

The PROCAS trial: looking at breast cancer risk during screening

Anthony Howell

Professor of Medical Oncology
Nightingale Screening & Genesis Prevention Centres
University Hospital of South Manchester
Institute of Cancer Sciences,
University of Manchester, UK



GISMa Meeting

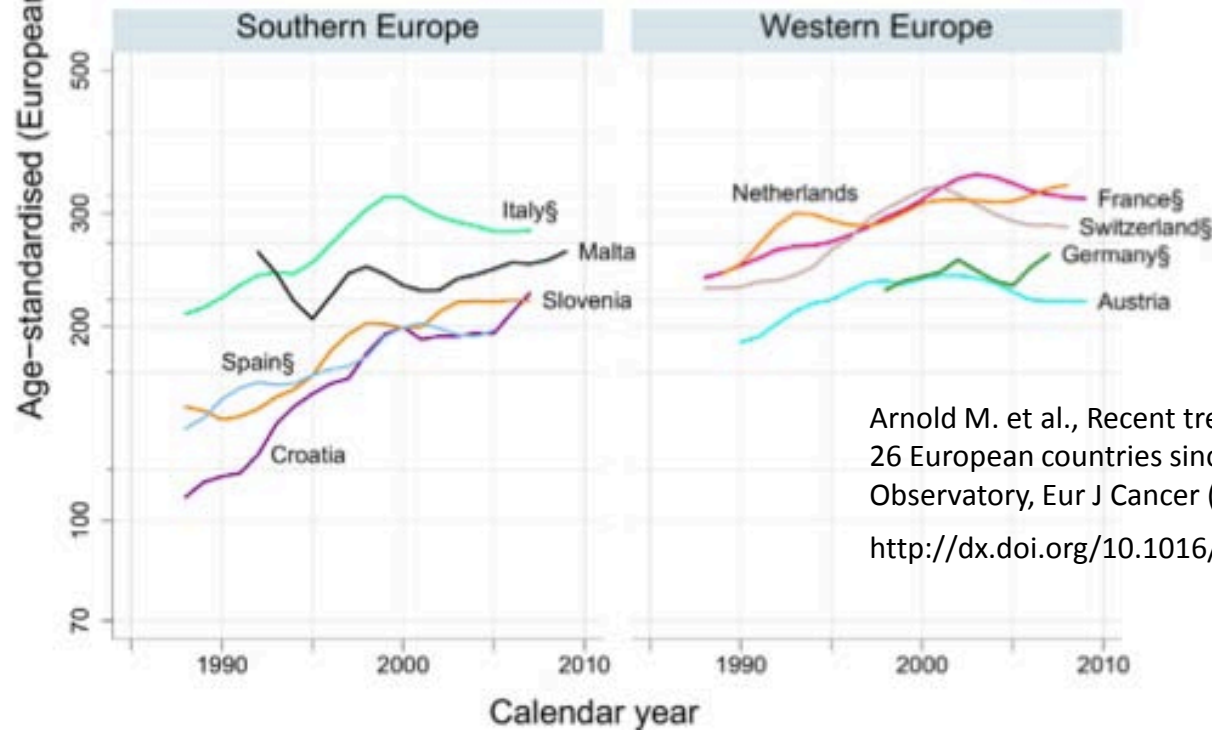
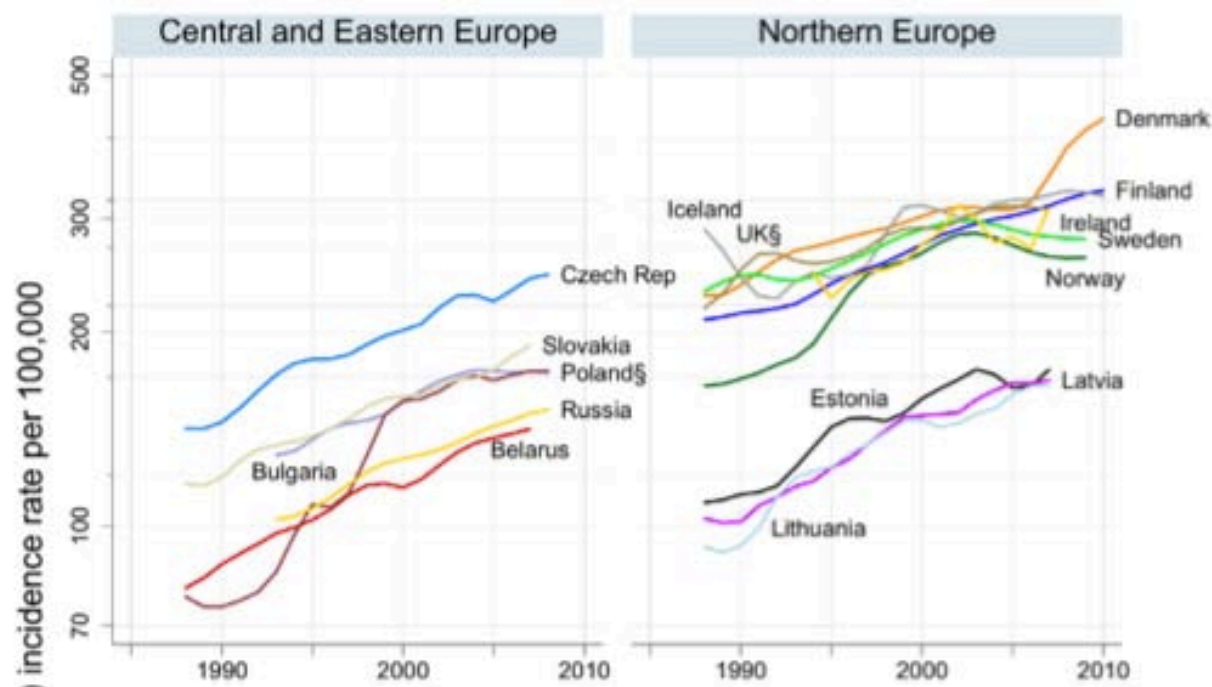
Sorrento 27th June 2014



Outline (work in progress)

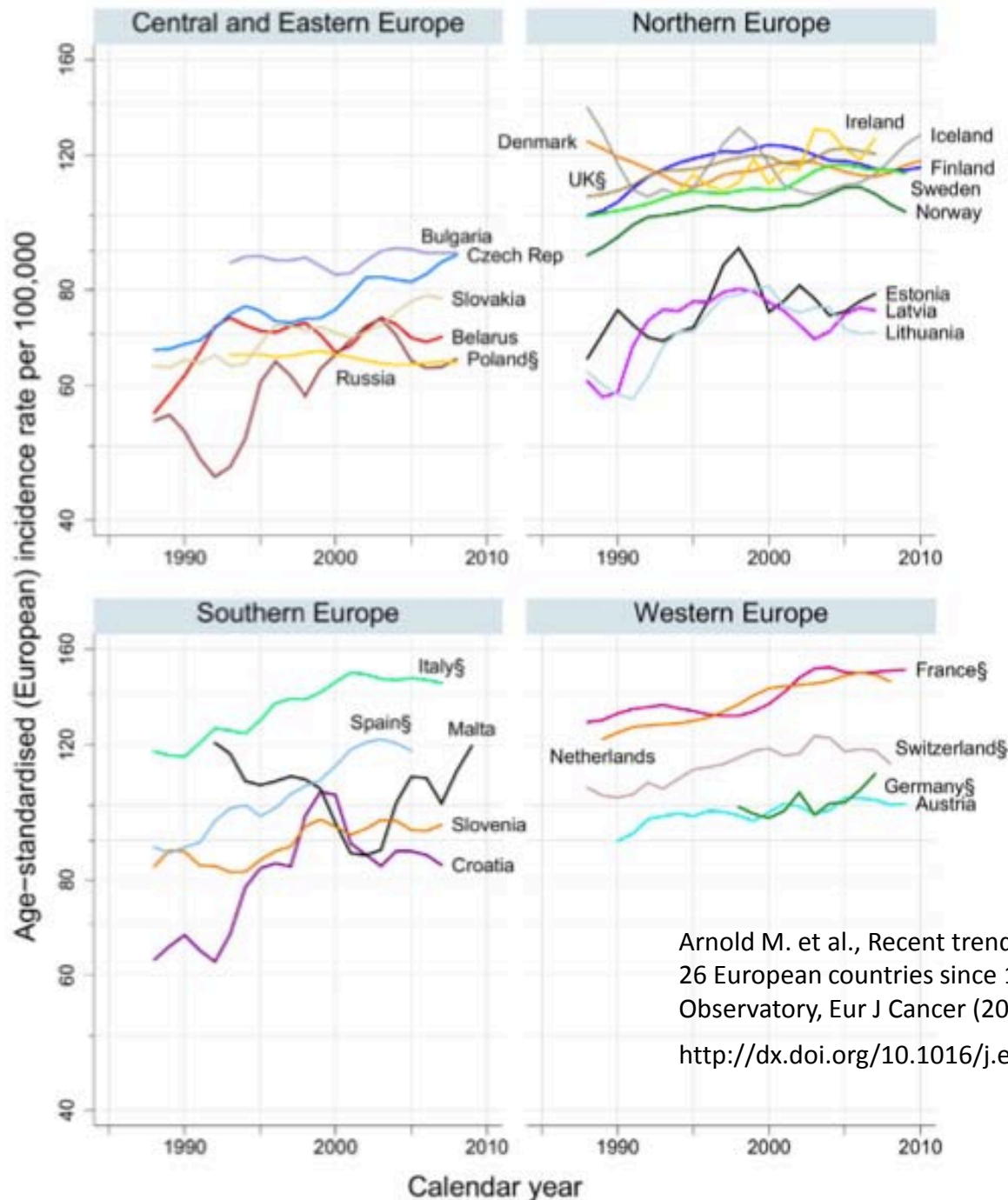
- Breast cancer incidence & mortality
- The PROCAS study
- Risk prediction models
- Mammographic density
- Single nucleotide polymorphisms
- Prevention

Postmenopausal Breast Cancer

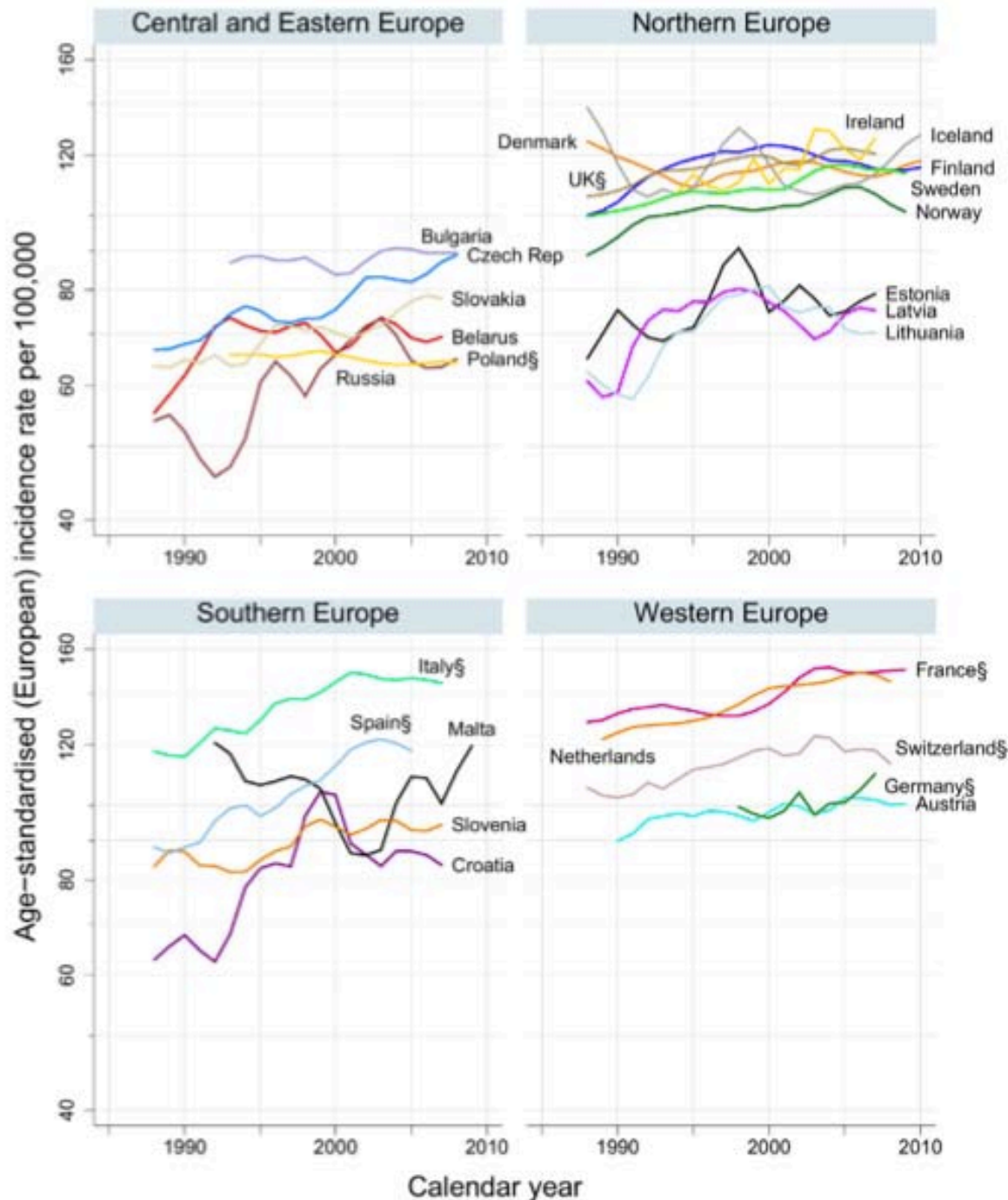


Arnold M. et al., Recent trends in incidence of five common cancers in 26 European countries since 1988: Analysis of the European Cancer Observatory, *Eur J Cancer* (2014), <http://dx.doi.org/10.1016/j.ejca.2013.09.002>

Premenopausal Breast Cancer



Arnold M. et al., Recent trends in incidence of five common cancers in 26 European countries since 1988: Analysis of the European Cancer Observatory, *Eur J Cancer* (2014),
<http://dx.doi.org/10.1016/j.ejca.2013.09.002>

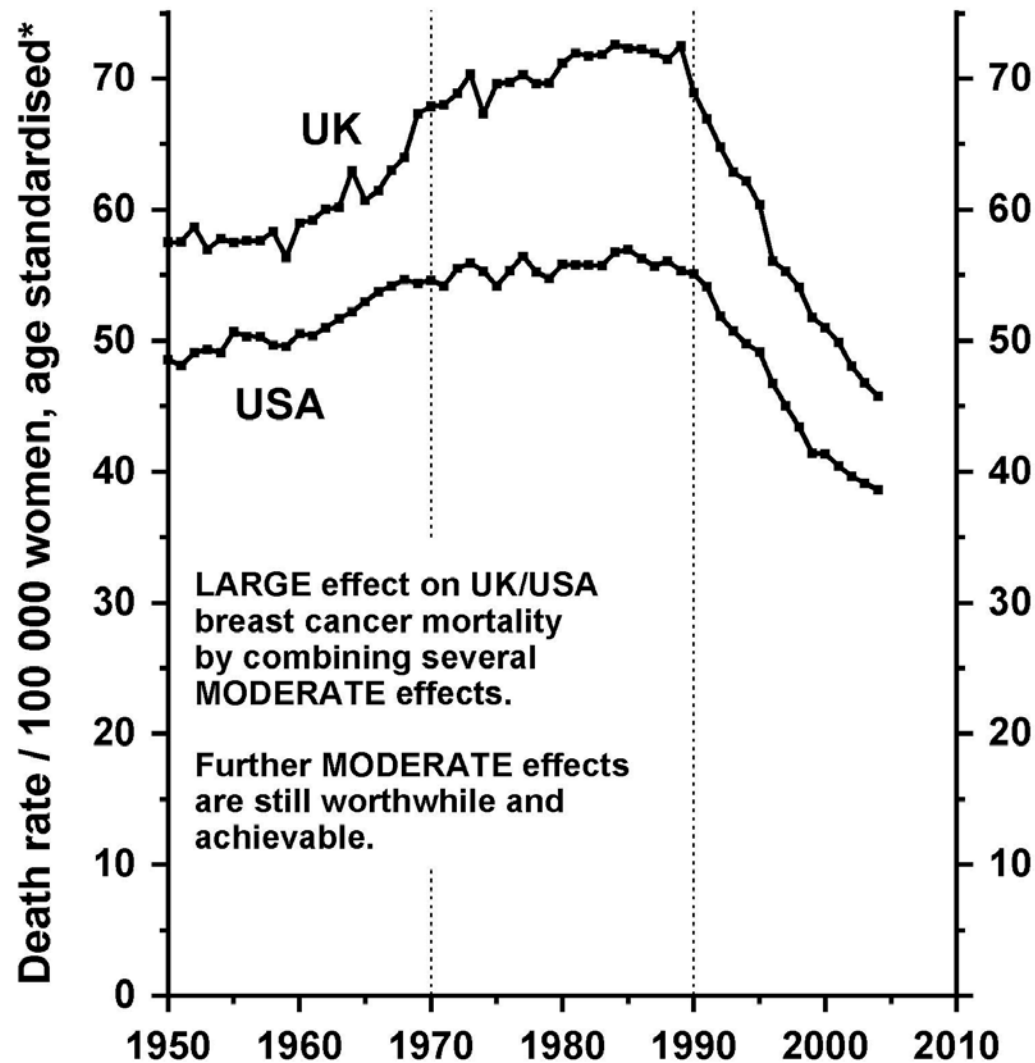


Premenopausal Breast Cancer

Why?

- Lifestyle
- Age of first pregnancy
- Screening

UK and USA 1950–2004: recent decrease in breast cancer mortality at ages 35–69



Why?

- Screening
- Treatment

*Mean of annual rates in the seven component 5-year age groups

Source: WHO mortality & UN population estimates

Comment - incidence and mortality

- Incidence is increasing
- Mortality declining but at a cost
- Women 'labelled' with cancer
- Can we detect 'good cancer' and prevent lethal cancer

Outline

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Use of screening programmes



Population based cancer screening programmes as a teachable moment for primary prevention interventions. A review of the literature

Carlo Senore*, Livia Giordano, Cristina Bellisario, Francesca Di Stefano and Nereo Segnan

Epidemiologia dei Tumori II, AOU S Giovanni Battista – CPO Piemonte, Torino, Italy

Howell A et al J Intern Med 2012 Apr;271(4):321-30
Evans DG et al Cancer Prev Res 2012 Jul; 5(7):943-51

Prediction Of Cancer At Screening

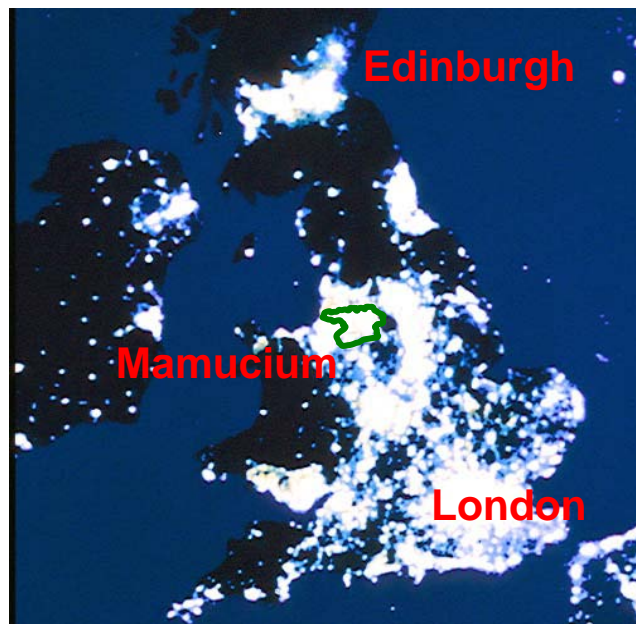
Could we:-

- determine risk at screening?
 - opportunity since ~70% of women seen
- improve on risk estimation?
 - add mammographic density and SNPs
- introduce risk adapted screening and prevention?
 - in conjunction with family doctors

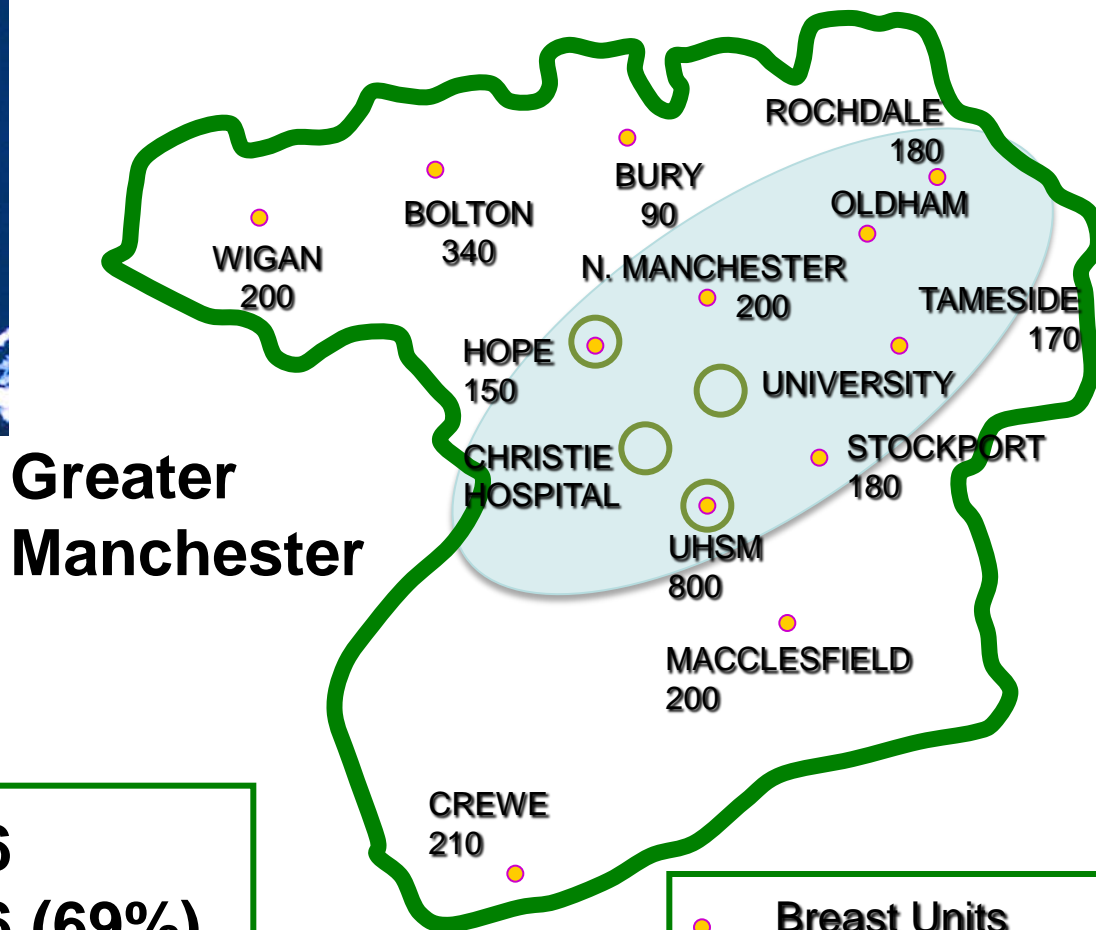
PRediction Of Cancer At Screening (PROCAS)



Mamucium



Started recruitment - 26.10.2009
Completed round - 31.10.2012



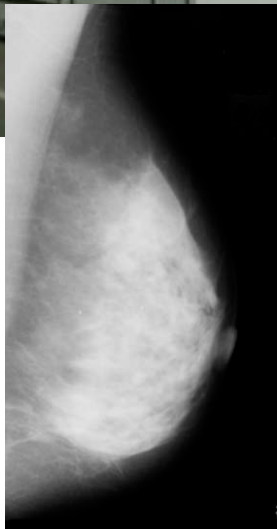
Greater Manchester

●	Breast Units
	University Hospitals

NHS
National Institute for Health Research

Invited	204,376
Attended	141,306 (69%)
Entered	54,498 (39%)

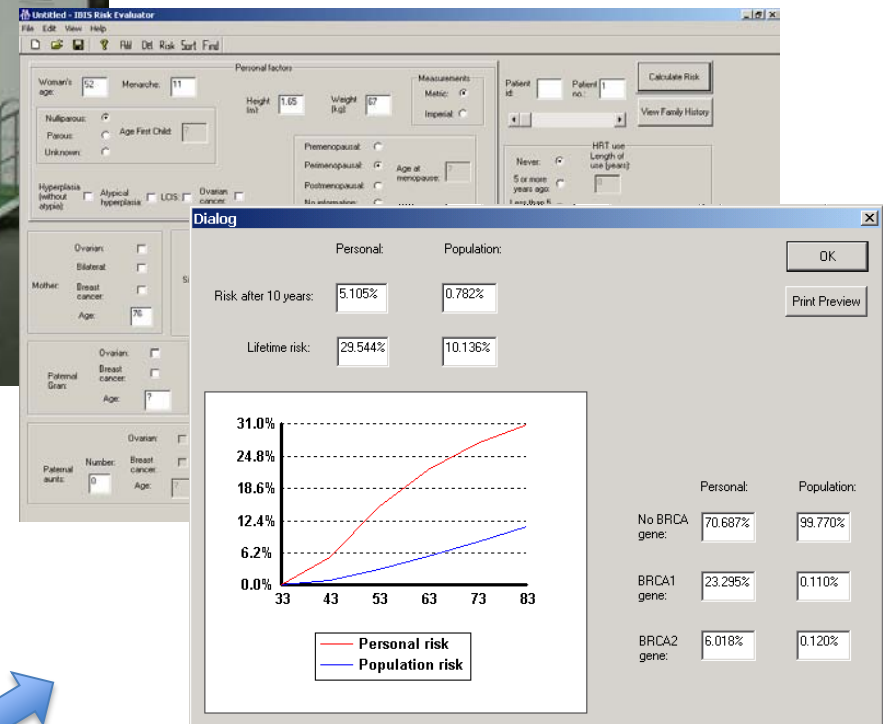
PROCAS investigations (n=54,498)



Density
(4 methods)

Sputum SNPs
(10,000)


Questionnaire



Risk algorithm

PROCAS forms

PROCAS
Predicting the Risk of Cancer At Screening

University Hospital
of South Manchester 
NHS Foundation Trust

We would be grateful if you would fill in this questionnaire before attending for screening. Please complete all sections. If you have any questions please call 0161 275 4438 or 07937 844402

Please try and give an accurate answer to each question and make sure you answer all questions. If you don't know the answer to a question, please write 'unknown'. If you can't remember precise dates or other information, please complete as best you can. If you run out of space, please provide any further relevant information on a separate piece of paper.

All information collected will be kept completely confidential and is for research purposes only.
Please complete the questionnaire in BLOCK CAPITALS and mark your answers with a cross 'X'.
Please bring your completed questionnaire to your mammogram appointment.

Name:

Postcode: Date of birth: / /

Height ft in OR m What is your current UK clothes size for trousers/skirts? (i.e. size 10,14,20)

Weight Now st lb OR kg

Weight age 25 st lb OR kg

At what age did you have your first period? yrs. Have you had a hysterectomy? Yes No

Have you had your ovaries removed? One ovary Both ovaries No. If yes, at what age did you have your hysterectomy? yrs

Menopausal status - Please select from the following:

Not been through menopause Been through menopause (i.e. not had a period for 2yrs)
 Currently going through menopause Unknown

If you have been through or are currently going through the menopause, how old were you when your periods stopped? yrs

Have you ever been on hormone Replacement Therapy (HRT)? Yes No. If yes, how long were you on HRT for? yrs mths

Please provide the name of the HRT:

Are you still on HRT? Yes No. If not how long ago did you stop? yrs mths

Have you ever taken anti-cholesterol drugs called statins (e.g. Simvastatin)? Yes No. If yes, how long for? yrs mths


What is the name of the anti-cholesterol medication you currently taking?

How many sisters do you have? 0 1 2 3 4 5 6 7+ Unknown

Have you had any children? Yes No. If yes, please answer the following questions:

How old were you when you gave birth to your first child? yrs

How many children have you given birth to?

PROCAS Questionnaire, version 10.0, 06/07/2011 PLEASE PRINT OVER  Page 1 of 2 40271

Please provide details of your mother's age if alive or her age at death. If you have sisters, please provide their ages below.

If either your mother or sisters have had breast or ovarian cancer, provide details of each occurrence of breast or ovarian cancer and age at diagnosis.

Mother Had breast or ovarian cancer? No Yes. If yes, please specify... 1 breast Both breasts Ovarian
Age yrs Unknown Age yrs yrs yrs

Sister 1 Had breast or ovarian cancer? No Yes. If yes, please specify... 1 breast Both breasts Ovarian
Age yrs Unknown Age yrs yrs yrs

Sister 2 Had breast or ovarian cancer? No Yes. If yes, please specify... 1 breast Both breasts Ovarian
Age yrs Unknown Age yrs yrs yrs

Sister 3 Had breast or ovarian cancer? No Yes. If yes, please specify... 1 breast Both breasts Ovarian
Age yrs Unknown Age yrs yrs yrs

If any other female relative has had breast or ovarian cancer, please provide full details below, including full details of relationship e.g. paternal gran, maternal gran, paternal aunt, maternal aunt, niece, maternal cousin, paternal cousin.

Relative: 1 breast Both breasts Ovarian
Age yrs yrs yrs

Relative: 1 breast Both breasts Ovarian
Age yrs yrs yrs

Relative: 1 breast Both breasts Ovarian
Age yrs yrs yrs

Relative: 1 breast Both breasts Ovarian
Age yrs yrs yrs

Have you ever been diagnosed with breast cancer? Yes No

Have you ever had a biopsy of your breast? Yes No

If yes, please state which hospital/breast screening centre you attended and the date:

Location:

Date: / /

Have you done any moderate/vigorous activity during the past week? Yes No
Only include activities where you felt warmingly out of breath, e.g. brisk walking, cycling, housework, etc. gardening, other sports or work related activities.


If yes, how much have you done in the past week? hrs min

Do you drink alcohol? Yes No. If yes, how many units per week, on average? units
(One single measure of 125ml 4% ABV, 16oz of 4% ABV, 10 units, standard 175ml glass 4% ABV units)

Ethnic or other origin (please tick all that apply): Asian Indian Black African/Caribbean
 Asian or Asian British (Bangladeshi, Indian, Pakistani, Chinese) Black British and Black African/Caribbean (African)
 Black or Black British (African or Caribbean) White British or Irish
 Mixed Origin Other (please specify)

PCAS (PROCAS) age

PCAS (PROCAS) sex

PROCAS (PROCAS)  Page 2 of 2 40271

Comment - PROCAS

- Questionnaire and consent feasible in context of busy a screening programme
- Uptake may be greater if not in a study?
- Risk estimate can be produced automatically
- Possible to role out in NHS Breast Screening programme?

Outline

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Assessment of risk prediction models

- 1933 women in Genesis FHC – 52 cancers (now 400)
- Compute Expected to Observed

	<u>E/O</u>	<u>95% CI</u>
• Gail	0.48	0.54-0.90
• Claus	0.56	0.59-0.99
• BRCAPRO	0.49	0.52-0.86
• Tyrer-Cuzick	0.81	0.85-1.41
• Claus X	0.89	0.95-1.58

Tyrer-Cuzick Risk Prediction Algorithm

Untitled - IBIS Risk Evaluator

File Edit View Help

Add Del Risk Sort Find

Personal factors

Woman's age: Menarche:

Nulliparous: Parous: Unknown: Age First Child:

Hyperplasia (without atypia): Atypical hyperplasia: LCIS: Ovarian cancer:

Height (m): Weight (kg):

Measurements: Metric: Imperial:

Premenopausal: Perimenopausal: Postmenopausal: No information: Age at menopause:

Patient id: Patient no.:

Calculate Risk

View Family History

HRT use Length of use (years):

Never: 5 or more years ago: Less than 5 years ago: Current user:

Ovarian: Bilateral: Mother: Breast cancer: Age:

Sisters: Ovarian: Bilateral: Breast cancer: Age:

Ashkenazi inheritance:

Half Sisters

Affected cousins

Affected Nieces

Genetic Testing

Paternal Gran: Ovarian: Breast cancer: Age:

Maternal Gran: Ovarian: Breast cancer: Age:

Show start up screen

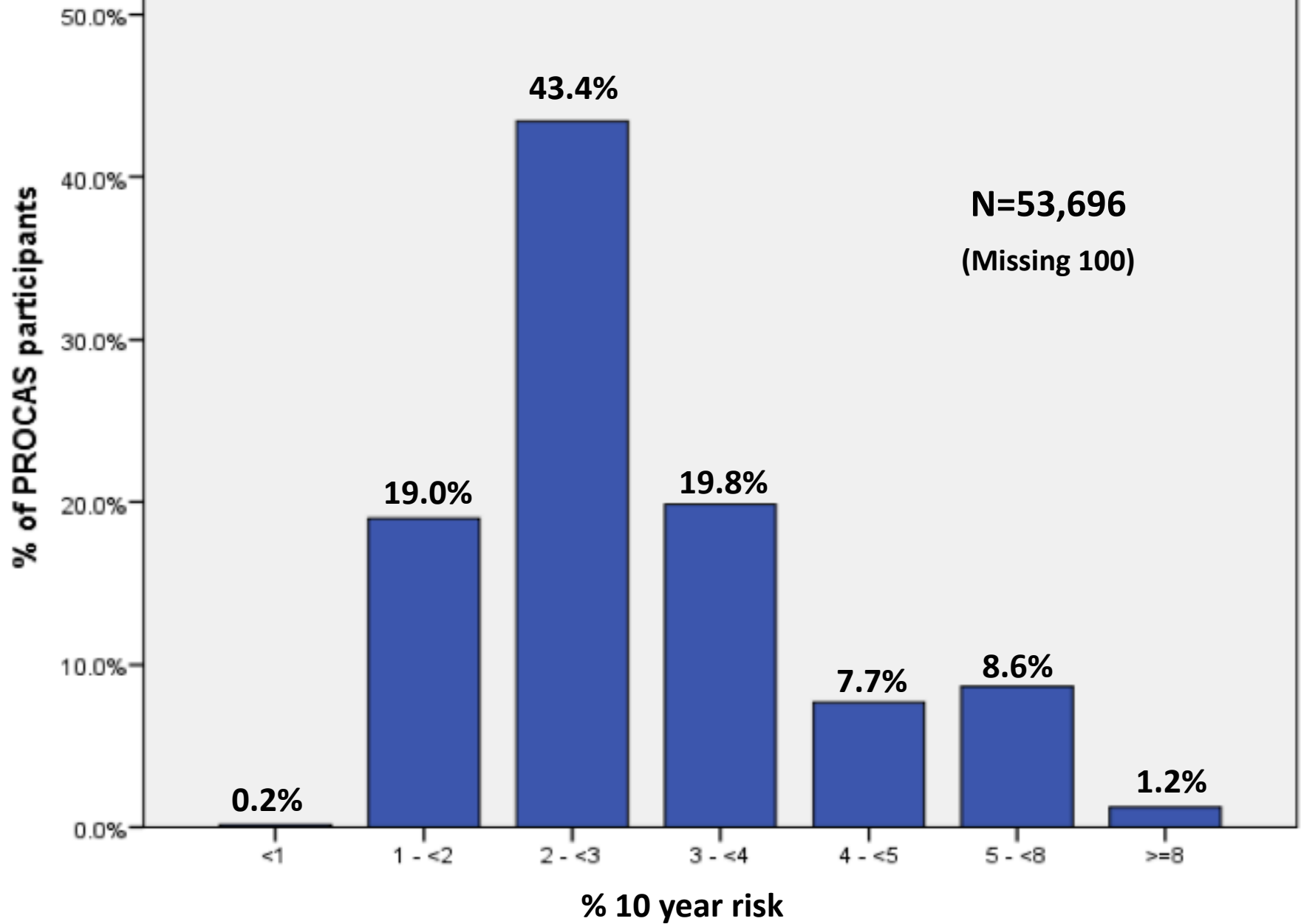
Paternal aunts: Number: Ovarian: Breast cancer: Age:

Maternal aunts: Number: Ovarian: Breast cancer: Age:

Daughters: Number: Ovarian: Breast cancer: Age:

Age	Personal Risk (%)	Population Risk (%)
33	0.0	0.0
43	6.2	2.5
53	12.4	5.0
63	18.6	7.5
73	24.8	10.0
83	31.0	12.4

PROCAS: Tyer-Cuzick risk distribution



Summary

- Several studies indicate T-C predicts well
- Risk estimation using T-C can be automated
- Identifies high risk groups – offer prevention
- Most women do not have risk factors but can still develop breast cancer!

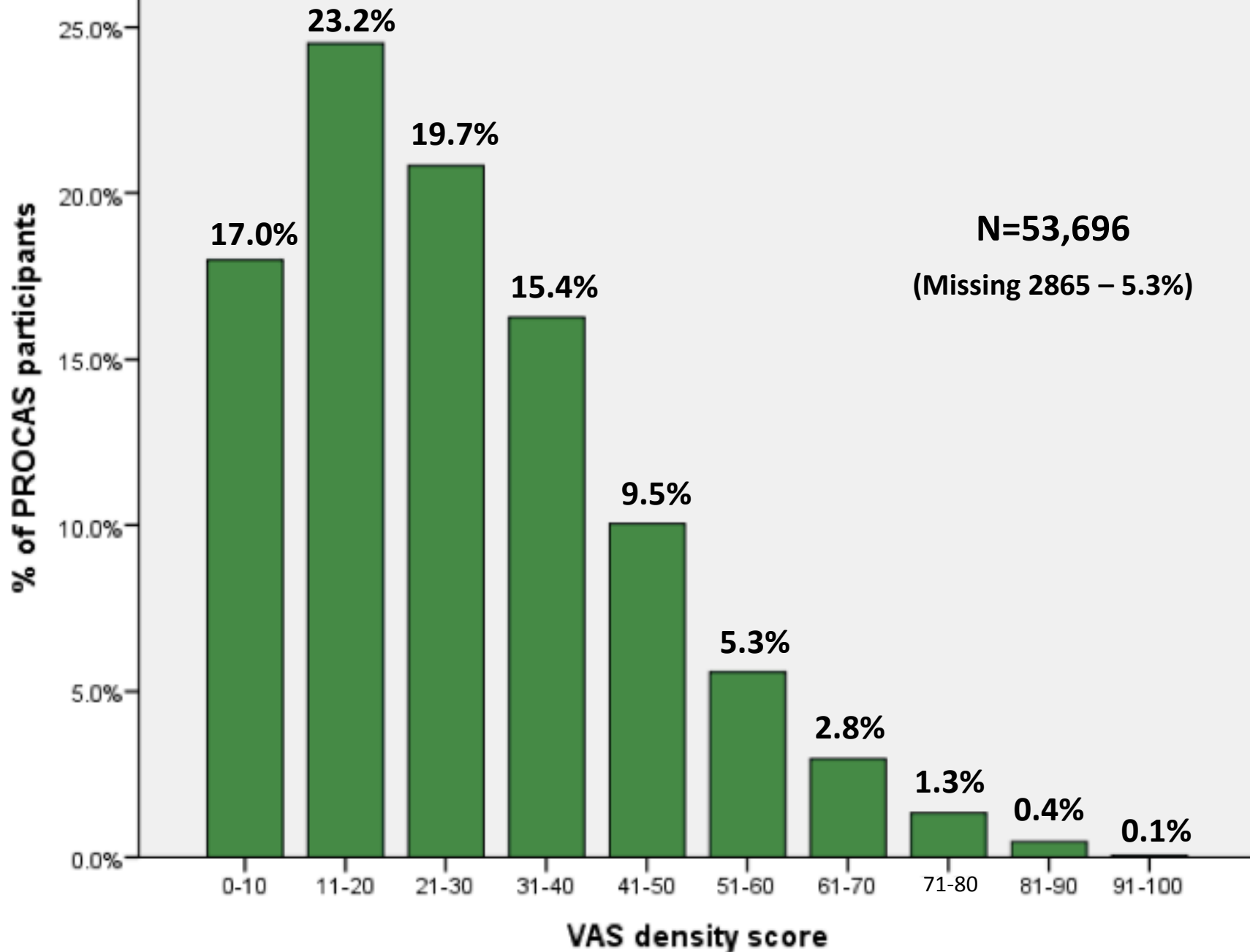
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Mammographic density measures

- Visual analogue scale - % density
- CUMULUS semi automated area
- Volumetric – Quantra and Volpara

PROCAS: % density – Visual Analogue Scale



Summary - density

- VAS difficult in busy screening programme
- Inter and intra reader variation
- Some extra discrimination when added to T-C
- Need to assess volumetric techniques which can give dense volume and be fully automated

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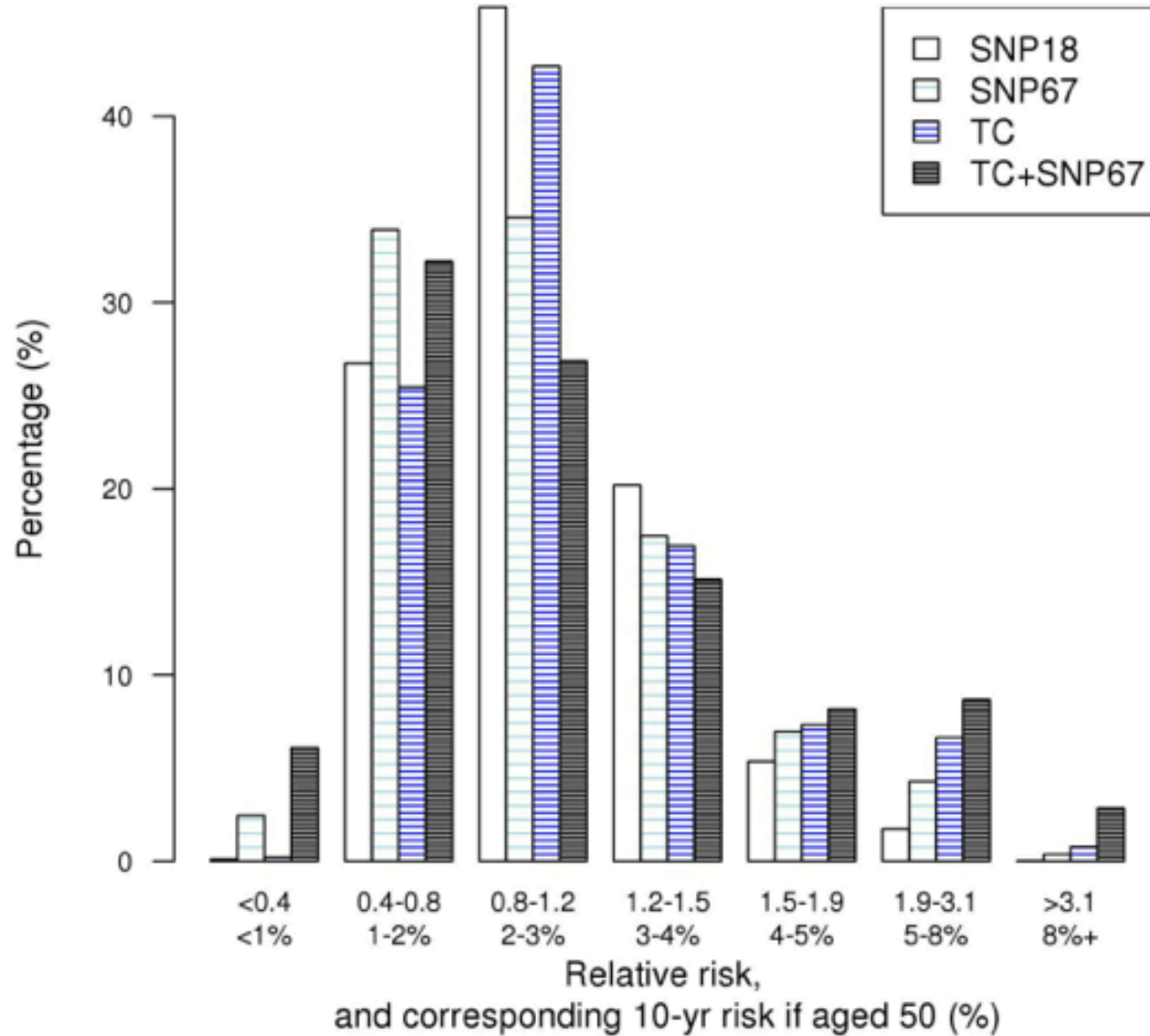
SNP -

Nat Genet. 2013 April ; 45(4): 353–361e2. doi:10.1038/ng.2563.

Large-scale genotyping identifies 41 new loci associated with breast cancer risk

Kyriaki Michailidou^{1,138}, Per Hall^{2,138}, Anna Gonzalez-Neira³, Maya Ghoussaini⁴, Joe Dennis¹, Roger L Milne⁵, Marjanka K Schmidt^{6,7}, Jenny Chang-Claude⁸, Stig E Bojesen^{9,10}, Manjeet K Bolla¹, Qin Wang¹, Ed Dicks⁴, Andrew Lee¹, Clare Turnbull¹¹, Nazneen Rahman¹¹, The Breast and Ovarian Cancer Susceptibility Collaboration¹², Olivia Fletcher¹³, Julian Peto¹⁴, Lorna Gibson¹⁴, Isabel dos Santos Silva¹⁴, Heli Nevanlinna¹⁵, Taru A Muranen¹⁵, Kristiina Aittomäki¹⁶, Carl Blomqvist¹⁷, Kamila Czene², Astrid Irwanto¹⁸, Jianjun Liu¹⁸, Quinten Waisfisz¹⁹, Hanne Meijers-Heijboer¹⁹, Muriel Adank¹⁹, Hereditary Breast and Ovarian Cancer Research Group Netherlands (HEBON)¹², Rob B van der Luijt²⁰, Rebecca Hein^{8,21}, Norbert Dahmen²², Lars Beckman²³, Alfons Meindl²⁴, Rita K

SNPs + Tyrer-Cuzick



Comment - SNPs

- 67+ available
- Estimated to be over 1,000
- Possibly predict tumour subtype
- Thus important for prevention

Outline (work in progress)

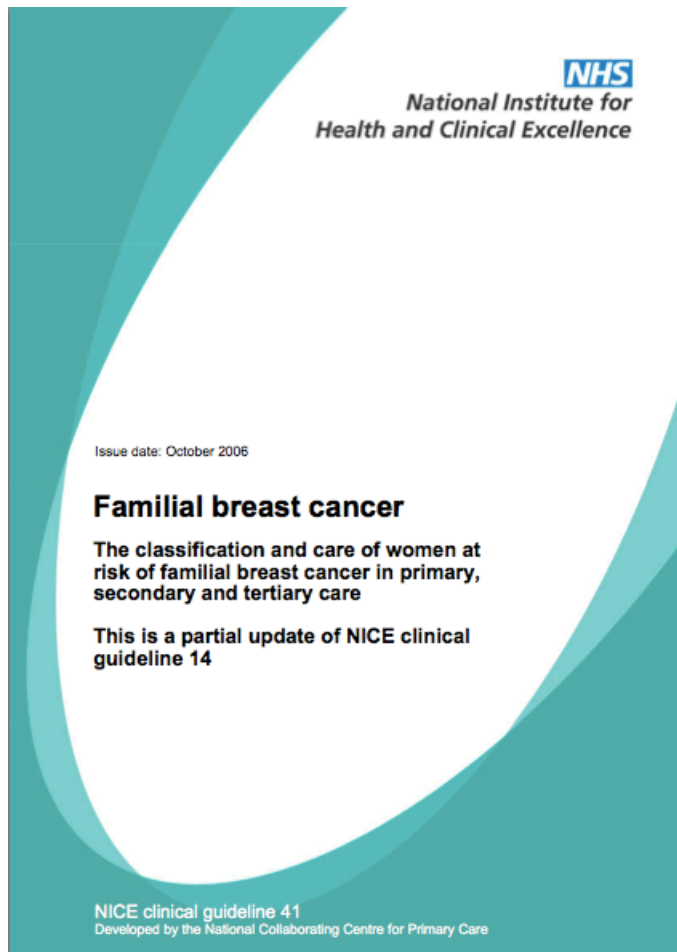
- Breast cancer incidence & mortality
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- **Prevention**

NICE Guidance on Familial Breast Cancer

2006

2013

NICE National Institute for
Health and Care Excellence



Familial breast cancer

Classification and care of people at risk of familial breast cancer and management of breast cancer and related risks in people with a family history of breast cancer

Issued: June 2013

NICE clinical guideline 164
guidance.nice.org.uk/cg164

- OFFER tamoxifen or raloxifene for women at >1 in 3 lifetime (high) risk and CONSIDER if >1 in 6 lifetime risk

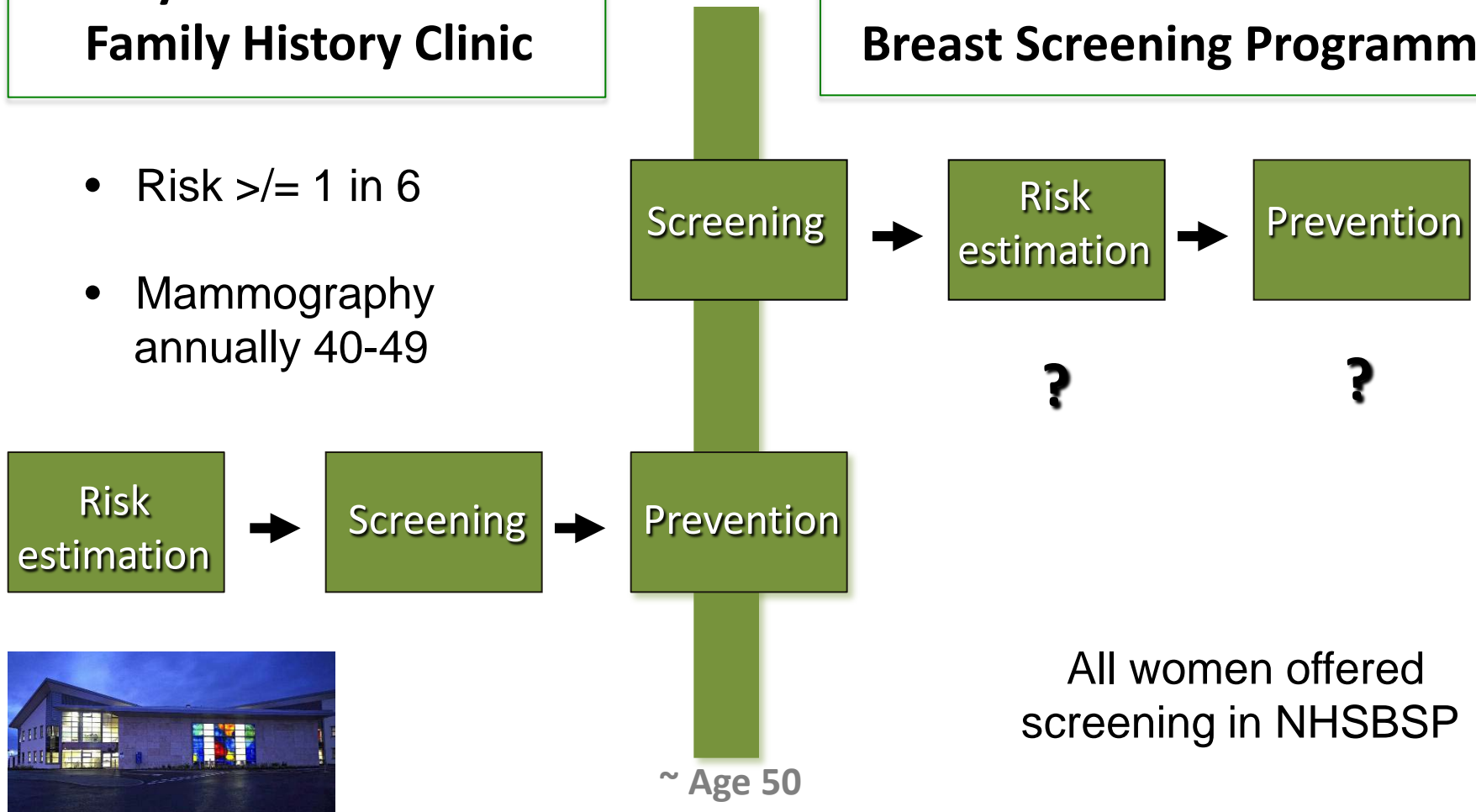
Identification of women at risk?



Family doctor referral to Family History Clinic

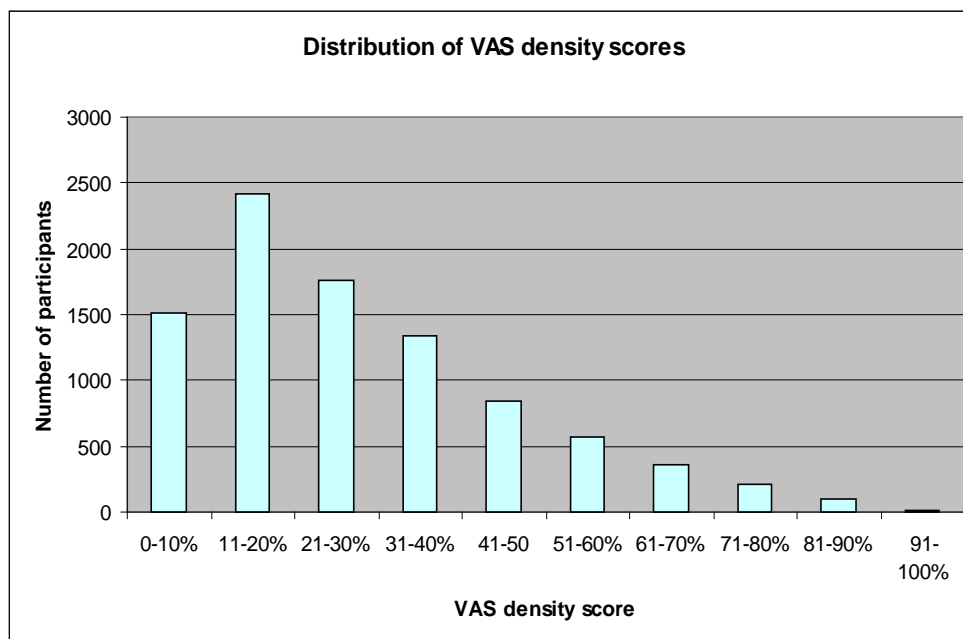
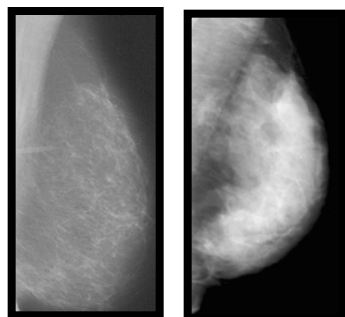
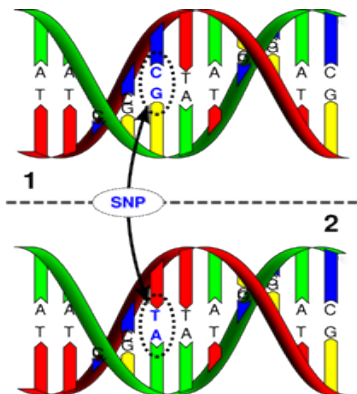
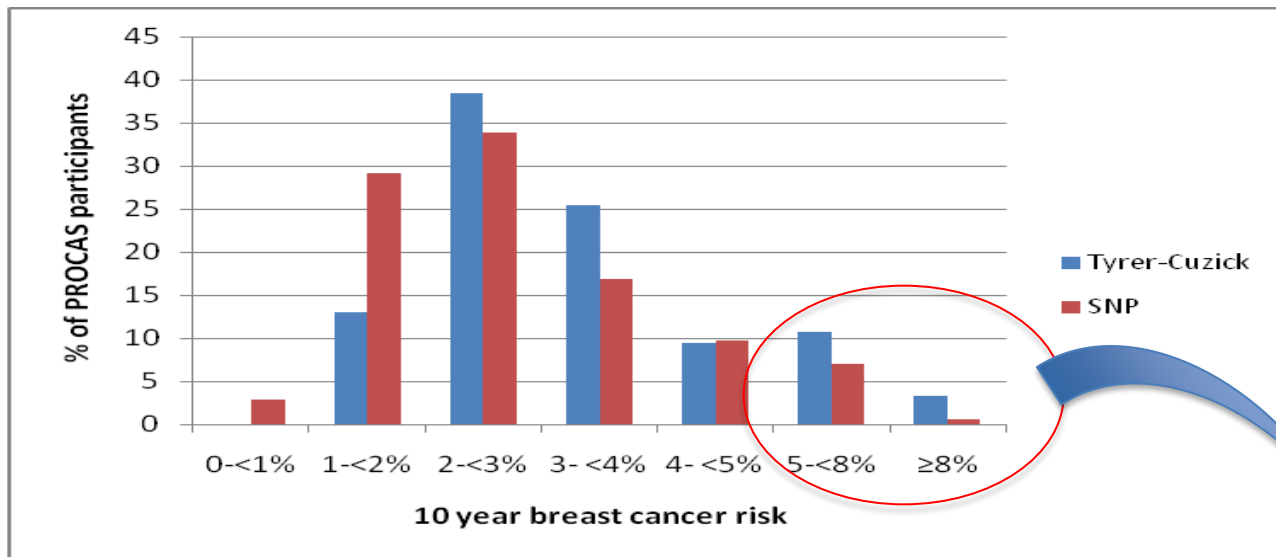
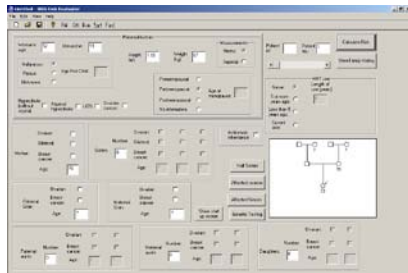
- Risk ≥ 1 in 6
- Mammography annually 40-49

NHS Breast Screening Programme



All women offered screening in NHSBSP

PRediction Of Cancer At Screening (PROCAS)



Offer interventions

Counseling in first 40,000 women

- Standard risk counseling offered to 8%+ group
- N=575 (1.4%)
- 391 (68%) accepted (visit or telephone)
- 93% attended for subsequent screen
- 73% wished to have information about chemoprevention

Comment – prevention

- Risk estimation ‘allows’ prevention
- Can offer tamoxifen & raloxifene (?AIs)
- Weight control, exercise & moderate alcohol for all!!

Summary

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Acknowledgements

Genesis Centre UHSM

- u Prof Anthony Howell
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