Medical Screening and Preventive Medicine

Dr Munir Abu-Helalah MD MPH PhD FPM
Department of Family and Community Medicine
School of Medicine, University of Jordan

Associate Professor of Epidemiology
and Preventive Medicine
Consultant Preventive Medicine
Director, Institute of Public Health

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 do something for genetic diseases?

Case of familial cancer management for family members with positive genetic mutations

- Can I change smoking habit as a risk factor?

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
- Based on best scientific evidence (meta-analysis, systematic reviews, clinical trials).
- Protocol for management
- Role of personalized medicine- Precision medicine
- Clinical indicators

Secondary prevention

- Interventions at early stages:
- prediabetes, stage 0 breast cancer, Cervical Cancer CIS, Subclinical hypothyroidism
- **Screening:** special consideration of secondary prevention aimed at asymptomatic individuals is necessary
- **Early detection** followed by evidence based interventions

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 Evidence Based Medicine

- One of the strongest methods to avoid unnecessary medical processes is **QUATERNERY Prevention**
- (EBM) in the sense that it was originally developed by David Sackett and colleagues
- **It is the evidence based approach for management of patients.**
- **Introduction of treatments and investigations according to solid scientific evidence and prevention of unnecessary medicine or the prevention of over-medicalisation and the prevention of unnecessary investigations**

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**	→	**Tertiary**		
	(Evidence Based Medicine) →					

Scope of preventive medicine

- High risk versus average risk

High risk strategy

- Checking lipid profile for everyone older than 50 or for smokers with family history of heart disease
- Influenza vaccines for patients with chronic cardiac and respiratory illnesses, pregnant women, aged 65 or more, cancer patients.
- **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 or 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.

Screening for breast cancer according to risk factors will detect only 30% of the cases

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.

1.1. Top Cancers among Jordanian population by sex, 2022

Table 7: Ten most common cancers among Jordanians, both sexes, 2022.

Rank	Cancer	No	%
1	Breast	1756	20.1
2	Colorectal	969	11.1
3	Trachea,Bronchus,Lung	650	7.4
4	Lymphoma	610	7.0
5	Bladder	471	5.4
6	Thyroid	365	4.2
7	Leukemia	355	4.1
8	Prostate	335	3.8
9	Brain,Nevous system	250	2.9
10	Stomach	208	2.4

Ten most common cancers among Jordanian Males, 2022

Rank	Site	Frequency	Percent
1	Trachea,Bronchus,Lung	518	12.9
2	Colorectal	515	12.8
3	Bladder	411	10.2
4	Prostate	335	8.3
5	NHL	234	5.8
6	Leukemia	200	5.0
7	HL	131	3.3
8	Brain,Nervous System	128	3.2
9	Kidney	126	3.1
10	Stomach	114	2.8

Ten most common cancers among Jordanian Females, 2022

Rank	Site	Frequency	Percent
1	Breast	1743	36.8
2	Colorectal	454	9.6
3	Thyroid	272	5.7
4	Corpus Uteri	208	4.4
5	Ovary	167	3.5
6	NHL	163	3.4
7	Leukemia	155	3.3
8	Trachea,Bronchus,Lung	132	2.8
9	Brain,Nervous System	122	2.6
10	Stomach	94	2.0

N.B: Total top ten female cancers accounted for 3510 (74.1%)

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**	

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)

Opportunistic screening (case finding):

- Do screening for someone when he/she comes into contact with the health system for another reason
- Check glucose profile for patient with gastric symptoms, older than 45 with family history of diabetes
- Refer lady aged 40 coming for URTI infection for breast cancer screening
- <u>If the patient has symptoms suggestive of the disease of interest, it is an EARLY DETECTION not screening</u>

Screening versus diagnosis

- Early detection: symptoms and signs
- It is essential to work in both directions in parallel way:
- Start your screening programs

&

- Invest in early detection at GPs and selected specialties & general population levels awareness.

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 Phenylketonuria in Jordan

In 2011, 7 out of 93000 screened babies.

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.
- 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.

- Screening for a disease or a risk factor

It is recommended to screen for diseases, while risk factors are bad screening tools

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.

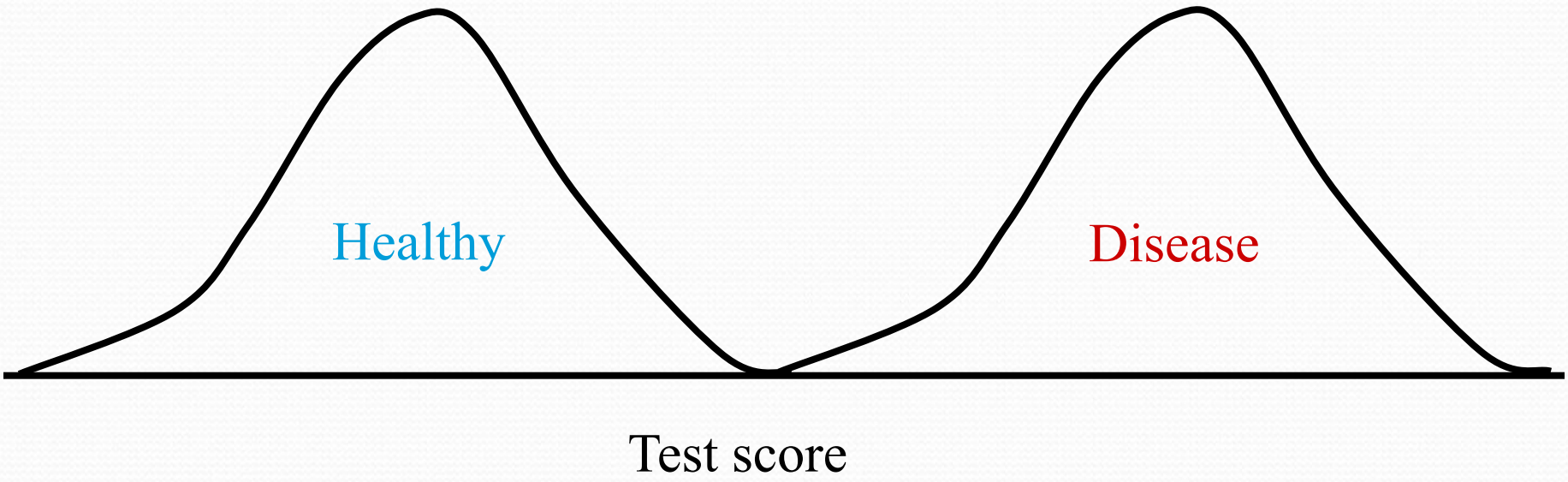
Screening test validity

- **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.

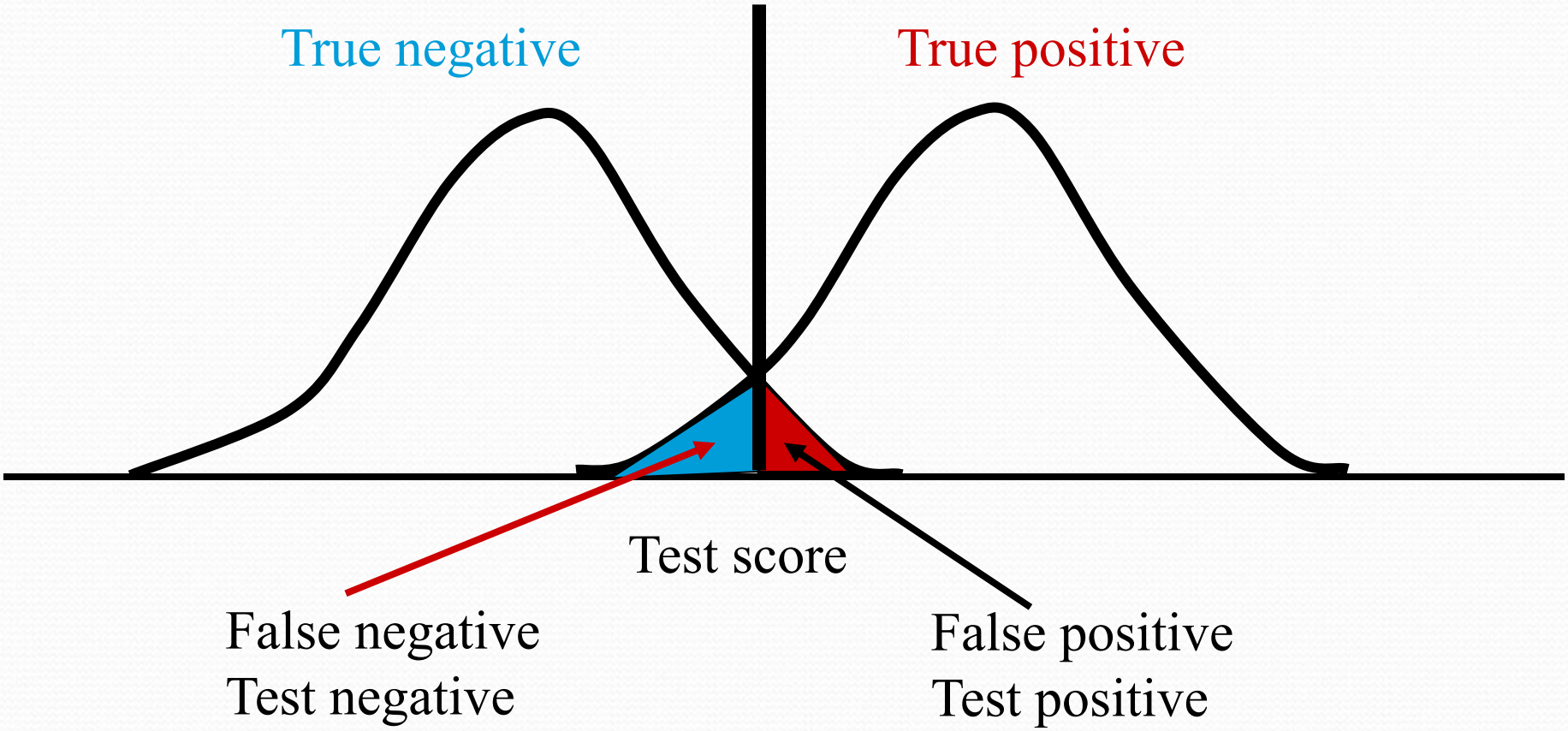
  B. Specificity is the ability of a screening tool to label people without the targeted condition as "unaffected" (for diseases, healthy people as non-diseased).

An ideal laboratory test would detect all people who have a disease and at the same time identify as normal all those who do not have the disease



Test based on continuous data

the values between normal/disease overlap



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 (further investigations) and other harmful effect such as psychological distress associated such outcomes.

Validity of a test

How well a test performs can be assessed based on the values in the following 2x2 table

	Disease present	Disease absent
Test positive or Surveillance Detection positive	True Positives TP a	False positives FP b
Test negative or Surveillance Detection negative	c False negatives FN	d True negative TN

	Disease present	Disease absent
Test positive or Surveillance Detection positive	True Positives TP **a**	False positives FP **b**
Test negative or Surveillance Detection negative	**c** False negatives FN	**d** True negative TN

$$\text{Sensitivity} = \frac{\text{Diseased people with a positive test}}{\text{All diseased people}} = \frac{TP}{TP + FN}$$

$$\textbf{\textit{Specificity}} = \frac{\textbf{\textit{Well people with a negaitive test}}}{\textbf{\textit{All well people}}} = \frac{\textbf{\textit{TN}}}{\textbf{\textit{TN + FP}}}$$

False positive rate= FP/FP+TN

False positive rate

- The proportion of unaffected individuals with positive test results.

- False positive rate= $\frac{b}{b+d}$ =1-specificty

Predictive values

- Positive predictive value= all true positives/all positives(all true and all false) ×100
- How likely it is that a positive test result indicates the presence of the disease.
- It is the percentage of all people who test positive and who really have the disease
- Negative predictive value= True negatives/all negatives ×100
- It is the percentage of all people who test negative who really do not have the disease

	Disease present	Disease absent
Test positive or Surveillance Detection positive	True Positives TP a	False positives FP b
Test negative or Surveillance Detection negative	c False negatives FN	d True negative TN

$$prevalence = \frac{Diseased\ people}{All\ \ people} = \frac{TP + FN}{TP + FN + FP + TN}$$

$$predictive\ value\ \ positive = \frac{Diseased\ people\ with\ a\ positive\ test}{All\ \ people\ with\ a\ \ positive\ test} = \frac{TP}{TP + FP}$$

$$predictive\ value\ \ negative = \frac{Well\ people\ with\ a\ \ negative\ test}{All\ \ \ people\ with\ a\ negative\ test} = \frac{TN}{TN + FN}$$

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	$\frac{d}{c+d}$

		Patients with bowel cancer (as confirmed on colonoscopy)		
		Positive	***Negative***	
Fecal occult blood screen test outcome	***Positive***	**True Positive (TP) = 20**	**False Positive (FP) = 180**	**→ Positive predictive value = TP / (TP + FP) = 20 / (20 + 180) = 20 / 200 = 10%**
	Negative	**False Negative (FN) = 10**	**True Negative (TN) = 1820**	**→ Negative predictive value = TN / (FN + TN) = 1820 / (10 + 1820) = 1820 / 1830 ≈ 99.5%**
		↓ Sensitivity = TP / (TP + FN) = 20 / (20 + 10) = 20 / 30 ≈ 66.67%	**↓ Specificity = TN / (FP + TN) = 1820 / (180 + 1820) = 1820 / 2000 = 91%**	

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

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:

- Where to refer your positive subjects
- What is the diagnostic tests
- Who will pay for the investigations and treatments
- 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

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.

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 1,000,000?

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

Notice: Screening interval depends on mean sojourn time, local data and health economics model.

Test it before you generalize it

- Start with pilot program
- Assess response rate
- Is my program cost-effective
- What is my cost-effective screening criteria
- Quality of all involved steps (single versus double reader mammography screening, FIT versus Haemoccult test)
- Compare respondents with non-respondents
- Assess success rates
- Look for determinants of success and failure
- Is there a specific group who needs different intervention?

Importance of Pilot Projects

1. Health economics evaluation
2. Setting age cut-off based on local data
3. Improve performance at national level by learning from experience at pilot phase
4. Comprehensive assessment of the screening program helpline, waiting time, film quality, guidelines such as double readers, false positive rate, false negative rate, diagnosis process, psychological counseling, treatment, prognosis, economic evaluation, how can we make it better at the national level.
5. Assessment of barriers to screening
6. Quality assessment of staff

Volunteer bias:

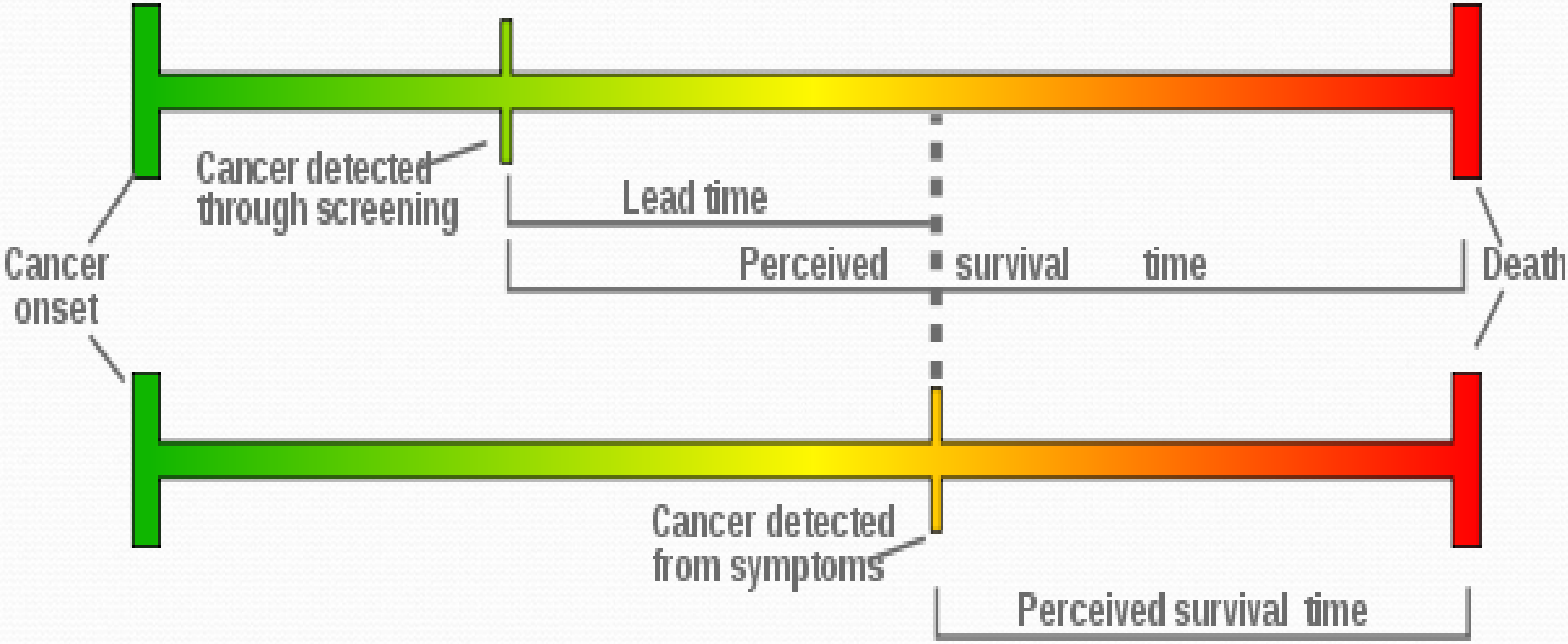
- They tend to be of higher socioeconomic class
- More health-conscious
- Comply better with prescribed advice
- Therefore, better results for a screening programme of volunteers compared with disease outcomes for non-voluntees may be relate to factors associated with the “volunteerism” rather than benefits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

- Therefore it is essential to analyse data on participants and ensure that all target group have the same access and received the same message

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

Lead time bias in Prostate cancer

- **Lead Times and Over detection Due to Prostate-Specific Antigen Screening: Estimates From the European Randomized Study of Screening for Prostate Cancer**
- Gerrit Draisma Rob Boer Suzie J. Otto Ingrid W. van der CruijsenRonald A. M. Damhuis Fritz H. Schröder Harry J. de Koning
- *JNCI: Journal of the National Cancer Institute*, Volume 95, Issue 12, 18 June 2003, Pages 868–878, https://doi.org/10.1093/jnci/95.12.868

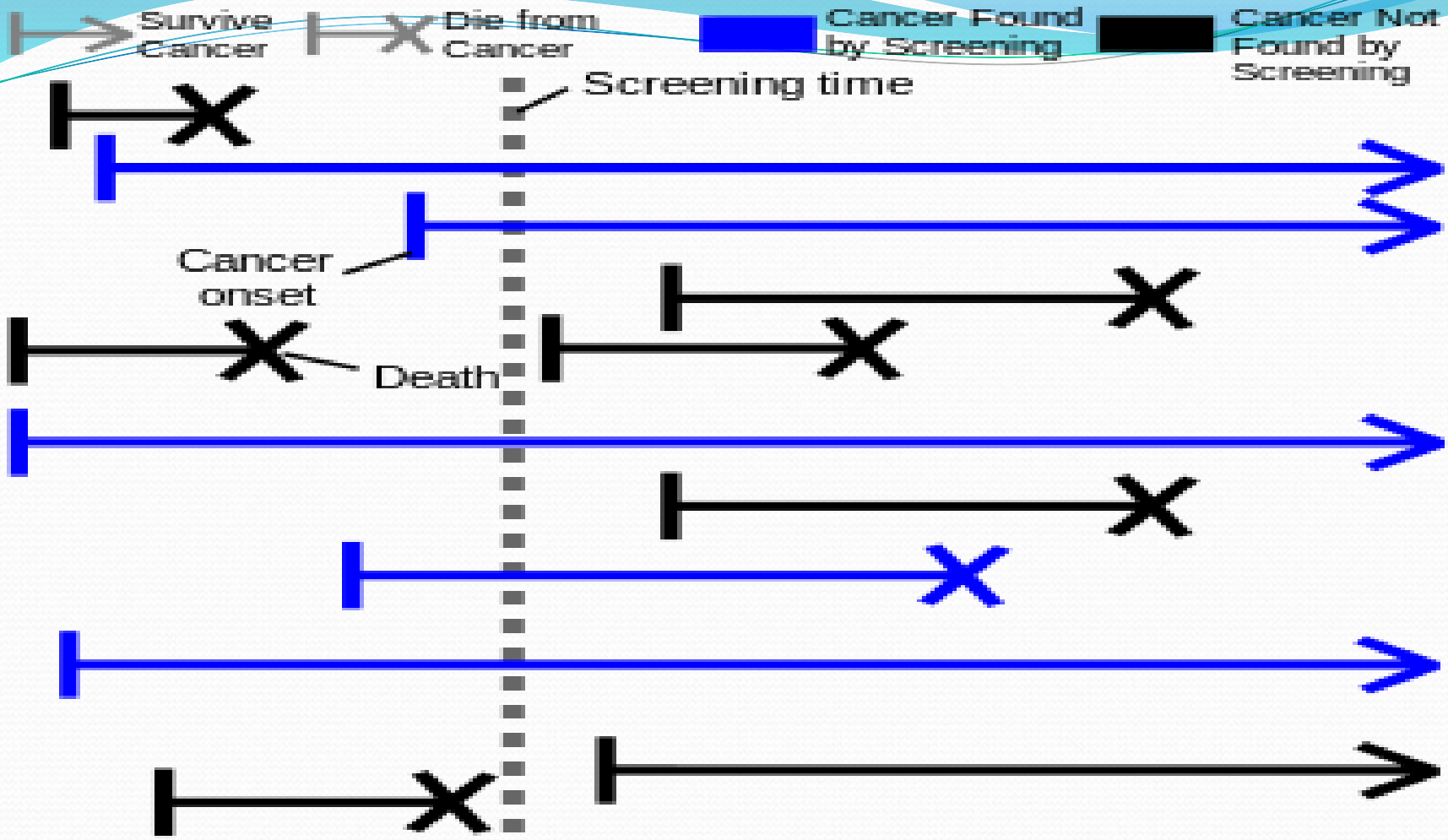
Global Center for Public Health and Disease Control, Global Academy for Health Sciences, OH USA

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.

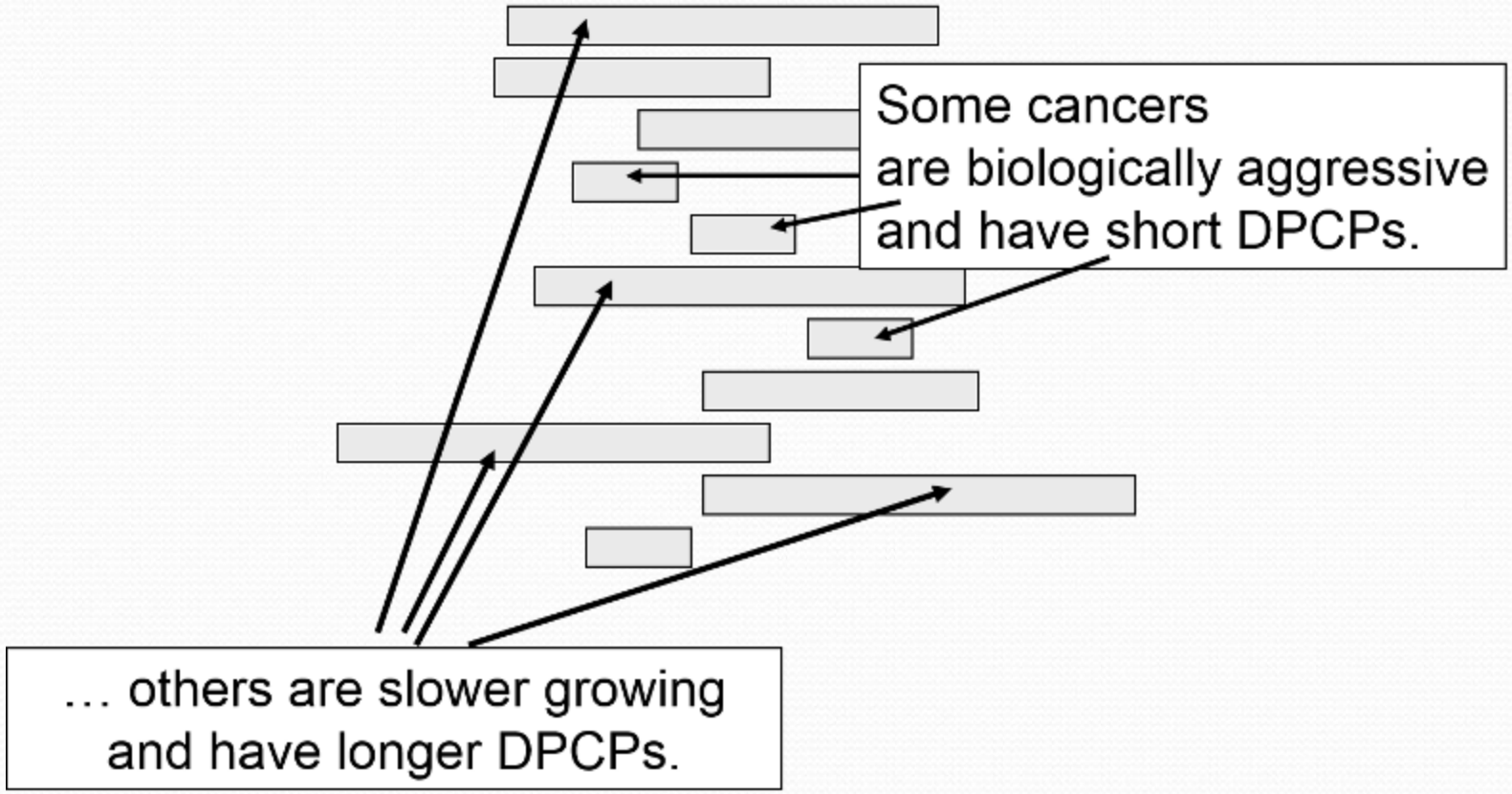
Length time bias

- 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%

Prostate Cancers With Varying DPCPs



DPCPs: detectable preclinical phase

Challenges

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