Screening for Chronic Disease

Prof. A. Miller

Non-communicable diseases (NCD)

Comprise:

- Cardiovascular diseases
- Cerebrovascular diseases
- Cancer
- Chronic respiratory diseases
- Diabetes

Non-communicable diseases (NCD)

Are responsible for:

- 60% of global mortality
- 43% of disease burden in the world
- The adverse health impact of Chronic diseases is increasing in the world

Non-communicable diseases (NCD)

Share common causes:

- Tobacco abuse
- Over-nutrition (high calorie diets)
- Obesity
- Lack of physical activity

Goals of a NCD Control Programme

- Prevent future NCD cases
- Diagnose NCD cases early
- Provide therapy
- Ensure freedom from suffering
- Reach all members of the population (equity)

Secondary prevention: Early diagnosis of NCDs

- Public education
- Professional education
- Self-awareness
- Professional examination
- Facilities for diagnosis
- Facilities for treatment

Secondary prevention: Screening in NCD Control

Principles:

- Use only effective strategies
- Educate professionals and public
- Base on Natural History of disease
- Screen at right ages and frequency
- Maintain high quality
- Ensure adequate facilities available
- Organisation

Efficacy of screening confirmed for cancer

Site	Reduction in mortality*
• Breast (age 50-69)	30%
• Cervix	90%
• Colon	30%

* *Providing adequate compliance achieved at the population level*

Efficacy of screening for other NCDs

Cardiovascular disease and stroke

- Hypertension
- Hypercholesterolaemia

Diabetes

- Testing for impaired glucose tolerance in the Obese
- (Testing for fundal abnormalities in known diabetics is tertiary prevention)

Disadvantages of screening for NCDs

- Requires different focus for each NCD
- Can not reduce disease incidence unless you can screen for a precursor
- Requires many (different) health care facilities and personnel
- Is only effective if there is effective treatment
- Requires organisation and continuing programme
- Is an expensive use of health care resources

Breast screening

IARC Working Group, 2002

There is *sufficient evidence* for the efficacy of screening women aged 50–69 years by mammography as the sole screening modality in reducing mortality from breast cancer.

There is *limited evidence* for the efficacy of screening women aged 40–49 years by mammography as the sole screening modality in reducing mortality from breast cancer.

IARC Working Group, 2002

Women aged 50–69:

- Mammography alone 0.75 (0.67, 0.85)

Women aged 40–49:

- Mammography alone 0.81 (0.65, 1.01)
- All valid trials 0.88 (0.74, 1.04)

Are there alternatives to mammography screening?

- Good therapy is complementary and essential. It may substitute for screening in many cases
- Possibly clinical breast examination (CBE) and BSE

IARC Working Group, 2002

There is *inadequate evidence* for the efficacy of screening women by clinical breast examination in reducing mortality from breast cancer.

There is *inadequate evidence* for the efficacy of screening women by breast self-examination in reducing mortality from breast cancer.

Canadian National Breast Screening Study (CNBSS)-2

- 39,405 volunteers age 50-59 randomized with informed consent to:
  - Annual two-view mammography + physical examination (CBE) + BSE (MP)
  - Annual physical examination (CBE) + BSE only (PO)
- 5 or 4 screens and 11-16 years follow-up

Occurrence of Invasive Breast Cancers in CNBSS-2

	MP	PO
Screen detected	267	148
Interval cancers	50	88
Incident cancers	305	374
Total	622	610
[Total in situ	*71*	*16]*

Characteristics of screen-detected invasive breast cancers in CNBSS-2

	MP		PO
Detected by:	Ma alone	CBE*	CBE
Number	126	141	148
Node positive	20%	33%	36%
15mm or more	38%	67%	72%

* *with or without mammography*

CNBSS-2 Deaths from breast cancer, 11-16 years follow-up

	MP	PO	
Women years (10^3)	216	216	
Breast cancer deaths	107	105	
Rate/10,000	4.95	4.86	
Rate ratio (95% CI)	1.02	(0.78, 1.33)	

Women with breast cancer age 50-59
Survival during 13 years follow-up

Trial and group	N	Alive	(%)
Swedish Two county (Late 1970s)			
ASP	349	290	(83)
PSP	290	221	(75)
CNBSS-2 (1980s)			
MP	622	515	(83)
PO	610	505	(83)

Conclusion on CNBSS-2

- The benefit from screening derives from the earlier detection of palpable breast cancers, coupled with good therapy, not from the early detection of impalpable cancers.
- This is accomplished both by good CBE + BSE and by mammography

Canadian National Breast Screening Study (CNBSS)-1

- 50,430 volunteers age 40-49 randomized with informed consent to:
  - Annual two-view mammography + CBE + BSE (MP)
  - Initial CBE + BSE only (UC)
- 5 or 4 screens and 11-16 years follow-up

Occurrence of Invasive Breast Cancers in CNBSS-1

	MP	UC
Screen detected	208	148
(Ma alone)	69	0
Interval cancers	47	24
Incident cancers	327	380
Total	592	552
[Total in situ	*71*	*29]*

CNBSS-1, Breast cancer mortality (11-16 year follow up)

	MP	UC
Women years (10^3)	282	282
Breast cancer deaths	105	108
Rate/10,000	3.72	3.82
Rate ratio (95% CI):	0.97 (0.74-1.27)	
Adjusted for mammograms outside CNBSS:	1.06 (0.80-1.40)	

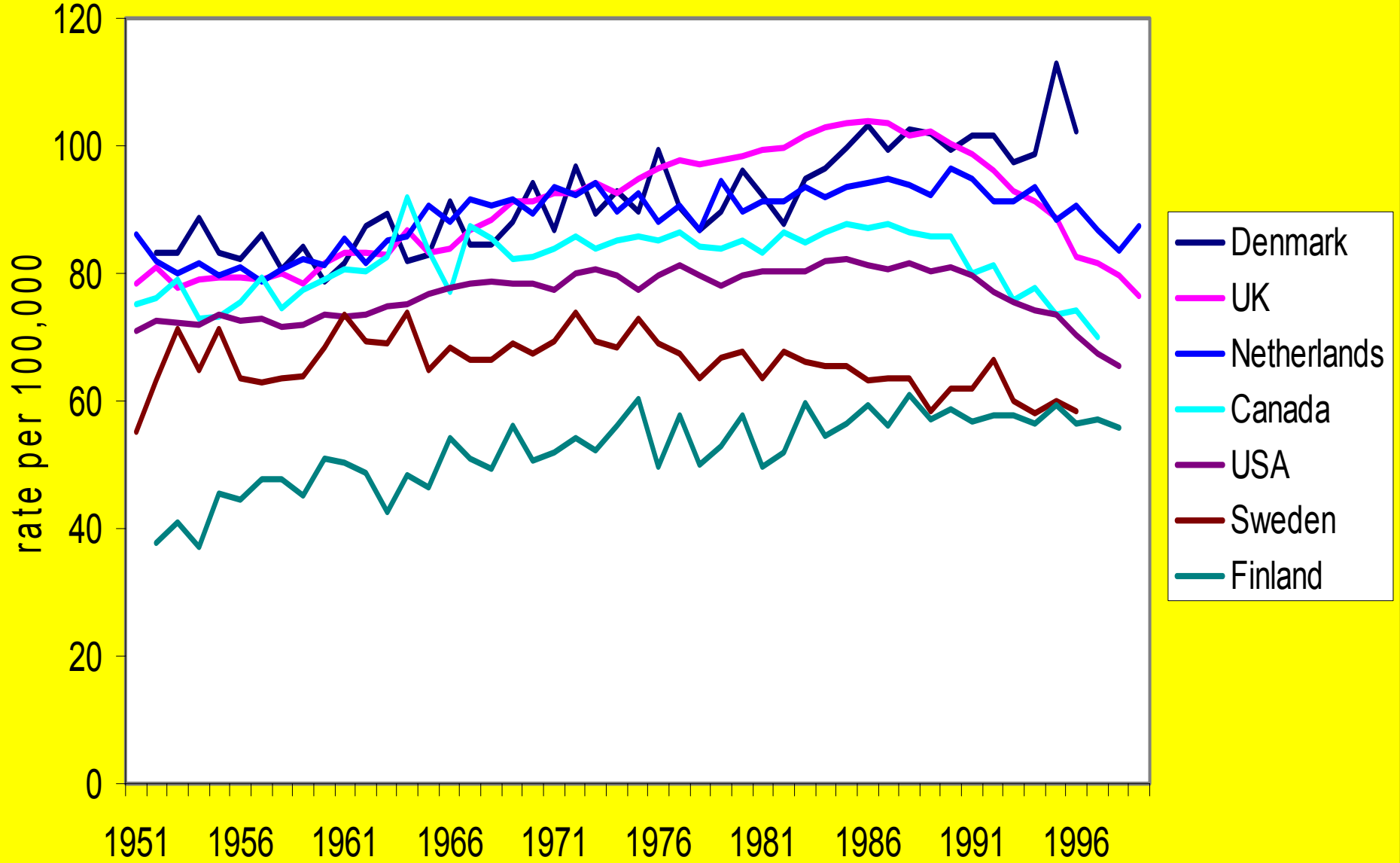
Conclusion on CNBSS-1

In a country where adjuvant therapy is available, and women are usually diagnosed with small cancers, it is not possible to demonstrate a benefit from annual mammography and CBE screening in women age 40-49 compared to good usual breast care

Effect of BSE within the CNBSS (Harvey et al, 1997)

Yr 2 BSE Score	Age	OR	(95% CI)
1-4		1.00	
5-8:	40-49	0.54	(0.27, 1.11)
	50-59	0.58	(0.35, 0.95)

Trends in mortality from breast cancer, women age 50-74



Effect of NHS programme on reduction in breast cancer mortality, England & Wales (Blanks et al, 2000)

Effect of:	Estimate 1990-98
Screening	6.4% (range 5.4-11.8%)
Treatment	14.9% (range 12.2-14.9%)

IARC Working Group, 2002

Recommendations for research:

A randomized trial of clinical breast examination versus no screening should be conducted in a country or countries where resources are unlikely to permit implementation of mammography screening in the foreseeable future.

A randomized trial of clinical breast examination versus mammography should be conducted, in a country or countries where resources may permit some mammography screening but insufficient to cover the whole at risk population.

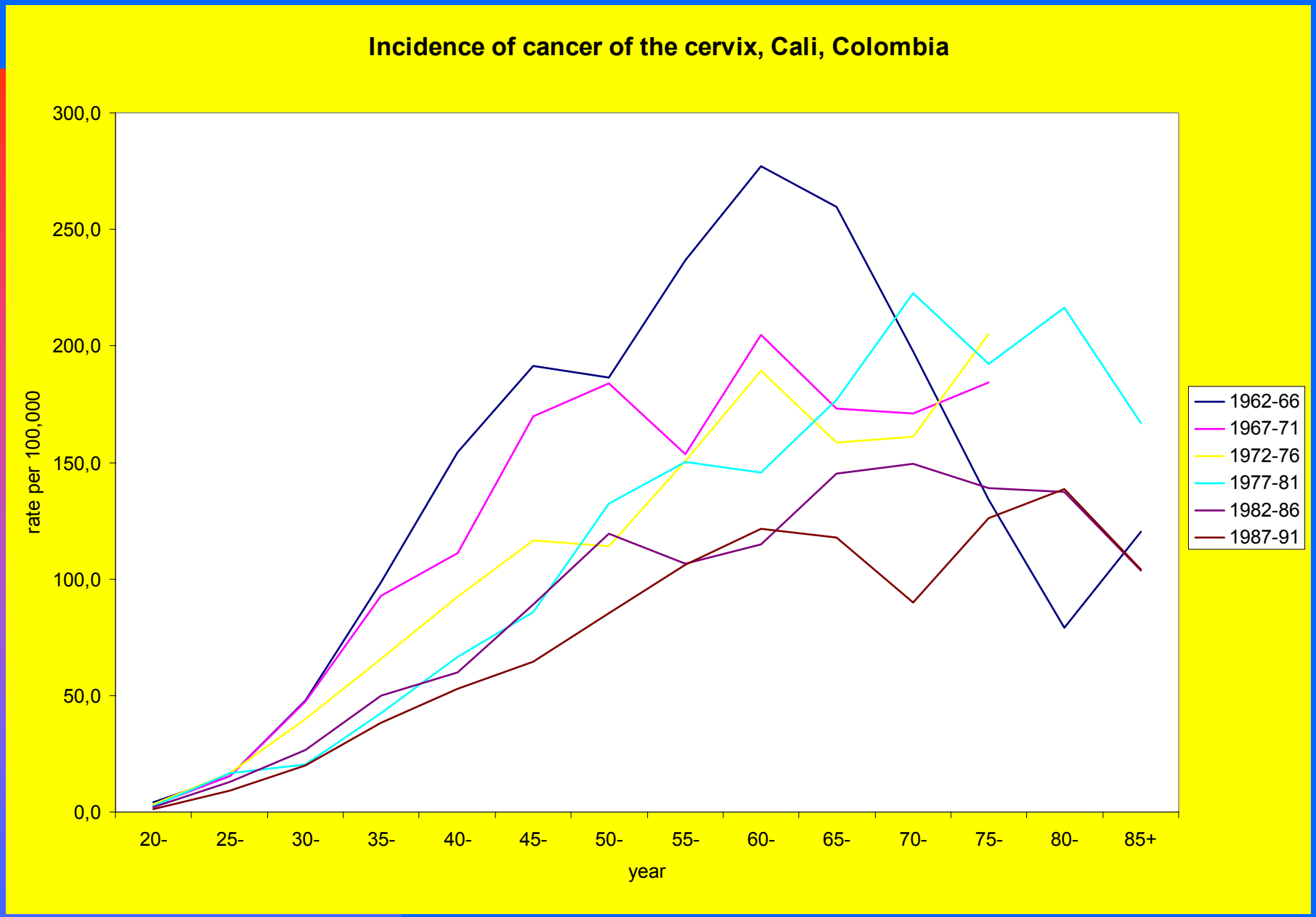
Research ongoing on CBE + BSE

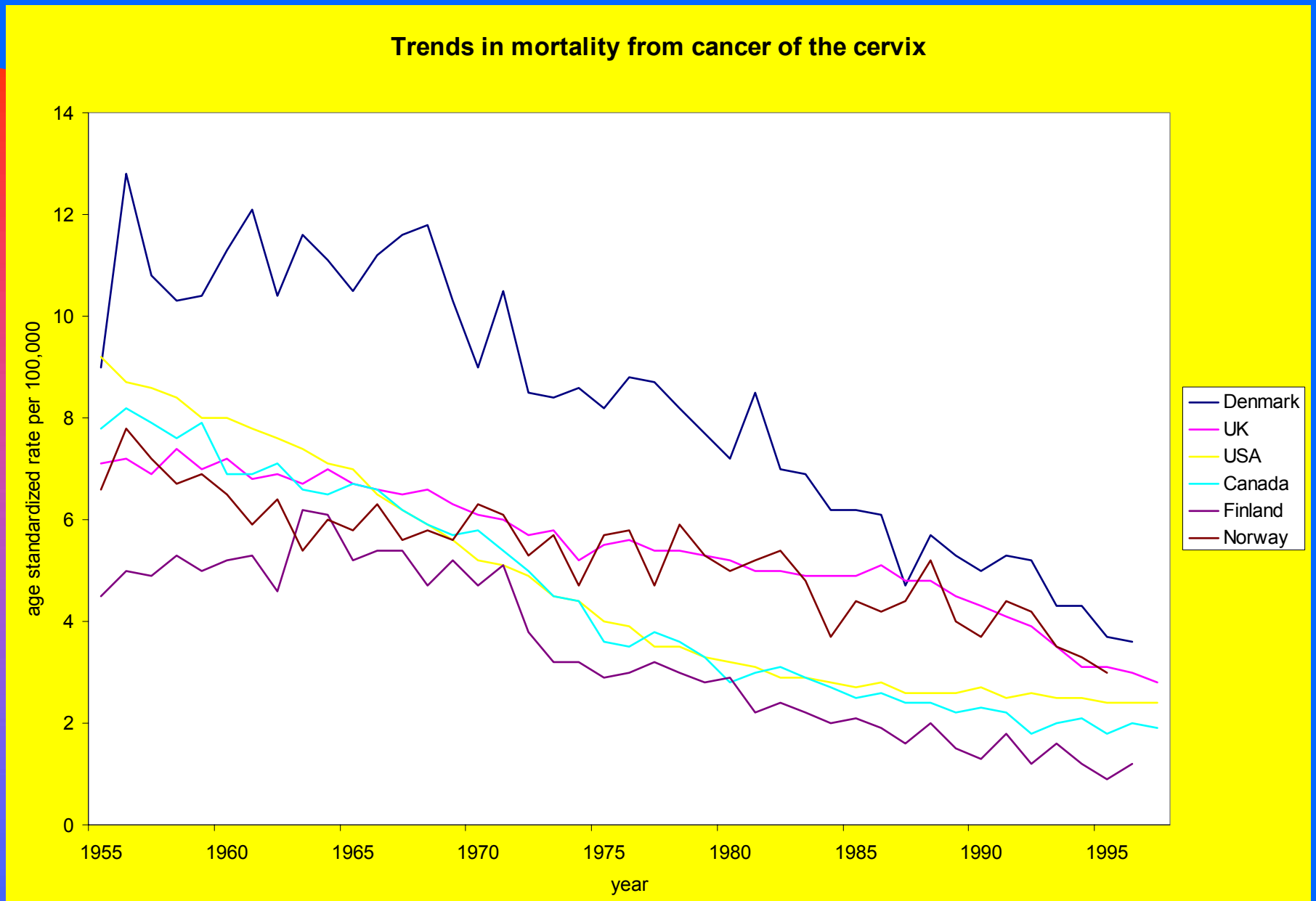
- The Russia/WHO trial of BSE
- Randomized trials in Mumbai and Cairo of CBE + BSE vs health education
- Studies of CBE + BSE are proposed in Iraq, Kuwait, Libya, Byelorussia
- Studies of CBE vs mammography proposed in South Africa and Colombia.
- There is an opportunity for other countries to contribute to this international endeavour.

Cervix cancer - the World problem

Cases		Deaths	
World:	470606	World:	233372
Developing countries:	379153	Developing countries:	194025

c.f Breast cancer		c.f Breast cancer	
World:	1050346	World:	372969
Developing countries:	471063	Developing countries:	183768


Incidence of cancer of the cervix, Cali, Colombia
300,0
250,0
200,0
150,0
100,0
50,0
0,0
rate per 100,000
20-
25-
30-
35-
40-
45-
50-
55-
60-
65-
70-
75-
80-
85+
year
1962-66
1967-71
1972-76
1977-81
1982-86
1987-91


Trends in mortality from cancer of the cervix
age standardized rate per 100,000
0
2
4
6
8
10
12
14
1955
1960
1965
1970
1975
1980
1985
1990
1995
year
Denmark
UK
USA
Canada
Finland
Norway

IARC study of effect of different screening policies*

Schedule	Cum. inc.	Reduction	No. of tests
None	1575		
20-64:			
Annual	105	93%	45
3 yrly	138	91%	15
5 yrly	258	84%	9
25-64:			
3 yrly	161	90%	13

* *Assumes 100% compliance, sensitivity 60-90%*

Duration of Preclinical Cancer (van Oortmarssen and Habbema, 1995)

Median duration from IARC study: 5-8 years

Median duration from model*: 15 years

* correcting for screen-detected cancers

Implication:

Screening every 5 (not 3) years will give 90% reduction in invasive cancer incidence and mortality, providing there is 100% compliance

Sensitivity of Pap tests

- Range in IARC study: 60-90%
- Range in Nanda et al, 2000: 6%-100% (median for HSIL/CIN II-III 58%)
- Blumenthal et al, 2001: 44.3% (women also received VIA and HPV tests)
- Boyes et al, 1982: 75% (population based programme)

IARC study - modified: 75% compliance, 75% sensitivity - high incidence country

Schedule	Cum. inc.	Reduction	No. of tests
None	5080		
25-64:			
3 yrly	1428	72%	13
5 yrly	1727	66%	8
35-64:			
5 yrly	1930	62%	6
10 yrly	2489	51%	3

IARC study - modified, 60% sensitivity, effects of different compliance levels - high incidence country

Schedule	Compliance	Reduction	No. of tests
35-64:			
3 yrly	40%	30%	6*
5 yrly	50%	34%	3*
10 yrly	80%	41%	2.4*
20-39:			
2 yrly	100%	39%	10

** averaged over the total population*

Failures of cervical screening

At the level of the woman:

- Failure to attend for screening at the recommended frequency
- Failure to attend for the recommended investigation and treatment

Failures of cervical screening

At the level of the primary care physician:

- Failure to use clinical contacts to take a smear
- Failure to take an adequate smear
- Failure to recommend further investigation and treatment of an abnormality

Failures of cervical screening

At the level of the laboratory:

- Inadequate fixation of the smear
- Inadequate staining of the smear
- Failure of the cytotechnologist to identify an abnormality on the smear
- Failure of the cytopathologist to classify the abnormality correctly

Failures of cervical screening

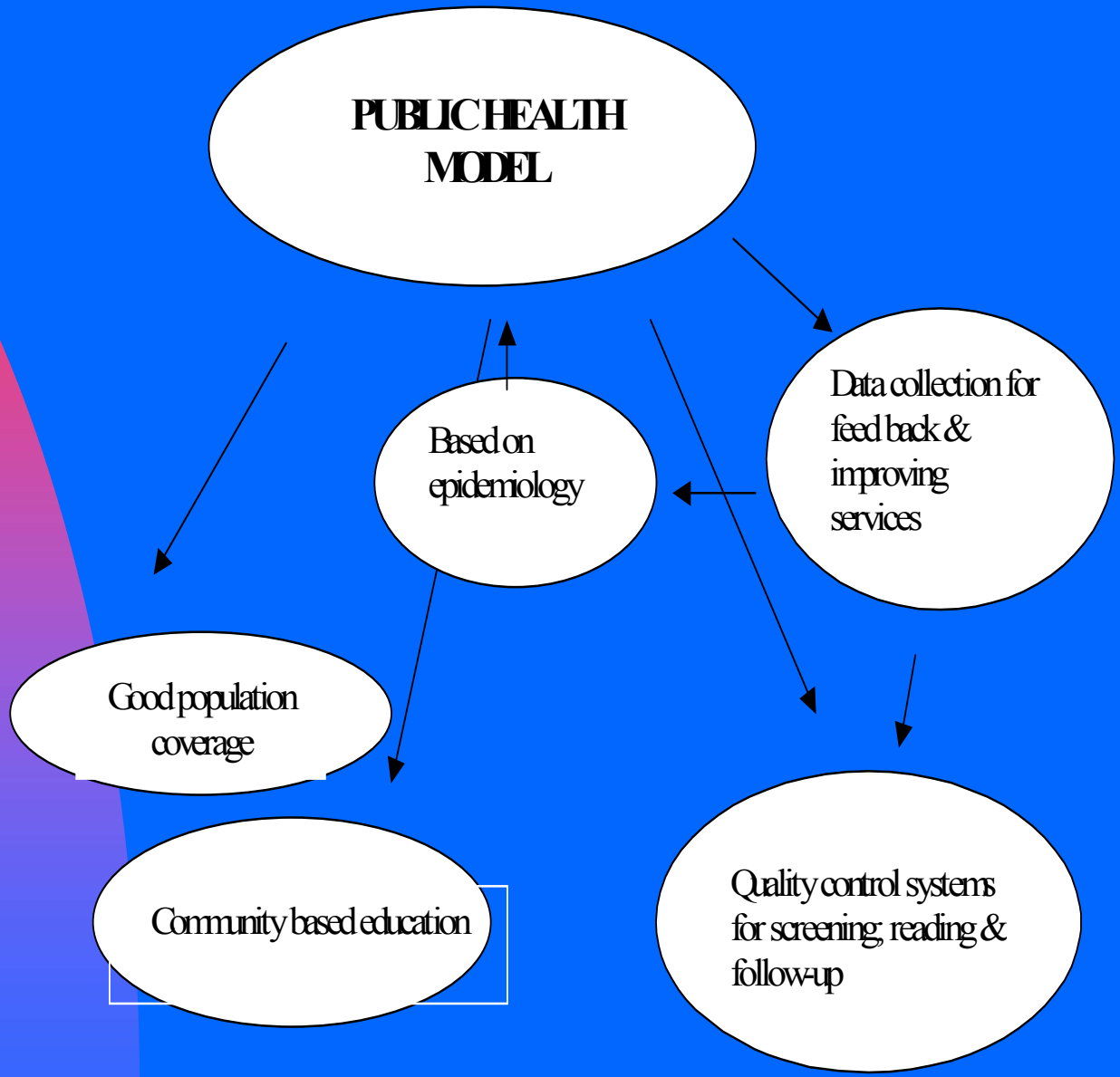
At the level of the gynaecologist:

- Failure to identify an abnormality during colposcopy
- Inadequate treatment of the abnormality
- Inadequate follow-up of the woman treated for an abnormality

Elements of an organised program

- The target population is identifiable
- Measures are available to guarantee high coverage and attendance
- There are adequate facilities for performing high quality screening tests
- There is an effective referral system for diagnosis and treatment of abnormalities
- There are adequate facilities for diagnosis and treatment

The Public Health model for cervical cancer screening



The WHO Steps

- Screen every woman once at age 45
- Once resources permit, expand to screen every woman at ages 35, 45 and 55
- When that has been achieved, expand to screen every 5 years from age of 35 to 59
- Only when the coverage is adequate for women age 35-59, extend screening to age 25 or more

Visual Inspection with Acetic Acid (VIA)

- Examiners can be trained to achieve as high sensitivity as cytology
- Laboratories are not required
- Specificity is lower than cytology
- If “See and treat” (cryotherapy) is safe, a major disadvantage of cytology is removed
- The long term benefits from VIA are unknown

HPV DNA testing

- Commercial test available, but expensive
- Sensitivity seems higher than cytology, but this may be spurious
- Specificity lower than cytology, especially in women under the age of 35
- Like cytology, test is unable to distinguish progressive disease
- Women HPV negative probably do not need to be re-screened for 6-10 years

Conclusions - Cervix cancer

- For full benefit, organisation must be introduced
- Cytology screening is still the established approach
- HPV testing shows promise, but further research required
- It is probable that many women are being overscreened and others underscreened

Colo-rectal screening

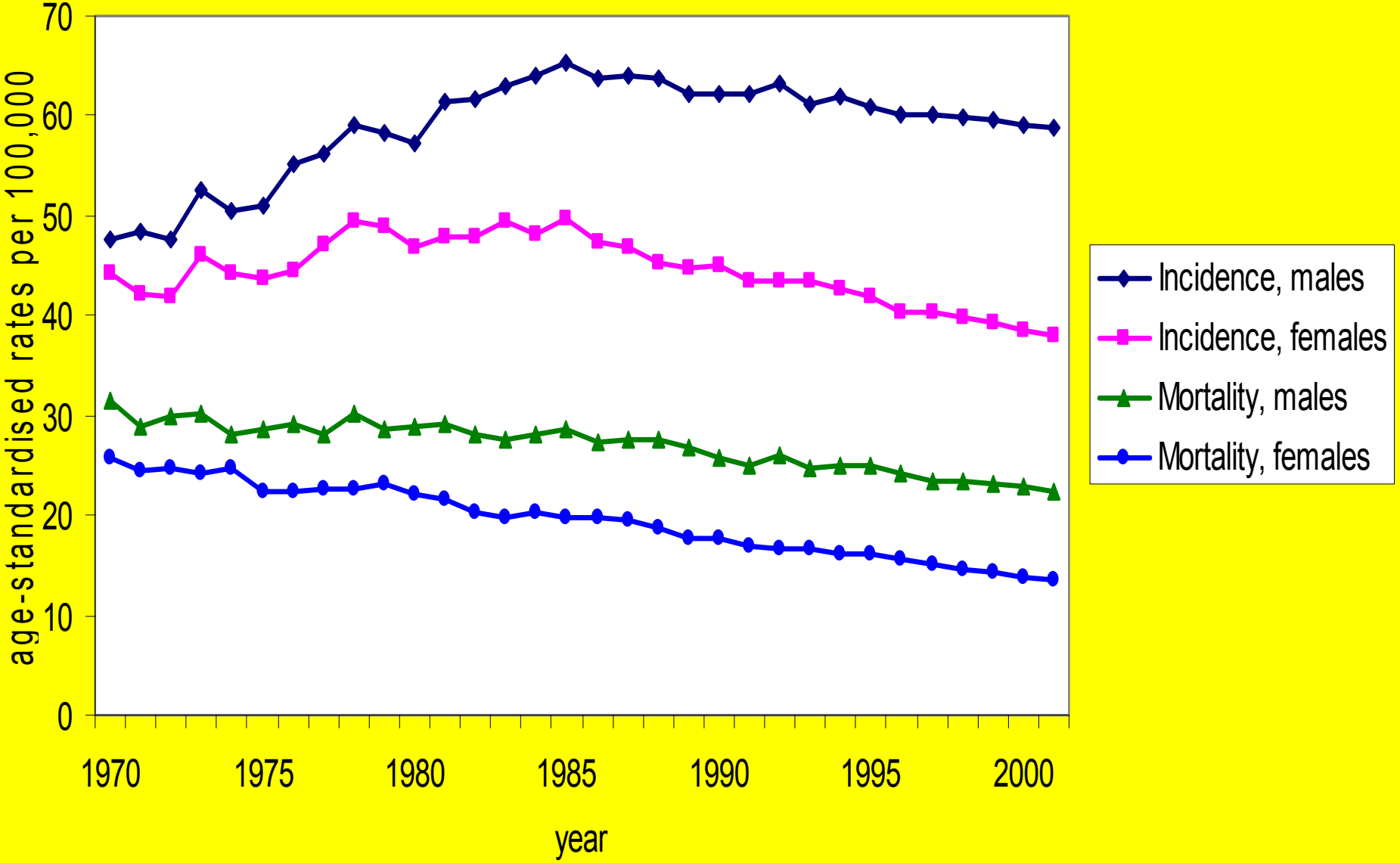
Trial of Fecal Occult Blood Test- 18 year follow-up
(Mandel et al,1999)

Group	CRC Mort R H (95% CI)
Annual	0.67 (0.51-0.83)
Biennial	0.79 (0.62-0.97)

Case-control study of screening sigmoidoscopy (Selby et al, 1992)

Cases	OR (95% C I)
Within reach of sigmoidoscope	0.31 (0.25-0.42)
Above reach of sigmoidoscope	0.96 (0.61-1.50)

Canada - Incidence and mortality from Colo-rectal cancer



Conclusions on colorectal screening

- Incidence and mortality from colorectal cancer are falling in many developed countries
- The screening tests for colorectal cancer have marginal acceptability
- The impact of primary prevention seems likely to be greater than for screening
- The opportunity cost from colorectal screening is too high

Final Conclusions

- Screening is an expensive use of health care resources
- Screening can not abolish mortality from cancer, and people who accept screening should not be deceived that it will
- As treatment improves, the benefit from screening will fall
- As prevention improves, the value of screening will diminish