

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

Article

Epidemiology of *Streptococcus pneumoniae* Serotypes in Jordan Amongst Children Younger than the Age of 5: A National Cross-Sectional Study

Munir Abu-Helalah ^{1,*}, Asma'a Al-Mnayyis ², Hamed Alzoubi ³, Ruba Al-Abdallah ⁴, Hussein Jdaitawi ⁵, Omar Nafi ⁶, Kamel Abu-Sal ⁷, Alaa Altawalbeh ⁸, Alia Khlaifat ⁹, Enas Al-Zayadneh ⁹, Ihsan Almaaitah ¹⁰, Ibrahim Borghol ¹¹, Fadi Batarseh ⁴, Omar Okkeh ⁴, Abdallah Dalal ⁴, Ahmad Alhendi ⁴, Mohammad Almaaitah ⁸, Adnan Al-Lahham ¹², Mahmoud Gazo ¹³, Faisal Abu Ekteish ¹⁴ and Ziad Elnasser ³

- ¹ Department of Family and Community Medicine, Faculty of Medicine, Jordan University, Amman 11942, Jordan
- ² Department of Clinical Sciences, College of Medicine, Yarmouk University, Irbid 21163, Jordan; asma.mnayyis@yu.edu.jo
- ³ Department of Pathology and Microbiology, King Abdullah University Hospital, Jordan University of Science and Technology, Irbid 22110, Jordan; hmalenabisi@just.edu.jo (H.A.); znasser@just.edu.jo (Z.E.)
- ⁴ Medical Department, MENA Center for Research & Development and Internship, Amman 11931, Jordan; ruba.yousef1995@gmail.com (R.A.-A.); bat.fadi97@yahoo.com (F.B.); okkeh123@gmail.com (O.O.); abood.dalal.ad@gmail.com (A.D.); alhindia23@yahoo.com (A.A.)
- ⁵ Ministry of Health, Princess Rahma Pediatrics Hospital, Irbid 21163, Jordan; jdaitawi_hussein@yahoo.com
- ⁶ Faculty of Medicine, Mutah University, Mutah 61110, Jordan; onaf2000@yahoo.com
- ⁷ Vaccines Department, Ministry of Health, Amman 11931, Jordan; d.abusal@yahoo.com
- ⁸ Royal Medical Services, Amman 1190, Jordan; altawalbeh@yahoo.com (A.A.); dralia.khlaifat@gmail.com (A.K.); adoctor77@hotmail.com (M.A.)
- ⁹ Department of Pediatrics, Faculty of Medicine, Jordan University, Amman 11942, Jordan; e.alzayadneh@ju.edu.jo
- ¹⁰ Pediatrics Department, Zarqa Governmental Hospital, Zarqa 13116, Jordan; ihsan.almaaitah66@gmail.com
- ¹¹ Alhashir Hospital, Amman 11931, Jordan; bob_borghol@hotmail.com
- ¹² Department of Biomedical Engineering, School of Applied Medical Sciences, German-Jordanian University, Amman 11931, Jordan; adnan.lahham@gju.edu.jo
- ¹³ Department of Central Laboratories, Ministry of Health, Amman 11931, Jordan
- ¹⁴ Department of Pediatrics, Faculty of Medicine, King Abdullah University Hospital, Jordan University of Science and Technology, Irbid 22110, Jordan; faisal@just.edu.jo
- * Correspondence: mabuhelalah@yahoo.co.uk



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Abstract: Introduction: *Streptococcus pneumoniae* infections are a major cause of mortality and morbidity worldwide. In Jordan, pneumococcal conjugate vaccines (PCVs) are not included in the national vaccination program. Due to the current availability of several PCVs, including PCV-10, PCV-13, and PCV-15, along with PCV-20, currently undergoing pediatric approvals globally, the decision to introduce PCVs and their selection should be based on valid local data on the common serotypes of *Streptococcus pneumoniae*. Methods: This cross-sectional study aimed to identify the frequency of serotypes of *Streptococcus pneumoniae* in children aged below 5 years hospitalized with invasive pneumococcal diseases (IPDs), including pneumonia, septicemia, and meningitis, during the study's duration in representative areas of Jordan. Serotyping for culture-positive cases was based on the capsular reaction test, known as the Quellung reaction. qPCR was conducted on the blood samples of patients with lobar pneumonia identified via X-ray or on cerebrospinal fluid for those with a positive latex agglutination test for *Streptococcus pneumoniae*. Results: This study was based on the analysis of the serotypes of 1015 *Streptococcus pneumoniae* cases among children younger than the age of 5: 1006 cases with pneumonia, 6 cases with meningitis, and 3 cases with septicemia. Only 23 culture-positive cases were identified in comparison to 992 lobar pneumonia cases, which were PCR-positive but culture-negative, with a PCR positivity rate of 92%. Serotypes 6B, 6A, 14, and 19F were the most common serotypes identified in this study, with prevalence rates of 16.45%, 13.60%, 12.12%, and 8.18%, respectively. PCV-10, PCV-13, PCV-15, and PCV-20 coverage rates were 45.32%,



REVIEW

Human Vaccines & Immunotherapeutics 11:9, 2158–2166; September 2015; Published with license by Taylor & Francis Group, LLC

Adult vaccination: Now is the time to realize an unfulfilled potential

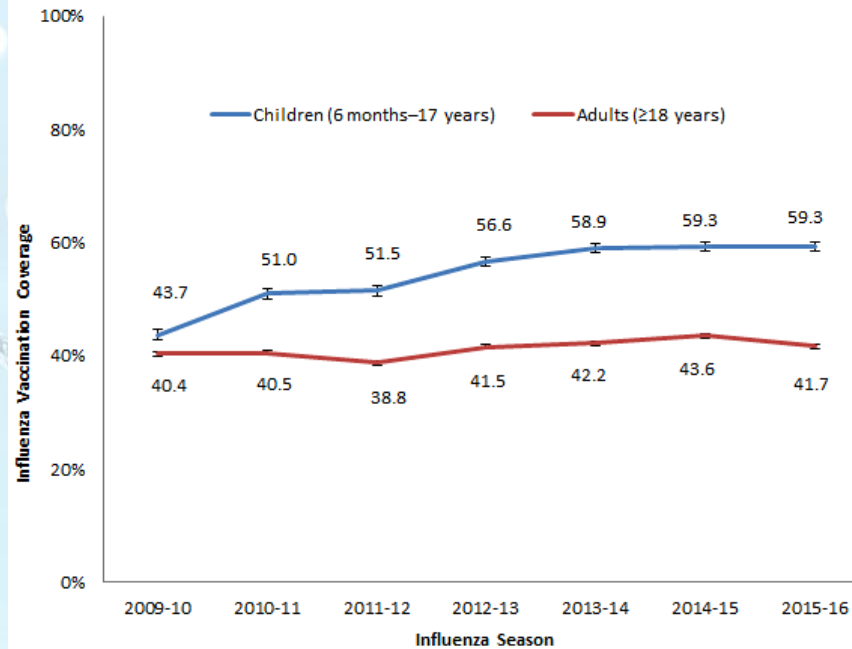
Litjen Tan*

Immunization Action Coalition; St Paul, MN USA

Keywords: adult immunization, immunization financing, immunization policy, immunization infrastructure, prevention, public health

Do you know the rate in Jordan??

Figure 1. Seasonal Flu Vaccination Coverage by Age Group and Season, United States, 2009–2016



Error bars represent 95% confidence intervals around the estimates.

The 2009-10 estimates do not include the influenza A (H1N1) pdm09 monovalent vaccine.

Starting with the 2011-12 season, adult estimates reflect changes in BRFSS survey methods: the addition of cellular telephone samples and a new weighting method.

Influenza infections : A frequent and serious disease leading to heavy public health burden



ANNUAL ATTACK RATE¹

- 5–10% in adults
- 20–30% in children



3 TO 5 MILLION CASES OF SEVERE ILLNESS²

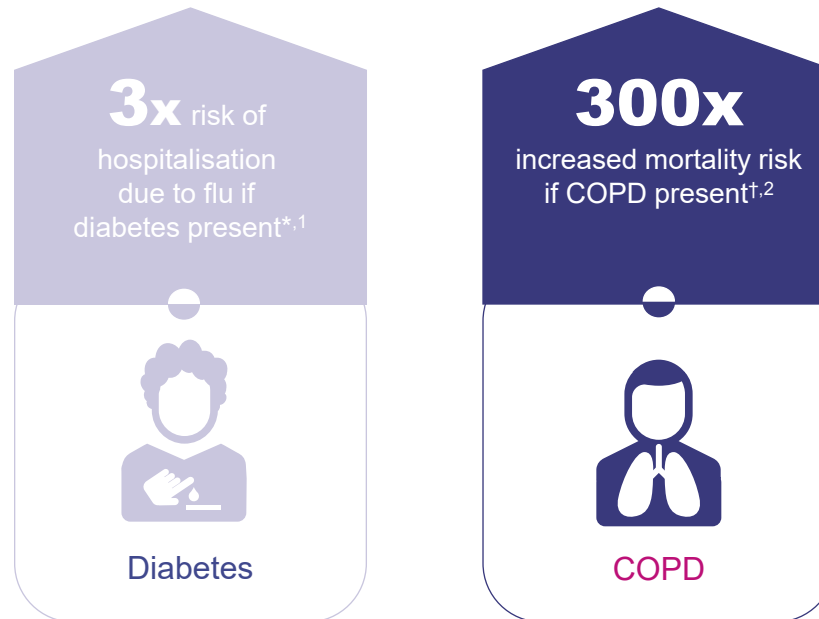


290,000 TO 650,000 ESTIMATED
DEATHS EVERY YEAR WORLDWIDE²

References: 1. WHO (<http://www.who.int/biologicals/vaccines/influenza/en/>) 2. WHO. Influenza (Seasonal) Fact Sheet. [http://www.who.int/news-room/fact-sheets/detail/influenza-\(seasonal\)](http://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal))

Concomitant NCDs increase the risk of complications of influenza

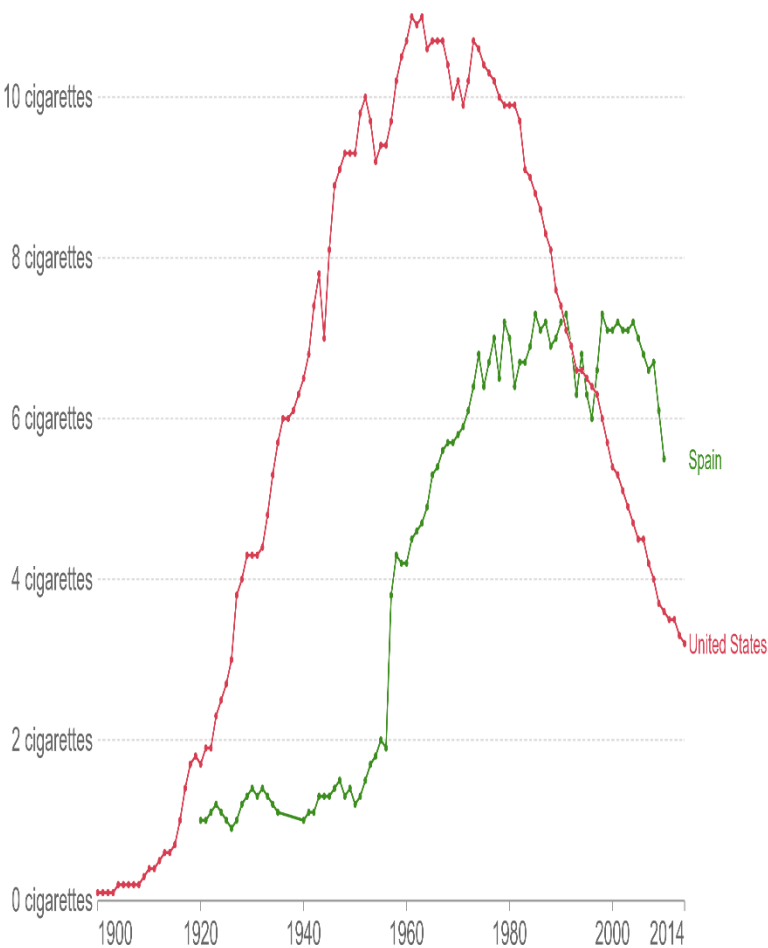
For individuals with influenza:



- COPD, chronic obstructive pulmonary disease; NCD, noncommunicable disease
- *Prevalence ratio for diabetes 3.10 (95% CI: 2.04–4.71) in 239 patients hospitalised with influenza A
- [†]Case fatality rate of influenza in patients with COPD ≥30% compared with 0.05–0.01% in otherwise healthy individuals
- Vallard R *et al. Diabetes Care* 2010;33:1491–1493; 2. Plans-Rubio P. *Int J Chron Obstruct Pulmon Dis* 2007;2:41–53

Sales of cigarettes per adult per day, 1900 to 2014

Figures include manufactured cigarettes, as well as estimated number of hand-rolled cigarettes, per adult (ages 15+) per day.

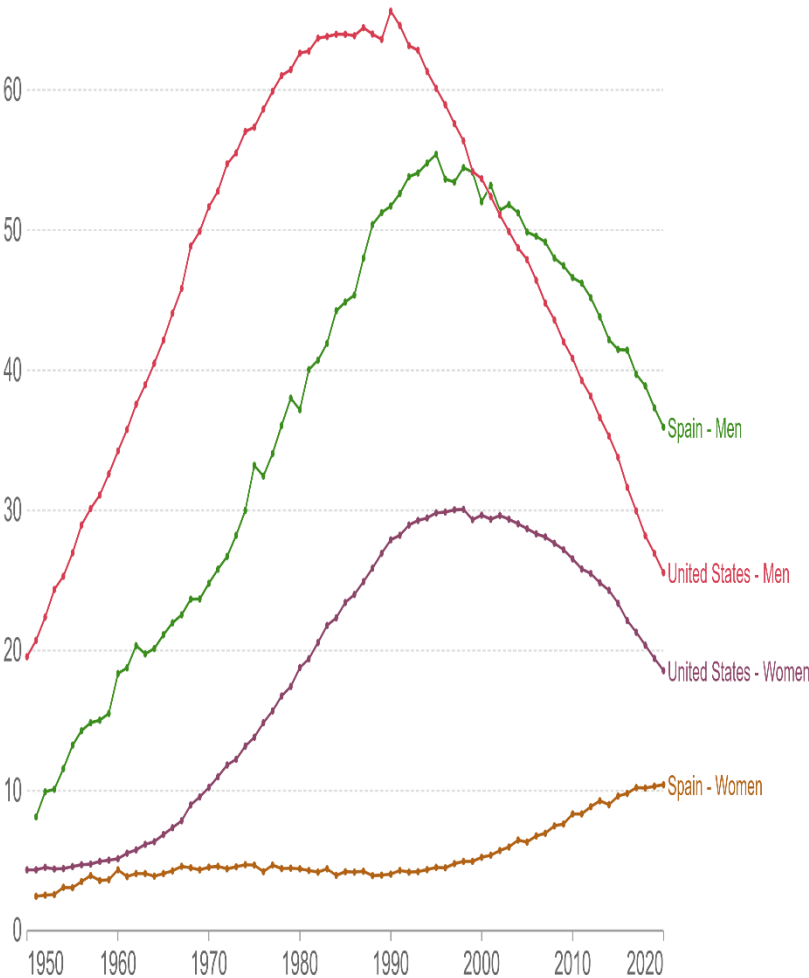


Source: International Smoking Statistics (2017)

OurWorldInData.org/smoking • CC BY

Lung cancer death rates, 1950 to 2020

Number of lung, bronchus and trachea cancer deaths per 100,000 people



Source: WHO Mortality Database (2022)

OurWorldInData.org/smoking • CC BY

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?

BRCA1 and BRCA2 genes mutations among 200 high risk breast cancer patients in Jordan

Referral to a specialist genetic clinic

1.4.4 People who meet the following referral criteria should be offered a referral to a specialist genetic clinic.

- At least the following female breast cancers only in the family:
 - 2 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 50 years (at least 1 must be a first-degree relative) **[2004] or**
 - 3 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years (at least 1 must be a first-degree relative) **[2004] or**
 - 4 relatives diagnosed with breast cancer at any age (at least 1 must be a first-degree relative). **[2004] or**
- Families containing 1 relative with ovarian cancer at any age and, on the same side of the family:
 - 1 first-degree relative (including the relative with ovarian cancer) or second-degree relative diagnosed with breast cancer at younger than age 50 years **[2004] or**
 - 2 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years **[2004] or**
 - another ovarian cancer at any age. **[2004] or**
- Families affected by bilateral cancer (each breast cancer has the same count value as 1 relative):
 - 1 first-degree relative with cancer diagnosed in both breasts at younger than an average age 50 years **[2004] or**
 - 1 first-degree or second-degree relative diagnosed with bilateral cancer and 1 first or second degree relative diagnosed with breast cancer at younger than an average age of 60 years. **[2004] or**
- Families containing male breast cancer at any age and, on the same side of the family, at least:
 - 1 first-degree or second-degree relative diagnosed with breast cancer at younger than age 50 years **[2004] or**
 - 2 first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years. **[2004] or**

From: *BRCA1* and *BRCA2* genes mutations among 200 high risk breast cancer patients in Jordan

Category	Number of patients	Prevalence (total 200)
Recurrent mutations		
BRCA1 Positive	15	7.50%
BRCA2 Positive	14	7.00%
BRCA1 or BRCA2 Positive	29	14.50%
Possible (recurrent and novel) mutations		
BRCA1 Positive	7	3.50%
BRCA2 Positive	14	7.00%
BRCA1 or BRCA2 Positive	21	10.50%
Recurrent and novel (VUS and pathogenic) mutations		
BRCA1 Positive	15	7.50%
BRCA2 Positive	21	10.50%
BRCA1 or BRCA2 Positive	36	18.00%

Abu-Helalah et al. <https://www.nature.com/articles/s41598-020-74250-2>

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

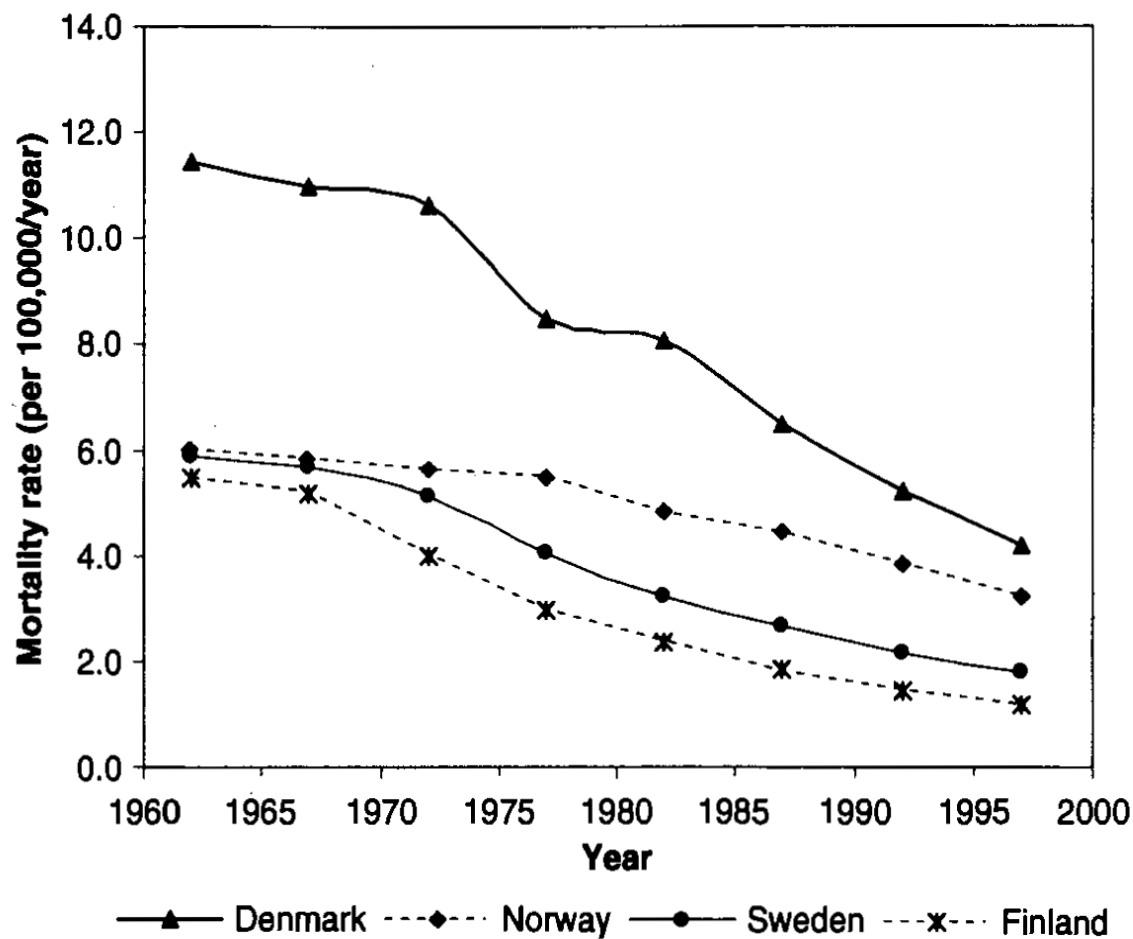


Fig. 14.5 Cervical cancer mortality rates (standardised relative to the world population) from 1950–1998 in the Nordic countries. (Data source: WHO Statistical Information System, accessed via <http://www-depdb.iarc.fr/who/menu.htm>, March 2004.).

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- Families containing male breast cancer at any age and, on the same side of the family, at least:
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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.

Under-diagnosed chronic kidney disease in Jordanian adults: prevalence and correlates

Amani A. Khalil, Mona A. Abed, Muayyad Ahmad, Ayman Hamdan Mansour

First published: 07 September 2017

<https://doi.org/10.1111/jorc.12214>

Background

Jordan has no relevant database or registry by which chronic kidney disease (CKD) would be early identified. The purpose of the present study is to uncover the prevalence of CKD in a national sample of Jordanian patients at high risk and examine the association of CKD with demographic and clinical factors.

Methods

This is a cross-sectional, correlational study that involved 540 outpatients at high risk for CKD. Demographic and clinical data were obtained in the period from September 2013 to March 2014. Prevalence of CKD was defined based on the National Kidney Foundation Kidney Disease Outcomes Quality Initiative Classification of CKD using estimated glomerular filtration rate. Associations of CKD and demographic and clinical factors were examined using bivariate analysis.

Results

The majority of the sample were females (64%), their mean age ($\pm$ SD) was 55.0 ± 12.5 years, their mean eGFR ($\pm$ SD) was 116.0 ± 47.5 . One third of patients had eGFR of 23.5%, 5.4%, 0.7% and 0.7% which corresponds with mild, moderate, severe and very severe reduction in eGFR, respectively. Ageing, being male, unemployment, packs/years of smoking, co-morbidities [hypertension (HTN), diabetes mellitus (DM) and cardiovascular disease] and low high density lipoprotein (HDL) correlated positively with development of CKD.

Conclusion

This study demonstrates a high rate of under-diagnosed CKD among Jordanians. Several demographic and clinical factors are linked with the development of CKD. Policymakers and healthcare providers need to establish an evidence-based practice project to prevent and screen for CKD in Jordan.

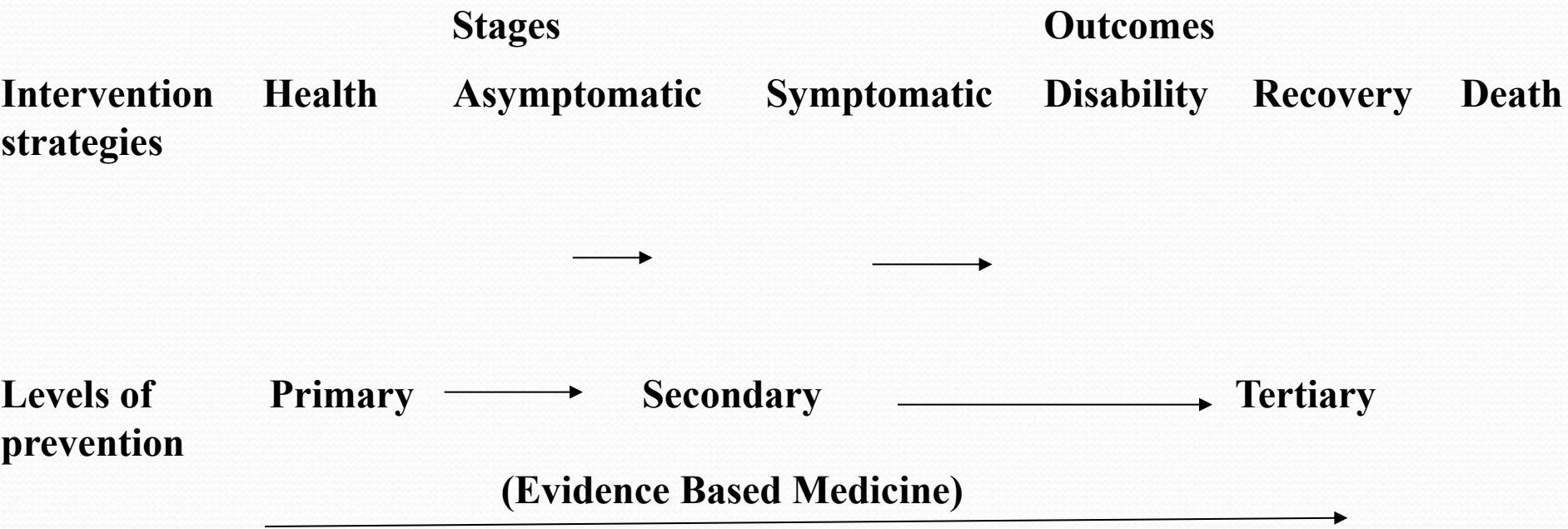
Quaternary prevention

Evidence Based Medicine

- One of the strongest methods to avoid unnecessary medical processes is **QUATERNARY 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





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.

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.)

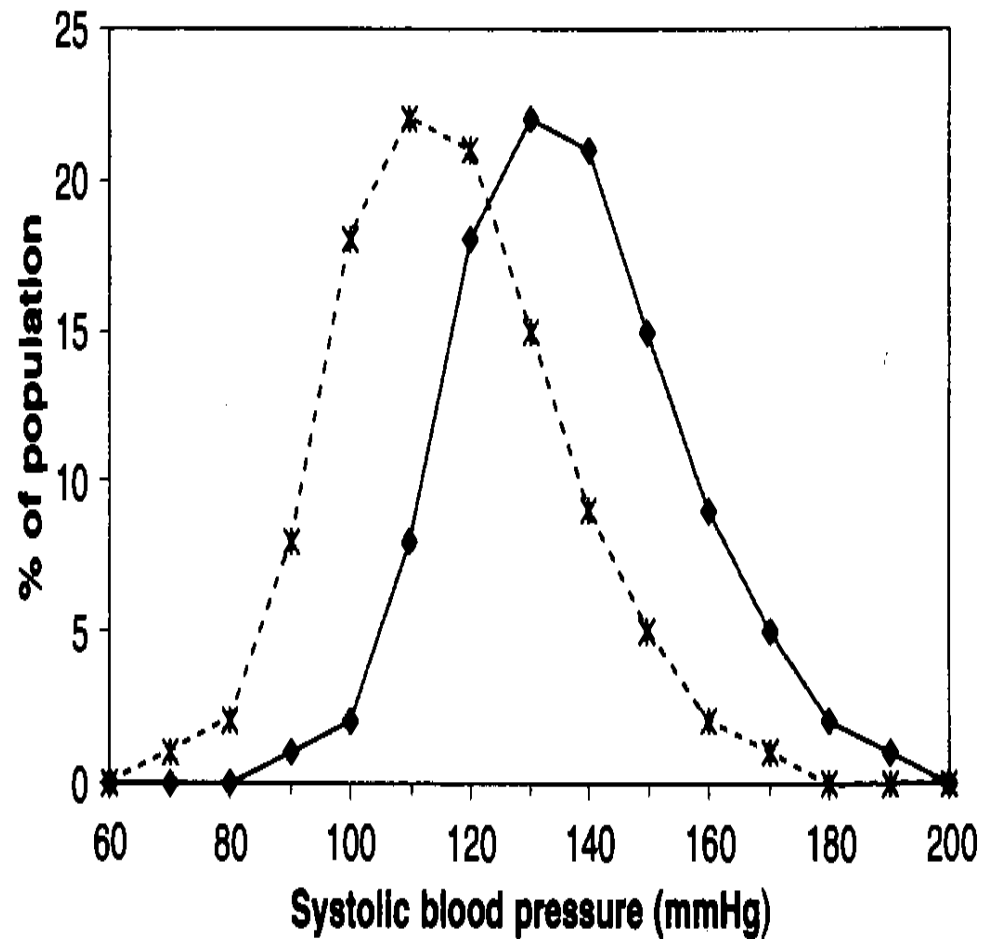


Fig. 13.6 Relative distributions of serum cholesterol levels in men who subsequently died of ischaemic heart disease and men who did not. (From Wald and Law, *BMJ*, 2003; 326: 1419–1425, reproduced with permission from BMJ Publishing Group.)

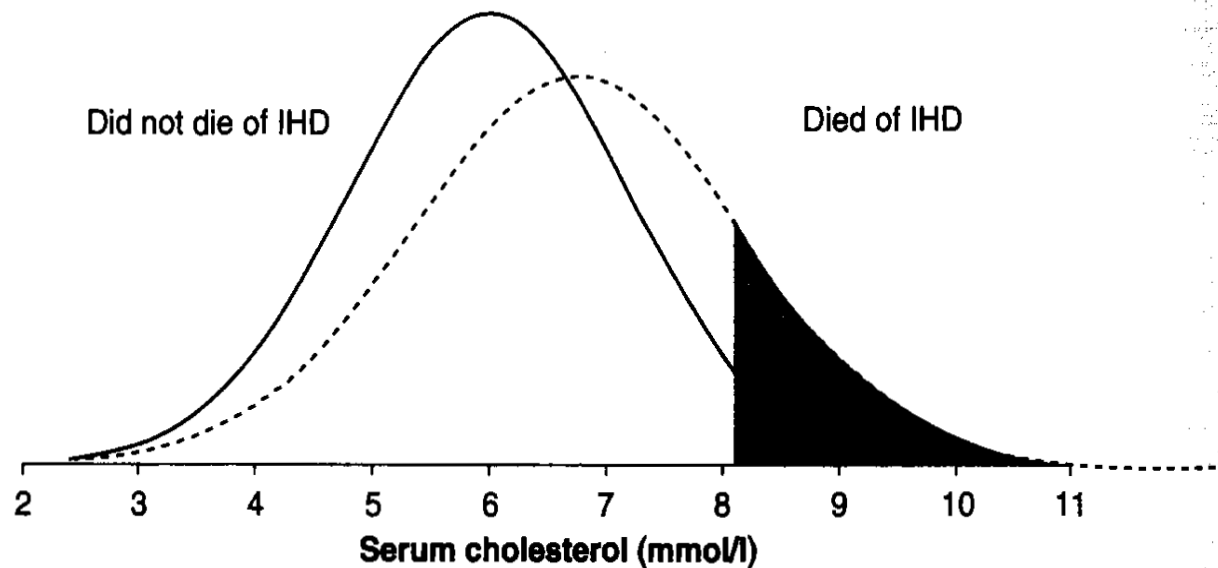


Figure 13.6 shows a concrete example of the close overlap in risk-factor distributions (in this case serum cholesterol level) between those who did and did not subsequently die from ischaemic heart disease (IHD). The whole curve for those who died from IHD is clearly shifted to the right, but the two 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.

Cancer Control Program

- An evidence based program aims to reduce cancer burden through:
 1. Reducing cancer incidence
 2. Minimizing cancer morbidity and mortality
 3. Prevention of cancer recurrence and complications
 4. Improvement of quality of life

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%)

FACTORS **I**NFLUENCING **S**URVIVAL FROM **C**ANCER

Treatment:

Availability

Access

Quality

Disease:

Natural history

Clinical extent

Definitions

Early Detection:

Early clinical detection

Screening

Host:

Age

Sex

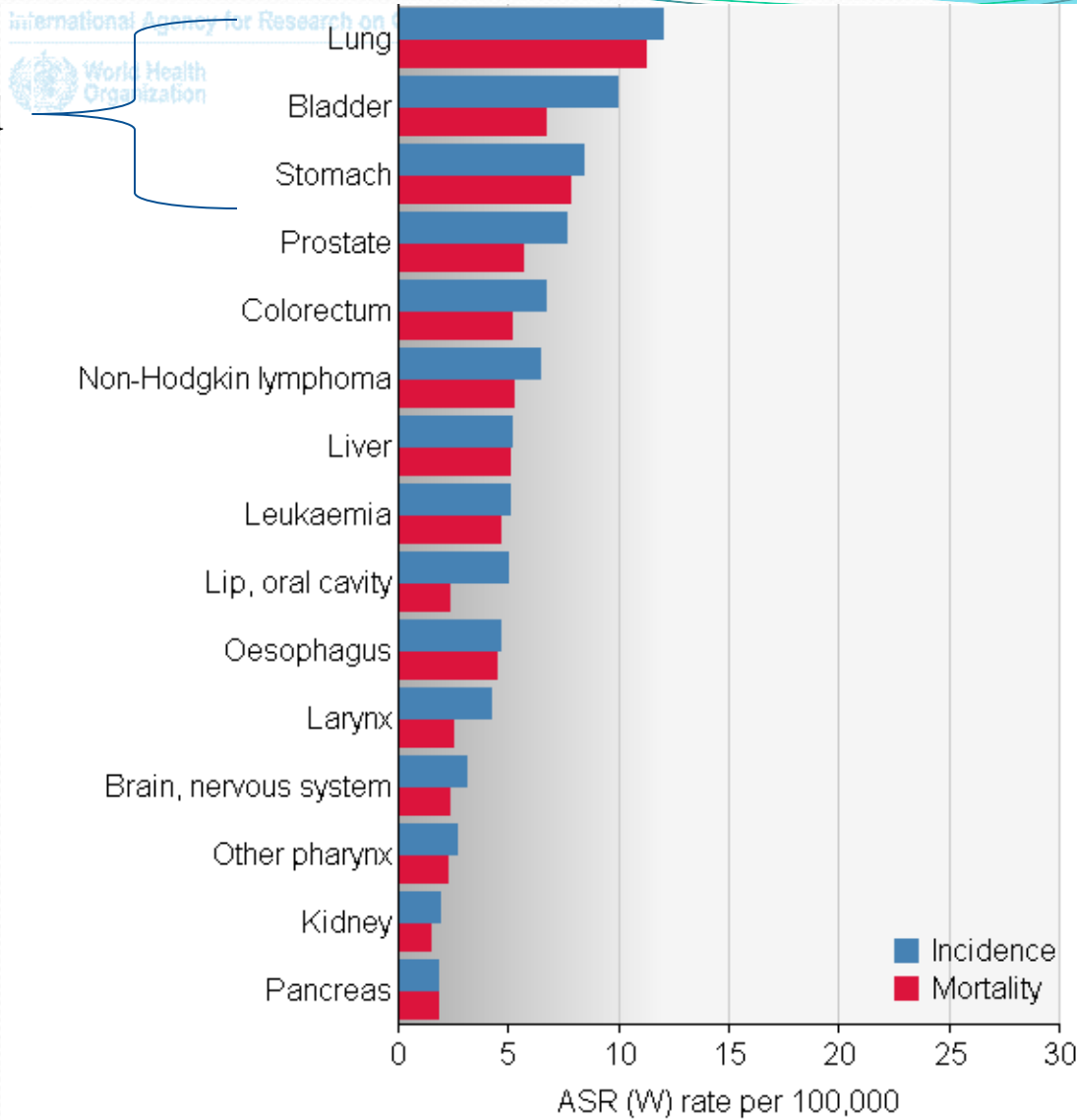
SES

Comorbidity

Behaviour

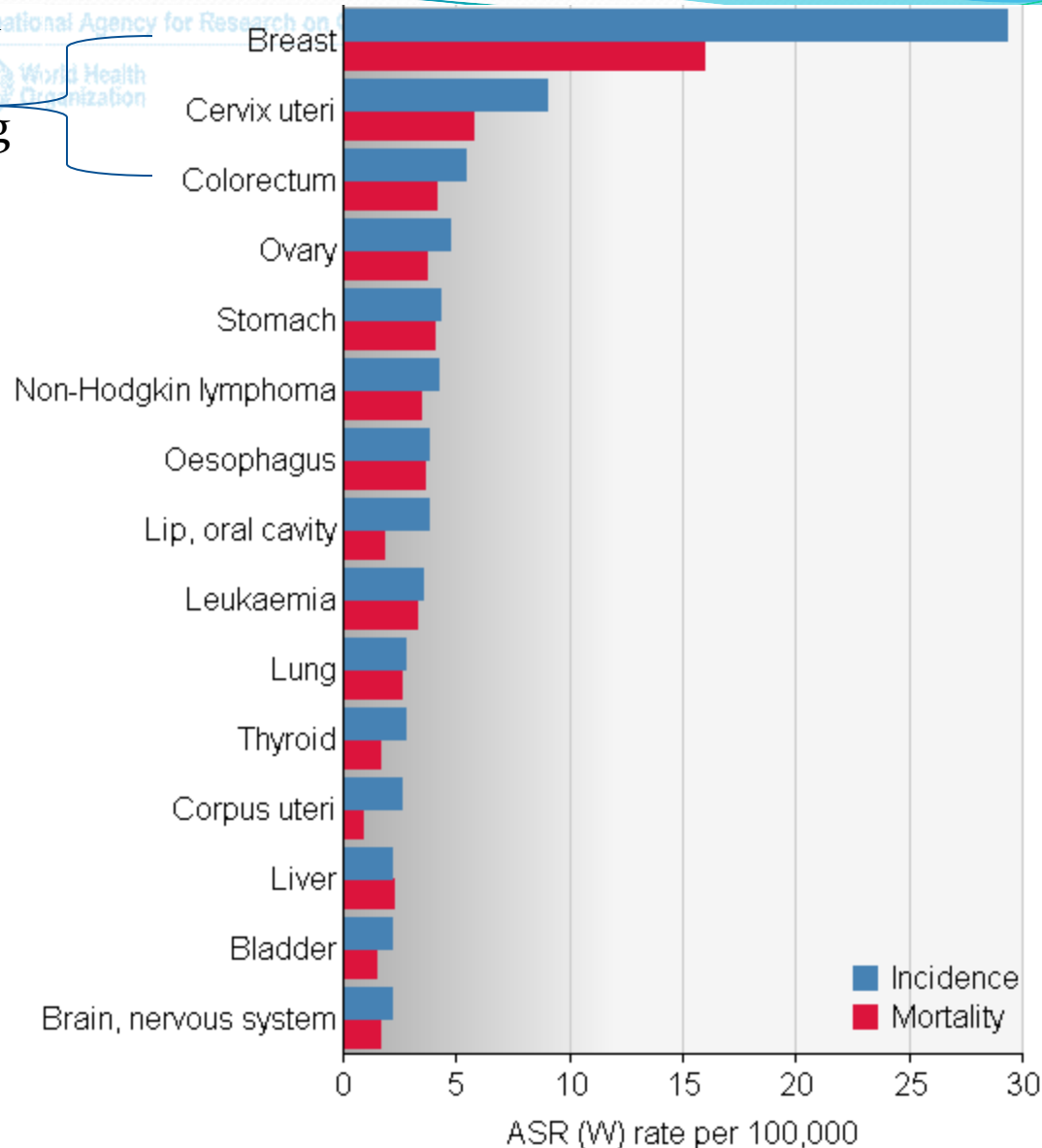
Estimated age-standardised incidence and mortality rates: men- Eastern Mediterranean region

Can be prevented



Estimated age-standardised incidence and mortality rates: women. Eastern Mediterranean region

We can detect them
through national
systematic screening
programmes

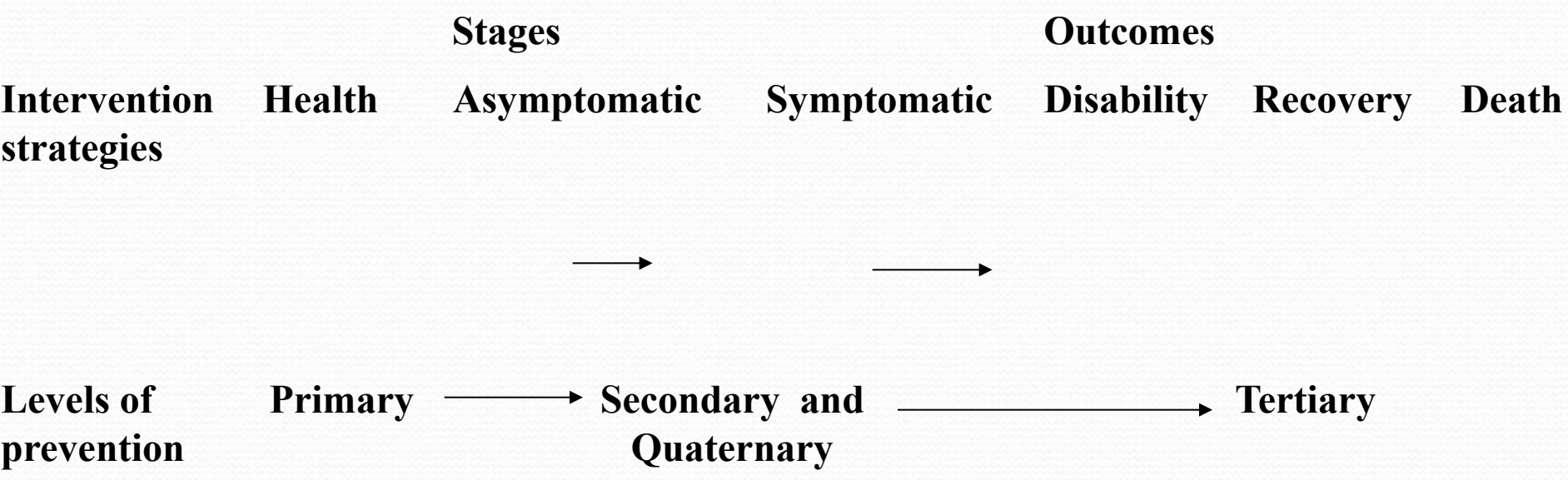




Compare
lung cancer prevention with
breast cancer prevention



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



What is screening

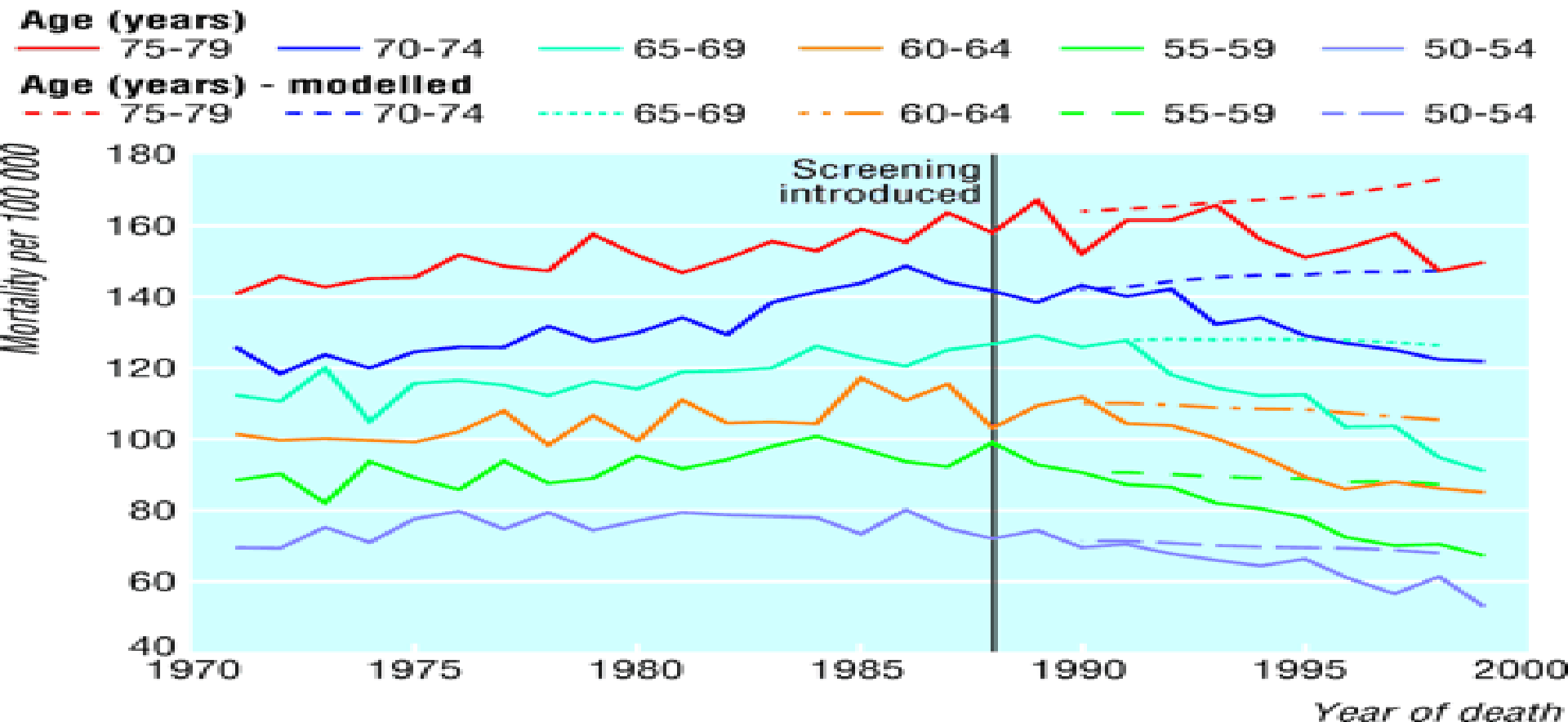
“The systematic application of a test or enquiry, to identify individuals at sufficient risk of specific disorder to benefit from further investigation or direct preventive action, among persons **who have not sought medical attention** on account of symptoms of that disorder.” Wald, 2004

Aims of screening

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

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 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
- If the patient has symptoms suggestive of the disease of interest, it is an EARLY DETECTION not screening

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.

Delay in presentation, diagnosis and treatment for Breast cancer patients in Jordan

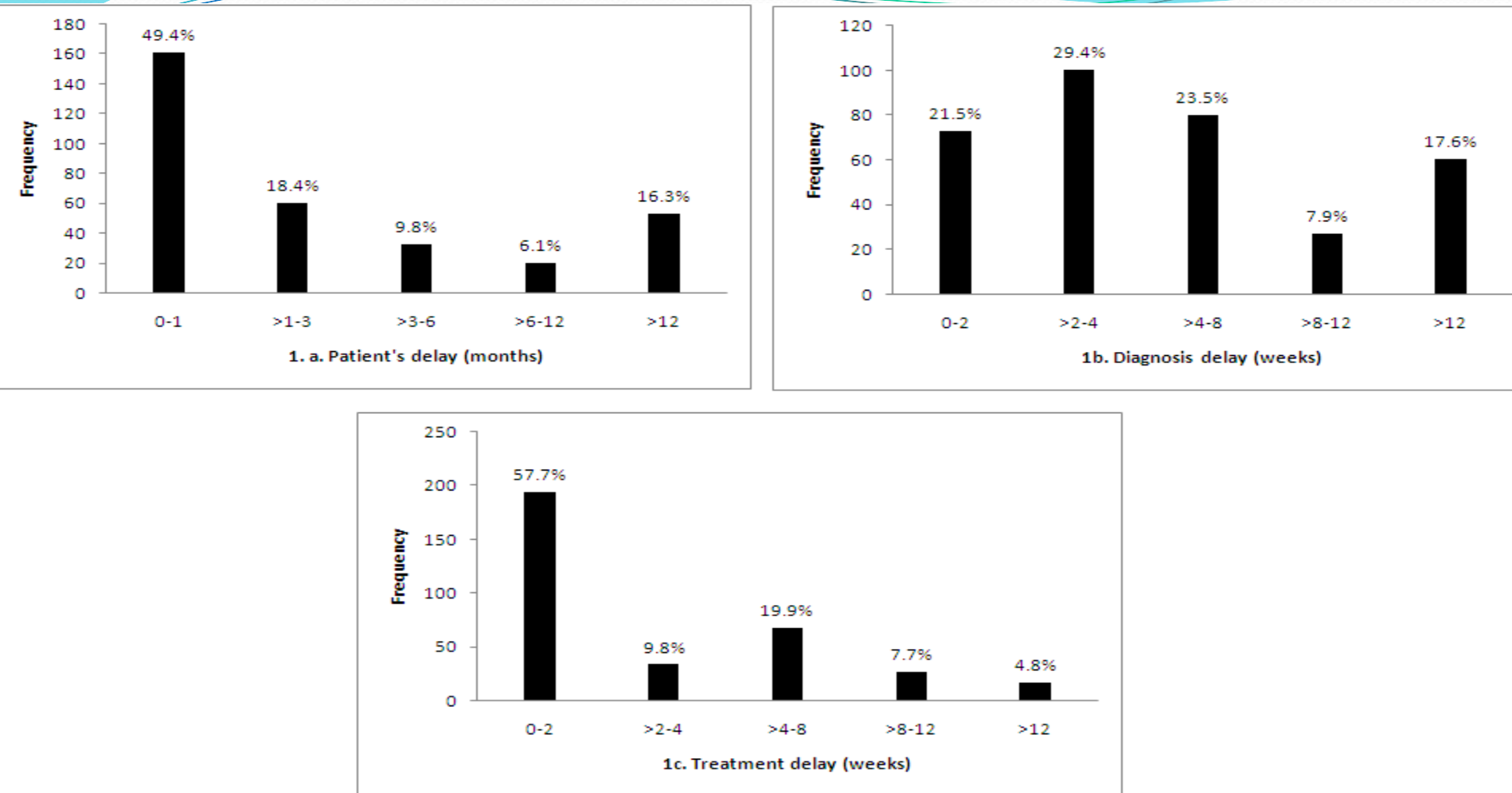
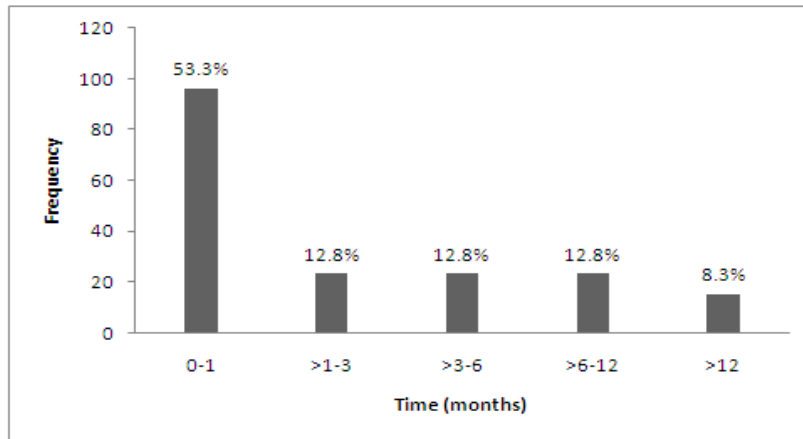


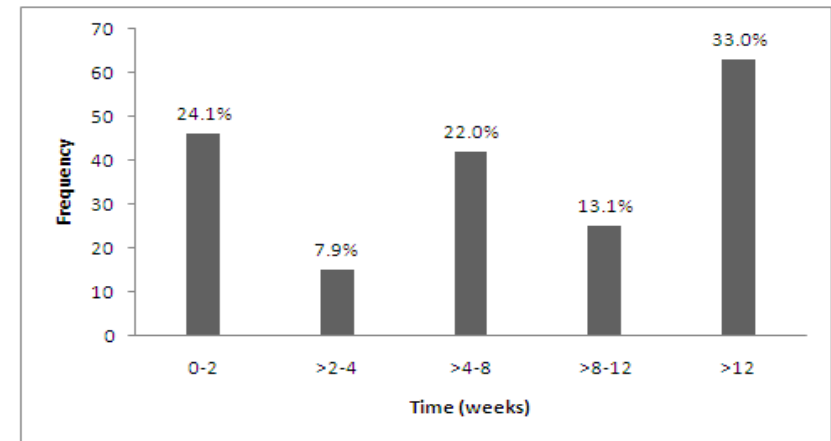
Figure 1: Proportion of participants by patient's delay, diagnosis delay, and treatment delay

Delay in presentation, diagnosis and treatment for colorectal cancer patients in Jordan

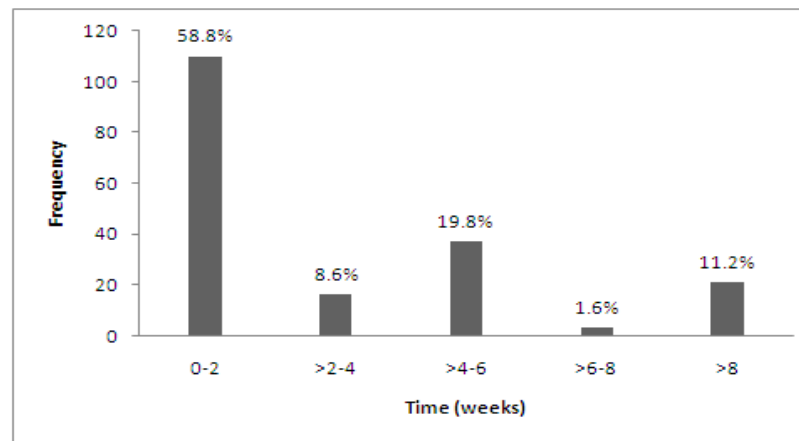
Fig1. Proportion of participants by patient's delay, diagnosis delay and treatment delay



(a)



(b)



(c)



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

Trial	Design	Subjects	<i>N</i> ; 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

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Original Article

A randomized double-blind crossover trial to investigate the efficacy of screening for adult hypothyroidism

M Abu-Helalah¹, M R Law², J P Bestwick³, J P Monson⁴, and N J Wald⁵

A Cross-Sectional Study to Assess the Prevalence of Adult Thyroid Dysfunction Disorders in Jordan

Munir Abu-Helalah,^{1,2} Hussam Ahmad Alshraideh,^{3,4} Sameeh Abdulkareem Al-Sarayreh,⁵
Ahmad Hassan Khalaf al Shawabkeh,⁶ Adel Nesheiwat,⁷ Nidal Younes,⁸ and Abdelfattah AL-Hader⁹

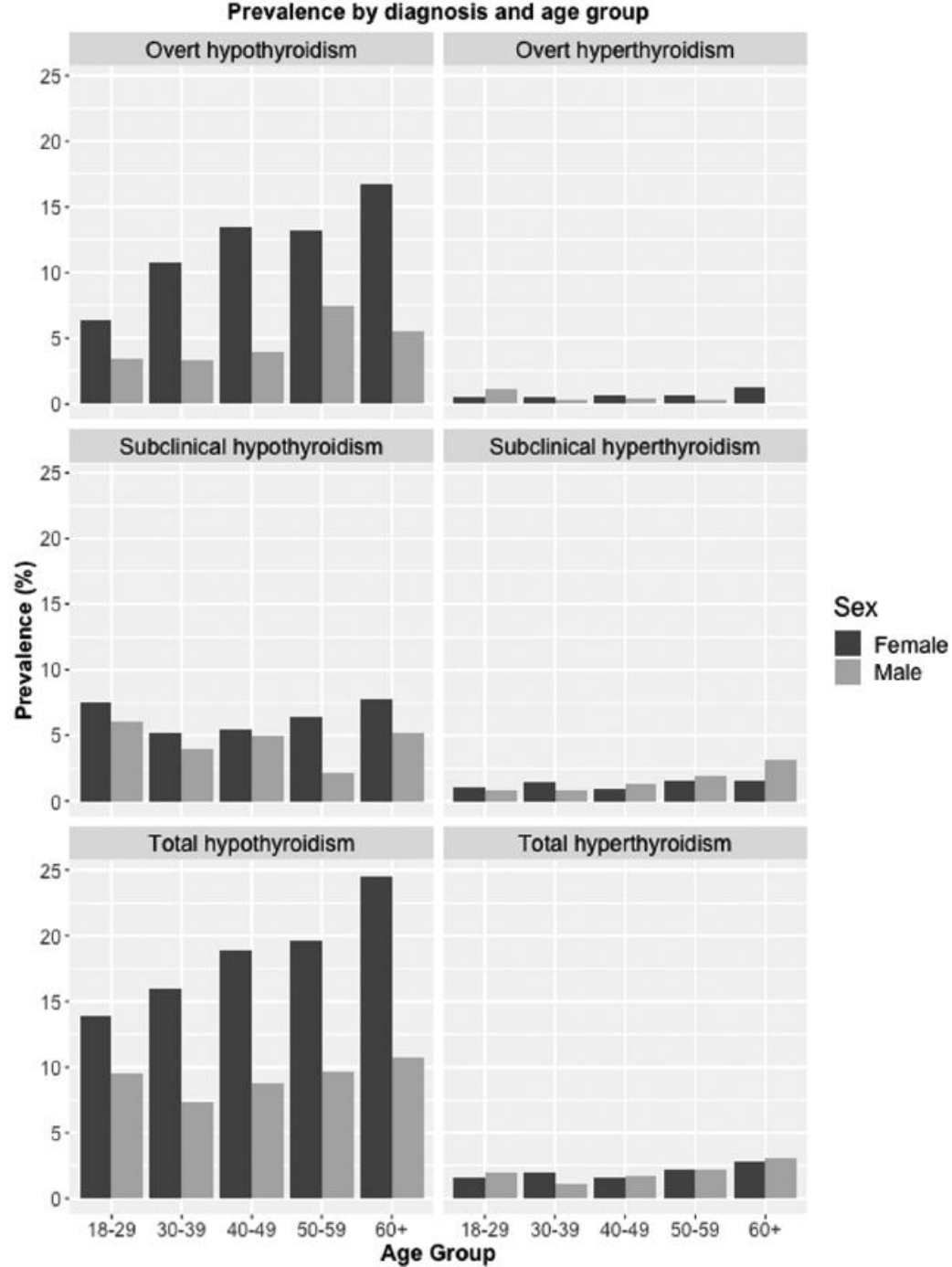
Background: Insufficient production of thyroid hormones results in hypothyroidism, while overproduction results in hyperthyroidism. These are common adult disorders, with hypothyroidism more common in the elderly. Jordan has had past problems with dietary iodine deficiency but there are no published studies assessing the population prevalence of these disorders in the Arab Middle East.

Methods: A cross-sectional study was conducted in three representative areas of Jordan. There were 7085 participants with a mean age of 40.8 years. Participants completed a questionnaire and had blood taken for thyroid analysis.

Results: *Hypothyroidism:* The prevalence of any hypothyroidism (already diagnosed and/or identified by blood testing) was 17.2% in females and 9.1% in males. Undiagnosed prevalence was 8% and 6.2% for females and males, respectively. The prevalence of subclinical hypothyroidism, defined as high serum thyrotropin (TSH) and normal serum-free thyroxine (fT4), was 5.98% among females and 4.40% among males. The prevalence of overt hypothyroidism, defined as high TSH and low fT4, was 2.00% among females and 1.80% among males. Only 53.5% (55.3% for females, 42.1% males) of those previously diagnosed with hypothyroidism had TSH levels within the appropriate range. *Hyperthyroidism:* The prevalence of any hyperthyroidism (already diagnosed and/or identified by blood testing) was 1.8% in females and 2.27% in males. The undiagnosed prevalence was 1.4% and 2.1% for females and males, respectively. The prevalence of subclinical hyperthyroidism (low TSH and normal fT4) was 1.20% and 1.80% among males and females accordingly. The prevalence of overt hyperthyroidism (low TSH and high fT4) was 0.2% among females and 0.3% among males. About 85.7% (83.3% for females, 100% males) of those previously diagnosed with hyperthyroidism had TSH levels within the appropriate range.

Conclusions: The results of this study reveal that the total prevalence of thyroid dysfunction among adult females and males in Jordan is very high compared with international statistics, particularly in the rates of undiagnosed cases. This indicates the need for further assessment of the value of screening for adult hypothyroidism in Jordan.

FIG. 1. Prevalence by diagnosis and age group.



What do you aim to achieve from your screening programme?

- Mortality
- Morbidity
- Quality of life and psychological wellbeing

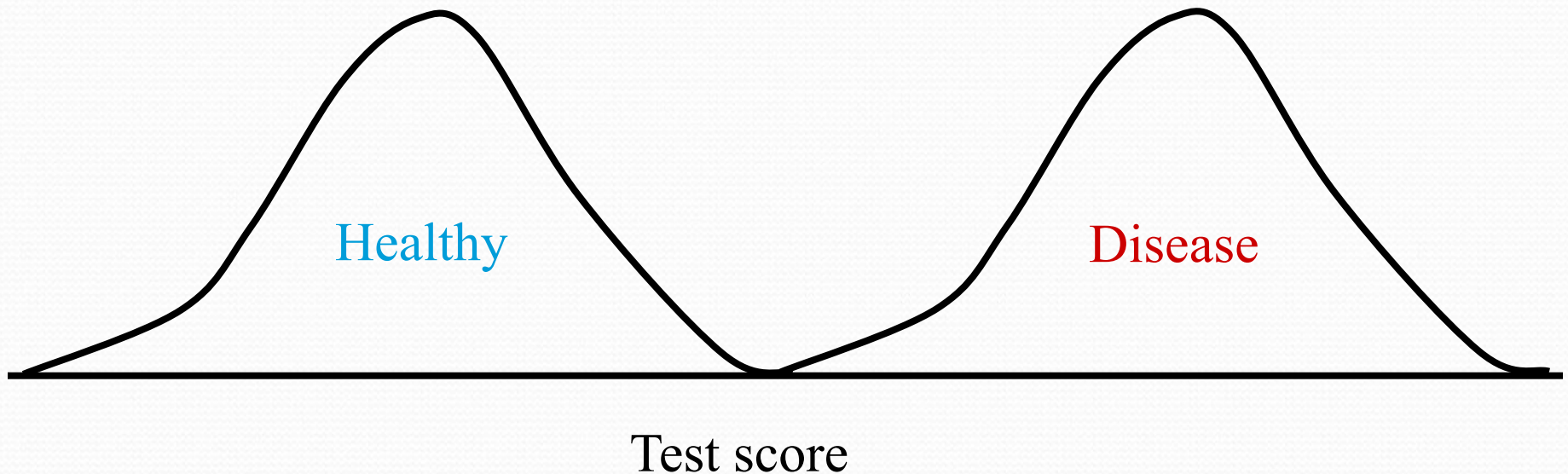
Screening test:

- 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

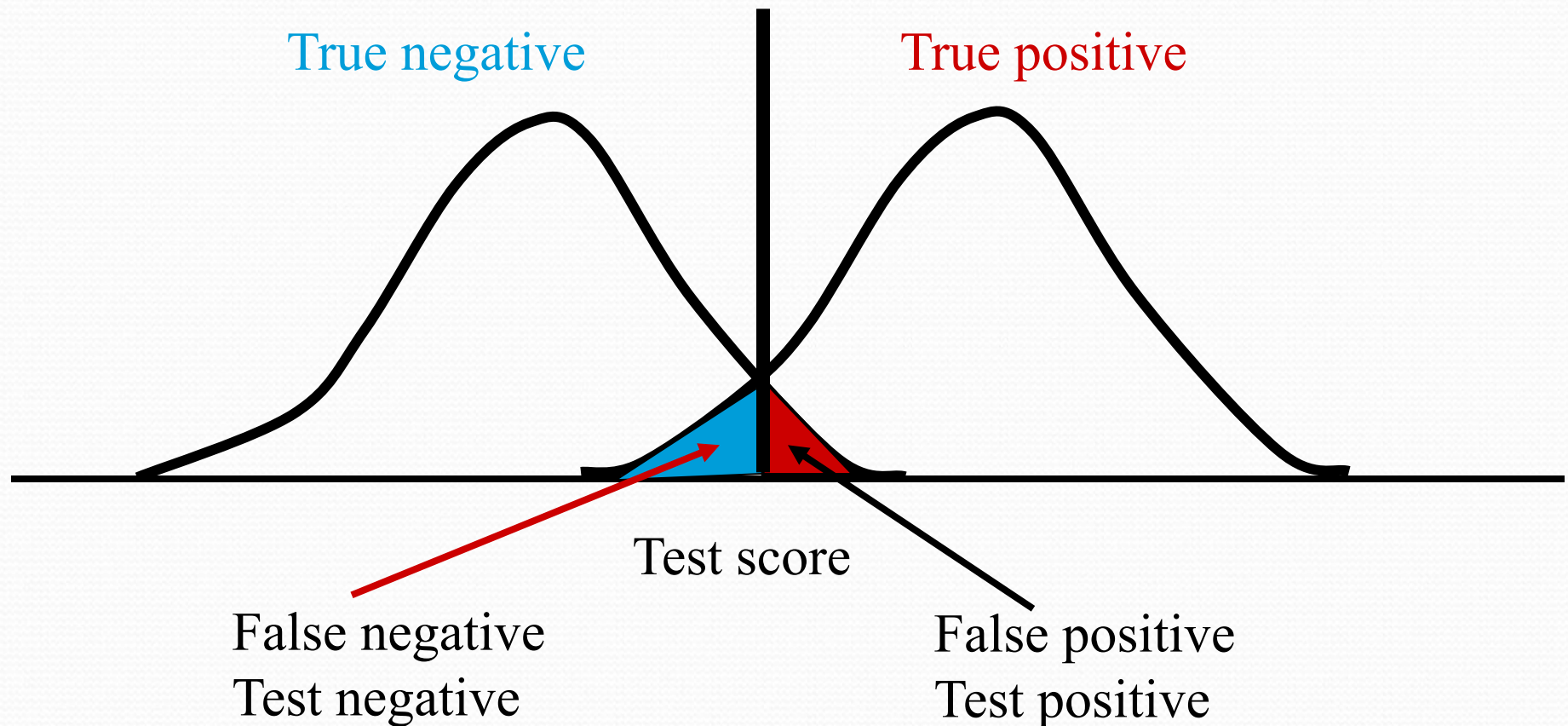
- The validity of a screening test can be evaluated through its detection rate (sensitivity) and specificity.
 - A. Detection rate (sensitivity) evaluates the ability of a screening tool to detect the disorder or problem. It represents the proportion of diseased individuals who have a positive screening 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	False negatives FN c	True negative TN d

	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

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

$$\text{Specificity} = \frac{\text{Well people with a negative test}}{\text{All well people}} = \frac{\text{TN}}{\text{TN} + \text{FP}}$$

$$\text{False positive rate} = \text{FP} / \text{FP} + \text{TN}$$

False positive rate

- The proportion of unaffected individuals with positive test results.
- False positive rate = $\frac{b}{b+d} = 1 - \text{specificity}$

Predictive values

- Positive predictive value= $\frac{\text{all true positives}}{\text{all positives (all true and all false)}} \times 100$
- 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= $\frac{\text{True negatives}}{\text{all negatives}} \times 100$
- 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

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

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

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

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	$\frac{b}{b+d} = (1 - \text{specificity})$	
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)		
		<i>Positive</i>	<i>Negative</i>	
Fecal occult blood screen test outcome	<i>Positive</i>	True Positive (TP) = 20	False Positive (FP) = 180	→ Positive predictive value = TP / (TP + FP) = 20 / (20 + 180) = 20 / 200 = 10%
	<i>Negative</i>	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%	

Example of validity assessment

	G-FOBT	FIT
Sensitivity	50.00% (6.76–93.24)	75.00% (19.41–99.37)
Specificity	77.87% (72.24–82.83)	90.12% (85.76–93.50)
Positive likelihood ratio	2.26 (0.83–6.18)	7.59 (3.86–14.94)
Negative likelihood ratio	0.64 (0.24–1.71)	0.28 (0.05–1.52)
Positive predictive value	3.45% (0.42–11.91)	10.71% (2.27–28.23)
Negative predictive value	98.99% (96.42–99.88)	99.56% (97.59–99.99)

False positive rates: $1 - \text{Specificity}$

More un-necessary colonoscopies and more cost
for the program

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

Sensitivities and specificities of different screening models for prediabetes

Screening model	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)
FPG $\geq$ 5.6 mmol/l	64.1 (61.7, 66.5)	65.4 (63.0, 67.8)
FPG $\geq$ 6.1 mmol/l	32.4 (30.0, 34.8)	88.3 (86.7, 89.9)
HbA1c $\geq$ 5.6%	66.2 (63.8, 68.6)	51.0 (48.5, 53.5)
FPG $\geq$ 5.6 mmol/l and HbA1c $\geq$ 5.6%	42.4 (39.9, 44.9)	82.4 (80.5, 84.3)
FPG $\geq$ 5.6 mmol/l or HbA1c $\geq$ 5.6%	87.9 (86.3, 89.5)	33.4 (31.0, 35.8)

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.

UKCCCR multicentre randomised controlled trial of one and two view mammography in breast cancer screening

Nicholas J Wald, Philip Murphy, Philippa Major, Carol Parkes, Joy Townsend, Chris Frost

Abstract

Objective—To compare one view (oblique) and two view (oblique and craniocaudal) mammography in breast cancer screening.

Design—Randomised controlled trial.

Setting—Nine breast screening centres in England.

Subjects—40 163 women aged 50–64 attending their first breast screening examination.

Interventions—Women were randomised to have one view mammography, two view mammography, or two view mammography in which one view was read by one reader and both views were read by another.

Main outcome measures—Prevalence of cancer detected, recall rates, cost per cancer detected, and marginal cost per extra cancer detected.

Results—Two view mammography detected 24% more women with breast cancer (95% confidence interval 16% to 31%) than one view mammography. Prevalence of detected cancer was 6.84 with two view mammography and 5.52 per 1000 women with one view. The proportion of women recalled for assessment was 15% lower (95% confidence interval 6% to 23%) with two view (6.97%) than with one view (8.16%) mammography. The cost of two view screening was higher (£26.46 compared with £22.00 per examination) but the average cost per cancer detected was similar (£5330 compared with £5310) and the marginal cost per extra cancer detected with two views was similar to the average cost (£5400).

Conclusion—Two view mammography is medically more effective than one view; it detects more

cases, knowing that the second film reading could correct the high recall rate.

To resolve the matter we, with the support of the United Kingdom Coordinating Committee on Cancer Research (UKCCCR) conducted a randomised trial allocating women to one view or two view mammography to determine (a) the additional breast cancer detection achievable with two views instead of one at the first screening examination, (b) the recall rates for the two policies, and (c) the economic implications of the two policies.

Patients and methods

A total of 40 163 women were recruited between 1990 and 1994 from nine centres in England (West London 10 610, Brighton 8048, Worthing 6564, North London 4260, Liverpool 3858, Reading 3141, Winchester 2388, Leeds 1060, and Southampton 234). Twenty one national breast screening programme film readers took part. All but two were radiologists. Women aged 50–64 were eligible for the trial at their first screening examination if they had not had breast surgery and could give consent. To be eligible for the trial, centres must have screened at least 5000 women as part of a general screening programme and identified at least four breast cancers for every 1000 women screened, with a recall rate of less than 10%, and have at least two film readers (X and Y).

In each centre women were randomised to one of three groups in the ratio 1:1:2 by means of a computerised random numbers generator. Group 1 had oblique view mammography alone, interpreted by film reader X; group 2 had two view mammography, interpreted by film reader X; and group 3 had two

Agreed plan on further investigation, diagnosis and treatment:

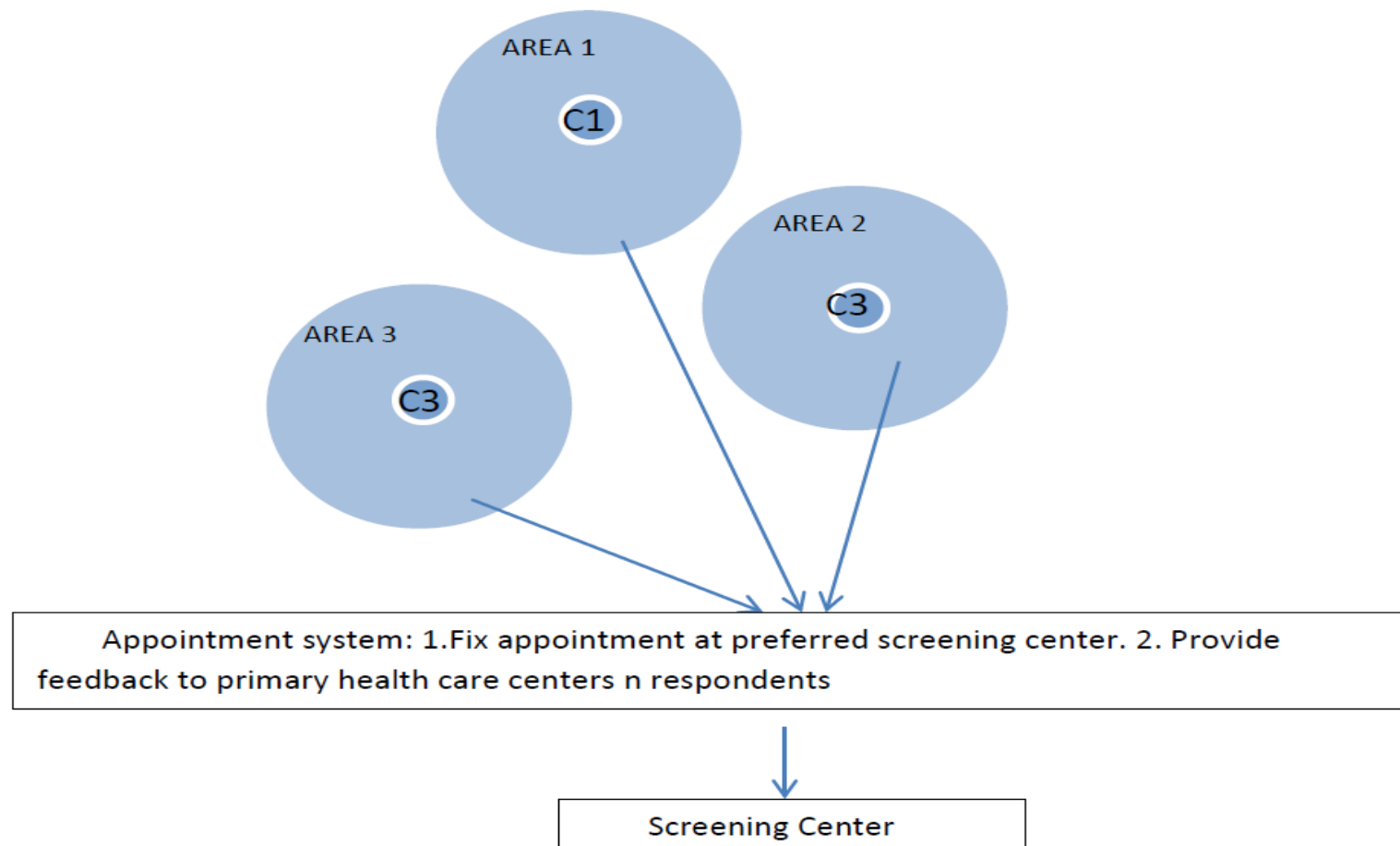
- Where to refer your positive subjects
- What is the diagnostic tests
- Who will pay for the investigations and treatments
- Diagnostic tools, screening intervals and treatment
- Facilities required for such steps should also be available or easily installed and equally accessed by the screened population

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.**



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 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.

Cut it down so it will be simple

Practical example: In country X, there are 1000000 women aged 40-70 who are eligible for screening

1000000	Women aged 40-70					
To be screened annually		500000				
75% response rate:		375000				
300 working days/ 6 days work			1250			
	if there are 12 main districts in your country					
25 centers in the whole country	2 mammograms per center	50 mammograms				
1250/50	25 subjects Per machine per day	7 working hours, means 4 subjects per hour	In the UK, 6-8 patients per hour per machine.			
If we have only 5 centers in Amman, 3 centers in Irbid, 2 centers in Zarqa, 2 centers in Karak and one center in the remaining governorates						
we need 50 machines in 25 centers for 1 million women across Jordan						
This number is already available and can be provided at the public sector						

Breast self-examination and death from breast cancer: analysis

AK Hackshaw^{*,1} and **EA Paul¹**

¹Barts & The London School of Medicine & Dentistry, Wolfson Institute of Environmental & Preventive Medicine, Queen Mary, University of London, Charterhouse Square, London EC1M 6BQ, UK

Breast self-examination (BSE) is widely recommended for breast cancer prevention. Following recent controversy over mammography, it may be seen as an alternative. We present a meta-analysis of the effect of regular BSE on breast cancer mortality. From a search of the medical literature, 20 observational studies and three clinical trials were identified that reported breast cancer death rates or rates of advanced breast cancer (a marker of death) according to BSE practice. A lower risk of mortality from breast cancer was only found in studies of women with breast cancer who reported practising BSE before diagnosis (pooled relative risk 0.64, 95% CI 0.56–0.73; advanced cancer, pooled relative risk 0.60, 95% CI 0.46–0.80). The results were not significant due to bias and confounding. There was no difference in death rate in studies on women who detected their breast cancer by self-examination (pooled relative risk 0.90, 95% CI 0.72–1.12). None of the trials of BSE training (in which most women practised it regularly) showed lower mortality in the BSE group (pooled relative risk 1.01, 95% CI 0.92–1.12). Thus, BSE is associated with considerably more women seeking medical advice and having biopsies. **Regular BSE is not associated with a reduction in breast cancer mortality.**

British Journal of Cancer (2003) **88**, 1047–1053. doi:10.1038/sj.bjc.6600847 www.bjcancer.com

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Keywords: breast self-examination; breast cancer; mortality; meta-analysis

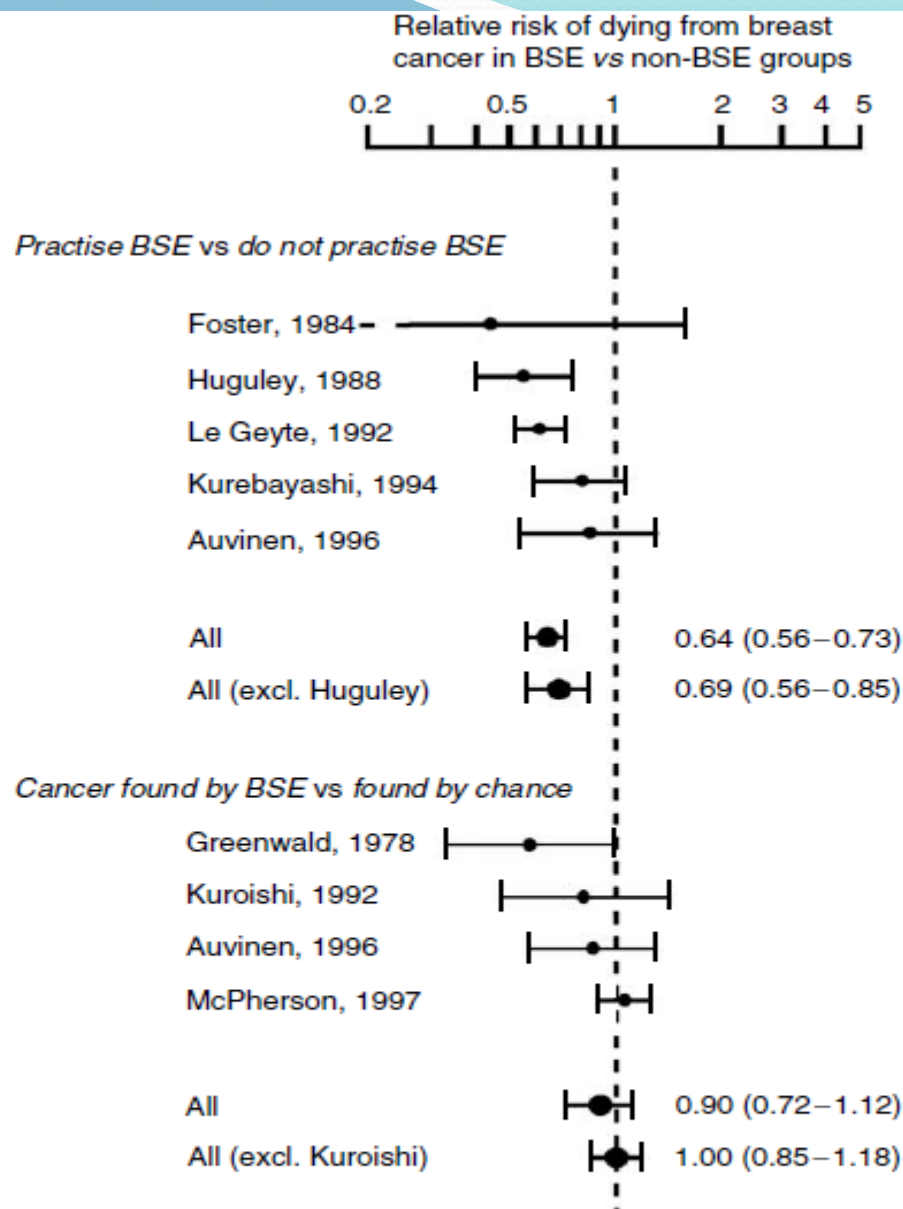
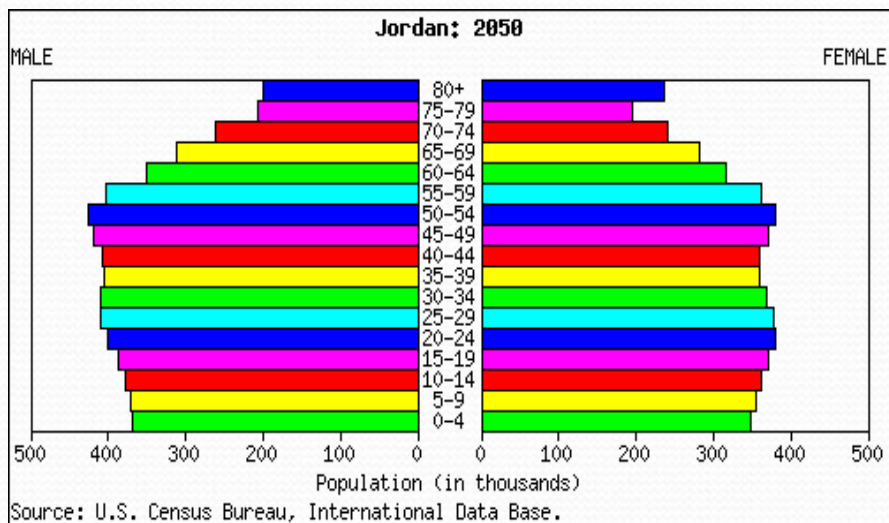
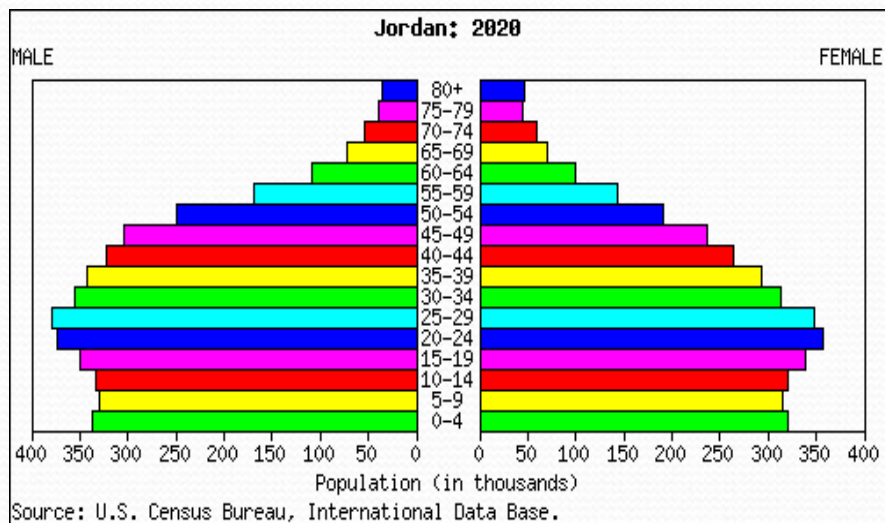
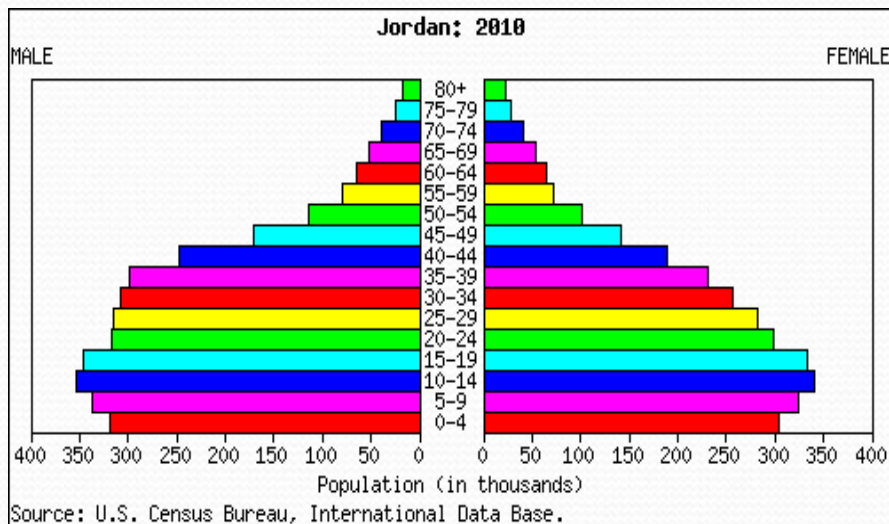
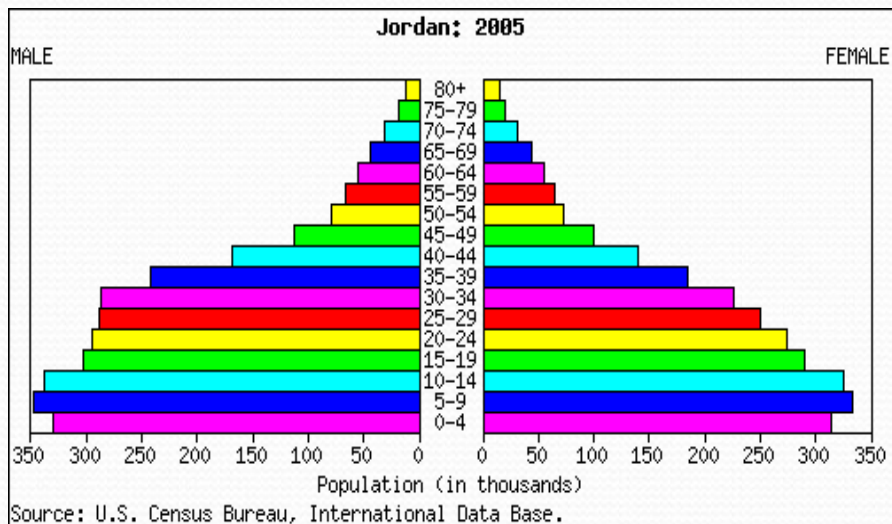


Figure 1 Observational studies of women with breast cancer, comparing the breast cancer death rates between the BSE and non-BSE groups. A test for heterogeneity between the studies yielded a *P*-value of 0.41 for those studies based on women who practise BSE and a *P*-value of 0.26 for those based on finding cancer by BSE.

Population pyramids- Jordan



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

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.
- **Each country should has its own studies and data**
- What is cost effective in the UK might not be cost effective in Jordan or India
- In breast cancer screening: age range for screening plays a key role in the cost-effectiveness of the program
- UK (Screening aged 50-70 Every three years, then in few years ago aged 40-49 at high risk)
- Sweden (age 40-70) annually

MAMMOGRAPHIC SCREENING

Economic evaluation of a mammography-based breast cancer screening programme in Spain

ROBERTO GARUZ, TARSICIO FORCÉN, JUAN CABASÉS, FERNANDO ANTONÁNZAS,
CRISTINA TRINXET, JOAN ROVIRA, FRANCISCO ANTÓN *

The aim of the study was to perform a cost-effectiveness analysis of a breast cancer (BC) mammography screening programme, compared to a do-nothing alternative, in Spain. Screening consisted of a biennial mammography performed on all women 50-65 years old. A marginal analysis including women 45-49 years old was also performed. With the aid of a decision tree model, the numbers of BC cases diagnosed through screening, BC cases missed by screening and false-positive BC cases were calculated. Costs were calculated by feeding local data into Markovian models and the cost-effectiveness ratio calculation was performed in a computer spread sheet. A sensitivity analysis was also conducted. Results were presented in ECUs of 1993. The cost-effectiveness ratio per avoided death is 115,500 ECUs and per saved life year 7,300 ECUs. Including women 45-49 years old in the programme raises this ratio to 229,000 and 9,400 ECUs respectively. The sensitivity analysis showed the efficacy of mammography, compliance of the programme and screening costs to be the more sensitive variables.

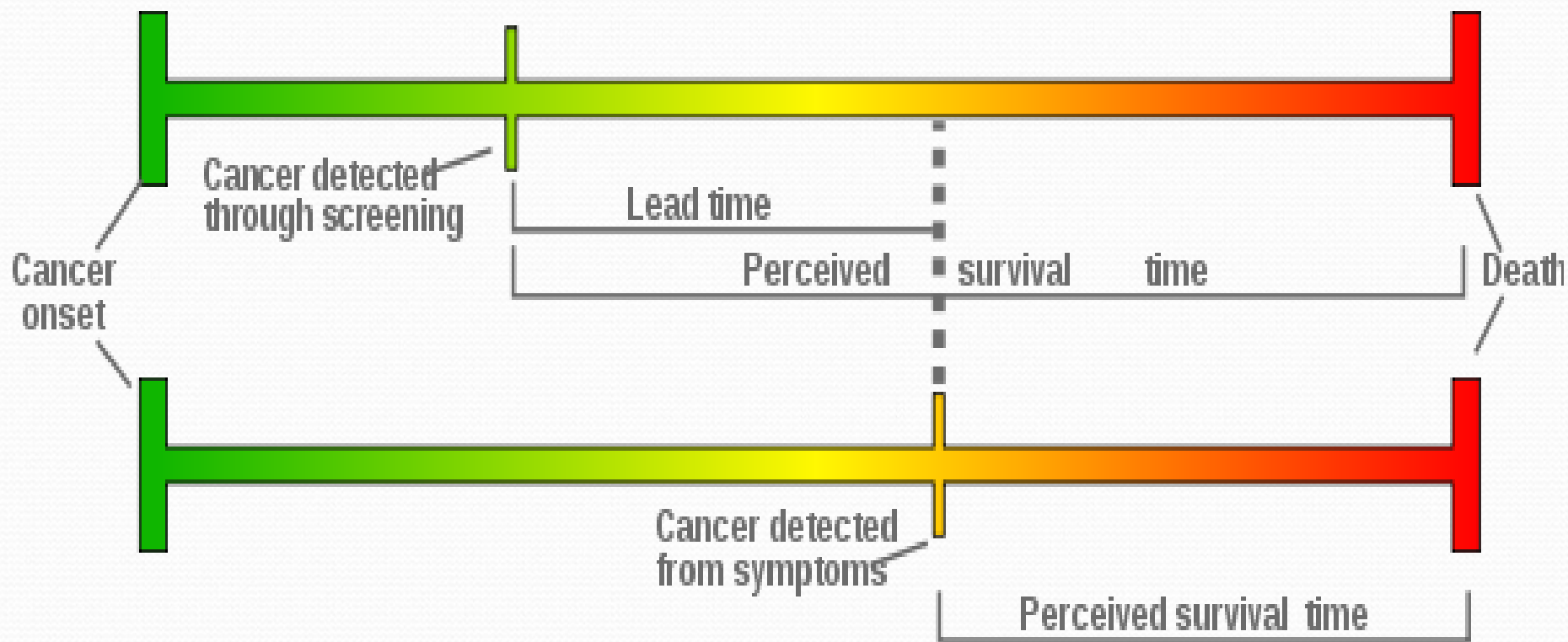
Key words: breast cancer, screening, economic analysis, cost-effectiveness analysis

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-volunteers may be related 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



Lead time bias in Prostate cancer

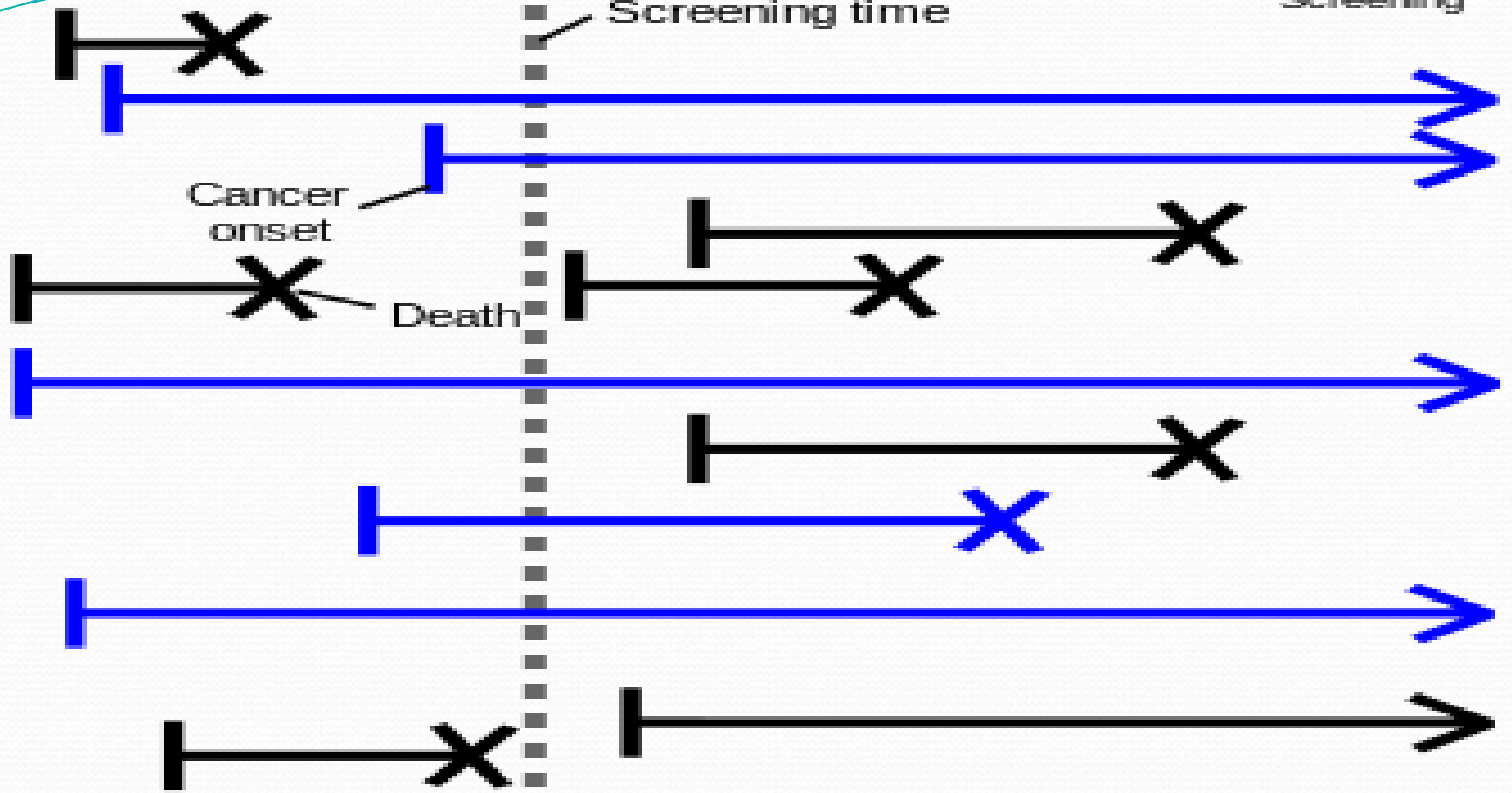
- **Lead Times and Over detection Due to Prostate-Specific Antigen Screening: Estimates From the European Randomized Study of Screening for Prostate Cancer**
- Gerrit Draisma Rob Boer Suzie J. Otto Ingrid W. van der Cruijsen Ronald A. M. Damhuis Fritz H. Schröder Harry J. de Koning
- *JNCI: Journal of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

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

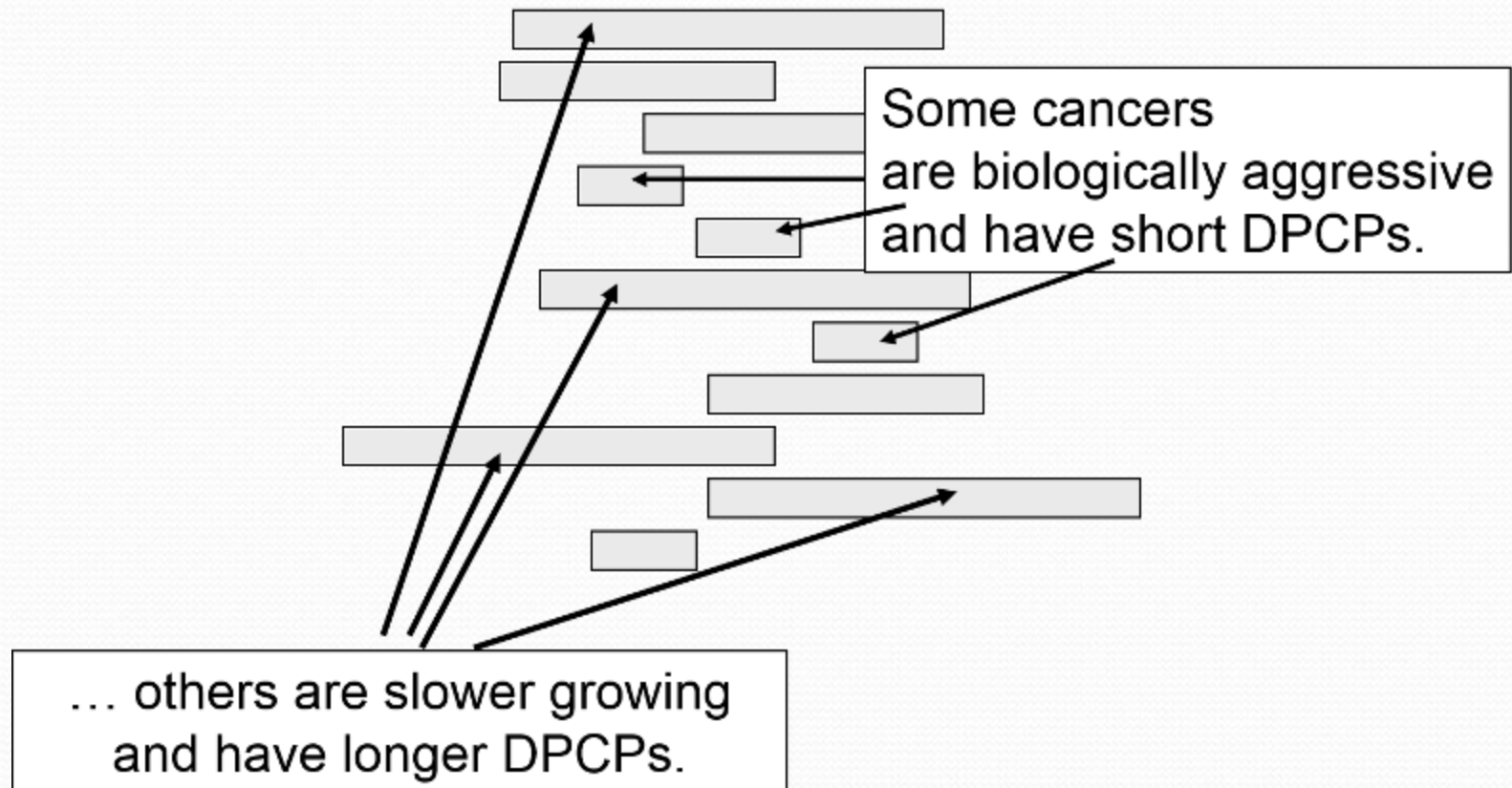
- Faster-growing tumors generally have a shorter asymptomatic phase than slower-growing tumours, and so are less likely to be detected. However, faster-growing tumors are also often associated with a poorer prognosis. Slower-growing tumors are hence likely to be over-represented in screening tests. This 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