

# Implementing population based screening programs

## Based on integrated risk profiling

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# **Health expectancy**

## Life expectancy

- Men: 75,5
- Women: 80,6

### Health expectancy

- Men: 61,3 (last 14 years sickness)
- Women: 60,8 (last 20 years sickness)

# Waiting for symptoms inefficient



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"A cardiovascular event must be regarded as a medical failure rather than the first indication for treatment".

Dr. William B. Kannel, a principal investigator for the Framingham Heart Study

## **Disease as process**



Symptoms are not the start of the disease

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Advantages in diagnostic testing enable early intervention



## Body Scan

SCAN

Cardiovascular disease and cancer for almost 3 out of every 4 deaths.

SCAN



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#### InnerVision Body Scans Price List

Heart Scan	\$450.00
Lung Scan	\$400.00
Heart and Lung Scan	\$750.00
Full Body Scan	\$950.00
Brain Scan	\$200.00
Virtual Colonoscopy	\$950.00

InnerVision accepts major credit cards (VISA and Mastercard), checks with proper ID, and cash.

Gift Certificates are available. Call toll-free 866 S BESURE (866-523-7673) for more information.



# Advanced diagnostics: how to apply?

#### **Total body scanning**

Advanced testing in an unselected population is undesirable, cost-ineffective and could even be 'dangerous'

- false positive results
- overdiagnosis
- unnecessary treatment
- medicalization and stigmatization

→ weighing risk versus benefit is important
 → adequate selection high-risk individuals is essential



# Disease

	Present	Absent
Positive	True positives	False positives
Line Test Negative	<b>False</b> negatives	<b>True</b> negatives







# True negative



# Certificate of health effect !?



















# Validity of Screening Tests

# **Key Measures**

- Sensitivity
- Specificity
- Positive Predictive Value
- Negative Predictive Value



# Disease





# Sensitivity

 Proportion of individuals who have the disease who test positive (true positive rate)

Tells us how well a positive test picks up disease



Sensitivity 
$$= \frac{a}{a+c}$$



# Specificity

 Proportion of individuals who don't have the disease who test negative (true negative rate)

Specificity \_\_\_\_

Tells us how well a normal test excludes disease





# In other words

## Sensitivity

 the ability of a test to correctly identify those who have a disease

A test with high sensitivity will have few false negatives

## Specificity

 the ability of a test to correctly identify those who do not have the disease

A test that has high specificity will have few false positives



# **Predictive Value**

 Measures whether or not an individual actually has the disease, given the results of a screening test

Affected by

- specificity
- sensitivity
- prevalence of preclinical disease

Prevalence =	a + c
	a+b+c+d



## **Predictive Value**

•Predictive Value of a Positive Test (PPV): Likelihood that a person with a positive test has the disease

•Predictive Value of a Negative Test (NPV): Likelihood that a person with a negative test does not have the disease

Relationship between Sensitivity, Specificity, and Prevalence of Disease

If prevalence is low, even a highly specific test will give large numbers of False Positives



# Prob=1% sens=90% spec=80%







# Screening for 2 diseases

Per disease: Prob=1% sens=90% spec=80%
Screen 100 000 individuals:

# ~ 35000 FPs

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# **Predictive value**

Prevalence = Pre-test likelyhood	99%	95%	80%	50%	20%	10%	5%	1%	0,5%	0,1%
disease upon posistive test result (= positive predictive value)	99,9%	99,7%	99%	95%	83%	68%	50%	16%	9%	2%
no disease upon positive test result (false positive)	0,1%	0,3%	1%	5%	17%	32%	50%	84%	91%	98%

#### Sensitivity and Specificity both 95%



### Enthusiasm for Cancer Screening in the United States

Lisa M. Schwartz, MD, MS

Steven Woloshin, MD, MS

Floyd J. Fowler, Jr. PhD

H. Gilbert Welch, MD, MPH

able 4. Experience of Persons Who Have Had False-Positive Screening Results

	No." for Papanicolaou Test (Weighted %†) (n = 103)	No." for Mammography (Weighted %†) (n = 109)	No." for Prostate-Specific Antigen Test (Weighted %† (n = 10)
low many [test] results have you had that required further			
testing?‡			
1	56 (55)	71 (88)	8 (59)
2	30 (29)	28 (24)	1 (12)
≥3	15 (16)	9 (8)	3 (29)
low many days or weeks were there between when you got the original [test] result and when you found out you did not have cancer?			
≤1 wk	24 (23)	34 (36)	1 (7)
1-2 wk	26 (30)	31 (33)	2 (27)
3-4 wk	20 (22)	17 (18)	1 (20)
>1 mo	26 (25)	13 (13)	3 (34)
low scary was that time for you?			
Scariest time of my life	10 (11)	8 (8)	3 (29)
Very scary	33 (32)	32 (29)	3 (29)
Somewhat scary	24 (25)	36 (33)	4 (41)
A little scary	30 (28)	23 (22)	0

JAMA 2004; 291:71-78

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#### Relation Between Number of Tests Ordered and Percentage of Normal People with at Least One Abnormal Test Result<sup>†</sup>

Number	People with at least one
of tests	abnormality, percent
1	5
5	23
20	64
100	99.4

<sup>†</sup>Data from Sackett, DL, Clin Invest Med 1978; 1:37.



# **Issues in Screening**

## Disease

-Disease/disorder should be an important public health problem High prevalence Serious disabling

-Early Detection in asymptomatic (pre-clinical) individuals is possible

-Early detection and treatment can affect the course of disease (or affect the public health problem?)





# Sources of Bias in the Evaluation of Screening Programs

## Lead time bias

- Length bias
- Volunteer bias



## Lead time

 Lead time: interval between the diagnosis of a disease at screening and the usual time of diagnosis (by symptoms)

Lead Time

Diagnosis by screening Diagnosis via symptoms



# Lead time bias

- Assumes survival is time between screen and death
- Does not take into account the lead time between diagnosis at screening and usual diagnosis.

Survival = 14 years

Diagnosis by screening in 1994

Death in 2008







## **Length Bias**

 Most chronic diseases, especially cancers, do not progress at the same rate in everyone.

 Screening will preferentially pick up slowly developing disease (longer opportunity to be screened) which usually has a better prognosis





## **Volunteer bias**

- Type of bias where those who choose to participate are likely to be different from those who don't
- Volunteers tend to have:
  - Better health
  - Lower mortality
  - Likely to adhere to prescribed medical regimens



# Screening

the systematic testing of risk factors for some target disease

to prevent, interrupt, or delay the development of this disease through early detection and treatment.



### Disease as a process



# classical risk factors atherosclerosis

smoking
hypertension
dyslipidemia
family history
diabetes
obesity

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Age-adjusted CHD death rates per 10,000 person-years

### Riskprofiling cardiovascular disease

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Yusuf et al. INTERHEART Lancet 2004



## Positive effect riskprofiling

- Less false positive results
- Less false normal results (certificate of health effect)
- Awareness
- Tailored advice
- Informed and shared desicion making
- Commitment



#### The European Strategy for the Prevention and Control of Noncommunicable Diseases



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Regional Committee for Europe Fifty-sixth session

Copenhagen, 11-14 September 2008

The greatest disease burden in Europe (= 86% of deaths and 77% of the disease burden) comes from non-communicable diseases (NCD); a group of conditions that includes cardiovascular disease, cancer, mental health problems, diabetes mellitus, chronic respiratory disease and musculoskeletal conditions. This broad group is linked by common risk factors, underlying determinants and opportunities for intervention.

Almost 60% of the disease burden in Europe, as measured by DALYs, is accounted for by seven leading risk factors: high blood pressure (12.8%); tobacco (12.3%); alcohol (10.1%); high blood cholesterol (8.7%); overweight (7.8%); low fruit and vegetable intake (4.4%;) and physical inactivity (3.5%).

A non-communicable disease is a disease which is not contagious

## The western society syndrome

#### On age 50 in Holland:

- 30% smoking
- 90% eating too much fat
- 50% lack of exercise
- 40% obese
- 15% hypertension
- 20% hypercholesterolemia
- per year 65.000 new diabetes patients

RIVM: Gezondheid op koers. 2002



#### **Causes of cancer**

roughly speaking:

**33%:** smoking (risk lungcancer 20x)

**33%:** poor food and lack of exercise

**33%:** other causes like genetic predisposition, UV-light, pollution (pesticides, radon, asbest)

Based on 500.000 papers, which were whittled down to 7000 relevant ones.



World Cancer Research Fund



American Institute for Cancer Research

# SUMMARY

Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective

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# **Riskprofiling algorythms for cancer**

Riskprofiling is more adequate to estimate pretest likelihood of disease than considering just one or two riskfactors

Breastcancer: riskprofiling algorithms

Claus E.B., et al. Cancer **73**, 643-651 (1994). Gail M.H. et al. J. Natl. Cancer Inst. **81**, 1879-1886 (1989). Amir E. et al. J. Med. Genet. **40**, 807-814 (2003). Tyrer J., et al. Stat. Med. **23**, 1111-1130 (2004).

#### - Coloncancer: multifactorial approach

Lieberman D.A., et al. JAMA 290, 2959-2967 (2003).

Betes M. et al. Am. J. Gastroenterol. 98, 2648-2654 (2003).



## Integrated risk assessment



#### Family, medical history and lifestyle

combination RF evaluation + intervention

(too) late

# **Coloscopy screening Norway**

#### **Population registry**

- Random sample: coloscopy and polypectomy
- Controles: no screening

#### **Results:**

- 5x less colorectal cancer, despite more riskfactors
- Overall mortality significantly higher in coloscopy group
   Due to CVD

Riskfactors CVD and cancer overlap !

*Thiis-Evensen E, et al. Scan J Gastro. 1999;34(4):414-20.* 





#### **ACS/ADA/AHA Scientific Statement**

#### Preventing Cancer, Cardiovascular Disease, and Diabetes A Common Agenda for the American Cancer Society, the American Diabetes Association, and the American Heart Association

Hannon Eyre, MD, Chief Medical Officer, American Cancer Society; Richard Kahn, PhD, Chief Scientific and Medical Officer, American Diabetes Association; Rose Marie Robertson, MD, FAHA, Chief Science Officer, American Heart Association; and the ACS/ADA/AHA Collaborative Writing Committee

#### ACS/ADA/AHA Collaborative Writing Committee Members

 Nathaniel G. Clark, MD, MS, RD, National Vice President for Clinical Affairs, American Diabetes Association; Colleen Doyle, MS, RD, Director, Nutrition and Physical Activity, American Cancer Society;
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 Thomas Glynn, PhD, Senior Director, International Tobacco Control, American Cancer Society;
 Robert A. Smith, PhD, Director of Cancer Screening, American Cancer Society;
 Kathryn Taubert, PhD, FAHA, Vice President of Science and Medicine, American Heart Association; Michael J. Thun, MD, Vice President, Epidemiology and Surveillance, American Cancer Society

2004: Circulation, Stroke, Diabetes Care, CA: A Cancer Journal for Clinicians

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## **Disability Adjusted Life Years (DALY)**





#### **The NIPED concept for prevention**

Focus on the most relevant diseases (DALY) with intervention options Integrate risk profiling for multiple disease processes

Early diagnostics based on stepped approach:

- high-risk identification by integrated risk profiling (pretest likelihood)
- advanced diagnostic as threshold is passed (threshold approach)

Prevention through personalized intervention strategies

- based on personal risk profile

#### Boost research in preventive medicine

- health information banking
- dynamic guideline development



### Population based screening for risk factors

**Personalized Prevention** 





# PreventieKompas®



#### How does it work?





# 2





#### LabCheck uitvoeren Na ontvangst van de LabBox bezoekt u een PrikPost. U laat bloed afnemen en levert gelijktijdig uw labmonster(s) in.

#### **Online questionnaire**

- Lifestyle
- Mental wellness
- Physical wellness
- Medical History
- Family history
- Medication use

#### Self measurement or CheckPoint / GP

- Blood pressure
- Waist circumference
- Length
- Weight

#### Laboratory testing

- Blood
- Urine
- Faeces



# One Box Self management alternative for CheckPoint visit





### **Communication of results**

#### **Health Course**



#### **Integrated Health Profile**



#### Health management plan

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Is your health 'on course' or should you take some action?

Gives you per health aspect information and educates about the effect on your health and on the interaction with other risk factors.

It shows were health improvement is possible

Provides a concrete and tailored health management plan, based on disease risk, motivation, preferences for of intervention methods.

It links to best-practice follow-up providers.



## **Intervention Matching**

#### **Risk profiling & health advice**



#### Advised health actions

- (Medical) health profile
- Preference (i.e. group,
- internet, guidance)
- Insurance/company
- Location

Individual intervention Matched for individual to increase success

#### **Intervention selection & ranking**



#### Intervention mapping

- Effectiveness
- Costs (compensation
- insurance/company)
- Evaluations
- Location

# **PreventionCompass results**

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#### combined Cardiometabolic and Psychological risk



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Health promoting behavior

#### Follow-up questionnaire: 6 months after participation



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#### Health promoting behavior

#### Follow-up questionnaire: 4-6 weeks after participation

#### Table 3

Self-reported initiation of health-behaviour-change of 638 employees who completed the HRA and responded to the satisfaction and health-behaviour change questionnaire.

Initiation of health-behaviour-change after receiving health advices

	Yes			No			na <sup>†</sup>	
Initiated overall health-behaviour-change after receiving tailored health advices	368	368 (58%) 243 (38%) From applicable				27	(4%)	
More physical activity	242	(38%)	<b>(</b> 53%)	212	(33%)	184	(29%)	
Quit smoking	20	(3%)	(14%)	125	(20%)	493	(77%)	
Reduced alcohol intake	64	(10%)	(24%)	198	(31%)	376	(59%)	
Improved diet	282	(44%)	(64%)	158	(25%)	198	(31%)	

Values are expressed as number of participants (%).

na<sup>†</sup>: Questionnaire responders who stated that health-behaviour change on item of interest was not applicable.

Colkesen et al. Journal of Occupational Medicine and Toxicology, 2011;6(1):1-5.



Effect CV risico in 7 months



#### Framingham 10-year CVD risk category

- Significant mean decrease in systolic blood pressure (5 mmHg) and 30% decrease in proportion with increased blood pressure
- Significant increase in HDL
- Significant decrease in total cardiovascular risk

B.E. Colkesen et al., Vascular Health and Risk Management, 2011;7:67-74

### **Overall 20% reduction in absenteeism** (p< 0.0001)

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**Figure:** Mean monthly days of absenteeism for health program participants and controls who had at least one recorded day of absence during the baseline period and no absenteeism at the start of participation

#### MAJ Niessen et al. EuroPrevent 2010





Colkesen et al. Journal of Occupational Medicine and Toxicology, 2011;6(1):1-5.