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## **Chronic Diseases:**

### **Role of environmental and infectious factors.**

*How can employers prevent cancer, cardiovascular diseases and Alzheimer's disease?*

# INTRODUCTION

# Emergence or reemergence of new epidemics due to :

- ✓ Globalization of exchanges and travels
- ✓ Demography: concentration in large cities
- ✓ Nutrition (pesticides, water)
- ✓ Environmental factors
- ✓ Climate changes, electromagnetic radiations
- ✓ Contacts with wild and farm animals
- ✓ Decline of immune defenses.

# The most important burden

## Chronic Diseases

- Cancers
- Cardiovascular
- Neurodegenerative
- Arthritic
- Autoimmune
- Multifactorial, but in common:
  - oxidative stress
  - infectious agents (?)

# Our microbial ecosystem :

Mucosa

Skin



Constant exposure to  
microbial agents and  
immune protection

# Extreme genetic plasticity of microorganisms:

- ✓ Virus : HIV, Influenza
- ✓ Bacteria (plasmids)
- ✓ Parasites (retrotransposons)

against reaction of the immune system

# *Noncommunicable diseases key facts*

- Noncommunicable diseases (NCDs), also known as chronic diseases, are not passed from person to person.
- They are of long duration and generally slow progression.
- Four groups of diseases account for around 80% of all NCD deaths.
  - Cardiovascular diseases (like heart attacks and stroke)
  - Cancers
  - Chronic respiratory diseases (such as asthma)
  - Diabetes
- NCDs share 4 risk factors: **physical inactivity**, tobacco use, the harmful use of alcohol and unhealthy diets

*WHO , NCDs Fact sheet, 2013*

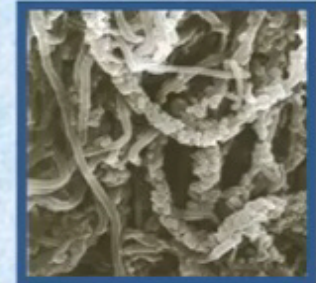
# Sedentarity increases susceptibility to environmental risk factors

- Disease susceptibility is higher in sedentary subjects as compared to subjects with regulated, moderate training (*Woods JA et al., 1999*)
- Disease susceptibility means a compromised immune response to risk of infections by environmental and infectious agents (*Deitch EA, 1988; Walsh NP, 2011*)





## The intestinal microbiota



- Over a trillion bacteria
- At least 500 species of bacteria
- Combined metabolic activity exceeds that of the liver
- Influence a variety of host functions within and outside the gastrointestinal tract, including physiological, immunological and metabolic functions
- Bacterial composition & activity subject to a variety of influences including host physiology and immunology, diet, antibiotic usage, and enteric infection
- Changes in microbiota (dysbiosis) associated with GI & metabolic disease

# Association between microbial and viral agents and NCDs

- Infectious agents have emerged as notable determinants of NCDs

Infectious agent(s)	Chronic disease(s)
<b>Established connections</b>	
Helicobacter pylori	Gastric cancers / peptic ulcer disease
Hepatitis B/C virus	Liver cancer
Human papillomavirus	Cervical cancer
Schistosoma hæmatobium	Bladder cancer
Epstein-Barr virus	Burkitt lymphoma, nasopharyngeal carcinoma
Kaposi-associated herpesvirus (HHV-8)	Kaposi's sarcoma, primary effusion lymphoma

Infectious determinants of chronic diseases (Gargano LM and Hughes JM, 2014).

# *NCDs environmental risk factors and prevention*

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- 24% of the global disease burden and an estimated 23% of all deaths are attributable to **environmental factors** (pollutants and infectious agents) (*WHO 2012; Pruss-Ustun A and Corvalan C, WHO 2006*).

Example of NCDs induced by environmental factors = part 1 of the presentation

- Employers can reduce NCDs health care costs, improve employee health and the business financial bottom line by using **community evidence-based practices and programs to reduce risks related to environmental factors.**

Setting prevention of NCDs at workplace = part 2 of the presentation

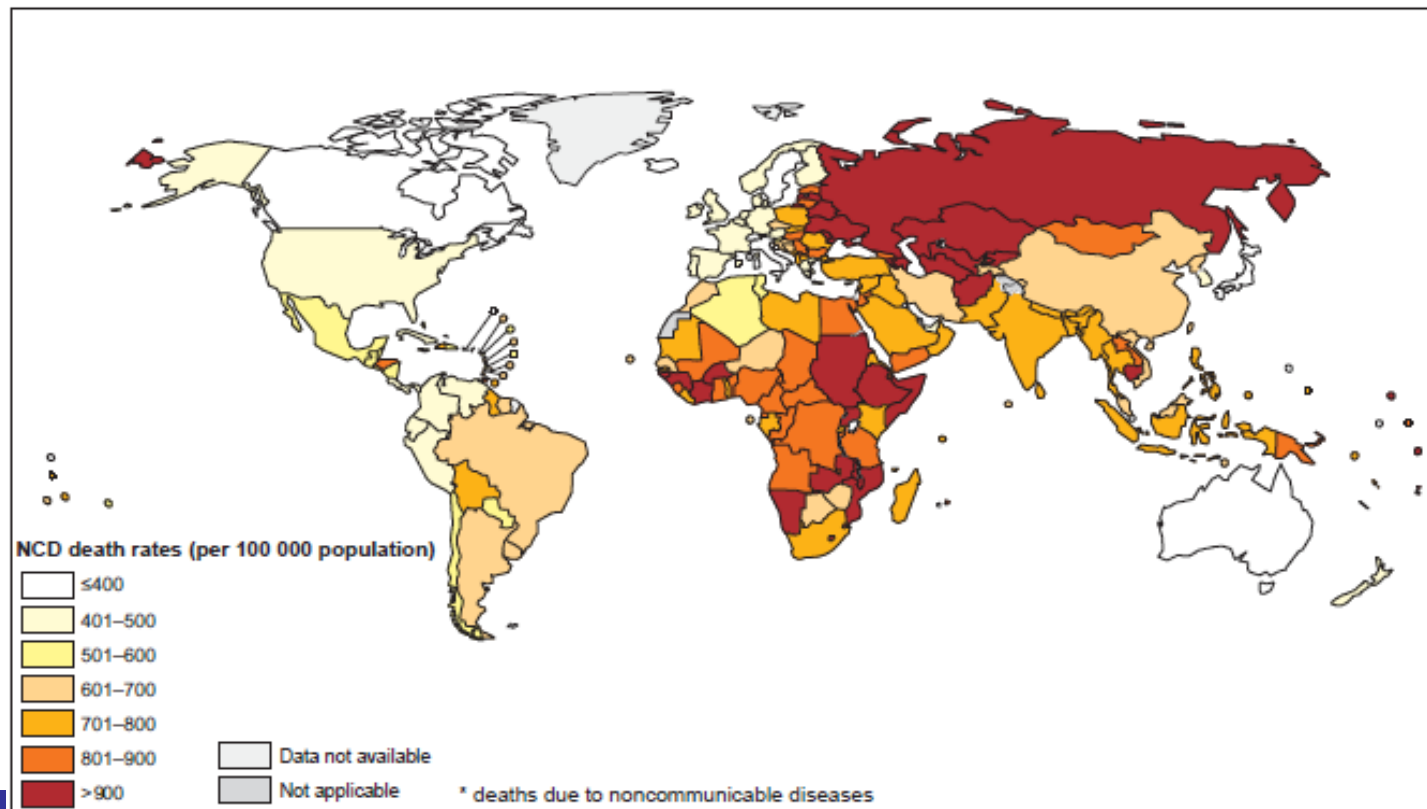
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## **PART I**

# **Example of NCDs induced by environmental factors**

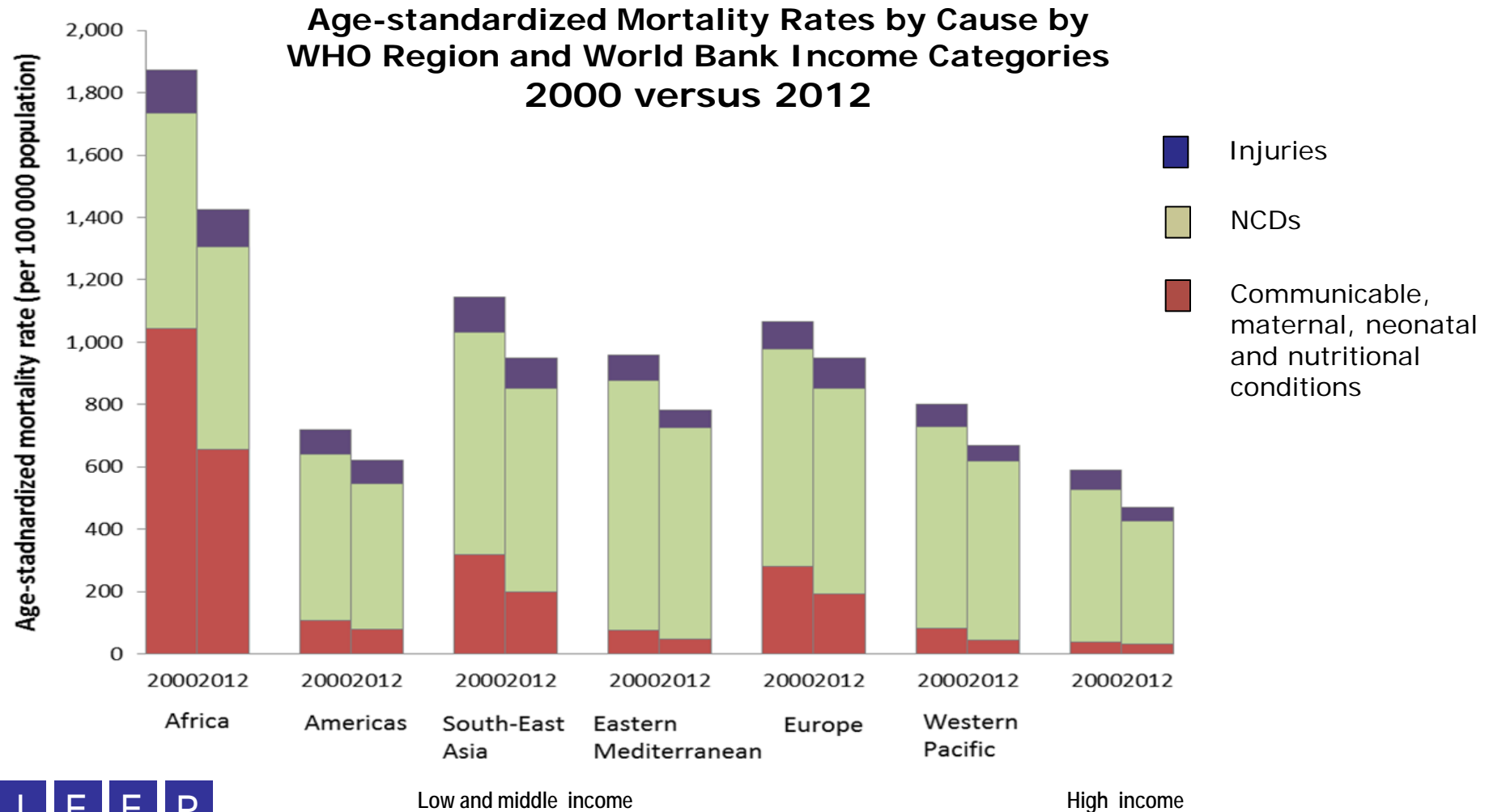
# Worldwide incidence of NCDs

- 36 millions of the 57 million global deaths in 2008 were due to NCDs.
- 29% of NCD deaths in low- and middle-income countries in 2008 occurred before the age of 60.



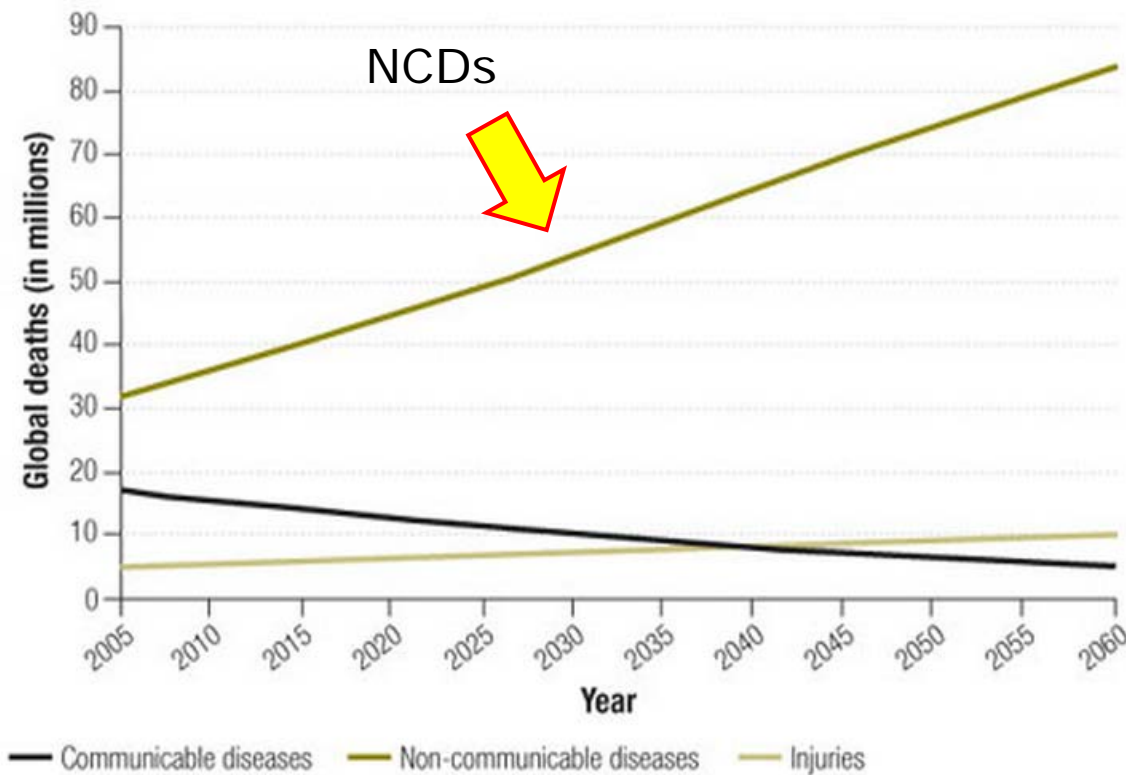
Total NCD death rates in male population in 2008 (WHO, 2010).

# *NCDs mortality rates did not decreased during the last decade*



# *NCDs mortality rates will progress in the next decades*

Fig. 4. Global deaths by major disease groups



Source: International Futures version 6.32 base case forecast.

Globally, the NCD burden will increase by 17% in the next 10 years, and in the African region by 27%.

The highest absolute number of deaths will be in the Western Pacific and South-East Asia regions.

From Bulletin of the World Health Organization, Hughes B et al.  
Bull World Health Organ vol.89 n.7 Geneva Jul. 2011

# *Cancer and pollutants*

## *The Lung cancer example*

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- Globally, about 19% of all cancers are related to environment (WHO, 2006).
- Lung cancer causes the largest disease burden of all cancers worldwide (WHO, 2006) and is the most costly cancer: 51,848 millions of US\$ in medical costs in 2010 (World Economic Forum 2011).
- The major risk factors related to lung cancer are:
  - Smoking and secondhand smoking
  - Exposure to radon and asbestos
  - Air pollution including diesel exhaust especially indoor
  - Arsenic in drinking water
- Simple means of prevention in a company:

### Counseling

Regular assessment of air and water quality at the workplace

Detection of radon level especially in basement of workplace

Provide a diet high in fruits and vegetables to population of work



# Cancer and Infectious agents

- Many cancers are caused by viral and bacterial agents:
  - Persistence of the infectious agents in the host > chronic inflammation
  - Direct cell transformation by infectious agent > inhibition of tumour suppressors and stimulation of proliferation
  - Immunosuppression by the infectious agents
- **But...**

*Journal of Internal Medicine* 2000; **248**: 171-183

## INTERNAL MEDICINE IN THE 21<sup>st</sup> CENTURY

### Infections as a major preventable cause of human cancer

H. KUPER<sup>1</sup>, H.-O. ADAMI<sup>1, 2</sup> & D. TRICHOPOULOS<sup>1, 2, 3</sup>

From the 1 Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA; 2 Department of Medical Epidemiology, Karoliska Institute, Stockholm, Sweden; and 3 Department of Hygiene and Epidemiology, University of Athens Medical School, Athens, Greece.

# *Helicobacter pylori and gastric cancer*

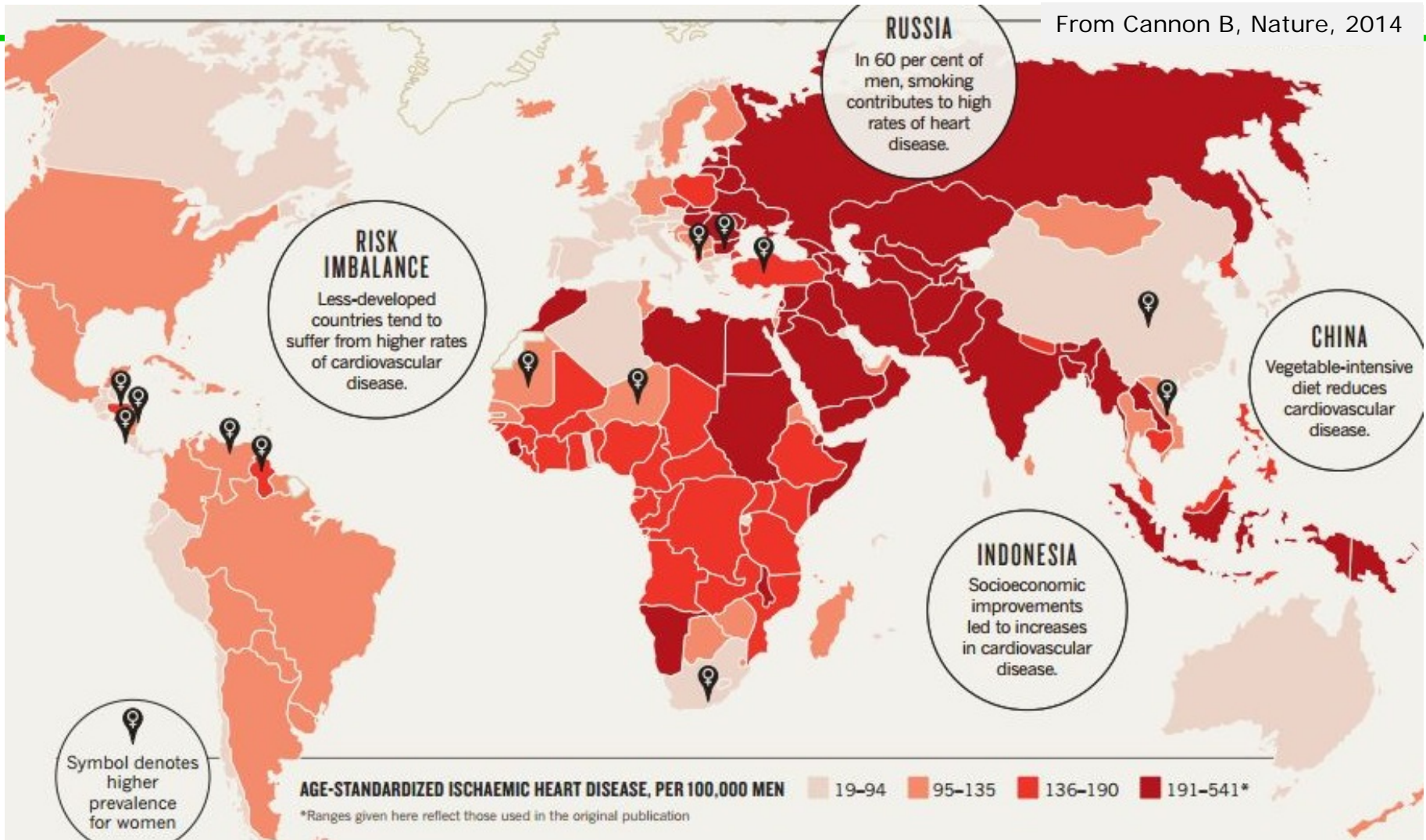
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- *Helicobacter Pylori* is a bacterium found in the stomach, initially identified in patients with chronic gastritis and gastric ulcers.
- *H. pylori* increases the risk of gastric cancer by 5 to 20-fold (*Huang QJ et al., 1998; Ekstrom AM et al., 2001; Helicobacter and Cancer Collaborative Group, 2001*).
- Gastric cancer is usually preceded by decades of chronic inflammation.
- Medical costs: 17,141 millions of USD in 2010 (World Economic Forum 2011).
- Simple means of prevention:
  - Wash hands thoroughly before handling food
  - Use safe sources of drinking water

# *Schistosoma haematobium* and bladder carcinoma

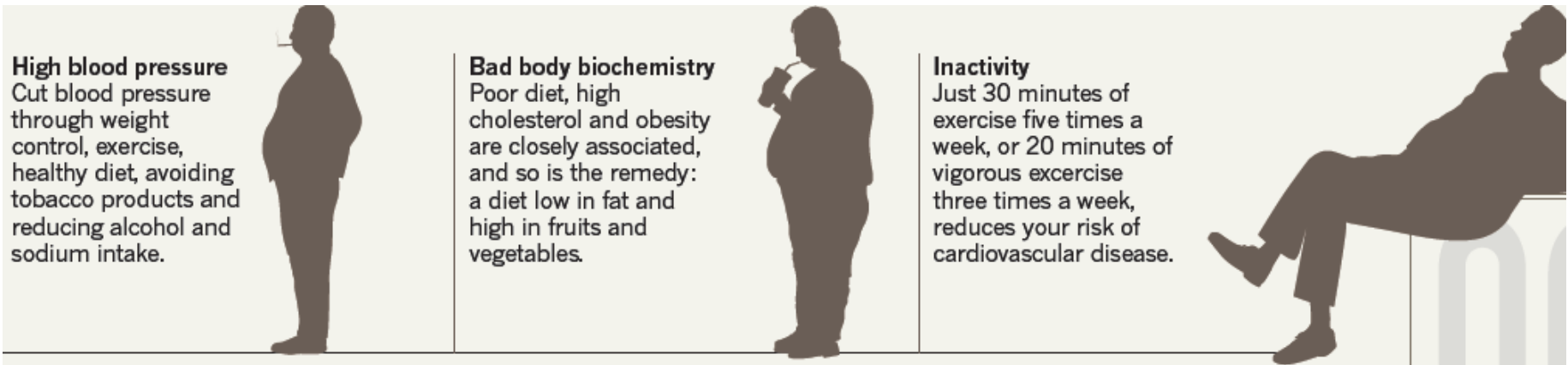
- *S. haematobium*, a trematode found in the Middle East, India, and Africa, causes urinary schistosomiasis (*Khurana S et al., 2005*).
- Studies have shown the relationship between *S. haematobium* infection and the development of squamous cell carcinoma of the bladder (*Mostafa MH et al., 1999*).
- Medical costs: 7,692 millions of USD in 2010 (World Economic Forum 2011).
- People are infected during routine agricultural, domestic, occupational and recreational activities which expose them to infested water. Simple prevention :
  - Optimization of hygienic conditions
  - Quality control of drinking water

# Cardiovascular diseases key facts



# Cardiovascular diseases key facts

- In 2008, CVDs were the leading cause of NCD deaths (17 million deaths)
- Global 2010 cost of CVD = US\$ 863 billion (mean per capita cost of US\$ 125) (World Economic Forum 2011).
- 23.6 millions: projected annual number of worldwide deaths from CVD in 2030
- Principles of prevention:



# Cardiovascular diseases and Environmental factors

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- 16% of the total burden of CVDs is attributed to environment, corresponding to 2.5 million deaths per year (*WHO, 2006*)
- Apart from diet, lifestyle, and stress, CVDs are associated with environmental risks factors such as :
  - air pollution (*Pope et al., 2002*)
  - exposure to lead (*Schwartz, 1995*)
  - exposure to tobacco smoke (*Kaur et al., 2004*)
- Simple prevention:
  - Air monitoring
  - Counselling for smoking cessation

# Cardiovascular diseases and Infectious agents

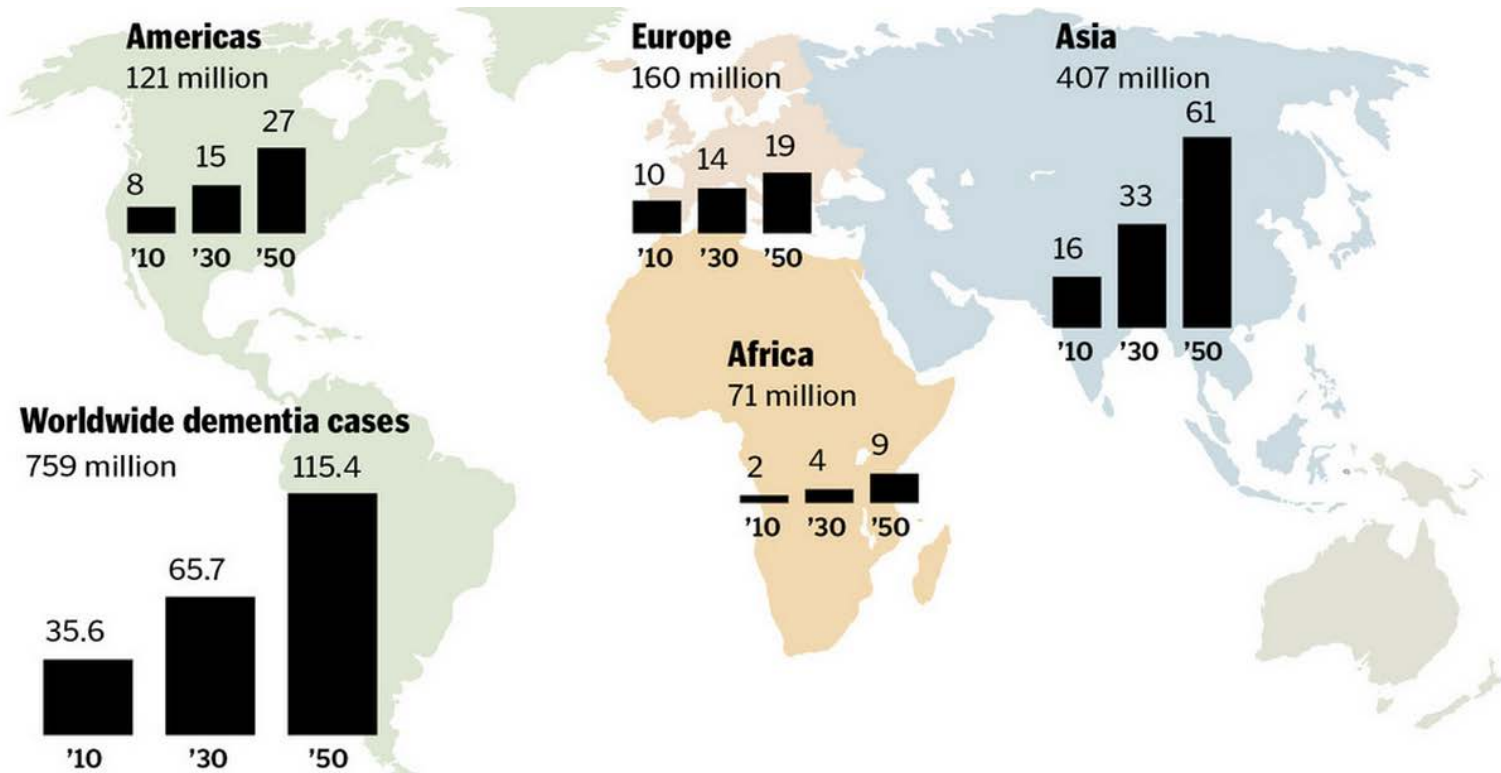
## *Porphyromonas gingivalis*

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- *P. gingivalis* is a pathogenic bacterium found in the oral cavity where it induces periodontitis, chronic infection in the tooth-supporting tissues, which may lead to loss of teeth
- Patients with periodontitis had a 19% increased risk of CVD (95% CI: 1.08–1.32) compared with subjects without periodontitis (*Pussinen PJ et al., 2007*).
- Medical costs of stroke: 73.7 billion USD in 2010 (AHA 2014)
- Simple mean of prevention:
  - Facilitate oral hygiene at workplace to allow teeth brush, floss and mouthwash use)

# Alzheimer's disease key facts

- Alzheimer's disease (AD) is the most common form of dementia affecting millions of people worldwide.
- Costs: US\$ 2.5 trillion in 2010 (World Economic Forum 2011).





# Alzheimer's disease and Environmental factors

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- AD is significantly related to social risk factors:
  - fewer years of formal education (*Evans DA et al., 1997*)
  - lower socioeconomic status, and lower occupational status (*Fratiglioni L et al., 1993*).
- This means that identification of subjects at risk is possible. This may facilitate prevention actions:
  - improve access and encourage education and mental activities
- AD is also related to vascular risk factors than can be prevented:
  - Promote lifestyle interventions including a healthy diet, physical activity and smoking cessation

# *Alzheimer's disease and Environmental factors*

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## ■ Other risks factors:

- smoking (Launer LJ et al., 1999)
- high alcohol consumption (Fratiglioni L et al., 1993)
- Metal ions, such as zinc and copper potentiate AD by participating in the aggregation of amyloid  $\beta$ -protein precursors and in the generation of reactive oxygen species (Adlard PA and Bush AI, 2006).

## ■ Prevention: *Encourage a brain-healthy lifestyle*

- *Facilitate physical activity and healthy diet*
- *Facilitate access to mental stimulation activities (reading, learn a foreign language, playing brain teasers and strategy games)*
- *Improve stress management*
- *Counselling for smoking cessation*

# *Infectious agents and Alzheimer's disease*

J. Miklossy

**Expert Reviews in Molecular Medicine**

Expert Reviews in Molecular Medicine / Volume 13 / 2011, e30 (34 pages)

## **Emerging roles of pathogens in Alzheimer disease**

- « There is a significant association between Alzheimer disease (AD) and
- various types of spirochete (including the periodontal pathogen *Treponemas* and *Borrelia burgdorferi*),
  - *Chlamydophyla pneumoniae*
  - Herpes simplex virus type-1 (HSV-1).

# *Infectious agents and Alzheimer's disease*

## *Herpes simplex-1 virus*

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- Herpes simplex-1 virus (HSV-1) or oral herpes causes sores around the mouth and lips
- As much as 90 percent of Americans age 50 and older have been exposed to it.
- HSV-1 has been found highly correlated with Alzheimer's disease (AD) diagnosis.
- A simple mean to prevent HSV1 infection
  - Follow proper hand washing procedure !

## **Part 2 - Prevention of NCDS at workplace**

# *Workplace prevention reduces risk of NCDs*

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- One year **telephone-based weight management programme** was beneficial for weight loss, improvement of physical activity, eating habits and overall health status in 1298 overweight/obese participants in 10 large workplace settings (Terry P et al.,2011).
- **Workplace physical activity and dietary behaviour** interventions significantly reduce body weight, BMI, and body fat percentage (Verweij LM, 2010).
- Employees undergone a three-year **worksite wellness program** had a significant reduction in total cholesterol, LDL-cholesterol, and triglyceride levels, and a robust increase in HDL-cholesterol (Byrd K et al., 2008).

# *Reduce contact with infectious agents*

Savolainen-Kopra *et al. Trials* 2012, **13**:10  
<http://www.trialsjournal.com/content/13/1/10>



RESEARCH

Open Access

## Hand washing with soap and water together with behavioural recommendations prevents infections in common work environment: an open cluster-randomized trial

**Results:** In the total follow-up period there was a 6.7% reduction of infection episodes in the soap-and water arm

# Promote physical activity to reduce risk of NCD

- Raise awareness: creation of the International Olympic Committee Non-Communicable Diseases ad-hoc Working Group in 2013

[Clin J Sport Med. 2013 Nov;23\(6\):419-29. doi: 10.1097/JSM.0000000000000038.](#)

**Prevention and management of noncommunicable disease: the IOC Consensus Statement, Lausanne 2013.**

- A regular physical activity :
  - Reduces the risk of CVD by 30% to 35% (*2008 Physical Activity Guidelines for Americans*)
  - Reduces the risk of colon cancer by 17%, breast cancer by 20% (*Wolin, 2011; Lynch, 2011*)
  - Reduces the risk of chronic respiratory diseases (*Hirayama, 2010*)
  - Reduces the risk of Alzheimer's disease (*Brown, 2013 and Buchman, 2012*)



# *Promoting physical activity to boost the immune system*

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- Exercise enhances immunity in several ways:
  - increase of macrophage production
  - increase of the circulation rate of immune cells
  - inhibition of bacterial growth by rising body temperature
  - reduction in stress-related hormones release
- Physical activity is associated with a reduced risk by 20% of upper-respiratory tract infection (URTI) (*Matthews CE et al., 2002*).

## *Health education, vaccination, diagnostic*

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### ■ **Develop vaccination campaign**

Today, only 37 percent of adults have had an annual flu vaccination.

### ■ **Develop diagnostic campaign**

14,000 additional lives would be saved each year if we increased to 90 percent the portion of adults age 50 and older who are up to date with any recommended screening for colorectal cancer.

A 2003 actuarial evaluation of one large U.S. company estimated savings of \$547 for each patient with a prior heart or stroke condition if they controlled their high blood pressure (HBP).

### ■ **Provide smoking cessation assistance**

Cigarette smoking is a substantial risk factor for important bacterial and viral infections.

# Conclusions

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- Preventing or mitigating chronic diseases of infectious and environmental etiology could have considerable positive impact on global and domestic health.
- Reducing impact of infectious and environmental risk factors will contribute substantially to decrease morbidity of preexisting chronic conditions.
- Further understanding of the connection between infectious and environmental agents and chronic diseases will result in a tremendous opportunity to reduce long-term illness and disability worldwide by maximizing infection prevention and control.