Medical Screening

Munir Abu-Helalah
MBBS MPH PhD
Associate Professor of
Epidemiology and Preventive Medicine

Preventive Medicine

- Prevention was defined by Last as:

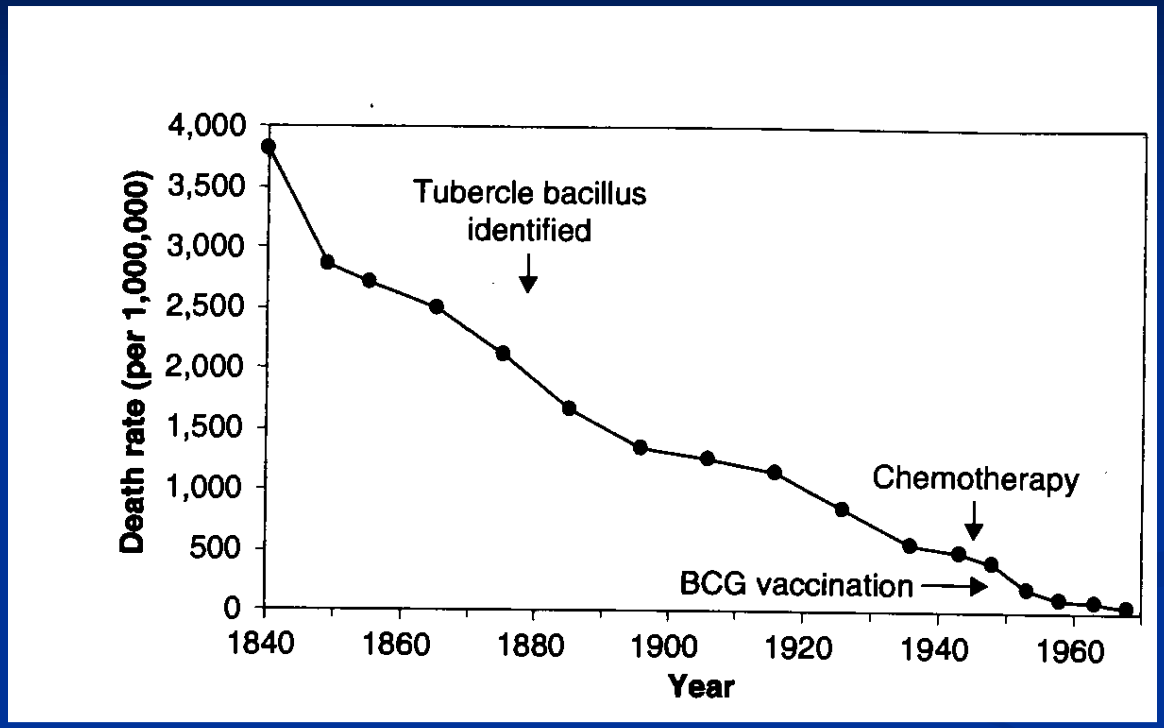
"Actions aimed at eradicating, eliminating, or minimizing the impact of disease or disability, or if none of these is feasible, retarding the progress of disease and disability".

Primary prevention

- Primary prevention aims to prevent disease from occurring in the first place
- Goal: decrease incidence of the disease
- Seeks actually to prevent the disease through altering some factors in the environment, change status of the host, or to change behaviour so that disease is prevented from occurring
- Vaccination programmes: has managed to reduce and eliminate infectious disease of childhood such as whooping cough, measles, rubella, poliomyelitis, and mumps.
- Eliminating environmental risks, such as contaminated drinking water supplies

Modifiable and non-modifiable risk factors

- Can I change age as a risk factor?
- Can I change smoking habit as a risk factor?


Death rate (per 1,000,000)
4,000
3,500
3,000
2,500
2,000
1,500
1,000
500
0
Tubercle bacillus identified
Chemotherapy
BCG vaccination
1840
1860
1880
1900
1920
1940
1960
Year

Secondary prevention

- Aims cure the disease or halt its progression if no available therapy can cure it
- Improving the outcomes of the disease that has already developed
- Early detection or early diagnosis followed by prompt, effective treatment.
- Special consideration of secondary prevention aimed at asymptomatic individuals is necessary

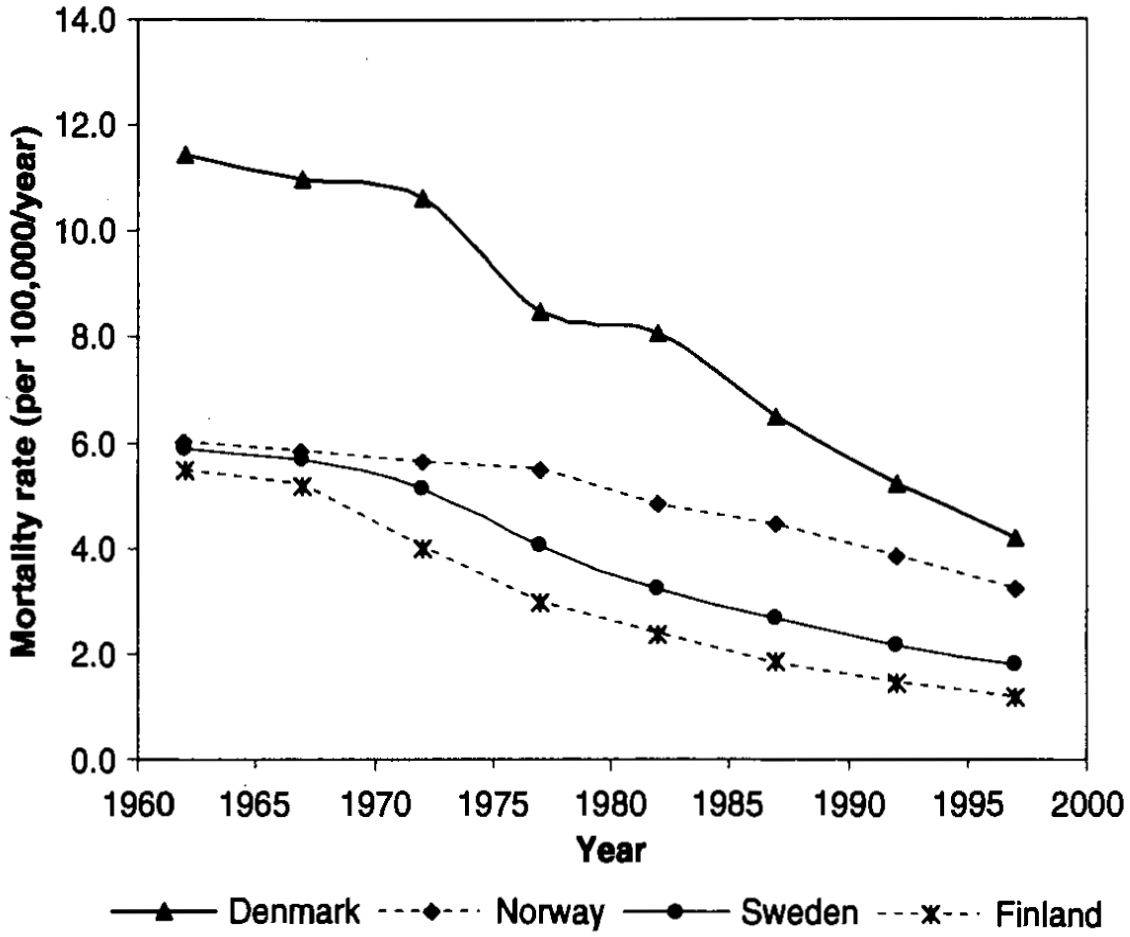


Fig. 14.5 Cervical cancer mortality rates (standardised relative to the world population) from 1950–1998 in the Nordic countries. (Data source: WHO Statistical Information System, accessed via http://www-depdb.iarc.fr/who/menu.htm, March 2004.).

Tertiary prevention

- implying better rehabilitation or quality of life in the longer term
- Preventing recurrence of the disease
- Concerned with rehabilitation of people with an established disease to minimize residual disabilities and complications, minimize suffering, and maximizing potential years or useful life.

Quaternary prevention

- **It is the prevention of unnecessary medicine or the prevention of over-medicalisation and the prevention of unnecessary investigations**
- **Aims to protect patients from unnecessary medicine.**
- Fibromyalgia: endless further diagnostic tests and prescriptions of never proven therapies with well known side-effects
- Antibiotics prescription for flu and other viral illness
- One of the strongest methods to avoid unnecessary medical processes is **Evidence based Medicine**
- (EbM) in the sense that it was originally developed by David Sackett and colleagues

Spectrum of health and disease with the main strategies for prevention at each level

		Stages		Outcomes		
Intervention strategies	Health	Asymptomatic	Symptomatic	Disability	Recovery	Death
Levels of prevention	Primary →	Secondary and Quaternary	→	Tertiary		

Scope of preventive medicine

- High risk versus low risk
- High risk versus average or low risk

High risk strategy

- Targeted rescue operation for vulnerable individuals.
- Checking lipid profile for everyone older than 50 or for smokers with family history of hear disease
- Advantages:
- The intervention is well matched to individuals and their concerns, thus should improve the benefit to risk and benefit to cost ratios
- Avoiding interference with the non-need group
- “Magic bullet approach”
- Easier to conduct and cheaper

High risk strategy

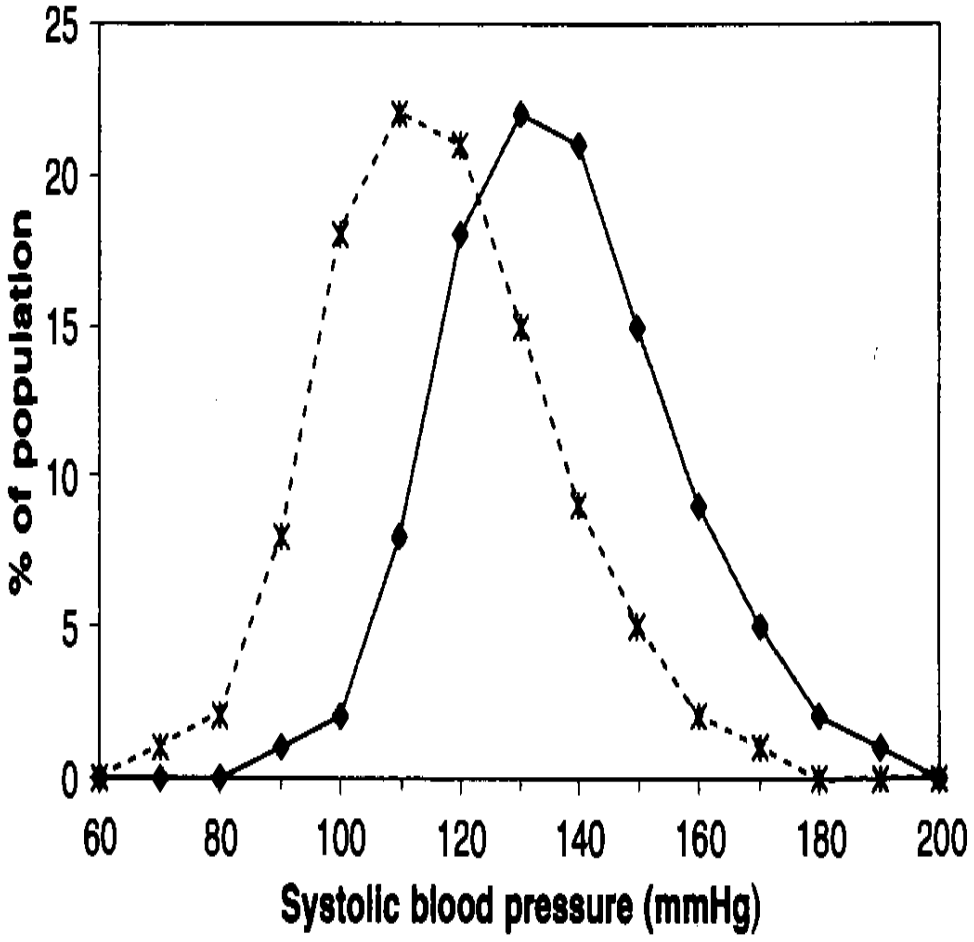
Disadvantages:

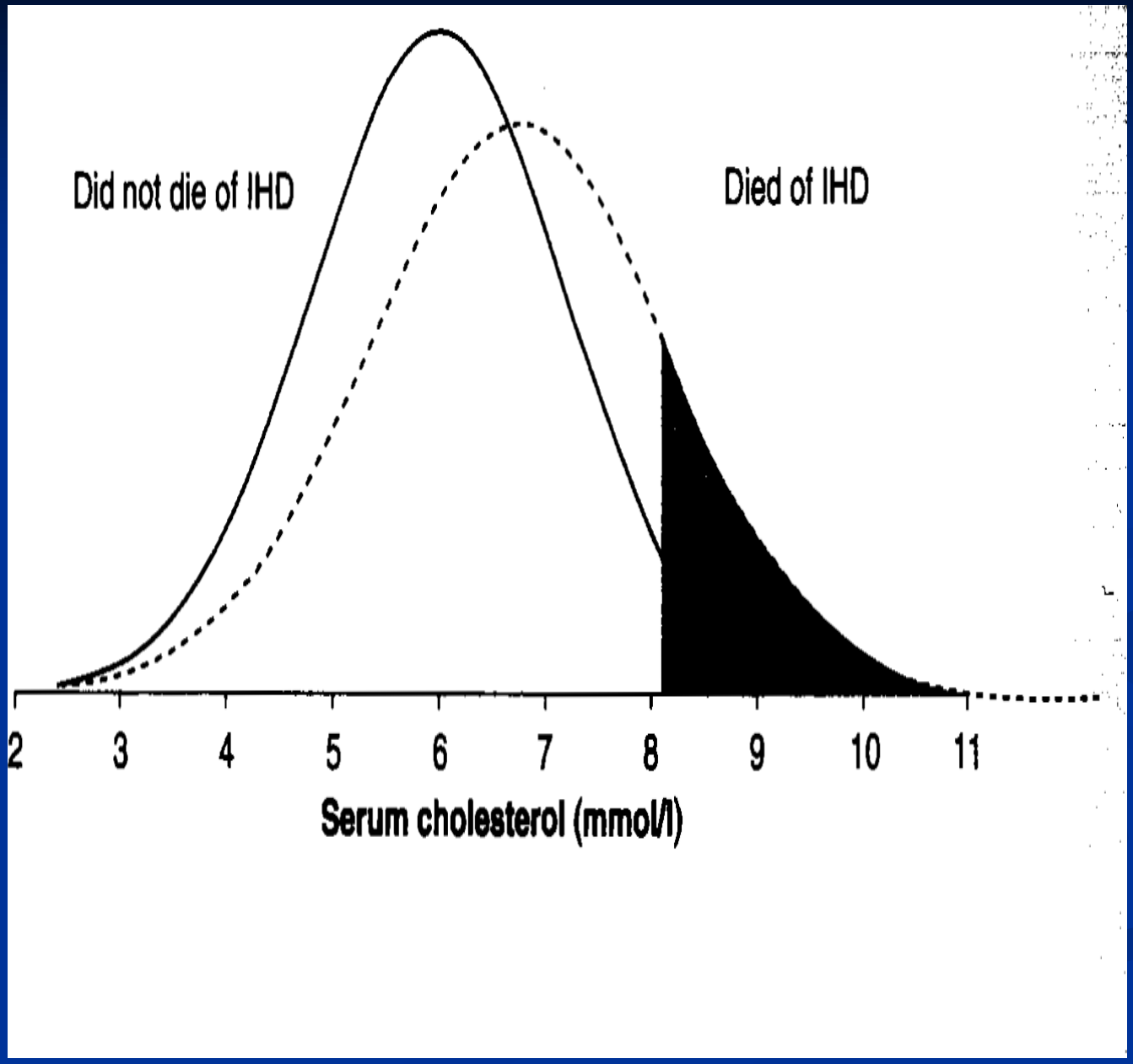
- If the cause or risk factor is widely spread o the disease is common, we need to be careful to limit our programmes to the so-called high-risk groups.
- Screening only older pregnant women, who are known to be at high risk of conceiving a child with Down's syndrome, will miss the majority of afflicted fetuses, which are conceived by younger women in who most pregnancies occur.

Mass strategy

- Aims to reduce the health risks of the entire population
- It is the alternative approach in the case of a common disease or widespread causes.
- Examples: Immunization programmes and water fluoridation
- This starts with the recognition that the occurrence of common diseases and exposures reflects the behaviour and circumstances of society as a whole.

Fig. 13.8 The distribution of systolic blood pressure in a population of middle-aged men before and after a hypothetical intervention. (From Figure 6.5, *The Strategy of Preventive Medicine*, G. Rose (1992), by permission of Oxford University Press.)




Did not die of IHD
Died of IHD
2
3
4
5
6
7
8
9
10
11
Serum cholesterol (mmol/l)

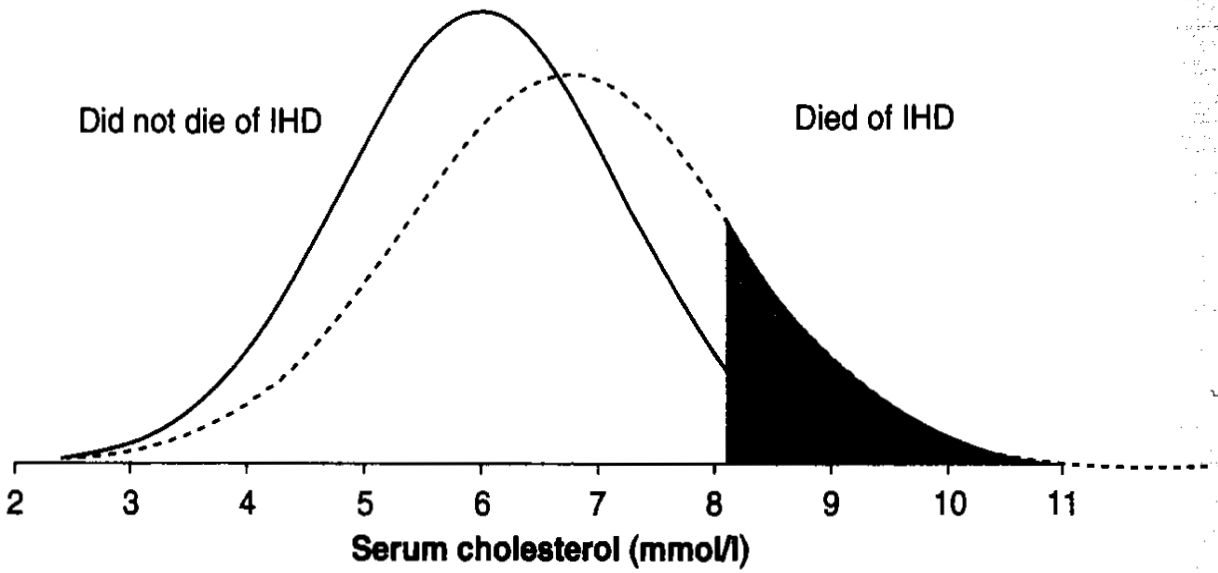


Fig. 13.6 Relative distributions of serum cholesterol levels in men who subsequently died of ischaemic heart disease and men who did not. (From Wald and Law, *BMJ*, 2003; 326: 1419–1425, reproduced with permission from BMJ Publishing Group.)

Figure 13.6 shows a concrete example of the close overlap in risk-factor distributions (in this case serum cholesterol level) between those who did and did not subsequently die from ischaemic heart disease (IHD). The whole curve for those who died from IHD is clearly shifted to the right, but the two overlap considerably and the cut-off point identifying the extreme upper 5% of the 'healthy' cohort identifies only 15% of those who will develop IHD. Again screening for high-risk individuals is not a good preventive strategy.

Compare lung cancer prevention with breast cancer prevention

Medical Screening

What is screening

"The systematic application of a test or enquiry, to identify individuals at sufficient risk of specific disorder to benefit from further investigation or direct preventive action, among persons who have not sought medical attention on account of symptoms of that disorder." Wald,2004

Aims of screening

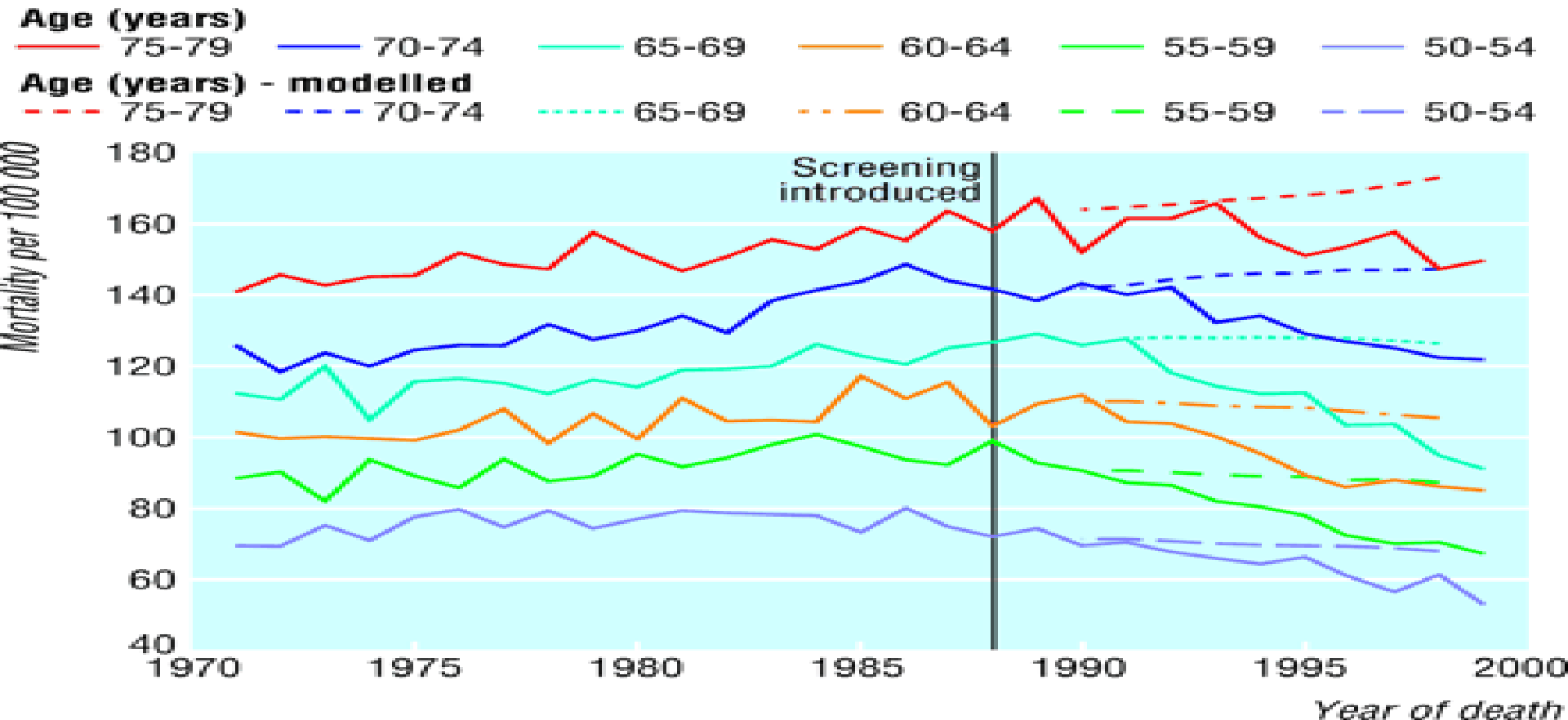
- Better prognosis/outcomes for individuals
- Protection of public from communicable diseases
- Rational allocation of resources
- Research (understanding natural history of disease)

Forms of screening

- Screening for communicable diseases
- Prior to entry to an organisation
- Protection of workforce: high risk industries
- Insurance purposes
- Early detection of diseases

Example of successful medical screening

- Mortality from breast cancer by year of death for selected age groups, England and Wales, 1971-99



Opportunistic screening (case finding):

- Do screening for someone when he/she comes into contact with the health system for another reason
- Check the lipid profile for your overweight or obese patients when they come to your clinic

Screening versus diagnosis

- Early detection: symptoms and signs
- Red flag system

Criteria for screening

1. The disease/condition is an important health problem:

- Well-defined disorder
- Known epidemiology
- Well-understood natural history
- Prevalence of undiagnosed cases

Shall we screen only for common illnesses?

- For serious diseases, even if it is not highly prevalent.
  e.g. Neonatal screening for inborn errors of metabolism.

Phenylketonuria screened for in the UK.

Incidence 1:12000 live births.

If undetected, it would lead to severe mental retardation and growth retardation. While detected cases could be treated simply by dietary restriction of phenylalanine.

If undetected leads to severe mental and growth retardation.

Early Detected cases easily treated by dietary restriction of PKU.

2. Presence of presymptomatic or early stage

- Is there an evidence from a randomised controlled trial that an earlier intervention would work?
- Detecting the disorder at this stage should help in getting better outcomes when compared with the situation without screening.
- Screening for a disease or a risk factor

Diabetes test	Normal	Prediabetes	Diabetes
Hemoglobin A_{1c}, %	< 5.7	5.7–6.4	≥ 6.5
Fasting blood glucose, mg/dL	< 100	100–125	> 125
Oral glucose tolerance, mg/dL	< 140	140–199	> 199

What do you aim to achieve from your screening programme?

- Mortality
- Morbidity
- Quality of life and psychological wellbeing

Screening test:

- Safe
- Inexpensive
- Acceptable
- Reliable
- Valid
- No or minimal adverse effects: pain or any possible adverse effects should be considered in addition to convenience and duration of the test.

Screening test validity

- The validity of a screening test can be evaluated through its detection rate (sensitivity) and specificity.

A. Detection rate (sensitivity) evaluates the ability of a screening tool to detect the disorder or problem. It represents the proportion of diseased individuals who have a positive screening test.

B. Specificity is the ability of a screening tool to label people without the targeted condition as "unaffected" (for diseases, healthy people as non-diseased).

False positive rate (1-specificity)

- More meaningful and practical than specificity because it shows the expected rate of those who would be falsely labelled as diseased or screen positive and might offered further investigations.
- It helps in estimation the magnitude of the economic and other harmful effect such as psychological distress associated such outcomes.

Screening test validity: Outcomes of screening tests

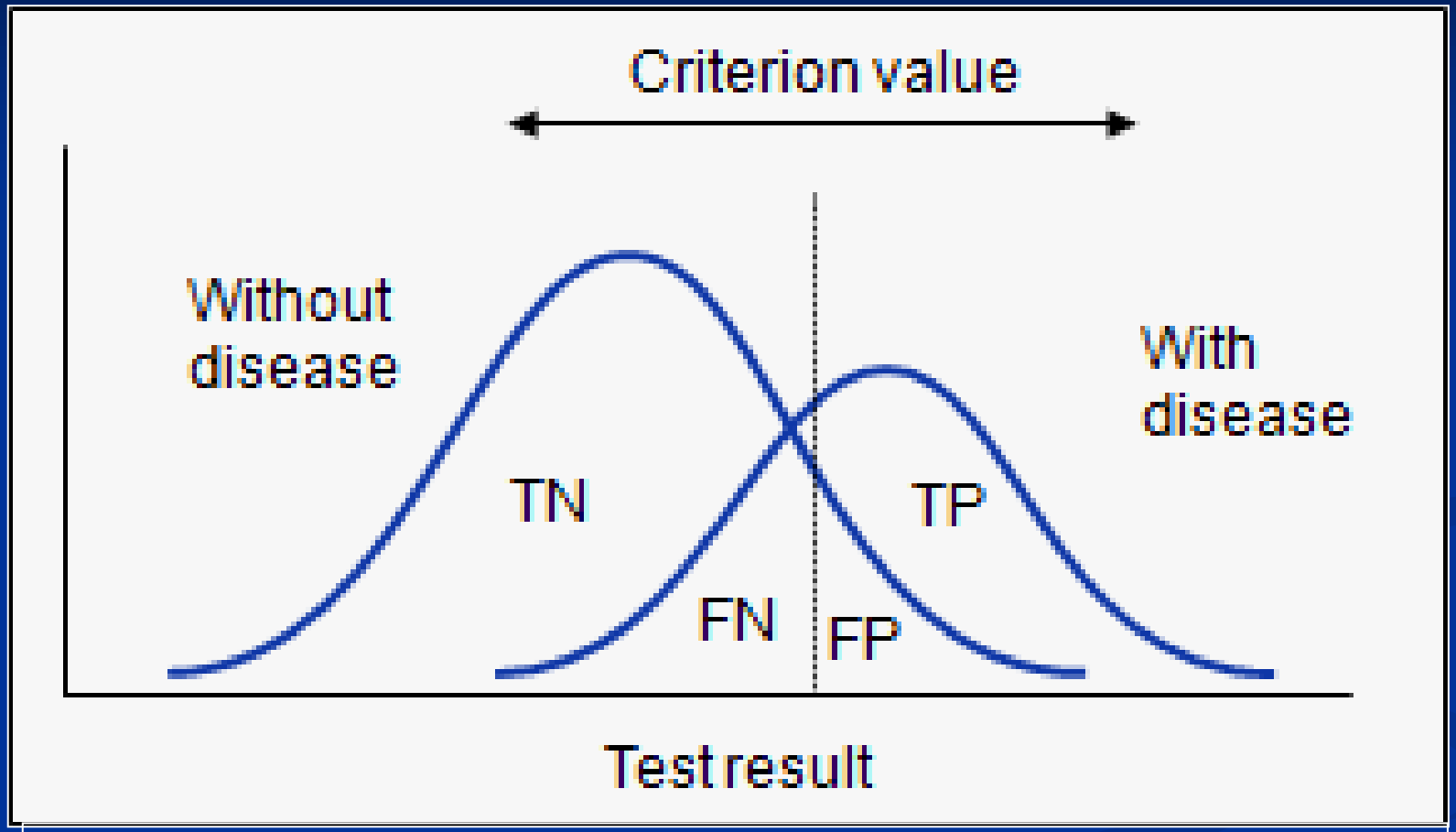
	Disease present	Disease absent	All
Positive screening test	***a*** **(true positive)**	***b*** **(false positive)**	***a + b***
Negative screening test	***c*** **(false negative)**	***d*** **(true negative)**	***c + d***
All	***a + c***	***b + d***	***a + b + c + d***

Detection rate	proportion of affected individuals with positive test results	$\frac{a}{a+c}$
Specificity	Proportion of unaffected individuals with negative test result	$\frac{d}{b+d}$
False positive rate	proportion of unaffected individuals with positive test results	$\frac{b}{b+d}$ =(1-specificity)
Positive predictive value	Probability of the disease being present given a positive test	$\frac{a}{a+b}$
Negative predictive value	probability of no disease being present given a negative test result	$\frac{d}{c+d}$

Screening test validity

- For biochemical tests such as serum hormone concentrations, which are considered as continuous outcomes, distribution of a screening test should be known amongst the screened population.
- This is essential in order to determine suitable cut off points
- This depends on both the screening test and prevalence of the health condition.

Outcomes of screening program



TP: true positives TN: true negatives
FP: False positives FN: False negatives

Example of validity assessment

Validity of various tests in detecting hypothyroidism					
	TSH	FT4	FT3	TT3	TT3
Detection rate	94-100%	65-80%	48%	60-61%	74%
False positive rate	8%	1%-6%	10%	3%-10%	13%

Reliability of screening test

- Reliability means that the same results should be obtained by different observer or the same observer at different occasions.
- In practice, it is hard to achieve 100% reliability
- Guidelines should be in place on decisions when two observers have different opinions.

Agreed plan on further investigation, diagnosis and treatment:

- Any interventional measures or early detection should be more worthwhile than both late diagnosis and/or intervention.
- This should be based on scientific-based evidence.
- Randomised controlled clinical trials could be needed to evaluate the impact of treatment on those detected from screening programmes as they could be different from those seeking medical attention for their conditions.

Agreed plan on further investigation, diagnosis and treatment:

- Diagnostic tools, screening intervals and treatment
- Facilities required for such steps should also be available or easily installed and equally accessed by the screened population

Trial	Design	Subjects	*N*; duration (years)	Control group	Active treatments	% change in diabetes risk
Principal diabetes prevention trials that evaluated metformin						
DPP (US) [19]	RCT	IGT and high–normal glucose	3234; 3	Placebo plus standard lifestyle advice	Metformin plus standard lifestyle advice	−31
					Intensive lifestyle intervention	−58
DPP Outcome Study (US) [69]	O	Epidemiological follow-up to DPP	2766; 5.7	Placebo plus intensive lifestyle advice	Metformin 1700 mg/day + intensive lifestyle advice	−13
					Intensive lifestyle advice	+5
IDPP (India) [20, 65]	RCT	IGT	531; 2.5	Standard lifestyle advice	Metformin plus standard lifestyle advice	−26
					Metformin plus intensive lifestyle intervention	−28
					Intensive lifestyle intervention	−29
Wenying et al. (China) [68]	NR	IGT	321; 3	Standard lifestyle advice	Metformin	−88
					Acarbose	−87
					Intensive lifestyle intervention	−43
Li et al. (China) [66]	RCT	IGT	70; 1	Placebo	Metformin	−66[a]
Iqbal Hydrie et al. (Pakistan) [67]	RCT	IGT	317; 1.5	Standard lifestyle advice	Metformin	−76.5
					Intensive lifestyle intervention	−71
CANOE (Canada) [64]	RCT	IGT	207; 3.9	Placebo	Metformin 500 mg plus rosiglitazone 2 mg twice daily	−66
Principal diabetes prevention trials that did not evaluate metformin						
Diabetes Prevention Study (Finland) [70]	RCT	IGT	522; 3.2	Standard lifestyle advice	Intensive, multifactorial lifestyle intervention	−58
Da Qing study (China) [71]	RBS	IGT	577; 6	Standard lifestyle advice	Diet, exercise, or both together	−31 to −46
STOP-NIDDM (International[b]) [72, 73]	RCT	IGT	1429; 3.3	Placebo	Acarbose	−25
XENDOS (Sween) [74]	RCT	IGT and obesity	694; 4[c]	Placebo	Orlistat	−45
DREAM (21 countries[d]) [75, 76]	RCT	IGT ± IFG	5269; 3	Placebo	Rosiglitazone	–62[e]
				Placebo	Ramipril	–9[f] (NS)
IDPP–2 (India) [77]	NR[f]	IGT	407; 3	Placebo + lifestyle intervention	Pioglitazone + lifestyle intervention	+8 (NS)
SOS study (Sweden) [78]	RCT	Obese, non-diabetic	3429; 10	No surgery[g]	Bariatric surgery	–83

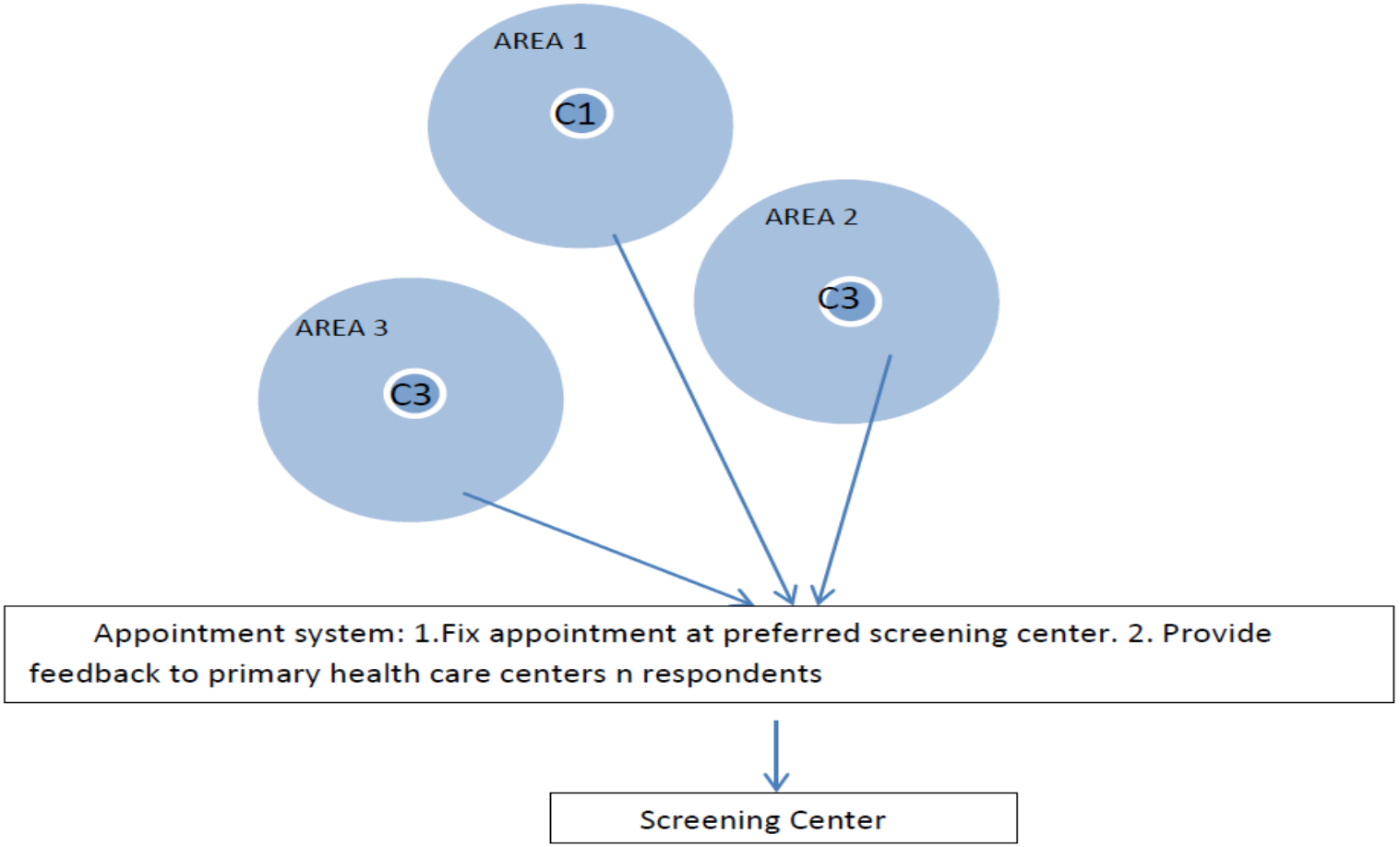
Systematic application

- This means that the test is offered routinely to the target group based on agreed criteria.

Do it in a systematic way!

- **Regular systematic national screening programs** for breast and colorectal cancers **should replace the current scattered campaigns and activities in many countries in the region.**

- Work should start with pilot systematic screening projects in representative area in the country of interest.



Obtain data from Ministry of Interior on residents in Areas 1,2,3 who fulfills screening criteria

Send letters through Health Centers C1,C2,C3

Send reminders through Health Centers C1,C2,C3 for non-respondents

Ask practice manager or health counselor to call non-respondents from the two calls and arrange for GP visit if needed.

Obtain data from the screening centers for respondents to screening calls.

Simplify your program

Is it too difficult to have a national systematic regular screening program for breast cancer in country "x" where the number of women aged 40-70 is 2,000,000?

In this country: it is recommended to screen women aged 40-69 once every two years

Notice: Screening interval depends on mean sojourn time and should not be fixed to be on annual basis unless there is clinical evidence for that

Cut it down so it will be simple

Practical example: In country X, there are 2000000 women aged 40-70 who are eligible for screening

2000000 Women aged 40-70

To be screened once every two years — 1,000,000 per year

75% response rate: — 750,000

300 working days/ 6 days work — **2500**

20 Main cities in the KSA (2 centers in each city except Riyadh 4, Jed3, Dam3= 44 Centers

2500/44 — 57

If two machines are available in each center: 29 per machine per day

4patients per hour — **For 7 working hours per day**

How can we reach target groups to achieve systematic screening??

- Our plan is that every woman within the target age range and meets other screening criteria should receive invitation letter and a reminder, if needed, to invite her to attend the screening.

Acceptability of programme to the public and health care staff.

- Screening test, diagnostic test and therapeutic options should be ethically and socially accepted by the general public and the health care professionals.

Economic evaluation:

- Implementing screening programmes should be more economically effective than the existing system.
- Cost of all steps related to the screening programme should be assessed and compared with outcomes of the screening and with other services.

Bias related to medical screening

- Lead time bias: screened cases are detected at an earlier stage than that in which treatment would be worthwhile.

  Does treatment work better at this stage?
- Length time bias: cases detected through screening are slowly progressive and may not harm the patient in lifetime
- Selection bias: respondents are different from decliners

Volunteer bias:

Epidemiological studies have shown that people who attend for screening are likely to be different from those who do not.

- They tend to be of higher socioeconomic class
- More health-conscious
- Comply better with prescribed advice
- Therefore, better results for a screening programme of volunteers compared with disease outcomes for non-voluntees may be relate to factors associated with the "volunteerism" rather than benefits of treatment following diagnosis

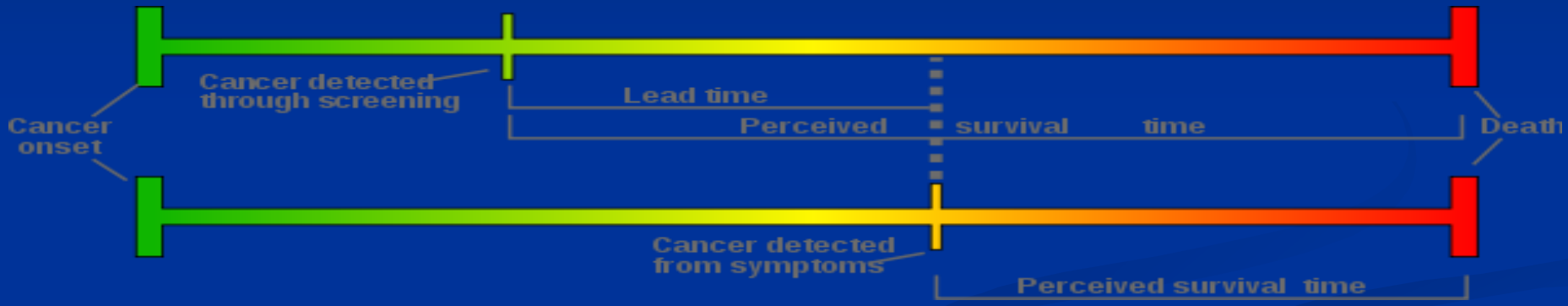
Volunteer bias:

To avoid this types of bias: conduct a preventive trial: Recruit a pool of volunteers and then assign them randomly to receive screening or no screening

Lead time bias

- Lead time: period between when the disease is detected by screening and when it would have become symptomatic and been diagnosed in the usual way.

- Prolongation between diagnosis and death
- There is no difference in outcomes between patients detected through screening and patients who is treated when the condition manifest clinically
- Screening simply makes the condition evident at an earlier stage without actually affecting its course. (appears to lead to longer survival because of earlier detection)
- If left with no screening the disease will be diagnosed at age of 50 and die at age of 54
- If screened disease will be diagnosed at age of 47 and die at the age of 54

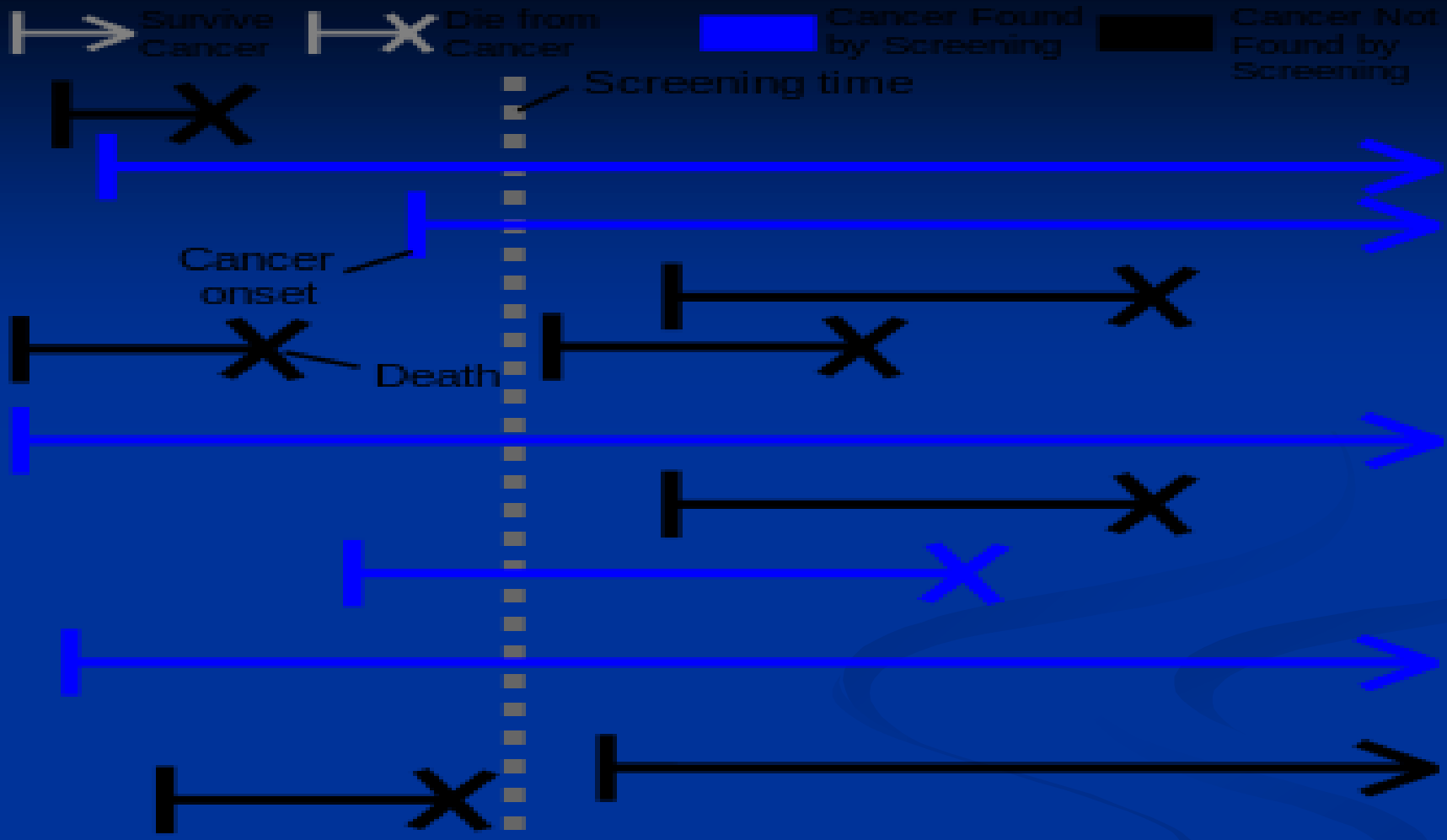

Cancer detected through screening
Lead time
Cancer onset
Perceived survival time
Death
Cancer detected from symptoms
Perceived survival time

Length time bias

- It is a form of selection bias.
- When we screen for disease were more likely to detect cases where the disease is progressing slowly
- Over-presentation of slowly progressing disease among cases detected by screening.
- Screening will detect more slowly growing tumours, while rapidly growing tumours are more likely to develop and to proceed to clinical presentation within the interval between two consecutive screening examinations.

Length time bias

- Faster-growing tumors generally have a shorter asymptomatic phase than slower-growing tumours, and so are less likely to be detected. However, faster-growing tumors are also often associated with a poorer prognosis. Slower-growing tumors are hence likely to be over-represented in screening tests. This can mean screening tests are erroneously associated with improved survival, even if they have no actual effect on prognosis.



	Death from Cancer	Survive Cancer	% Surviving Cancer
Cancer Discovered Through Screening	1	4	80%
Not detected through Screening	7	5	41.7%

Challenges

- Validity of the screening test
- Healthy people need further tests
- Anxiety caused
- Health care resources

Criteria for introducing screening

- Important health problem
- Presence of presymptomatic or early stage

- Screening test
- Agreed plan on further investigation, diagnosis and treatment
- Acceptability of programme to the public and health care staff
- Systematic application
- Economic evaluation

Pilot basis

- What is my next step?
- Learn from other countries or sites' experience
- Consult others who have the programme already in place
- Start your programme on pilot basis

Quality Assurance

- Quality assurance means that the assessment of the service provided and applying modifications when necessary.
- This includes various steps such as recruitment, registration, waiting time, test procedures, results handling and follow up or referral for treatment procedures.
- Clinical audit is a term that have been used to describe quality assurance for clinical settings, although some consider it as a part of the quality assurance.

My programme is already in place

- Continuous monitoring and regular evaluation

Questions

Thank you!