTTATGTAAACCAAAA
ATAAAATTTCTGAAGATGTCTGATCATCTGAATGGACCTTCTCTGGACCCAGGGCATTTCCAAAGTTAACCI
GAAAATTTGGTTGGCCATGATGGGAAGGGAGGTTGGATATGCCTCATTATGCCCTCTTCCCTTTTCAGAAI
TCAGGAAAAGCCAACCAGCATTAACATCAACACAGATTTTTCAGATCTTAGGTTTTCTTTCCGATCTATTCTCI
CTGAACCCCTGCTACCTGGAGGCTTCATCTGCATAATAAAAATTTAGTCTCCACAACCCCTTATCTTACCCCA
GACATTTCTTTCTAATTGATAATAACTCTTTCAACCAATTTGCCAATCAGGGTATGTTTAAATCTACCTATGAC
CTGGAAGCCCCACTTTGCACCCTGAGATCAAAACAGTGAATCTTATATGTATTGATTTGTCAATGAAAA
CAGTCAAAGCCAGTCAAGGCACAGTGGCTCACTGCCTGTAATCCAGCACTTTGGGAGGCTGAGGCGGGTAGAI
CACCTGAGGTGAGGAGTTTCGACACCAGCCTGGCCAAACATGGTGAACCCCGTCCCTACTAAAATACAAAAI
TAGCCAGCTTGGTGGTGGGACCTGTAATCTTAGCTACTGTGAGAGACTGAGGCAAGGAGATCGCTTGAACC
CAGGAGGTGGAGGTTGCAGTGCCTGAGATTTTGGCATTGCACTCCAGCCTGGGCAACAGAGCAAGACTCTA
TCTCAAAAAACA
TTCTGAACCAAAATATGAATGACCATGGTCCATGACACAGCCCTCAGAAGACCCTGAGAACATGTGCCAAGE
TGGTACAGTGCATCTTAGTTTGTACATTTAGGGAGATATGAGACTTCAGTCAAATACATTTTAAAAAA
TACATTTGGTTTTGTCCAGAAAGCCAGAACCCTCAAAGCAGGGGTTTTCCAGGTTATAAGTAGATTTAAAAATI
TTTTCTGATTGACAATTTGGTTGAAAGAGTTGTCAATAGAAAAGGAATGTCTGCATTGTGACAAGAGGTTGTGGA
GACCAAGTTTCTGTCTATGCAGATGAAGCCTTCAGGTAGCAGGCTTCCAAGATAACAGGTTGTAAATAGTTCTI
TATCAGACTTAAGTTCTGTGGAGAGTAAAATGAGGCATATCTGACCTCCACTTCCAAAAACATCTGAGACA
GGTCTCAGTTAATTAAGAAAAGTTTGTCTGCTAGTTTAAAGACATGCCCATGACACTGCCTCAGGAGGTC
TGACAGCATGTGCCAAGGTGGTTCAGGATACAGCTTGTCTATATATTTTAGGGAGAAAATACATCAGCCI
GTAAACAAAAAATTAATTTCTAAGGTCCCTGAACCATCTGAATGGGCTTTCTTCTAGGCCAGGGCACTCTAA
AATTTGAAGAACCTGAACATTCCCTTTCTATTGATAAATACTTTAGCAGGTTGAGCCATTTCAGACCACAGCAA
GGTGCAGGCCAGGCAAGGGCTGACTTGTAGATCACTGCCAGATGAGTCACTGGCAAAAGGTGCTGCTCCCTG
GTGAGGGAGAAAACACCAGGGGCTGGGAGAGCCCAAGAGGCTCTGAAGGAGTTTTTGGTTTGGCTGGCCATGI
GTGCAATTAGCCTGATGAGCTCTGACATGGCCCTTGCATGGACGGATTGGGCAGGACACCAGCTGAGGAGG
ATGGCAGGAGTGTGAGGCACAGGGGAAAGGTTGGCATAACCCAGGTGACAGCTCCCACTACCTCCACTCTGTG
CTGCAGCTCAGGGGCTGGGTCTTCTGCTGCAACTGACCCCTCTGTACCAGCCCTGGCCTCATTCCCTTGGI
TCCAGGACACCAGCTGACAAAAGGGACTTGCCTGTACCCCTGCTGACCTGGTCTACACTGGCTCCTGGGTI
GTCAGCAGGTGTTTTGTTGGGCCAACGAGTGCATGGATGGAAACACAGACAGAAGGACAGATGGAGAGATGGI
GGGTGGCCAGACAAGGAGTAACCTTGGTGAAGGATGTGCATTAGGAAATCACAGAAGAGCCAGAAACTGTTTG
AAAATTTCAAAGTGGGGAAAAGTGGGAGGTGAAGCAGGGCTGAAGGGCTCCCTCAGAGCCTTCTCCACTCI
GTGGTGTCCACATCCCTTTGGTCTGCTTGTGGGAGGCACCTACCTTTTGTCTCAGCCTATTGTGGCTACAGC
CCAGAGGTTCCAGGTTGGCACCAGCCAAAGATGAAGTTGGCATTGAGGGCTGAAGTCTCCTCACCATGAAGG
GATGATGTATAGTGGGTGGGGCCCTCAGGAGGAAGAGGGCCAAACCCCTACCTGGCCCCCTAACCTGTGCCI
GGAGTAGGCAGGTACCAGAGGCATGGGGTGAAGGCTGAGGTTGACAGGTCGAGGACCAGGGCCATCTCACTGCCT
AGCCCATGGACTGGCTCAGGGGTCTGTGAGATGATTCTAGAGTGTAGTTGGAGGTAAGGGCAGGGGGTTTGI
TCCTGGGTTCAAGACCATGGAAGGAAGGGGTAGAGAAGGAGGCCAACAAAGTGAAGGAGGCAAAATTACAGTGGC
TGGCAGAAGGAGAGAGAAGCCAGGACAGGTGGCTGTGGGCTGTCCCTGCAGGCAGACCCAGGAAGGAGCTC
AGAGACAGGATTCATGCCAAGCCTGCCTACCCAGCAGCATCTCTCCTCATGGACATGAGAGAAAACCCCTCCAG
CTTGGCCCTCACATCTGTGAAACCCACAGTATGGGGCTGACATCTCTGCCCCTATGCAAGAGAGGTTTTCC
AAGCACTTGCAGCAAGTGAACCTGCACAGGATGGCGAATCCACAAGAAACACGTTTGTCTCATGCTCTTTGG
AAGCACAATTTACATTTCTGACAGTTTTGTGGGGAGATGAGACCAAGTGAAGGAGGAGGAAACCCCTGCTCATT
GGGGAACCCCTTGGTGGTCTCTGCTTGGAAAGCCGGGCTGCAGAGGACTGTAAGATCAACCAGCCGGGGCTGTAG
GTGATGGCTCAGGCACTGGATTCTCCATGGAGGACCCCAATGAAATGCACTTTGAAAGGTCAGCTCCATGGGT
TCAGCTGGCTGGGCCCATTTGGGAGTTCTATCTTTGGGGAAGGATGCTTTCTTAGGCTCTGTTGCACGCTGC
CCCTAGGCTCAGGCCAGGATCAAAATCAAAGTCAAGTTCACTGAGTCCCAAGGAGGCACTACCTCCTCCA
GGGCCACAGGTTGGGGCCTAAATTTCCATCTGCGGGATCCAGGTCAGGAACAAGGCCAGGGGATGCTGCTI
CTGGGTTGAACCCCAAGTATGGGTCAAGAGGGCTCAACTCAAGGGTGAAGTTATTCATGGTGAAGAAA
CTGTAAGTCTCCAGGACATTTCCCTCCATGTAAGCAGGAAAGCTGCCCTTTGCTTCCCAAGCAAAAAGGTA
TGAGGCTGGTTGTCTCAGCACCAGCCCTTGGGGCTGGAAAGGCTGGGAGGGCAGGTTGGCATTCCAG
TTTTGAGGGAGCCAGGTGTATCTTCTGAGCTGGGCTGGATGAAATGTTAGGGTGGCCCTATGATTGGCC
TGAGAGGTTGTTTTGTCTCCCATCAGTGGAGCTGGCAATCTGACGATGCCTCTCTTTGGACCCTGGCCTTCAG

Gene alterations (mutations) are usually small

CAAATATGAATGACCATGGTCCATGACACAGCCCTCAG/
AGTGCATCTTAGTTTTGTACATTTAGGGGAGATATGAGACTTC
;TTTTGTCCAGAAAGCCAGAACCCTCAAAGCAGGGGTTT
GACAATTGGTTGAAAGAGTTGTCAATAGAAAGGAATGTCTC
;TTTCTGTCATGCAGATGAAGCCTTCAGGTAGCAGGCTTC
>TTAAGTTCTGTGGAGACGTAAAATGAGGCCATATCTGACCT
GTTAATTAAGAAAGTTTGTCTGCCTAGTTTAAGGACATGCC
ATGTGCCCAAGGTGGTCAGGATACAGCTTGCTTCTATATA
AAAAATTAATTTCTAAGGTCCCTGAACCATCTGAATGGGC1
;AACCTGAACATTCCTTTCTATTGATAATACTTTTCAGCCAGTT
;GGCCAGGCCAAGGGCTGACTTGAGATACCTGCCAGATC
;AGAAACACCAGGGGCTGGGAGAGGGCCAGAAAGGCT
;AGCGTGATGAGCTCTGACATGGCCTTGCATGGACGGAT
;GAGTGATGGCACAGGGGAAAGGGTGGCATAACCAGG
;TCAGGGGCTGGGTCTTCTGCTGCAACTCAGCCCCTCTG
;CACCCAGCTGACAAAAGGGACTTGCCTGTACCCCTGC/
;GGTGTGTTGTTGGGCCAACGAGTG **CATGG** ATGGA/
>CAGACAAAGGAGTAACCTGGTGAGGAATGTGCATTAGG
>AAGTGGGGAAAGTGAGGAGGTGAAG **CATGG** GGGCTGAAG
>CACATCCCCTTGGTCGTCCTTGTGGGA **CATGG** CACTCACCT
>GTCCCAGGTGGCACCAGCCAAGATG **CATGG** GTGGCATT
[ATAGTGGGTGGGGCCTCAGGAGGAAG **CATGG** GGCCACC/
;GCAGGTACCAGAGGCATGGGGTGAGG **CATGG** GTTGCAG
GGACTGGCTCAGGGGTCTGTGATGATTC **CATGG** GAGCTG/
TTCAAGACCATGGAAGGAAGGGGTAGAGA **CATGG** AGGCC
;AGGAGAGAGAAGCCAGGACAGGTGGCTGT **CATGG** CCTC
;GGATTGATGCCAAGCCTGCCTACCCAGCACATC **CATGG** CCT
CTCACATCTGTGAAACCCACAGTAATGGGGCTGACA **CATGG**
TGCAGCAAGTGAGACTGCACAGGATGGCGAATCCACA
>AATTTACATTCTGACAGTTTTGTGGGGAGATGAGACCAGT
>CCTTGGTGGTCTCTGCTTGAAGCCGGGCTGCAGAGG
CTCAGGCACTGGATTCTCCATGGAGGACCCCATGAATG

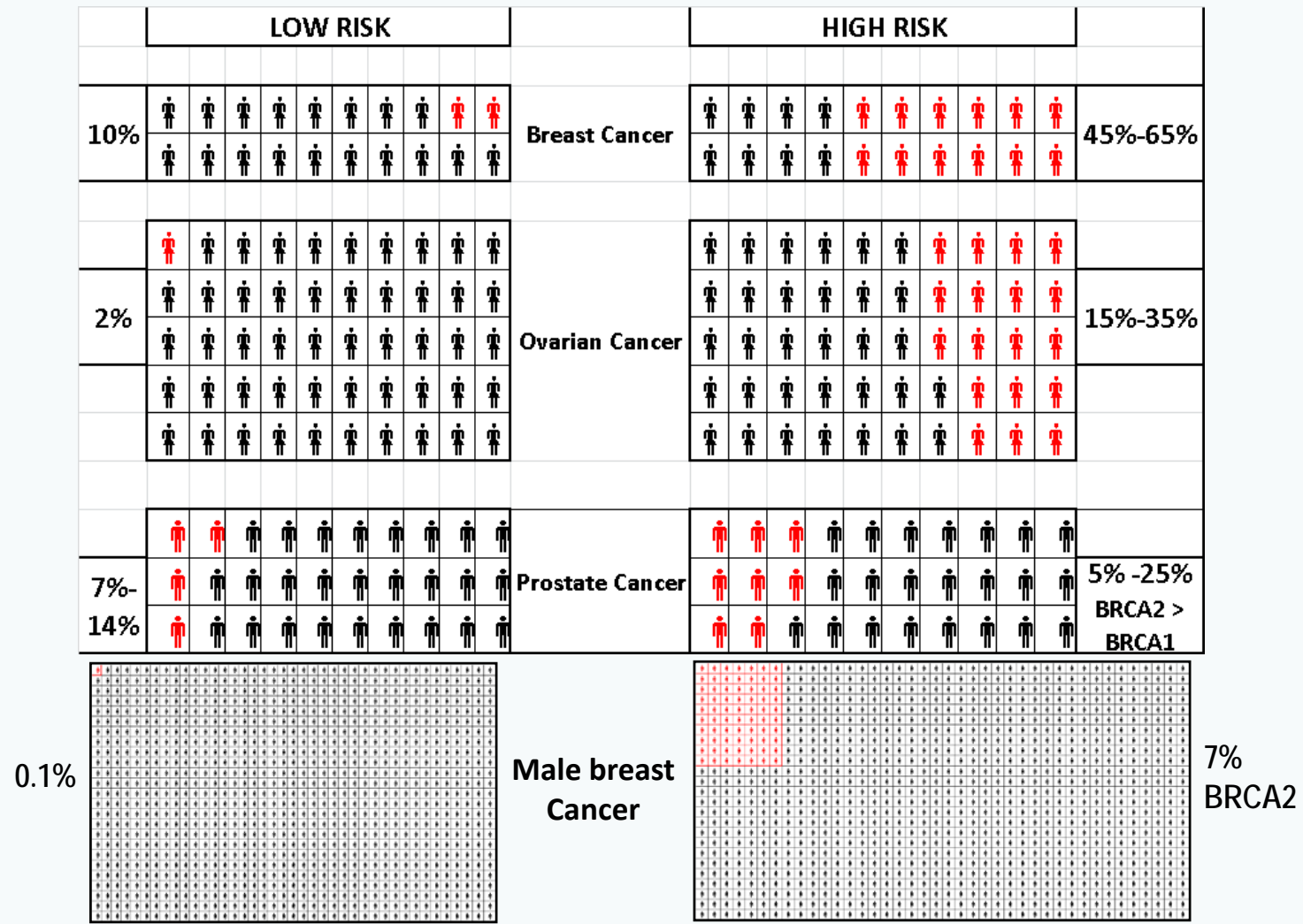
CAGTGCATCTTAGTTTTGTACATTTAGGGGAGATATGAGAC
;GTTTTGTCCAGAAAGCCAGAACCCTCAAAGCAGGGG
TTGACAATTGGTTGAAAGAGTTGTCAATAGAAAGGAATGT
AGTTTCTGTCATGCAGATGAAGCCTTCAGGTAGCAGGC1
ACTTAAGTTCTGTGGAGACGTAAAATGAGGCCATATCTGA/
AGTTAATTAAGAAAGTTTGTCTGCCTAGTTAAGGACATG
;CATGTGCCCAAGGTGGTCAGGATACAGCTTGCTTCTAT.
AAAAATTAATTTCTAAGGTCCCTGAACCATCTGAATGG/
;AGAACCTGAACATTCCTTTCTATTGATAATACTTTTCAGCCA/
>AGGCCAGGCCAAGGGCTGACTTGAGATACCTGCCAG
>GAGAAACACCAGGGGCTGGGAGAGGGCCAGAAAG/
>TAGCGTGATGAGCTCTGACATGGCCTTGCATGGACGC
>GGAGTGATGGCACAGGGGAAAGGGTGGCATAACCCA
>CTCAGGGGCTGGGTCTTCTGCTGCAACTCAGCCCCTC
>ACACCCAGCTGACAAAAGGGACTTGCCTGTACCCCTC/
>AGGTGTTGTTGGGCCAACGAGTG **CAT G** ATGC
>CCAGACAAAGGAGTAACCTGGTGAGGAATGTGCATTA
>CAAGTGGGGAAAGTGAGGAGGTGAAGCAGGGGCTG/
;TCCACATCCCCTTGGTCGTCCTTGTGGGAGGCCACTCA
AGGTCCCAGGTGGCACCAGCCAAGATC **CATGG** GTGGC/
>STATAGTGGGTGGGGCCTCAGGAGG **CATGG** GGCCA/
>GGCAGGTACCAGAGGCATGGGG **CATGG** GTTGC.
ATGGACTGGCTCAGGGGTCTGT **CATGG** CAGC
GTTCAAGACCATGGAAGGA **CATGG** AGC
>AAGGAGAGAGAAGCCAGGACAGC **CATGG** GCTGTGGCC
>AGGATTGATGCCAAGCCTGCCTAC **CATGG** AGCACATCTC1
CCTCACATCTGTGAAACCCACAG **CATGG** TGGGGCTGACA
>TTCAGCAAGTGAGACTGCACAGGATGGCGAATCCACA
>CAATTTACATTCTGACAGTTTT **CATGG** GGGAGATGAGACCA/
ACCCTTGGTGGTCTCT **CATGG** GAAGCCGGGCTGCAGA
GG **CATGG** GACT **CATGG** CTCCATGGAGGACCCCATGA/
GGCTGGGGCCCAATTTGGGAGTTCTATCTTTGGGGAAAGGA
;GCTCAGGCCAGGATCAAATCAAAGTCAGCTTCATGC

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



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

A diagram consisting of a horizontal row of six shapes: three circles followed by three squares. A large blue oval is superimposed over the text, partially overlapping the circles and squares. The text is centered within the oval.

Advantages of BRCA Carrier Identification



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
IDENTIFICATION
OF HIGH RISK
GROUPS**

**BETTER
TARGETED
PREVENTION**

**REDUCED
CANCER
INCIDENCE &
MORTALITY**

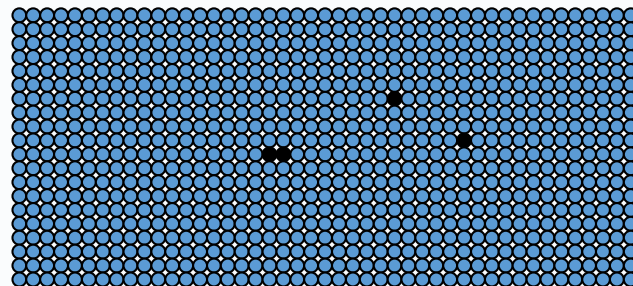
**WHY DO WE NEED TO WAIT FOR PEOPLE
TO GET CANCER TO IDENTIFY PEOPLE IN
WHOM WE CAN PREVENT CANCER??**

CAN WE TEST POPULATIONS?

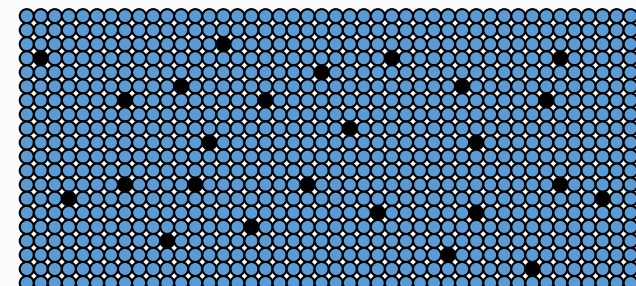


- Increased Carrier identification?
- Risk/ Penetrance?
- Psychological / QoL Impact?
- Acceptable?
- Cost effective?
- New approaches for delivery?

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.

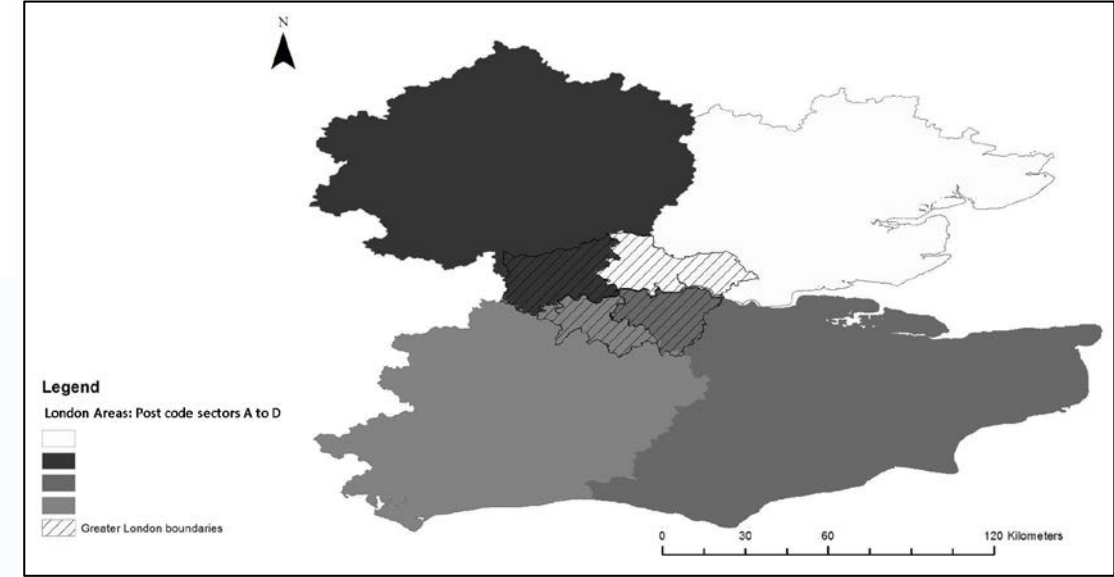
Current detection rates and time-to-detection of all identifiable *BRCA* carriers in the Greater London population

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 Jacobs¹²



AJ = 0.0261 1:40
Gen Pop = 0.00677 1:200



Map of London coverage areas (A, B, C, D) based on postcode sectors covered by NHS Genetics Services

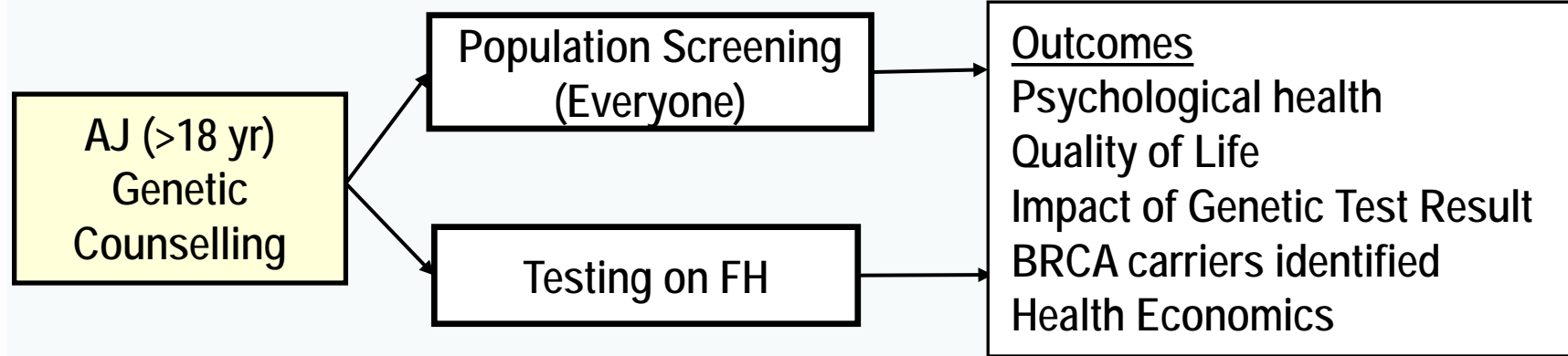
Gen pop BRCA – 3%
AJ Pop – 10%

Vast majority are unidentified

1995 – 2014, 16 Million pop
All BRCA carriers detected
Mapped for London Post Code

THE RESEARCH

THE AJ MODEL



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

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

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



JNCI 2015

Cost-effectiveness of Population Screening for BRCA Mutations in Ashkenazi Jewish Women Compared with Family History-Based Testing

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

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

AJOG 2017

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

Ranjit Manchanda,^{1,2} M Burnell,³ F Gaba,^{4,5} S Sanderson,⁴ K Loggenberg,⁶ S Gessler,⁷ J Wardle,^{4,1} L Side,⁸ R Desai,⁹ AF Brady,⁹ H Dorkins,¹⁰ Y Wallis,¹¹ C Chapman,¹² C Jacobs,^{1,1} I Tomlinson,¹⁰ U Beller,¹⁵ U Menon,¹ I Jacobs¹⁶

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

2019

96% interest
60% intention
88% uptake

Reassurance
Reducing Uncertainty
Married/Cohabiting – 4x

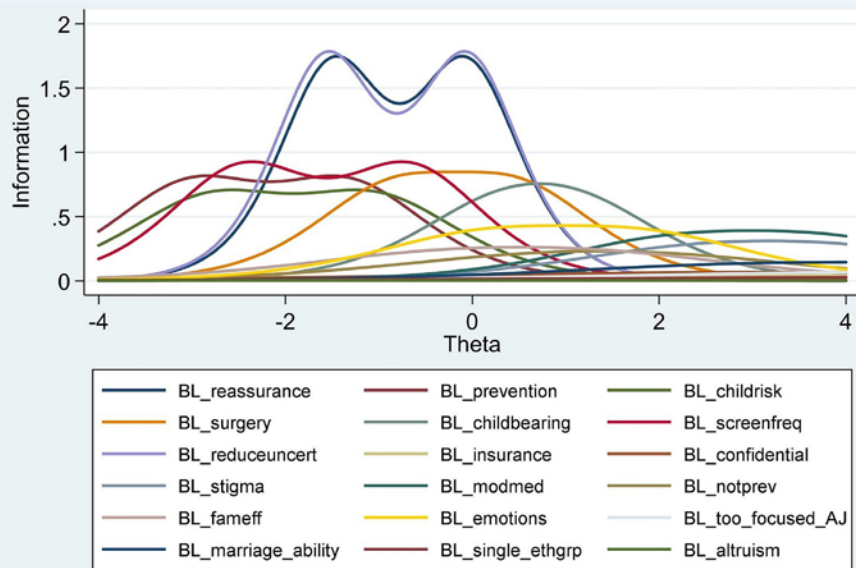
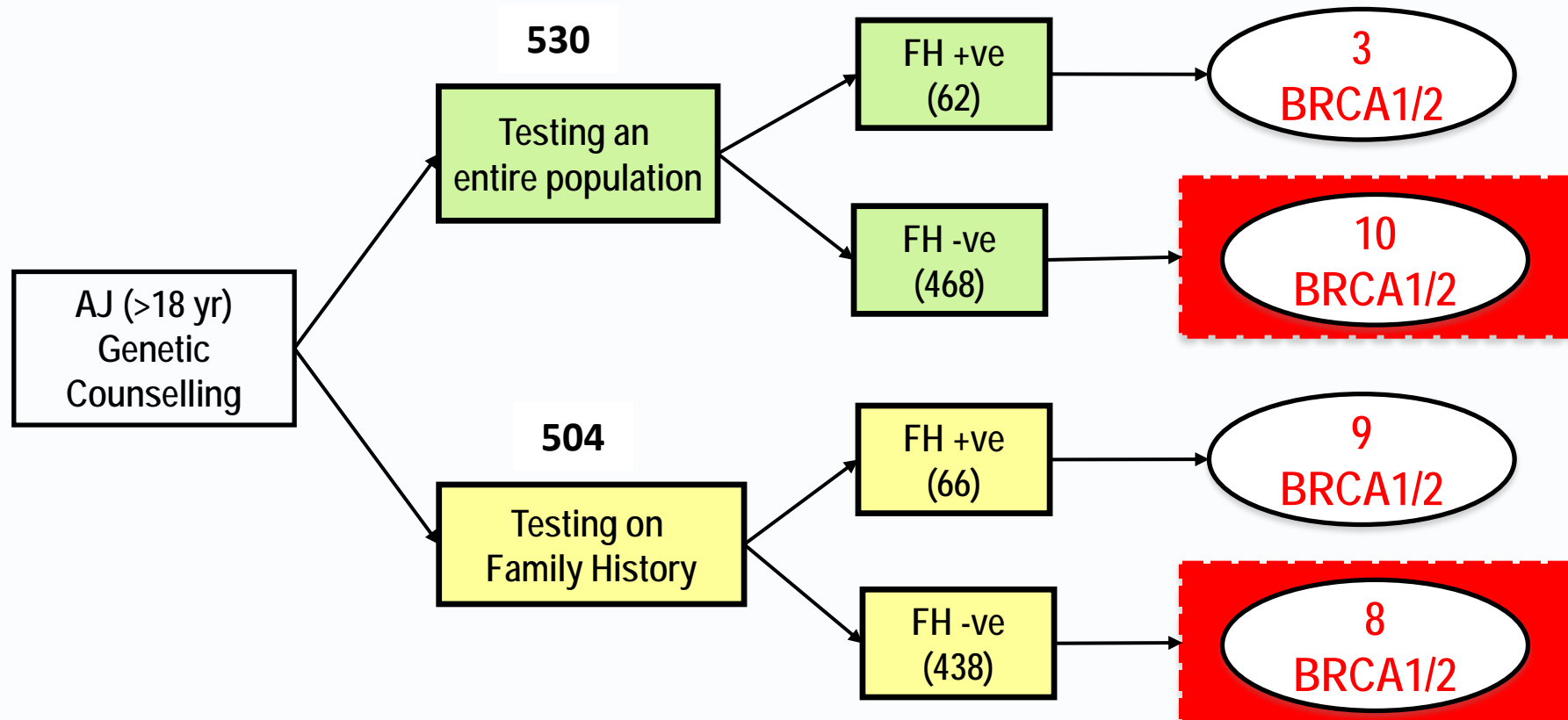
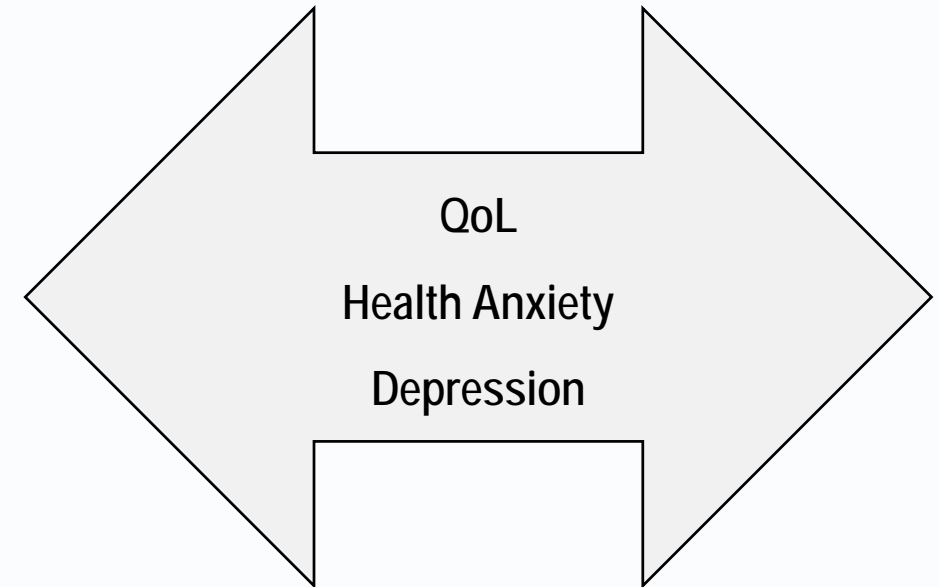
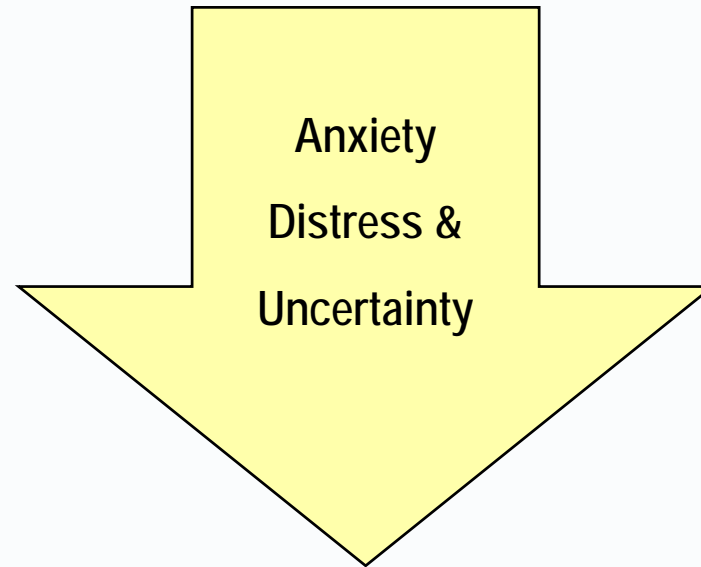


Figure S1. Item Information Functions



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

Effect of Time



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

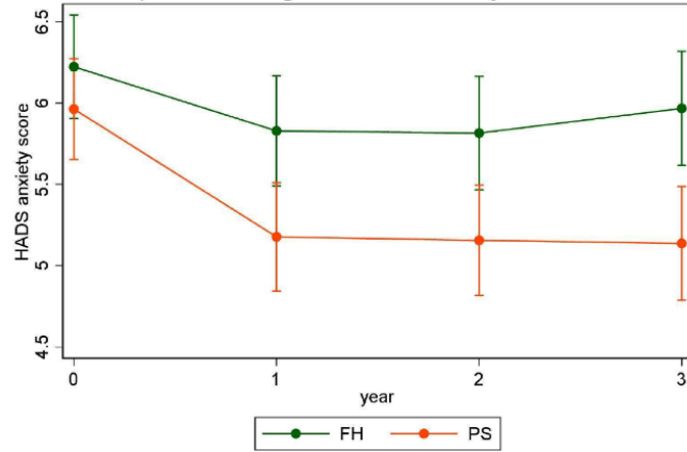
60% carriers do NOT have a strong FH & are identified by Population Testing Only

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

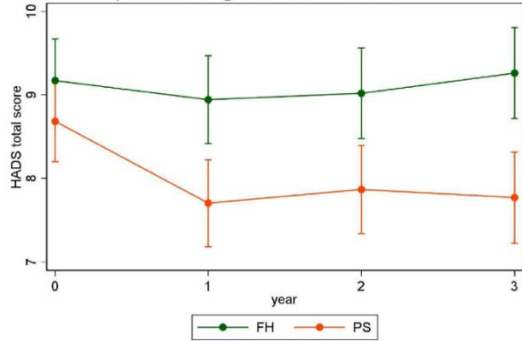
predictive margins for HADS anxiety score



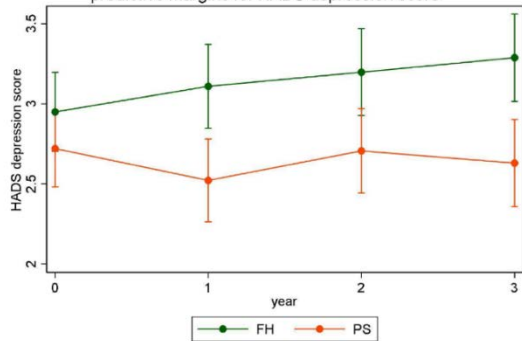
Decrease in anxiety following testing

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

predictive margins for HADS total score



predictive margins for HADS depression score

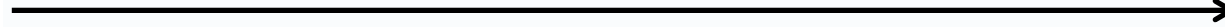


**No Difference in
QOL
Health Anxiety
Uncertainty
Distress**

$$QALY = (\text{Survival}) \times (\text{Utility score})$$



0



1



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

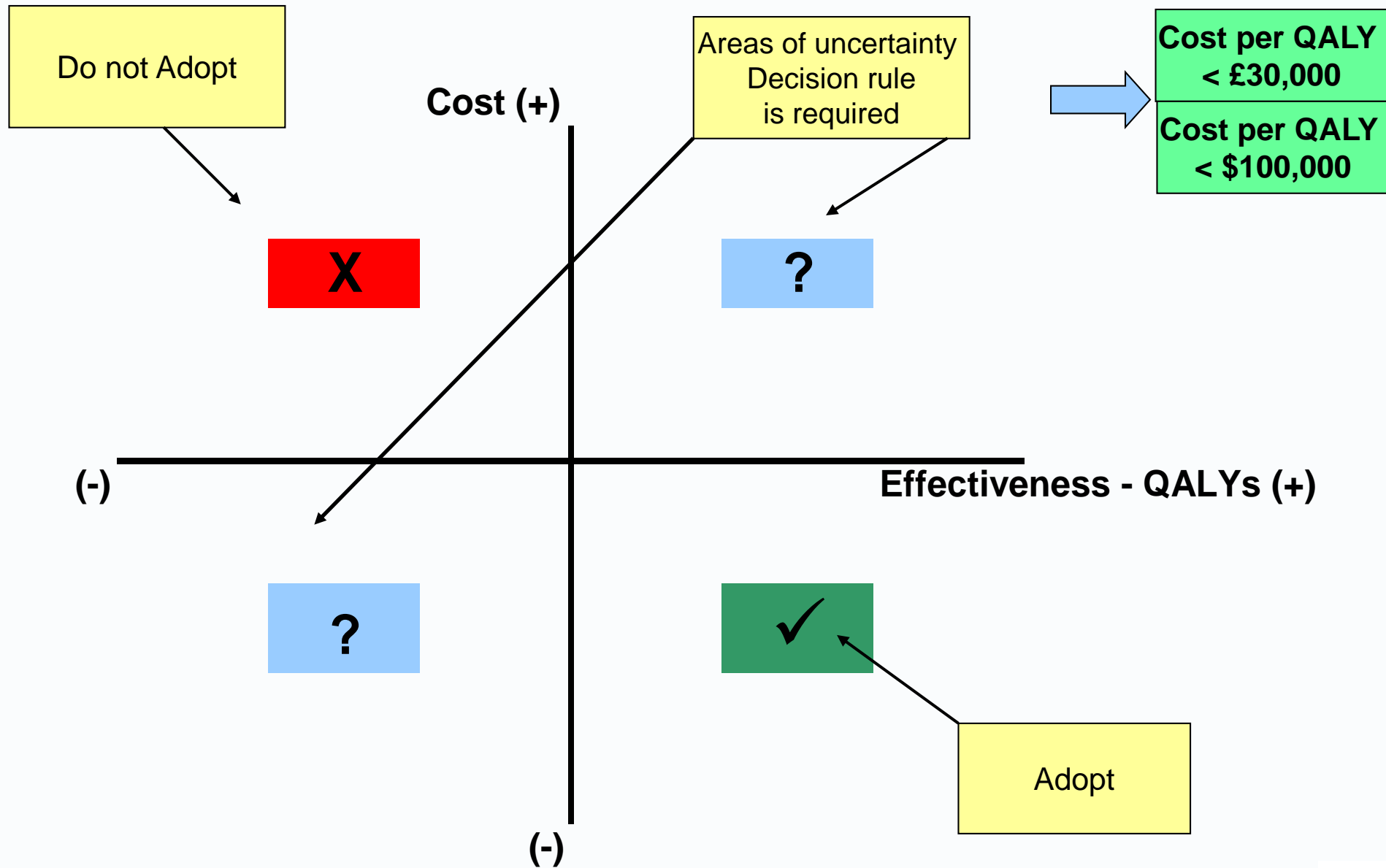
HEALTH ECONOMICS (HE)

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



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

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

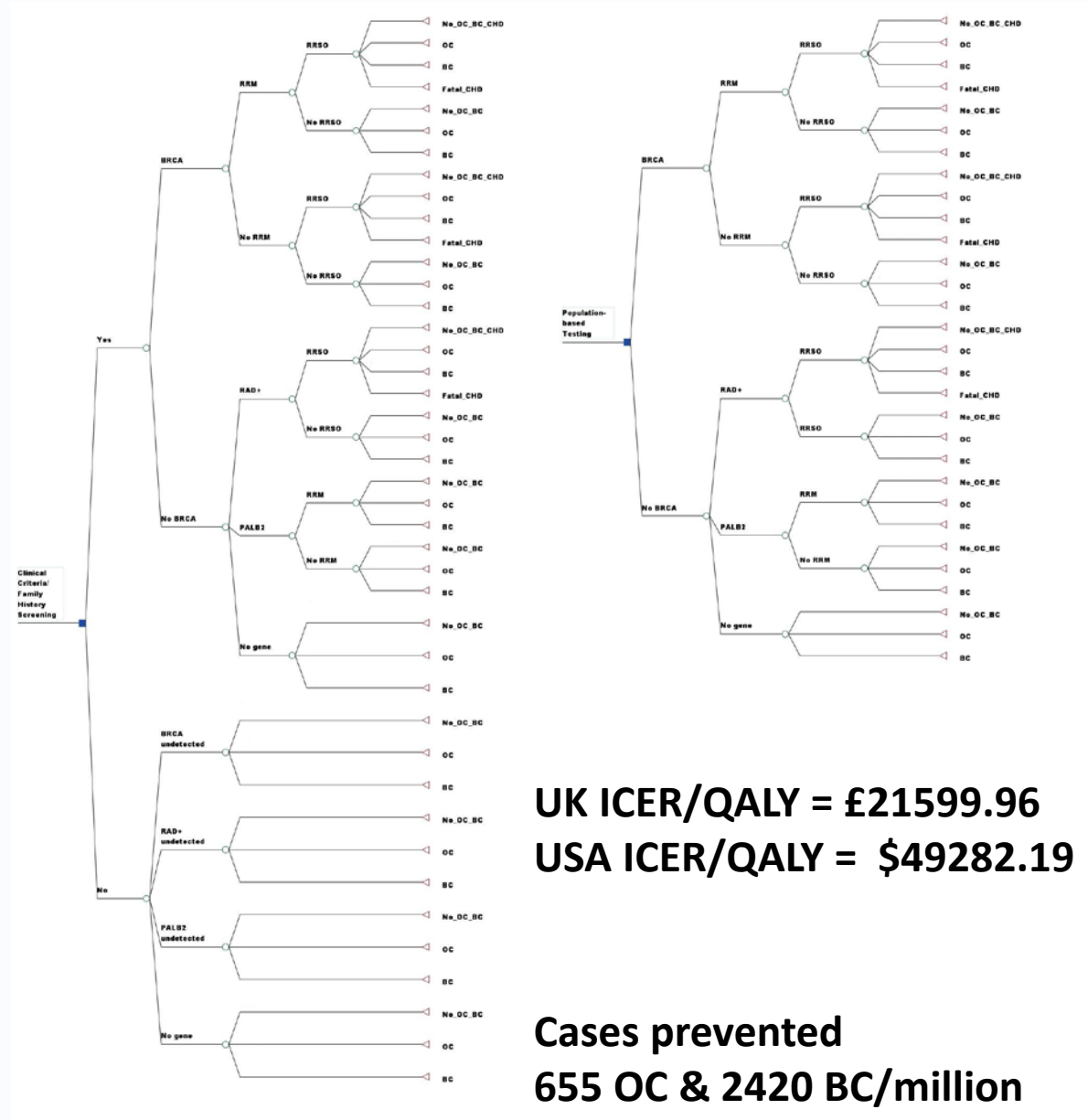
doi: 10.1093/jnci/djx265

First published online January 18, 2018

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 faulty 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.

BBC | Your account | News | Sport | Weather | iPlayer | TV | RA

NEWS

Home | UK | World | Business | Politics | Tech | Science | Health | Family & Education

Health

Angelina Jolie gene testing for all?

By James Gallagher
 Health and science correspondent, BBC News

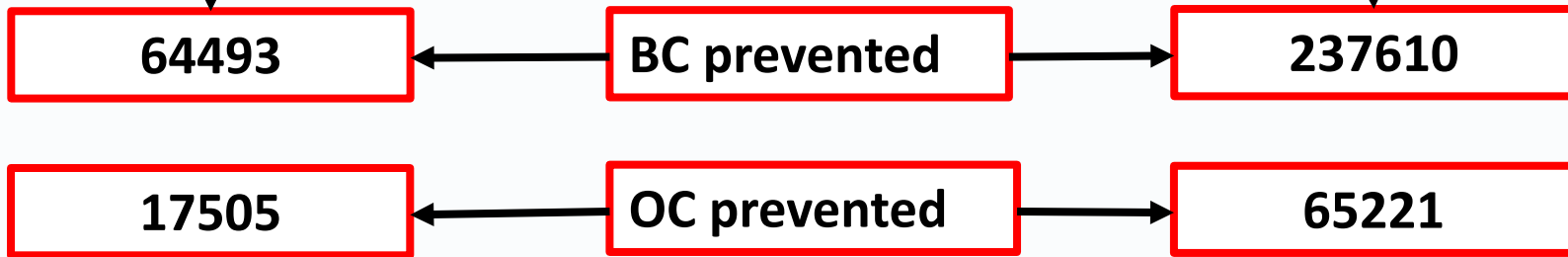
18 January 2018 | 109

f | | | | | | | | | |





IMPACT!



**MODEL OF CARE FOR
PREVENTING CHRONIC
DISEASE**

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

Ian Jacobs
Usha Menon
Matthew Burnell
Faiza Gaba
Rakshit Desai
Jane Wardle
Sue Gessler
Lucy Side
Saskia Sanderson
Kelly Loggenberg
Angela F Brady
Huw Dorkins
Yvonne Wallis
Cyril Chapman
Chris Jacobs
Rosa Legood
Uziel Beller
Ian Tomlinson
Rohan Taylor
Katriina Whitaker
Mahesh Parmar

Anthony Silverstone
Margaret Jacobi
Marlena Schmool
Elizabeth Bancroft
Imelda Udeh
Naila Balogun
Judith Soloway
Jennifer Wiggins
Adina Roth
Hannah Lyons
Jane Lyons
Sarah Chamberlain
Michelle Johnson
Helen Mitchell
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

