The Importance of Prevention and Early Detection

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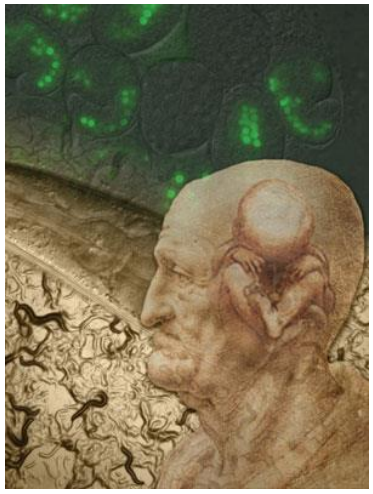
MANCHESTER 1824

NHS Manchester University NHS Foundation Trust

breast cancer now

prevent breast cancer

"Prevention is better than healing because it saves the labour of being sick"



Thomas Adams

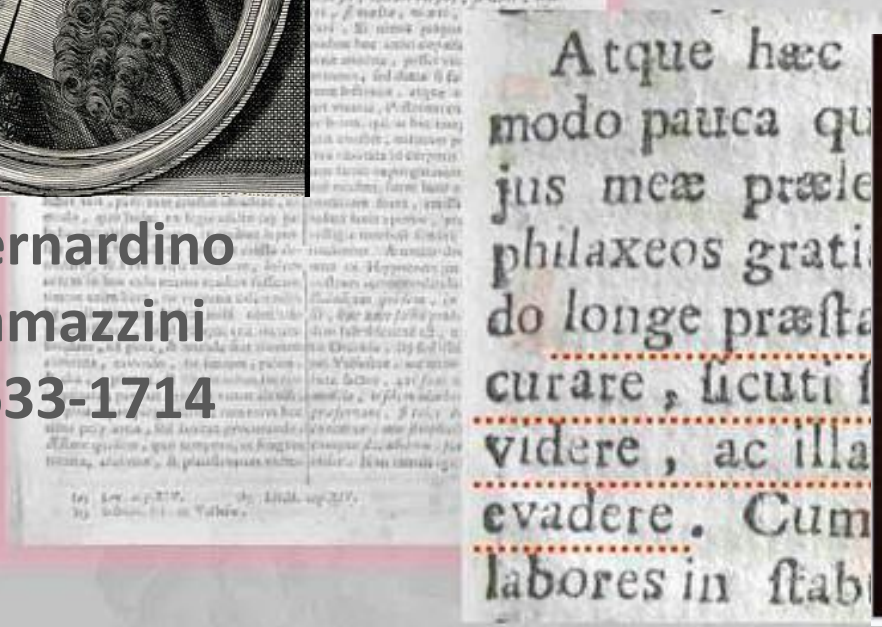
17th Century physician

"An ounce of prevention is worth a pound of cure"

Bernardino Ramazzini 1633-1714

'This marvelous sympathy of the breasts and uterus, those two sources of desire'

Described the high frequency of breast cancer in nuns


Atque hæc
modo pauca qu
jus meæ præle
philaxeos grati
do longe præſta
curare, ſicuti
videre, ac illa
evadere. Cum
labores in ſtab


DE
MORBIS
ARTIFICUM
BERNARDINI RAMAZZINI
IN PATAVINO GYMNASIO
DIATRIBA
MUTINÆ OLIM EDITA.
AC DISSERTATIO
DE
SACRARUM VIRGINUM
VALETUDINE TUENDA.
PATAVII · M.DCC.XIII.

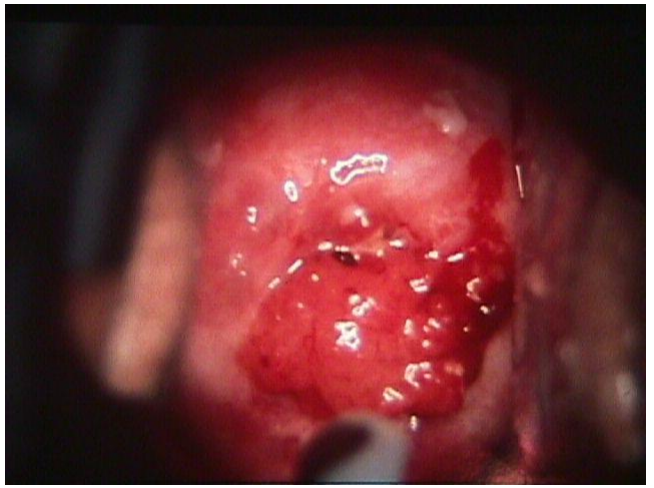
"…it is much better to prevent than to cure, and so much easier to foresee future harm and avoid it rather than have to get rid of it after having fallen prey" (XIII Oratio, 1711)

Prevention Early detection paradigms

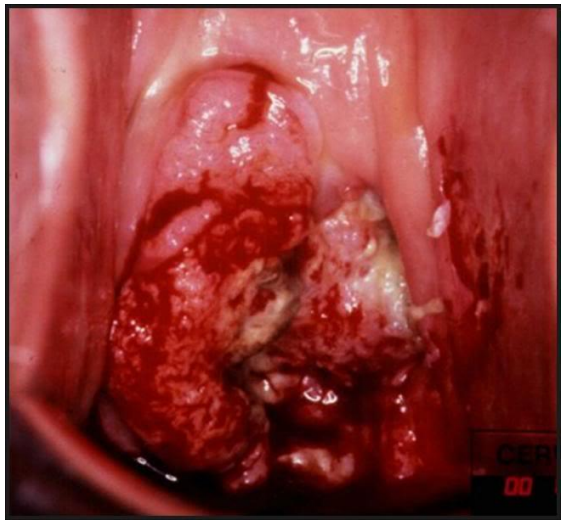
- Cervical Cancer
- Screening, HPV vaccination
- Breast cancer
- Screening, Chemoprevention

Introduction (CC slides courtesy Emma Crosbie)

- Cervical cancer is the second leading cause of cancer-related death among women worldwide



- Cervical cancer is caused by persistent high risk human papillomavirus infection



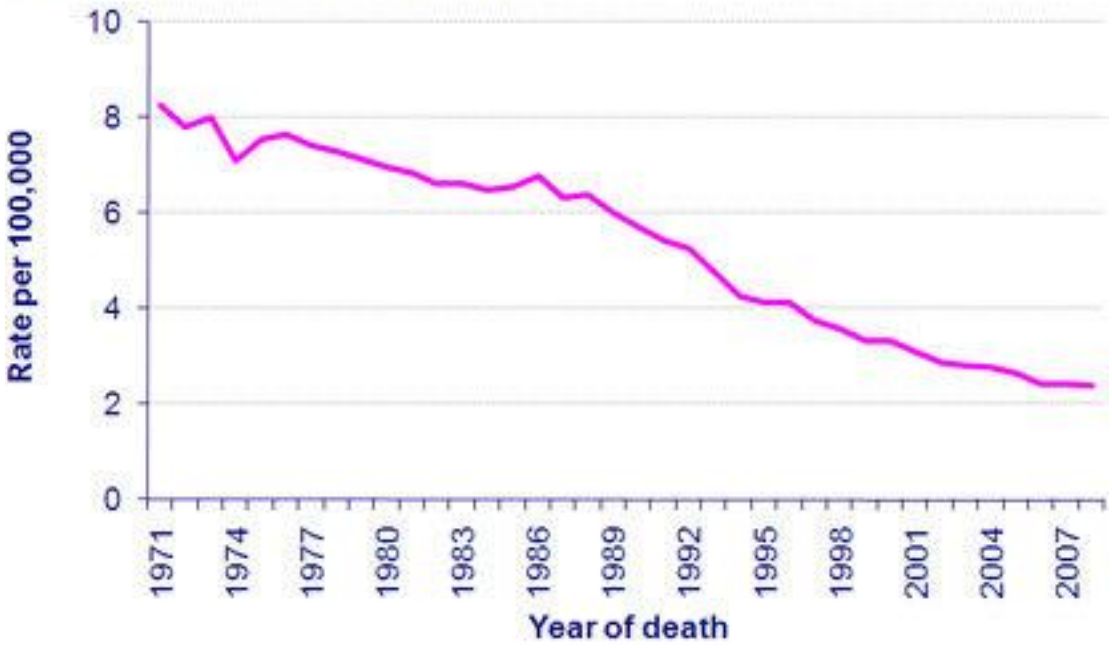
Global burden of cervical cancer

CRUK Cancer Stats

- There were 275,000 deaths from cervical cancer worldwide in 2008
- 8% of all female cancer deaths
- 88% of these occurred in developing countries
- Death rates vary 15-fold across the world:
  - 2 per 100,000 in North America/ Western Europe
  - 25 per 100,000 in Eastern Africa (in 2008)

Cervical screening is effective at reducing deaths from cervical cancer

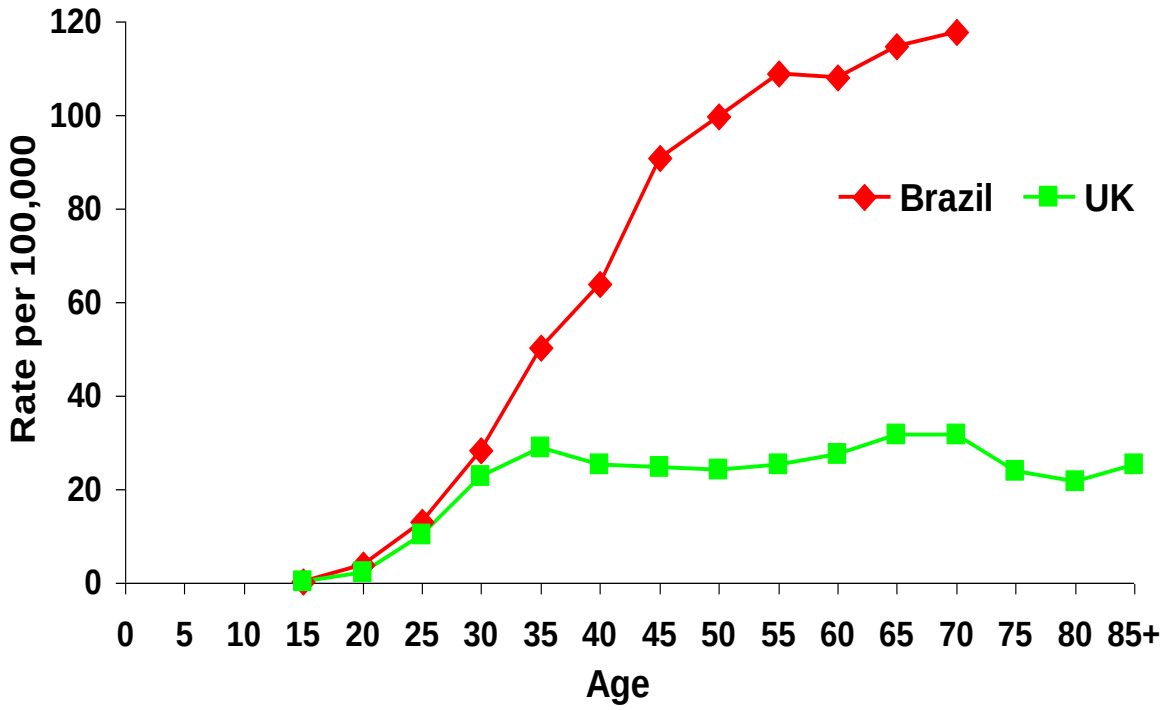
Figure 2.2: Age standardised (European) mortality rates, cervical cancer, UK, 1971-2008



- Age-standardised incidence has dropped by 44% in 30 years
- Cancer mortality rates are 70% lower

CRUK Cancer Stats

Age-specific incidence of cervical cancer in screened (UK) and unscreened (Brazil) women



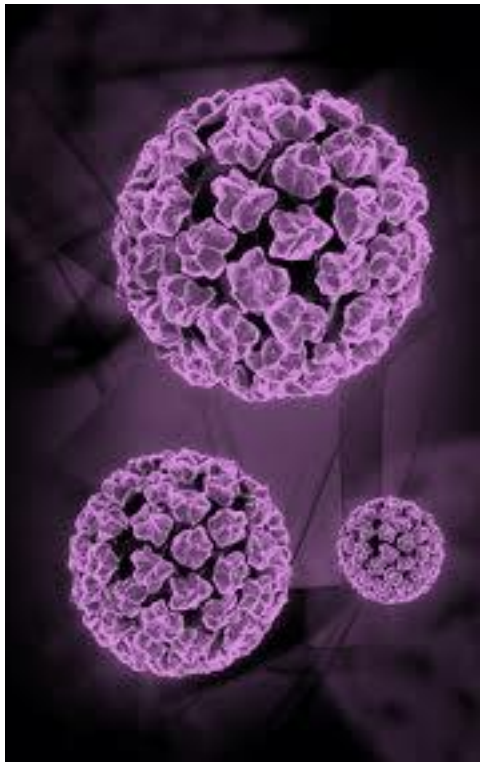
The success of cervical screening

- It has been estimated that:
  - 1/65 UK women born since 1950 would have contracted cervical cancer in their lifetime
  - This would equate to approx 6000 deaths per year
  - As a result of screening 80% of these have been prevented
  - This equates to 5000 lives per year being saved

Peto et al Lancet 2005

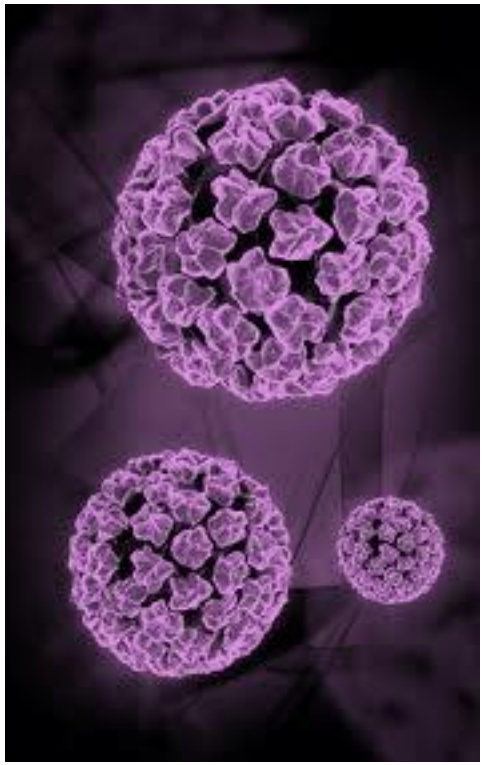
Primary screening with HPV

- Compared to cervical cytology, HPV testing is:
  - 25% more sensitive
  - 6% less specific at detecting borderline smears (or worse)
- Detects more than 90% CIN 2+
- ***Excellent negative predictive value over two rounds of screening***
- Automated to aid throughput & reduce costs
- Primary screening has been tested in 6 'sentinel sites' across the UK and is now being rolled out to whole population

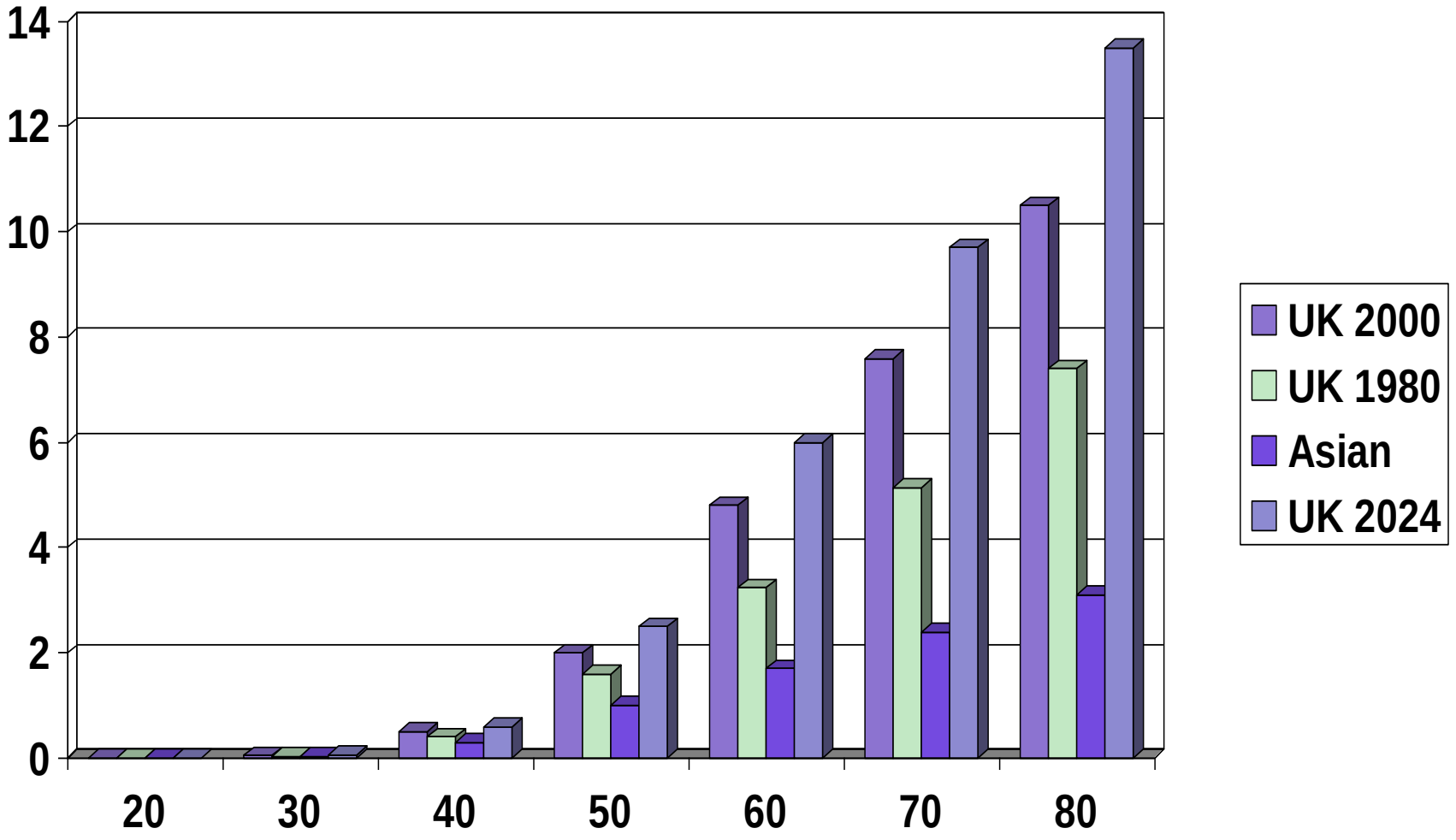


Primary prevention with HPV Vaccination

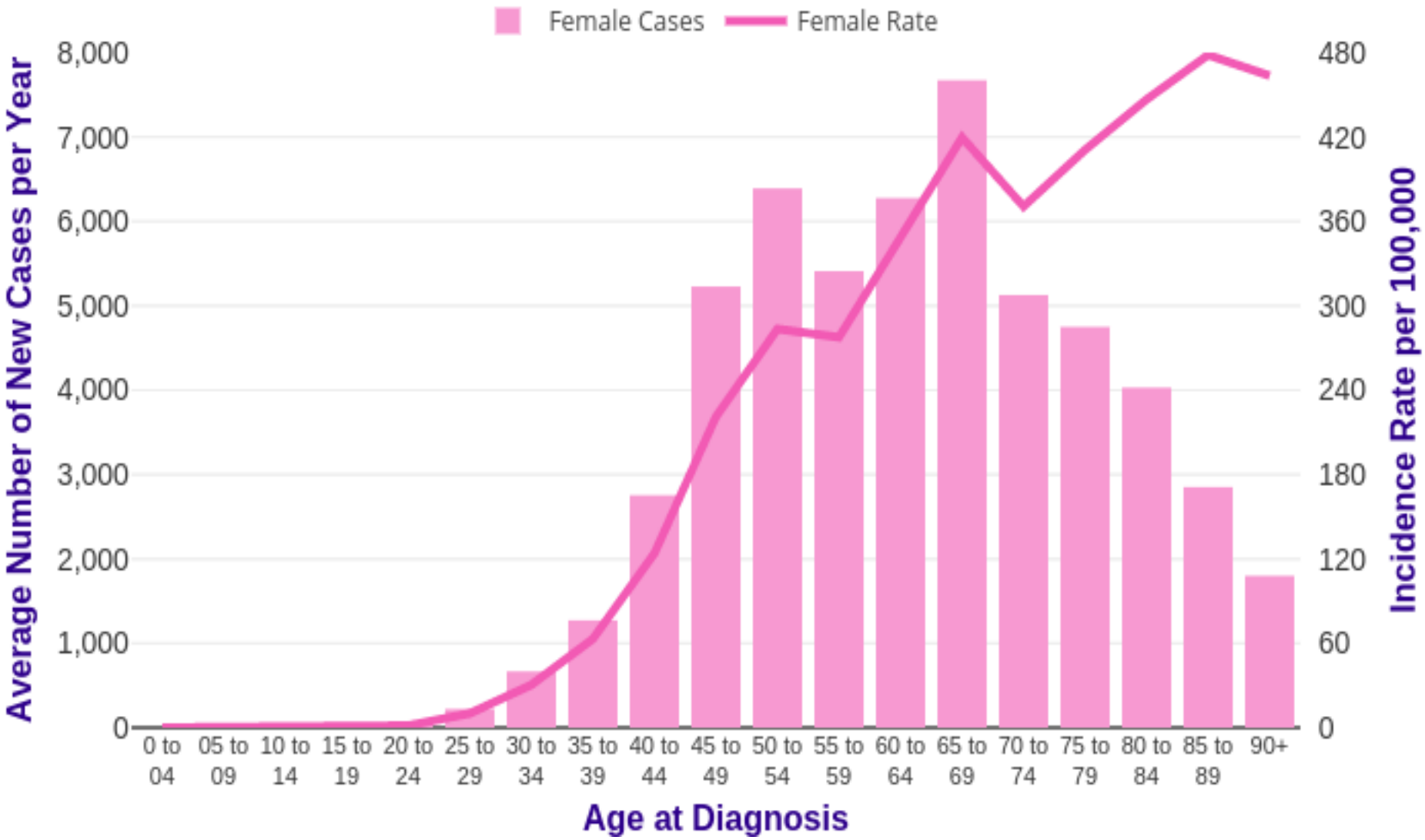
- Introduced in 2008
- ***Excellent coverage and efficacy***
- More than ten million doses of HPV vaccine have been given to young women in this country
- Over 80% of women aged 15-24 have received the vaccine
- Will potentially prevent 99% of cervical cancer due to HPV



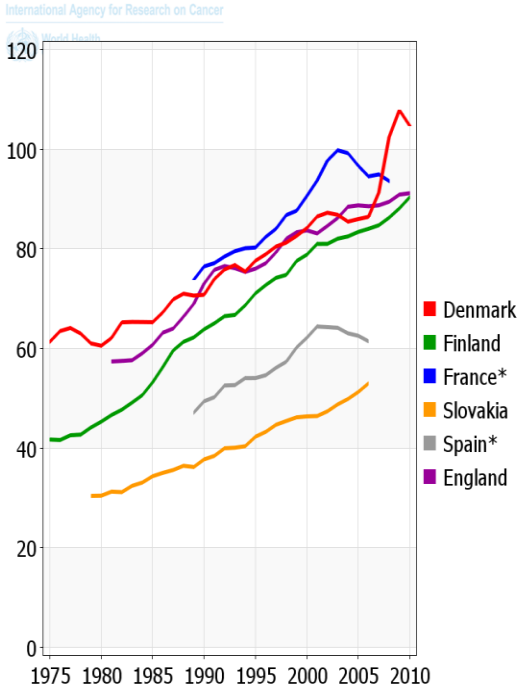
Breast cancer cumulative risk UK population and Asia

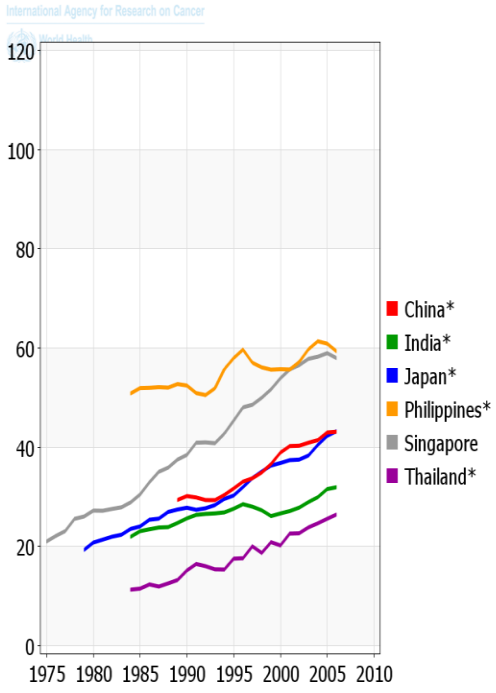


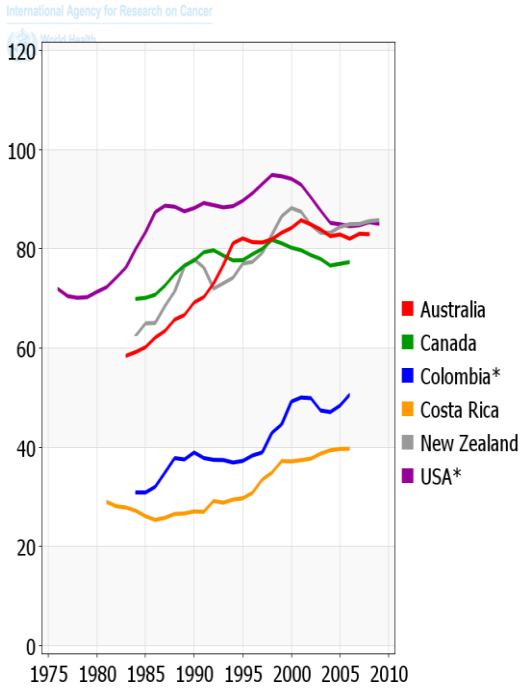
Breast cancer age specific risk



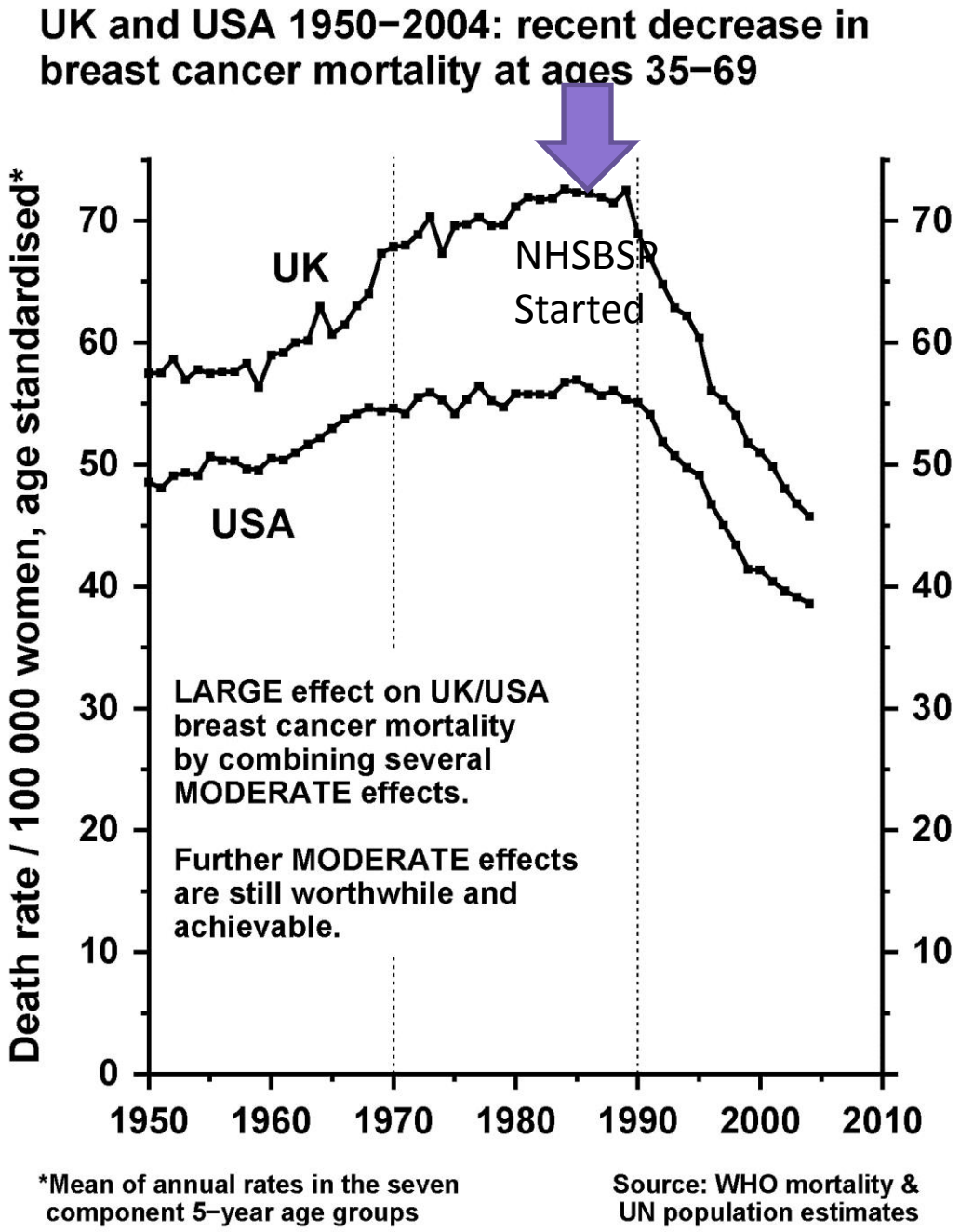
Breast cancer is increasing worldwide







http://globocan.iarc.fr



Why?

- Screening
- Treatment

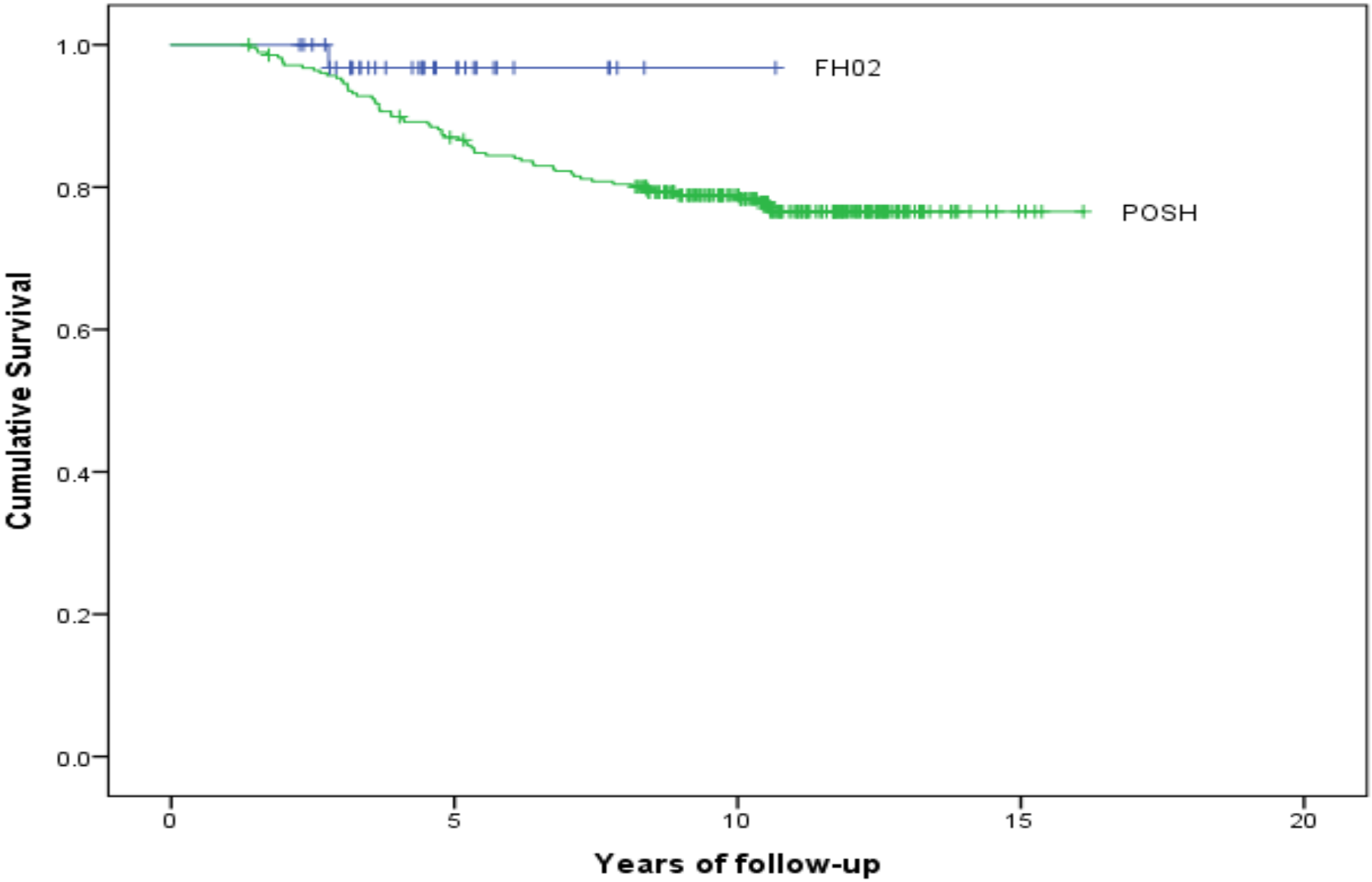
FH02 prospective compared to previous studies

Age at Diagnosis	POSH FHpos Unscreened 35-40 (%)	FH01 40-49 Prospective (%)	retrospective FH02 35-39+ (%)	Prospective FH02 35-40 (%)
N	293	136	47	50
Years of diagnosis	2000-2008	2003-2010	1990-2008	2007-2016
Years follow up	1-12 years	0-7 years	1-12 years	0-9 years
Histology				
Invasive (%)	293 (100%)	96 (74)	35 (74)	35 (70)
Grade 1 (% of invasive)	18 (6)	17 (19)	3 (8.6)	6 (17)
Grade 3 (% of invasive)	177 (60.5)	40 (45)	17 (48.6)	21 (60)
In-situ (%)	0 not included in POSH	34 (26)	12 (26)	15 (30)
Unknown		6	-	0
P value compared to prospective FH02	N/a as POSH only invasive			
Size (in situ excluded)	N=293	N=87	N=35	N=35
≤2cm	138 (47)	61/87 (70)	25 (74)	28 (80)
2-4.9cm	122 (41.5)		8 (23)	6 (18)
≥5cm	23 (8)		1 (3)	1 (3)
Unknown	10	9	1	0
P value for ≤2cm compared to prospective POSH				P<0.0001

FH02 prospective compared to previous studies

Age at Diagnosis	POSH FHpos Unscreened 35-40 (%)	FH01 40-49 Prospective (%)	retrospective FH02 35-39+ (%)	Prospective FH02 35-40 (%)
Node Involvement (in situ excluded)	N=293	N=82	N=35	N=35
0	133 (45)	56 (68)	25 (77)	28 (80)
1-4	110 (38)		7 (23)	5 (15)
>4	48 (16)		-	2 (6)
Not sampled/[not known]	3 (1)	[14]	3	0
P value for LN0 compared to POSH Stage 1 of invasive	83 (28%)	-	21 (60)	P=0.0002 24 (68.5%)
P value POSH ref				P<0.0001
Status	N=289		N=47	N=49*
Alive (no metastasis)	204 (70)	NK	43 (91)	49 (98)
Alive (with metastasis)	23 (8)		0 (0)	0
Died (of disease)	63 (21.5)		4 (9)	1 (2)
Died (other)	10 (3.5)		0	0
P value compared to POSH				P=0.0009
Annual Incidence Rate/ 1000			4.77	3.7

Survival in FH02



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Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer

Clinical guideline [CG164] Published date: June 2013 Last updated: March 2017 Register as a stakeholder

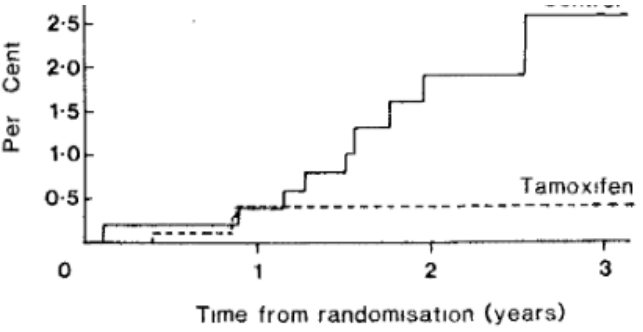
- Update on chemoprevention stimulated by 2 yearly review process (2015)
- Literature search by NICE didn't identify additional data
- Topic experts identified
  - IBIS-1 long term tamoxifen vs placebo
  - IBIS-2 anastrozole vs placebo

Recruitment periods and trial numbers

Lancet. 1985 Aug 3;2(8449):282.

Tamoxifen and contralateral breast cancer.

Cuzick J, Baum M.



MAP1 4,560

IBIS II 3,864

AIs Post

STAR 19,747

RUTH 10,101

Raloxifene Post

MORE 7,705 CORE 3,510

IBIS I 7,140

Italian 5,408

NSABP P1 13,388

Royal Marsden 2,471

Tamoxifen Pre & Post

1985 1990 1995 2000 2005 2010 2015

Recruitment period

NICE 2004

NICE 2013

NICE 2017

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

NICE guidelines [CG164] Published date: June 2013

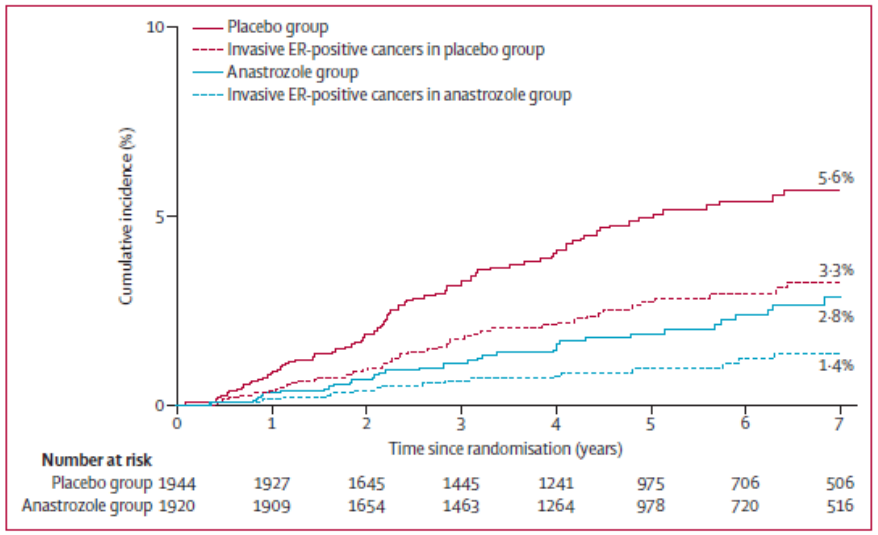
RISK	premenopausal	postmenopausal	
		Uterus	No uterus
High (>8% 10 yr) 30%+	Offer TAM*	Offer TAM* or RAL	Offer TAM*
Moderate (3%+, 5-8%) 17-29%	Consider TAM*	Consider TAM* or RAL	Consider TAM*
Low	Do not consider	Do not consider	

* unless they have a past history or may be at increased risk of thromboembolic disease or endometrial cancer.

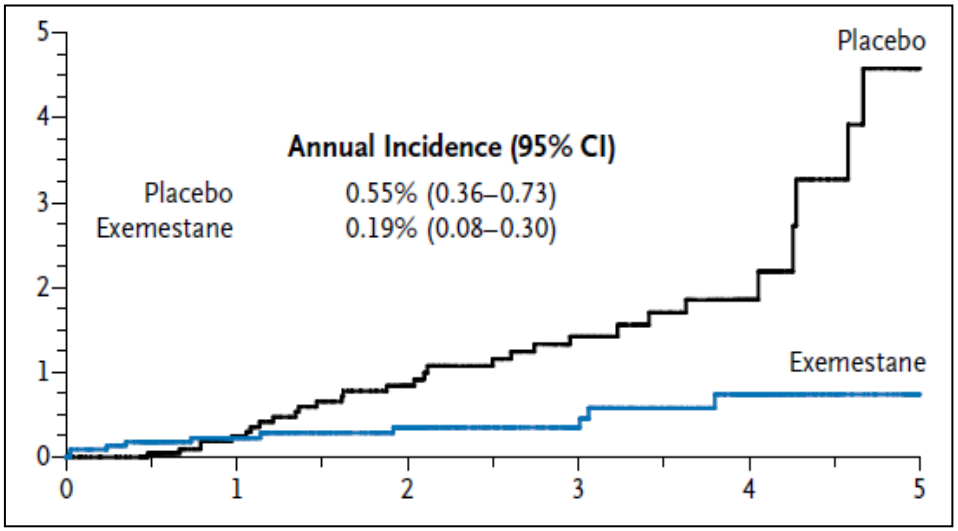
The update question for NICE

What is the effectiveness of chemoprevention for the reduction of the incidence of breast cancer in women with a family history of breast, ovarian or related (prostate/pancreatic) cancer? (More than 70% with FH)

IBIS II



MAP3



MAP3 study of exemestane (steroidal AI) vs placebo

Did not define the proportion of women at risk due to FH –not considered

Cuzick J…Howell A Lancet. 2014 Mar 22;383(9922):1041-8

Goss P et al N Eng J Med 2011 Jun 23;364(25):2381-9

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

NICE guidelines [CG164] Published date: June 2013

Updated 2017

RISK	premenopausal	postmenopausal	
		Uterus	No uterus
High (>8% 10 yr) 30%+	Offer TAM*	Offer Anastrozole or Tam* or RAL	Offer Anastrozole or TAM*
Moderate (3%+, 5-8%) 17-29%	Consider TAM*	Consider Anastrozole or TAM* or RAL	Consider Anastrozole or TAM*
Low	Do not consider	Do not consider	

* unless they have a past history or may be at increased risk of thromboembolic disease or endometrial cancer.

Anastrozole found by NICE HE analysis to be COST SAVING to NHS

University Hospital of South Manchester NHS Foundation Trust

Making Choices

For women at **high risk** deciding on whether to take **tamoxifen** for prevention of breast cancer

genesis preventing breast cancer

UHSM Your Hospital

University Hospital of South Manchester NHS Foundation Trust

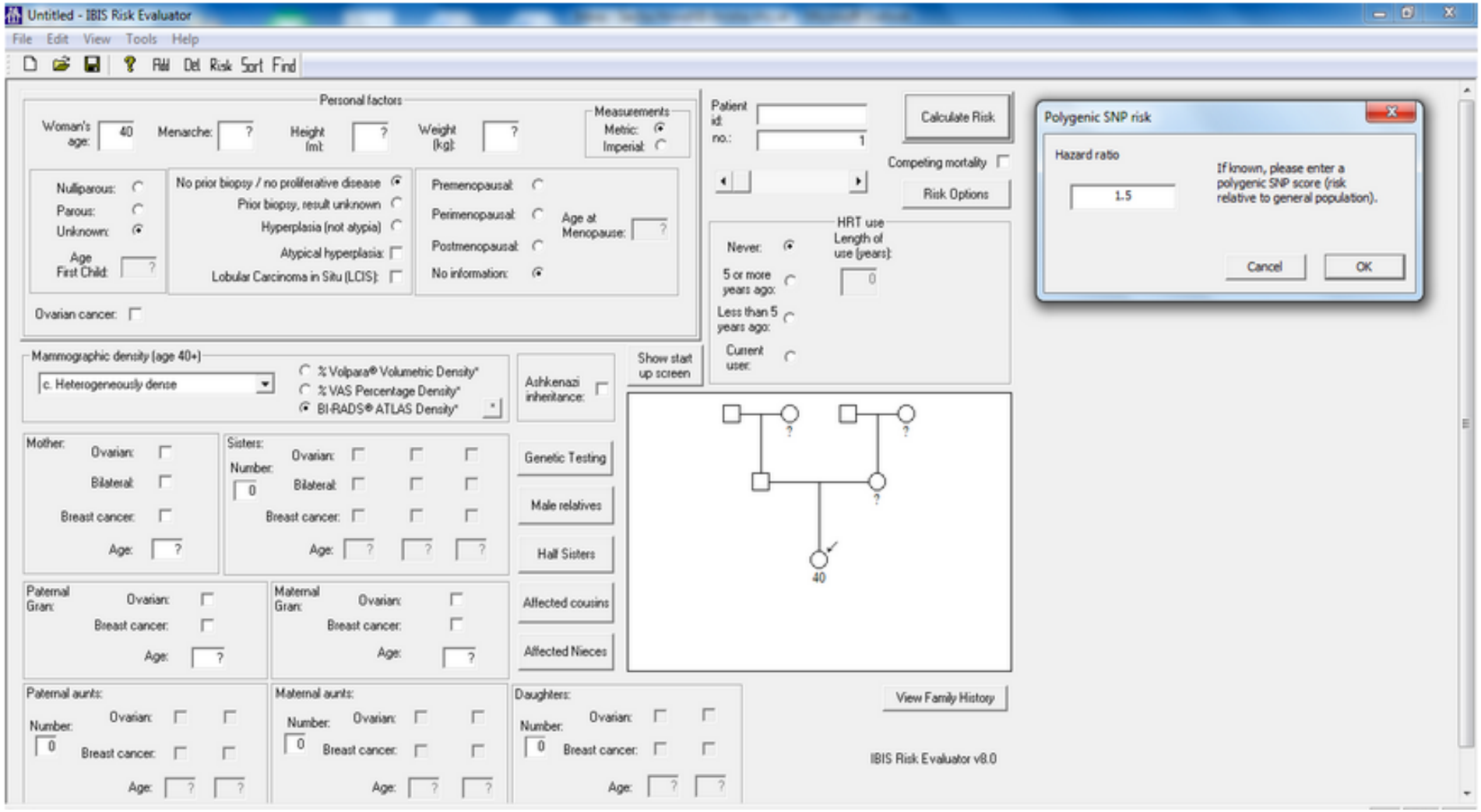
Making Choices

For women at **moderate risk** deciding whether to take **raloxifene** for prevention of breast cancer

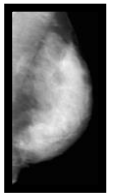
genesis preventing breast cancer

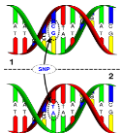
UHSM Your Hospital

Tyrer-Cuzick v8

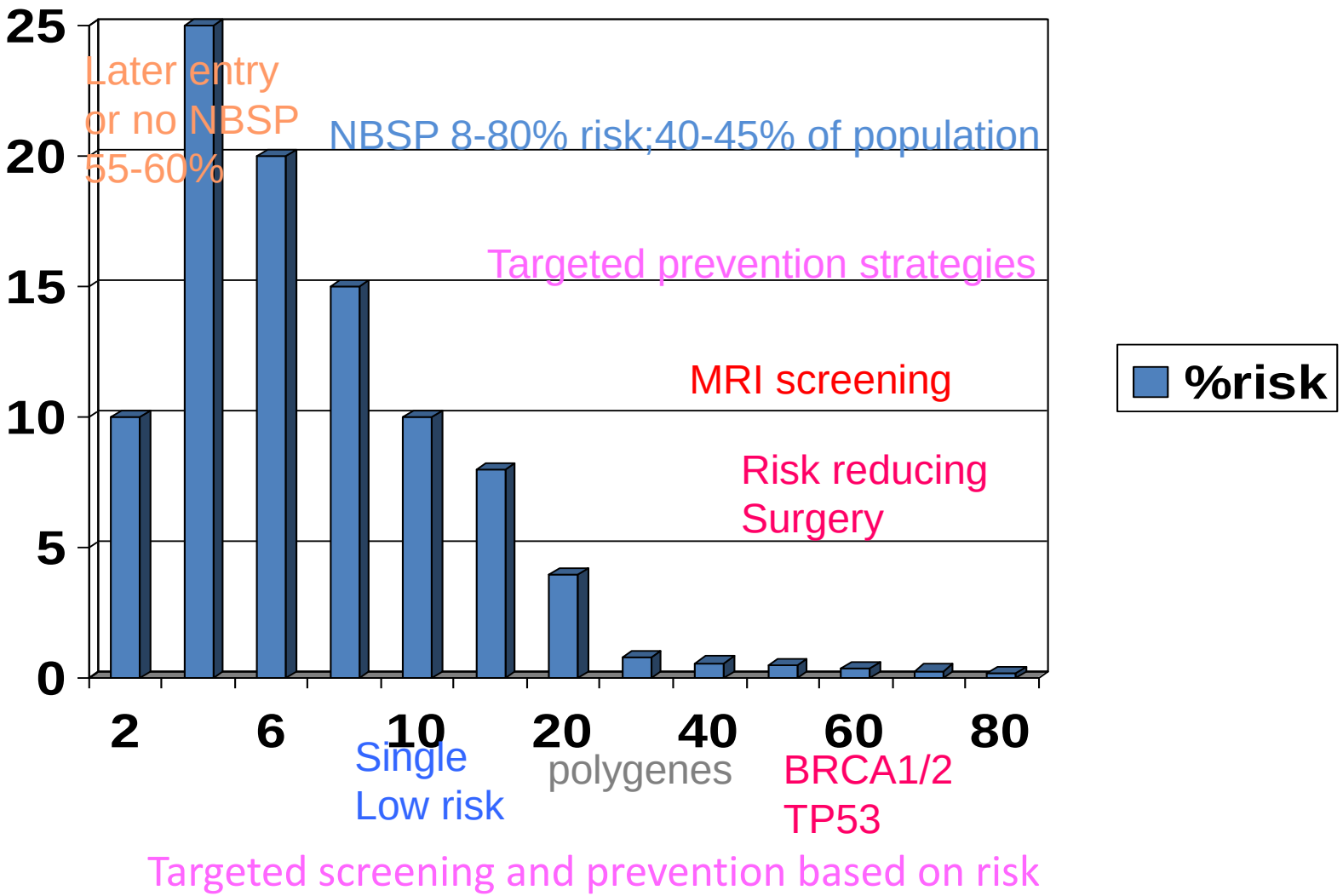


Risk in the screening population





Breast cancer risk in general population



Risk Reducing mastectomy

Manchester experience (update 2018)

- **621 operations**
- **Age range 21-60 yrs**
- **92 carried out on contralateral breast**
- **34 simple bilateral mastectomy/modified**
- **242 operations on known *BRCA1/2* mutation carriers**
- **Manchester: 6474 yrs fu: 75.3 cancers expected 4 occurred OR 0.053**
- **16/621 (2.5%) occult tumours identified**
- **One 3mm cancer nipple sparing surgery (BRCA2)10 years post RRM**
- **One Chest wall 23 mm LN) 6.5 yrs post BRRM BRCA1**
- **One IDC TNT 15mm in BRCA1 carrier 5 years post RRM**
- **One IDC 45mm TNT in BRCA1 carrier 7 years post RRM**

Summary

- Huge role for Screening and Prevention in cancer
- Cervical cancer revolutionised
- Huge potential benefits in Breast Cancer
- Many other areas of potential benefit

  Lung, Colorectal, Endometrial etc etc

Acknowledgments

MANCHESTER 1824

The University of Manchester

Programme to predict risk in the NHSBSP and in the Family History Clinic population (PROCAS)

Paula Stavrinos, Sarah Sampson, Jill Fox, Lynne Fox, Donna Watterson, Helen Ruane, Jake Southworth, Ellie Tinning, Bill Newman, Helen Byers, Elaine Harkness, Iain Buchan, Wendy Watson, Fiona Harrison, Katherine Payne, Michelle Harvie, Mary Wilson, Sue Astley, Alan Hufton, Tony Howell, Gareth Evans.

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Asian Breast Cancer Support Group

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Breast Research Nurses and team

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Risk reducing surgery service

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Family History Clinic service

Rosemary Greenhalgh, Julia Wiseman, Jayne Beesley, Helen Morgan, Liz Lee, Lorraine Roberts, Tara Clancy, Fiona Lalloo, Tina Henderson, Gareth Evans, Tony Howell.

Cervical cancer

Emma Crosbie

Cancer PED

Emma Thorpe

The Christie NHS
NHS Foundation Trust

breast cancer now

NHS
National Institute for Health Research

prevent breast cancer

NHS
Manchester University
NHS Foundation Trust