

FRESHER



FORESIGHT AND MODELLING FOR EUROPEAN HEALTH POLICY AND REGULATION

Project Acronym: FRESHER

Project Full Title: Foresight and Modelling for European Health Policy and regulation

Grant Agreement: 643576

Project Duration: 36 months (January 2015 - December 2017)

Coordinator: AMU - Jean Paul Moatti

D 3.1 Horizon Scanning report with annotated short list of drivers

Title: Drivers and Trends of Future Developments of Non-communicable Diseases
WP WP3 Horizon Scanning and Driver Identification
Authors: Susanne Giesecke, Giovanna Guiffrè, Marianne Hörlesberger, Taavi Lai, Benedetta Mattioli, Maria Giovanna Quaranta, Masha Smirnova, Liina Üksik, Stefano Vella, Beatrix Wepner
Organisations: AIT, ISIS, FVC, EPHA
Dissemination: Public
Date of publication: 31/03/2016

TABLE OF CONTENTS

INTRODUCTION TO THE FRESHER PROJECT	4
Horizon Scanning and Foresight.....	4
Workshops for Trend- and Driver Identification	5
PART I.....	6
1 NON-COMMUNICABLE DISEASES	7
1.1 Cardiovascular diseases.....	7
1.2 Cancer.....	10
1.3 Diabetes.....	13
1.4 Chronic respiratory diseases	16
1.5 Obesity.....	18
1.6 Musculoskeletal diseases	21
1.7 Mental Health and Neurological Disorders.....	23
PART II.....	27
2 DETERMINANTS OF NON-COMMUNICABLE DISEASES	28
2.1 Introduction.....	28
2.2 Smoking	29
2.3 Diet	32
2.4 Physical (In)Activity	34
2.5 Alcohol use	36
PART III.....	38
3 TRENDS & DRIVERS OF NON-COMMUNICABLE DISEASES	39
INTRODUCTION	39
Defining Drivers & Trends	39
Drivers.....	39
Trends	39
3.1 Innovation in medicine.....	40
3.1.1 Human genome sequencing	40
3.1.2 Epigenetics	43
3.1.3 Stem Cells.....	44
3.1.4 Microbiota.....	45
3.1.5 Organ transplantation.....	46
3.1.6 Minimally invasive and robotic surgery	49
3.1.7 Smart medical devices	50

3.1.8	Immune checkpoints in cancer therapy.....	51
3.1.9	Biomarkers in medicine	51
3.1.10	Gender Specific Medicine and Care	53
3.2	Environment	55
3.3	Urban Development	59
3.3.1	Built Environment and Physical Activity	60
3.3.2	Built Environment and Depression	60
3.3.3	Built Environment of Schools.....	60
3.3.4	Attractive Environments	61
3.3.5	Health Equity and Built Environment	62
3.3.6	Healthy and Sustainable Cities.....	62
3.4	Health Systems shared values and operating principles.....	62
3.5	Social Developments	74
3.5.1	Inequity and Prosperity.....	74
3.5.2	Quality of Life, Unemployment, and Mental Well-being.....	75
3.5.3	Social Networks and Social Cohesion	77
3.5.4	Social Innovations	78
3.5.5	Changes in Gender Roles	80
3.5.6	Family Values	81
3.5.7	Migration.....	82
3.6	Agriculture	84
3.6.1	General Aspects	84
3.6.2	Chemistry and Pesticides	88
3.6.3	Organic Farming.....	89
3.7	Nutrition	89
3.7.1	General nutritional aspects.....	89
3.7.2	Food Labelling	92
3.7.3	Taxation of unhealthy foods and drinks	93
3.8	Industrialisation of Food Production.....	95
3.9	Marketing and Advertising	97
4	REFERENCES.....	101

INTRODUCTION TO THE FRESHER PROJECT

FRESHER is a collaborative research project that aims to detect emerging health scenarios to test and assess future policy options to tackle the burden of chronic non-communicable diseases (NCDs) in Europe. As one of the largest threats to public health globally, the exponential growth of NCDs in Europe has a serious negative impact on human development, reduces productivity, contributes to poverty and creates a significant burden on health systems. Therefore, one of the main goals of FRESHER is to identify core determinants that could be targeted to lessen the impact of NCDs, focusing on a set of chronic diseases which currently constitute the bulk of the mortality rate in Europe: cardiovascular diseases, cancers, diabetes, chronic respiratory diseases obesity, musculoskeletal diseases, mental health and neurologic disorder.

Rather than just extrapolating past health trends, the project consortium uses a variety of foresight techniques that account for the interdependencies of structural long-term trends in demographic, gender relations, technological, economic, environmental, and societal factors for European countries. Supported by a mapping of determinants of NCDs in Europe, the developed model will capture the complex set of inter-relationships between individuals' history of engagement in risk-taking behaviours, exposure to environmental risks and the resulting distribution of health, social and economic consequences across gender and across social groups. All of these efforts will fuse to elaborate and produce inputs for the empirically-based dynamic micro-simulation tool capable of quantifying the current and future health and economic impacts of risk factors as well as potential new policies and policy combinations.

HORIZON SCANNING AND FORESIGHT

Recent health related Foresights and Forecasts show widespread use of visions, scenarios and forecasts with demographic shifts, rising healthcare costs, and emerging technologies predominating.

Statistical forecasting combined with perceived and extrapolated trends sketch scary future developments with regard to the rise of NCDs and health systems collapse. Even though a lot is known on the determinants of NCDs, one wonders why so little is done effectively at individual, community and political levels. One of the aims of WP3 of the Fresher Project is to identify trends and drivers that contribute to the determinants of NCDs and for opportunities for change. The identification and analysis of trends and drivers are set in the context of horizon scanning and foresight.

Foresight is defined as a systematic, participatory, future-intelligence-gathering and medium-to-long-term vision-building process aimed at enabling present-day decisions and mobilizing joint actions. It can be envisaged as a triangle combining "Thinking the Future", "Debating the Future" and "Shaping the Future". Foresight is neither prophecy nor prediction. It does not aim to predict the future – to unveil it as if it were predetermined – but to help us build it. It invites us to consider the future as something that we can create or shape, rather than as something already decided (www.foresight-plattform.eu).

Horizon scanning implies a search process, which is extended at the margins of 'the known' environment and possibly beyond this (Loveridge, 2009) with the aim of identifying emerging issues

and events which may present themselves as threats or opportunities for society and policy. In line with this explanation, the UK Department for Environment, Food and Rural Affairs (DEFRA) defined Horizon Scanning in 2002 as “the systematic examination of potential threats, opportunities and likely future developments which are at the margins of current thinking and planning” and, continuing, horizon scanning “may explore novel and unexpected issues, as well as persistent problems or trends”(www.foresight-plattform.eu).

In this context, the FRESHER team tapped into a large variety of sources and expert knowledge to come up with those trends and drivers that are discussed as the most prominent ones within the scientific community of researches working in the field or in related fields. We organized group discussions with stakeholders of various field but all with a relation to NCDs to discuss our findings and get additional inputs and points of views. (The workshops are briefly described below) We are well aware of the deficits that our report here presents. Due to time and output orientation we had to be rather brief and selective in our result presentation. For each driver and trend, for each determinant and disease libraries could be filled. But it is also a task of foresight to present drivers and trends in a concise way and understandable for a broad (lay) audience in order to continue the process, e.g. by giving input to scenario building and micro-simulation. Beyond the work package results presented in this report, one additional target of FRESHER is to develop future scenarios that could form the basis for discussions for future policy formulations and options.

WORKSHOPS FOR TREND- AND DRIVER IDENTIFICATION

In the three workshops the discussion went beyond the common and well-researched determinants. Participants and organizers asked for the wider correlations, such as in the context of food production and consumption, city planning and green spaces for individual physical activities, the impact of environmental pollution, the organisation of social life and many more. All three workshops started with a short introduction to the project and the trends and drivers identified. The workshop continued with interactive work in small groups where every participant was asked to speak out and share their knowledge with the others. Their contributions were very important not only for the workshop but also for the further course of the project. They assessed the findings of the horizon scanning on trends and drivers in a discursive and moderated manner and collected additional drivers that had not been considered so far.

There were between 25 and 28 participants at each workshop. They came from very different areas but all were somehow related to non-communicable diseases. When selecting the participants the FRESHER team took care to have a fair representation of experts with different backgrounds such as medicine and care, society, policy, media, research and industry.

The workshops took place in Vienna, Brussels and Lisbon. Even though the agendas were quite similar, each workshop had also a special focus. In Vienna, the discussion centered on NCDs and people living in the city. In Brussels the focus was on differences in Eastern and Western Europe. And in Lisbon special aspects of people living in Southern Europe and suffering from austerity measures were taken into account. In each workshop, participants formed four groups to discuss four drivers or trends in particular and from different perspectives. There were drivers or trends already identified in the preliminary version of this reports or drivers and trends newly identified by the groups. All workshop results were documented by the FRESHER team.

PART I

1 NON-COMMUNICABLE DISEASES

Non-communicable diseases (NCDs), also known as chronic diseases, are mainly represented by cardiovascular diseases, cancers, diabetes, chronic respiratory diseases, obesity, musculoskeletal diseases and mental disorders. NCDs represent a leading threat to human health and human development in today's world, and continue to be the leading cause of morbidity and mortality in the European Region but also globally and in the majority of low- and middle- income countries (LMICs). These NCD are the world's leading causes of death, and kill an estimated 35 million people each year - 60% of all deaths globally – with 80% (28 million) in LMIC. Of these, cardiovascular diseases account for most NCDs deaths (17.5 million people annually), followed by cancers (8.2 million), respiratory diseases (4 million), and diabetes (1.5 million) (WHO, Global status report on non-communicable diseases; 2014).

All age groups and all regions are affected by NCDs. WHO estimates that total deaths from non-communicable diseases will increase by a further 17% over the next 10 years. NCDs are often prevalent in disadvantaged socio-economic populations and areas and represent a major obstacle to the economic development of many countries. WHO predicts the greatest increase in incidence of NCDs in Europe in the Eastern Mediterranean region with 25% rise.

NCDs are often associated with older age groups, but evidence shows that 16 million of all deaths attributed to NCDs occur before the age of 70. Of these "premature" deaths, 82% occurred in LMICs (WHO, Non communicable diseases, fact sheet, 2015).

Common, modifiable risk factors underlie the major NCDs. They include tobacco, harmful use of alcohol, unhealthy diet, insufficient physical activity, and overweight/obesity, raised blood pressure, raised blood sugar and raised cholesterol. These diseases are driven by forces that include ageing, rapid unplanned urbanization, and the globalization of unhealthy lifestyles. The NCD threat can be overcome using existing knowledge. The solutions are highly cost-effective. Comprehensive and integrated action at country level, led by governments, is the means to achieve success (<http://www.euro.who.int/en/health-topics/noncommunicable-diseases>).

Sources:

- WHO/Europe, Non communicable diseases - - <http://www.euro.who.int/en/health-topics/noncommunicable-diseases>
- WHO, Non communicable diseases fact sheet, 2015 - - <http://www.who.int/mediacentre/factsheets/fs355/en/>
- WHO, Global status report on non-communicable diseases 2014 – <http://www.who.int/nmh/publications/ncd-status-report-2014/en/>

1.1 CARDIOVASCULAR DISEASES

The Burden

Cardiovascular disease (CVD) is the leading cause of death and a major cause of disability and lost of productivity in adults worldwide. Every year, an estimated 17.5 million people globally die from CVDs, representing 31% of all global deaths (or 48% of NCD deaths). Of these deaths, an estimated 7.4 million were due to coronary heart disease and 6.7 million were due to stroke. By 2030, it is

estimated that 23 million people will die from CVDs each year (WHO, Cardiovascular diseases, Fact sheet N°317, 2015).

CVD causes more than half of all deaths across the European Region. CVD causes 46 times the number of deaths and 11 times the disease burden caused by AIDS, tuberculosis and malaria combined in Europe.

The lifetime risk for a forty-year-old developing coronary heart disease is roughly 50% in men and 32% in women. Research has shown that males between 20 and 64 years of age in semi- and unskilled manual occupations run a three times higher risk of premature death from CVD compared to those in professional and managerial positions. Moreover, when improvements to health do occur, the benefits are unevenly distributed within society. These conditions and their causes contribute to differences in healthy life expectancy between and within European countries (<http://www.euro.who.int/en/health-topics/noncommunicable-diseases/cardiovascular-diseases>).

The Diseases

Cardiovascular diseases are a group of disorders of the heart and blood vessels and include:

Coronary heart disease and cerebrovascular disease: disease of the blood vessels supplying the heart muscle or the brain, respectively. Heart attacks and strokes are usually acute events and are mainly caused by a blockage that prevents blood from flowing to the heart or brain. The most common reason for this is a build-up of fatty deposits on the inner walls of the blood vessels that supply the heart or brain. Strokes can also be caused by bleeding from a blood vessel in the brain or from blood clots.

Peripheral arterial disease: disease of the blood vessels supplying the arms and legs.

Rheumatic heart disease: damage to the heart muscle and heart valves from rheumatic fever, caused by streptococcal bacteria. Rheumatic fever is caused by an abnormal response of the body to infection with streptococcal bacteria, which usually begins as a sore throat or tonsillitis in children. Rheumatic fever mostly affects children in developing countries, especially where poverty is widespread. Globally, about 2% of deaths from cardiovascular diseases are related to rheumatic heart disease.

Congenital heart disease: malformations of heart structure existing at birth.

Deep vein thrombosis and pulmonary embolism: blood clots in the leg veins, which can dislodge and move to the heart and lungs (NCD Alliance, Cardiovascular diseases).

The Socioeconomic Impact

CVD expenditures vary from country to country, but most countries spend 8-22% of their health budget on CVD. Nevertheless, CVD remains a major cause of health disparities and rising health care costs. At least three quarters of the world's deaths from CVDs occur in LMICs. Out of the 16 million deaths under the age of 70 due to NCDs, 82% are in LMICs and 37% are caused by CVDs. People in LMICs often do not have the benefit of integrated primary health care programs for early detection and treatment of people with risk factors compared to people in high-income countries. As a result, many people in LMICs are detected late in the course of the disease and die younger from CVDs and other NCDs, often in their most productive years (<http://www.ncdalliance.org/node/38>).

Prevention and Risk Factors

These diseases occur in infants, children, and adults of both sexes, and they affect people of all races and ethnicities. The majority of CVDs are caused by risk factors that can be controlled, treated or modified, such as high blood pressure, cholesterol, overweight/obesity, tobacco use, lack of physical activity and diabetes. Cessation of tobacco use, reduction of salt in the diet, consuming fruits and vegetables, regular physical activity and avoiding harmful use of alcohol have been shown to reduce the risk of CVDs. Moreover, drug treatment of diabetes, hypertension and high blood lipids may be necessary to reduce cardiovascular risk and prevent heart attacks and strokes. In terms of attributable deaths, the leading CVD risk factor is raised blood pressure (to which 13% of global deaths is attributed), followed by tobacco use (9%), raised blood glucose (6%), physical inactivity (6%) and overweight and obesity (5%) (<http://www.cdc.gov/heartdisease/index.htm>).

In addition to the modifiable risk factors, there are some risk factors that cannot be changed (age, gender, hereditary factors). However, people in these high-risk categories should receive regular check-ups.

There are also a number of underlying determinants of CVDs or "the causes of the causes". These are a reflection of the major forces driving social, economic and cultural change, globalization, urbanization and population ageing. Other determinants of CVDs include poverty, stress and family history.

At the individual level, for prevention of first heart attacks and strokes, individual health-care interventions need to be targeted to those at high total cardiovascular risk or those with single risk factor levels above traditional thresholds, such as hypertension and hypercholesterolemia. The former approach is more cost-effective than the latter and has the potential to substantially reduce cardiovascular events. This approach is feasible in primary care in low-resource settings, including by non-physician health workers (<http://www.cdc.gov/stroke/index.htm>).

For secondary prevention of CVD in those with established disease, including diabetes, treatment with aspirin, beta-blockers, angiotensin-converting enzyme inhibitors or statins are necessary. It has been estimated that a regimen of aspirin, statin and blood pressure-lowering agents may significantly reduce the risk of death from CVD in people at high cardiovascular risk. Providing such a regimen to those eligible between 40-79 years of age has been estimated to avert about one fifth of cardiovascular deaths in the next 10 years, with 56% of deaths averted in people younger than 70 years.

The benefits of these interventions are largely independent, but when used together with smoking cessation, nearly 75% of recurrent vascular events may be prevented. Currently there are major gaps in the implementation of these interventions particularly at the primary health care level. In addition costly surgical operations (i.e. coronary artery bypass; balloon angioplasty; valve repair and replacement; heart transplantation; artificial heart operations) or medical devices (i.e. pacemakers, prosthetic valves, patches for closing holes in the heart) are sometimes required to treat some CVDs.

Prevention of heart attacks and strokes through a total cardiovascular risk approach is more cost-effective than treatment decisions based on individual risk factor thresholds only and should be part of the basic benefits package for pursuing universal health coverage. Achieving this target will

require strengthening key health system components, including health-care financing to ensure access to basic health technologies and essential NCD medicines (<http://www.cdc.gov/heartdisease/index.htm>).

Sources:

- WHO/Europe, Cardiovascular diseases - <http://www.euro.who.int/en/health-topics/noncommunicable-diseases/cardiovascular-diseases>
- WHO, Cardiovascular diseases, Fact sheet N°317, 2015 - <http://www.who.int/mediacentre/factsheets/fs317/en/>
- NCD Alliance, Cardiovascular diseases - <http://www.ncdalliance.org/node/38>
- Center for disease control and prevention (CDC), Heart disease - <http://www.cdc.gov/heartdisease/index.htm>
- Center for disease control and prevention (CDC), Stroke - <http://www.cdc.gov/stroke/index.htm>

1.2 CANCER

The Burden

Cancer is a leading cause of death worldwide and accounts for 7.6 million deaths (around 15% of all deaths) per year. 66% of all cancer deaths occurred in LMICs. Deaths from cancer worldwide are projected to continue rising, with an estimated 13.1 million deaths in 2030 (WHO, Cancer, Fact sheet N°297, 2015).

With more than 3 million new cases and 1.7 million deaths each year, cancer represents the second most important cause of death and morbidity in Europe after CVDs.

The Diseases

Cancer refers to any one of a large number of diseases characterized by the development of abnormal cells that divide uncontrollably and have the ability to infiltrate and destroy normal body tissue. This arises from a change in one single cell, and may be started by external agents and inherited genetic factors and can affect almost any part of the body.

The transformation from a normal cell into a tumor cell is a multistage process where growths often invade surrounding tissue and can metastasize to distant sites. These changes result from the interaction between a genetic factors and external agents such as the chemicals in tobacco smoke, or radiation, such as ultraviolet (UV) rays from the sun.

The main types of cancer are: lung (1.4 million deaths/year); stomach (737,000 deaths); liver (695,000 deaths); colorectal (609,000 deaths); breast (458,000 deaths) (<http://www.ncdalliance.org/node/40>).

In particular the most common types of cancer in males are lung cancer, prostate cancer, colorectal cancer, and stomach cancer, and in females, the most common types are breast cancer, colo-

rectal cancer, lung cancer, and cervical cancer. In children, acute lymphoblastic leukemia and brain tumors are most common except in Africa where non-Hodgkin lymphoma occurs more often. In 2012, about 165,000 children under 15 years of age were diagnosed with cancer.

The Socioeconomic Impact

The first EU-wide analysis of the economic impact of cancer in European Union countries (2009) revealed that the total cost was 126 billion euro and of that 51 billion euro was down to healthcare costs including doctors' time and drug costs. Lost productivity, because of work missed through sickness or dying young, cost 52 billion euro while the cost to families of providing care was put at 23 billion euro (<http://www.who.int/cancer/en/>).

Lung cancer accounted for more than a tenth of all cancer costs in Europe. The deadly cancer tends to affect people at an earlier age than other cancers so the lost productivity through early deaths is a major factor.

Prevention and Risk Factors

The most-studied known or suspected risk factors for cancer include:

Age: advancing age is the most important risk factor for cancer overall, and for many individual cancer types. According to the most recent statistical data from NCI's Surveillance, Epidemiology, and End Results program, the median age of a cancer diagnosis is 66 years (<http://www.who.int/cancer/prevention/en/>).

Cancer-Causing Substances: cancer is caused by changes to certain genes that alter the way our cells function. Some of these genetic changes occur naturally when DNA is replicated during the process of cell division. But others are the result of environmental exposures that damage DNA. These exposures may include physical carcinogens, such as ultraviolet and ionizing radiation or asbestos, chemical carcinogens, such as vinyl chloride, or betanaphthylamine, components of tobacco smoke, aflatoxin (a food contaminant) and arsenic (a drinking-water contaminant), biological carcinogens, such as infections from certain viruses, bacteria or parasites.

Tobacco: tobacco use is a leading cause of cancer and of death from cancer. People who use tobacco products or who are regularly around environmental tobacco smoke (also called secondhand smoke) have an increased risk of cancer because tobacco products and secondhand smoke have many chemicals that damage DNA. Tobacco use causes many types of cancer, including cancer of the lung, larynx (voice box), mouth, esophagus, throat, bladder, kidney, liver, stomach, pancreas, colon and rectum, and cervix, as well as acute myeloid leukemia. People who use smokeless tobacco (snuff or chewing tobacco) have increased risks of cancers of the mouth, esophagus, and pancreas.

Alcohol Drinking: alcohol can increase the risk of cancer of the mouth, throat, esophagus, larynx (voice box), liver, and breast. The more you drink, the higher your risk. The risk of cancer is much higher for those who drink alcohol and also use tobacco.

Radiation: radiation of certain wavelengths, called ionizing radiation, has enough energy to damage DNA and cause cancer. Ionizing radiation includes radon, x-rays, gamma rays, and other forms of high-energy radiation. Lower-energy, non-ionizing forms of radiation, such as visible light and the energy from cell phones and magnetic fields, do not damage DNA and have not been found to

cause cancer.

Infectious Agents: certain infectious agents, including viruses, bacteria, and parasites, can cause cancer in infected people or increase the risk that cancer will form. Some viruses can disrupt normal controls on cell growth and proliferation. They may also increase the chance that a person will be affected by other cancer risk factors, such as UV radiation or substances in tobacco smoke that cause cancer. In the developing world nearly 20% of cancers are due to infections such as hepatitis B, hepatitis C (liver cancer), human papillomavirus (HPV) (cervical cancer) and helicobacter pylori (stomach cancer).

Chronic Inflammation: in chronic inflammation, the inflammatory process may begin even if there is no injury, and it does not end when it should. Why the inflammation continues is not always known. Chronic inflammation may be caused by infections that don't go away, abnormal immune reactions to normal tissues, or conditions such as obesity. Over time, chronic inflammation can cause DNA damage and lead to cancer. For example, people with chronic inflammatory bowel diseases, such as ulcerative colitis and Crohn disease, have an increased risk of colon cancer.

Diet: the dietary component is associated with a change in cancer risk (i.e. vegetables, fruits, whole grains, processed and red meat), not that the dietary component is responsible for, or causes, the change in risk. For example, study participants with and without cancer could differ in other ways besides their diet, and it is possible that some other difference accounts for the difference in cancer.

Obesity: people who are obese may have an increased risk of several types of cancer, including cancers of the breast (in women who have been through menopause), colon, rectum, endometrium (lining of the uterus), esophagus, kidney, pancreas, and gallbladder. Conversely, eating a healthy diet, being physically active, and keeping a healthy weight may help reduce risk of some cancers. These healthy behaviors are also important to lessen the risk of other illnesses, such as heart disease, type II diabetes, and high blood pressure.

Sunlight: the sun, sunlamps, and tanning booths all give off UV radiation. Exposure to UV radiation causes early aging of the skin and skin damage that can lead to skin cancer.

Many of the most common high-impact cancers – breast, cervical, oral and colorectal cancers – lend themselves to affordable and accessible early detection through screening, with high potential for recovery if diagnosed at an early stage and appropriate treatment is provided.

More than 30 % of cancers are preventable through modification of behavior and lifestyles. Tobacco consumption and excessive alcohol consumption cause about 40% of the total cancer burden. If the consequences of inappropriate diet, obesity and insufficient physical activity are added, the percentage of cancers due to an unhealthy lifestyle rises to 60%.

In addition, a significant proportion of cancers can be cured, by surgery, radiotherapy or chemotherapy and targeted therapy, especially if they are detected early.

Sources:

- WHO/Europe, Cancer - <http://www.euro.who.int/en/health-topics/noncommunicable-diseases/cancer>

- WHO, Cancer - <http://www.who.int/cancer/en/>
- NCD Alliance, Cancer - <http://www.ncdalliance.org/node/40>
- WHO, Cancer, Fact sheet N°297, 2015 - <http://www.who.int/mediacentre/factsheets/fs297/en/>
- WHO, Cancer Prevention - <http://www.who.int/cancer/prevention/en/>

1.3 DIABETES

The Burden

Diabetes is one of the most common NCDs globally. It is the fourth or fifth leading cause of death in most high-income countries and there is substantial evidence that it is epidemic in many economically developing and newly industrialized countries. Diabetes can lead to cardiovascular disease, blindness, kidney failure, loss of limbs and loss of life. It causes suffering and hardship for the approximately 60 million people in the European Region currently living with the disease (about 10.3% of men and 9.6% of women aged 25 years and over), while also straining the Region's economies and health systems.

387 million people had diabetes in 2014, and without effective prevention and management programmes this number is expected to rise to 592 million by 2035. 77% of people with diabetes live in LMICs. Prevalence of diabetes is increasing in the European Region, already reaching rates of 10-12% of the population in some Member States. This increase is strongly associated with increasing trends towards overweight and obesity, unhealthy diets, physical inactivity and socioeconomic disadvantage (WHO, Diabetes, Fact sheet N°312, 2015).

The Diseases

Diabetes is a chronic disease that arises when the pancreas does not produce enough insulin, or when the body cannot effectively use the insulin it produces. Failure of insulin production, insulin action or both leads to raised glucose levels in the blood (hyperglycaemia). This is associated with long-term damage to the body and the failure of various organs and tissues (Alberti KG, et al. 1998).

Type1 diabetes, although less common than type 2 diabetes, is increasing each year in both rich and poor countries. In most high-income countries, the majority of people with diabetes in the younger age groups have type 1. Type 1 diabetes is an autoimmune disease characterized by the destruction of the insulin-producing cells in the pancreas. Consequently, people with type 1 diabetes produce very little or no insulin and must take insulin to survive. Type 1 diabetes is not preventable with current knowledge.

Type 2 diabetes makes up about 85 to 95% of all diabetes in high-income countries and may account for an even higher percentage in LMICs. Type 2 diabetes results from the body's ineffective use of insulin (insulin resistance). Type 2 diabetes is largely preventable and can often be managed through exercise and diet. However, in many cases, oral drugs are needed and often insulin is required. Impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG) are intermediate conditions in the transition between normality and diabetes. People with IGT or IFG are at high risk of progressing to type2 diabetes, although this is not inevitable.

Gestational diabetes mellitus (GDM) is common and, like obesity and type 2 diabetes, is increasing throughout the world. GDM is a condition of hyperglycaemia during pregnancy in women without previously diagnosed diabetes. GDM affects about 4% of all pregnant women. Gestational diabetes is most often diagnosed through prenatal screening, rather than reported symptoms. It is generally temporary, but women with gestational diabetes may develop type 2 later in life.

If diabetes is not managed correctly, sufferers are likely to become progressively ill and debilitated. Over time, diabetes can damage the heart, blood vessels, kidneys, eyes and nerves. 50% of people with diabetes die of cardiovascular disease (primarily heart disease and stroke), and 10-20% of people with diabetes die of kidney failure.

Long-term accumulated damage to the small blood vessels in the eye leads to diabetic retinopathy, an important cause of blindness. After 15 years of diabetes, approximately 2% of people become blind, and about 10% develop severe visual impairment.

Damage to the nerves (diabetic neuropathy) affects up to 50% of people with diabetes. Although many different problems can occur as a result of diabetic neuropathy, common symptoms are tingling, pain, numbness, or weakness in the feet and hands. Combined with reduced blood flow, neuropathy in the feet increases the chance of foot ulcers and eventual limb amputation.

The overall risk of dying among people with diabetes is at least double the risk of their peers without diabetes.

The Socioeconomic Impact

Diabetes creates an economic burden at the personal, national, and global level. In 2013, 10.8% of global health spending was directed at diabetes, and at the national level, the majority of countries dedicate between 5% and 18% of health spending to diabetes. Global health expenditure for diabetes was 548 billion USD in 2013, and this amount is projected to increase to 627 billion USD by 2035 (<http://www.ncdalliance.org/node/37>).

Prevention and Risk Factors

Genetics, some environmental factors and viral infections have been shown to increase one's risk of type 1 diabetes, though research is still needed to further define type 1 diabetes risk factors. Conversely, preventative measures can be taken with type 2 diabetes (for example lifestyle changes in diet and physical activity can be preventative actions), where risk factors are well known: Unhealthy diet: eating high levels of refined carbohydrates and saturated fat and not enough fruits and vegetables contributes to weight gain, thereby increasing the risk of diabetes (<http://www.euro.who.int/en/health-topics/noncommunicable-diseases/diabetes>).

Physical inactivity: studies have shown that just 30 minutes of moderate exercise a day, five days a week is enough to promote good health and reduce the chance of developing type 2 diabetes. Overweight and obesity (BMI over 25 kg/m²): have been estimated to account for about 65-80% of new cases of type 2 diabetes. The risk is a function of the age of onset and the duration of obesity, and weight gain during adult life. Overweight people run a lower relative risk than obese people, however the fraction of disease attributable to overweight may be as high as, if not higher than, that due to obesity. This demonstrates the importance of preventing weight gain in all ranges. Low birth weight is also associated with increased risk of developing type 2 diabetes.

Age: the older a person is, the greater their risk of diabetes. However, type 2 diabetes is increasing in all age groups and is now also reported among children and adolescents.

Gestational diabetes: women who have had GDM have an increased risk of developing type 2 diabetes in later years. GDM is also associated with increased risk of obesity and abnormal glucose metabolism during childhood and adult life in the offspring.

Socioeconomic determinants: socioeconomic disadvantage contributes to the development of diabetes and its complications through inequitable access to quality treatment and environmental conditions that promote unhealthy choices. Almost 80% of diabetes cases occur in LMICs. However, high rates of diabetes are also found among the lower-income groups in many middle- and high-income countries. For example, morbidity from diabetes complications is three and a half times higher among the poorest people in the United Kingdom than the richest.

Other risk factors are: family history of diabetes, high blood pressure, poor nutrition during pregnancy, ethnic group, experiences and influences in early life.

Though type 2 diabetes is largely preventable, it is unfair to believe that people have only themselves and their lifestyle to blame. Individual responsibility is important, but governments and societies must also play a part. In general, energy-dense, nutrient-poor foods, such as refined grains, added sugar and fats are not only convenient and tasty but also less expensive than nutrient-dense lean meats, fish, fresh vegetables and fruit. Additionally, quitting smoking is a positive lifestyle change that can prevent the development of type 2 diabetes.

Healthy choices are easier when the policy environment nudges people in that direction or when the environment makes them the automatic choices.

Sources:

- WHO Europe, Diabetes - <http://www.euro.who.int/en/health-topics/noncommunicable-diseases/diabetes>
- WHO, Diabetes, Fact sheet N°312, 2015 - <http://www.who.int/mediacentre/factsheets/fs312/en/>
- NCD Alliance, Diabetes - <http://www.ncdalliance.org/node/37>
- Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med.* 1998 Jul;15(7):539-53. [http://onlinelibrary.wiley.com/doi/10.1002/\(SICI\)1096-9136\(199807\)15:7%3C539::AID-DIA668%3E3.0.CO;2-S/epdf](http://onlinelibrary.wiley.com/doi/10.1002/(SICI)1096-9136(199807)15:7%3C539::AID-DIA668%3E3.0.CO;2-S/epdf)
- Definition, diagnosis and classification of diabetes mellitus and its complications : report of a WHO consultation. Part 1, Diagnosis and classification of diabetes mellitus - See more at: <http://apps.who.int/iris/handle/10665/66040#sthash.OYeb5K1l.dpuf>
- Center for disease control and prevention (CDC), Diabetes - <http://www.cdc.gov/diabetes/data/index.html>

1.4 CHRONIC RESPIRATORY DISEASES

The Burden

Chronic respiratory diseases (CRDs) can cause ill health, disability and death, they adversely impact the quality of life of affected individuals and can lead to premature death. They also have large adverse economic effects on families, communities and societies in general. WHO/Europe aims to support Member States in their efforts to reduce the toll of morbidity, disability and premature mortality related to chronic respiratory diseases.

Lung health is less well recognized as a critical health factor than other indicators, such as weight and blood pressure. However, anyone who has struggled to breathe, even for a short time, knows how essential it is. Preventable chronic respiratory diseases are currently under-recognised, under-diagnosed, under-treated and insufficiently prevented. Respiratory conditions are believed to be the most commonly managed problems in general practice. Data from the Bettering the Evaluation and Care of Health survey of general practitioners suggest that respiratory conditions were managed in approximately 1 in 5 encounters from 2004–05 to 2013–14. According to the latest available data for 1997–2006, over 12% of infant deaths in the European Region are due to respiratory diseases. In general, rates are considerably higher in eastern than in western Europe. Worldwide 235 million people are affected by asthma. It is the most common chronic disease among children and also affects adults. The causes of asthma and the reasons for its increasing prevalence in LMICs are not well understood (<http://www.ncdalliance.org/node/39>).

64 million people suffer from chronic obstructive pulmonary disease (COPD), a term that covers emphysema and chronic bronchitis. 90% live in LMICs. COPD caused more than 3 million deaths in 2005. The number of COPD deaths is expected to increase by more than 30% in the next 10 years and WHO projects it will be the 3rd leading cause of death worldwide by 2030.

The Diseases

The term CRDs describes a range of diseases of the airways and the other structures of the lungs including:

Asthma: a chronic inflammatory disorder of the airways. People with asthma experience episodes of wheezing, breathlessness and chest tightness due to widespread narrowing of the airways (<http://www.who.int/respiratory/en>).

COPD: limits airflow in the lungs, which can lead to mild or severe shortness of breath that is not fully reversible even with treatment. COPD is a serious long-term disease that mainly affects older people, and includes conditions such as emphysema and chronic bronchitis.

'Hay fever': is a term commonly used to describe allergic rhinitis when it is caused by seasonal exposure to pollen. Allergic rhinitis is one of the most common chronic respiratory conditions.

Bronchiectasis: refers to an abnormal and irreversible widening of air passages in the lungs. People with bronchiectasis are prone to infections as mucus accumulates in the airways and becomes stagnant. It has a number of causes, including COPD, cystic fibrosis, low antibody levels and infections such as tuberculosis, whooping cough and measles.

Chronic sinusitis: is the inflammation of the lining of one or more sinuses (large air cavities inside the face bones). It occurs when normal draining of the sinuses is obstructed by swelling, excessive mucus, or an abnormality in the structure of the sinuses. It can cause discomfort and pain and is often linked to similar inflammation inside the nose.

Cystic fibrosis (CF): is a hereditary disease in which mucus from glands is thicker and stickier than normal, affecting the lungs and other organs. Difficulty in clearing mucus from the airway leads to chest infections and airflow obstruction, with related problems such as bronchiectasis and shortened life expectancy.

Occupational lung diseases: result from breathing in harmful dusts or fumes, such as silica, asbestos and coal dust. This exposure typically occurs in the workplace. Pneumoconiosis, or scarring of the lung tissue caused by inhaled dust, is one of the most common forms of occupational lung disease.

Sleep apnoea: is a condition that affects breathing while asleep. It reduces airflow which causes intermittent dips in the amount of oxygen in the blood and disturbs sleep. The individual with sleep apnoea is often unaware of the night-time breathing difficulties.

Pulmonary fibrosis: is a scarring or thickening of the lungs. It affects the transfer of oxygen into the blood. Sometimes a cause can be identified for this but often the cause is not known. In this case it is described as idiopathic pulmonary fibrosis.

The Socioeconomic Impact

Similar to other NCDs, chronic respiratory diseases place a financial burden on those affected, their families and communities.

Prevention and Risk Factors

WHO/Europe aims to support Member States in their efforts to reduce the toll of morbidity, disability and premature mortality related to chronic respiratory diseases. Specific objectives include surveillance to assess the current problem and monitor progress, reduction of exposure to risk factors and strengthening of health systems to improve care for people suffering from chronic respiratory diseases (<http://www.euro.who.int/en/health-topics/noncommunicable-diseases/chronic-respiratory-diseases>).

The major risk factors for lung disease are well known. Mitigation of these risks can prevent or reduce the impact of lung disease.

Tobacco Control: direct or indirect exposure to tobacco smoke is a major risk factor for all lung diseases. Effective tobacco control is essential to any strategy for preventing lung disease. According to the WHO Global Status Report on NCDs 2010, smoking is estimated to cause about 71% of all lung cancer deaths and 42% of chronic respiratory disease worldwide. Of the six WHO regions, the highest overall prevalence for smoking in 2008 was estimated to be the in the European Region, at nearly 29%. Survey data from 2002–2007 indicate that over half of all children aged 13–15 years in many countries in the European Region are exposed to second-hand tobacco smoke at home. This exposure exceeds 90% in the Balkans and the Caucasus. Second-hand smoke causes severe respiratory health problems in children, such as asthma and reduced lung function; and

asthma is now the most common chronic disease among children throughout the Region.

Occupational Health: preventive measures, such as adequate ventilation and early detection are vital to addressing occupational lung diseases.

Indoor and Outdoor Air Quality: improvements in cook stove technology can help reduce exposure to indoor air pollution in homes. Smoke-free legislation protects air quality in workplaces, public places, health care facilities, educational facilities and public transportation. Other air quality controls can reduce and eliminate exposure from industrial emissions, traffic, etc. Indoor air pollution from biological agents related to damp and mould increases the risk of respiratory disease in children and adults. Children are particularly susceptible to the health effects of damp, which include respiratory disorders such as irritation of the respiratory tract, allergies and exacerbation of asthma. Damp is often associated with poor housing and social conditions, poor indoor air quality and inadequate housing hygiene, which includes factors such as overcrowding, low air exchange rate, low indoor temperature and poor insulation.

Diet and Nutrition: associations have been reported between chronic respiratory disease and diet. It is therefore feasible that dietary strategies compatible with those already existing for the control of coronary heart disease, diabetes and cancer could be developed for the primary and secondary prevention of CRDs as well.

Early life: evidence shows that a child's health in the first year of life affects the subsequent respiratory health. Maternal smoking during pregnancy adversely affects the lung function of the child at birth. Long-term average exposure to particulate matters determines both the risks of chronic effects of pollution on children's health and the frequency of acute effects, such as the aggravation of asthma or incidence of respiratory symptoms.

Socioeconomically disadvantaged populations in low and middle-income countries are especially vulnerable to the development and exacerbation of respiratory diseases, in part because: they are more exposed to indoor solid fuels and unsafe occupational environments; occupational chronic respiratory diseases are often not adequately recognized as a problem; treatment drugs are often unavailable or not affordable and tobacco use tends to be higher among poor people than among wealthier members of society.

Sources:

- WHO/Europe, Chronic respiratory diseases - <http://www.euro.who.int/en/health-topics/noncommunicable-diseases/chronic-respiratory-diseases>
- WHO, Chronic respiratory diseases - <http://www.who.int/respiratory/en/>
- NCD Alliance, Chronic respiratory diseases - <http://www.ncdalliance.org/node/39>

1.5 OBESITY

The Burden

Obesity is a leading preventable cause of death worldwide, with increasing rates in adults and children. It is one of the greatest public health challenges of the 21st century. Its prevalence has

tripled in many countries of the WHO European Region since the 1980s, and the numbers of those affected continue to rise at an alarming rate. According to estimates for 2008, over 50% of both men and women in the WHO European Region were overweight, and roughly 23% of women and 20% of men were obese. Based on the latest estimates in European Union countries, overweight affects 30-70% and obesity affects 10-30% of adults. In the European Region up to 27% of 13 years old and 33% of 11 years old child are obese.

In 2013, the American Medical Association classified obesity as a disease. In addition to causing various physical disabilities and psychological problems, excess weight drastically increases a person's risk of developing a number of NCDs, including CVD, cancer and type 2 diabetes. The risk of developing more than one of these diseases (co-morbidity) also increases with increasing body weight. Obesity is already responsible for 2–8% of health costs and 10–13% of deaths in different parts of the European Region (<http://www.euro.who.int/en/health-topics/noncommunicable-diseases/obesity>).

The WHO predicts that overweight and obesity may soon replace more traditional public health concerns such as under nutrition and infectious diseases as the most significant cause of poor health.

The Diseases

Obesity is a complex disorder involving accumulation of an excessive amount of body fat to the extent that it may have a negative effect on health, leading to reduced life expectancy and/or increased health problems. Obesity is diagnosed when the body mass index is 30 or higher (<http://www.who.int/topics/obesity/en/>).

Obese people are more likely to develop a number of potentially serious health problems, including:

- High triglycerides and low high-density lipoprotein (HDL) cholesterol
- Type 2 diabetes
- High blood pressure
- Metabolic syndrome: a combination of high blood sugar, high blood pressure, high triglycerides and low HDL cholesterol
- Heart disease
- Stroke
- Cancer, including cancer of the uterus, cervix, endometrium, ovaries, breast, colon, rectum, esophagus, liver, gallbladder, pancreas, kidney and prostate
- Breathing disorders, including sleep apnea, a potentially serious sleep disorder in which breathing repeatedly stops and starts
- Gallbladder disease
- Gynecological problems, such as infertility and irregular periods
- Erectile dysfunction and sexual health issues
- Nonalcoholic fatty liver disease, a condition in which fat builds up in the liver and can cause inflammation or scarring

The Socioeconomic Impact

Obesity is a public health and policy problem because of its prevalence, costs, and health effects. Reported relative economic burdens ranged from 0.09% to 0.61% of each country's gross domestic product (GDP). Obesity appears to be responsible for a substantial economic burden in many Eu-

European countries, and the costs identified in the available studies presumably reflect conservative estimates.

In addition to its health impacts, obesity leads to many problems and social stigmatization, including disadvantages in employment and increased business costs. These effects are felt by all levels of society from individuals, to corporations, to governments. Moreover, the overall quality of life of an obese person may be diminished (causing depression, disability, sexual problems, shame and guilt, social isolation, lower work achievement).

Prevention and Risk Factors

Obesity usually results from a combination of causes and contributing factors, including:

Physical inactivity: although there are genetic, behavioral and hormonal influences on body weight, obesity occurs when you take in more calories than you burn through exercise and normal daily activities. With a sedentary lifestyle, you can easily take in more calories every day than you use through exercise and normal daily activities (<http://www.who.int/topics/obesity/en>).

Unhealthy diet and eating habits: an excessive food energy intake and a diet lacking in fruits and vegetables, full of fast food, and laden with high-calorie beverages and oversized portions contribute to weight gain.

Medical problems: in some people, obesity can be traced to a medical cause, such as Prader-Willi syndrome, Cushing's syndrome and other conditions such as endocrine disorders or psychiatric illness. Medical problems, such as arthritis, also can lead to decreased activity, which may result in weight gain.

Genetics: genes may affect the amount of body fat stored, and where that fat is distributed. Genetics may also play a role in how efficiently the body converts food into energy and how the body burns calories during exercise.

Family lifestyle: obesity tends to run in families. That's not just because of genetics. Family members tend to share similar eating and activity habits (Sonntag D, et al. *Nutrients*. 2015 Oct 16;7(10):8565-76.).

Certain medications: some medications can lead to weight gain if you don't compensate through diet or activity. These medications include some antidepressants, anti-seizure medications, diabetes medications, antipsychotic medications, steroids and beta blockers.

Social and economic issues: research has linked social and economic factors to obesity. Avoiding obesity is difficult if you don't have safe areas to exercise. Similarly, you may not have been taught healthy ways of cooking, or you may not have money to buy healthier foods. In addition, the people you spend time with may influence your weight (you're more likely to become obese if you have obese friends or relatives).

Age: obesity can occur at any age, even in young children. But with age, hormonal changes and a less active lifestyle increase the risk of obesity. In addition, the amount of muscle in the body tends to decrease with age, leading to a decrease in metabolism. These changes also reduce calorie needs, and can make it harder to keep off excess weight.

Pregnancy: during pregnancy, a woman's weight necessarily increases. Some women find this weight difficult to lose after the baby is born. This weight gain may contribute to the development of obesity in women.

Quitting smoking: quitting smoking is often associated with weight gain. And for some, it can lead to enough weight gain that the person becomes obese. In the long run, however, quitting smoking is still a greater benefit to your health than continuing to smoke.

Lack of sleep: not getting enough sleep or getting too much sleep can cause changes in hormones that increase the appetite.

Sources:

- WHO/Europe, Obesity - <http://www.euro.who.int/en/health-topics/noncommunicable-diseases/obesity>
- WHO, Obesity - <http://www.who.int/topics/obesity/en/>
- Dobbs R, Sawers C, Thompson F, Manyika J, Woetzel J, Child P, McKenna S, Spatharou A. How the world could better fight obesity. Report McKinsey Global Institute, 2014 <http://ncdalliance.org/news/how-world-could-better-fight-obesity>
- Sonntag D, Schneider S, Mdege N, Ali S, Schmidt B. Beyond Food Promotion: A Systematic Review on the Influence of the Food Industry on Obesity-Related Dietary Behaviour among Children. *Nutrients*. 2015 Oct 16;7(10):8565-76.
- Center for disease control and prevention (CDC), Division of Nutrition, Physical Activity, and Obesity - <http://www.cdc.gov/nccdphp/dnpao/index.html>

1.6 MUSCULOSKELETAL DISEASES

The Burden

Musculoskeletal conditions (MSCs) are extremely common and have important consequences for the individual, society and the health service due to their frequency, chronicity, and resultant disability and they affect hundreds of millions of people around the world. Typically around 50% of the population report musculoskeletal pain at one or more sites for at least one week in the last month. MSCs are the second most common cause of disability worldwide, measured by years lived with disability (YLDs), with low back pain being the most frequent condition. Disability due to MSC is increased by 45% from 1990 to 2010, in particular osteoarthritis (OA), and is expected to continue to rise with an increasingly obese, sedentary and ageing population (Woolf AD et al, 2003).

MSCs significantly affect the psychosocial status of affected people as well as their families and careers. The pain and physical disability brought about by MSCs affect social functioning and mental health, further diminishing the patient's quality of life.

The Diseases

MSCs are a diverse group with regard to pathophysiology but are linked anatomically and by their

association with pain and impaired physical function. They encompass a spectrum of conditions, from those of acute onset and short duration to lifelong disorders.

They can broadly be categorized as joint diseases, physical disability, spinal disorders, and conditions resulting from trauma. Example of MSCs include spains, strains, carpal tunnel, hernia. Those conditions with the greatest impact on society include rheumatoid arthritis, OA, osteoporosis, low back pain, and limb trauma.

Population surveys show that back pain is the most common site of regional pain in younger and middle aged adults, and knee pain in older people. The prevalence of physical disability is higher in women than men and it rises with age: around 60% of women aged over 75 living in the community report some physical limitations (<http://www.hse.gov.uk/msd/>).

The Socioeconomic Impact

The cost of treating major MSCs is greater than for treatment of many other common health conditions. Yet research dollars to identify causes, create new treatments, and reduce pain and disability remain much lower than that of other health conditions.

The costs of MSCs include those to healthcare services, to society and indirect costs. MSCs are among the most commonly reported causes of work-related ill health. In individuals of working age, MSCs (in particular back pain and generalised widespread pain) are a common cause of sick leave and long term work disability and hence a big problem for the individuals affected, with huge economic consequences for society.

Among older people rheumatoid arthritis, OA and osteoporosis are associated with a loss of independence and a need for more support in the community or admission to residential care. Rheumatoid arthritis alone costs the UK economy between £3.8 and 4.8 billion a year. The average cost of a major hip procedure is £7800 and of a major knee procedure £6000.

Around 15-20% of consultations in primary care are for MSCs. Many of these people are referred to allied health professions such as physiotherapists, occupational therapists or chiropractors; or to medical specialists such as rheumatologists, orthopedic surgeons or rehabilitation specialists. Total joint replacement (mainly of the hip or knee) is one of the most common elective operations for older people in most European countries. The major consequences for the health services of osteoporosis are forearm and vertebral fractures and hip fractures, significantly associated with higher mortality (Woolf AD, et al 2003).

Prevention and Risk Factors

The prevalence of certain MSCs varies depending on non-modifiable and modifiable risk factors.

Non-modifiable risk factors are:

Age: The risk of developing most types of MSCs increases with age. The increasing number of older people and the changes in lifestyle throughout the world mean that the burden on people and society will increase dramatically (<http://www.cdc.gov/arthritis/temp/pilots-201208/pilot1/online/arthritis-challenge/02-Epidemiology/modrisks.htm>).

Gender: Most types of arthritis are more common in women; 60% of all people with arthritis are women. Gout is more common in men.

Genetic: Specific genes are associated with a higher risk of certain types of arthritis, such as rheumatoid arthritis, systemic lupus erythematosus, and ankylosing spondylitis.

Demographic factors: such as lower levels of education and lower income are associated with some MSCs. Although these risk factors are potentially modifiable, it is not clear if modifying them would reduce the risk of arthritis since the mechanisms by which they increase the risk are not yet understood.

Modifiable risk factors are:

Obesity: is a risk factor for several common forms of arthritis such as OA of the knee in women and gout in men. Obesity is a risk factor for both the development and progression of OA. Reducing weight, among the overweight, will decrease the risk of developing MSCs. About 66% of adults with doctor-diagnosed arthritis are overweight or obese (compared with 53% of adults without doctor-diagnosed arthritis) (Wearing SC, et al 2006).

Joint injuries and damage to ligaments or cartilage: resulting from occupation, sports, or other sources of injury can increase the risk of MSCs. For example, a history of joint trauma is the strongest risk factor for unilateral OA of the knee or hip.

Specific occupations: numerous studies have demonstrated an excess of site-specific MSCs in occupational groups with repetitive use of specific joints. For example, occupations requiring knee bending have been associated with knee OA in both retrospective and prospective studies. In addition, farming has been associated with hip OA in several retrospective studies.

Sources:

- Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. Bulletin of the World Health Organization 2003;81:646-656.
- Wearing SC, Hennig EM, Byrne NM, Steele JR, Hills AP. Musculoskeletal disorders associated with obesity: a biomechanical perspective. Obes Rev. 2006 Aug;7(3):239-50.
- Health and Safety Executive. Musculoskeletal disorder - <http://www.hse.gov.uk/msd/>
- Center for disease control and prevention (CDC), Arthritis, Osteoporosis, and Chronic Back Conditions. Final Review 2010 - http://www.cdc.gov/nchs/data/hpdata2010/hp2010_final_review_focus_area_02.pdf
- Center for disease control and prevention (CDC), Arthritis - The Arthritis Challenge - <http://www.cdc.gov/arthritis/temp/pilots-201208/pilot1/online/arthritis-challenge/02-Epidemiology/modrisks.htm>

1.7 MENTAL HEALTH AND NEUROLOGICAL DISORDERS

The Burden

Mental ill health accounts for almost 20% of the burden of disease in the WHO European Region and mental health problems affect one in four people at some time in life. Six out of the 20 countries with the highest suicide rates in the world are in the European Region.

In many western countries, mental disorders are the leading cause of disability, with an estimated 83 million people being affected. Yet even these figures are likely to underestimate the scale of the problem, as only a limited number of disorders were included and it did not collect data on those aged over 65, a group that is at particular risk.

Rates for women are significantly higher as compared to those for men, except for substance use disorders, and psychotic disorders. These figures also fail to capture the complexity of the problems many people face. 32% of those affected had one additional mental disorder, while 18% had two and 14% three or more (http://www.who.int/topics/mental_disorders/en/).

Neuropsychiatric disorders are the third leading cause of disability-adjusted life years (DALYs) and the first cause of years lived with disability (YLD) in Europe.

In the European Region six European countries fall within the top 20 countries with the highest estimated suicide rates globally.

The Diseases

Mental disorders are "psychiatric illnesses" or diseases which appear primarily as abnormalities of thought, feeling or behaviour, producing either distress or impairment of function. Mental diseases represent a wide spectrum of afflictions and often are considered to be comorbid with other common NCDs due to potential bidirectional causality.

There are currently two widely established systems for classifying mental disorders:

- Chapter V of the International Classification of Diseases (ICD-10) produced by the World Health Organization (WHO). Chapter V focuses on "mental and behavioral disorders" and consists of 10 main groups: organic, including symptomatic, mental disorders; mental and behavioral disorders due to use of psychoactive substances; schizophrenia, schizotypal and delusional disorders; mood [affective] disorders; neurotic, stress-related and somatoform disorders; behavioural syndromes associated with physiological disturbances and physical factors; disorders of personality and behavior in adult persons; mental retardation; disorders of psychological development; behavioral and emotional disorders with onset usually occurring in childhood and adolescence; a group of "unspecified mental disorders".

- The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) produced by the American Psychiatric Association (APA). It consists of five axes on which disorder can be assessed: clinical disorders (all mental disorders except personality disorders and mental retardation); personality disorders and mental retardation; general medical conditions (must be connected to a Mental Disorder); psychosocial and environmental problems (for example limited social support network); global assessment of functioning (psychological, social and job-related functions are evaluated on a continuum between mental health and extreme mental disorder).

One of the most common mental diseases is depression. Depression is characterized by depressed or sad mood, diminished interest in activities which used to be pleasurable, weight gain or loss, psychomotor agitation or retardation, fatigue, inappropriate guilt, difficulties concentrating, as

well as recurrent thoughts of death.

Neurological disorders are diseases of the central and peripheral nervous system (brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles). These disorders include epilepsy, Alzheimer disease and other dementias, cerebrovascular diseases including stroke, migraine and other headache disorders, multiple sclerosis, Parkinson's disease, neuro-infections, brain tumors, traumatic disorders of the nervous system such as brain trauma, and neurological disorders as a result of malnutrition.

Dementia is a class of degenerative brain syndromes that negatively affect multiple cognitive processes, including memory, behavior, emotional processing and control, and cognition. There are multiple forms of dementia, with Alzheimer's disease being the most common type.

It is estimated that 50-75% of dementia cases can be classified as Alzheimer's disease (AD). AD causes the destruction of brain cells and associated nerves and interferes with neurotransmitter functions. Particularly, the memory system of the brain is compromised. As the disease progresses, an individual's capacity to communicate, think, and remember deteriorates (http://www.who.int/topics/mental_health/en/).

The Socioeconomic Impact

In 2015, the estimated global cost of dementia was US \$818 billion, or about 1.09% of the world's GDP. In many western countries, mental disorders are responsible for 30-40% of chronic sick leave and costing some 3% of GDP. At the national level, country GDP percentages dedicated to dementia ranged from 0.24% in low-income countries to 1.24% in high-income countries.

Prevention and Risk Factors

There is overlap of risk factors with the other NCDs, and mental and neurological diseases are also often chronic in nature. Mental and neurological diseases occur in all racial, ethnic, and socioeconomic groups. Although the specific causes are not known, many risk factors have been identified or suggested. These include: genetics, older age, tobacco use, harmful alcohol use, unhealthy diet, physical inactivity, cranial injuries, psychological factors (e.g., stressful events) and sociocultural factors (e.g., poverty). A family history of mental and addictive disorders also put individuals at risk. (<http://www.ncdalliance.org/mental-health-and-neurological-disorders>)

Smoking: Previous research suggests depression is an established risk factor for smoking, with nicotine stimulating receptors in the brain which may improve mood in certain types of depression. The significance of nicotine use as a means of ameliorating depressive symptoms was supported by a longitudinal study examining smoking cessation. The study found that smokers with depressive symptoms in a control group continued to be highly symptomatic, while those who received nicotine replacement therapy did not have significantly higher depressive symptom scores relative to their non-depressed peers. Smokers have been found to be more likely than nonsmokers to experience daily symptoms of depression (29% vs. 19%). Notably as depressive symptom scores increase, the probability of smoking cessation decreases. Thus, depression is associated with an increased risk for smoking and, furthermore, may impede smoking cessation efforts.

Alcohol Consumption: Early onset of drinking has been reported to be associated with a range of problematic outcomes, including depressive symptoms. Assessing a clinical population, investiga-

tors reported a dynamic association between negative affect and lapses in sobriety following alcohol treatment.

Physical Inactivity: Physical inactivity and its strong correlate, obesity, have been identified as modifiable risk factors for depression: major depression is associated with an increased risk of transition from an active to an inactive pattern of activity. These findings may have therapeutic implications, with physical activity reported to reduce depressive symptoms – even among individuals who are not clinically depressed.

Sleep Disturbance: Depression appears to be associated with poor sleep throughout the lifespan. Some antidepressant agents are reported to commonly foster sleep disturbance.

Much is now known about what works in mental health promotion, prevention, care and treatment. The challenge is now to implement this knowledge.

Services and practice do not always reflect the knowledge of what works in mental health care and treatment. Many countries have limited community-based mental health services and little specialist help for young or elderly people.

Many people in large mental institutions are subject to neglect and abuse of human rights, reflected in high mortality rates. Stigma and prejudice are widespread and affect every aspect of mental health, including whether people seek and receive help.

Though there currently is no cure for this class of NCDs, some specific diseases have treatments available. For Alzheimer's disease, there is a class of drug treatments known as cholinesterase inhibitors that can slow the progression of the disease. Other drugs are available to dampen some specific symptoms of these diseases, such as mood swings and sleeplessness. Beyond drugs, emotional support and therapy is often employed to help those affected by these diseases.

Sources:

- WHO/Europe, Mental health - <http://www.euro.who.int/en/health-topics/noncommunicable-diseases/mental-health>
- WHO, Mental disorders - http://www.who.int/topics/mental_disorders/en/
- WHO, Mental Health - http://www.who.int/topics/mental_health/en/
- NCD Alliance Mental Health and Neurological Disorders - <http://www.ncdalliance.org/mental-health-and-neurological-disorders>
- Center for disease control and prevention (CDC), Mental Health Awareness - <http://www.cdc.gov/genomics/resources/diseases/mental.htm>
- Center for disease control and prevention (CDC), Mental Illness - <http://www.cdc.gov/mentalhealth/basics/mental-illness.htm>

PART II

2 DETERMINANTS OF NON-COMMUNICABLE DISEASES

2.1 INTRODUCTION

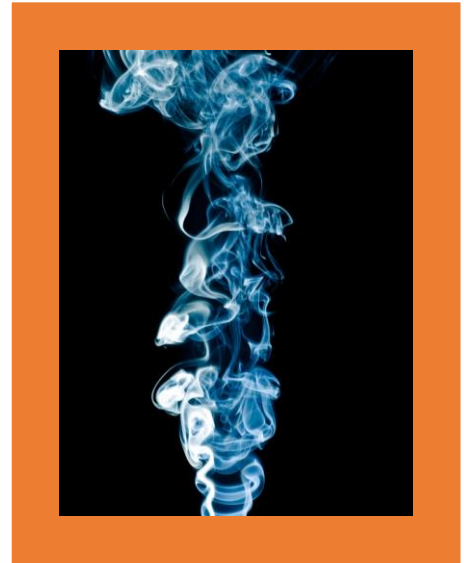
Non-communicable diseases (NCDs) are a leading cause of death in the world. It is well known fact that four health behavior factors, i.e. tobacco and alcohol use, unhealthy diet and physical inactivity, are the main contributors to the burden of NCDs. In fact, these factors contribute to over 20% of global disability-adjusted life years (DALYs; sum of years lived with disability [YLD] and years of life lost [YLL]) (Lim et al. 2012). It can be further exemplified by the fact that all four risk factors together increase mortality risk up to 2.5 times (Martin-Diener et al. 2014).

From the estimates it can be concluded that the burden of NCDs could be substantially diminished through these four risk factors. Decreasing the prevalence of smoking would undoubtedly be the largest input to harm reduction, as smoking together with second-hand smoking is globally accounting for more than 6 million deaths each year. It is followed by alcohol misuse, which accounted for 3.3 million of deaths in 2012. Combination of poor diet and physical inactivity is contributing 10% to the burden of disease worldwide (Lim, Meigs 2014, World Health Organization 2014b). Following discussion gives an overview of these four risk factors and their relation to NCDs. In this context, risk factors equal determinants. We define determinants as factor which contributes to the generation of a trait and which affect the occurrence or rate of occurrence of a disease.

2.2 SMOKING

Tobacco use is stated as one of the leading contributor to preventable deaths globally (World Health Organization 2014b). It is annually responsible for more than 6 million deaths in the world and it contributes 6.3% to the global burden of disease (Lim et al. 2012). Compared to the rest of world, Europe has one of the highest tobacco-attributable mortality rates. Proportion of all deaths attributable to tobacco in Europe among people age of 30 years and older is 16%. In men, it is as high as 25% and among women 7% of deaths due to tobacco use (World Health Organization 2012).

Tobacco smoke includes besides the main ingredient nicotine thousands of different chemicals and over 60 carcinogens (Mainali et al. 2015). Thereby it is clear that tobacco smoke is not harmful only to tobacco users, but has also a significant impact to the health of people surrounded by tobacco smoke. It has been found that every tenth person killed by tobacco is due to secondhand smoking. Furthermore, besides cigarette smoking there are many tobacco products used smokeless (World Health Organization 2014b). Alternative tobacco products do not show as high morbidity and mortality effects, but despite that the health risks of these products should not be underestimated (Mainali et al. 2015). The most recent tobacco product of interest for researchers, policy makers and general public in the last decade has been electronic cigarettes. These are quickly gaining popularity despite the lack of evidence about their impact on public health. It is ongoing process to get answers to questions about their safety, effectiveness for smoking cessation and total impact on public health (Grana, Benowitz & Glantz 2014).



Tobacco smoke has been associated with multiple cardiovascular risks. It is found to affect inflammatory processes, vasomotor dysregulation, oxidative stress, heart rate, cardiac output and blood pressure. Through these processes the risk of atherosclerosis, coronary artery disease, ischemic heart disease and peripheral arterial disease is significantly increased (Mainali et al. 2015). For example, Arain and Cooper (2008) note that tobacco users have approximately 4 times higher odds of getting peripheral arterial disease compared to non-smokers (Arain, Cooper 2008). The effect of smoking is dose-dependent which means that tobacco smoke even in very small doses is harmful (Mainali et al. 2015).

Even if an individual has chosen not to smoke, second-hand smoking can expose the cardiovascular risks of tobacco smoke. For example, it is stated that second-hand smokers have around 30% higher risk of developing an ischemic heart disease compared to those not being exposed to tobacco smoke (Barnoya, Glantz 2005).

Despite the multiple damages that tobacco smoke can do, the evidence shows that benefits from smoking cessation are noticeable even after decades of smoking. It takes only up to five years after cessation to diminish the cardiovascular risks to a level of a never smoker (Glantz, Gonzalez 2012) (Mainali et al. 2015).

It is no news that next to cardiovascular diseases tobacco smoke has had a tremendous effect on global burden of cancer diseases. Tobacco smoke has more than 60 carcinogens and around one third of all cancer deaths are attributed to smoking (Warren, Cummings 2013).

Lung cancer is the most common form of cancer worldwide and cigarette smoking is the main cause of lung cancer. It is attributable for nine lung cancer cases out of ten. Global trends of smoking and lung cancer show that the prevalence of smokers is particularly high in Europe. Smoking among men is the highest in Eastern Europe. Furthermore, the prevalence of smoking among women in Europe is especially high compared to global estimates of female smoking. At the same time, Europe is also experiencing highest burden of cancer deaths attributable to smoking (Islami, Torre & Jemal 2015). Also, it should be noted that compared to smoking women, men who smoke have 61% higher risk of getting smoking-attributable lung cancer (Yu et al. 2014). Despite the fact that tobacco control regulations have achieved some significant decreases in the rates of smoking, it is still causing overwhelming harm (Islami, Torre & Jemal 2015).

Besides lung cancer, smoking is also associated with oral upper aerodigestive tract, stomach, pancreas, liver, bladder, myeloid leukemia and cervix cancer. Furthermore, second-hand smoking is associated not only with lung cancer, but as well with upper aerodigestive tract, nasopharynx or sinonasal cavity cancer (International Agency for Research on Cancer 2012).

It is noteworthy here that the evidence shows a positive effect of cessation even if quitting after the cancer diagnosis. Quitters have lower mortality rates and better treatment outcome, they also have lower chance of second primary malignancies and their quality of life is better (Florou et al. 2014).

Tobacco smoke has also an inverse relationship with one of the main NCDs, type 2 diabetes. Studies show that smokers have almost 1.4 times higher risk of getting type 2 diabetes and it has found to have a dose-response relation (U.S. Department of Health and Human Services 2014).

Regarding chronic respiratory diseases smoking is the most common risk factor for obstructive pulmonary disease (COPD). Moreover, the association with second-hand smoking has been declared. Although tobacco smoke does not contribute as much to COPD like it does to cardiovascular diseases or cancer, it has still a significant impact on the disease (Burney, Jarvis & Perez-Padilla 2015).

It has been often discussed that quitting smoking might contribute to the risk of obesity. In fact, smoking cessation is indeed attributable to approximately five kilograms weight gain on average. However, the findings show that in overall major reduction in smoking increases only slightly the prevalence of obesity and smoking is highly associated with increased risk of metabolic syndrome (Cena, Fonte & Turconi 2011).

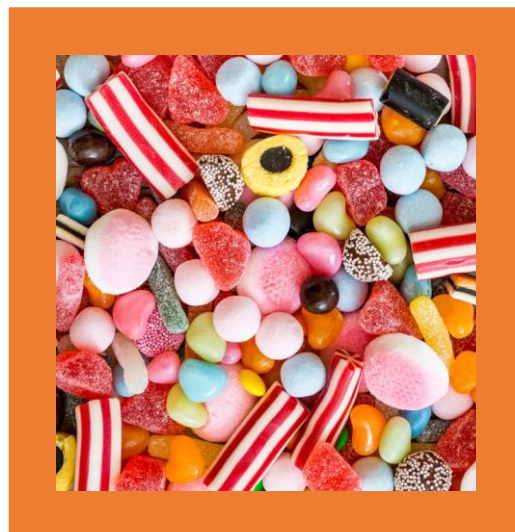
The most common mental health problem worldwide is depression. The role of smoking can be extremely important in developing depression. Luger et al (2014) found in their meta-analysis that current smokers have almost twice as high risk of getting depression compared to former or never smokers (Luger, Suls & Vander Weg 2014).

Finally, smoking has also a negative impact on different cognitive impairments. Diseases that have been most at interest are all-cause dementia, vascular dementia and Alzheimer's disease (Peters

2012). Zhong et al (2015) and Reitz et al (2015) found that smokers have 30-40% higher risk of all-cause dementia, vascular dementia and Alzheimer's disease compared to non-smokers. However, after cessation the risk of all three diseases decreases to the level of never smokers (Reitz et al. 2007; Zhong et al. 2015).

2.3 DIET

Diet has been repeatedly acknowledged as a modifiable risk factor in the development of NCDs. Globally, 2.7 million deaths are attributable to diets low in fruits and vegetables (World Health Organization 2009). Diet has an essential, yet complex role to play in the burden of NCDs. In regards to diet related diseases, obesity and diabetes have the most important role to play, because these diseases lead to many other NCDs. It can be illustrated by the fact that overweight and obesity accounted for 3.4 million deaths and 93.6 million DALYs in 2010 (Lim et al. 2012). Besides obesity and diabetes, diet is directly related to diseases such as cancer, cardiovascular disease, skeletal disease and sarcopenia (Fardet, Boirie 2014).



Obesity as a result of imbalanced calorie intake and expenditure leads to multiple risks. Obesity is associated with diabetes, hypertension, coronary heart disease, stroke, certain cancers, obstructive sleep apnea, COPD, asthma and osteoarthritis (World Health Organization 2014b, Khazrai, Defeudis & Pozzilli 2014).

Diabetes increases the risk of several diseases, from NCDs the most prevalent are cardiovascular diseases. The prevalence of diabetes has increased substantially during the last decade; in 2012 it was responsible for 1.5 million deaths and 89 million DALYs. In 2014, the prevalence of diabetes was 9% (World Health Organization 2014b).

The relation between diet and the risk of different cancer forms has been a research topic for some time. Although there is no clear evidence that certain nutrients have a causal relationship with cancer, it is found that the different diet patterns can significantly contribute to the development of cancer. Diet is attributable for over 30% of risk factors that contribute to the onset of cancer (Baena Ruiz, Salinas Hernandez 2014).

The share of fats in diet is primarily affecting the risk of obesity, but besides that it has also a direct impact on cardiovascular diseases. It is found that it is not the total fat intake that is the threat to cardiovascular diseases, but more importantly, it is trans-fats and saturated fats. While the damaging effect of saturated fats on CVDs was established long ago, studies about trans-fats stated relatively recently that these can have as harmful impact as saturated fats (Bhupathiraju, Tucker 2011).

High salt intake, or more precisely high intake of sodium, is mainly a risk factor for cardiovascular diseases. High levels of sodium increase the risk of hypertension and stroke. However, the association between sodium intake and the risk of CVD is not linear. There are findings stating that very low levels of sodium, i.e. less than 3g/day, may not be beneficial any more. The evidence base is though insufficient and the debate is ongoing (Adler et al. 2014). In terms of high salt intake, most of the research is studying its impact on hypertension. Results show that sodium has a dose-response effect on blood pressure. Resulting from this, the international recommendations of salt

intake have been set to 5-6g per day. However, it is found that a further decrease to 3g per day would have additionally significant benefits (He, MacGregor 2015). Besides elevating blood pressure, the decrease of salt intake could have a possible effect on reducing the risk of gastric cancer (D'Elia, Galletti & Strazzullo 2014).

One of the problematic aspects of diet during the last decades has been rapid increase of carbohydrates and refined sugar intake. Evidence shows that high levels of carbohydrates and refined sugar have connections with several diseases. In terms of carbohydrates, two different values should be kept in mind: these are glycemic load and glycemic index. The former term indicates the level of carbohydrates in the food portion and the latter means the speed of the carbohydrate turning into glucose in the organism. High level of glycemic index can increase the risk of breast cancer as much as 8%. Connection to other types of cancer forms has not been found so far (Bae-na Ruiz, Salinas Hernandez 2014). Besides the impact on cancer risk, high level of added sugars has also a direct effect on blood pressure (He, MacGregor 2015).

Finally, there is found a relationship between diet and aging of muscle and bone. Sarcopenia and osteoporosis is affected by certain diet aspects, such as calcium, Vitamin D and protein intake (Curtis et al. 2015).

2.4 PHYSICAL (IN)ACTIVITY

Physical inactivity is one of the 10 leading risk factors for mortality worldwide (Lim et al. 2012). Globally, around 30% of adults are not meeting the recommended physical activity levels. The highest prevalence of physical inactivity is in the regions of America and Eastern Mediterranean with estimates of over 40% (Hallal et al. 2012). In Europe, levels of physical inactivity are varying in wide range, but are stated to be as high as 30% (World Health Organization 2015). Insufficient physical activity is one of the 10 leading risk factors for global mortality. People who are insufficiently physically active have a 20% to 30% increased risk of all-cause mortality compared to those who engage in at least 150 minutes of moderate intensity physical activity per week, or equivalent, as recommended by WHO. Regular physical activity reduces the risk of ischemic heart disease, diabetes, breast and colon cancer. Additionally, it lowers the risk of stroke, hypertension, and depression. Furthermore, physical activity is a key determinant of energy expenditure and thus fundamental to energy balance and weight control. (http://www.who.int/gho/ncd/risk_factors/physical_activity_text/en/)

Numerous factors influence the level of physical activity; especially in urban areas a high level of physical inactivity can be observed (Adams et al., 2014). Sedentary behaviors (involving prolonged sitting) can be associated detrimentally with health outcomes. Older adults, the most sedentary age group, are especially at risk due to their high levels of television viewing time (van Cauwenberg et al 2014). Furthermore higher sedentary behavior at workplaces due to higher degree of automation and computerization create opportunities for insufficient physical activity.

The built environment has been identified as an important correlation of residents' physical and social activities. In contrast to automobile-dependent developments, walkable communities typically feature high density, mixed land uses, and sufficient pedestrian, bicycle, and transit facilities. They have been associated with higher levels of physical activities and more social interactions. However, previous studies are mostly cross-sectional; only a few studies conducted a pre–post comparison to better isolate the impact of moving into walkable communities (Zhu, Yu, Lee, Lu, & Mann, 2014). Numerous other studies confirm the influence of built environment both at home and at workplaces on physical activities (e.g. Adlakha et al., 2015; or references in WHO reports).

World Health Organization has developed recommendations of physical activity with aim to prevent NCDs (World Health Organization 2010). These guidelines are linking frequency, duration, intensity, type and total amount of physical activity. Recommendations are directed separately to three age groups and are following:

- 5-17 years of age – at least 60 minutes of moderate- to vigorous intensity physical activity daily, most of which should be aerobic in nature. Vigorous-intensity activities should be incorporated at least 3 times per week.
- 18-64 years of age – at least 150 minutes of moderate-intensity aerobic physical activity throughout the week or at least 75 minutes of vigorous-intensity aerobic physical activity throughout the week or an equivalent combination of moderate- and vigorous-intensity activity. Aerobic activity should be performed in bouts of at least 10 minutes duration. Vigorous-intensity activities should be done on 2 or more days a week.
- 65 years of age and above - at least 150 minutes of moderate-intensity aerobic physical activity throughout the week or at least 75 minutes of vigorous-intensity aerobic physical activity throughout the week or an equivalent combination of moderate- and vigorous intensity activity. Aerobic activity should be performed in bouts of at least 10 minutes duration. People with

poor mobility should perform physical activity to enhance balance and prevent falls on 3 or more days per week. Muscle-strengthening activities should be done on 2 or more days a week (World Health Organization 2010).

There are many factors to consider when one seeks to understand why people are not being physically active. Bauman et al (2012) found that health status or simply intentions to exercise is affecting it. They also reported that men and those having well-established habit of exercising are more likely to be physically active. Besides individual level there are also environmental factors, such as family support in adolescents, transport use, leisure time activities and finally, policy at wider aspect (Bauman et al. 2012).

In 2008, premature mortality attributable to physical inactivity was estimated to be as high as 9% of all-cause mortality globally. Not meeting the recommendations listed above is predominantly associated with coronary heart disease, high blood pressure, stroke, metabolic syndrome, type 2 diabetes, breast cancer, colon cancer depression, cardio-respiratory and muscular fitness, body mass and composition, bone health, functional health and cognitive function (Lee et al. 2012).

Likewise the association between diet and obesity, physical inactivity is often related to NCDs through obesity as a start point risk factor. For example, it is found that inactive and obese people have 40-90% higher mortality risk compared to non-active obese people. However, there are also contradicting findings stating that physically active overweight and obese people who have cardiovascular disease have better prognosis than normal weight equivalents. Therefore, it is suggested that it is cardio-respiratory fitness instead of adiposity that is a determining factor in cardiovascular risks, such as coronary heart disease and heart failure (Myers et al. 2015).

60 million people in European Region have been diagnosed with diabetes and it is one of the leading causes of death worldwide. It is estimated that physical inactivity alone contributes around 7% to the burden of type 2 diabetes (World Health Organization Regional Office for Europe 2015). Physical activity can reduce the risk of type 2 diabetes around 25-35% depending on the level and duration of activity (Aune et al. 2015).

Study findings regarding the association between physical activity and stroke vary in detail, but the overall conclusion is that physical activity reduces the risk of stroke. Depending on the type and level of activity the risk of stroke can be reduced from 15% to as high as 55%. However, there is still need for further investigation to get clearer knowledge what are the intensity and duration thresholds in order to reduce the stroke risk and also, if there is any difference between men and women (Howard, McDonnell 2015).

Physical activity has also a significant role to play in the prevention of mental diseases, namely depression. Even low intensity activities such as walking have a beneficial effect on preventing depression (Mammen, Faulkner 2013).

Finally, in regards to physical activity it is relevant to separately bring out the term of sedentary behavior, i.e. time spent sitting. It is now clear that sedentary behavior is exclusively a risk factor for burden of disease. Increased sedentary time is associated with all-cause mortality, risk of cancer, cardiovascular disease and type 2 diabetes regardless of the physical activity level (Biswas et al. 2015).

2.5 ALCOHOL USE

The burden of disease deriving from alcohol misuse is one of the most significant contributors to morbidity and mortality in the world. Alcohol is attributable to around 6% of deaths globally, which is 3.3 million deaths yearly (World Health Organization 2014a).

European region has the highest consumption of alcohol in the world. In 2011, pure alcohol consumption in the European Union was 9.99 liters per capita among population of 15 years of age and older (Health for All Database).

Factors affecting alcohol consumption on societal level are culture and traditions, economic development and alcohol regulations of the country, religion, historic background. The main individual level factors are age, gender and socioeconomic status (World Health Organization Regional Office for Europe 2009).

Alcohol has been associated with over 200 different diseases and conditions (Shield, Parry & Rehm 2013). Alcohol related harm is mostly associated with non-communicable diseases. The leading diseases and conditions that are contributing most to the alcohol-attributable harm, are cancer, cardiovascular diseases, liver diseases and mental disorders (Parry, Patra & Rehm 2011).

The association between cardiovascular diseases is specifically interesting, as the effect of alcohol on this disease group is not unidirectional. It has been found that light to moderate levels of alcohol consumption can be protective against certain diseases, such as ischemic heart disease, ischemic stroke and among females, also hypertension (Shield, Parry & Rehm 2013, Parry, Patra & Rehm 2011). On the other hand, any episode of heavy drinking will remove this protective effect (Roerecke, Rehm 2010). Misuse of alcohol is associated with alcoholic cardiomyopathy, systemic hypertension, arrhythmias, cerebrovascular disease, coronary artery disease and heart failure (Klatsky 2015).

Interestingly, it has been noted that alcohol has also a protective effect against type 2 diabetes. The protective effect is appearing when drinking up to about 20g of pure alcohol per day. However, the relationship turns inverse when drinking more than 50 g of pure alcohol per day among women and 60 g per day among men (Baliunas et al. 2009).

In 2010, alcohol-attributable cancer deaths formed 4.9 deaths per 100 000 people globally, but the indicator is the highest in Eastern Europe, i.e. 10.3 deaths per 100 000 people (Rehm, Shield 2013). Consumption of alcoholic beverages is causally related to cancer of oral cavity, pharynx, larynx, colorectum, liver and female breast cancer (International Agency for Research on Cancer 2012).

In regards to gastrointestinal diseases, liver cirrhosis is the main contributor to alcohol related deaths. In 2010, alcohol-attributable liver cirrhosis was responsible for 47.9 % of all liver cirrhosis deaths (Rehm, Shield 2013). It is found that there is clear dose-response relationship between alcohol and the risk of liver cirrhosis. Also, studies indicate that the risk of



liver cirrhosis starts to increase with more than two drinks among both men and women (Rehm et al. 2010).

Finally, World Health Organization (2014) reported that in 2012, the biggest proportion of alcohol-attributable DALYs, i.e. one fourth was due to neuropsychiatric disorders (World Health Organization 2014a). Most important neuropsychiatric conditions caused by alcohol are alcohol use disorders. Alcohol use disorders are entirely attributable to alcohol use and according to the International Classification of Disease; Tenth Edition (ICD-10), the term is standing for harmful use of alcohol and alcohol dependence. It is found that under the age of 40, alcohol use disorders increase the mortality risk as much as nine times among men and 13 times among women (Roerecke, Rehm 2013).

PART III

3 TRENDS & DRIVERS OF NON-COMMUNICABLE DISEASES

INTRODUCTION

Chapter three of the report is an assessment of trends and drivers influencing the determinants of non-communicable diseases today and in the future. The FRESHER Project applied a tailored horizon scanning approach to examine what future drivers of health and wellbeing in Europe may be. The scope of this document is focused on already evident drivers and those that are not yet evident in the published literature. It documents expert opinion regarding new ideas or emerging findings that are accessible in published journals, online documents, scientific books and media coverage but also sources not yet published. The analysis of scientific literature, research and foresight projects is supposed to identify present trends and drivers, and gain insight into possible future issues. Specifically, the work focuses on the “Grand Challenges” in the future of health in Europe and beyond. The rather random definition of what an NCD is and which disease belongs to this group of indications sometimes make the distinction between determinants on the one hand and trends and drivers on the other hand unprecise. In fact, some diseases may themselves be determinants for other indications such as obesity can be a determinant for diabetes type 2. Similarly, depression can be defined as a trend in our modern society today as statistics have been showing a steady increase over the years. Some forms of depression may be a determinant for other NCDs, e.g. cardio-vascular diseases; or depression can also perform as a trend and have effects on determinants such as alcohol abuse and smoking. Thus the line between on and the other is often opaque and NCDs remain complex issues to deal with.

DEFINING DRIVERS & TRENDS

DRIVERS

We define drivers as developments causing change, affecting or shaping the future. A driver is the cause of one or more effects.¹ For example, taxation can be a driver for regulating alcohol consumption.

TRENDS

Trend is a general tendency or direction of a development or change over time. It can be called a megatrend if it occurs at global or large scale. A trend may be strong or weak, increasing, decreasing or stable. There is no guarantee that a trend observed in the past will continue in the future. Megatrends are the great forces in societal development that will very likely affect the future in all areas over the next 10-15 years, for example urbanization or demographic change.

“Trends are experienced by everyone and often in more or less the same contexts insofar as they create broad parameters for shifts in attitudes, policies and business focus over periods of several years that usually have global reach. What is interesting about trends is that normally most players, organizations or even nations cannot do much to change them – they are larger than the power of individual organizations and often nation states as well”.²

¹ Definition adapted from ‘Global Foresight Glossary and Drivers of Change in Ecosystems and Their Services’

² Definitions adapted from Saritas O., Smith J. (2011, p. 294): The Big Picture – trends, drivers, wild cards, discontinuities and weak signals, Futures, 43(3): 292-312, and from ‘Global Foresight Glossary and Drivers of Change in Ecosystems and Their Services’

3.1 INNOVATION IN MEDICINE

In the last 20 to 30 years, many innovations in medicine have impacted significantly on the prevention, diagnosis and treatment of chronic diseases, from the laboratory, to the operating room, bedside, clinics, and day to day treatment of chronic patients. In different areas big revolution occurred, game-changing innovations that have dramatically improved human health and transformed medicine, both influencing specific fields (e.g. use of statins for secondary prevention) or having an impact on a wide range of fields like the human genome sequencing.



Management guru Peter Drucker defined innovation as “change that creates a new dimension of performance and it “includes both improvements in technology and better methods or ways of doing things” as stated by Michael Porter (Dzau et al 2013). There is a real need for innovation in health care delivery, as well as in medicine, in drug- or device-related biomedicine, to address challenges of access, quality, and affordability through new and creative approaches

The path from a promising discovery to an effective treatment often takes a decade or more. The completion of the Human Genome Project sparked optimism that cures for debilitating diseases were just around the corner. Cures still generally elude us, but now the ability to map human DNA cheaply and quickly is yielding a torrent of data about the genetic drivers of disease—and a steady stream of patients who are benefiting from the knowledge. On other fronts, technology is putting more power in the hands of patients, and researchers are learning to combat disorders by harnessing the body's own ability to heal and grow. Advances bring other challenges, including how to pay for them. Meanwhile, the complex biology that impedes gains for some patients sets goals for new advances.

Here are some of today's potentially transformative trends, resulting from biomedical sciences, engineering and computer science advances, new findings in genomics, stem cells, new pharmaceuticals, medical devices, imaging and diagnostic devices, new surgical approaches, digital medicine and the wireless revolution.

3.1.1 HUMAN GENOME SEQUENCING

For years, doctors have been able to test specific genes to detect the presence of mutations associated with disorders such as cystic fibrosis and sickle cell disease. But only recently have scientists been able to map out a person's entire genetic code, or genome, by sequencing all 20,000 or so genes in one fell swoop. The Human Genome Project (HGP) was the international, collaborative research program whose goal was the complete mapping and understanding of all the genes of human beings. The HGP was one of the great feats of exploration in history, an international research effort to sequence and map all of the human genome.

Since the first sequencing of the human genome was completed in 2003, the challenge to researchers and scientists is to determine how to read the contents of all these pages and then understand how the parts work together and to discover the genetic basis for health and the pathol-

ogy of human disease. In this respect, genome-based research will eventually enable medical science to develop highly effective diagnostic tools, to better understand the health needs of people based on their individual genetic make-ups, and to design new and highly effective treatments for disease.

Individualized analysis based on each person's genome will lead to a very powerful form of preventive medicine. We'll be able to learn about risks of future illness based on DNA analysis. Then, through our understanding at the molecular level of how things like diabetes or heart disease or schizophrenia come about, we should see a whole new generation of interventions, many of which will be drugs that are much more effective and precise than those available today. It's important to be careful about raising expectations. Most new drugs based on the completed genome are still perhaps 10 to 15 years in the future, although more than 350 biotech products - many based on genetic research - are currently in clinical trials.

Testing, however, will arrive more quickly, especially the ability to predict individual future health risks, and the ability to implement an enhanced approach to preventive medicine. These new developments not only point to innovation in diagnostics but also in treatment: not everyone responds to a drug the same way. Genomics may help predict the right therapy with the fewest side effects for individual patients. It can improve the quality of care and decrease cost at the same time.

Since May 2015, the Oxford Nanopore Technologies company unveiled the first of a generation of tiny DNA sequencing devices that many predict will eventually be as ubiquitous as cellphones—it's already the size of one (more information available at: <https://www.nanoporetech.com/>). Nanopore sequencing devices, which are designed to be even smaller and more affordable, could speed efforts to make gene sequencing a routine part of a visit to the doctor's office. DNA molecules are exceedingly long and complicated; that makes them hard to read. Nanopore technology measures changes in the molecules' electrical current as the DNA is threaded in a single strand through tiny holes created in a membrane.

In the next decade, we may also be better able to determine which drugs work best for individuals, based on their genetic make-up. The results of drug therapy can vary within a population. Although some individuals obtain the desired effects, others can have minimal or no therapeutic response. Furthermore, certain patients might experience adverse effects that can range from bothersome to life threatening. Several factors can contribute to variable drug response, including age, race, gender, interactions with other drugs, concomitant diseases, and renal and hepatic function. However, there is increasing evidence that genetic differences can be an important (and in some cases predominant) factor influencing drug response variability. Although pharmacogenetics is an established field, it has seen rapid growth in recent years in part owing to technological advances in the molecular sciences. Currently, pharmacogenetic investigations, particularly those focused on proteins other than the drug metabolizing enzymes, usually begin with an understanding of the sequence variability in a relevant gene, and then focus on how this genetic variability influences the drug response phenotype.

Foundation Medicine Inc., in 2015, officially launched an innovative test to analyze a tumor sample for 280 different genetic mutations suspected of driving tumor growth. To date about 70% of ana-



lyzed samples have turned up a mutation that is potentially targeted by a drug on the market or in a clinical trial. This can change the way to approach patients with cancer: recently, a sample from a female patient with advanced pancreatic cancer yielded a response for "her2," an alteration associated with a certain form of breast cancer. She was treated and her cancer responded to the breast-cancer drug Herceptin. Few oncologists would think to look for her2 in a patient with pancreatic cancer.

Personalized health care and personalized medicine are relative new trends in the health sector and have the potential to revolutionize medicine. Both topics are connected but they are not the same: while personalized health care involves the tailoring of care to the unique characteristics of each patient, personalized medicine refers specifically to the use of genetics and genomics (e.g. the use of specific tumor markers to guide therapy for breast cancer).

Personalized health care uses also other biologic information that helps predict risk for disease or how a patient will respond to treatments. An example of personalized healthcare would be the inclusion of specific biomarkers like lipoprotein (a) that can help to better predict risk for heart disease or stroke in some individuals. These biomarkers can augment traditional means of assessing risk based on age, diabetes, high blood pressure, or high cholesterol levels.

After the sequencing of the **Human Genome**, the next critical stage is to develop and implement health information systems that can capture, help interpret, and share complex yet accurate patient data, including genomic information along with phenotypic and medical data. Health IT is the basis for personalized medicine. Yet it is not fully available in hospitals and physician's offices. The ongoing challenges include creating an instant connection between real-world clinical results and molecular data to establish and refine correlations in real-time so that health care providers can make clinical decisions based on a body of scientific knowledge that is beyond the training, experience, or memory of any single practitioner (<http://www.phsforesight.eu/>).

In the US, where more than 90 percent of the physicians are using the **Electronic Health Records**, the framework is in place to leverage health IT investments and address ongoing concerns such as interoperability, data sharing, and complex consent. One of the expectations is that widespread use of EHRs creates the potential for the millions of files of data they hold to be analyzed by researchers, test developers, and regulators to better develop, refine, and understand the underpinnings and real-world applications of personalized medicine. Hopes are that EHR data can be used in longitudinal cohort studies, where the availability of a sufficient amount of high-quality data can enable retrospective analysis and better use of tests and tools for identifying health trends and predicting disease (Personalized Medicine Coalition, 2014). This development touches issues of data privacy that still need to be dealt with. One prerequisite is informed consent that both allows patients to understand how their data may be used and enables researchers to respect the limits of data use.

Finally, the sequencing of the human genome opened the way to **gene therapy**: after years of controversy, gene therapy is poised to become a viable option for a variety of often life-threatening medical conditions. Gene therapy is particularly attractive for diseases that currently do not have satisfactory treatment options, and is probably easier for monogenic disorders than for complex diseases (Griesenbach U. et al 2009). The treatment involves loading a functional gene onto a fragment of a deactivated virus that transports the gene to a cell's nucleus, where it is intended to take over.

The need for gene transfer into specific cell types is clearly dependent on the target disease. Over the past decade the gene therapy community has recognized that there is no one vector that is good for all applications, but that the gene transfer agent has to be carefully chosen depending on the cell type to be targeted, the number of treatments (one vs. repeat administration) required, and the size and nature (secreted vs. cellular product) of the gene to be delivered. In addition extracellular barriers such as mucus/sputum and the degree of inflammation may be disease dependent both on disease type, and severity within a given disease.

In 2013 the European Union approved the first gene-therapy medicine for treatment of a rare genetic disease in the Western world, Glybera, designed to restore the LPL enzyme activity required to enable the clearance of fat-carrying chylomicron particles formed in the intestine after a fat-containing meal. The product consists of an engineered copy of the human LPL gene packaged with a tissue-specific promoter in a non-replicating vector, which has a particular affinity for muscle cells. Glybera is administered in a one-time series of up to 60 intramuscular injections in the legs. Gene therapy is currently being evaluated for a wide range of acute and chronic lung diseases including acute respiratory distress syndrome (ARDS), cancer, asthma, emphysema and cystic fibrosis (CF), not least because of the comparatively easy non-invasive accessibility of the lungs through aerosols (e.g MinION MkI produced by nanoporetech <https://www.nanoporetech.com/>)

Further Information

- <https://www.genome.gov/10001772>
- <https://www.nanoporetech.com/>
- <http://www.lina-schwab.de/Publikationen/z66.pdf>
- <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2629647/pdf/bph0157-0153.pdf>
- http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/002145/WC500135476.pdf

3.1.2 EPIGENETICS

Epigenetics, information transmitted during cell division via a means other than the DNA sequence, links genetics and environment through modification of gene expression. External factors, such as diet, viral exposure, and environmental insults, including smoking, all have the potential to alter the normal genome functions of DNA methylation, histone post-translation modifications, and nucleosome remodeling, thus modifying the epigenome. Epigenetic modifications are now recognized to play a key role in the development of disease, and epigenetic marks on the genome have shown promise as biomarkers of environmental exposure, thus providing data that allow improved risk prediction and insights into disease etiology. Changes to the epigenome can be long-lasting and even inheritable; although in some cases damaging epigenetic marks may be reversible, leading to the possibility of novel epigenetic drugs and other non-pharmacologic lifestyle therapies.

Current trials are examining the potential for pretreatment of cancer progenitor cells with epigenetic therapies to eliminate resistance to chemotherapeutic agents. The next few decades are likely to bring multiple new inhibiting agents targeting various epigenetic processes to treat a range of diseases from cancer to cardiovascular disease. Promising early work examining the leptin gene in mice with diet-induced obesity even holds the potential for the development of an epigenetic treatment of obesity, though Joel Dudley, PhD, assistant professor of genetics and genomic sci-

ences at the Icahn School of Medicine at Mount Sinai in New York, cautions that epigenetic therapies are likely to be only one of many tools needed to tackle complex diseases, such as obesity, where the pathogenesis is attributable to genetics, epigenetics, lifestyle, and even the microbiome (e.g. gut bacteria).

Further Information

- <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1392256/pdf/ehp0114-a00160.pdf>

3.1.3 STEM CELLS

Stem cells are a class of undifferentiated cells that are able to differentiate into specialized cell types. Commonly, stem cells come from embryos formed during the blastocyst phase of embryological development (embryonic stem cells) and adult tissue (adult stem cells). Both types are generally characterized by their potential to differentiate into different cell types (such as skin, muscle, bone, etc.).

Stem cells are either extracted from adult tissue or from a dividing zygote in a culture dish. Once extracted, scientists place the cells in a controlled culture that prohibits them from further specializing or differentiating but usually allows them to divide and replicate. The process of growing large numbers of embryonic stem cells has been easier than growing large numbers of adult stem cells, but progress is being made for both cell types. Once stem cells have been allowed to divide and propagate to a stem cell line that can be stimulated to specialize in a process known as directed differentiation. Embryonic stem cells are able to differentiate into more cell types than adult stem cells.

Stem cells extracted from embryos can be induced to become any desired cell type. This property makes stem cells powerful enough to regenerate damaged tissue under the right conditions. **Tissue regeneration** is probably the most important possible application of stem cell research. Currently, organs must be donated and transplanted, but the demand for organs far exceeds supply. Stem cells could potentially be used to grow a particular type of tissue or organ if directed to differentiate in a certain way. Stem cells that lie just beneath the skin, for example, have been used to engineer new skin tissue that can be grafted on to burn victims.

A team of researchers from Massachusetts General Hospital reported in PNAS Early Edition (July 2013 issue) that they were able to **create blood vessels** in laboratory mice using human stem cells. The scientists extracted vascular precursor cells derived from human-induced pluripotent stem cells from one group of adults with type1 diabetes as well as from another group of “healthy” adults. They were then implanted onto the surface of the brains of the mice. Within two weeks of implanting the stem cells, networks of blood-perfused vessels had been formed - they lasted for 280 days. These new blood vessels were as good as the adjacent natural ones (Rekha S. et al 2013) . The authors explained that using stem cells to repair or regenerate blood vessels could eventually help treat human patients with cardiovascular and vascular diseases.

Additionally, replacement cells and tissues may be used to **treat brain disease** such as Parkinson's and Alzheimer's by replenishing damaged tissue, bringing back the specialized brain cells that keep unneeded muscles from moving. Embryonic stem cells have recently been directed to differentiate into these types of cells, and so treatments are promising.

Healthy heart cells developed in a laboratory may one day be transplanted into patients with heart disease, repopulating the heart with healthy tissue. Similarly, people with type I diabetes may receive pancreatic cells to replace the **insulin-producing cells** that have been lost or destroyed by the patient's own immune system. The only current therapy is a pancreatic transplant, and it is unlikely to occur due to a small supply of pancreases available for transplant.

Further Information

- <http://stemcells.nih.gov/info/basics/pages/basics1.aspx>
- http://ac.els-cdn.com/S0006295216001118/1-s2.0-S0006295216001118-main.pdf?_tid=57f74efc-e057-11e5-883d-00000aacb360&acdnat=1456910324_3006ba18e2d8c9828525fb7fc2690006

3.1.4 MICROBIOTA

An area of research showing a lot of promise has to do with our guts, specifically all the bacteria residing there. The human microbiota consists of the 10-100 trillion symbiotic microbial cells harbored by each person, primarily bacteria in the gut; the human microbiome consists of the genes these cells harbor. Microbiome projects worldwide have been launched with the goal of understanding the roles that these symbionts play and their impacts on human health. This partnership between the gut and its microbiota is not always so harmonious, and a number of studies have focused on the influence that these bacteria have on disease.

There are trillions of microbes in the human microbiome, although the entire microbiome only accounts for about 1-3% total body mass, with some weight-estimates ranging as high as 3 pounds (approximately 48 ounces or 1,400 grams). Research into the role that microbiota in the gut might play in the human immune system started in the late 1990s. The microbiome of the gut has been characterized as a "forgotten organ",¹ and the possibility has been raised that "the mammalian immune system, which seems to be designed to control microorganisms, is in fact controlled by microorganisms".

The human microbiome may have a role in auto-immune diseases like diabetes, rheumatoid arthritis, muscular dystrophy, multiple sclerosis, fibromyalgia, and perhaps some cancers. A poor mix of microbes in the gut may also aggravate common obesity. Since some of the microbes in the human body can modify the regulation of some neurotransmitters, it may be possible to use certain microorganisms to supplement treatments for depression, bipolar disorder and other stress-related psychiatric disorders.

The human gut is home to trillions of microorganisms, and there is vast diversity within this gut microbiota. Research into the association of the gut microbiota with health and disease continues to expand, with the field advancing at a rapid pace especially the emerging clinical applications of manipulating this microbiota. The challenge ahead of us, as Fergus Shanahan points out in his Perspectives article, is how we can translate these new research findings into clinical practice. With better understanding of the microorganisms in our gut, one hope is that their manipulation might prove to be a future targeted therapy for a number of conditions. Outnumbered (on a cellular level alone) by our microbial 'mates' by 10 to 1, a question arises: as medicine moves towards taking a personalized approach, should we be tailoring treatment to both our human and microbial 'selves'? (Shanahan F. 2012)

Recent research has proved dependency of *gut microbiota and brain disorder* (Dash, 2015). The human intestinal microbiome is seeded at birth; it is influenced initially by delivery and feeding mode, and reaches an adult-like state within the first few years of life (Bergstrom et al., 2014). Alterations in the composition, diversity, and stability of gut microbiota have been linked to a broad range of diseases, including autoimmune, metabolic, gastrointestinal, and brain disorders (see Guinane et al. 2013 and Collins et al. 2012). Although the composition of the gut microbiota remains relatively stable during our middle years, it continues to be influenced by such factors as geography, antibiotics, exercise, and diet. This is particularly important when considering possible prevention and intervention in brain disorders.

It is well known that bidirectional gut/brain communication may occur directly and indirectly via the central and enteric nervous systems, the vagus nerve, and the endocrine and immunoinflammatory systems and through the modulation of neurotransmitters (Grenham et al., 2011). Diet could also utilize these pathways, because the gut microbiota supports optimal nutritional bioavailability, for example, by maintaining normal plasma tryptophan levels, an important building block for making serotonin, a key central nervous system neurotransmitter (Grenham et al., 2011). Advances in this field have come from the development of DNA sequencing technology, which allows researchers to conduct large-scale screening of the bacteria in the gut and their associated physiologic functions. This has helped researchers to link disruption of the gut microbiota with biological markers of the communication pathways mentioned above.

Further Information

- <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3426293/pdf/nihms369735.pdf>
- <http://www.nature.com/nrgastro/journal/v9/n10/pdf/nrgastro.2012.145.pdf>

3.1.5 ORGAN TRANSPLANTATION

There are more than five times as many people on the waiting list for organ transplants as will actually receive one. This acute shortage of human organs has prompted significant research and development into alternatives. (Levitt 2015). The idea of **xenotransplantation**, defined as the transplantation of organs from non-human animals to human patients is not new, but historically, it's been essentially a surgical research tool.

The principal obstacle to organ xenotransplantation has been rejection of the donor organ by the recipient's immune system. Based on complex interactions of various genes, cells of humans, pigs, cows, apes, and other animals all express certain molecules on the cell surface. Seeing those surface molecules as "foreign", the immune system mounts a massive attack. This is a major issue even for human-to-human organ transplants, but using donor-recipient genetic matching and also immunosuppressive drugs, transplant medicine has been able to overcome the problem, although the risk is always present.



With transplantation between species, however, the genetic mismatch between the donated organ and the recipient's immune system is bigger. Thus, even when a xenograft organ is the correct size anatomically –as a pig heart is to replace a human

heart, for instance— the rejection potential is a showstopper. Another concern has been the possibility of viruses transmitted from the donor animal to the human recipient, but this type of infection has not shown up in all the years of pig and cow heart valve transplantation to humans.

Due to advances in biotechnology, genetics, and immunology, xeno-organ transplantation now beckons as a viable, long-term solution to the organ shortage. One particular xenotransplant area that's advancing is for the treatment of type 1 diabetes. While only the tissue containing islet beta cells is needed, not the entire pancreas, to harvest enough islet beta cells to cure a type 1 diabetic, actually more than a full human pancreas is needed. However, the state of technology for harvesting the cells from a pig pancreas has advanced such that recent analysis shows that it would be cost effective, particularly for young diabetics, and the patient would be cured and no longer depend on constant insulin injections to stay alive. Xenotransplantation is also being developed for non-whole organ scenarios such as neurodegenerative disorders, chronic pain control, and ex vivo perfusion events.

Toward the goal of **transplanting entire organs** into humans from other species, in 2014 a study (Mohiuddin M. 2014) reported pig hearts remaining viable for more than a year after transplantation into baboons. Genetically, the difference between pigs and baboons is no greater than the difference between pigs and humans. Consequently, this is a major achievement that could pave the way to pig-to-human heart transplants –not as a research tactic, nor even for stalling in a patient awaiting a human heart, but to provide the patient a heart for the long-term. This approach is under investigation for a wide range of conditions, including replacement of the heart, lungs, liver, and kidneys.

An ethically contested issue is **fetal tissue engineering**. On the medical side there are a lot of expectations and hopes in fetal tissue engineering to help relieve the symptoms, if not cure, many, previously, incurable chronic diseases, incl. Parkinson's, Alzheimer's, diabetes mellitus, hepatic enzyme/factor deficiencies and many more. Companies such as Advanced Tissue Sciences, Organogenesis, Life Cell, and Bio Surfarace Technology are using neonatal foreskins, a normally discarded piece of tissue from circumcision, to isolate fibroblasts used to create bioartificial skin grafts. Fetal tissues have the advantage to grow, divide and differentiate better than adult tissues. Moreover, fetal tissues have been shown to have the ability to withstand hypoxia and also have decreased immunogenic effects (Patrick et al. 1998).

Strategies presently either under development, in clinical trials, or available via medical tourism include stem cell transplants, manipulation of a patient's own stem cells, and the use of implanted scaffold materials that emit biochemical signals to spur stem cells into action. In the field of tissue engineering, researchers have generated sections of **tissue outside the body** for transplant, using the patient's own cells to minimize the possibility of transplant rejection. Regenerative therapies have been demonstrated in the laboratory to at least partially heal broken bones, bad burns, blindness, deafness, heart damage, worn joints, nerve damage, the lost brain cells of Parkinson's disease, and a range of other conditions. Less complex organs such as the bladder and the trachea have been constructed from a patient's cells and scaffolds and successfully transplanted. To create genetically tailored organs out of a patient's own cells, abolishing compatibility issues is still in its infancy. It is speculated that mass-producing artificial scaffolds will make organ engineering even more cost-effective than xenotransplantation (Soto-Gutierrez A, 2010).

In the field of organ transplantation, **3D printing** will have a leading role. It is just one of the many revolutionary technologies currently being used in healthcare, and refers to various processes used to synthesize a three-dimensional object. In 3D printing, successive layers of material are formed under computer control to create an object. These objects can be of almost any shape or geometry and are produced from a 3D model or other electronic data source. Medical researchers have already turned to 3D printing to create human body parts and they're just getting started. Recently scientists from Cornell University (Cornell scientists) printed out an artificial outer ear that looks and works like looks and acts like a natural ear (Cornell Chronicle Feb. 20, 2013.). Meanwhile, researchers at the University of Pennsylvania and M.I.T. have used printers to produce blood vessels (Webster A. 2012), while scientists at Wake Forest have developed a way to print skin cells directly on to wounds (Brooke K. 2013). A San Diego company named Organovo is now working on printing print a human liver to be used in a lab for drug research —therefore not suitable to implant in a human—but its more evidence that human tissue from a printer can be kept alive (Organovo <http://www.organovo.com/tissues-services/exvive3d-human-tissue-models-services-research/exvive3d-liver-tissue-performance/>)

3D printing in medicine has been skyrocketing and the list of objects that have already been successfully printed in this field demonstrates the potential that this technology holds for healthcare in the near future. Researchers at Harvard University are making great progress in bioprinting blood vessels, a crucial step towards printing tissues with a blood supply. The lab of Dr. Jennifer Lewis designed a custom-built 3D printer and a dissolving ink to create a swatch of tissue containing skin cells interwoven with structural material that can potentially function as blood vessels.

At Cornell University has printed a Heart valve that will be tested in sheep. They have been able to print a combination of alginate, smooth muscle cells, and valve interstitial cells, to control the valve's stiffness. Organovo announced in 2014 the commercial launch of their bioprinted liver as-says, 3D printed liver cells that able to function for more than 40 days. While, at the moment, the product is used for testing new pharmaceuticals, Organovo's top executives and other industry experts suggest that within a decade we will be able to print solid organs such as liver, heart, and kidney. Hundreds of thousands of people worldwide are waiting for an organ donor; imagine how such a technology could transform their lives.

3D printing has also been used to print bone, tailor-made sensors, low-cost prosthetic parts and also medical equipment (eg. groups like iLab/Haiti have taken to 3D printing umbilical chord clamps for local hospitals in Haiti). And of course 3D printers can be used for medical models like models of cancerous tumors to aid discovery of new anti-cancer or to better understand how tumors develop, grow, and spread. Creating patient-specific models from CT and MRI scans expands from medical research into practical application with the ability to prepare doctors for surgeries, thus drastically reducing surgery times. Taking this one step further, there are numerous examples of using medical scan data to 3D print implants tailor-made to the patient.

Further Information

- The pathobiology of pig-to-primate xenotransplantation: a historical review. Cooper DK, Ezzelarab MB, Hara H, Iwase H, Lee W, Wijkstrom M, Bottino R. Xenotransplantation, 2016 Jan 27. 12219.
- <http://www.sciencedirect.com/science/article/pii/S000349751501677X>
- Fetal tissue engineering: Regenerative capacity of fetal stem cells. Wu P, Moschidou D, Fisk NM. (2009) In: Meyer U, Meyer T, Handschel J and Wiesmann HP eds. Fundamentals of Tissue Engineering and Regenerative Medicine. pp. 139-157.

- <https://www.etde.org/etdeweb/servlets/purl/977185-WKsl8c/977185.pdf>
- <http://www.news.cornell.edu/stories/2013/02/bioengineers-physicians-3-d-print-ears-look-act-real>

3.1.6 MINIMALLY INVASIVE AND ROBOTIC SURGERY

Advances in surgery have focused on minimizing the invasiveness of surgical procedures, such that a significant paradigm shift has occurred for some procedures in which surgeons no longer directly touch or see the structures on which they operate.

Building on the precedent of **pelviscopy** in gynecology and **arthroscopy** in orthopedic surgery, the use of minimally invasive approaches into other surgical specialties, including general surgery, urology, thoracic surgery, plastic surgery, and cardiac surgery, has changed not only the performance of specific operations but more important the strategic approach to all surgeries. Advancements in **video imaging**, **endoscope technology**, and instrumentation have made it possible to convert many procedures in many surgical specialties from open surgeries to endoscopic ones. **Robotic surgery**, **computer-assisted surgery**, and **robotically-assisted surgery** are terms for technological developments that use robotic systems to aid in surgical procedures. The use of computers and robotics promises to facilitate complex endoscopic procedures by virtue of voice control over the networked operating room, enhancement of dexterity to facilitate microscale operations, and development of virtual simulator trainers to enhance the ability to learn new complex operations (Michael J. 2001).

The technologies that facilitated this shift include: development of **the charge coupling device (CCD) chip** that allowed high resolution video images to be transmitted through an optical scope to the surgeon, **high intensity xenon and halogen light sources** that improved visualization of the surgical field, and improved **hand instrumentation designed** for endoscopic approaches. The surgeon did not look directly at the target structure but viewed digitally enhanced images that provided a better visualization because of the magnification and illumination.

Due to robotic use, the surgery is done with precision, miniaturization, smaller incisions; decreased blood loss, less pain, and quicker healing time. Medical robots may be classified in many ways:

- by manipulator design (e.g. kinematics, actuation);
- by level of autonomy (preprogrammed versus teleoperation versus constrained cooperative control),
- by targeted anatomy of technique (e.g. cardiac, intravascular, percutaneous, laparoscopic and microsurgical);
- or intended operating environment (e.g. in-scanner, conventional operating room).

The Da Vinci Surgical System, approved by the Food and Drug Administration (FDA) in 2000, is currently the only commercially available surgical robotic system. The da Vinci System has been designed to facilitate complex surgery using a minimally invasive approach, and is controlled by a surgeon from a console. Da Vinci robots operate in hospitals worldwide, with an estimated 200,000 surgeries conducted in 2012, most commonly for hysterectomies and prostate removals. As of June 30, 2014, there was an installed base of 3,102 units worldwide, up from 2,000 units at the same time the previous year. The locations of these units are as follows: 2,153 in the United States, 499 in Europe, 183 in Japan, and 267 in the rest of the world (Palep JH 2009). The da Vinci

System consists of a surgeon's console that is typically in the same room as the patient, and a patient-side cart with four interactive robotic arms controlled from the console. The instruments' jointed-wrist design exceeds the natural range of motion of the human hand; motion scaling and tremor reduction further interpret and refine the surgeon's hand movements. The da Vinci System always requires a human operator, and incorporates multiple redundant safety features designed to minimize opportunities for human error when compared with traditional approaches.

Further Information

- <http://www.intuitivesurgical.com/>
- <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2699074/>

3.1.7 SMART MEDICAL DEVICES

A wide range of healthcare products for screening and monitoring indicators related to NCDs is already on the market and includes home usage **blood pressure monitors, blood glucose monitors, nebulizers, body composition monitors, pedometers**, etc. and hospital usage blood pressure monitors.

The concept of patient-generated data is nothing new, but the days of blood pressure cuffs and fingerstick glucose tests are coming to an end. There's a good chance that you already own one of the most ubiquitous health-care innovations: a **smartphone**. This area is expanding to wearable technology in general and these new gadgets not only measure data, they immediately interpret that data. FDA cleared a new iPhone add-on that lets doctors take an electrocardiogram just about anywhere. Other smartphone apps help radiologists read medical images and allow patients to track moles for signs of skin cancer. At \$199, Alive Cor consists of a case that snaps onto the iPhone, with electrodes on the back. It reads heart rhythms and relays the recording to an iPhone app, allowing physicians to read the data. Dr. David E Albert, who has developed medical and other life-saving technologies and products over the last 30 years, and is founder of the AliveCor company, says a \$99 version should be available soon that will let patients capture their own heart data, documenting sometimes-fleeting arrhythmias when they feel symptoms or tracking the success of lifestyle changes at curbing heart troubles.

Doctors say that mainstream EKG machines provide more information but the iPhone version is sufficient for many diagnostic needs. The FDA has cleared a handful of apps, beginning with an iPad- and iPhone-based medical imaging reader in 2011. The smartphone lets us "bring health care into the home," says Erik Douglas, CEO of Cell Scope. His company is developing an iPhone-based otoscope that would allow parents to upload images of the inside of children's ears when they show signs of infections, with the aim of avoiding unnecessary doctor's visits (See Celloscope website <https://www.cellscope.com/clinicians>).

Soon **smart watches** will be available to continuously monitor blood pressure or blood oxygen concentration, and wearable sensors will track hemodynamic metrics like cardiac output and stroke volume. Routine lab work is also moving in the direction of the smartphone.

The next wave of wearable health tech will focus on gathering personal data more meaningful to a doctor, and send it directly to his or her office--such as a remote stethoscope that can transmit a person's heart rhythm to a physician. Finally, devices that try to replicate the pancreas have moved out of controlled trial centers into real-world settings, representing a significant advance in

the technology. The system includes a continuous glucose monitor and a "brain"—such as a smartphone—that calculates what the patient needs to maintain appropriate glucose levels, and then communicates with an infusion device that delivers insulin and, in some cases, glucagon. Researchers say a dependable, user-friendly system could be available in the next 5 years.

Further Information

- <http://www.hindustantimes.com/india/smartphone-clinic-your-health-is-in-your-hands/story-Mxdzk2ruJV8NwsXhvxUosN.html>

3.1.8 IMMUNE CHECKPOINTS IN CANCER THERAPY

Few advances in cancer care are generating more enthusiasm than harnessing the power of the immune system to fight the disease. For decades, cancer researchers have wondered why the immune system typically doesn't treat tumor cells as invaders and target them. Among the most promising approaches to activating therapeutic antitumor immunity is the blockade of immune checkpoints. Immune checkpoints refer to a plethora of inhibitory pathways of the immune system that are crucial for maintaining self-tolerance and modulating the duration and amplitude of physiological immune responses in peripheral tissues in order to minimize collateral tissue damage. It is now clear that tumors co-opt certain immune-checkpoint pathways as a major mechanism of immune resistance, particularly against T cells that are specific for tumor antigens. Because many of the immune checkpoints are initiated by ligand–receptor interactions, they can be readily blocked by antibodies or modulated by recombinant forms of ligands or receptors. Cytotoxic T-lymphocyte-associated antigen 4 (CTLA4) antibodies were the first of this class of immunotherapeutics to achieve US Food and Drug Administration (FDA) approval. Preliminary clinical findings with blockers of additional immune-checkpoint proteins, such as programmed cell death protein 1 (PD1), indicate broad and diverse opportunities to **enhance antitumor immunity** with the potential to produce durable clinical responses.

The number of cases where immunotherapy has been tested is still relatively small, but the results have been encouraging. Immunotherapy marks an entirely different way of treating cancer—by targeting the immune system, not the tumor itself.

Further Information

- <http://www.nature.com/nrc/journal/v12/n4/pdf/nrc3239.pdf>

3.1.9 BIOMARKERS IN MEDICINE

Biomarkers are any measurable characteristics of an organism that reflect a particular physiological state. In medicine, biomarkers are often compounds isolated from serum, urine, or other fluids that can be used as **an indicator of the presence or severity of a particular disease** state and can also be used to assess the effectiveness of particular therapies. Biomarkers are also important in the development of **new drug therapies** through the discovery of "**druggable targets**." In addition to identifying drug targets, biomarkers have the potential to speed development of new disease therapies through the use of "progression" markers to delineate the development and course of a disease.

Biomarkers can take many different forms, proteins, antibodies, cell types, metabolites, lipids, hormones, enzyme levels, physiological states such as blood pressure or fever, or imaging studies of particular organs or organ systems. It can also be a substance introduced into a patient to as-

sess how internal organ systems are functioning, such as radioactive iodine used to measure thyroid function. Ultimately, biomarkers can be used to detect a change in the physiological state of a patient that correlates with the risk or progression of a disease or with the susceptibility of a disease to a given treatment. Biomarkers hold great promise for personalized medicine as information gained from diagnostic or progression markers can be used to tailor treatment to the individual for highly efficient intervention in the disease process (The Coriell Institute for Medical Research web-site).

An ideal biomarker may fill one of many different roles. A biomarker may be suitable for the **early diagnosis** of a disease, either as part of a routine screening exam or at the first sign of a questionable symptom. A biomarker may also appear or disappear over the course of disease progression and thus be useful in determining the **prognosis of a disease** within an individual. Another biomarker may change as a drug therapy is started, adjusted or discontinued, ultimately aiding in the monitoring of the patient's response to that particular therapy.

In addition, the rapid return of results for early initiation of treatment and monitoring effectiveness is highly desirable. This could be a test performed during a patient's office visit with an immediate result. Finally, a reliable biomarker will have a detection method that is both sensitive and specific and is highly reproducible among clinical laboratories (S. Vasan, 2006)

Large-scale studies are currently underway on the discovery and validation of new and more effective biomarkers. The driving force behind these studies is the revolution of **"omic" medicine**. Instead of looking at one potential biomarker at a time, new techniques in genomics, transcriptomics, proteomics, metabolomics, lipidomics, glycomics, and secretomics have allowed investigators to identify patterns in the changes of tens, hundreds and even thousands of genes and compounds that correlate with disease state. A single biomarker is often inconclusive or ambiguous because diseases with very different pathophysiologies can affect the same molecule or marker. The sum of changes of a metabolic pathway or a suite of genes would be a much better indicator of the underlying pathology. These omic studies require thousands of blood, urine, or other samples to reveal subtle, but definitive, pattern changes.

In particular, the development of CVD biomarkers has been a challenging field since the urgent need for additional tools to aid clinical assessment and to enhance the ability to identify the “vulnerable” patient at risk for CVD. Biomarkers are one such tool to better identify high-risk individuals, to diagnose disease conditions promptly and accurately, and to effectively prognosticate and treat patients with disease.

Three parallel developments have revolutionized the field of biomarker discovery: First, the completion of the Human Genome Project, the development of microarrays, proteomics, and nanotechnology together provide new avenues for developing exceptionally informative biomarkers of CVD, including high-throughput, highly sensitive, functional assays. Second, the advances in bioinformatics coupled with cross-disciplinary collaborations (e.g. of biologists, clinicians, chemists, computer scientists, physicists) have greatly enhanced our ability to retrieve, characterize, and analyze large amounts of data generated by the technological advances noted above. Third, there is increased recognition that diseases arise out of the dynamic dysregulation of several gene regulatory networks, proteins, and metabolic alterations, reflecting complex perturbations (genetic and environmental) of the “system.” The expectation that single biomarkers can capture these intricate derangements and can unambiguously identify disease or that targeting single molecules or

signaling pathways is adequate for treating complex pathology is simplistic. Rather, a “systems biology” approach that investigates multiple components of malfunctioning regulatory networks (referred to as multi-parameter analysis of tens of hundreds of molecules) may provide better insights into disease diagnosis, prognosis, and treatment (Marko-Varga G. et al. 2005).

It is generally believed that the biomarker industry will continue to rapidly expand and flourish in the near future. The burgeoning research in biomarker development mandates a systematic organization of data with the use of standardized taxonomies that facilitate the **online sharing of biomarker** metadata among researchers. Large epidemiological and clinical studies will be required to assess the cost-effectiveness of biomarkers. Screening biomarkers will likely compete for limited healthcare budgets, and only those with excellent performance characteristics will find utility in primary care settings. It is conceivable that some biomarkers may find use as **over-the-counter tests** as the public continues its informed interest in its own health. Biomarkers that are cost-effective in preventing late sequelae of CVD will likely survive such competition. Diagnostic markers will find use in point-of-care testing in emergency departments and by the bedside. Biomarkers that perform well and cost-effectively in the testing of rapid “rule out” or “rule in” strategies and those that help to triage patients into low- and high-risk treatment strategies will be integrated into clinical decision-making protocols. Biomarkers (including pharmacogenetic ones) that facilitate choice of the most appropriate drug, that enable titration of drug dose to avoid side effects, and that maximize therapeutic effects are likely to be attractive to clinicians.

Further Information

- <https://www.coriell.org/research-services/biomarkers/challenges-of-biomarker-research>
- <http://circ.ahajournals.org/content/113/19/2335.full.pdf+html>

3.1.10 GENDER SPECIFIC MEDICINE AND CARE

The field of gender-specific medicine examines how normal human biology and physiology differ between men and women and how the diagnosis and treatment of disease differs as a function of gender. This research covers various conditions that predominantly occur in men as well conditions that predominantly occur in women. Among the areas of greatest difference are cardiovascular disease, mood disorders, the immune system, lung cancer as a consequence of smoking, osteoporosis, diabetes, obesity, and infectious diseases. Recent research focuses on the essentials of gender-specific medicine and the current study of sex and gender differences in human physiology and pathophysiology, for example how the gender-specific risks of one organ system’s disease affects the health of other organ systems. Research is also done to examine the results of new drug therapies designed with gender-specific differences such as hormone therapy in men and women for the prevention and treatment of cardiovascular disease.



Examples of sex-related illnesses and disorders in female humans³:

Examples of sex-related illnesses and disorders in male humans:

³ http://www.gutenberg.us/articles/sex-related_illness

<ul style="list-style-type: none"> • 99% of breast cancer occurs in women. • Ovarian cancer, and other diseases of the female reproductive system occur only in women. Endometriosis, another female reproductive disorder occurs almost exclusively in women, but has rarely been found in men undergoing estrogen treatment for prostate cancer. • More women than men suffer from osteoporosis • Autoimmune diseases, such as Sjögren's syndrome and scleroderma, are more prevalent in women. An estimated 75 percent of those living with autoimmune diseases are female. • In Western cultures, more women than men suffer from eating disorders such as anorexia nervosa and bulimia • Alzheimer's disease has a higher rate in women than in men. • Women are more likely to suffer from unipolar clinical depression (although bipolar disorder appears to affect both sexes equally) • Psychologists are more likely to diagnose women than men with borderline or histrionic personality disorder. There is no current agreement on whether this is because of a real underlying difference between the sexes, or simply because of deeply ingrained social attitudes. 	<ul style="list-style-type: none"> • Prostate cancer and other diseases of the male reproductive system occur only in men. • Diseases of X-linked recessive inheritance, such as colour blindness, occur more frequently in men. Abdominal aortic aneurysms are six times more common in men, and thus some countries have introduced screening for males at risk of suffering the condition. • Autism is approximately 4 times more prevalent in males than females. • Psychologists are more likely to diagnose men than women with antisocial personality disorder and substance-abuse disorders.
---	--

Gender-specific care is not limited to physiological gender differences; instead it addresses total health from a gender-specific perspective. When you take away the obvious reproductive differences, men and women experience many of the same diseases in different ways. For that reason they benefit from a different approach to healthcare. For example, pancreatic cysts occur more frequently—and differently—in women than they do in men. The symptoms of heart disease are different in women compared with those that are common in men. Even musculoskeletal injuries are different in women—in fact, women are prone to more and different injuries than are men (Adams et al. 2007).

Women have four times the number of ACL (Anterior cruciate ligament) tears than men and a greater incidence of ankle injuries compared with men. Medical experts say that this has to do with estrogen and the fact that women can bear children. The angle from the hip to the knee is different in women, which places more strain on the knee. After puberty women do not land in the same way as men do when they jump. But there are things women can do to prevent injury—like muscle training and core training.

Literature incorporating sex/gender analysis increased over time and displays a stronger trend if compared to overall publication increase.⁴ As Oertelt-Prigione showed, all disciplines, but cardiology (22%), demonstrated an underrepresentation of research about gender differences in management, which ranges from 3 to 14%. While the use of animal models for identification of sex differences in basic research varies greatly among disciplines, studies involving human subjects are frequently conducted in large cohorts with more than 1,000 patients (24% of all human studies). Although large cohorts are often analysed, sex and gender differences in clinical management are insufficiently investigated leading to potential inequalities in health provision and outcomes.

⁴ Analysis of sex and gender-specific research reveals a common increase in publications and marked differences between disciplines, Sabine Oertelt-Prigione, Roza Parol, Stephan Krohn, Robert Preißner and Vera Regitz-Zagrosek

Men tend to have an unhealthy life-style compared to women; they get sick more often, have more accidents and die earlier. Male employees are more on sick leave than women. Psychological problems such as depression occur more often in men than women and their suicide rate is also much higher. They make up two thirds of the people with alcohol abuse (Apfel, 1982; Waldron, 1994; (Verbrugge, 1985; Walsh, et al., 1995). When social discrimination decreases, women's life expectancy increases (Waldron, 1983). Men have higher rates of fatal illnesses. Men have more toxic occupational exposure; Men have higher rates of injuries (both intentional and non-intentional) (Verbrugge, 1985; Walsh, et al., 1995). Even though men in our society do not have to do the hard physical labour their ancestors had to do one or two generations ago, and they do not have to go to war anymore (at least the majority), they are not in a good position concerning health. Most of them only see a doctor when already in a very critical stage, doing more "repair" than prevention. The US psychologist Herb Goldberg formulated seven "masculine imperatives" attempting an analysis for the male health situation:

"The less sleep I need, the more pain I can take, the more alcohol I can hold, the less I concern myself with what I eat, the more I control and repress my emotions, the less attention I pay to myself physically, the more masculine I am."

Gender-specific care is a more individualized, nuanced approach to healthcare. Research and health services are specializing in this direction. Dedicated to gender medicine, for example, is the 'Foundation for Gender Specific-Medicine', supporting the investigation of the ways in which biological sex and gender affect normal human function and the experience of a disease. One of the discipline's pioneers, Marianne J. Legato, FACP, MD established this Foundation as a continuation of her work with 'The Partnership for Gender-Specific Medicine' at Columbia University.⁵

3.2 ENVIRONMENT

The environment must be recognised as not only a source of potential hazards, but also a health-promoting and health-protecting asset that can extend life, improve its quality and increase overall well-being. A comprehensive understanding of the relationship between health and the environment requires a forward-looking perspective and insight into the composite interactions among the physical, biological and social spheres (WHO 2013). An overview of impacts of environmental changes to health is given in figure 3:

⁵ <https://gendermed.org/dr-legato/>

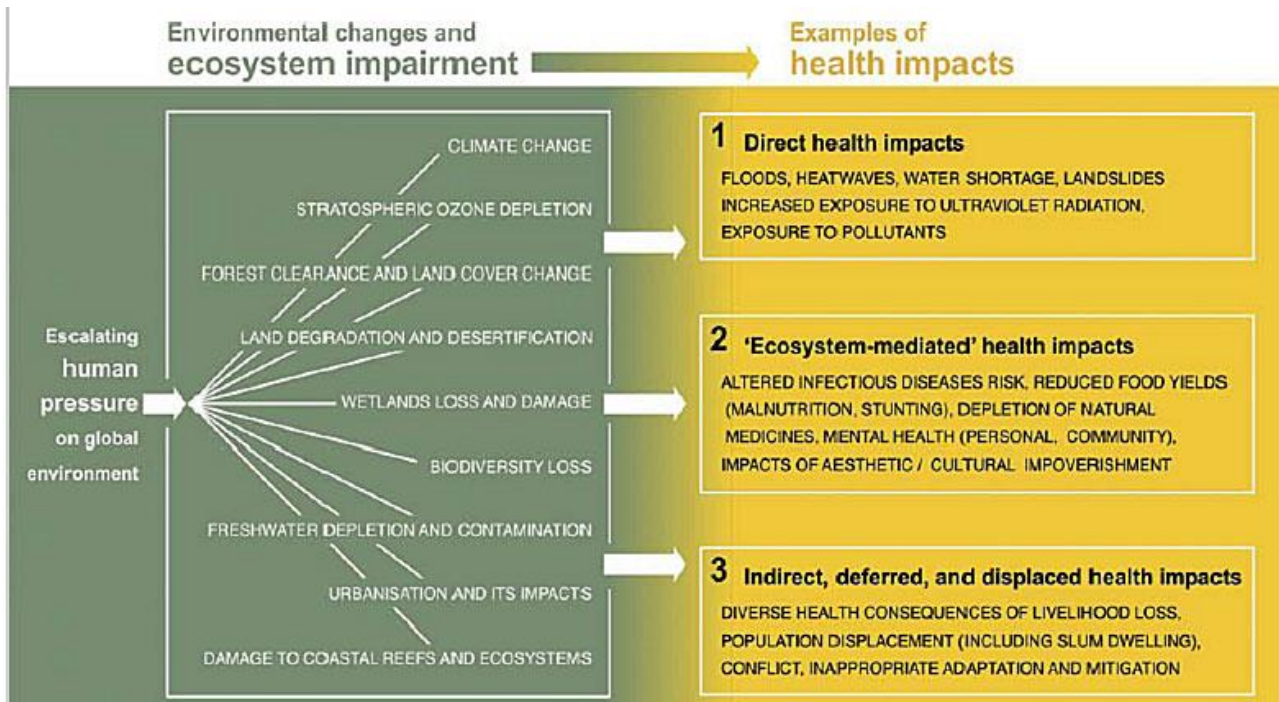


Figure 1: Millennium Ecosystem Assessment (2005) (Source: <http://www.who.int/globalchange/environment/en/>)

Environmental hazards influence over 80% of the communicable and non-communicable diseases and injuries monitored by WHO. What is included in the term “environment” can be best depicted by Figure 2, adapted by the WHO from Smith et al. (1999), but was defined in a more practical sense by the WHO: “the environment is all the physical, chemical and biological factors external to a person, and all the related behaviors, but excluding those natural environments that cannot reasonably be modified” (Prüss-Üstün & Corvalán 2006).

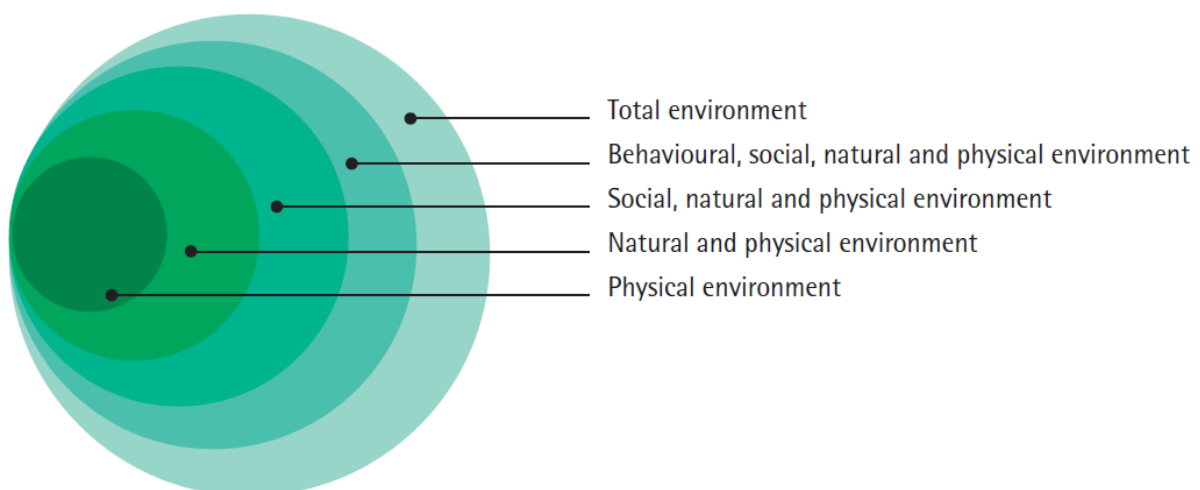


Figure 2: Definition of the environment (adapted after Smith et al., 1999)

Thus various factors need to be taken into consideration and the most important risk hazards are addressed by the global strategy of WHO Public Health & Environment (2011):

- Water, sanitation & hygiene guidelines to inform policy making and prevent waterborne diseases
- Indoor air policies to substitute fuels & cook stoves
- Outdoor air policies to minimize the health impact of urban transport
- Housing standards and policies to reduce exposure to radon, lead, asbestos and other harmful chemicals
- Chemical regulation policies to restrict or stop the use of highly hazardous chemicals in industry, agriculture and in consumer products and promote the use of safer alternatives

Environmental and occupational exposures account for a significant part of the NCD burden. Physical activity is influenced by **urban environments and transport policies**, which can promote cycling and walking for transport by developing safe infrastructure, as well as fostering the establishment of accessible green spaces for leisure-time physical activity and encouraging behaviour modification. Occupational health and safety programmes can also be advocates for workplace wellness interventions. On a larger scale, lessons learned from the climate change and sustainable development movements serve as a model for developing advocacy for NCDs and development. There are deep connections with the causes of air and noise pollution and with efforts to control them. Sound and sustainable policies relating to the environment and health will contribute directly to reducing the burden of NCDs: from agricultural practices and policies, to protection of children from adverse environmental exposures.

Agriculture influences health directly through the **quantity and the nutritional composition** of the foods available for consumption in the household and in the market (see also chapter 3.6 and chapter 3.8). This is influenced by what we grow. Choices within agriculture between the production of food and cash crops influence competition for land, water and labour resources, and influence food availability. Agricultural practices and policies can therefore have a direct health impact by influencing the price and availability of foods. Another direct effect of agriculture on health is the exposure of human subjects to **food-borne diseases and to toxicants such as herbicides and pesticides**, associated with farming and food chains. (Dangour et al., 2012) The same chemicals that are used to assist agricultural production, develop medicines and produce consumer goods can be hazardous to human health over the long term, accumulating in our bodies through environmental exposure.

There has been an increasing awareness in recent years of the presence and potential impacts of **pharmaceuticals** and personal care products **in the environment**, including surface water, groundwater, soil, bed sediment, and in tissue. The potential routes of environmental entry include patient excretion either as parent compound or metabolites via the sewer system, direct release into the waste water system from manufacturing, hospitals or disposal via toilets/ sinks, and terrestrial depositions, for example via sludge application to land, leaching from solid waste landfills, or irrigation with treated or untreated wastewaters.

Even in trace amounts active pharmaceuticals are of great concern due to their continuous introduction into the environment, their impact on ecosystem and human and veterinary health. This has given birth to the science of Ecopharmacovigilance (EPV). It aims to ensure that significant environmental issues associated with pharmaceuticals in the environment are identified and managed appropriately. Environmental Risk assessment (ERA) is now a regulatory requirement prior to launch of any new drug. The biggest difference and greatest challenge concerns signal detection in the environment and the dilemma of identifying cause and effect (e.g. Brown, 2014; Holm et al,

2013; Kaplan, 2013; Wand & Hu, 2014).

A growing body of research in the United States and Western Europe documents significant effects of the physical environment (**toxins, pollutants, noise, crowding, chaos, and housing, school and neighborhood quality**) on children and adolescents' cognitive and socioemotional development (Ferguson et al., 2013). Over the last three decades there has been increasing global concern over the public health impacts attributed to environmental pollution, in particular, the global burden of disease. The World Health Organization (WHO) estimates that about a quarter of the diseases facing mankind today occur due to prolonged exposure to environmental pollution. Most of these environment-related diseases are however not easily detected and may be acquired during childhood and manifested later in adulthood. Improper management of solid waste is one of the main causes of environmental pollution and degradation in many cities, especially in developing countries. Many of these cities lack solid waste regulations and proper disposal facilities, including for harmful waste. Such waste may be infectious, toxic or radioactive.

Chemical pollution provokes irreparable damage to our ecosystems and communities, causing dramatic effects on the health of the most vulnerable, especially children, the poor and indigenous peoples. Although some progress has been made on chemical safety, impacts on the health of workers remain enormous. Every minute, a person dies from exposure to toxic substances at work. Out of the 160 million occupational illnesses per year, the bulk is caused by chemical agents (UNEP, 2015).

WHO's International Agency for Research on Cancer (IARC) has classified 107 agents, mixtures, and exposure situations as carcinogenic to humans. These include all forms of asbestos and a number of agents found in the environment such as benzene, arsenic in water, cadmium, ethylene oxide, benzo[a]pyrene, silica, ionizing radiation including radon, ultraviolet radiation including tanning devices, aluminium and coke production, iron and steel founding, or the rubber manufacturing industry (WHO, 2011).



Air pollutants, taken as an example of environmental influence on health, such as carbon monoxide (CO), sulphur dioxide (SO₂), nitrogen oxides (NO_x), volatile organic compounds (VOCs), ozone (O₃), heavy metals, and respirable particulate matter (PM_{2.5} and PM₁₀), differ in their chemical composition, reaction properties, emission, time of disintegration and ability to diffuse in long or short distances. Air pollution has both acute and chronic effects on human health, affecting a number of different systems and organs. It ranges from minor upper respiratory irritation to chronic respiratory and heart disease, lung cancer, acute respiratory infections in children and chronic bronchitis in adults, aggravating pre-existing heart and lung disease, or asthmatic attacks. In addition, short- and long-term exposures have also been linked with premature mortality and reduced life expectancy (Kampa & Castanas, 2008).

Noise exposure at work places, schools and in living environment has been investigated in various studies. Noise has been associated with a number of adverse health effects, apart from Noise Induced Hearing Loss, manifesting in the form of physiologic damage or psychological harm through

a variety of mechanisms (Seidman & Standring, 2010). Adverse effects from noise have been studied in detail deriving from physical and urban environment, both at home and at workplaces. Studies have shown that noise is strongly related to reduced cognitive function, inability to concentrate, increased psychosocial activation, nervousness, feeling of helplessness and other stress related symptoms ranging from high blood pressure to sleeplessness and cardiovascular diseases (Viet et al 2010; Evans et al. 2001; Guite et al, 2006; Leather et al, 2003; Lamb & Kwok, 2016; Liebl et al., 2012; Smith-Jackson & Klein, 2009).

In developing countries, the burden of disease due to environmental hazards is heavily weighted towards communicable diseases. In developed countries, environmental hazards have a bigger impact on non-communicable diseases. In the Parma Declaration on Environment and Health (2010), European Member States have explicitly set themselves the goal of contributing to the prevention of NCDs through actions directed at reducing the relevant environmental exposures, also addressed in the European Environment Health Process (EHP)⁶:

- A. Protecting children's health
 - a. Ensuring public health by improving access to safe water and sanitation
 - b. Addressing obesity and injuries through safe environments, physical activity and healthy diet
 - c. Preventing disease through improved outdoor and indoor air quality
 - d. Preventing disease arising from chemical, biological and physical environments
- B. Protecting health and the environment from climate change
- C. Involvement of children, young people and other stakeholders
- D. Knowledge and tools for policy-making and implementation

Further Information

- <http://www.ipenproject.org/>
- <http://www.euro.who.int/en/health-topics/environment-and-health>
- http://www.who.int/quantifying_ehimpacts/publications/preventingdisease.pdf?ua=1

3.3 URBAN DEVELOPMENT

Over half the world's population now lives in cities, and urbanization will be among the most important global health challenges during the 21st century. Urbanization is associated with many health challenges – infectious diseases and non-communicable diseases, including cancer and heart disease – as well as unhealthy life choices such as tobacco use and alcohol abuse. City dwellers are more exposed to road traffic accidents, injuries, violence and crime. The urban poor suffer disproportionately from a wide range of diseases and other health challenges.

To reverse this trend, representatives of local and national governments are urged to develop policies to protect and promote health, across multiple sectors, including the environment, transport, education and urban planning.⁷

⁶ <http://www.euro.who.int/en/health-topics/environment-and-health/pages/european-environment-and-health-process-ehp/health-and-environment-in-the-who-european-region-creating-resilient-communities-and-supportive-environments>

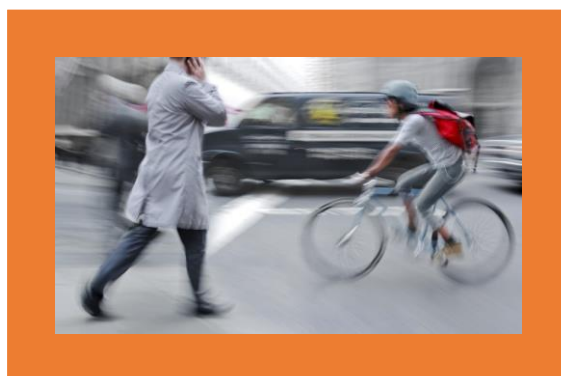
⁷ <http://www.euro.who.int/en/health-topics/environment-and-health/urban-health/activities/healthy-cities/who-european-healthy-cities-network/meetings-of-the-who-european-healthy-cities-network/annual-meeting-of-the-who-european-healthy-cities-network-2010.-theme-the-hidden-cities-addressing-equity-in-health-and-inclusiveness-in->

3.3.1 BUILT ENVIRONMENT AND PHYSICAL ACTIVITY

Built environment may influence health behaviours directly or indirectly (Cradock/Duncan 2014, p. 442). It is obvious that built environment can promote physical activity via respective promoting facilities and environments, for example with regard to walkable community design, density, connected streets, mixed land uses, access to transit and public transportation, pedestrian and bicycle facilities, building designs such as stair cases, parking places; the location of workplaces and schools, parks and trails, playgrounds, landscape aesthetics, sidewalks and safety. Among children and adolescents, research suggests that walkability, traffic speed and volume, access and proximity to recreational facilities, and the urban form characteristics of land-use mix and residential density present important correlates of physical activity participation (Ding et al., 2011).

Local stores, supermarkets, and fast food restaurants can influence nutrition-related behaviors via access and marketing of foods and beverages, e.g. with regard to distance and availability for special needs. There are some studies that indicate that perceived availability is linked to healthy nutritional behavior. Other correlations still need to be evaluated and researched more.

A growing body of studies shows that accessibility to **tobacco** retailers is associated with increased tobacco use (Chan & Leatherdale, 2011; Henriksen et al. 2008; Leatherdale & Strath 2007). Concerning **alcohol** the issue is more complex. Research results concerning alcohol availability in the neighborhood and alcohol consumption are ambiguous (Halonen et al., 2011; Connor, Kypri, Bell, Cousins, 2011).



3.3.2 BUILT ENVIRONMENT AND DEPRESSION

Built environment and depression are associated as several studies show. Greater access to social destinations and community design features in the built environment may promote socialization and prevent or work against symptoms of depression. No definite evidence is available yet concerning the walkable distance in a particular neighborhood and depression.

Interventions in the built environment are generally sustainable interventions, that is to say they influence the structure and function of the physical environment in which health behaviors occur but do not require repeated introduction in order to be maintained. It goes without saying that interventions of this kind are usually very costly, but since they last very long and can reduce the health care budget they might often be the cheaper expenditure. Cost effectiveness studies of built environment interventions however are just lately becoming an area of research (Wu et al., 2011). Built environment interventions are increasingly becoming multi-disciplinary partnerships between urban planners, parks/recreation officials, transportation engineers, public health officials, and citizens.

3.3.3 BUILT ENVIRONMENT OF SCHOOLS

Schools are an important for influencing health-related behavior of both students and teachers and other employees working at the school site. Interventions within the built environments of

[cities/quick-facts-on-urban-health](#)

schools have been developed to address dietary behaviours as well as physical activity and tobacco consumption. Interventions in schools often include physical infrastructure change and also campaigns to raise awareness for the connection between built environment, behaviour and health. Many students consume food and beverages while on school property thus making the built environment of schools a popular setting for interventions to promote healthy eating and drinking (Giles et al. 2012).

School playgrounds and public playgrounds are a common device to promote play and physical activity among students and smaller children. Studies have shown that physical activity is more attractive to children if sufficient playground materials and space are provided (Hannon/Brown, 2008).

3.3.4 ATTRACTIVE ENVIRONMENTS

Built environment can also promote or hamper the physical activities of adults. Taking the stairs is one way to be more physically active in everyday environments and has proven to strengthen fitness over short intervention periods (Boreham et al., 2005). Examples of interventions promoting stair use in place of elevators and escalators have generally relied on point-of-decision signage frequently demonstrating statistically significant increases in stair use with potential for longer-term sustainability (Soler et al., 2010). Certain design characteristics can impede or promote stair use.

To make neighborhoods more attractive for walking they have to have a certain infrastructure and they have to be safe from accidents. There are several design features to help reduce speed of cars and to raise more awareness in car drives for the needs of pedestrians. Pedestrian crossing countdown signals, visual signals that provide information on the amount of time for the next green light, auditory information for pedestrians with visual impairment, installations of traffic calming measures (speed bumps, blocks on the road), and shared spaces are options to reduce traffic speed and grant more right to the pedestrians. (Dumbaugh/Frank, 2007; Bunn et al., 2009)

The other major strategy to improve or maintain health through intelligent neighborhood built environment is to support biking, e.g. by more biking lanes, off- as well as on-road, bike parking lots, bicycle sharing programs, public electric stations to charge e-bikes, etc.

There is quite some room for action at the political level to influence health behavior by regulating physical infrastructure, e.g. through local zoning policies. What is more, several studies have shown links between the density of tobacco retail outlets around schools or homes and smoking prevalence. (Mozaffarian et al., 2012; Center for Tobacco Policy & Organizing, 2011)

In the U.S., the “Safe Routes to School Programs” were established as part of federal transportation policy that provided funding to support local programs in each state, supporting walking and bicycling of kids to school and thus be more physically active. One approach for more physical activity of children in a safe environment is called “multi-component intervention” and comprises information campaigns for parents and children together with changes in the built environment. Within school buildings, multi-component intervention can ameliorate healthy eating by designing teaching kitchens, storage of food, serving and eating zones, display of healthy foods and on-site food production facilities (Huang et al., 2013).

3.3.5 HEALTH EQUITY AND BUILT ENVIRONMENT

The health equity debate is based on the assumption that health inequities often occur among disadvantage groups and are unjust. Built environment strategies can play an important role in promoting social and environmental justice and reduce health inequities by eliminating health-harming environments. As several studies have shown, low income populations and some racial/ethnic minorities are exposed to features of built environment that may contribute to obesity and other NDC-related factors (Larson et al., 2009).

3.3.6 HEALTHY AND SUSTAINABLE CITIES

The WHO European Healthy Cities Network consists of cities around the WHO European Region that are committed to health and sustainable development: nearly 100 cities and towns from 30 countries. The WHO European Healthy Cities Network has six strategic goals:⁸

1. to promote policies and action for health and sustainable development at the local level and across the WHO European Region, with an emphasis on the determinants of health, people living in poverty and the needs of vulnerable groups;
2. to strengthen the national standing of Healthy Cities in the context of policies for health development, public health and urban regeneration with emphasis on national–local cooperation;
3. to generate policy and practice expertise, good evidence, knowledge and methods that can be used to promote health in all cities in the Region;
4. to promote solidarity, cooperation and working links between European cities and networks and with cities and networks participating in the Healthy Cities movement;
5. to play an active role in advocating for health at the European and global levels through partnerships with other agencies concerned with urban issues and networks of local authorities; and
6. to increase the accessibility of the WHO European Network to all Member States in the European Region.

3.4 HEALTH SYSTEMS SHARED VALUES AND OPERATING PRINCIPLES

Health systems are primarily regulated at national level and health systems organisation, services and outcomes differ widely among European countries. For all Member States, however, healthcare is a cornerstone of social protection, 75% financed by public funding and constitutes almost 15% of all governments expenditures. Chronic diseases' cure accounts for 70%-80% of all health care costs, estimated €700bn in the EU every year, and affect 8 out of 10 of people over 65. Considering the demographic megatrend that projects 37% of the European population over 60 by 2050 and the recent cut at health care expenditures, the need clearly emerges to reform the health systems in order to safeguard the health system values and its social protection function in the future (Acting Together: A Roadmap for Sustainable Healthcare 2015).

In 2006, the Council of EU (2006) has recognised the overarching **values** common to all the European health care systems. “**Universality** means that no-one is barred access to health care; **soli-**

⁸ <http://www.euro.who.int/en/health-topics/environment-and-health/urban-health/activities/healthy-cities/who-european-healthy-cities-network/six-strategic-goals>

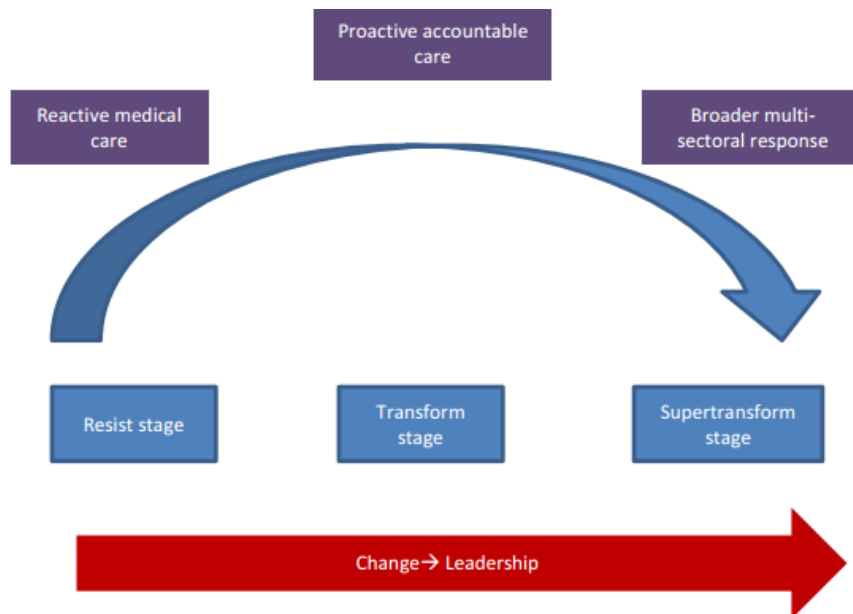


parity is closely linked to the financial arrangement of our national health systems and the need to ensure accessibility to all; **equity** relates to equal access according to need, regardless of ethnicity, gender, age, social status or ability to pay. EU health systems also aim to reduce the gap in health inequalities, which is a concern of EU Member States; closely linked to this is the work in the Member States' systems on the prevention of illness and disease by inter alia the promotion of healthy lifestyles". The Resolution recognised also six operating principles that are shared by health systems across the EU: *safety, care that is based on evidence and ethics, patient involvement, redress, privacy and confidentiality*.

In 2006, Member States have also increased their cooperation on health reforms through the Open Method of Coordination (OMC) with the aim of the establishment of guidelines and indicators, the organization of exchange of best practice, and the preparation of the necessary elements for periodic monitoring and evaluation (SPC 2011c). OMC is a policy method that collects voluntary, non-binding targets and heavily relies on the national government actions and follow-up measures. The Commission identified **three principles**, reinvigorated over time, all-important and mutually dependent, that should serve as basis for the reform of the national health systems:

- **access for all to adequate health and long-term care** and ensuring that the need for care does not lead to poverty and financial dependency; and that inequities in access to care and in health outcomes are addressed;
- **quality in health and long-term care and by adapting care, including developing preventive care**, to the changing needs and preferences of society and individuals, notably by developing quality standards reflecting best international practice and by strengthening the responsibility of health professionals and of patients and care recipients;
- adequate and high quality **health and long-term care remains affordable and financially sustainable** by promoting a rational use of resources, notably through appropriate incentives for users and providers, good governance and coordination between care systems and public and private institutions. Long-term sustainability and quality require the promotion of healthy and active life styles and good human resources for the care sector.

Health systems are complex, have an important legacy from the past and resist to changes. Following the economic crisis, Member States have reduced the health care budget and started including Health system reform in their National Reform Plan. In 2015, the Social Protection Committee (SPC) and the Council Working Party on Public Health at Senior Level (WPPHSL) reached joint conclusions on the health-related country specific recommendations (CSRs) and analysis of health challenges in member states (SPC 2015). Most countries have implemented sectoral and often-unfair measures whereas few States have taken the opportunity to initiate more complex actions that could bring better quality, increase the access and generate savings. Health systems are urged to shift from reactive model toward a broader multi-sectoral response, and political leadership needs to move from a sectoral perspective toward a more comprehensive vision. The future will depend upon the systems' ability to become "proactive rather than reactive, comprehensive and continuous rather than episodic and disease specific and founded on lasting patient-provider relationship rather than incidental, provider-led care" (WHO 2014).



Source: Rafael Bengoa

Figure 3 Health systems – Adapted from WHO (2015) Health system strengthening in the context of Health 2020: challenges and priorities in the WHO European Region

Trends for innovations are emerging regarding all systems components (resources, organisations and management), and failing to understand and adapt them will put the values and principles on which health systems are built at risk.

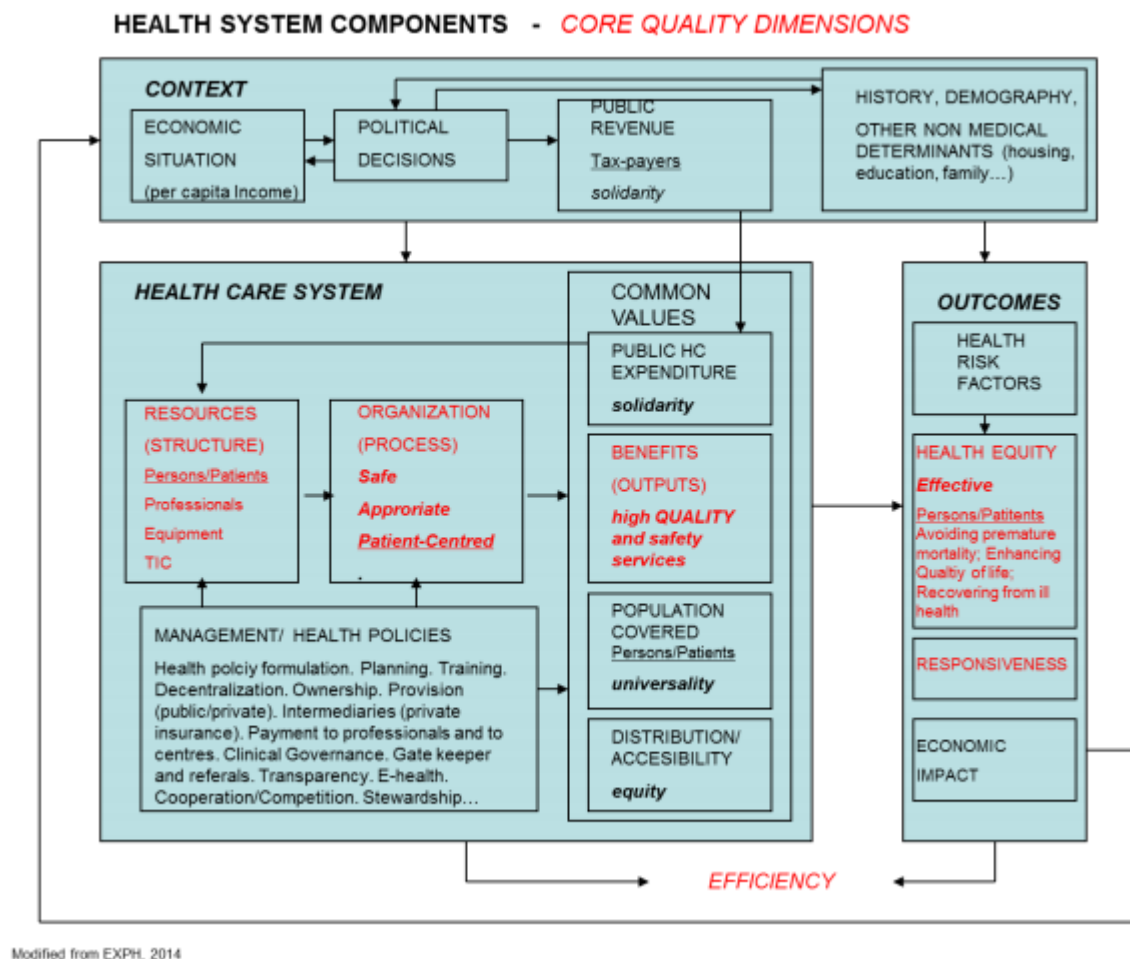


Figure 4 Health systems components -

EXPH- Future EU Agenda on quality of health care with a special emphasis on patient safety

1 Increasing transparency and improving the evaluation of Health Systems

Steering the change requires first knowledge and comparison of systems, an assessment of the performances, an analysis of the threats and the identification of opportunities. In line with this, a number of initiatives have been recently launched by the European Union and by WHO.

In 2014 the EC set up an Expert Group on Health Systems Performance Assessment (HSPA) with the aim of:

- Providing participating Member States with a forum for exchange of experience on the use of HSPA at national level.
- Support national policy-makers by identifying tools and methodologies for developing HSPA.
- Defining criteria and procedures for selecting priority areas for HSPA at national level, as well as for selecting priority areas that could be assessed EU-wide in order to illustrate and better understand variations in the performance of national health systems
- Intensifying EU cooperation with international organisations, in particular the OECD and the WHO

This action is strongly related to the “Tallin Charter: Health System for Health and Wealth” (WHO, 2008). Among EU countries, one of the most advanced countries in this field is Belgium, whose latest HSPA report covers five main dimensions of performance: quality, accessibility, efficiency, sustainability, and equity, featuring 74 indicators to assess the levels of performance.

WHO Regional Office for Europe has produced a Country Assessment framework and guide to evaluate the health system performance in reaching the goal of decreasing the premature mortality from NCDs by 25% by 2025. Five countries participated in a first round of assessments: Hungary, Kyrgyzstan, the Republic of Moldova, Tajikistan and Turkey. The work and the results cross-comparison will help to:

1. produce pragmatic and implementable policy recommendations for health system strengthening, to allow faster improvements in key NCD outcomes;
2. synthesize knowledge and experience in the countries of the Region on common health system challenges and promising approaches to overcome them;
3. build capacity in policy analysis, policy development, and implementation through dialogue around HSS and NCD

The framework lists the fifteen system features that can represent a challenge or present an opportunity for improved delivery of core NCD interventions and services.

Political commitment to NCDs	Explicit priority-setting approaches	Interagency cooperation	Population empowerment
Effective model of service delivery	Coordination across providers	Regionalization	Incentive systems
Integration of evidence into practice	Distribution and mix of human resources	Access to quality medicines	Effective management
Adequate information solutions	Managing change	Ensuring access and financial protection	

Figure 5 Roberts MJ, Stevenson MA. Better Non-communicable Disease Outcomes: Fifteen Challenges and Opportunities for Health Systems. Copenhagen: WHO Regional Office for Europe, 2014 (forthcoming)

2 Economic crisis undermines the access to health services

Access to quality health care is a human right recognized in the EU and contributes in achieving the objectives of the long-term savings and productivity increase of the Social Investment packages as well as the inclusive growth pursued by Europe 2020 strategy. Accessibility means “ensuring that the resources required to deliver relevant, appropriate, and cost-effective health services are as closely matched to need as possible”. (Access to health services in the European Union”, Preliminary Opinion 2015)

Between 2005 and 2009, EU Member States made huge progress in improving access to health care. The number of people reporting unmet needs fell steadily from 24 million in 2005 to 15 million in 2009. Since 2009, however, this positive trend has been reversed – a visible sign of the damage caused by the financial and economic crisis. By 2013, the number of people reporting unmet need for health care had risen to 18 million (3.6% of the population). (EC Preliminary Opinion). This negative trend is directly related to the reduction of health spending. The question is now whether the health systems will uptake the technological and management innovations able to ensure access to health adequate services without raising the healthcare expenditure.

Access to care is the result of interaction between different factors; the following indicators monitor the accessibility of the health systems:

- **Health system coverage** Except Bulgaria, Greece and Cyprus, the EU countries have achieved universal (or near-universal) coverage of health care costs. Alarming phenomena of the recent years is the decrease of population covered by health system in Bulgaria and Greece (Health at glance, 2014).
- **Depth of coverage and affordability** The health coverage, whether provided through public or private insurance, generally covers a defined “basket” of benefits, which usually include consultations with doctors, tests and examinations, and hospital care. In order to ensure that services are requested in a responsible way, people are asked to contribute financially toward the service they require, in the form of cost-sharing or co-payment. On average, curative care and pharmaceuticals are more than 70% of all medical spending by households but the share varies across countries (Health at glance, 2014).

- **Availability (health workforce, distance from point of care, waiting time)** Patients should have reasonable access to healthcare services: they should not have to travel too far or wait too long to access the service they need. As shown in the table above, there are wide differences in the situation in Europe and margins for improvement in many European countries. In the period 2008–2013, 9 countries recorded an increase of 1 percentage point or more in the share of the population reporting unmet needs for care and only 3 countries registered significant improvements in access (Social Europe Aiming for inclusive growth 2014).

		EU28	EU27	EA18	BE	BG	CZ	DK	DE	EE	IE	EL	ES	FR	HR	IT
2013		3.6	3.6	0.0	1.9	8.9	1.0	1.3	1.6	8.4	3.3	9.0	0.8	2.7	3.3	7.1
2012-2013 change in pp		~	~	n.a.	~	~	~	~	~	~	~	1.0	~	~	~	1.5
2008-2013 change in pp		n.a.	~	n.a.	n.a.	-6.4	~	~	~	1.1	1.5	3.6	~	~	n.a.	1.9
	CY	LV	LT	LU	HU	MT	NL	AT	PL	PT	RO	SI	SK	FI	SE	UK
2013	4.4	13.8	3.2	0.9	2.4	0.9	0.4	0.4	8.8	3.0	10.4	0.0	1.9	4.3	1.9	1.6
2012-2013 change in pp	~	1.4	~	~	~	~	~	~	~	~	~	~	~	~	~	~
2008-2013 change in pp	1.6	4.1	-2.3	~	-1.0	~	~	~	2.8	1.9	~	~	~	3.5	~	~

Figure 6 Self-reported unmet needs for medical care in % and changes 2012-2013 and 2008-2013

Note: i) Break in series in BE in 2011 means that evolutions between years before 2011 and years from 2011 on cannot be interpreted; ii) Only statistically significant changes have been marked in green/red (positive/negative changes) with a 1pp threshold. “~” stands for stable performance (i.e. statistically insignificant change). EUROSTAT -

Survey data suggest that financial barriers to access are the largest driver of unmet need in the EU. The figure below shows how unmet need disproportionately affects people of lower socio-economic status, those with low health literacy, poor education and low incomes; people with greater healthcare needs in general or those who belong to a specific disadvantaged ethnic minority, as well as homeless people and migrants. Moreover, the crisis has resulted in the emergence of new groups that were not considered vulnerable previously due to increased unemployment, especially among young men, and increased household debt problems, particularly for young couples facing housing and job insecurity. (EUROFUND- “Access to healthcare in times of crisis 2014)

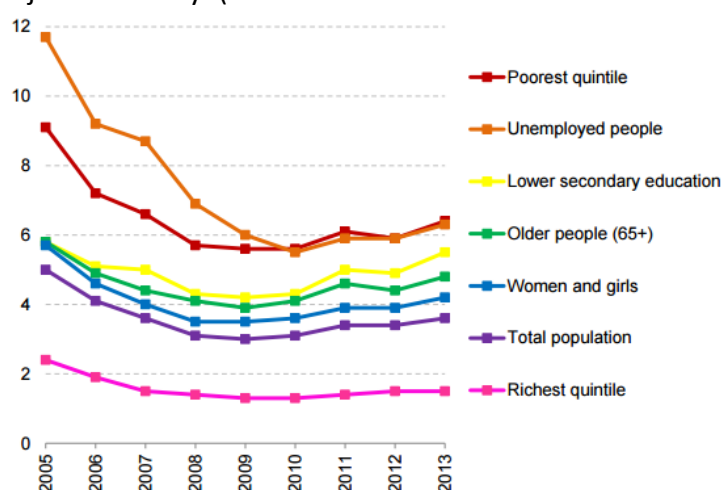


Figure 7 Share (%) of the population reporting unmet need for health care due to cost travel distance and waiting time, EU27, 2005-2013 Source: Access to health services –summary of preliminary opinion - based in EU-SILC

The opinion “Access to health services in the European Union” (2014) identifies the main barriers to access healthcare at the level of individuals, services providers and health systems. The opinion calls for policy responses that take into account the “multi-dimensional nature of access problems, the importance of inter-sectoral action and the specifics of national and regional context”.

Measures are proposed in the following policy areas:

- Financial resources are linked to health need;
- Services are affordable for everyone;
- Services are relevant, appropriate and cost effective;
- Well-equipped facilities are within easy reach;
- There are enough workers, with the right skills, in the right place;
- Quality of medicine and medical devices at fair prices;
- People can use services when they need them;
- Services are acceptable to everyone.

EUROFUND Report “Access to healthcare in times of crisis” (2014) highlights measures adopted by providers to sustain access during the crisis among which: economising, seeking funds from other public sources, and expanding coverage or leniency in enforcing co-payments for people in need. Other mitigation strategies identified in the research include:

- accelerating trends of deinstitutionalization, reducing hospital stays and keeping older people in the community, combined with development of an alternative care infrastructure;
- retaining and motivating staff, drawing on less costly workers, and work reorganisation;
- seeking new funding sources from alliances with local actors;
- ensuring basic services, such as scaled-down replacement services, when a service provider is closed;
- group sessions for patients with crisis-related mental health problems; self-help, medical help-lines or e-healthcare for people in remote areas;
- scaling up screening and measures to prioritise most urgent needs and services.(EUROFUND 2014)

3 Risk of health workforce shortage

Healthcare is highly labour intensive and one of the largest sectors in the EU, accounting for about 17 million or 8% of all jobs in the EU. Despite the economic downturn, the sector continues to grow and, with an ageing population and the rising demand for healthcare, will remain a key driver for jobs with an estimated 8 million job openings between 2010-2020. The EC estimates a potential shortfall of around 1 million healthcare workers by 2020 rising up to 2 million if long term care and ancillary professions are taken into account. This means around 15% of total care will not be covered compared to 2010. Potential shortfalls might worsen the working conditions and increase pressures on the healthcare workforce raising concerns over the impacts on patient safety and quality of care. Recognised challenges for the health workforce are:

1. an aging workforce and too few new recruits to replace retirees;
2. significant turnover due to demanding working conditions and relatively low pay;
3. the need of new skills shift toward more integrated delivery models and the growth of new technologies, new medical appliances and diagnostic techniques (Action Plan for the EU Health Workforce 2012).

The Action Plan for the EU health workforces (2012) and the EU Joint Action on Health Workforce Planning & Forecasting aim at improving the health workforce planning, anticipating future skills, improving professional development and the retention of health professionals.

4 Rising costs of medicine and medical device

Medicine and medical devices account for around 25% of total spending on health care and the efficient use of this resource is key for equitable access to health services. In some countries, high out of the pocket costs are a significant barrier to access and medicines are frequently the most important driver of financial hardship when using health services. And the high price of many medicines is becoming an increasing problem also for EU health system as recent experience on cancer drug have shown. (EC preliminary opinion, 2015). The EC recommends Member States to:

4. Ensure fairer prices by identifying more efficient ways to fund R&D, requiring much greater transparency around costs, prices, and developing joint procurement agreements for medicines and medical devices.
5. Define national policies on medical devices
6. Systematically use Health Technology Assessment (HTA), including cost-effectiveness and cost-utility analysis, to inform coverage decisions and disinvestment for medicines and medical devices.
7. Encourage rational prescribing and use of medicines and medical devices through ‘wise lists’, algorithms, guidelines, capacity planning of big-ticket equipment and specialised medical equipment management units.
8. Improve information systems and data collection at regional, national and EU level

5 The search for sustainability of the health systems

For all EU Member States, health expenditure is a major component of public finances. Public budget (social security and government spending) financed traditionally on average three quarters of health expenses and the “out of the pocket spending” and insurance covering the rest.

Total health care spending, both public and private, increased rapidly during the 1960s and 1970s and at a slower rate, in the 1980s. It picked up again in the 1990s in most Member States and continued growing in the first decade of the 21st century (Przyawara 2010). In 2012, it amounted an average of 8.7% of GDP in the EU, up significantly from 7.3% in 2000. Changes in the ratio in health spending to GDP are the result of combined effects of growth in both GDP and health expenditure. Healthcare expenditure per capita in the EU countries is €2.193 but it varies significantly among countries depending on the overall income level of a country and how much the country spends in health. Since 2008, health spending has in real terms fell in half of EU countries and significantly slowed in the rest. On average across the EU, health-spending decrease by 0.6% each year between 2009-2012 compared with the annual growth of 4.7% between 2000 and 2009. (Health at Glance 2014).

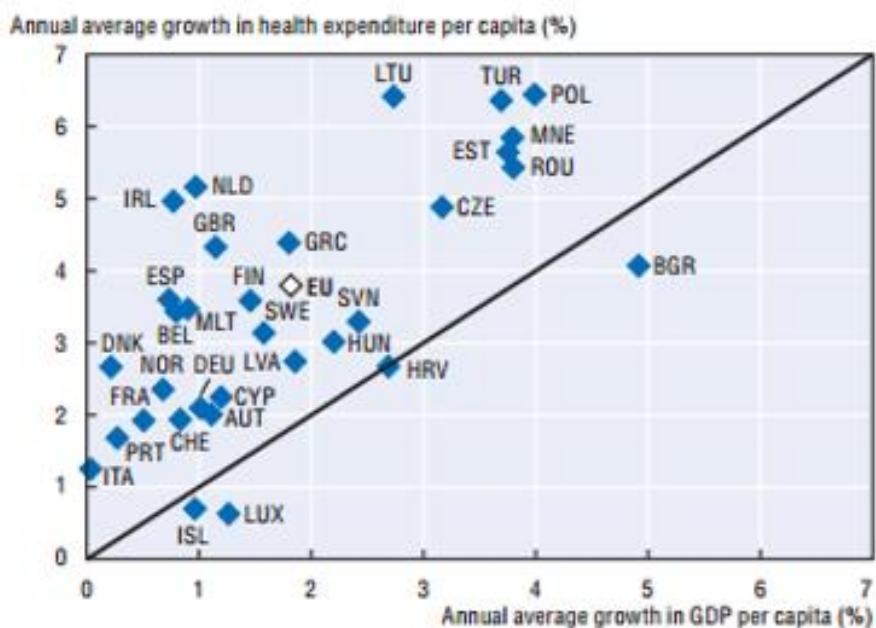


Figure 8 annual growth in health expenditure and GDP per capita, in real terms 2000-2010 (or nearest year) OECD Data 2012 EUROSTAT Statistic database, WHO global health expenditure

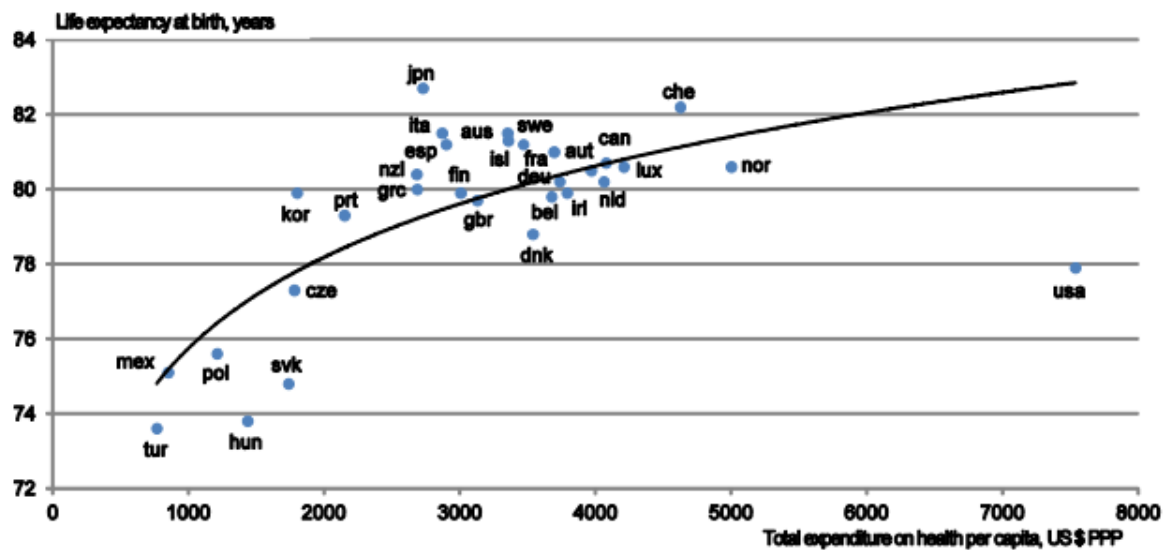
Recognised drivers of health spending include both demographic factors (population size and structure and health status) and non-demographic factors (income, technological advances in medical treatments, relative prices and regulations). In the past decades, health expenditure has been growing much faster than what would be expected from changes in demography and income alone. Many studies claim that the gap is filled by technologic advances in the health sector.

Medical innovations produce two opposite effects: reducing the unit costs and increasing total spending. The first effect is due to the more efficient equipment, the second derives from the demand of a wider population to the new or more accessible health treatments. The elasticity of the demand of a given treatment will determine the influence of the medical innovation in the total health spending. Smith et al. (2009) suggest that in the US between 27% to 48% of health spending growth since 1960 is explained by innovations in medical technology. Earlier studies estimated that about 50% to 75% of increases in total health expenditure were driven by technology (European Economy Economic Papers 507 | October 2013)

For the future, the health expenditure is projected to 8 % of GDP in 2060 only on account of demographic ageing– and to higher levels when other push up factors are accounted for. The projections show that whilst ageing per se has a non-negligible effect on expenditure growth, it is rather moderate. In effect, much depends on whether gains in life expectancy are spent in good or bad health (2015 Ageing Report). As regards technology, the future patterns of its development and diffusion can be more difficult to assess as innovation can be basically considered as a constant process, ground-breaking discoveries affecting strongly health care spending are to a large extent unpredictable (European Economy Economic Papers 417, July 2010).

Evidence shows that the relationship between healthcare expenditure and health outcomes is however not linear. If it were, any additional euro spent on healthcare would result in a corresponding improvement in the population's health status (measured, for instance, in terms of healthy life expectancy). In reality, the greater the expenditure, the lower the marginal improvement in health status as a result of its increase. Countries also vary significantly in their ability to

translate a similar level of resources into health outcomes. International comparisons show that the same amount of per capita healthcare expenditure can be associated with very different health outcomes even after taking into account the differences in lifestyle and socio-economic realities among countries. (Investing in Health 2014)



1. Or latest year available.

Source: OECD Health Data 2010.

Figure 9 - life expectancy and health care spending across OECD countries (OECD 2010 Health care systems: getting more value for money)

Through cross-comparing health data and systems, OECD has recently assessed the health system sustainability. The report highlights that in all OECD countries there is room to improve the effectiveness of their health care system. Life expectancy could rise more than two years across OECD countries while holding health care spending steady, if all countries were to become as efficient as the best performers. By way of comparison, assuming no reform, a 10% increase in health care spending would increase life expectancy by only three to four months. The report stresses that there is no health care system that performs systematically better in delivering cost-effective health care. It may thus be less the type of system that matters but rather how it is managed. (OECD 2010 Health care systems: getting more value for money)

Currently, spending on inpatient care and outpatient care covers the major part of health expenditure across EU member states – almost two-thirds of current health expenditure on average in 2012. A further quarter of overall health spending was allocated to medical goods (mainly pharmaceuticals), while 10% went towards long-term care and the remaining 6% to collective services, including public health and prevention services and administration. (Health at glance 2015)

The EC and the European Steering Group on Sustainable Healthcare (ESG) indicate **investing in public health and prevention programme as the priority policy areas** that could reduce high long-term treatment costs and improve health outcomes by avoiding tens of thousands of premature deaths and chronic diseases. However, current data are not encouraging: in 2010, only six EU countries have reached the EU target of involving in **breast screening programme** at least 75% of eligible target. Although there is great uniformity amongst national breast screening programmes, participation varies considerably across European countries, ranging from 8% in Romania and 16% in the Slovak Republic, to over 80% in Finland, Denmark, Austria and the Netherlands. Most worryingly, the screening rates fell in six countries in the past decade. A recent study showed that evi-

dence-based workplace interventions to promote mental health could help save up to €135 billion a year by reducing absenteeism and early retirement. There is a wide array of health promotion and disease prevention measures authorities can and should make use of in many different settings (at work, at school and in health institutions). (Investing in Health 2015)

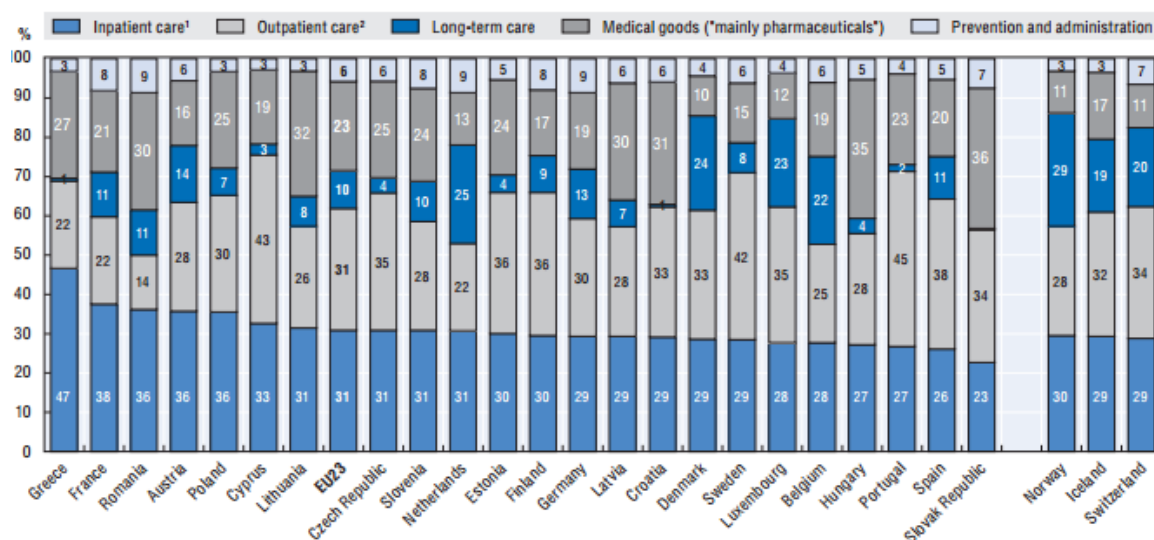


Figure 10 Current health expenditure by function, 2012 (or nearest year) Source: OECD Health Statistics 2014, <http://dx.doi.org/10.1787/health-data-en>; Eurostat Statistics Database 1 2 for non-OECD countries- Europe at glance

6 Integration of care and people-centred services: the way forward

Health systems have reached great health outputs: European citizens live longer and better. These gains in longevity can be attributed to a number of factors, including improved lifestyle, better education and as well as greater access to quality health care. *The question is now whether the health systems will be able to reorient their services for responding to the rise of chronic diseases and multi-morbidity.* The **life expectancy at birth** in the 28 countries reached 79.2 years on average in 2012, an increase of 5.1 since 1990. With variations among countries, the gender gap in life expectancy has generally decreased since 1990, coming down from 7.2 to 6.1 years in 1992. In 2080, population aged over 85 will represent nearly 7% of the all population. However, the success on life expectancy needs to be cross-compared with the data related to Healthy Life Years (HLY). At EU level, the number of **healthy life years (HLY)** at 65 is now quite similar for both women and men, with the EU average for both being 8.5 years in 2012. Over the period 2008-2012, there was a significant increase in HLY for women and men, respectively, in 10 and 15 Member States but significant falls in HLY were registered in 5 Member States (Health at glance 2014). To what extent the health status may change in the future in relation to the growing life expectancy is subjected to different explanation and three main hypotheses, represented in the figure below, are quoted in the literature:

- the expansion of morbidity hypothesis
- the compression of morbidity hypothesis
- the dynamic equilibrium/postponement of morbidity hypothesis

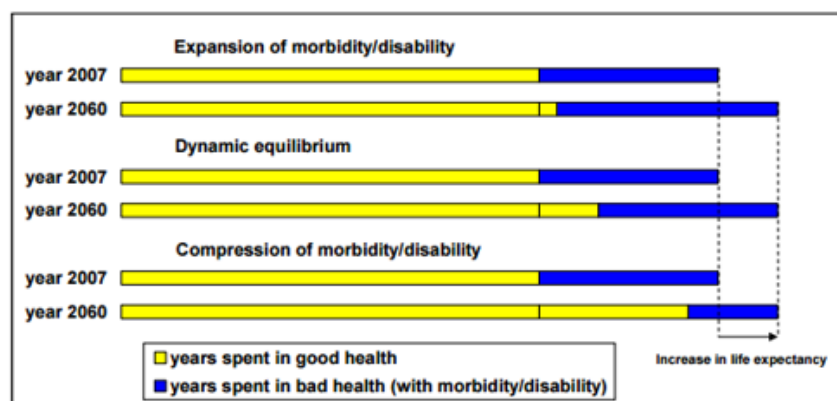


Figure 11 Different hypotheses on the evolution of healthy life expectancy Source European Economy Economic Papers 417, July 2010

Integration of care is on the agenda of the EU for a sustainable, resilient and efficient health system (EC 2014) and reorganising care delivery is one of the three priorities of the recently published White paper by European Steering Group on Sustainable Healthcare (ESG). Taking different prospective, integration of care and disease management aim both at improving outcomes for those with (complex) chronic diseases problems by overcoming issues of fragmentation through linkage of services of different providers along the continuum care. (Caring for people with chronic conditions. A health system perspective 2008)

The Chronic Care Model (CCM) is among the most influential framework for promoting the integration of care and the organisation of healthcare to improve the outcomes for people with chronic disease. Developed by E. Wagner in the United States, has been adopted and adapted to a global perspective by WHO. In brief, the framework is based on a set of guiding principles acting at three levels. The *micro level* emphasizes the partnership between patients/families, healthcare teams and community partners. The *meso level* refers to the healthcare organization and community, with a particular emphasis on the need for continuity and coordination as well as for “organized and well-equipped” healthcare teams rather than decision support, in recognition that decision-support tools may not be applicable in low-resource settings. The *macro level*, finally, explicitly considers the policy and financing contexts, which are seen as key factors in any successful system response to chronic conditions (Epping-Jordan et al. 2004). Evidence on the impact on quality of care of the adoption of CCM model are still limited, but models with explicit patient-oriented have proven to be more effective. In line with this, WHO has recently elaborated the framework and criteria for creating a people-centred health services delivery function. Transforming health services delivery towards coordinated/integrated services is stressed as a mean and design principle for creating people-centred health services (WHO 2014).

The Investing in Health (EC 2013) promotes the ideas of patient empowerment and the practices of self-management to improve citizens’ health status and reduce the drug treatment costs and the time spent in the hospital. The European Innovation Partnership (EIP) on Active and Healthy Ageing, applies an innovative approach to policy making by providing a forum for key stakeholders (end users, public authorities, industry) in which they can cooperate, united around a common vision that values older people and their contribution to society, identify and overcome potential innovation barriers and mobilise instruments. The EIP focuses on the following areas throughout a person’s life: prevention, screening and early diagnosis, care and cure, active ageing and inde-

pendent living.

As regards patient empowerment, the 1998 ECJ ruling Kohll and Decker has shown that informed patients claim the right to choose their own providers. The directive 2011/24 on the application of patients' rights in cross-border regulates the procedure and the limits for seeking cross-border health care but includes also articles on the cross-border recognition of prescriptions, the Health Technology Assessment and the European reference network. Among others, the Directive requires Member State to set-up national contact points to provide information to citizens, including on their rights and entitlements, patient safety and quality of care standards. A recent Eurobarometer survey indicates that fewer than two out of ten citizens feel that they are informed about their cross-border healthcare rights and one in ten knew about the existence of NCPs. The Directive has been transposed into national law by 2013 thus the meaning in practice will emerge in the upcoming years.

3.5 SOCIAL DEVELOPMENTS

3.5.1 *INEQUITY AND PROSPERITY*

In most countries, people who have a low socioeconomic status and those who live in poor or marginalised communities have a higher risk of dying from NCDs than more advantaged groups and communities. NCDs are the greatest contributor to morbidity and mortality in low- and middle-income countries.

Smoking rates, blood pressure, and several other NCD risk factors are often higher in groups with low socioeconomic status than in those with high socioeconomic status. The social gradient also depends on the country's stage of economic development, cultural factors, and social and health policies (see Di Cesare et al., 2013).

Insurance is associated with higher treatment likelihood for NCDs in low and middle-income countries, and helps mitigate socioeconomic and regional disparities in treatment likelihood, as the study by El-Sayed et al. (2015) outlines. These influences are particularly strong among women. Insurance also predicted lower likelihood of borrowing or selling to pay for health services among the poorest women. Taken together, insurance coverage may serve as an important policy tool in promoting NCD treatment and in reducing inequities in NCD treatment by household wealth, urbanity, and sex in low and middle-income countries.



Focusing on the European Region the studies “Action Plan for implementation of the European Strategy for the Prevention and Control of Non-communicable Diseases 2012–2016” (2012) and “Gaining health: the European Strategy for the Prevention and Control of Non-communicable Diseases”(2006) state that there is an uneven distribution of conditions of key social determinants of health and their causes throughout the population, with higher concentration among the poor and vulnerable. People in low socioeconomic groups have at least twice the risk of serious illness and premature death as those in high socioeconomic groups. Inequalities in health between peo-

ple with higher and lower educational level, occupational class and income level have been found in all European countries where measured. The increasing concentration of risk factors in the lower socioeconomic groups is leading to a widening gap in future health outcomes.

Mental health and many common mental disorders are shaped by the social, economic and physical environments and social gradient in which people live and work. Risk factors for many common mental disorders are heavily associated with social inequalities, whereby the greater the social inequality the higher the risk. The poor and disadvantaged suffer disproportionately, but everyone in society is affected to an extent (Allen et al, 2014).

People are made vulnerable to mental ill-health by deep-rooted poverty, social inequality, and discrimination. Social arrangements and institutions, such as education, social care, healthcare and work, also have a considerable impact on mental health, for better or for worse. To reduce inequalities and promote good mental health, it is vital that action is taken to improve the conditions of everyday life, beginning before birth and progressing into early childhood, older childhood and adolescence, during family-building and working ages, and through to older age. Action throughout these life stages would provide opportunities for both improving population mental health, and for reducing risk of those mental disorders that are associated with social inequalities. Not only must such action be throughout these life stages, but also across various sectors within and outside the country, which will provide opportunities for both improving population mental health, and for reducing risk of those mental disorders that are associated with social inequalities. As mental disorders are fundamentally linked to a number of other physical health conditions, these actions would also reduce inequalities in physical health and improve health overall.

A workshop during the project⁹ worked out the following frame. The challenges are the restrained budget for increasing needs. There is money in the health system, but a better allocation is required. There is some recovery from economy crisis but incomes do not rise. The productivity increase is led by technology. The challenge is that there will be less jobs and this will have an impact on income growth. Europe has to cope with the aging, the social security, bankruptcy, the decline of the power of labour organisations. There is the risk of the breakdown of the well organised healthcare systems. On the other hand the awareness of what is good for the body will increase on the individual level. The government will develop the support more patronising. On the global level more wars and revolutions might emerge in the next decades. The creation of new social contracts could emerge; new social contracts and institution competitions might increase. The health systems might become more similar in Europe. The key assumptions for that development are that we are not able to reverse aging; technology is good; there might be more European integration; people will be working less. The drivers of changing could be the role of technology in shaping job creations as well as destruction; the population dynamics regarding aging and migration; energy sources. The inhibitors of change might be the status quo institutions (resistance to change at institutional level) and the current regulation and norms (e.g. current laws about labour mobility).

3.5.2 QUALITY OF LIFE, UNEMPLOYMENT, AND MENTAL WELL-BEING

There are many studies which address the problem of depression, unemployment, and stress. Some of the excerpts are presented here. Rayens et al. (2013) study depressive symptoms and their patterns. Depressive symptoms may be influenced by work patterns, work satisfaction,

⁹ Lisbon Workshop Group (26 October 2015).

stress, and health status. In addition, members of a couple may affect each other's depressive symptoms. The study was done for depressive symptoms in older rural couples. The main question was whether depressive symptoms score is predicted by hours worked on the farm, satisfaction with work, number of health conditions, perceived stress, and demographics in a sample of older farm couples, and to assess the degree of influence on depressive symptoms spouses have on each other. Men's depressive symptoms scores were predicted by their own number of health conditions and stress and by their wives' stress and health conditions. Women's depressive symptoms scores were predicted by their own work satisfaction, stress, and number of health conditions and their husbands' time spent working on the farm and stress. Stress management may be particularly important in older farm couples (but not only there). Work factors and health conditions also affect depressive symptoms in older rural couples.

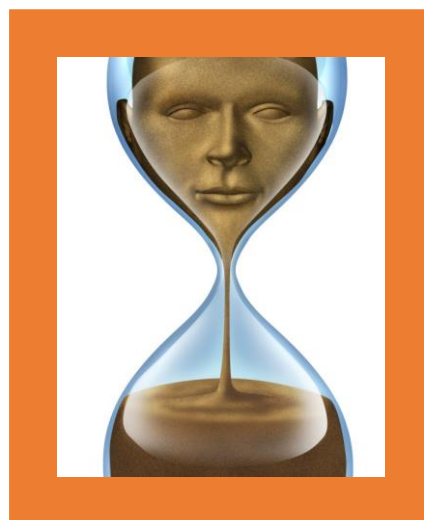
Walker et al. (2014) study the independent effects of socioeconomic and psychological social determinates of health and find significant associations for quality of life included depression, serious psychological distress, social support, and perceived stress. Social determinants of health were significantly associated with diabetes self-care and outcomes with socioeconomic factors being most often associated with diabetes outcomes and psychological factors, specifically self-efficacy and perceived stress being most often associated with self-care and quality of life.

Mustard et al. (2013) worked on the association between unemployment and cause-specific mortality for a cohort of working-age Canadians (aged 30-69). Consistent with results reported from other long-duration cohort studies, unemployed men and women in this cohort had an elevated risk of mortality for accidents and violence, as well as for chronic diseases. The persistence of elevated mortality risks over two consecutive multi-year periods suggests that exposure to unemployment in 1991 may have marked persons at risk of cumulative socioeconomic hardship.

High unemployment expands the population vulnerable to homelessness and influences health care needs and social needs, so Burke et al. (2013). Adeyi et al (2007) investigated the effect of NCD on unemployment, so the other way round. People with NCDs are also more likely to miss work, become unemployed or retire early.

How changes in socioeconomic factors affect health outcomes is evident in countries in the midst of the current economic crisis. In Spain, for example, the number of people displaying mental health disorders (who attended primary care) has increased significantly, particularly the prevalence of mood, anxiety, somatoform and alcohol related disorders, with the rise in prevalence of major depression being the highest. Researchers have estimated that at least half the increase in mental health disorders can be attributed to the combined risks of individual or family unemployment and difficulty in making mortgage payments. In Greece, between January and May 2011, economic hardship caused a 40% rise in suicide compared with the same period in 2010. In Portugal, there is concern about the 40% of people older than 65 years who live alone and are unable to keep their homes adequately heated during winter (Karanikolas et al. 2013).

There is inconsistent evidence linking early life development and later depression. The aim of a study by Colman et al (2014) was



to investigate relationships between low birthweight, infant neurodevelopment, and acute and chronic stress as components in pathways to depression in adulthood. Depression in adulthood is influenced by an accumulation of stressors across the life course, including many that originate in the first years of life. Effects of early-life development on mental health appear by adolescence.

Janowski et al. (2014) found that task-oriented style of coping with stress correlated positively with suppression of depression and anxiety, whereas acceptance of illness correlated negatively with suppression of anger. Levels of emotional control are only weakly related to the type of diagnosis; however, some clinical samples may show lower suppression of anger. Suppression of negative emotions is weakly related to adjustment indicators such as certain coping styles and acceptance of illness.

3.5.3 SOCIAL NETWORKS AND SOCIAL COHESION

Quite a number of studies published over the last 30 years have documented the correlation between social support and health. The ability to develop positive social relations is dependent on satisfactory early relationships with both mother and father. Disrupted patterns of early relationships may be related to ill health, either through development of abnormal or excessive responses to stress or through the adoption of unhealthy behavior such as excessive eating, drinking, or smoking as a partial substitution for satisfactory emotional relationships. Some aspects of an individual personality work against the development of positive social relations: Hostility, which has been shown in several studies to be predictive of future coronary heart disease tends to have an inverse with measures of social support (Barefoot et al., 1995). Positive social support is important for coping with a disruptive life event. This can also be the development of an illness that is attenuated by protective factors such as support. Likewise, vulnerability factors such as lack of support, predispose the person to the development of ill health following the experience of a life event (Stensfeld, 2011).

Support from networks, family or friends may encourage healthier lifestyles such as reducing fat in a diet, taking exercise, or give up smoking (Cohen et al., 2000). By the same token, the perception of control over the environment, and giving an assurance of self-worth, which in turn may improve well-being and immunity to disease (Bisconti/Bergeman, 1999). On the other hand, poor health might also be a barrier to maintaining or participating in social relationships, especially observed with elderly people (Cornmen et al., 2003).



Environmental stressors may have direct effects on bodily systems and especially on hormones. Acute stressors may stimulate the adrenal system, resulting in the classic fight-or-flight response in which adrenal medullary hormones, such as adrenaline and noradrenaline, are secreted and increase levels of lipids and glucose. Similarly, stimulation of the hypothalamic-pituitary-adrenal (HPA) axis will lead to raised cortisol secretion, often also found in severe depressive illness, and may cause suppression of immune functioning and, thus, increase the susceptibility of infection (Williams et al., 1991; Seeman et al., 1994). Depression has also been associated with increased mortality risk of post-myocardial infarction (Lespérance et al. 1996; Brown et al., 1987).

Studies in the US showed that social isolation was related to increased cardiovascular disease mortality and post-myocardial infarction and deaths from accident and suicide (Berkman/Syme, 1979; Welin et al., 1985; Kaplan et al., 1988; Kawachi et al. 1996; Lindsay et al., 2001;).

Social support, or lack of it, also seems to be related to physical morbidity. Social isolation has been linked to stroke incidence in a large study of US male health professionals (Kawachi et al. 1996). Welin's (1985) longitudinal study in Sweden found a significant protective effect of social integration on the incidence of non-fatal myocardial infarction in those found to be free of heart disease at baseline. Social support may not only have a protective effect in preventing or decreasing the risk of developing an illness, it may also be helpful for people who have to adjust to or cope with the stress of a chronic illness (Lindsay et al., 2001). Ruberman et al. (1984) found evidence that isolated man have an increased risk of death by post-myocardial infarction; and Berkman et al. (1992) added that low levels of emotional support may be the reason why social isolation conveys greater mortality risk in post-myocardial infarction patients.

Social support has been shown to be helpful when coping with chronic disabling and painful diseases such as rheumatoid arthritis, preventing the onset of secondary depression and limiting disability (Fitzpatrick et al., 1991). Social support may not only be contributing practical help to people who are restricted in activities of everyday life, but also providing crucial emotional support. Social support has also been shown to be influential in some studies of cancer survival (Kiecolt-Glaser/Glaser, 1995).

3.5.4 SOCIAL INNOVATIONS

In recent years, social innovation has become an increasingly prominent concept employed by political leaders and administrations. It has been posited as a solution to both old and new social risks at a time of heightened uncertainty and pressure on public administrations and finances (Bonoli, 2005; OECD, 2011; Sinclair and Baglioni, 2014). While innovation more generally has been an enduring interest and concern of policy direction (Borzaga and Bodini, 2014), only in the last two decades has social innovation captured the political interest of supranational organisations and domestic institutions (Pol and Ville, 2009; Grisolia and Ferragina, 2015). Particularly since 2003, the Organisation for Economic Co-Operation and Development (OECD) has supported a range of initiatives and research to promote inclusive entrepreneurship and 'improve social cohesion through the identification and dissemination of local innovations'. Constraints on public expenditure have challenged the state's capacity to respond to and address social problems. Within this context, social innovation has regularly been cited as a means 'to do and achieve more with less' (TEPSIE, 2014).

Social innovation as a strategy is underlined by a series of flagship initiatives and process innovations to encourage EU member states to realise their economic *and* social potential. These activities are being informed and supported by the EU's largest public research funding programme *Horizon 2020* (European Commission., 2013b). This and the Europe 2020 Agenda are also designed to tackle poverty, inequality, structural unemployment, health and demographic challenges.

We find social innovations with relevance not only in the health sector as we have a broader understanding of the factors that affect NCDs. One of the important networks arising from the Ottawa Charta is the so called Community-based health research.

3.5.4.1 *Community-based health research*

Community-based health research (sometimes Community-based participatory (health) research (CBPR), collaborative research, action research, interactive research, participatory health research (PHR)) signifies cooperation between research, health care and engaged citizens to commonly achieve new insights in the improvement of public health. Especially socially marginalized parts of our society benefit from this approach because it facilitates innovative practice that can contain negative determinants of health. Research is not done “on” people as passive subjects providing “data,” but “with” them to provide relevant information for improving their lives (Israel 1998; Minkler & Wallerstein 2008; Macaulay 1998 & 1999; Green & Kreuter, 2005).

It is regarded as an effective method for transferring evidence-based research from clinical settings to communities that can most benefit thereby improving health. CBPR's community-partnered research processes offer the potential to generate better-informed hypotheses, develop more effective interventions, and enhance the translation of the research results into practice. Thus, CBPR is an essential tool for action-oriented and community-driven public health research.

Considering social innovation for the benefit of marginalized people in our society the health sector offers a vast field of study objects. Community-based health research, for example, has been recognized as a field of activity for both researchers and activist in the public health sector to engage in the quality assurance of health promotion and disease prevention with socially disadvantaged groups. Based on the observation that in most OECD countries life expectancy and at the same time compression of morbidity are growing if a person belongs to the privileged group that could gain from the progress in health research, care, better education and improved standard of living, we have to acknowledge a dark side as well: There is one fifth of the population falling through the grid. Those who have low income, poor education, grew up in an underprivileged parental home are more inclined to suffer from poor health than others. This is partly rooted in the fact that chronic-degenerative diseases are the major cause of health problems and death in OECD countries and they appear earlier in the life of the underprivileged and are more often and earlier the cause of death (WHO et al., 2011). Chronic-degenerative diseases, however, are to a large degree avoidable if primary prevention measures are taken early enough. This is one major focus of community-based, participatory health research. Other foci are for example women health, migrants, and old age.

Very different ways to this kind of research developed. Besides their differences they usually have two features in common:

1. New insights are directly connected with new forms of action to improve the living conditions of the marginalized.
2. Researchers, practitioners and citizen scientists work at the same level to conduct a research project together at all phases, and this is meant by the term participatory.

Action research today charts very different ways and has yet to find a basis for consolidation. It is present in various fields and areas and there is no common definition of even title. The health sector is one of the most established ones when it comes to action research. This was historically accompanied by the emergence of Public Health and the Ottawa Charta for Health Promotion.

These prerequisites can only be provided in collaboration with the local communities. Local communities are thus often involved in community-based health research and essential for the funding of such projects. Some of the principles of this common activity in the health sector are:

- Mutual learning and transfer of expertise
- Divided decision making
- Common ownership of all products and process achieved in the common work/project (Wright 2012, p. 419)

3.5.5 CHANGES IN GENDER ROLES

The WHO defines “gender” as a dynamic concept, which looks at the interrelationship between men and women in the context of their society and roles in that society. **Gender roles** are defined as the social and cultural traits that different societies assign to males and females. Such gender roles are the patterns of behaviour, rights and obligations defined by a society as appropriate for each sex. A gender perspective is a way of looking at situations and issues taking into account the respective roles and contributions of men and women in society.¹⁰

With **increasing female employment** over the last century the roles of “male breadwinner” and “female gatekeeper at home” has shifted, the past decennia are characterized by a decreasing amount of male breadwinner families and increasingly more female autonomy (Aboim, 2010). During the transitional period from male breadwinner to dual earner households, men’s depression scores were high because they had to conquer the feelings of embarrassment or guilt due to having a wife in employment. Variations in women’s or men’s earnings seemed to have no effect on depression (Dereuddre et al., 2014).

Employment preserves or improves psychological well-being for both men and women (Aube, Fleury, & Smetana, 2000; Boye, 2011; Kalmijn & Monden, 2011; Ross & Mirowsky, 1995). Increased income appears beneficial for both men’s and women’s psychological well-being (Rogers & DeBoer, 2001). Earning less, by contrast, is considered as an indicator of relative disadvantage, leading to depression via feelings of powerlessness or lack of control (Mirowsky, 1985). However, working part-time is associated with a lower sense of control in comparison with working full-time, because it is generally more routine and less autonomous (Ross & Wright, 1998).

The discussion on the division of unpaid work is coming along with the increase in paid work and dual earner households. Researchers have focused on equity in the division of both paid and unpaid labour. Both Glass and Fujimoto (1994) and Kalmijn and Monden (2011) argue that a more equal distribution of **paid and unpaid labour** hours is associated with lower levels of depression. However, according to the former researchers, this relationship is mediated by perceptions of equity. Perceived inequity in paid labour increased depressive symptoms for men, as did perceived inequity in performing household labour for women. The studies of Roxburgh (2004)



¹⁰ <http://www.who.int/trade/glossary/story032/en/>

and Boye (2010) indicated no significant effects of equity on men's levels of depression. Roxburgh (2004) argues that more than 10 hours of weekly housework increased women's depression scores, although mediated by time pressure. In contrast, Boye (2010) found that being employed as well as doing housework was associated with higher psychological wellbeing. Too much time in paid work, however, decreased the beneficial effects of unpaid work, and vice versa (Dereuddre et al., 2014).

Dereuddre et al., 2014, conclude that "although employed women nowadays are the rule rather than the exception, the labour market keeps changing and differentiating by variations on part-time employment, working from home, etc. (Margherita, O'Dorchai, & Bosch, 2009). This increasing complexity and flexibility and the possible consequences for mental health of both men and women requires continued attention and further research into the complex intertwinements between gender, power and mental health in intimate relationships. Worse mental health of men goes hand in hand with conditions that signal lower social standing vis-à-vis their partner: Greater financial dependence and taking up low prestige, low-schedule-control tasks."

Considering further health aspects **maternal employment** is often linked to overweight children (Couch potatoes), Wills & Brauer, 2012 indicate a "negligible influence of maternal employment on children's cognitive and behavioral development". The contemporary milieu of maternal employment is different than it was decades ago. For instance, child care now is more readily available and arguably of higher quality, cultural attitudes about women's work roles have become less traditional as women have established rewarding and successful careers, and fathers have assumed more active parenting responsibilities within families. It is worth stressing the more salient variables that do exert effects on child outcomes, such as sex, race, maternal education and AFQT scores, and mother's age at her child's birth are clearly consequential for children's development. Perhaps the more future scholarship brings these factors to the forefront, along with focusing on how employed parents across a variety of households manage work and family life such that well-being is optimized, the less attention will be devoted to the alleged general harm of maternal employment on children. The context of maternal employment certainly has changed over the past several decades. Child care arrangements are more abundant, fathers are more involved in family life, women are benefitting from the financial and psychological rewards that come from having a career, and cultural attitudes about maternal employment are more supportive (Wills & Brauer, 2012).

3.5.6 FAMILY VALUES

The scientific literature discusses family values connected to NCD in context with patient care and the burden of the family also regarding the health care costs. The WHO study from 2006 (see ¹ WHO Regional Office for Europe. Gaining Health (2006)) summarises that living with long-term illness or disability has economic implications for families and society. Families and society carry a burden of direct and indirect health care costs, reduced income, early retirement and increased reliance on social care and welfare support. This WHO study continuous that treatment may not be accessible, available or affordable, and the burden of costs can push families further into poverty.

Family plays an important role in triggering and implementing new life styles. Arena et al. (2015) underline the importance of educating women, particularly in racial and ethnic minorities, as women are often the key decision-makers about diet and lifestyle in the family.

Family is therefore an important driver for the health system. But in which direction will the societal structure “family” develop in the future in Europe, in the western part of the world? The group discussion in Lisbon¹¹ projected ideas of the family in the future in Europe, which is influenced by the newest technology of ubiquitous available Internet. The ubiquitous availability of intelligence in a technological way might create a new form of family. It could be called “family networks evolution”. Intergenerational communication within the family has improved in the last decades. The traditional nuclear family composed of parents, children, and grandparents might be overturned. A postmodern family might emerge as “tribe social network virtual families”. Individuals build ad hoc families on a temporarily basis. Educative and health models move outside the spheres of family and school. Social network is predominating. People handle NCDs on an individual level influenced by the virtual models provided by their “new family”. More “family time” might be spent on Internet such as social network (Skype connections, Facebook “groups”). There will be continuous investment in ICT technologies reducing individual lost and increasing connection capacity. Drivers of change for such a development could be the increased availability of virtual communication means. Economic and industrial groups might influence consumption behaviour. There might be a transformation of habitat to accommodate recomposed families poly-nuclear ad hoc families.

The individual action is already discussed in the report of WHO “Gaining Health. The European Strategy for the Prevention and Control of Non-Communicable Diseases” (see WHO Regional Office for Europe. Gaining Health (2006)). Community action for health involves individuals acting collectively to gain greater influence and control over the determinants of health and the quality of life and well-being in their community. The arena or setting where people engage in daily activities, such as a school or workplace, is a place where people can actively shape the environment and solve problems relating to health. Communities may have organized themselves so that individuals and families have assumed some responsibility for their, and the community’s, health and welfare. So, for example, patient clubs or support groups may have developed to support families and life-long sufferers of a particular chronic condition. Empowerment of communities to facilitate their organization and involvement in public debate and decision-making is central to progress if greater equity in health is to be achieved.

3.5.7 *MIGRATION*

With over 800.000 refugees arriving on Europe’s shores in 2015 alone according to the UNHCR¹², migration has become a top priority on the EU political agenda. The difficulty to cope and respond to the political, social and public health challenges of migration is exacerbated by austerity measures in the aftermath of the economic crisis that have led to severe cut backs in the welfare system, particularly strongly experienced by the Mediterranean EU Member States. The number of refugees arriving on Greek shores alone soared by 408% over the first six months of 2015 compared with the same period last year, driven in large part by a surge in Syrians fleeing the brutal civil war in their country.¹³

¹¹ Lisbon FRESHER Workshop 26 October 2015.

¹² <http://data.unhcr.org/mediterranean/regional.php>

¹³ <http://www.theguardian.com/global-development/datablog/2015/jul/24/greece-migrant-influx-overtakes-italy-syria-afghanistan>

There is a central role for NCDs within the migration context to be considered. First, as the burden of disease in low- and middle-income countries begins to shift from infectious diseases to non-communicable diseases, NCDs become a major public health challenge. Refugees and migrants in an irregular situation also very often suffer from specific health risks such as those resulting from exploitative working conditions, violence, precarious housing, lack of social protection, mental health issues, nutrition disorders etc. that increases their susceptibility to NCDs. For example, chronic diseases have substantially increased in conflict zones, due to poor treatment, interruption of care and general medical systems failure. According to the latest report on the health situation in Aleppo, Syria by Physicians for Human Rights¹⁴, shortages of personnel, equipment, medicine, and necessities such as clean water and electricity have caused a breakdown in Aleppo's health care system, resulting in an increase in chronic and acute illnesses. Similarly, Doctors Without Borders/ Médecins Sans Frontières (MSF) conclude that nearly 90 percent of the Syrian patients in Lebanon arrive with prior diagnoses of chronic disease such as hypertension and diabetes.¹⁵

In Europe, different healthcare systems and the limited enforceability of legally binding international law provisions on the right to health have resulted in different healthcare services being offered to migrants in an irregular situation¹⁶. In many EU Member States, access is limited to emergency healthcare only, thus continuity of care with chronic conditions cannot be provided by the State. A study by the EU Agency for Fundamental Rights on the Cost of Exclusion from Healthcare¹⁷ however illustrated that for example in the case of hypertension, providing timely access to health screening and treatment not only contributes to fulfilling the right to health, but is also cost-saving compared to providing medical treatment in emergency cases only. The study established that cost-saving of around 9 % in Germany and Greece and about 8 % in Sweden can be achieved just within one year if preventative healthcare is provided, compared to costs that incur if only emergency care is provided. It is clear that further research, improved data availability and better preparedness are needed to respond to public health concerns and NCDs within the context of migration. Barriers such as access to health services, cultural issues that call for a culturally trained health workforce, structural problems such as transport as well as bureaucratic barriers need to be dealt with in a more systematic manner. In October 2015, the European Commission amended its current Health Work Programme and launched a new call with the aim of supporting Member States under particular migratory pressure, and to help addressing health related issues of arriving migrants¹⁸. Based on available evidence, the WHO put forward following policy recommendations regarding refugee health:¹⁹

- improved access to services by removal of legal restrictions
- provision of full health coverage for all pregnant women and for children regardless of immigration status
- adoption of approaches to improve communications, such as provision of interpreters, good documentation for patients; and
- adjustment of health care provision to improve service utilization, for example longer appointment times, transport provision.

¹⁴ https://s3.amazonaws.com/PHR_Reports/aleppo-abandoned.pdf

¹⁵ <http://www.doctorswithoutborders.org/news-stories/field-news/treating-chronic-diseases-among-syrian-refugees>

¹⁶ http://fra.europa.eu/sites/default/files/fra_uploads/fra-2015-cost-healthcare_en.pdf

¹⁷ Ibid.

¹⁸ <https://ec.europa.eu/research/participants/portal/desktop/en/opportunities/3hp/topics/7050-ha-01-2015.html>

¹⁹ http://www.euro.who.int/__data/assets/pdf_file/0004/289246/WHO-HEN-Report-A5-2-Refugees_FINAL.pdf?ua=1

3.6 AGRICULTURE

3.6.1 GENERAL ASPECTS

Generally agriculture is closely linked to industrialization of food production (see also chapter 3.8). The last 50 years has brought giant changes and developments in agriculture worldwide. The world's human population and food consumption are growing. The authors of Agropoly ask whether the number of companies involved in the food sector is growing as well. But they investigated the situation and found that the opposite is true. Big corporations buy smaller companies and thus increase their market share and power. This has extensive consequences for all involved parties, such as companies producing fertilizers and pesticides, controlling livestock breeding and seeds, famers, food producers, consumers. Companies can dictate prices, terms and conditions and, increasingly, the political framework. Much of what we consume in the North is being produced more cheaply in the Global South. The profits are made by only a few, predominantly Northern, companies. The big losers are the plantation workers and small farmers in the South, as they are the weakest links in the “value chain”. In no other section of the population is hunger so widespread. More and more ecosystems are being degraded and destroyed.

Seeds, young animals, feed, fertilizer, all things that used to be produced on the farm itself, are today separate sectors of the industrialized and globalized food value chain. This also includes trade, processing and selling of foodstuffs. The most vulnerable in this chain are those who cultivate and produce these foods: the farmers. Small-scale farmers in the Global South come under great pressure through horizontal and vertical integration (concentration) in food production. Their right to food can be violated in many ways: by patents on seeds, expulsion from land, unfair working conditions or prices, or the squeezing out of informal markets. The authors of Agropoly document the processes of concentration in food production and show how, with corporate concentration, a few major global companies have increasing powers to dictate prices, conditions, and in some cases even government policies.

There are many other studies, which demonstrate that it is evident that agriculture has been the foundation for nutrition and food industry till today. The dependency of nutrition and health is widespread. The structure in agriculture (e.g. large areas of one-crop agriculture farming) and applied methods and procedures in agriculture influences the health of soil, plants, animals, and the whole environment and consequently human health. But also the property situation of agriculture land influences the nutrition and food situation of people in question.



Food and agriculture is strongly linked to providing food for mankind, because without any food people are dying. Therefore also the study “The Future of Food and Farming: Challenges and choices for global sustainability” (2011) list five challenges:

- Balancing future demand and supply sustainably to ensure that food supplies are afforda-

- ble to everyone and in particular the poorest groups.
- Ensuring that there is adequate stability in food supplies – and protecting the most vulnerable from the volatility that does occur.
- Achieving global access to food and ending hunger – producing enough food in the world so that everyone can potentially be fed is not the same thing as ensuring food security for all.
- Managing the contribution of the food system to the mitigation of climate change. - Maintaining biodiversity and ecosystem services while feeding the world.

The study by Giovannucci et al. (2012) demonstrates the influence of agriculture and argue that the current trajectory of growth in agricultural production is unsustainable because of its negative impacts on natural resources and the environment. One-third of farm land is degraded, up to 75 percent of crop genetic diversity has been lost and 22 percent of animal breeds are at risk. More than half of fish stocks are fully exploited and, over the past decade, some 13 million hectares of forests a year were converted into other land uses.

Agriculture is one of the biggest threats to a healthy environment. It uses most of our available fresh water and some 20,000 – 50,000 km² of potentially productive lands are lost annually through soil erosion and degradation, much of it in developing countries. Besides its production function, agriculture needs to integrate other vital functions of ecosystem management as central features of its development.

The overarching challenges are the growing scarcity and fast degradation of natural resources, at a time when the demand for food, feed, fibre and other goods and services from agriculture (including crops, livestock, forestry, fisheries and aquaculture) is increasing rapidly. Some of the highest population growth is predicted in areas which are dependent on agriculture and already have high rates of food insecurity.

The report of the United Nation 2012 entitled “Food and Agriculture: The Future of Sustainability” (Giovannucci et al., 2012) points out that yet, agriculture policy concentrates mostly on production and trade and is curiously divorced from the vital issues of good nutrition. For the first time in history we have as many overweight people as undernourished people and the consequences of our emerging dietary habits are on a disastrous trajectory for human health and for ecosystem health. In addition this report outlines that we need to actively shift our focus to two areas:

- more exercise since we already have more than 4000 kcal per person per day in traded foods; and
- more nutrition or healthy food because the explosion of empty calories in many developing countries reflects the meteoric rise of the clinically overweight in many industrial economies.

Agriculture has also been strongly connected to policies, international emphasis on trade liberalization, and increasing foreign investment by large transnational food companies since the 1980s. The article by Lock et al. (2010) presents a model about the effects of agriculture, health, and economy on chronic diseases. Increased globalization of agriculture food systems has affected the availability and access to food through changes in food production and distribution, facilitating shifts in food culture, patterns of dietary consumption, and nutritional status (Hawkes et al., 2012). The studies WHO/FAO. Codex alimentarius, animal food production” (2008) and WHO. The global strategy on diet, physical activity and health (2010) indicate that agricultural and health sec-

tors are largely disconnected in their priorities and policy objectives. Typically, agricultural priorities center on production and processing systems, markets, and livelihoods, with concern for food safety only as it affects trade, rather than on broad public health issues. By contrast, public health traditionally centers on agriculture insofar as it affects food security and food safety, with only recent consideration of agriculture's potential role in prevention of non-communicable diseases.

Agriculture is food producer on the one hand but also an important key contributor to economy on the other hand. Especially in low-income countries agriculture is the biggest sector of economy. Agriculture is crucial for rural development. Agriculture products are traded worldwide. On the contrary health policies are regulated and organized mainly on the national or European level. The study by Lock et al. (see Lock et al., 2010) argue that for example, a public-health policy aimed at reduction of dietary intake of saturated fat in the EU would lead to a decline in domestic demand for food from animal sources (and thereby production or import), and increased demand for substitute foods. Moreover, a reduction in imports of food from animal sources into the EU could alter the global demand for imports from Brazil, which would result in either increased domestic consumption, increased export to other countries, or reduced overall Brazilian production. The authors of the study (Lock et al., 2010) show how important it is to work in a holistic approach regarding agriculture, health, and economy (including employment and trade).

The study by Lock et al. (2010) discuss the fact that agriculture and trade policies are crucial determinants of what food is produced, sold, and consumed. To identify how agricultural policies can usefully contribute toward promotion of healthy diets and tackle non-communicable diseases related to diet, public health policy makers need to judge whether present agriculture and trade are contributing to efforts to attain dietary goals, and how agricultural policy interventions could help achieve dietary goals. Accompanying, policy makers also need to consider a holistic approach in this triangle "agriculture-health-economy".

The GFAR (Global Forum on Agricultural Research²⁰) conducted an inventory of forward thinking activities and organized workshops and a conference documented in briefs. Brief 42 gives a short overview on "The Future of Food and Farming". The GFAR outlines the drivers of change affecting the food system in the following:

- Global population increases
- Changes in the size and nature of per capita demand
- Future governance of the food system at national and international levels
- Climate change
- Competition for key resources
- Changes in values and ethical stances of consumers

These drivers converge to shape a global food system, which will experience an unprecedented confluence of pressures over the next 40 years.

The project about "The Future of Food and Farming" (The Future of Food and Farming, 2011) conclude that many systems of food production are unsustainable, putting at great risk future food production. There are widespread problems with soil loss due to erosion, loss of soil fertility, salinization and other forms of degradation; rates of water extraction for irrigation are exceeding rates of replenishment in many places; over-fishing is a widespread concern; and there is heavy

²⁰ <http://www.gfar.net/>

reliance on fossil fuel-derived energy for synthesis of nitrogen fertilizers and pesticides. In addition, emissions to air and water from food production systems are frequently in excess of the levels considered environmentally benign. Livestock and nitrogenous fertilizer are major sources of emissions of the greenhouse gases methane and nitrous oxide, while losses of nitrates and phosphates from soil cause loss of water quality. Despite these long-standing failings, and likely confluence of future pressures, the food system has until recently received relatively little attention from policy-makers. The available resources for forest (fresh air producer) and land for agriculture has changed a lot over the last 17 years as Figure 12 shows.

The GFAR group for “The Futures of Agriculture” state (see Brief No. 42: The Future of Food and Farming) that while the global food system currently delivers for many, it is currently failing in two major ways, which demand decisive action. It is consuming the world’s natural resources at an unsustainable rate and it is failing the world’s poorest, with almost 1 billion still suffering from hunger.

Robin Bourgeois from GFAR argues that drivers, trends and disruptions for agriculture are the same as for NCDs, namely globalization, connectivity, consumption patterns, resources, population dynamics, urbanization, technology development, and prosperity. Granted he might be right but on a very macro level. The following figure demonstrates the changes in the areas for forest and agricultures in 17 years.

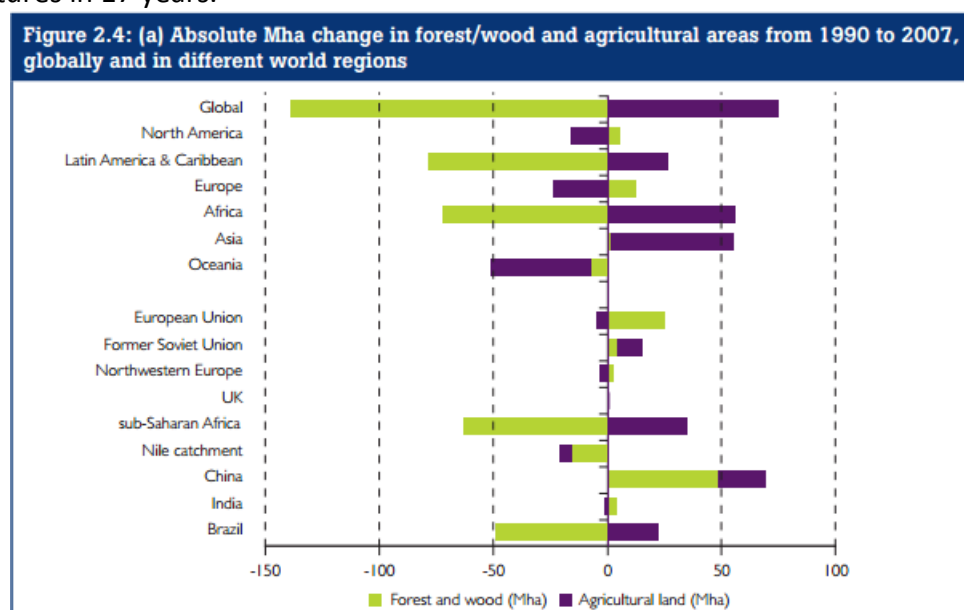


Figure 12. Loss and gain in agriculture and forest areas from 1990 to 2007 (Source: The Future of Food and Farming (2011), see The Future of Food and Farming. Final Project Report., 2011).

Foresight Brief No. 42 “The Futures of Agriculture” highlights that interconnected policy making is critical, with policy in other sectors outside the food system also needing to be developed in much closer conjunction with that for food. These areas include energy, water supply, land use, the sea, ecosystem services and biodiversity. Any policy decision needs to be informed by being built on a strong evidence base. Additionally, action is required simultaneously on four fronts:

- More food needs to be produced sustainably through use of existing technology; this needs more investment in new science and technology, social institutions and infrastructure, (water, transport, markets).
- Demand for resource-intensive types of food needs to be contained.

- Waste in the food system should be minimized.
- Political and economic governance of the food system should be improved.

3.6.2 CHEMISTRY AND PESTICIDES

The application of chemistry in agriculture, nutrition, food science and food technology has contributed not only to a safe and abundant food supply but also to the growing consumer awareness of the roles that food and food constituents have in maintaining and improving health and reducing the risk of major chronic diseases. (Richardson 2014).

Concern about food security and its effect on persistent undernutrition has increased interest in how agriculture could be used to improve nutritional outcomes in developing countries. Yet the evidence base for the impact of agricultural interventions targeted at improved nutrition is currently poor. There is comparatively little current research on indirect effects of agriculture on nutrition, or the effect of policies or governance, rather than technical interventions. Most research is focused on undernutrition and small farmer households, and few studies target consumers generally, urban populations, or nutrition-related non-communicable diseases. (Turner et al. 2013,).

Greenpeace and especially Allsop et al. (2015) investigated the impact of pesticides on human health. They found that health impacts that have been reported for children exposed to elevated levels of pesticides in the womb include delayed cognitive development, behavioural effects and birth defects. There is also a strong correlation between pesticide exposure and incidences of childhood leukemia. Studies have also related higher pesticide exposures to increased incidence of several types of cancer (prostate, lung and others), and neurodegenerative diseases such as Parkinson's and Alzheimer's disease. There is also evidence that suggests some pesticides can disrupt normal endocrine function and immune systems in the body. Whilst the mechanisms of such impacts are poorly understood, it is clear that, in some cases, enzyme function and important signalling mechanisms at cellular levels can be disrupted.

Studies using DNA-based methods also indicate that certain chemicals disrupt gene expression and this may follow on to generations that are not exposed to pesticides through epigenetic inheritance. This means that the negative impacts of pesticide usage can be extremely long term, even after the substance has been outlawed.

Lyons and Watterson outline (Lyons and Watterson 2010) that

- Exposures to certain pesticides may interact with other chemical exposures and life circumstances (e.g. those causing a weakened immune system) and genetic factors to increase the risk of cancer.
- Extensive data highlight the role pesticide exposures are suspected to play in several cancers.
- There are studies which strongly suggest an association between pesticide exposure and NHL²¹, leukemia and prostate cancer. In addition, there are strong reasons to consider that pesticides can play an important role in breast and testicular cancer. Moreover, some researchers consider it can also confidently be stated that there is at least some association between pesticide exposure and some childhood cancers.

²¹ Non Hodgkin Lymphoma (also known as non-Hodgkin's lymphoma, NHL, or sometimes just lymphoma) is a cancer that starts in cells called lymphocytes, which are part of the body's immune system. Lymphocytes are in the lymph nodes and other lymphoid tissues (such as the spleen and bone marrow).

- Some studies suggest pesticide exposure prior to conception, during pregnancy or during childhood seems to increase the risk of childhood cancer, with maternal pesticide exposure during pregnancy often being most consistently associated with childhood cancer.
- Given the available evidence of the role pesticides play in ill health, substantial financial and future health benefits are likely to accrue from the better regulation of pesticides.
- Pesticides with endocrine disrupting properties, or those with known or suspected human carcinogenic properties, should be substituted with safer alternatives. This is particularly because of the overwhelming evidence showing that simultaneous exposure to chemicals with endocrine disrupting properties can cause additive effects – and similarly, evidence to show that carcinogenic substances can work together to exert tumorigenic responses after sequential or simultaneous exposures.

3.6.3 ORGANIC FARMING

Organic farming affects nutrition, fat, vitamins, environment, and so on. A number of comparative studies showed lower nitrate contents and less pesticide residues, but usually higher levels of vitamin C and phenolic compounds in organic plant products, as well as higher levels of omega-3 fatty acids and conjugated linoleic acid in milk from organically raised animals. However, the variation in outcomes of comparative studies is very high, depending on plant fertilization, ripening stage and plant age at harvest, and weather conditions. Moreover, there appeared no simple relationship between nutritional value and health effects. It is difficult therefore to draw conclusions from analytical data about the health effects of organic foods. Some in vitro studies comparing health-related properties of organic vs conventional foods showed higher antioxidative and anti-mutagenic activity as well as better inhibition of cancer cell proliferation of organically produced food. (Hubera et al., 2011)

Animal studies carried out so far have demonstrated positive effects of an organic diet on weight, growth, fertility indices and immune system. Recent human epidemiological studies associated consumption of organic foods with lower risks of allergies, whereas findings of human intervention studies were still ambiguous. The hypothesis might be that organic food increases the capacity of living organisms towards resilience. (Hubera et al., 2011)

3.7 NUTRITION

3.7.1 GENERAL NUTRITIONAL ASPECTS

An unhealthy diet is one of the major risk factors for the major non-communicable diseases, besides tobacco use, physical inactivity and harmful use of alcohol. The World Health Organisation recommends five priority interventions for the control of non-communicable diseases, three of them related to nutrition:

1. promoting healthy consumption via fiscal and marketing policies;
2. elimination of trans fats in food (and their replacement with polyunsaturated fats);
3. salt reduction.

About 25% of scientific publications on non-communicable diseases deal with the influence of nutrition and healthy diets on origins of NCDs. Increased attention in dietary research and guidance has been focused on dietary patterns, rather than on single nutrients or food groups, because die-

tary components are consumed in combination and correlated with one another. In order to make “diets” measurable various factors have been examined (Glycaemic index, dietary fibres, vitamin levels), or general factors such as Healthy Eating Index–2010 (HEI-2010), the Alternative Healthy Eating Index–2010 (AHEI-2010), the alternate Mediterranean Diet (aMED), and Dietary Approaches to Stop Hypertension (DASH) to name only a few (e.g. Reedy et al. 2014).



Research has also led to new developmental models indicating the origin of disease already by nutrition during fetal life, infancy and early childhood, as gene expressions are established and thereby functional capacity, metabolic competence and responses to the later environment are set (Barker 1995 & 2012, Vaisermann 2014). Nutritional genomics or Nutrigenomics is the study of how foods affect the expression of genetic information in an individual and how an individual's genetic makeup affects the metabolism and response to nutrients and other bioactive components in food. Personalised, genotype-based nutrition is a concept that links genotyping with specific nutritional advice in order to improve the prevention of nutrition-associated, chronic diseases (Kaput & Dawson 2007, Joost et al. 2007).

The microbiome appears to play a major role in health and disease and has been cited as being involved in a number of clinical problems, including the frailty of the elderly, inflammatory bowel disease, irritable bowel syndrome, colorectal cancer, and gut-derived infections. More generally, there are proposed links between the gut microbiota and appetite control, energy balance, obesity, diabetes, immune function, allergies, behavioral perturbations, cardiovascular disease, and cancers such as stomach cancer. The diet on one hand might be expected to have a strong influence on the gut microbiota and to be able to modify the impact of the microbiota upon health, with either beneficial or deleterious consequences (Flint, 2012). Maternal microbiome transferred during childbirth and through breast feeding is the basis for a healthy microbiome in infants, strongly influenced by diets and nutritional habits going hand in hand with health and diseases.



Of course nutrition cannot be seen as a single factor influencing the origins of NCDs but the whole subject has to be considered in a broader sense in combination and correlation with other factors. Social status, income or education for example influence nutritional patterns in households. In the USA 14.5 % of households were food insecure at least some time during the year 2013, including 5.7 % with very low food security—meaning that the food intake of one or more household members was reduced and their eating patterns were disrupted at times during the year because the household lacked money and other resources for food. Food-insecure adults may consume more highly palatable foods as a coping mechanism, leading to poorer diet quality and increased risks of

chronic disease over time. The problem of food insecurity increases with decreased social income and status as well as increasing migration and insecure political conditions (Coleman-Jensen et al 2013, Leung et al 2014).

Factors influencing people's choice for their diets are first of all the relative price of healthy and unhealthy options, transaction costs, meaning the time and skills required to make a healthy dinner versus the time buying fast food and perceived benefits of consumption. Policies and interventions can strongly influence the attractiveness of healthy choices, e.g. by expanding the range of options available, reducing the price of products and services that encourage healthy choices, by education and information or regulation of unhealthy choices or even their advertisement (Nicola, 2015).

If diets and nutrition are considered in a very broad sense, then we find a link to environmental and human health. Rising incomes and urbanization are driving a global dietary transition in which traditional diets are replaced by diets higher in refined sugars, refined fats, oils and meats. By 2050 these dietary trends, if unchecked, would be a major contributor to an estimated 80 per cent increase in global agricultural greenhouse gas emissions from food production and to global land clearing. Moreover, these dietary shifts are greatly increasing the incidence of type II diabetes, coronary heart disease and other chronic non-communicable diseases that lower global life expectancies. Alternative diets that offer substantial health benefits could, if widely adopted, reduce global agricultural greenhouse gas emissions, reduce land clearing and resultant species extinctions, and help prevent such diet-related chronic non-communicable diseases. The implementation of dietary solutions to the tightly linked diet-environment-health trilemma is a global challenge, and opportunity, of great environmental and public health importance. (Tilman & Clark, 2014)

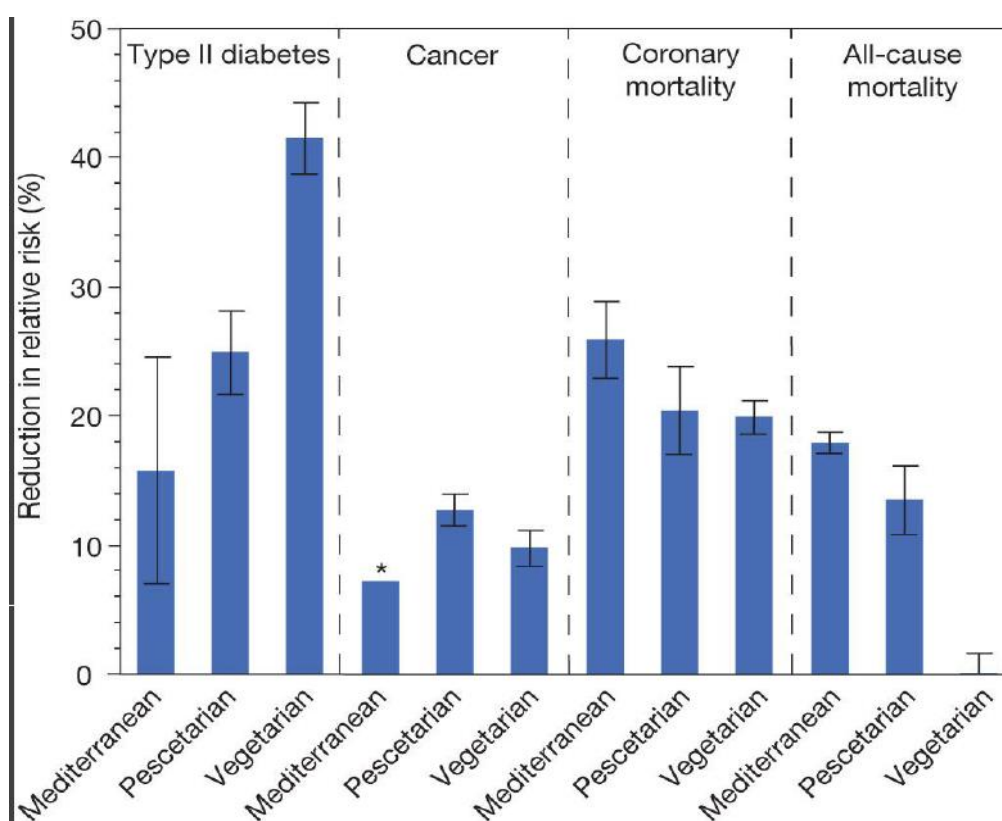


Figure 13: Diet-dependent percentage reductions in relative risk of type II diabetes, cancer, coronary

heart disease mortality and of all-cause mortality when comparing each alternative diet (Mediterranean, pescetarian and vegetarian) to its region's conventional omnivorous diet (Tilman & Clark, 2014)

Running along this line of close connection of environmental factors, food production, marketing and nutrition one of the groups in a workshop²² within WP 3 of this project considered different scenarios of development of nutritional aspects: a positive development going along with the availability of healthy but at the same time cheap food and a sustainable food system; on the other hand a negative scenario indicated by an increase in NCDs and especially obesity and a loss of traditional and fresh food. Further along the line a loss of diversity in agriculture and highly processed food lead to malnourishment and changes in microbiota, again resulting in negative health aspects. Key assumptions that global population will grow and diets will have to change away from highly processed to healthy and fresh food were seen as closely linked to environmental and health factors. This change to healthy diets is driven by marketing, education and consumer awareness, but also strongly by policies in health insurance, agriculture and employment (e.g. maternity leave). Especially commercially driven interests of industry and trade were seen as inhibitors for a positive development (see also chapter 3.6 Agriculture).

The WHO has adopted Global action plan for the prevention and control of non-communicable diseases 2013-2020 recommending where policies and programmes regarding nutrition should aim to²³:

- Promote and support exclusive breastfeeding for the first six months of life, continued breastfeeding until two years old and beyond and adequate and timely complementary feeding.
- Implement WHO's set of recommendations on the marketing of foods and non-alcoholic beverages to children, including mechanisms for monitoring.
- Develop guidelines, recommendations or policy measures that engage different relevant sectors, such as food producers and processors, and other relevant commercial operators, as well as consumers, to:
 - Reduce the level of salt/sodium added to food (prepared or processed).
 - Increase availability, affordability and consumption of fruit and vegetables.
 - Reduce saturated fatty acids in food and replace them with unsaturated fatty acids.
 - Replace trans-fats with unsaturated fats.
 - Reduce the content of free and added sugars in food and non-alcoholic beverages.
 - Limit excess calorie intake, reduce portion size and energy density of foods.

3.7.2 FOOD LABELLING

The U.K. Food Standards Agency, in 2013, has developed a traffic light label that gives consumers independent expert scientific dietary advice to help make healthier choices quickly and easily. Products have with green, amber or red coloured labels on the front of the pack. These show consumers at a glance if the food they are thinking about buying has low, medium or high amounts of fat, saturated fat, sugars and salt. This policy is supposed to helping consumers get a better balance. However, Italy backed by several other Member States has opposed the scheme from the

²² Brussels Workshop, 15th October 2015

²³ http://www.who.int/nmh/events/ncd_action_plan/en/

start and says that the fact it was launched through a Department of Health recommendation means that it is not really voluntary but quasi mandatory. It pushed the European Commission to take action on what it said is a hidden trade barrier, since traditional Italian foods are hard hit by the scheme. <http://www.eurofoodlaw.com/labelling/health-and-nutrition/no-legal-action-against-uk-over-traffic-lights-105740.htm>

In October 2014, the European Commission has formally opened infraction proceedings against the UK for its voluntary traffic light labelling system, giving the state two months to defend itself against business complaints. The decision follows an investigation by the European Commission earlier into the compatibility of the UK's traffic light scheme. No further steps have been taken so far.

3.7.3 TAXATION OF UNHEALTHY FOODS AND DRINKS

3.7.3.1 Alcohol

As Alemanno and Garde in their latest volume on life style risk regulation point out, other than tobacco, for alcohol there have only been EU harmonizing rules to contain alcohol-related harm. One exception is the Audiovisual Media Services Directive (AVMS Directive) regulating promotion of alcohol in the audiovisual media. The experts complain about the weakness of this provision and the fact that most Member States comply only with the minimum standard and the high degree of fragmentation this has led to within the internal market (Alemanno/Garde 2014, p. 10).

At national level, tax measures have been in all countries on alcohol, traditionally for fiscal reasons but increasingly also to regulate alcohol consumption and the harms caused through over consumption (mortality, injury rate, traffic-crash deaths, violence and crime episodes, sexually-transmitted diseases). Quite an impressive numbers of studies document that high taxes do actually have positive effects on citizens' health. However the results and difference of such measures have to be analysed and evaluated in detail (see also Sassi et al 2014). For example, increased taxes generally affect citizens with low socio-economic status more than others. What is more is the combination with tobacco consumption and increase of tobacco taxes. E.g. alcohol is often used as a substitute for cigarettes when tobacco taxes are increased (Decker/Schwarz 2000). Another study concluded that alcohol and tobacco have complementary effects as smokers respond to increases in alcohol prices by reducing their tobacco consumption, while drinkers respond less or not at all to changes in cigarette prices. The authors explain this phenomenon with the hypothesis that smokers smoke more in social settings, when also drinking alcohol (Koksal/Wohlgenant 2011).

3.7.3.2 Tobacco

Experience from tobacco tax regulation highlights the power of price changes to affect purchasing behavior and public health (Jha et al., 2006). In addition to direct price effects on purchases, tobacco taxes have generated significant revenues that some states have used to support comprehensive tobacco control programs that further reduced smoking (Chaloupka, 2010). However, taxation is not the only anti-smoking policy and not always the most effective one.

The very low rates of cessation shown in disadvantaged groups are inconsistent with the idea that, for them, price is an effective means of promoting cessation. Price increases may influence poor people to switch to cheaper and higher yield brands (Jarvis 1998), to roll their own cigarettes, and to cut down on the number of cigarettes, rather than to quit altogether. Because of the phenome-

non of nicotine compensation, lowering cigarette consumption is unlikely to confer any benefit in lowering risk of smoking-related disease.

Restrictions on smoking in public places and the workplace carry an effective message about social acceptability of cigarettes, as well as protecting non-smokers. This it may enhance the motivation and attempts to give up smoking. In some countries, legislative bans have been recently introduced with quite good acceptance and success (e.g. Ireland, Italy, Norway) (Jarvis/Wardle 2011).

3.7.3.3 Sugary Food

Consumption of sweets has grown significantly in recent decades and is related to the increase of many NCDs such as diabetes, obesity, cardio-vascular problems and others. In Finland, the Act on the Excise Tax of Sweets, Ice Cream and Soft Drinks (1127/2010), popularly known as the sweets tax, came into force at the beginning of 2011 was increased in 2012. The tax levied is 95 cents per kilogram of sweets and ice-cream and 11 cents per litre of beverage on soft drinks. However, due to political pressure, the Finnish government is likely to withdraw the tax, at least until the EU regulation (1169/2011) demanding reporting of sugars content comes into effect in the beginning of 2017.

The Danish government has imposed tax increases of 25% on 1st July this year on ice cream, chocolate, and sweets and will also increase taxes on soft drinks, tobacco, and alcohol products in a bid to reduce the burden on public health services and to tackle obesity, heart disease, and other illnesses. (www.skm.dk/foreign/english/8013.html). The aim of the tax rises was 'to reduce the prevalence of a broad range of illnesses and improve life expectancy.' However, this tax was abandoned as well.

In February 2015, the US Dietary Guidelines Advisory Committee recommended the Obama administration to impose a tax on sugary foods in order to fight obesity. In what would be the committee's first target on "added sugars" from food processing, the group set a level of no more than 10 percent of all calories, down from the average 13 percent now consumed by U.S. adults. The recommendation comes after studies tying snacks and sugary beverages to high obesity rates. (<http://www.bloomberg.com/news/articles/2015-02-19/tax-on-sugary-foods-proposed-by-u-s-panel-to-help-fight-obesity>)

3.7.3.4 Sugar-Sweetened Beverages

Beverage taxes came into light with increasing concerns about obesity, particularly among youth. Sugar-sweetened beverages (SSB) have become a target of anti-obesity initiatives with increasing evidence of their link to obesity. Studies show that with an excise tax on sugar-sweetened beverages governments could prevent obesity at least to some degree. The public health impact of beverage taxes could be substantial. This debate on policy intervention has to be seen in the context of tobacco taxation mentioned above.

Further Information

- <http://www.who.int/topics/nutrition/en/>
- http://www.who.int/nmh/events/ncd_action_plan/en/
- <https://www.fmhs.auckland.ac.nz/en/soph/global-health/projects/informas/objectives.html>

3.8 INDUSTRIALISATION OF FOOD PRODUCTION

The industrialisation of food production is indispensable connected to agriculture. The agriculture system has to be considered from a global point of view, because agriculture production follows the concept of industry and the associated economy precept.

The basic principle of economic activating has three characteristics:

- Minimum principle: An output has to be achieved with the least possible use of resources (or input).
- Maximum principle: The applied use of resources (input) should a maximum possible output.
- Optimization principle: The ratio allocation of resources to achievement has to be optimized (taking into account existing criteria).

The industrialisation of food production has very serious or even fatal consequences for nature, for the population and diversity of animals and plants, and as a consequence for mankind (see also chapter 3.6 Agriculture).

While the agricultural system or rather the industrialized food production plays on the global stage, the health system is often organized only nationally or partly on the EU level. These two different principles are in a contradiction with a high potential for political creativity and shaping.

Diets link environmental and human health. Rising incomes and urbanization are driving a global dietary transition in which traditional diets are replaced by diets higher in refined sugars, refined fats, oils and meats. By 2050 these dietary trends, if unchecked, would be a major contributor to an estimated 80 per cent increase in global agricultural greenhouse gas emissions from food production and to global land clearing. Moreover, these dietary shifts are greatly increasing the incidence of type II diabetes, coronary heart disease and other chronic non-communicable diseases that lower global life expectancies. (Tilman and Clark 2014)

High-yielding cereals and other staples have produced adequate calories to ward off starvation for much of the world over several decades. However, deficiencies in certain amino acids, minerals, vitamins and fatty acids in staple crops, and animal diets derived from them, have aggravated the problem of malnutrition and the increasing incidence of certain chronic diseases in nominally well-nourished people (the so-called diseases of civilization). Enhanced global nutrition has great potential to reduce acute and chronic disease, the need for health care, the cost of health care, and to increase educational attainment, economic productivity and the quality of life. However, nutrition is currently not an important driver of most plant breeding efforts, and there are only a few well-known efforts to breed crops that are adapted to the needs of optimal human nutrition. Technological tools are available to greatly enhance the nutritional value of our staple crops. However, enhanced nutrition in major crops might only be achieved if nutritional traits are introduced in tandem with important agronomic yield drivers, such as resistance to emerging pests or diseases, to drought and salinity, to herbicides, parasitic plants, frost or heat. There is the need and means for agriculture, food processing, food transport, sociology, nutrition and medicine to be integrated into new approaches to food production with optimal human nutrition as a principle goal. (Sands et al. 2009)

Industrialised food production implies refined sugar, refined fat, refined oil, and more meat in the food. These dietary causes the increase of type II diabetes, heart diseases, and other NC-diseases (Tilman and Clark 2014). The industrialisation of food production provides an oversupply of available calories. This is a likely driver of overconsumption of those calories and can readily explain the weight gain seen in most countries.

Walker et al. already argued in 2005 that the high level of meat and saturated fat consumption in the USA and other high-income countries exceeds nutritional needs and contributes to high rates of chronic diseases such as cardiovascular disease, diabetes mellitus and some cancers. Affluent citizens in middle- and low-income countries are adopting similar high-meat diets and experiencing increased rates of these same chronic diseases. The industrial agricultural system, now the predominant form of agriculture in the USA and increasingly world-wide, has consequences for public health owing to its extensive use of fertilisers and pesticides, unsustainable use of resources and environmental pollution. In industrial animal production there are public health concerns surrounding feed formulations that include animal tissues, arsenic and antibiotics as well as occupational health risks and risks for nearby communities. It is of paramount importance for public health professionals to become aware of and involved in how our food is produced.

3.9 MARKETING AND ADVERTISING

Advertising and marketing in connection with NCDs are mainly discussed in connection with the effect on children. WHO has worked on that problem in several projects and has published the findings and recommendations (WHO, 2010).

Advertising and other forms of food and beverage marketing to children are widespread across the world and are influencing children's food preferences, purchase requests and consumption patterns. A significant amount of this marketing is for products with a high content of fat, sugars or salt, consumption of which may increase the risk of overweight, obesity or certain NCDs.

Overweight and obese children are at higher risk of developing serious health problems including diabetes type 2, high blood pressure, asthma, and other respiratory problems, sleep disorders and liver disease. They may also suffer from psychological effects, such as low self-esteem, depression and social isolation. Childhood obesity also increases the risk of obesity, NCDs, premature death and disability in adulthood (WHO, 2011²⁴).

Television advertising is responsible for a large share of the marketing of unhealthy foods and, according to systematic reviews of evidence, advertisements influence children's food preferences, purchase requests, and consumption patterns.

In May 2010 (see WHO, 2010), WHO Member States endorsed a new set of recommendations on the marketing of foods and non-alcoholic beverages to children. The recommendations call for national and international action to reduce the exposure of children to marketing messages that promote foods high in saturated fats, trans-fatty acids, free sugars, or salt, and to reduce the use of powerful techniques to market these foods to children.

"NCDs, such as cardiovascular diseases, cancers and diabetes, today represent a leading threat to human health and socioeconomic development," says Dr Ala Alwan, WHO's Assistant Director-General for NCDs and Mental Health. "Implementing these recommendations should be part of broad efforts to prevent unhealthy diets - a key risk factor for several NCDs."

WHO data shows that 43 million pre-school children worldwide are obese or overweight. Scientific reviews have also shown that a significant portion of television advertising that children are exposed to promotes "noncore" food products which are low in nutritional value.

Poor diet is one of the four common factors associated with the four main NCDs (cancers, diabetes, cardiovascular diseases and chronic lung diseases), which are responsible for around 60% of all deaths worldwide, or over 35 million people annually. More than 9 million deaths are premature (people dying before reaching 60 years of age) and could have



²⁴ http://www.who.int/chp/media/news/releases/2011_1_marketing/en/

been prevented through low-cost measures at the world's disposal today, including measures to stop tobacco use, reduce the harmful use of alcohol, and to promote healthy diets and physical activity (see footnote 24).

WHO organized also a United Nations General Assembly High-level Meeting on the Prevention and Control of NCDs in New York in September 2011.

WHO developed a set of 12 recommendations (see WHO 2010), endorsed by the World Health Assembly, aimed at reducing the impact of marketing foods high in saturated fats, trans-fatty acids, free sugars, or salt. The main purpose of these recommendations is to guide efforts by Member States in designing new and/or strengthening existing policies on food marketing communications to children in order to reduce the impact on children of marketing of foods high in saturated fats, trans-fatty acids, free sugars, or salt. The recommendations are structured into the following five sections: Rationale; Policy development; Policy implementation; Policy monitoring and evaluation; and Research.

Rationale

1. The policy aim should be to reduce the impact on children of marketing of foods high in saturated fats, trans-fatty acids, free sugars, or salt.
2. Given that the effectiveness of marketing is a function of exposure and power, the overall policy objective should be to reduce both the exposure of children to, and power of, marketing of foods high in saturated fats, trans-fatty acids, free sugars, or salt.

Policy development

3. To achieve the policy aim and objective, Member States should consider different approaches, i.e. stepwise or comprehensive, to reduce marketing of foods high in saturated fats, trans-fatty acids, free sugars, or salt, to children.
4. Governments should set clear definitions for the key components of the policy, thereby allowing for a standard implementation process. The setting of clear definitions would facilitate uniform implementation, irrespective of the implementing body. When setting the key definitions Member States need to identify and address any specific national challenges so as to derive the maximal impact of the policy.
5. Settings where children gather should be free from all forms of marketing of foods high in saturated fats, trans-fatty acids, free sugars, or salt. Such settings include, but are not limited to, nurseries, schools, school grounds and preschool centres, playgrounds, family and child clinics and paediatric services and during any sporting and cultural activities that are held on these premises.
6. Governments should be the key stakeholders in the development of policy and provide leadership, through a multistakeholder platform, for implementation, monitoring and evaluation. In setting the national policy framework, governments may choose to allocate defined roles to other stakeholders, while protecting the public interest and avoiding conflict of interest.

Policy implementation

7. Considering resources, benefits and burdens of all stakeholders involved, Member States should consider the most effective approach to reduce marketing to children of foods high in saturated fats, trans-fatty acids, free sugars, or salt. Any approach selected should be set within a framework developed to achieve the policy objective.
8. Member States should cooperate to put in place the means necessary to reduce the impact of

cross-border marketing (in-flowing and out-flowing) of foods high in saturated fats, trans-fatty acids, free sugars, or salt to children in order to achieve the highest possible impact of any national policy.

9. The policy framework should specify enforcement mechanisms and establish systems for their implementation. In this respect, the framework should include clear definitions of sanctions and could include a system for reporting complaints.

Policy monitoring and evaluation

10. All policy frameworks should include a monitoring system to ensure compliance with the objectives set out in the national policy, using clearly defined indicators.
11. The policy frameworks should also include a system to evaluate the impact and effectiveness of the policy on the overall aim, using clearly defined indicators.

Research

12. Member States are encouraged to identify existing information on the extent, nature and effects of food marketing to children in their country. They are also encouraged to support further research in this area, especially research focused on implementation and evaluation of policies to reduce the impact on children of marketing of foods high in saturated fats, trans-fatty acids, free sugars, or salt.

There are just as many studies and publication on this topic in scientific journals. In 1999 Gallo stated that the most heavily advertised foods tend to be of dubious nutritional value. He found that candy, sweetened breakfast cereals, and fast-food restaurants accounted for over half of all food ads in Norway, Australia, the United States, and 10 European Union nations. In the United States, fast-food restaurants alone account for one third of food advertising expenditures. And among all companies—not just food companies—Coca-Cola and McDonald's are among the top 10 advertisers (Gallo 1999).

The significant increase of obesity in children in the European Union is of major concern to all Member States. It is imperative that comprehensive strategies be put in place to combat this increase in obesity and that measures be taken as a matter of urgency. One factor which is known to have an impact on children's consumption patterns is the marketing of unhealthy food to them, but there is a lack of agreement amongst stakeholders over what should be done. It is clear that food manufacturers are increasingly using integrated and sophisticated marketing strategies to promote their products directly and indirectly to children. It is also clear from this report, as well as from other international reports and surveys, that globally the commercial marketing to children of food and drink is dominated by unhealthy products. Whilst television continues to be used as a powerful tool for food marketing, and in-school marketing is increasingly exploited, many other non-traditional marketing techniques are becoming more prominent. One of the fastest growing ways to market food to children is via the Internet.

Behavioral components are strongly influencing obesity spread and development, especially when considering TV and advertising. There is, therefore, the need of multi-cultural and cross-cultural research, in order to gain a full understanding of the association between obesity and different risk factors, in different scenarios, providing the best evidence to decision makers, grounding prevention on evidence-based strategies rather than focusing on single factors without the recognition of their mutual influence.

Yancey et al. (2009) investigated advertising in the context of the income in the different countries and found that living in an upper-income neighbourhood, regardless of its residents' predominant ethnicity, is generally protective against exposure to most types of obesity-promoting outdoor advertising (food, fast food, sugary beverages, sedentary entertainment, and transportation). The density of advertising varied by zip code area race/ethnicity, with African American zip code areas having the highest advertising densities, Latino zip code areas having slightly lower densities, and white zip code areas having the lowest densities. Conclusions: The potential health and economic implications of differential exposure to obesity-related advertising are substantial. Although substantive legal questions remain about the government's ability to regulate advertising, the success of limiting tobacco advertising offers lessons for reducing the marketing contribution to the obesogenicity of urban environments.

4 REFERENCES

- Aboim, S. (2010). Gender cultures and the division of labour in contemporary Europe: a cross-national perspective. *Sociological Review*, 58(2), 171-196.
- Action Plan for implementation of the European Strategy for the Prevention and Control of Non-communicable Diseases 2012–2016; World Health Organization 2012; ISBN 978 92 890 0268 4
- Adams, J., Baskett, S., Brookman, R. et al. (2007): 21 Reasons Why Gender Matters. Fatherhood Foundation, New South Wales. http://www.gendermatters.org.au/Home_files/21%20Reasons%20Why%20Gender%20Matters%28low%20res%29.pdf
- Adams, M., Frank, L., Schipperijn, J., Smith, G., Chapman, J., Christiansen, L., Sallis, J. et al. (2014). International variation in neighborhood walkability, transit, and recreation environments using geographic information systems: the IPEN adult study. *International Journal of Health Geographics*, 13(1), 1-17. doi: 10.1186/1476-072x-13-43
- Adeyi, O.; Smith, O.; Robles, S. (2007). Public policy and the challenge of chronic non-communicable diseases. Washington: The World Bank.
- Adlakha, D., Hipp, A. J., Marx, C., Yang, L., Tabak, R., Dodson, E. A., & Brownson, R. C. (2015): Home and Workplace Built Environment Supports for Physical Activity. *American Journal of Preventive Medicine*, 48(1), 104-107. doi: 10.1016/j.amepre.2014.08.023
- Agropoly – A handful of corporations control world food production. (2013). English Edition PUBLISHER Berne Declaration (DB) & EcoNexus. EvB: Zürich, Switzerland. (<http://www.econexus.info/publication/agropoly-handful-corporations-control-world-food-production>)
- Ahmad, Summiya, et al. "Gender Differences in Depression Among the Affectees of War on Terrorism and the Role of Psychological Interventions in the Rehabilitation." *Pakistan Journal of Criminology* 6.2 (2014): 95-112
- Allen, Jessica; Balfour, Reuben; Bell, Ruth; Marmot, Michael. (2014). Social determinants of mental health. *International Review of Psychiatry*. ; 26(4): 392–407. : <http://dx.doi.org/10.3109/09540261.2014.928270>. (WOS:000340824500002).
- Allsop, M; Huxdorff, C; Johnston, P; Santillo, D; Thompson, K. (2015). Pesticides and our Health. A GROWING CONCERN. Greenpeace Research Laboratories. <http://www.greenpeace.org/international/Global/international/publications/agriculture/2015/Pesticides-and-our-Health.pdf>
- Andreyeva, T. et al. (2011), Estimating the potential of taxes on sugar-sweetened beverages to reduce consumption and generate revenue. In: *Preventive Medicine* 52, pp. 413–416
- Arena, Ross; Guazzi, Marco; Lianov, Liana; Whitsel, Laurie; Berra, Kathy; Lavie, Carl J.; Kaminsky, Leonard; Williams, Mark; Hivert, Marie-France; Franklin, Nina Cherie; Myers, Jonathan; Dengel, Donald; Lloyd-Jones, Donald M.; Pinto, Fausto J.; Cosentino, Francesco; Halle, Martin; Gielen, Stephan; Dendale, Paul; Niebauer, Josef; Pelliccia, Antonio; Giannuzzi, Pantaleo; Corra, Ugo; Piepoli, Massimo F.; Guthrie, George; Shurney, Dexter. (2015). Healthy Lifestyle Interventions to Combat Noncommunicable Disease—A Novel Nonhierarchical Connectivity Model for Key Stakeholders: A Policy Statement From the American Heart Association, European Society of Cardiology, European Association for Cardiol. *Mayo Clinic Proceedings*. DOI: 10.1016/j.mayocp.2015.05.001
- Aschemann-Witzela, J.; Maroscheckb, N.; Hammb, U. (2013). Are organic consumers preferring or avoiding foods with nutrition and health claims? IN: *Food Quality and Preference*, Volume 30, Issue 1, October 2013, Pages 68–76. doi:10.1016/j.foodqual.2013.04.011.

- Aube, J., Fleury, J., & Smetana, J. (2000). Changes in women's roles: Impact on and social policy implications for the mental health of women and children. *Development and Psychopathology*, 12(4), 633–656.
- Barefoot, J.C., S. Larsen, L. v.d. Lieth et al. (1995): Hostility, incidence of acute myocardial infarction, and mortality in a sample of Ider Danish men and women. In: *Am. J. Epeidemiol.*, 142, pp. 477-484.
- Barker DJP. Fetal origins of coronary heart disease. *Br Med J.* 1995;311:171–174.
- Bergstrom, A; Skov, TH; Bahl, MI; et al. (2014). Establishment of intestinal microbiota during early life: a longitudinal, explorative study of a large cohort of Danish infants. IN: *Appl Environ Microbiol.* 2014, 80:2889-2900.
- Berkman, L.F. and S.L. Syme (1979): Social networks, host resistance, and mortality: a nine-year follow-up study af Alamedy County residents. *Am. J. Epidemiol.*, 109, pp. 108-203
- Bioengineers, physicians 3-D print ears that look, act real, *Cornell Chronicle* (Feb. 20, 2013), Retrieved from <http://www.news.cornell.edu/stories/2013/02/bioengineers-physicians-3-d-print-ears-look-act-real>
- Bisconti, T.L. and C.S. Bergeman (1999): Perceived social control as a mediator of the relationships among social support, psychological well-being and perceived health. In: *The Gerontologist*, 39, pp. 94-103.
- Bonoli, G. 2005. The politics of the new social policies: providing coverage against new social risks in mature welfare states. *Policy & politics*, 33, 431-449.
- Boreham, C.A.G., R.A. Kennedy. M.H. Murphy et al. (2005): Training effects of short bouts of stair climbing on cardiorespiratory fitness, blood lipids, and homocysteine in sedentary young women. *Britisch Journal of Sports Medicine*, 39 (9), pp. 590-593
- Borgzaga, C. & Bodoni, R. 2014. What to Make of Social Innovation? Towards a Framework for Policy Development. *Social Policy and Society*, 13, 411-421.OECD, 2011.
- Boye, K. (2010). Time spent working. *European Societies*, 12(3), 419–442.
- Boye, K. (2011). Work and well-being in a comparative perspective – The role of family policy. *European Sociological Review*, 27(1), 16–30.
- Brackbill, R. M., S. D. Stellman, et al. (2013). "Mental health of those directly exposed to the World Trade Center disaster: Unmet mental health care need, mental health treatment service use, and quality of life." *Social Science & Medicine* 81: 110-114.
- Brandta, K.; Leifertb, C.; Sandersonc, R.; Seala, C.J. (2011). Agroecosystem Management and Nutritional Quality of Plant Foods: The Case of Organic Fruits and Vegetables. IN: *Critical Reviews in Plant Sciences*, Volume 30, Issue 1-2, pages 177-197, Special Issue: Towards a More Sustainable Agriculture. DOI:10.1080/07352689.2011.554417.
- Brief No. 42: The Future of Food and Farming. Camilla Toulmin, IIED and Charles Godfray, University of Oxford. <http://www.gfar.net/content/foresight-write-workshops>[http:// or here: www.fao.org/docs/eims/upload/307711/Toulmin_Future%20of%20Food_Brief%2042.pdf](http://www.fao.org/docs/eims/upload/307711/Toulmin_Future%20of%20Food_Brief%2042.pdf)
- Brooke, K., (July 19, 2013), "Wake Forest 3D Prints skin cells onto burn wounds", 3D Printer world, Retrived from: <http://www.3dprinterworld.com/article/wake-forest-3d-prints-skin-cells-burn-wounds>
- Brown, A. R. (2014). "In response: Industry perspective." *Environmental Toxicology and Chemistry* 33(9): 1915-1918.
- Brown, G.W and T. Harris (1987): *The social origins of depression*. Tavistock Publications, London
- Bungum, T., M. Meacham, and N. Truax (2007): The effects of signage and the physical environment on stair usage. *Journal of Physical Activity & Health*, 4 (3), pp. 237-244
- Bunn, F., T. Collier, C. Frost, K. Ker et al. (2009): Area wide traffic calming for preventing traffic related injouries. *Chochrane Database of Systematic Reviews* 2003, issue 1

- Burke, C; Johnson, EE; Bourgault, C; Borgia, M; O'Toole, TP. (2013). Losing Work: Regional Unemployment and its Effect on Homeless Demographic Characteristics, Needs, and Health Care. IN: JOURNAL OF HEALTH CARE FOR THE POOR AND UNDERSERVED, 2013 Aug; 24(3):1391-402. doi: 10.1353/hpu.2013.0150
- Camilla Toulmin, IIED and Charles Godfray. (2012) Brief No. 42: The Future of Food and Farming. University of Oxford. (<http://www.gfar.net/content/foresight-write-workshops>[http://](http://www.gfar.net/content/foresight-write-workshops))
- Casas, Maria I.; Duarte, Silvia; Doseff, Andrea I.; Grotewold, Erich. (2014). Flavone-rich maize: an opportunity to improve the nutritional value of an important commodity crop. IN: FRONTIERS IN PLANT SCIENCE, Volume 5. DOI: 10.3389/fpls.2014.00440. WOS:000343311800001.
- Chaloupka, FJ (2010): The effects of pricing and tax policies on youth tobacco use. Prepared for the Global Consultation on Effective Youth Tobacco Control Policy Interventions. World Health Organization, Tobacco-Free Initiative.
- Chan, W.C. and S.T. Leatherdale (2011): Tobacco retailer density surrounding schools and youth smoking behavior: A multi-level analysis. Tobacco Induces Diseases, 9 (1), p. 9
- Clarke J, Wu HC, Jayasinghe L, Patel A, Reid S, Bayley H. Continuous base identification for single-molecule nanopore DNA sequencing. Nat Nanotech. 2009; 4:265-70.
- Cohen, S, L.G. Underwood and B.H. Gottlieb (2000): Social support measurement and intervention: a guide for health and social scientists. Oxford University Press.
- Coleman Jensen, A.; Nord, M.; and Singh, A. (2013): Household Food Security in the United States in 2012, ERR-155, U.S. Department of Agriculture, Economic Research Service, September 2013.
- Collins, SM; Surette, M; Bercik, P. (2012). The interplay between the intestinal microbiota and the brain. IN: Nat Rev Microbiol. 2012;10:735-742.
- Colman, I; Jones, PB; Kuh, D; Weeks, M; Naicker, K; Richards, M; Croudace, TJ. (2014). Early development, stress and depression across the life course: pathways to depression in a national British birth cohort. IN: Psychol Med. 2014 Oct;44(13):2845-54. doi: 10.1017/S0033291714000385. Epub 2014 Feb 27.
- Connor, J., K. Kypri, M. Bell, and K. Cousins (2011): Alcohol outlet density, levels of drinking and alcohol-related harm in New Zealand: A national study. Journal of Epidemiology and Community Health, 65 (10), pp. 841-846
- Cornman, J.C., N. Goldman, D.A. Gleib et al. (2003): Social ties and perceived support: two dimensions of social relationships and health among the elderly in Taiwan. In: J. Aging Health, 15, pp. 616-644.
- Cradock A, Duncan DT. 2014. The role of the built environment in supporting health behavior change. In: The Handbook of Health Behavior Change (Riekert K, Ockene J, Pbert L, eds). Vol. 4. New York:Springer Publishing Company, 437–462.
- Dangour, A. D., Green, R., Häslar, B., Rushton, J., Shankar, B., & Waage, J. (2012). Linking agriculture and health in low- and middle-income countries: an interdisciplinary research agenda. Proceedings of the Nutrition Society, 71(02), 222-228. doi: 10.1017/S0029665112000213
- Dash, Sarah R. (2015). The Microbiome and Brain Health: What's the Connection? IN: Medscape Psychiatry. March 24, 2015. (<http://www.medscape.com/viewarticle/841748>)
- Dereuddre, R., Missinne, S., Buffel, V., & Bracke, P. (2014). Gender specific effects of financial and housework contributions on depression: A multi-actor study among three household types in Belgium. Health Sociology Review, 23(2), 78-90.
- Di Cesare, M; Khang, YH; Asaria, P; Blakely, T; Cowan, MJ; Farzadfar, F; Guerrero, R; Ikeda, N; Kyo-butungi, C; Msyamboza, KP; Oum, S; Lynch, JW; Marmot, MG; Ezzati, M; Lancet NCD Action

- Group. (2013). Inequalities in non-communicable diseases and effective responses. IN: *Lancet*. 2013 Feb 16; 381(9866):585-97. doi: 10.1016/S0140-6736(12)61851-0. Epub 2013 Feb 12. PMID: 23410608 [PubMed - indexed for MEDLINE]
- Dibb, Sue. (1996). *A Spoonful of Sugar, Television Food Advertising Aimed at Children: An International Comparative Survey*. Ed. Haggart, Kelly; Harris, Lucy; Tugend, Alina. Consumers International. ISBN 0 9524388 3 6. <http://www.consumersinternational.org/media/308610/a%20spoonful%20of%20sugar%20-%20television%20food%20advertising%20aimed%20at%20children-%20an%20international%20comparative%20survey.pdf>.
- Dibildox, J. (2014). Analysis of TV, advertising and other behavioral determinants of overweight and obesity in childhood. IN: *Salud Publica Mex*. 2014 ;56 Suppl 2:s162-6. PMID: 25629249.
- Ding, D., J. Sallis, J.F. Kerr et al. (2011): Neighborhood environment and physical activity among youth: A review. *American Journal of Preventive Medicine*, 41 (4)
- Dumbaugh, E. and L. Frank (2007): Traffic safety and safe routes to school – Synthesizing the empirical evidence. *Transportation Research Records* (2009), pp. 89-97
- Dzau, Victor J., MD, Ziggy Yoediono, MD, MBA, William F. ElLaissi, MBA, MHA, and Alex H. Cho (October 2013), MD, MBA. *Fostering Innovation in Medicine and Health Care: What Must Academic Health Centers Do?* *Academic Medicine*, Vol. 88, No. 10 /
- Edwards, P; Tsouros, A: Promoting physical activity and active living in urban environments. The role of local governments, World Health Organization 2006; ISBN 92-890-2181-0
- El-Sayed, AM; Palma, A; Freedman, LP; Kruk, ME. (2015). Does health insurance mitigate inequities in non-communicable disease treatment? Evidence from 48 low- and middle-income countries. IN: *Health Policy*. 2015 Sep;119(9):1164-75. doi: 10.1016/j.healthpol.2015.07.006. Epub 2015 Jul 29.
- Evans, G. W., Lercher, P., Meis, M., Ising, H., & Kofler, W. W. (2001). Community noise exposure and stress in children. [Article]. *Journal of the Acoustical Society of America*, 109(3), 1023-1027. doi: 10.1121/1.1340642
- Experts call for 'all hands on deck' to tackle global burden of non-communicable disease. *European Society of Cardiology*. July 2, 2015. <http://www.sciencedaily.com/releases/2015/07/150702073559.htm>.
- ExVive3D Liver Tissue Performance (10 March 2016) retrieved <http://www.organovo.com/tissues-services/exvive3d-human-tissue-models-services-research/exvive3d-liver-tissue-performance/>
- Fergus, Shanahan (October 2012), The gut microbiota—a clinical perspective on lessons learned. *Nature Reviews Gastroenterology and Hepatology* 9, 609-614
- Ferguson, K. T., Cassells, R. C., MacAllister, J. W. and Evans, G. W. (2013), The physical environment and child development: An international review. *International Journal of Psych*, 48: 437–468. doi: 10.1080/00207594.2013.804190
- FOODCONFERENCE-EU Project: Report Summary 2011. Project reference: 280424 http://cordis.europa.eu/result/rcn/55902_en.html
- Gallo, Anthony E. (1999). Food Advertising in the United States. IN: Elizabeth Frazao, ed., *America's Eating Habits: Changes and Consequences*, Washington, DC: United States Department of Agriculture (USDA), Economic Research Service (ERS), April 1999.
- Gardner, Gary T. ; Halweil, Brian; Peterson, Jane A.. (2000). Underfed and Overfed: The Global Epidemic of Malnutrition World Watch Institute. Watch Paper 150.
- Giles, C. M., E.L. Kenney, S.L. Gortmaker et al. (2012): Increasing water availability during after-school: Evidence, strategies and partnerships from the OSNAP Group Randomized Trial.

- American Journal of Preventive Medicine, 43 (3S2), S136
- Giovannucci, Daniele; Scherr, Sara J.; Nierenberg, Danielle; Hebebrand, Charlotte; Shapiro, Julie; Milder, Jeffrey; Wheeler, Keith. (2012). Food and Agriculture: The Future of Sustainability. The Sustainable Development in the 21st century (SD21) Report for Rio+20, New York: United Nations, 2012 (http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2054838).
- Glass, J., & Fujimoto, T. (1994). Housework, paid work, and depression among husbands and wives. *Journal of Health and Social Behavior*, 35(2), 179–191.
- Global action plan for the prevention and control of noncommunicable diseases 2013-2020. World Health Organization 2013; ISBN 978 92 4 150623 6.
- Goenjian, Armen K., et al. (2000) "Prospective study of posttraumatic stress, anxiety, and depressive reactions after earthquake and political violence." *American Journal of Psychiatry* 2000; 157:911–916
- Gold, Mary. "What is organic production?". National Agricultural Library. USDA. Retrieved 1 March 2014.
- Grenham, S; Clarke, G; Cryan, JF; et al. (2011). Brain-gut-microbe communication in health and disease. IN: *Front Physiol*. 2011;2:94.
- Griesenbach, U. Alton EW (2009 Feb 27), Gene transfer to the lung: lessons learned from more than 2 decades of CF gene therapy. UK Cystic Fibrosis Gene Therapy Consortium. *Adv Drug Deliv Rev*;61(2):128-39. http://ac.els-cdn.com/S0169409X08002639/1-s2.0-S0169409X08002639-main.pdf?_tid=714a55e2-e6a7-11e5-a835-00000aabb0f02&acdnat=1457604433_318c11928ab06f3d9635346d64a51fb4
- Grisolia, F. & Ferragina, E. 2015. Social Innovation on the Rise: yet another buzzword in time of austerity? *Salute e Società*.
- Guinane, CM; Cotter, PD. (2013). Role of the gut microbiota in health and chronic gastrointestinal disease: understanding a hidden metabolic organ. IN: *Therap Adv Gastroenterol*. 2013, 6:295-308.
- Guite, H. F., Clark, C., & Ackrill, G. (2006). The impact of the physical and urban environment on mental well-being. *Public Health*, 120(12), 1117-1126. *Proceedings Paper*, 14th UK Public Health Forum doi: 10.1016/j.puhe.2006.10.005
- Halonen, J.; Kiyimaki, M.; Virtanen M. et al. (2013): Living in proximity of a bar and risky alcohol behaviors: A longitudinal study. *Addiction*, 108 (2), pp. 320-328
- Hannon, J.C; Brown, B.B. (2008): Increasing preschoolers' physical activity intensities: An activity friendly preschool playground intervention. *Preventive Medicine*, 46 (6), pp. 532-536.
- Hasin, D.; Hatzenbuehler, ML.; Keyes, K.; Ogburn, E. (2006). The Diagnostic and Statistical Manual of Mental Disorders. Fourth edition (DSM-IV)- *Addiction*, 2006. Wiley Online Library.
- Hawkes C, Murphy S. In: Trade, Food, Diet and Health Perspectives and Policy Option. Hawkes C, Blouin C, Henson S, Drager N, Dube L, editor. (2010). Oxford: John Wiley & Sons Inc. An overview of global food trade.
- Hawkes, Corinna; Turner, Rachel; Waage, Jeff. (2012). Current and Planned Research on Agriculture for Improved Nutrition: A Mapping and a Gap Analysis. Report for the Department of International Development (DFID). London: Leverhulme Centre for Integrative Research on Agriculture and Health/University of Aberdeen/Center for Sustainable International Development.
- Henriksen, L., Feighery, E. C., Schleicher, N. C., Cowling, D. W., Kline, R. S., Fortmann, S. P. 2008 Is adolescent smoking related to the density and proximity of tobacco outlets and retail cigarette advertising near schools? *PREVENTIVE MEDICINE*, 47 (2): 210-214
- Holm, G., J. Snape, et al. (2013). "Implementing Ecopharmacovigilance in Practice: Challenges and Potential Opportunities." *Drug Safety* 36(7): 533-546.

- Hubera, M.; Rembiałkowskab, E.; Średnickab, D.; Bügelc, S.; van de Vijvera, L.P.L. (2011). Organic food and impact on human health: Assessing the status quo and prospects of research. IN: *NJAS - Wageningen Journal of Life Sciences*, Volume 58, Issues 3–4, December 2011, Pages 103–109. doi:10.1016/j.njas.2011.01.004.
- Janowski, K; Kurpas, D; Kusz, J; Mroczek, B; Jedynak, T. (2014). Emotional Control, Styles of Coping with Stress and Acceptance of Illness among Patients Suffering from Chronic Somatic Diseases. IN: *Stress Health*. 2014 Feb;30(1):34-42. doi: 10.1002/smi.2493. Epub 2013 May 8.
- Jarvis, M.J., (1998): Supermarket cigarettes: the brands that dare not speak their name. in: *British Medical Journal*, 316, pp. 929-931
- Jarvis, M.J., J. Wardle (2011): Social patterning of individual health behaviours; the case of cigarette smoking. In: Marmot, M, R. Wilkinson (eds.): *Social Determinants of Health*. Second edition. Oxford University Press, pp.224-237
- Jensen, Maja M.; Jørgensen, Henry; Lauridsen, Charlotte. (2013). Comparison between conventional and organic agriculture in terms of nutritional quality of food – a critical review. IN: *CAB Reviews* 2013 8, No. 045. doi: 10.1079/PAVSNNR20138045.
- Jha P. et al., (2006): Social inequalities in male mortality, and in male mortality from smoking: indirect estimation from national death rates in England and Wales, Poland, and north America. *Lancet*, 368:367–370.
- Johansson, Eva; Hussain, Abrar; Kuktaite, Ramune; Andersson, Staffan C.; Olsson, Marie E. (2014). Contribution of Organically Grown Crops to Human Health⁹ IN: *NATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH*, Volume: 11, Issue: 4, Pages: 3870-3893, DOI: 10.3390/ijerph110403870. WOS:000335762700061.
- Joost, H.G.; Gibney, M.J.; Cashman, K.D.; Görman, U.; Hesketh, J.E.; Mueller, M.; van Ommen, B.; Williams, C.M.; and Mathers, J. C. (2007). Personalised nutrition: status and perspectives. *British Journal of Nutrition*, 98, pp 26-31. doi:10.1017/S0007114507685195.
- Kalmijn, M., & Monden, C. W. S. (2011). The division of labor and depressive symptoms at the couple level: Effects of equity or specialization? *Journal of Social and Personal Relationships*, 29(3), 358–374.
- Kampa, M., & Castanas, E. (2008). Human health effects of air pollution. *Environmental Pollution*, 151(2), 362-367. doi: http://dx.doi.org/10.1016/j.envpol.2007.06.012
- Kaplan, G.A., J.T. Salonen, R.D. Cohen et al. (1988): Social connections and mortality from all causes and cardiovascular disease: prospective evidence from eastern Finland. In: *Am. J. Epidemiol.*, 128, pp. 370-80.
- Kaplan, S. (2013). "Review: Pharmacological Pollution in Water." *Critical Reviews in Environmental Science and Technology* 43(10): 1074-1116.
- Kaput J, Dawson K. (2007) Complexity of type 2 diabetes mellitus data sets emerging from nutrigenomic research: a case for dimensionality reduction? *Mutat Res*. 2007 Sep; 622(1-2) 19-32. doi:10.1016/j.mrfmmm.2007.02.033.
- Karanikolas, M.; Mladovsky, P.; Thomson, S.; Basu, S.; Stuckler, D.; Mackenbach, J.; McKee, M. (2013). "Financial Crisis, austerity, and health in Europe". *Lancet* 381: 1323-1331.
- Kawachi, I., G.A. Colditz, A. Ascherio et al. (1996): A prospective study of social networks in relation to total mortality and cardiovascular disease in men in the USA. In: *J. Epidemiol. Commun. Hlth.*, 50. pp. 245-251.
- Kennedy, ET. (2005). The global face of nutrition: What can governments and industry do? IN: *JOURNAL OF NUTRITION*, Volume 135, Issue 4, pages 913-915. WOS:000228149500045.
- Kozo, Justine; Sallis, James F.; Conway, Terry L.; Kerr, Jacqueline; Cain, Kelli; Saelens, Brian E.; Frank, Lawrence D.; Owen, Neville (2012): Sedentary behaviors of adults in relation to neighborhood walkability and income. *Health Psychology*, Vol 31(6), Nov 2012, 704-713.

- <http://dx.doi.org/10.1037/a0027874>
- Lamb, S., & Kwok, K. C. S. (2016). A longitudinal investigation of work environment stressors on the performance and wellbeing of office workers. *Applied Ergonomics*, 52, 104-111. doi: <http://dx.doi.org/10.1016/j.apergo.2015.07.010>
- Leather, P., Beale, D., & Sullivan, L. (2003). Noise, psychosocial stress and their interaction in the workplace. *Journal of Environmental Psychology*, 23(2), 213-222. doi: 10.1016/s0272-4944(02)00082-8
- Leatherdale ST, Strath JM. (2007). Tobacco retailer density surrounding schools and cigarette access behaviors among underage smoking students. *Ann Behav Med*. 2007 Feb;33(1):105-11. PMID: 17291176
- Lespérance, F.; Frasure-Smith, N.; Talajic, M. (1996): Major depression before and after myocardial infarction: its nature and consequences. In: *Psychosom. Med.*, 58, pp. 99-110.
- Leung, CW; Epel, ES; Ritchie, LD; Crawford, PB; Laraia, BA. (2014). Food insecurity is inversely associated with diet quality of lower-income adults. *J Acad Nutr Diet*. 2014 Dec;114(12):1943-53.e2. doi: 10.1016/j.jand.2014.06.353.
- Lewis, A.; Eves, F. (2012). Testing the theory underlying the success of points-of-choice-prompts: A multi-component staircase intervention. In: *Psychology of Sport and Exercise*, 13 (2), pp. 126-132.
- Liebl, A., Haller, J., Jodicke, B., Baumgartner, H., Schlittmeier, S., & Hellbruck, J. (2012). Combined effects of acoustic and visual distraction on cognitive performance and well-being. *Applied Ergonomics*, 43(2), 424-434. doi: 10.1016/j.apergo.2011.06.017
- Lindsay, G.M, L.N. Smith, P. Hanlon et al. (2001): The influence of general health status and social support on symptomatic outcome following coronary artery bypass grafting. In: *Heart*, 85, pp. 80-86.
- Lock, K.; Smith, R.D.; Dangour, A.D.; Keogh-Brown, M.; Pigatto, G.; Hawkes, C.; Fisberg, R.M.; Chalabi, Z. (2010). Health, agricultural, and economic effects of adoption of healthy diet recommendations. IN: *The Lancet*, Volume 376, Issue 9753, 13–19 November 2010, Pages 1699–1709.
- Lyons, Gwynne; Watterson, Andrew. (2010). A Review of the Role Pesticides Play in Some Cancers: Children, Farmers and Pesticide Users at Risk? Report, CHEM Trust. <http://www.chemtrust.org.uk/wp-content/uploads/CHEM-Trust-Report-Pesticides-Cancer-July-2010.pdf>.
- Mack, Michael J., (2001), Minimally Invasive and Robotic Surgery. *JAMA*. 285(5):568-572. doi:10.1001/jama.285.5.568.
- Mairi, Levitt (2015) Could the organ shortage ever be met? *Life Sciences, Society and Policy* 11:6 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4513003/pdf/40504_2015_Article_23.pdf
- Margherita, A., O'Dorchai, S., & Bosch, J. (2009). Reconciliation between work, private and family life in the European Union. Luxembourg, Luxembourg: Office for Official Publications of the European Communities.
- Matthews, Anne; Cowburn, Gill; Rayner, Mike; Longfield, Jeanette; Powell Charlie. (2005). The marketing of unhealthy food to children in Europe. A report of Phase 1 of the 'Children, obesity and associated avoidable chronic diseases' project. www.ehnheart.org. or <http://www.ehnheart.org/projects/children-a-obesity/publication/54.html>.
- McFarlane, AC. (2010). The long-term costs of traumatic stress: intertwined physical and psychological consequences. *World Psychiatry*. 9:3–10.[Medline]
- Mirowsky, J. (1985). Depression and marital power: An equity model. *American Journal of Sociology*, 91(3), 557–592.
- Mohiuddin, Muhammad M, Avneesh K. Singh, Philip C. Corcoran, Robert F. Hoyt, Marvin L. Thom-

- as, David Ayares, Keith A. Horvath (2014), Genetically engineered pigs and target-specific immunomodulation provide significant graft survival and hope for clinical cardiac xenotransplantation, *The Journal of Thoracic and Cardiovascular Surgery*, 148 (3): 1106 DOI: 10.1016/j.jtcvs.2014.06.002
- Mustard, CA; Bielecky, A; Etches, J; Wilkins, R; Tjepkema, M; Amick, BC; Smith, PM; Aronson, KJ.(2013). Mortality following unemployment in Canada, 1991-2001. IN: *BMC Public Health* 2013, 13:441 doi:10.1186/1471-2458-13-441.
- Nicola, P. (2015). Diet and physical activity: risk factors and foresight. Presentation at FRESHER- 3rd Workshop on Drivers & Trends of the Future Developments of Non-communicable Diseases, Lisbon, 26th Oct 2015
- Nicoll, G. (2007): Spatial measures associated with stair case use. In: *American Journal of Health Promotion*, 21, (4S), pp. 346-352.
- Organic Farming EU: http://ec.europa.eu/agriculture/organic/organic-farming/what-is-organic-farming/index_en.htm
- Palep JH.(2009)Robotic assisted minimally invasive surgery. *Journal of Minimal Access Surgery*.;5(1):1-7. doi:10.4103/0972-9941.51313. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2699074/> Patrick, C.W., A.G. Mikos, L.V. McIntire (1998): *Frontiers in Tissue Engineering*.
- Personalized Medicine Coalition (2014): *THE CASE FOR PERSONALIZED MEDICINE*. 4th edition. Washington, D.C.
- Pol, E. & Ville, S. 2009. Social innovation: Buzz word or enduring term? *The Journal of Socio-Economics*, 38, 878-885.
- Prüss-Üstün, A. and Corvalán, C. (2006): Preventing disease through healthy environments. *World Health Organization* 2006; ISBN 92 4 159382 2; http://www.who.int/quantifying_ehimpacts/publications/preventingdisease.pdf?ua=1
- Ramachandran S. Vasan, (2006), Biomarkers of Cardiovascular Disease Molecular Basis and Practical Considerations, *MD. Circulation*; 113: 2335-2362 <http://circ.ahajournals.org/content/113/19/2335.full.pdf+html>
- Rayens, Mary Kay; Deborah, B. Reed RN. (2013). Predictors of Depressive Symptoms in Older Rural Couples: The Impact of Work, Stress and Health. IN: *The Journal of Rural Health* Volume 30, Issue 1, pages 59–68. DOI: 10.1111/jrh.12028.
- Reedy J, Krebs-Smith SM, Miller PE, Liese AD, Kahle LL, Park Y, Subar AF (2014). Higher diet quality is associated with decreased risk of all-cause, cardiovascular disease, and cancer mortality among older adults. *J Nutr*. 2014;144:881–89.
- Rekha, S., Daheron L, Liao S, Vardam T, Kamoun WS, Batista A, Buecker C, Schäfer R, Han X, Au P, Scadden DT, Duda DG, Fukumura D, Jain (2013 Jul 30) Generation of functionally competent and durable engineered blood vessels from human induced pluripotent stem cell RK. *Proc Natl Acad Sci U S A*. 110(31):12774-9 <http://www.pnas.org/content/110/31/12774.long>
- Rhodes, R. E., Mark, R. S., & Temmel, C. P. (2012). Adult Sedentary Behavior: A Systematic Review. *American Journal of Preventive Medicine*, 42(3), e3-e28. doi: <http://dx.doi.org/10.1016/j.amepre.2011.10.020> Barker DJ. Human growth and chronic disease: a memorial to Jim Tanner. *Ann Hum Biol*. 2012;39: 335–341.
- Richardson, David P. (2014). Ensuring That Nutrition and Health Claims in the European Union on Foods and Food (Dietary) Supplements Are Justified and Scientifically Substantiated. In: *Science and The Law: Analytical Data In Support Of Regulation In Health, Food, And The Environment*. Proceedings Paper. WOS:000344714200009.
- Riggs, D. S., Byrne, C. A., Weathers, F. W., & Litz, B. T. (1998). The quality of the intimate relation-

- ships of male Vietnam veterans: problems associated with posttraumatic stress disorder. *Journal of Traumatic Stress*, 11(1), 87e101.
- Rogers, S. J., & DeBoer, D. D. (2001). Changes in wives' income: Effects on marital happiness, psychological well-being, and the risk of divorce. *Journal of Marriage and Family*, 63(2), 458–472.
- Ross, C. E., & Mirowsky, J. (1995). Does employment affect health? *Journal of Health and Social Behavior*, 36(3), 230–243.
- Ross, C. E., & Wright, M. P. (1998). Women's work, men's work, and the sense of control. *Work and Occupations*, 25(3), 333–355.
- Roxburgh, S. (2004). 'There just aren't enough hours in the day': The mental health consequences of time pressure. *Journal of Health and Social Behavior*, 45(2), 115–131.
- Ruberman, W., E. Weinblatt, J.D. Goldberg et al. (1984): Psychosocial influences on mortality after myocardial infarction. In: *N. Engl. J. Med.*, 311, pp. 552-559.
- Sands, David C.; Morris, Cindy E.; Dratz, Edward A.; Pilgeram, Alice L. (2009). Elevating optimal human nutrition to a central goal of plant breeding and production of plant-based foods. IN: *PLANT SCIENCE*, Volume 177, Issue 5, pages 377-389. WOS:000269873800001.
- Schifferstein, Hendrik, N.J.; Peter A.M. Oude Ophuis, Peter, A.M. (1998). Health-related determinants of organic food consumption in The Netherlands. IN: *Food Quality and Preference*, Volume 9, Issue 3, May 1998, Pages 119–133. doi:10.1016/S0950-3293(97)00044-X.
- Seeman, T.E., L.F. Berman, D. Blazer et al., (1994): Social ties and support as modifiers of neuro-endocrine function. *MacArthur studies of successful aging*. In: *Ann. Behav. Med*, 16, pp. 95-106.
- Seidman MD, Standring RT. Noise and Quality of Life. *International Journal of Environmental Research and Public Health*. 2010;7(10):3730-3738. doi:10.3390/ijerph7103730.
- Shalev, A. Y., S. Freedman, et al. (1998). "Prospective Study of Posttraumatic Stress Disorder and Depression Following Trauma." *American Journal of Psychiatry* 155(5): 630-637
- Sinclair, S. & Baglioni, S. 2014. Social Innovation and Social Policy – Promises and Risks. *Social Policy and Society*, 13, 469-476.
- Skrove, M; Romundstad, P; Indredavik, MS. (2013). Resilience, lifestyle and symptoms of anxiety and depression in adolescence: the Young-HUNT study. IN: *SOCIAL PSYCHIATRY AND PSYCHIATRIC EPIDEMIOLOGY*, 2013 Mar; 48(3):407-16. doi: 10.1007/s00127-012-0561-2. Epub 2012 Aug 8.
- Slusser, W.M., W.G. Cumberland, B.L. Browdy et al. (2007): A school salad bar increases frequency of fruit and vegetable consumption among children living in low-income households. In: *Public Health Nutrition*, 10 (12), pp. 1490-1496.
- Smith KR, Corvalàn FC, Kjellström T (1999). How much ill health is attributable to environmental factors? *Epidemiology*, 10(5):573—584. Also available online at http://www.who.int/quantifying_ehimpacts/methods/en/smith.pdf.
- Smith-Jackson, T. L., & Klein, K. W. (2009). Open-plan offices: Task performance and mental workload. *Journal of Environmental Psychology*, 29(2), 279-289. doi: 10.1016/j.jenvp.2008.09.002
- Soler, R.E., K.D. Leeks, L.R. Buchanan et al. (2010): Point-of-decision prompts to increase stair use. A systematic review update. In: *American Journal of Preventive Medicine*, 38, 29, pp. 292-300.
- Soto,-Gutierrez A, Yagi H, Uygun BE, et al. (2010) Cell Delivery: From Cell Transplantation to Organ Engineering. *Cell transplantation*; 19(6): 655-665. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2957541/pdf/nihms227248.pdf>
- Stefler D, Pikhart H, Jankovic N, et al. Healthy diet indicator and mortality in Eastern European

- populations: prospective evidence from the HAPIEE cohort. *European journal of clinical nutrition*. 2014; 68(12):1346-1352. doi:10.1038/ejcn.2014.134.
- Steven S. Coughlin. (2013). *Post-Traumatic Stress Disorder and Cardiovascular Disease*. Chapter 7. IN: *Post-Traumatic Stress Disorder and Chronic Health Conditions*. eSBN: 978-0-87553-262-2, print ISBN: 978-0-87553-016-1. Read More: <http://ajph.aphapublications.org/doi/abs/10.2105/9780875530161ch07>
- The Coriell Institute for Medical Research web-site. Retrived from <https://www.coriell.org/research-services/biomarkers/role-of-biomarkers-in-medicine>
- The Future of Food and Farming (2011). Final Project Report. The Government Office for Science, London, https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/288329/11-546-future-of-food-and-farming-report.pdf.
- Tilman, D., & Clark, M. (2014). Global diets link environmental sustainability and human health. *Nature*, 515(7528), 518-522. doi: 10.1038/nature13959
- Titze, S., B.W. Martin, R. Seiler et al. (2001): A worksite intervention module encouraging the use of stairs: Results and evaluation. *Sozial- und Präventionsmedizin*, 46 (1), pp. 13-19.
- Turner, Rachel; Hawkes, Corinna; Waage, Jeff; Ferguson, Elaine; Haseen, Farhana; Homans, Hilary; Hussein, Julia; Johnston, Deborah; Marais, Debbi; McNeill, Geraldine; Shankar, Bhavani (2013). *Agriculture for improved nutrition: The current research landscape*. IN: *FOOD AND NUTRITION BULLETIN*. Article. WOS:000329556100001.
- Umans-Eckenhausen MA, Defesche JC, van Dam MJ, et al. Long-term compliance with lipid-lowering medication after genetic screening for familial hypercholesterolemia. *Arch Intern Med*. 2003; 163(1):658.
- UNEP United Nations Environment Programme (2015): <http://web.unep.org/ourplanet/september-2015/articles/help-wanted-industrial-transformation>
- US patent 20060029957, ZS Genetics. Systems and methods of analyzing nucleic acid polymers and related components. Issued July 2006
- Vaiserman, A. M. (2014). Early-life nutritional programming of longevity. [Review]. *Journal of Developmental Origins of Health and Disease*, 5(5), 325-338. doi: 10.1017/s2040174414000294
- Van Cauwenberg J, De Donder L, Clarys P, De Bourdeaudhuij I, Owen N, Dury S, De Witte N, Buffel T, Verté D, Deforche B (2014): Relationships of individual, social, and physical environmental factors with older adults' television viewing time. *J Aging Phys Act*. 2014 Oct;22(4):508-17. doi: 10.1123/japa.2013-0015.
- Vandevijvere, Stefanie; Chow, Carson C.; Hall, Kevin D.; Umali, Elaine; Swinburna, Boyd A. (2015). Increased food energy supply as a major driver of the obesity epidemic: a global analysis. IN: *Bull World Health Organ*. 2015 Jul 1; 93(7): 446–456. doi: 10.2471/BLT.14.150565.
- Varga, György Marko- et all. *J. Proteome Res.* (2005) , Discovery of Biomarker Candidates within Disease by Protein Profiling: Principles and Concepts., 4 (4), pp 1200–1212 Viet SM, Del-larco M, Dearborn DG, Neitzel R. Assessment of Noise Exposure to Children: Considerations for the National Children's Study. *Journal of pregnancy and child health*. 2014;1(1):105. doi:10.4172/2376-127X.1000105
- Walker, P; Rhubart-Berg, P; McKenzie, S; Kelling, K; Lawrence, RS. (2005). Public health implications of meat production and consumption. *Public Health Nutr.*, 8(4):348-56. PMID: 15975179.
- Walker, RJ; Gebregziabher, M; Martin-Harris, B; Egede, LE. (2014). Independent effects of socio-economic and psychological social determinants of health on self-care and outcomes in

- Type 2 diabetes. IN: Gen Hosp Psychiatry. 2014 Nov-Dec;36(6):662-8. doi: 10.1016/j.genhosppsy.2014.06.011. Epub 2014 Jul 9.
- Walker, RJ; Gebregziabher, M; Martin-Harris, B; Egede, LE. (2015). Understanding the influence of psychological and socioeconomic factors on diabetes self-care using structured equation modeling. PATIENT EDUCATION AND COUNSELING, 2015 Jan; 98(1):34-40. doi: 10.1016/j.pec.2014.10.002. (a).
- Walker, RJ; Gebregziabher, M; Martin-Harris, B; Egede, LE. (2015). Quantifying direct effects of social determinants of health on glycemic control in adults with type 2 diabetes. IN: Diabetes Technology & Therapeutics, 2015 Feb; 17(2): 80-7. doi: 10.1089/dia.2014.0166. Epub 2014 Oct 31. (b).
- Walter, C. M., & Du Randt, R. (2011). Socio-cultural barriers to physical activity among black isixhosa speaking professional women in the Nelson Mandela metropolitan municipality. South African Journal for Research in Sport Physical Education and Recreation, 33(2), 143-155.
- Wang, J. and X. M. Hu (2014). "Ecopharmacovigilance: Current state, challenges, and opportunities in China." Indian Journal of Pharmacology 46(1): 13-17.
- Webster A. (July 3, 2012), "3D printers and sugar used to create blood vessel networks", Retrived from <http://www.theverge.com/2012/7/3/3135317/3d-printer-sugar-blood-vessel>
- Welin, L., Tibblin, G., Tibblin B., et al. (1985): Prospective study of social influences on mortality: The study of men born in 1913 and 1923. In: Lancet, 1, pp. 915-918.
- WHO 2010. Set of recommendations on the marketing of foods and non-alcoholic beverages to children. Geneva, World Health Organization. (<http://www.who.int/dietphysicalactivity/publications/recsmarketing/en/>).
- WHO 2011. http://www.who.int/chp/media/news/releases/2011_1_marketing/en/
- WHO Global action plan for the prevention and control of noncommunicable diseases 2013-2020. World Health Organization 2013; ISBN 978 92 4 150623 6.
- WHO Regional Office for Europe (2006) Gaining health: The European Strategy for the Prevention and Control of Noncommunicable Diseases. Denmark, ISBN 92-890 2179 9. (<http://www.euro.who.int/pubrequest>).
- WHO. The global strategy on diet, physical activity and health. Geneva: World Health Organization, 2004. Hawkes C, Blouin C, Henson S, Drager N, Dubé L. Trade, food, diet and health: perspectives and policy options. Oxford: Wiley Blackwell, 2010.
- WHO/FAO. Codex alimentarius, animal food production (first edition). Geneva: World Health Organization; Rome: Food and Agriculture Organisation, 2008.
- WHO: Action Plan for implementation of the European Strategy for the Prevention and Control of Noncommunicable Diseases 2012–2016; World Health Organization 2012; ISBN 978 92 890 0268 4. (http://www.euro.who.int/__data/assets/pdf_file/0019/170155/e96638.pdf, accessed 18 November 2013).
- WHO: Environmental and occupational cancers (2011). Fact sheet N°350, March 2011 <http://www.who.int/mediacentre/factsheets/fs350/en/>
- WHO: Health and Environment in the WHO European Region: Creating resilient communities and supportive environments (2013). <http://www.euro.who.int/en/health-topics/environment-and-health/pages/european-environment-and-health-process-ehp/health-and-environment-in-the-who-european-region-creating-resilient-communities-and-supportive-environments>
- WHO: WHO European Healthy Cities Network <http://www.euro.who.int/en/health-topics/environment-and-health/urban-health/activities/healthy-cities/who-european-healthy-cities-network/six-strategic-goals>

- WHO Regional Office for Europe (2006). Gaining health: the European Strategy for the Prevention and Control of Noncommunicable Diseases. Copenhagen; (http://www.euro.who.int/__data/assets/pdf_file/0008/76526/E89306.pdf, accessed 18 November 2013).
- Williams, J.K., J.A. Vita and S.B. Manuck (1991): Psychosocial factors impair vascular responses of coronary arteries. In: *Circulation*, 84, pp. 2146-2153.
- Wills, J. B., & Brauer, J. R. (2012). Have children adapted to their mothers working, or was adaptation unnecessary? Cohort effects and the relationship between maternal employment and child well-being. *Social Science Research*, 41(2), 425-443. doi: 10.1016/j.ssresearch.2011.10.004
- World Health Organisation. (2005a). Briefing notes on psychosocial/mental health assistance to the tsunami affected region. Singapore: WHO South East Asia Office. Retrieved from http://www.alnap.org/tec/pdf/who_briefing_note_mentalhealth_Feb_2005.pdf
- World Health Organisation. (2005b). Gender considerations in disaster assessment. Geneva: WHO. Retrieved from <http://www.reliefweb.int/library/documents/2005/who-gen-11jan.pdf>
- World Health Organisation. (2005c). Mental health and psychosocial care of children affected by natural disasters. Geneva: WHO. Retrieved from <http://www.reliefweb.int/library/documents/2005/who-gen-11jan.pdf>
- Wu, S.Y., D. Cohen, Y.Y. Shi et al. (2011): Economic analysis of physical activity interventions. In: *American Journal of Preventive Medicine*, 40 (2), pp. 149-158.
- Wu, S.Y., D. Cohen, Y.Y. Shi et al. (2011): Economic analysis of physical activity interventions. In: *American Journal of Preventive Medicine*, 40 (2), pp. 149-158.
- www.fao.org/docs/eims/upload/307711/Toulmin_Future%20of%20Food_Brief%2042.pdf.
- Yancey, AK; Cole, BL; Brown, R; Williams, JD.; Hillier, A.; Kline, RS.; Ashe, M.; Grier, SA.; Backman, D.; McCarthy, WJ. (2009). A cross-sectional prevalence study of ethnically targeted and general audience outdoor obesity-related advertising. *Milbank Q.* 2009 Mar; 87(1):155-84. doi: 10.1111/j.1468-0009.2009.00551.x.
- Zhu, X., Yu, C.-Y., Lee, C., Lu, Z., & Mann, G. (2014). A retrospective study on changes in residents' physical activities, social interactions, and neighborhood cohesion after moving to a walkable community. *Preventive Medicine*, 69, Supplement, S93-S97. doi: <http://dx.doi.org/10.1016/j.ypmed.2014.08.013>.