Chapter 2

Chapter 2

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CARDIOVASCULAR DISEASES (CVD)

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2.6. GENERAL EPIDEMIOLOGY OF NON-COMMUNICABLE DISEASES
CARDIOVASCULAR DISEASES

The public health care means the practical activity of theoretical based preventive medicine,which is a pre-eminent influencing factor of the health status of people . Among these determinant factors have special importance the lifestyle and life circumstances ,the social and economic environment and epigenetical influences, the different health-damaging factors and its abuse,more than the age and gender and the genetic factors .The most informative indicators of their effects on the health seemed the

life expectancy and the mortality statistics in their specific distribution . Investigation of them is a crucial requirement of this learning .The last years and decades in the developed and developing countries also the greatest epidemiological problems were represented with the wide- range occured non communicable diseases enhanced appeareance of which seems to be clearly connected to these factors . Increased appereance of them is in primary connection (dependence) of the enhancing phenomen of urbanisation ang globalisation having the durest effect on human life with the increasing production of industry –not negligently on the field of foods also-generating by the easy of attainment of them and the other harmful processes and effects as : lower physical activity constructed in the life style(cars ,hypermarkets ,ample choice of different products ,wide use of free ranged tobacco,alcohol-products and other s enriched in harmful on health contents of consumer's goods. Have great importance in this question the connecting stressed and incertained life enforced with the legislational gaps and immoralties increasing the depressive factors influencing the immunosystem badly at once. The effect of psychical stress on the imunosystem and consequently of the diseases are also well-known phenomens.
Nowadays more than 90% of all deaths caused by representants of this illness-group:
-cardiovascular diseases
-tumours
-diseases of digestive system
-diseases of respiratory system and
-violence
Enormous number of diseases with low fatality case among the non –communicable diseases improves the meaning of this extented disease-group. Among the goals of public health the first place is to roll back them because of their extraordinary medical and social dangers.
There are 4 main steps to surpass these diseases:
1.to assess the situation the extension range of the given disease in the population,using epidemiological methods(demographics)
2.data –collection about the causes and risk-factors for the development of disease(methods of analytical epidemiology and animal-experiments)
3.to elaborate preventional methods and arrangements for decrease the extension of disease and realise the early recognition of the disease with intervening the development of late their consequences
4.setting in law the good preventive measures and to control them.
among these points the greatest importance has the epidemiological method –collection directed on the answering of these problems.

2.6.1.1. Noncommunicable diseases (NCD) short review

- **A total of 57 million deaths occurred in the world during 2008; 36 million (63%) were due to NCDs,**
- **principally**
- **-cardiovascular diseases,**
- **-diabetes,**
- **-cancer and**

- **-chronic respiratory diseases**
- **Nearly 80% of these NCD deaths (29 million) occurred in low- and middle-income countries**
- **The leading causes of NCD deaths in 2008 were:**
- **-cardiovascular diseases (17 million deaths, or 48% of NCD deaths);**
- **-cancers (7.6 million, or 21% of NCD deaths); and**
- **-respiratory diseases, including asthma and chronic obstructive pulmonary disease (COPD), (4.2 million).**
- **Diabetes caused an additional 1.3 million deaths.**
-
- **Over 80% of cardiovascular and diabetes deaths, and**
- **almost 90% of deaths from COPD, occurred in low- and middle-income countries**

- **Mortality/morbidity**
  Mortality and morbidity due to Cardiovascular Disease (CVD), cancer, chronic respiratory diseases and diabetes
- **see here „total NCD death-view interactive map „-to see the global situation by countries**

Situation

Of the 57 million global deaths in 2008, 36 million, or 63%, were due to noncommunicable diseases.

2.6.1.2. Death rates: World Bank regions

In this section:

- East Asia and Pacific
- Europe and Central Asia
- High income
- Latin America and Caribbean
- Middle East and North Africa
- South Asia
- Sub-Saharan Africa

2.6.1.3. The top 10 causes of death

Fact sheet N°310
Updated July 2013

The 10 leading causes of death in the world, 2000 and 2011

Ischaemic heart disease,

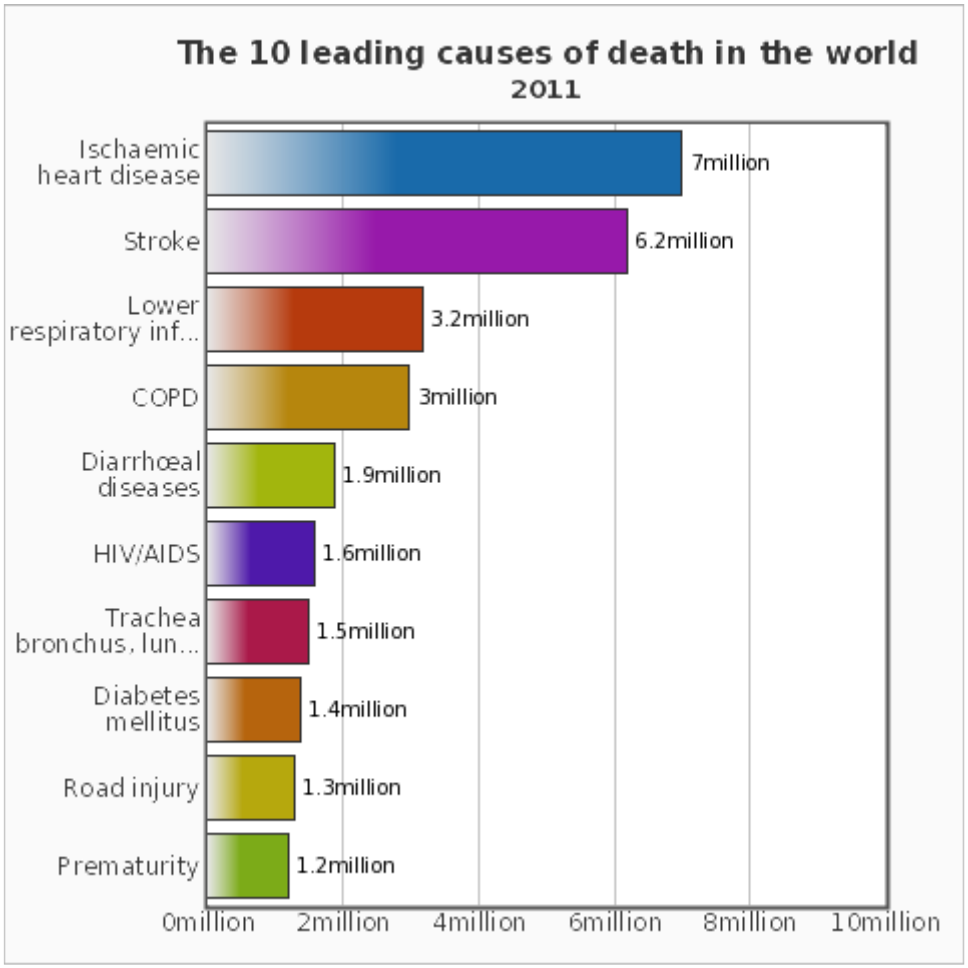
-stroke,

-lower respiratory infections,

chronic obstructive lung disease, diarrhoea and HIV/AIDS have remained the top major killers during the past decade.

Tuberculosis is no longer among the 10 leading causes of death, but is still among the top 15, killing one million people in 2011.

Chronic diseases cause increasing numbers of deaths worldwide. Lung cancers (along with trachea and bronchus cancers) caused 1.5 million (2.7%) deaths in 2011, up from 1.2 million (2.2%) deaths in 2000. Similarly, diabetes caused 1.4 million (2.6%) deaths in 2011, up from 1.0 million (1.9%) deaths in 2000.



atherosclerosis in the world 2012

http://www.nationmaster.com/graph/mor_ath-mortality-atherosclerosis

Showing latest available data.

Rank	Countries	Amount
# 1	Poland:	29,511 deaths
# 2	Romania:	16,215 deaths
# 3	United States:	14,393 deaths
# 4	Germany:	13,920 deaths
# 5	Czech Republic:	10,474 deaths
# 6	Egypt:	7,824 deaths
# 7	Hungary:	7,404 deaths
# 8	Spain:	4,217 deaths
# 9	Cuba:	3,143 deaths
# 10	Slovakia:	2,490 deaths
# 11	Brazil:	2,457 deaths
# 12	Sweden:	2,062 deaths
# 13	Argentina:	1,836 deaths
# 14	Netherlands:	1,331 deaths
# 15	Canada:	1,313 deaths
# 16	Austria:	1,256 deaths
# 17	Latvia:	1,235 deaths
# 18	Lithuania:	1,071 deaths
# 19	Japan:	1,043 deaths
# 20	Denmark:	954 deaths
	Total:	131,222 deaths
	Weighted average:	2,343.3 deaths

Mortality Statistics > Cardiomyopathy (most recent) by country

http://www.thrombosisadviser.com/en/_global/sitemap/

http://www.thrombosisadviser.com/en/acs/a-leading-cause-of-mortality/

Mortality Statistics > Cardiac arrest (most recent) by country

figures for:

- **Cardiac arrest**
- **Cardiac arrest with successful resuscitation**
- **Sudden cardiac death, so described DEFINITION: Total for all ages and sexes. Database compiled January 2004. Total of**
- **Cardiac arrest, unspecifiedl> The mortality statistic**

VIEW DATA: Totals **Definition** **Source** **Printable version**

Bar Graph **Pie Chart** **Map**

Health statshun usa.doc

Health stats: Hungary vs United States

	 Hungarian Health stats	 American Health stats
Abortions	76,957 Ranked 10th.	1,210,880 Ranked 2nd. **15 times more** than Hungary
Age of women at first childbirth	25.1 years old Ranked 13th. **1% more** than United States	24.9 years old Ranked 15th.
Breast cancer incidence	26.6 per 100,000 females Ranked 7th. **25% more** than United States	21.2 per 100,000 females Ranked 17th.
Daily smokers	33.8% Ranked 3rd. **93% more** than United States	17.5% Ranked 29th.
Death from cancer	411 deaths per 100,000 peopl Ranked 3rd. **28% more** than United States	321.9 deaths per 100,000 peopl Ranked 9th.
Drug access	95% Ranked 43rd.	95% Ranked 27th.
Heart disease deaths	192.1 per 100,000 people Ranked 2nd. **80% more** than United States	106.5 per 100,000 people Ranked 13th.
Hospital beds	8.3 per 1,000 people Ranked 10th. **131% more** than United States	3.6 per 1,000 people Ranked 27th.
Hospital beds > per 1,000 people	7.8 per 1,000 people Ranked 9th in 2003. **136% more** than United States	3.3 per 1,000 people Ranked 37th in 2003.
Maternal mortality	15 per 100,000 Ranked 108th. **88% more** than United States	8 per 100,000 Ranked 121st.
Obesity	18.8% Ranked 8th.	30.6% Ranked 1st. **63% more** than Hungary
Physicians > per 1,000 people	3.2 per 1,000 people Ranked 16th in 2002. **39% more** than United States	2.3 per 1,000 people Ranked 31st in 2002.
Spending > Per person	318 Ranked 37th.	4,271 Ranked 1st. **12 times more** than Hungary
Suicide rate > Females	8.6 Ranked 6th. **91% more** than United States	4.5 Ranked 17th.
Suicide rate > Gender ratio	3.3 per 100,000 people Ranked 39th.	4.5 per 100,000 people Ranked 17th. **36% more** than Hungary
Suicide rate > Males	37.1 Ranked 1st. **110% more** than United States	17.7 Ranked 17th.
Teen birth rate	41 Ranked 7th.	64 Ranked 1st. **56% more** than Hungary
Teenage pregnancy	9,175 births	494,357 births

Statistics health topics
http://www.who.int/topics/statistics/en/

Cardiovascular diseases health topic
http://www.who.int/topics/cardiovascular_diseases/en/

Estimates and analysis are available at:
http://www.who.int/gho/mortality_burden_disease/en/index.html
For further information about the estimates and methods, please contact healthstat@who.int
estimates for 2004 by cause for WHO Member States [Internet]. Geneva: World Health Organization; 2009. Available from:http://www.who.int/healthinfo/global_burden_disease/estimates_country/en/index.html
SOURCE: World Health Organisation Statistical Information System

Mortality Statistics > Death rate, crude > per 1,000 people (most recent) by country

DEFINITION: Crude death rate indicates the number of deaths occurring during the year, per 1,000 population estimated at midyear. Subtracting the crude death rate from the crude birth rate provides the rate of natural increase, which is equal to the population growth rate in the absence of migration.

VIEW DATA: **Totals** Definition Source Printable version

Bar Graph **Map**

Showing latest available data. Select another time period:

Rank	Countries	Amount	Date
# 1	Botswana:	27.06 per 1,000 people	2005
# 2	Lesotho:	25.39 per 1,000 people	2005
# 3	Sierra Leone:	22.95 per 1,000 people	2005
# 4	Zimbabwe:	22.9 per 1,000 people	2005
# 5	Central African Republic:	21.92 per 1,000 people	2005
# 6	Zambia:	21.88 per 1,000 people	2005
# 7	Angola:	21.54 per 1,000 people	2005
# 8	South Africa:	21.38 per 1,000 people	2005
# 9	Afghanistan:	21.1 per 1,000 people	1987
# 10	Malawi:	20.63 per 1,000 people	2005
# 11	Equatorial Guinea:	20.55 per 1,000 people	2005
# 12	Liberia:	20.43 per 1,000 people	2005
# 13	Swaziland:	20.26 per 1,000 people	2005
# 14	Niger:	20.19 per 1,000 people	2005
# 15	Mozambique:	19.99 per 1,000 people	2005
# 16	Chad:	19.72 per 1,000 people	2005
# 17	Congo, Democratic Republic of the:	19.65 per 1,000 people	2005
# 18	Guinea-Bissau:	19.37 per 1,000 people	2005
# 19	Ethiopia:	19.16 per 1,000 people	2005
# 20	Nigeria:	18.82 per 1,000 people	2005

# 38	Hungary:	13.5 per 1,000 people	2005

# 39	**Mauritania**:	13.37 per 1,000 people	2005

SOURCE: World Development Indicators database

See also

See this stat for year: 2005 2004 2003 2002 2001 2000 1999 1998 1997 1996 1995 1994 1993 1992 1991 1990 1989 1988 1987 1986 1985 1984 1983 1982 1981 1980 1979 1978 1977 1976 1975 1974 1973 1972 1971 1970 1969 1968 1967 1966 1965 1964 1963 1962 1961 1960

NOTES: These statistics are derived from official causes of death detailed on certificates of death by each country. Rather than being a true indicator of the number of deaths attributed to a particular cause, mortality statistics reveal more about a particular country's reporting processes.

Mortality Statistics > Heart failure (most recent) by country

DEFINITION: Total for all ages and sexes. Database compiled January 2004. Total of figures for:

- Heart failure
- Congestive heart failure
- Left ventricular failure
- Heart failure, unspecifiedl> The mortality statistics consist of deaths registered i

VIEW DATA: **Totals** Definition Source Printable versio

Bar Graph Pie Chart Map

"Mortality > Heart failure" also viewed these world stats:

- Other specified diabetes mellitus
- Unspecified diabetes mellitus
- Lack of expected normal physiological development
- Disorders of orbit
- Exposure to excessive natural heat
- Other sudden death, cause unknown
- Other neurotic disorders
- Q fever
- Fall involving chair
- Abnormal involuntary movements

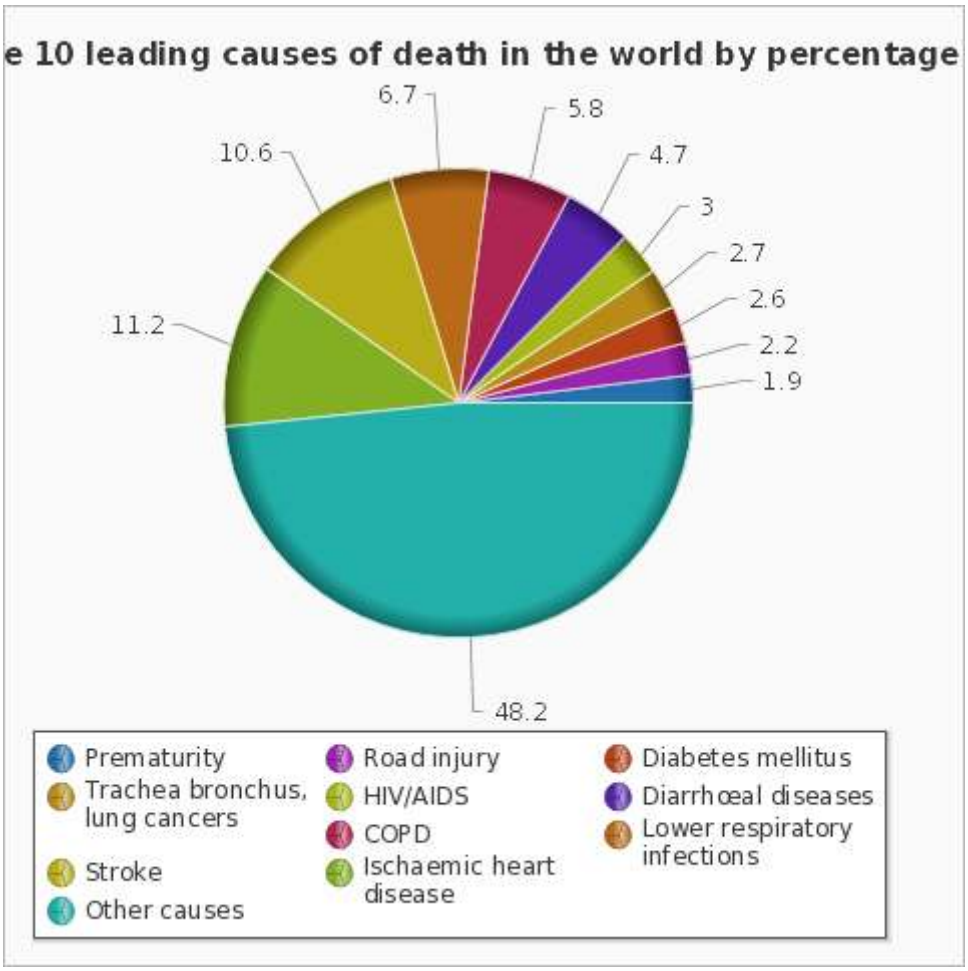
Total:	396,406 deaths
Weighted average:	6,834.6 deaths

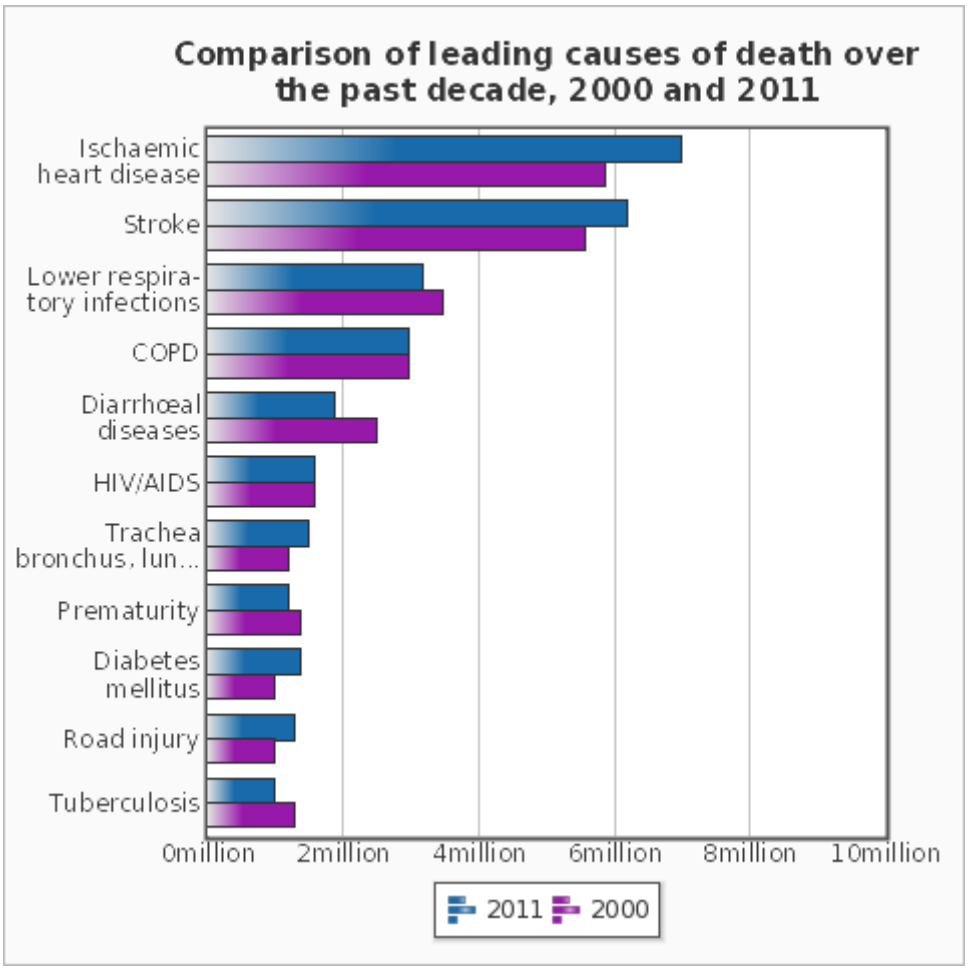
SOURCE: World Health Organisation Statistical Information System
SEE ALSO

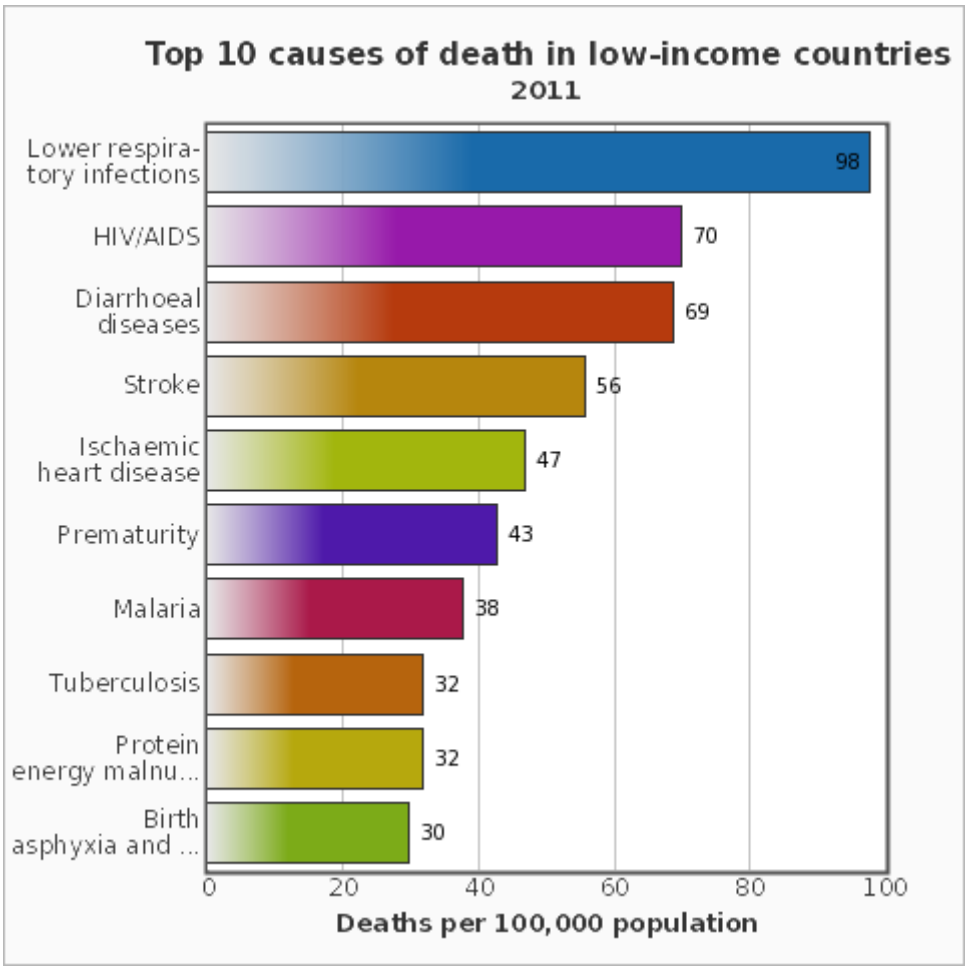
NOTES: These statistics are derived from official causes of death detailed on certificates of death by each count attributed to a particular cause, mortality statistics reveal more about a particular country's reporting processes.

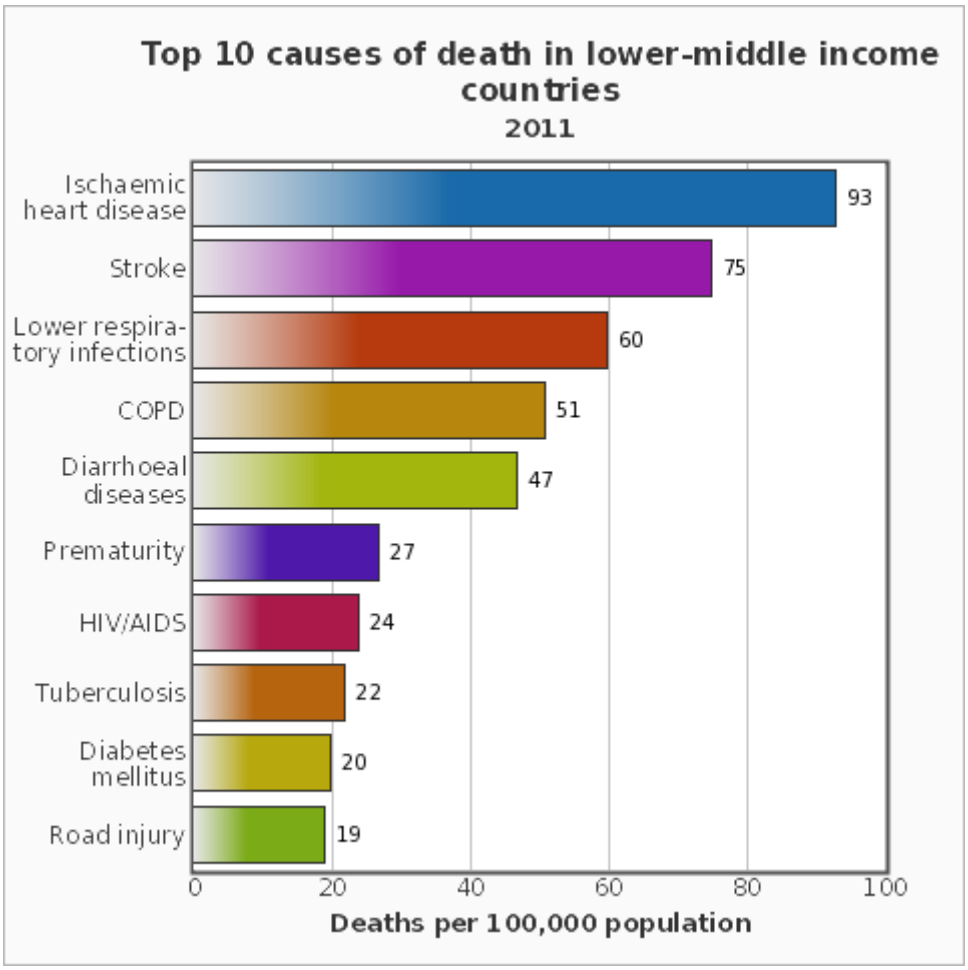
Search for: congestive heart failure graph statistics; heart failure peru

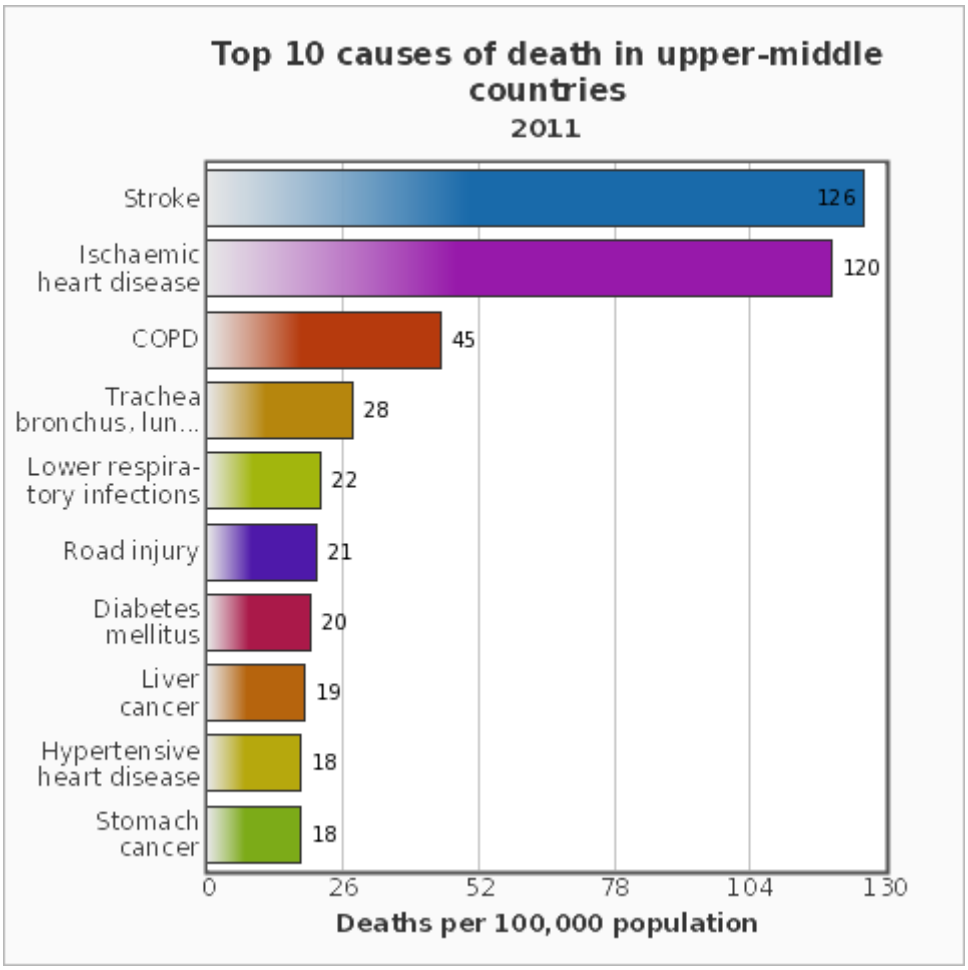
TOP STATS

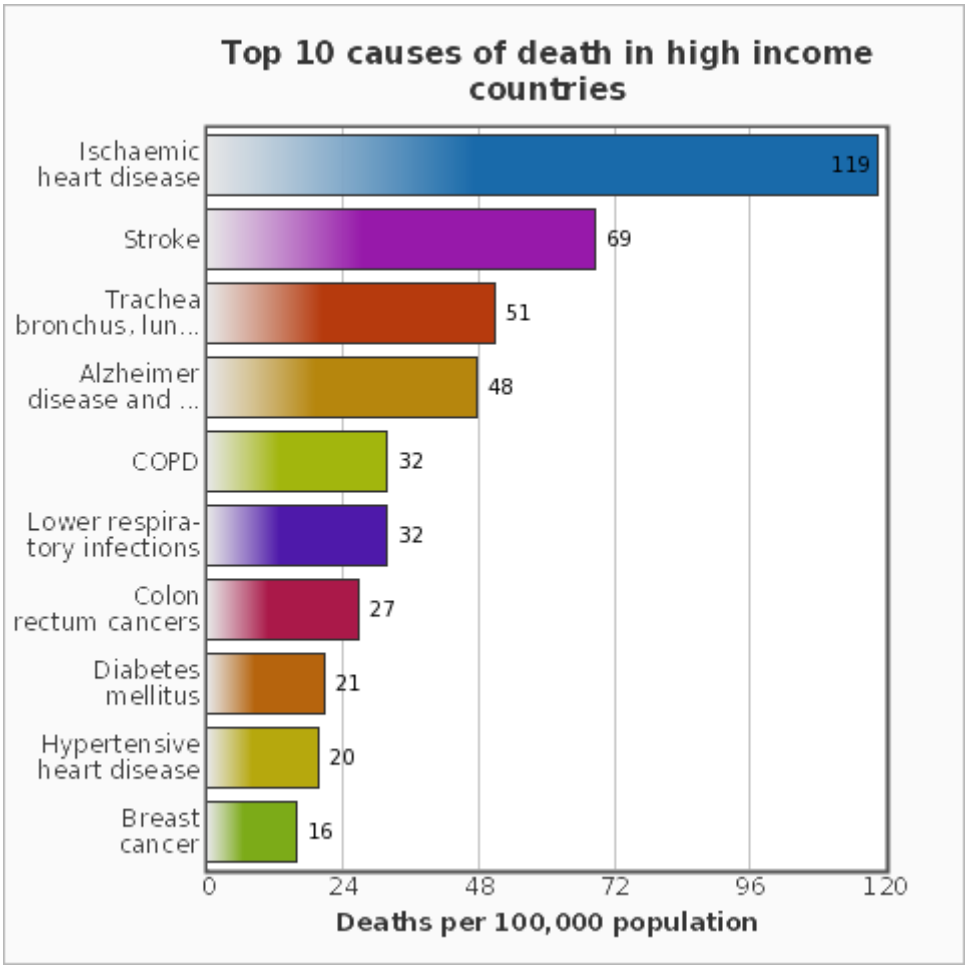

e 10 leading causes of death in the world by percentage
6.7
5.8
10.6
4.7
3
2.7
2.6
11.2
2.2
1.9
48.2
Prematurity
Trachea bronchus, lung cancers
Stroke
Other causes
Road injury
HIV/AIDS
COPD
Ischaemic heart disease
Diabetes mellitus
Diarrhœal diseases
Lower respiratory infections


Comparison of leading causes of death over the past decade, 2000 and 2011
Ischaemic heart disease
Stroke
Lower respira-tory infections
COPD
Diarrhoeal diseases
HIV/AIDS
Trachea bronchus, lun...
Prematurity
Diabetes mellitus
Road injury
Tuberculosis
0million
2million
4million
6million
8million
10million
2011
2000


Top 10 causes of death in low-income countries
2011
Lower respira-tory infections
98
HIV/AIDS
70
Diarrhoeal diseases
69
Stroke
56
Ischaemic heart disease
47
Prematurity
43
Malaria
38
Tuberculosis
32
Protein energy malnu...
32
Birth asphyxia and ...
30
0
20
40
60
80
100
Deaths per 100,000 population


Top 10 causes of death in lower-middle income countries
2011
Ischaemic heart disease
93
Stroke
75
Lower respira-tory infections
60
COPD
51
Diarrhoeal diseases
47
Prematurity
27
HIV/AIDS
24
Tuberculosis
22
Diabetes mellitus
20
Road injury
19
0
20
40
60
80
100
Deaths per 100,000 population


Top 10 causes of death in upper-middle countries
2011
Stroke
126
Ischaemic heart disease
120
COPD
45
Trachea bronchus, lun...
28
Lower respira-tory infections
22
Road injury
21
Diabetes mellitus
20
Liver cancer
19
Hypertensive heart disease
18
Stomach cancer
18
0
26
52
78
104
130
Deaths per 100,000 population



2.6.1.3. Why do we need to know the reasons people die?

Measuring how many people die each year and why they died is one of the most important means – along with gauging

-how diseases and injuries are affecting people

- for assessing the effectiveness of a country's health system.

Cause-of-death statistics help health authorities determine their focus for public health actions.

A country where deaths from heart disease and diabetes rapidly rise over a period of a few years, for example, has a strong interest in starting a vigorous programme to encourage lifestyles to help prevent these illnesses. Similarly, if a country recognizes that many children are dying of malaria, but only a small portion of the health budget is dedicated to providing effective treatment, it can increase spending in this area.

High-income countries have systems in place for collecting information on causes of death in the population. Many low- and middle-income countries do not have such systems, and the numbers of deaths from specific causes have to be estimated from

incomplete data. Improvements in producing high quality cause-of-death data are crucial for improving health and reducing preventable deaths in these countries.

2.6.1.4 Major causes of death

In 2011, an estimated 55 million people died worldwide.

What diseases and injuries cause the most death and disability globally?

http://www.healthmetricsandevaluation.org/gbd/visualizations/regional

on this web adress are given data (IHME Regional Visualization –interactive maps and figures 1a-d) are compared the changed relations in global death by causes ,sex and age

Noncommunicable diseases were responsible for 2/3 of all deaths globally in 2011, up from 60% in 2000. The four main NCDs are cardiovascular diseases, cancers, diabetes and chronic lung diseases. Communicable, maternal, perinatal and nutrition conditions collectively were responsible for a quarter of global deaths, and injuries caused 9% of all deaths. cardiovascular diseases killed nearly 17 million people in 2011, that is 3 in every 10 deaths. Of these, 7 million people died of ischaemic heart disease and 6.2 million from stroke.

In terms of number of deaths, 26 million (nearly 80%) of the 36 million of global NCD deaths in 2011 occurred in low- and middle-income countries. In terms of proportion of deaths that are due to NCDs,

high-income countries have the highest proportion – 87% of all deaths were caused by NCDs – followed by upper-middle income countries (81%). The proportions are lower in low-income countries (36%) and lower-middle income countries (56%).

Tobacco use is a major cause of many of the world's top killer diseases – including cardiovascular disease, chronic obstructive lung disease and lung cancer. In total, tobacco use is responsible for the death of about 1 in 10 adults worldwide. Smoking is often the hidden cause of the disease recorded as responsible for death.

In high-income countries, 7 in every 10 deaths are among people aged 70 years and older. People predominantly die of chronic diseases: cardiovascular diseases, cancers, dementia , chronic obstructive lung disease or diabetes. Lower respiratory infections remain the only leading infectious cause of death. Only 1 in every 100 deaths are among children under 15 years.

In low-income countries, nearly 4 in every 10 deaths are among children under 15 years, and only 2 in every 10 deaths are among people aged 70 years and older. People predominantly die of infectious diseases: lower respiratory infections, HIV/AIDS, diarrhoeal diseases, malaria and tuberculosis collectively account for almost one third of all deaths in these countries. Complications of childbirth due to prematurity, and birth asphyxia and birth trauma are among the leading causes of death, claiming the lives of many newborns and infants.

Ischaemic heart disease, stroke, lower respiratory infections, chronic obstructive lung disease, diarrhoea and HIV/AIDS have remained the top major killers during the past decade.

Noncommunicable diseases (NCDs) were responsible for two-thirds (36 million) of all deaths globally in 2011, up from 60% (31 million) in 2000.

Cardiovascular diseases alone killed nearly 2 million more people in 2011 than in the year 2000.

Tuberculosis, while no longer among the 10 leading causes of death in 2011, was still among the 15 causes, killing one million people in 2011. Maternal deaths have dropped from 420 000 in the year 2000 to 280 000 in 2011, but are still unacceptably high: nearly 800 women die due to complications of pregnancy and childbirth every day.

Injuries continue to kill 5 million people each year. Road traffic injuries claimed nearly 3500 lives each day in 2011 – about 700 more than in the year 2000 – making it among the top 10 leading causes in 2011.

In 2011, 6.9 million children died before reaching their fifth birthday; almost all (99%) of these deaths occurred in low- and middle-income countries. The major killers of children aged less than five years were pneumonia, prematurity, birth asphyxia and birth trauma, and diarrhoeal diseases. Malaria was still a major killer in sub-Saharan Africa, causing about 14% of under-five deaths in the region.

About 43% of deaths in children younger than 5 years in 2011 occurred within 28 days of birth – the neonatal period. The most important cause of death was prematurity, which was responsible for one-third of all deaths during this period.

imagine a diverse international group of 1000 individuals representative of the women, men and children from all over the globe who died in 2011.

Of those 1000 people:

- **141 would have come from low-income countries, 368 from lower-middle-income countries, 322 from upper-middle-income countries and 169 from high-income countries.**
- **153 would have been children under 15 years of age, 412 adults aged 15-69 years old and 435 adults aged 70 years and older.**

More than half (517) of these 1000 deaths would have been caused by the following 10 conditions:

A new report published by the World Health Organization calculates that

almost 2/3 of all worldwide deaths are now in the result of non-communicable diseases.

These mainly comprise cardiovascular diseases, cancers, diabetes and chronic lung diseases, and their epidemic, is being driven by powerful forces now touching every region of the world: demographic ageing, rapid unplanned urbanisation, and the

globalisation of unhealthy lifestyles. While many chronic conditions develop slowly, changes in lifestyles and behaviours are occurring with a stunning speed and sweep. The report also points out that,

contrary to popular opinion, nearly 80% of deaths from non-communicable disease occur in low- and middle-income countries.

And the culprit risk factors

-tobacco use,

-unhealthy diet,

-insufficient physical activity

-harmful use of alcohol and the

–stressed and the unstable,uncertained life of masses of people are now the "pervasive aspects of economic transition, rapid urbanization and 21st-century life".

Within the context of cardiovascular diseases this is a reminder of how important the prevention and management of chronic disease - and its impact .We have made great progress in managing CVD in the acute phase, but the WHO research emphasises the extent to which avoidable risk factors and unhealthy lifestyle contribute to global mortality.

only through simple improvements in lifestyle - with attention to diet, exercise, smoking and weight - will this epidemic of chronic disease be reversed. This can only be achieved through the concerted efforts of populations, professionals and politicians.

Among "best-buys" recommended by the WHO report at the population level are restrictions on smoking (sales and community bans), raised taxes on tobacco and alcohol, reduced salt in foods, the replacement of trans-fats with polyunsaturated fat, and public awareness about diet and physical activity.

Best-buys at the individual intervention level include counselling and multidrug therapy, including glycaemic control for diabetes, and aspirin therapy for AMI.(acute myocardial infarceation)

The report estimates that the worldwide number of deaths attributable to non-communicable disease will increase by 15% between 2010 and 2020, with the greatest increases in Africa and South-East Asia. Most of these deaths will be associated with the four risk factors noted above. Tobacco use, for example, if unchecked will account for 10% of all deaths by 2010.

The report emphasises the power of primary prevention initiatives, and particularly their effect on CVD. More than half the dramatic decline in CHD mortality in the UK between 1981 and 2000 was attributed to risk factor reduction. The WHO's own MONICA data indicate that population-wide primary prevention and individual

healthcare interventions go hand-in-hand to reduce the burden of CVD. Yet many of these initiatives and interventions are unavailable in many poor resource countries.

Chronic non-communicable diseases kill 86% of all people in the WHO European Region.

-Cardiovascular diseases,

-cancer,

- respiratory diseases,

-diabetes, kidney and

- liver diseases account for more than 40% the disease burden in Europe.

Heart disease, stroke and diabetes alone are projected to lead to loss of national income in the billions, e.g. almost $33 billion in the United Kingdom (from 2005 to 2015).

2.6.1.5. Cardiovascular Diseases in general

EU-cardiovascular-disease-statistics-2012.pdf

cvdglobalatlaswho_eng.pdf

WHO health 2011.pdf

cardiovascular2012-european-cvd-statistics-visuals.aspx.htm

cvd australiaAbsoluteCVD_GL_webready.pdf

cardiovascPocketGL.ENGLISH.AFR-D-E.rev1.pdf

The cardiovascular diseases and the most frequently occured atherosclerotic organic manifestations at fist range (coronary heart disease,ischemic cerebrovascular events.,disease of peripheric arterias) mean the greatest health problem of the developed countries because of the caused death,invalid and needs in hospitalization which represent higher burden as the summary of other diseases together

Cardiovascular disease (also called heart disease) is a class of diseases that involve the heart, the blood vessels (arteries, capillaries, and veins) or both.[1]

Cardiovascular disease refers to any disease that affects the cardiovascular system, principally cardiac disease, vascular diseases of the brain and kidney, and peripheral arterial disease.[2] The causes of cardiovascular disease are diverse but atherosclerosis and/or hypertension are the most common. Additionally, with aging come a number of physiological and morphological changes that alter cardiovascular function and lead to subsequently increased risk of cardiovascular disease, even in healthy asymptomatic individuals.[3]

Cardiovascular disease is the leading cause of deaths worldwide, though since the 1970s, cardiovascular mortality rates have declined in many high-income countries.[4][5] At the same time, cardiovascular deaths and disease have increased at a fast rate in low- and middle-income countries.[6] Although cardiovascular disease usually affects older adults, the antecedents of cardiovascular disease, notably atherosclerosis, begin in early life, making primary prevention efforts necessary from childhood.[7] There is therefore increased emphasis on preventing atherosclerosis by modifying risk factors, such as healthy eating, exercise, and avoidance of smoking tobacco.

Cardiovascular diseaes are the most frequent diseases almost in all countries of the world and give the leading cause of death in them.
The pathophysiological basis of them is the atheroscerosis developing for years and symptomes of the disease appears only at the devloped stadiums and in high proportions become fatal,mainly the cases of ischemic heart diseases as AMI and stenocardial attacks and at people diagnosed with high risk-factor influence.
The main health-advices to prevent the disease and the fatal outcomes are:
-avoid smoking
-healthy nutrition
-enough physical activity
-decrease the BMI and the waist/hip ratio to the healthy levels
-hold on the healthy level also the blood pressure,blood-cholesterol and the LDL-levels ,and the blood-glucose level

MORTALITY FROM HEART DISEASE AND STROKE

Cardiovascular diseases are the main cause of mortality in almost all EU member states, accounting for 36% of all deaths in the region in 2010.

They cover a range of diseases related to the circulatory system, including ischemic heart disease (known as IHD, or heart attack) and cerebro-vascular disease (or stroke).
Together, IHD and stroke comprise 60% of all cardiovascular deaths, and caused more than one-fifth of all deaths in EU member states in 2010.
Ischemic heart disease is caused by the accumulation of fatty deposits lining the inner wall of a coronary artery, restricting blood flow to the heart.
IHD alone was responsible for 13% of all deaths in EU member states in 2010.
Mortality from IHD varies considerably, however ; Baltic countries report the highest IHD mortality rates, Lithuania for both males and females, followed by Latvia, the Slovak Republic and Estonia. IHD mortality rates are also relatively high in Finland and Malta, with rates several times higher than in France, Portugal, the Netherlands and Spain. There are regional patterns to the variability in IHD mortality rates. Besides the Netherlands and Luxembourg, the countries with the lowest IHD mortality rates are four countries located in Southern Europe: France, Italy, Portugal and Spain, with Cyprus and Greece also having low rates. This lends support to the commonly held hypothesis that there are underlying risk factors, such as diet, which explain differences in IHD mortality across countries.
Death rates for IHD are much higher for men than for women in all countries (Figure 1.4.1).

On average across EU member states, IHD mortality rates in 2010 were nearly two times greater for men.
The disparity was greatest in Cyprus, France and Luxembourg, with male rates two-tothree times higher, and least in Malta, Romania and the Slovak Republic, at 60% higher. Since the mid 1990s, IHD mortality rates have declined in nearly all countries. The decline has been most remarkable in Denmark, Ireland, the Netherlands and the United Kingdom. Estonia and Norway also saw IHD mortality rates cut by one-half or more, although rates in Estonia are still high. Declining tobacco consumption contributed significantly to reducing the incidence of IHD, and consequently to reducing mortality rates.
Improvements in medical care have also played a part [see Indicator 3.8 "Cardiac procedures (coronary angioplasty)"]. A small number of countries, however, have seen little or no decline since 1995. Declines in Hungary, Poland and the Slovak Republic have been moderate, at under 20%.
Stroke was the underlying cause for about 9% of all deaths in 2010. It is a loss of brain function caused by the disruption of the blood supply to the brain. In addition to being an important cause of mortality, the disability burden from stroke is substantial (Moon *et al.*, 2003). As with IHD, there are large variations in stroke mortality rates across countries. Again, the rates are highest in Baltic and central European countries, including Bulgaria, Hungary, Latvia, Lithuania, Romania and the Slovak Republic. They are the lowest in Cyprus, France, Ireland and the Netherlands. Rates are also low in Switzerland, Iceland and Norway. Looking at trends over time, stroke mortality has decreased in all EU member states since 1995, with a more pronounced fall after 2003. Rates have declined by around 60% in Austria, Estonia and Portugal. The decline has only been moderate in Lithuania, Poland and the Slovak Republic. As with IHD, the reduction in stroke mortality can be attributed at least partly to a reduction in risk factors. Tobacco smoking and hypertension are the main modifiable risk factors for stroke. Improvements in medical treatment for stroke have also increased survival rates (see Indicator 4.4 "In-hospital mortality following stroke").

Definition and comparability

Mortality rates are based on numbers of deaths registered in a country in a year divided by the size of the corresponding population. The rates have been directly age standardised to the WHO European standard population to remove variations arising from differences in age structures across countries and over time. The source is the *Eurostat Statistics*

Database.

Deaths from ischemic heart disease are classified to ICD-10 Codes I20-I25, and stroke to I60-I69. Mathers *et al.* (2005) have provided a general assessment of the coverage, completeness and reliability of data on causes of death.

Trends in mortality rates
healthglance2013index.aspx.htm
health at a glance2013oecdhealthdata.htm
healthglance2013EXECUTIVE SUMMARY.doc
health glance mortality rates 2012.doc

health_glance_2012_en.pdf

„Chapter 1. Health status
1.3. Mortality from all causes 20
1.4. Mortality from heart disease and stroke 22
1.5. Mortality from cancer . 1.13. Cancer incidence 40
1.14. Diabetes prevalence and incidence. . . . ."

2.6.1.6. The burden of cardiovascular disease

**- Cardiovascular disease (CVD), including heart disease and stroke, is the world's largest killer,
claiming 17.1 million lives a year1**

**- In 2004, an estimated
7.2 million of these deaths were due to coronary heart disease and
5.7 million were due to stroke**

- Over 80 per cent of CVD deaths take place in low-and middle-income countries and occur almost equally in men and women

1. **By 2030, almost 23.6 million people will die from CVD, mainly from heart disease and stroke. It is projected to remain the single leading cause of death**

- **CVD is responsible for 10 %of disability adjusted life years (DALYs)a lost in low- and middle-income countries, and for 18% of DALYs lost in high-income countries.**

The World Heart Federation, of the which the ESC is a member, has described the forecasted trend in rising CVD incidence as „unacceptable" and has urged a global response which puts CVD prevention at the centre of national development initiatives.

The Chronic Disease Alliance, an association of ten science-based European organisations of which the ESC is a founding member, has also declared its objective in reversing the rise in chronic non-communicable diseases by urging political action against tobacco use, poor nutrition, lack of physical activity and alcohol.

2. World Health Organization. Global status report on noncommunicable disease 2010.

Notes to editor
**ESC Press Office
+ 33 4 92 94 77 56
press@escardio.org**

References 1. World Health Organization. Global status report on noncommunicable disease 2010.
http://www.who.int/nmh/publications/ncd_report_full_en.pdf

The diagnostic group *cardiovascular diseases* is used here to mean diseases and congenital malformations of the circulatory system as coded in the ICD.

Charts 3–1 through 3–3 show the distribution of deaths in 2008 specific to CVD,

heart disease, and stroke deaths, respectively.31 Chart 3–4 lists CVD;

ICD-9-CM codes for CVD; 2009 estimates of hospital discharges, lengths of stay, and physician office visits for those diagnostic codes;

ICD-10 codes for CVD; and the number of deaths in 2008 for those codes.31, 32, 34 Subsequent charts display morbidity and mortality for total CVD and selected subgroups.

health_glance_2012_en.pdf

2.6.2.1. Pathophysiology of cardiovascular diseases

Population based studies show that atherosclerosis the major precursor of cardiovascular disease begins in childhood. (high salt intake!)

The Pathobiological Determinants of Atherosclerosis in Youth Study demonstrated that intimal lesions appear in all the aortas and more than half of the right coronary arteries of youths aged 7–9 years.

2.6.2.2. SPECTRUM OF CARDIOVASCULAR DISEASES

Key Words: Previous Section

Next Section

- cardiovascular diseases
- diabetes mellitus
- drugs
- heart diseases
- stents
- prevention
- risk factors

2.6.2.3. CVD as a chain of events

CVD as a chain of events, initiated by a myriad of related and unrelated risk factors and progressing through numerous physiological pathways and processes to the development of end-stage heart disease (Figure 1).[1]

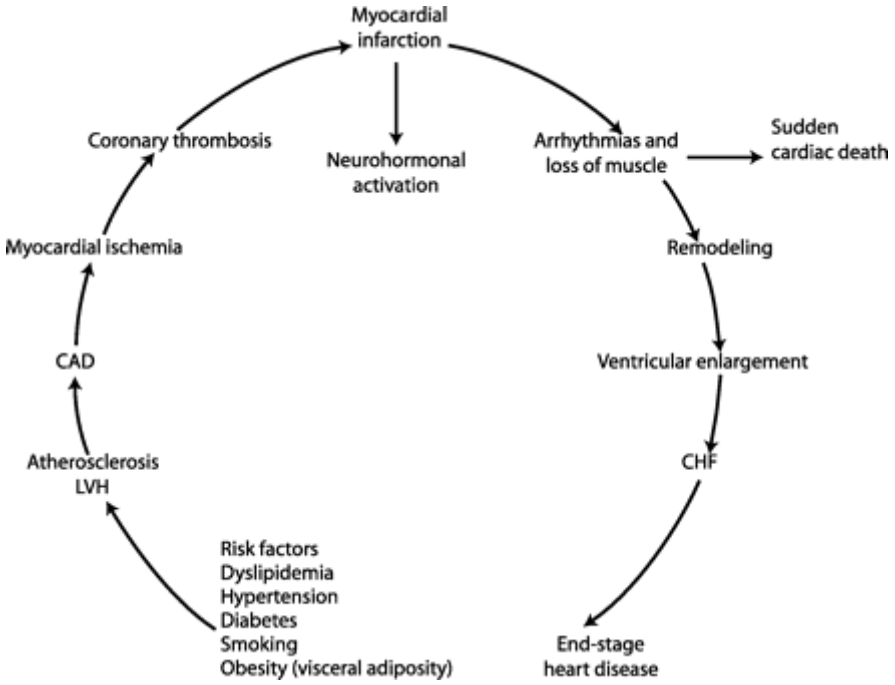


Figure 1. The cardiovascular disease continuum. LVH indicates left ventricular hypertrophy; CHF- congestive heart failure. Adapted from Dzau et al[1] with permission from Elsevier.

They further hypothesized that intervention anywhere along the chain of events leading to CVD could disrupt the pathophysiological process and confer cardioprotection. The workshop participants endorsed this paradigm but also identified the unresolved issues relating to the concept of a CVD continuum. There was limited availability of clinical trial data and pathobiological evidence at that time, and the experts recognized that critical studies at both the mechanistic level and the clinical level were needed to validate the concept of a chain of events leading to end-stage CVD.

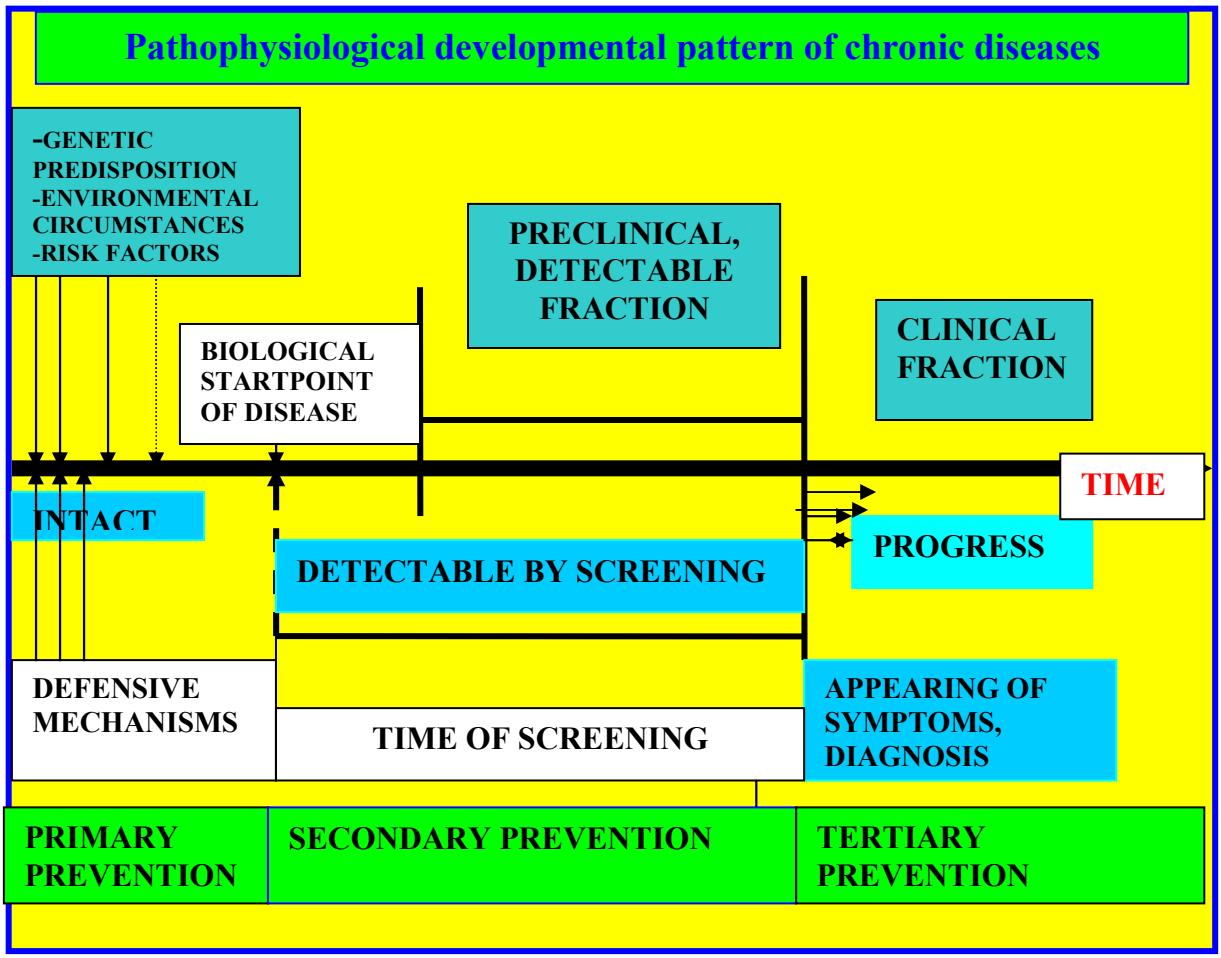
In the intervening 15 years, new evidence for underlying pathophysiological mechanisms, the development of novel therapeutic agents, and the release of additional landmark clinical trial data have confirmed the concept of a CVD continuum and reinforced the notion that intervention at any point along this chain can modify CVD progression. In addition, the accumulated evidence indicates that the events leading to disease progression overlap and intertwine and do not always occur as a sequence of discrete, tandem incidents. Furthermore, although the original concept focused on risk factors for coronary artery disease (CAD) and its sequelae, the CVD continuum has expanded to include other areas such as cerebrovascular disease, peripheral vascular disease, and renal disease. Since its conception 15 years ago, the CVD continuum has

become much in need of an update. Accordingly, this 2-part article will present a critical and comprehensive update of the current evidence for a CVD continuum based on the results of pathophysiological studies and the outcome of a broad range of clinical trials that have been performed in the past 15 years. It is not the intent of the article to include a comprehensive listing of all trials performed as part of the CVD continuum; instead, we have sought to include only those trials that have had the greatest impact. Part I briefly reviews the current understanding of the pathophysiology of CVD and discusses clinical trial data from risk factors for disease through stable CAD. Part II continues the review of clinical trial data beginning with acute coronary syndromes and continuing through extension of the CVD continuum to stroke and renal disease. The article concludes with a discussion of areas in which future research might further clarify our understanding of the CVD continuum.

2.6.2.4. New Understanding of a Pathophysiological Continuum

Our understanding of the pathophysiology of CVD has expanded considerably since 1991. A pathophysiological continuum, which underlies the clinical CVD continuum, describes the progressive processes at molecular and cellular levels that manifest as clinical disease (Figure 2).[2] In addition, cardiovascular risk factors, such as elevated cholesterol, hypertension, diabetes mellitus, and cigarette smoking, are now known to promote oxidative stress and to cause endothelial dysfunction, initiating a cascade of events, including alterations in vasoactive mediators, inflammatory responses, and vascular remodeling, that culminates in target-organ pathology (Figure 3).[3] Considerable evidence suggests that these processes begin earlier in life than previously recognized, indicating that CVD arises over decades. Beyond traditional risk factors, the role of biomarkers/biomediators and surrogate markers in CVD continues to be elucidated. In addition, it is now recognized that neurohormones contribute to disease at both the systemic and local level, exerting direct trophic and inflammatory effects on

tissue.


Pathophysiological developmental pattern of chronic diseases
-GENETIC PREDISPOSITION
-ENVIRONMENTAL CIRCUMSTANCES
-RISK FACTORS
PRECLINICAL, DETECTABLE FRACTION
CLINICAL FRACTION
BIOLOGICAL STARTPOINT OF DISEASE
TIME
INTACT
PROGRESS
DETECTABLE BY SCREENING
DEFENSIVE MECHANISMS
TIME OF SCREENING
APPEARING OF SYMPTOMS, DIAGNOSIS
PRIMARY PREVENTION
SECONDARY PREVENTION
TERTIARY PREVENTION

CHAIN OF CARDIOVASCULAR EVENTS

INICIATIVE AND AGGRAVATING MECHANISMS ,MEDIATORS

PATHOLOGICAL MORPHOLOGICAL,STRUCTURAL AND FUNCTIONAL REMODELING OF CARDIOVASCULAR SYSTEM

SYMPTOMLESS CARDIOVASCULAR INJURY

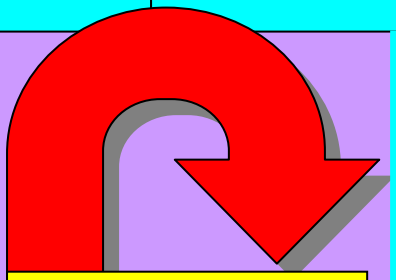
ORGANIC INJURIES: MI, VASCULAR NEPHROPATHY STROKES EXTREMITAL ISCHEMICS

PATOLOGICAL MORPHPLOGICAL,STRUCTURAL AND FUNCTIONAL ALTERATIONS-TRANSFORMATIONS

PROGREDIENT INJURIES OF TARGET-ORGANS

CARDIOVASCULAR RECONSTRUCTION HYPERTROPHY, SYMPTOMLESS ATHEROSCLEROSIS

ENDOTHELIAL DYSFUNCTION



SYMPATHO-ADRENAL SYSTEM ,RENIN-ANGIOTENZIN-ALDOSTERON-SYSTEM

AGGRAVATING FUNCTIONAL DISORDERS OF TARGET-ORGANS HEART- AND RENAL FAILURE, DEMENTIA

ORGANIC FAILURES IN FINAL STADIUM

DEATH

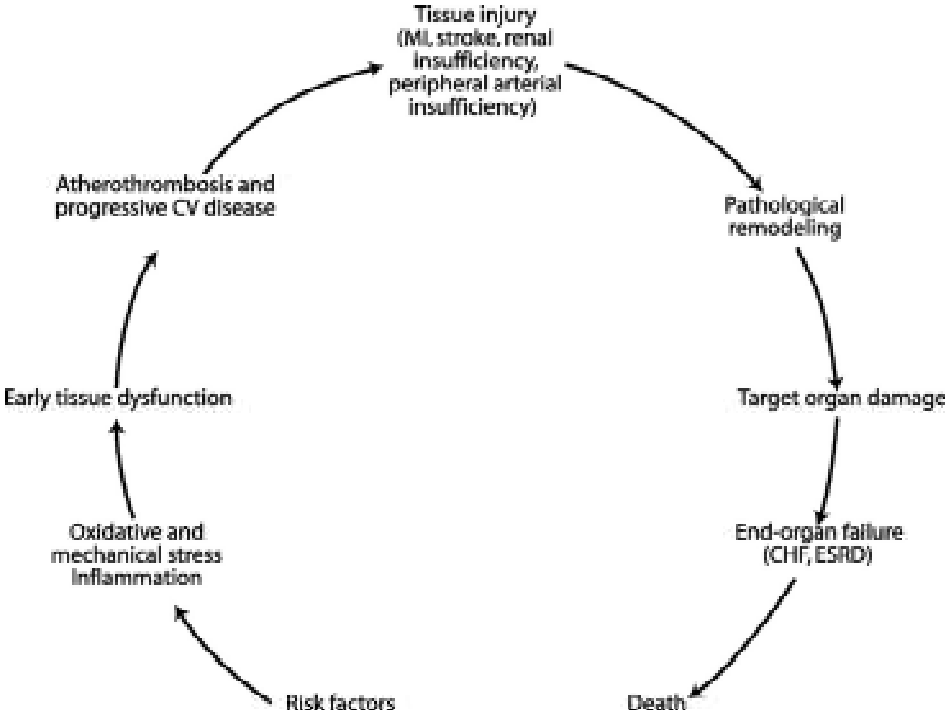
RISK FACTORS :AGE,FAMILIAR ANAMNESIS, HYPERTONIA, DIABETES DYSLIPIDAEMIA, TOBACCO USE OBESITY

GENETIC PREDISPOSITION
SOCIO-ECONOMIC BACKGROUND
ENVIRONMENTAL EFFECTS

MI-MYOCARDIAL INFARCEATION

AFTER DZAU AND BRAUNWALD

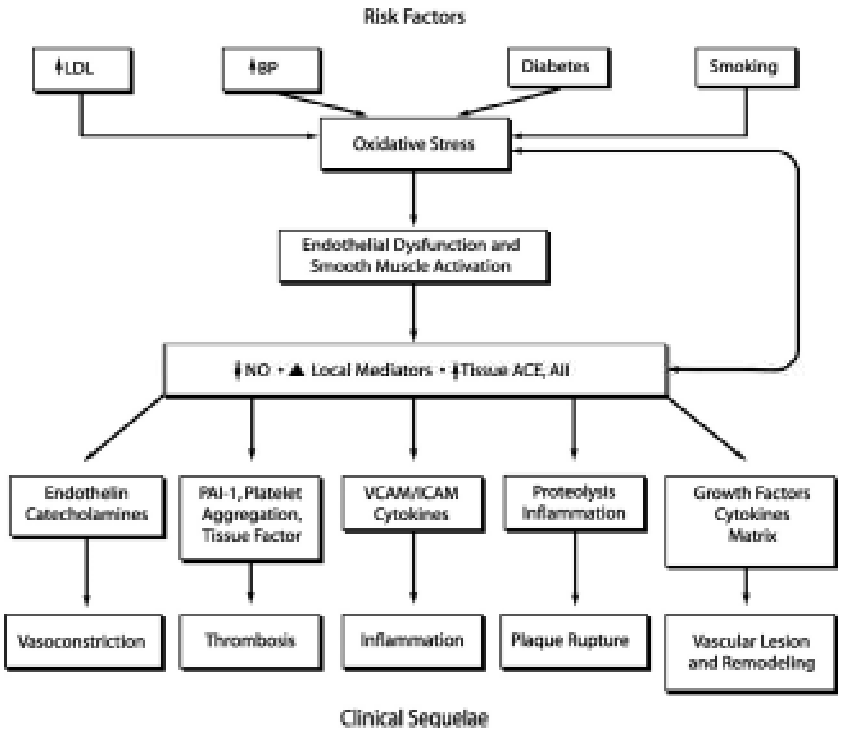
Figure 2. Cardiovascular and renal pathophysiological continuum.



Dzau V J et al. Circulation 2006;114:2850-2870

Figure 2. Cardiovascular and renal pathophysiological continuum. CHF indicates congestive heart failure; CV, cardiovascular; ESRD, end-stage renal disease; and MI, myocardial infarction.

Figure 3. Integrated model of tissue angiotensin and vascular pathobiology.



Dzau V J et al. Circulation 2006;114:2850-2870

Figure 3. Integrated model of tissue angiotensin and vascular pathobiology. AII indicates angiotensin II; BP, blood pressure; ICAM, intracellular adhesion molecule; PAI-1, plasminogen activator inhibitor-1; and VCAM, vascular cell adhesion molecule. Adapted with permission from Dzau VJ.

2.6.2.5. Neurohormones

The renin-angiotensin-aldosterone system (RAAS) is now understood to play a significant role in CVD pathophysiology.[3] Interacting with the adrenergic system and various mediators, the RAAS mediates adaptive and maladaptive responses to tissue injury, such as may result from hypertension, ischemic heart disease, cardiomyopathy, other systemic or pulmonary diseases, or the effects of CVD risk factors.[14] The important biologically active component of the RAAS is angiotensin II. Angiotensin II mediates hemodynamic and renal actions in addition to having direct cardiovascular tissue effects and has been implicated at every stage along the CVD continuum.

The identified pathological effects of angiotensin II are myriad and include, but are not limited to, vasoconstriction, cardiac and vascular remodeling, inflammation, thrombosis, and plaque rupture.[3] Although angiotensin II stimulates 2 major receptors, angiotensin II type 1 (AT_1) and type 2 (AT_2), the pathological effects of angiotensin II appear to be mediated through the AT_1 receptor.[15] Evidence suggests that stimulation of the AT_2 receptor mediates more favorable actions, inducing NO and bradykinin release and promoting cGMP-mediated vasodilation.[15] Furthermore, stimulation of AT_2 receptors may promote cell differentiation and apoptosis and inhibit cell proliferation.

Angiotensin II increases the tissue generation of reactive oxygen species, creating an environment of oxidative stress and decreased NO activity.[3] These changes contribute to inflammatory responses, including the induction of monocytes and smooth muscle cells to release chemoattractant proteins such as monocyte chemotactic protein-1, as well as other cytokines and adhesion molecules. Angiotensin II promotes vascular remodeling by stimulating expression of growth factors in vascular smooth muscle cells, promoting smooth muscle cell proliferation, inducing the production and release of matrix metalloproteinases, and modulating vascular cell migration.[3]

The RAAS, and specifically angiotensin II, also plays a role in fibrinolytic responses via the endothelium. ACE stimulates plasminogen activator inhibitor-1 production via angiotensin II and also degrades bradykinin. Bradykinin stimulates tissue-type plasminogen activator release from the endothelium.[16,17] Accordingly, the interaction between bradykinin and angiotensin II at the endothelial surface modulates the prothrombotic/fibrinolytic state of the blood vessel.[18,19]

An increase of tissue ACE in atherosclerotic lesions sets up a positive feedback mechanism for angiotensin II production.[3] Increased ACE promotes an inflammatory response via angiotensin II, and inflammatory cells such as monocytes/macrophages, neutrophils, and mast cells release enzymes that generate angiotensin II. The increased level of angiotensin II creates an environment of oxidative stress and induces the release of cytokines, adhesion molecules, and growth factors, which leads to further inflammation and promotes atherogenesis. Tissue ACE and angiotensin II accumulate in the shoulder regions of vulnerable plaques and may contribute to the susceptibility of these plaques to rupture.

Other neurohormones are involved in the pathophysiology of CVD. A-type natriuretic peptide (also called atrial natriuretic peptide) and B-type natriuretic peptide (also called brain natriuretic peptide) are smooth muscle relaxants that cause vasodilation and lower blood pressure. B- and A-type natriuretic peptide are released in response to myocyte stretch.[20] A-type natriuretic peptide also inhibits the RAAS by blocking secretion of renin and aldosterone, and B-type natriuretic peptide appears to have direct relaxant effects on the myocardium. In addition, both A- and B-type natriuretic peptide inhibit sympathetic nervous system activity in the heart. Both B- and A-type natriuretic peptide generally act to oppose the actions of angiotensin II.[21] Arginine vasopressin has been implicated in hyponatremia in heart failure patients.[22] Arginine vasopressin acts on the V_2 vasopressin receptor, which causes antidiuresis activity in the collecting duct of the kidney. In addition, arginine vasopressin binds to vasopressin V_1 receptors on vascular smooth muscle, which may increase vascular resistance.

Other hormones that may also be important include vasodilating prostaglandins and the vasoconstrictor endothelin. Prostacyclin and prostaglandin E generally act to counterbalance the vasoconstrictor actions of angiotensin II.[22]

2.6.2.6. Inflammatory Processes

An inflammatory state has been associated with atherosclerosis. In the inflammatory response to endothelial injury, release of chemoattractant proteins (chemokines) promotes entry of monocytes into the vessel wall, where they can transform into macrophages. Macrophages then take up modified and oxidized LDL, becoming foam cells.[3] Foam cells contribute to formation of fatty streaks, an early stage of atherosclerotic plaque.[23] Repetitive cycles involving ongoing arterial injury, lipid uptake, and vascular remodeling can result in complicated plaques with large necrotic cores, thin fibrous caps, and accumulation of macrophages in the shoulder regions, where plaque rupture tends to occur. When activated by T cells, macrophages release proteolytic matrix metalloproteinases that degrade the fibrous cap and interstitial collagen, which promotes rupture.[23,24] One important signaling pathway between T lymphocytes and macrophages is the CD40:CD402 system. Macrophage accumulation appears to be associated with increased levels of inflammatory markers, such as fibrinogen and C-reactive protein.[23,25] Thrombosis that results in a clinical event (eg, acute coronary syndrome) may also be caused by a superficial erosion, rather than intimal rupture, of the atherosclerotic plaque; in either case, the immediate site of plaque rupture or erosion is always marked by an inflammatory process.[26]

C-reactive protein has emerged as a useful predictor of atherosclerotic CVD risk.[27] Data suggest that C-reactive protein may also be a mediator and not just a marker of inflammation. C-reactive protein induces the expression of tissue factor and cell adhesion molecules, binds and activates complement, stimulates monocytes to enter the vessel wall, promotes the production of monocyte chemotactic protein-1, and mediates macrophage uptake of LDL.[13] The role of C-reactive protein as a biomarker for CVD is discussed further in part II of this article.

2.6.2.7. Coagulation Cascade

When a plaque ruptures, the thrombogenic lipid core is exposed to circulating blood, which activates the coagulation cascade that initiates and sustains thrombus formation. During this process, platelets adhere to the site of trauma and contribute to the formation of thrombin, which converts fibrinogen into strands of fibrin. Fibrin strands trap additional platelets, blood cells, and plasma to form a clot that can partly or completely block an artery.

2.6.2.8. Vascular Remodeling

Vascular remodeling occurs in response to chronic alterations in hemodynamic conditions that precipitate structural changes in the vessel wall, such as increased ratio of wall to lumen width, changes in luminal dimensions with minimal changes in wall thickness, neointima formation in response to injury, and rarefaction of the microcirculation.[4] Inward remodeling typically occurs in response to reduced blood flow

and results in decreased vessel size; conversely, outward remodeling usually is a reaction to increased flow and results in increased vessel size.[28] Locally produced biologically active mediators, such as NO and matrix metalloproteinases, and growth factors, such as platelet-derived growth factor and transforming growth factor-β, in addition to hemodynamic stimuli, such as shear stress, interact to promote cell migration, cell growth, cell death, and the production and degradation of extracellular matrix, which results in these structural alterations.[4,28] The pathophysiological changes in vascular structure that result from alterations in endothelial function have clinical implications.[4]

Vascular remodeling in small resistance arteries may be the initial step in the progression from hypertension to target-organ damage.[29] Small resistance arteries that have undergone hyperplastic/hypertrophic remodeling have an enhanced response to vasoconstrictor substances, further reducing vascular reserve. This reduction may contribute to tissue ischemia if surrounding arteries are stenotic. Small-artery remodeling is more common among persons with hypertension than those without, and patients with the highest blood pressures are also the most likely to develop left ventricular hypertrophy (LVH) and have the greatest incidence of small-artery changes.[29]

Figure 1
Endothelial dysfunction: Leukocyte adhesion and migration into the deep layer of the intima (9). (From Ross I. Reproduced with permission. © 1999 Massachusetts Medical Society.)
Endothelial permeability
Leukocyte migration
Endothelial adhesion
Leukocyte adhesion

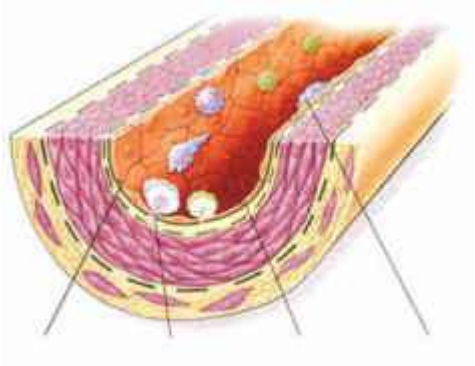


Figure 2
Fibrous cap formation and the necrotic core (9). (From Ross I. Reproduced with permission. © 1999 Massachusetts Medical Society.)

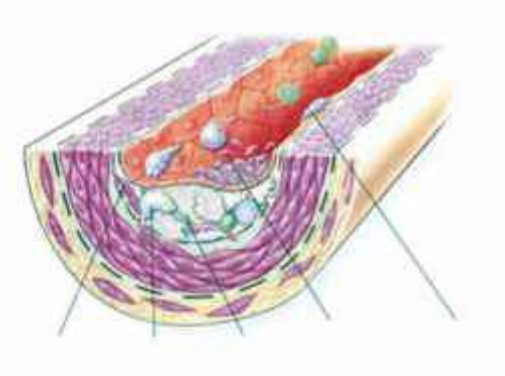


Figure 3
The ruptured plaque (9). (From Ross I. Reproduced with permission. © 1999 Massachusetts Medical Society.)
Macrophage accumulation
Formation of necrotic core
Fibrous-cap formation Plaque rupture
Thining of fibrous cap
Hemorrhage from plaquemicrovessels

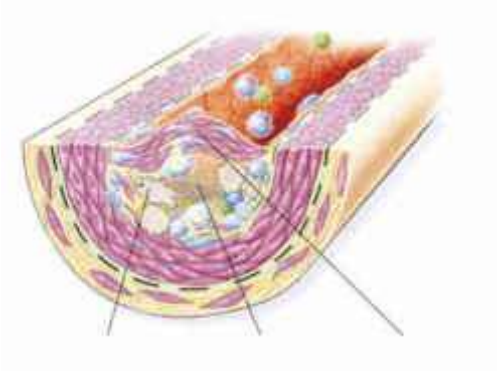
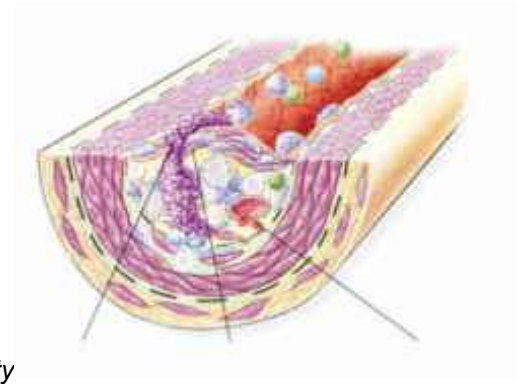


Figure 4
Fatty streak formation revealing platelet aggregation on the endothelial surface, foam-cell formation and smooth muscle migration (9). (From Ross I. Reproduced with permission. © 1999 Massachusetts Medical



Society

2.6.2.9. Cardiac Remodeling and Target-Organ Damage

Cardiac remodeling is mediated by diverse endocrine, paracrine, and autocrine effects of a number of different hormones that result in hypertrophy.[14] The hormones involved in changing the structure, function, and phenotype of the myocardium include angiotensin II, vasopressin, peptide growth factors, endothelin, natriuretic peptides, cytokines, and NO. Evidence indicates that insulin and insulin-like growth factor may be myocardial growth factors, which suggests that altered glucose and insulin metabolism, such as occurs in diabetes and the metabolic syndrome, further contributes to LVH and accelerated heart failure.[30,31] Oxidative stress also plays an important role in the cardiac remodeling process; in animal studies, inhibition of antioxidant systems disrupts normal cell growth and apoptosis in cardiac myocytes.[14] If uninterrupted, cardiac remodeling results in impaired systolic and diastolic functioning and progresses to heart failure.[32]

Basic science investigations have rendered obsolete the concept that each disease event on the CVD continuum is mediated by a specific and single pathophysiological pathway; rather, common pathophysiological processes participate in multiple steps across the continuum. It is now apparent that common and overlapping mechanisms are involved in disease development across the entire spectrum of CVD. This understanding has therapeutic implications in that many interventions and drugs are effective in treating multiple disease events across the CVD continuum. Clinical trials supporting this conclusion will be discussed next.

Previous SectionNext Section

Clinical Trial Evidence for a Clinical Continuum

Validation of the concept of a clinical CVD continuum is based on clinical trial evidence that intervention disrupts the progression of disease. This review will examine interventional efforts at points along the CVD continuum to prevent or delay CVD and its consequences, with primary focus on major clinical trials published since the CVD continuum was first proposed in 1991. Potential trials to include were identified by performing a search of the MEDLINE literature from 1991 to 2005. Search terms used included the well-established risk factors for CVD and major points along the clinical CVD continuum. The resulting trial lists, organized by therapeutic category, were supplemented by a review of major clinical guidelines. Finally, the trial lists were sent to a panel of expert validators, who determined which trials were the most important to be discussed and who suggested additional trials to be included.

2.6.3.1.

Types of cardiovascular diseases

cvdglobalatlaswho_eng.pdf

cvdglobalatlaswho_eng.pdf

The human heart is only the size of a fist, but it is the strongest muscle in the human body.The heart starts to beat in the uterus long before birth, usually by 21 to 28 days after conception.

The average heart beats about 100 000 times daily or about two and a half billion times over a 70 year lifetime. With every heartbeat, the heart pumps blood around the body. It beats approximately 70 times a minute, although this rate can double during exercise or at times of extreme emotion. Blood is pumped out from the left chambers of the heart. It is transported through arteries of ever-decreasing size, finally reaching the capillaries in all the tissues, such as the skin and other body organs.

Having delivered its oxygen and nutrients and having collected waste products, blood is brought back to the right chambers of the heart through a system of ever-enlarging veins.
During the circulation through the liver, waste products are removed. This remarkable system is vulnerable to breakdown and assault from a variety of factors, many of which can be prevented and treated.

Cardiovascular disease: types and symptoms
January 2011

Types of cardiovascular diseases

- CVD is a group of disorders/diseases of the heart and blood vessels
- Types of CVD include:

1.ISCHEMIC ORIGINED:
o -Coronary heart disease–a disease of the blood vessels supplying the heart muscle that can lead to a heart attack

Coronary Heart Disease

CHD includes AMI and angina pectoris. charts provide information about the prevalence and hospitalization rates of AMI and angina pectoris. Mortality data are not shown for them individually because good diagnostic information is often not available at the time in which death certificates are completed
Over the years, multiple revisions of the ICD have resulted in changes in diagnostic terms and codes included in the CHD category that compromised direct comparability of CHD deaths over time. For example, ICD-10 expanded CHD (over ICD-9) to include

"Atherosclerotic CVD." To maintain comparability over time, CHD death rates in ICD-9 (1979–1998) were retabulated to include deaths coded to the additional term.

-Myocardial infarceation
-Angina pectoris

2.CEREBROVASCULAR ORIGINED:

A stroke happens when blood supply to the brain is interrupted. Blood is carried to the brain by blood vessels called arteries. Blood contains oxygen and important nutrients for your brain cells. Blood may be interrupted or stop moving through an artery, because the artery is blocked (ischaemic stroke) or bursts (haemorrhagic stroke). When brain cells do not get enough oxygen or nutrients, they die. The area of brain damage is called a cerebral infarct.

Brain cells usually die shortly after the stroke starts. However, some can last a few hours, if the blood supply is not cut off completely. If the blood supply can be returned in the minutes and hours after the stroke, some of these cells may recover. If not, they will also die.

A transient ischaemic attack (TIA) happens when there is a temporary interruption to the blood supply to the brain. It causes the same symptoms as a stroke, but these go away completely within 24 hours.

-Stroke (cerebrovascular disease) − the brain- equivalent to a heart attack.
STROKE : -named a very fast developed syndrome coincidenced with the the general or focal dysfunction of brain –activity and its functions which consists more than 24 hours and may lead to death of patients.
the 25% of patients are less than 60 years .it is not only the diseases of older people there are attacked the younger and middle-aged population also.

Cerebrovascular Diseases (Stroke)

Cerebrovascular disease (i.e., stroke) is the fourth leading cause of death. Only a small proportion of deaths from stroke can be classified as cerebral hemorrhage, occlusion, thrombosis, or embolism. Most are coded to ill-defined forms of cerebrovascular diseases (Chart 3–3).

-Ministroke or TIA :
named a transitoric ischemic attack (TIA) not attached to brain-cell death. Symptomes will be ordered in 24 hours,but it signes the bad brain circulation-vascular status. After a TIA the danger of stroke increases with 10 times and appears in 5-8 years maximum. Should be threated immediately ! To control the status applied the TIA-test: smile (assymmetric alterations on face) hands up and try to put out the tongue(assymmetric signes!)-call the ambulance
In each hours of not threated stroke the brain aged with 3 and half of years and in each minutes dye 2 millions neurons . The length of lost neural tracts is about 700km/hours.

Over 50 years the risk of stroke increased 2 times /10 years and depends on the sex: among the males is more frequent with 25 % .
In case of stroke will be interrupted the blood-supply of brain and the brain –tissues will be damaged.
It may occur anywhere in the brain with consequented lack of blood-supply and brain – infarceation.
Main causative factors may be any kind of unsatisfactory blood-supply of brain:

1. block of blood-vessels of brain
a,by thrombus (adhered to the endothelium of blood-vessels of brain)
b,embolies,disrupted from the endothelium or any other thing hampering the blood – flood to the tissues
2.vascular lesions: disruptional injuries of blood-vessels in brain
apoplexia cerebri: inhaemorrhage of brain tissue
apoplexias counted about 20% of strokes

Blood must to flow through the brain for help it to performe its function. If this flow in a part of the brain is blocked or interrupted, that part is deprived of oxygen and nutrients and begins to die
Warning signs of heart attack or stroke

- A heart attack or stroke may be the first warning of an underlying disease

- Heart attack warning signs include:
o Chest discomfort – most attacks have discomfort in the centre of the chest that lasts more than a few minutes, or that goes away and comes back. It can feel like uncomfortable pressure, squeezing, fullness or pain
o Pain or discomfort in other areas of the body – can include one or both arms, the back, neck, jaw or stomach
o Shortness of breath – can occur with or without chest discomfort

o Other signs – may include breaking out in a cold sweat, nausea or light-headedness

- Warning signs of a stroke include:
o Sudden weakness of the face, arm, or leg, most often on one side of the body
o Sudden confusion, trouble speaking or understanding
o Sudden trouble seeing in one or both eyes
o Sudden trouble walking, dizziness, loss of balance or coordination
o Sudden, severe headache with no known cause

3.PERIPHERIC VASCULAR DISEASES:
a,hypertonia
b,arteriosclerosis (stenosis of arterias)
c,sclerotic disease of blood-vessels: atherosclerosis

4.INFECTIOUS ORIGINED DISEASES:

- **Chlamydia pneumoniae caused atherosclerosis :**

the atherosclerotic process will be fastered because these pathogens are intracellular bacterias,living in the leukocytes collected to the endothelium- and epidermal –cells to kill these Chlamydias. But these cells will be killed by the Chlamydias and accumulating in the atherosclerotically altered thrombus these decay-or lesion- products riches the waste containing calcaryferous and fatty products and penetrate into the injured endothelium. The triggered greatly frighteening mysterious death cases were the basis of the new investigation of infectious origined atherosclerosis:

in very short time were died 8 sweden athlets in myocardial infarceation which attacked them generally after the trainings and it happened generally during the training together with other sportsmen: all of them seemed healthy before.The internal examination showed in the miocardium the Chlamydia pneumoniae,which believed to this time a simple respiratory pathogen. At the same time in the blood of investigated by other causes heart attacked patients were shown very high level of Chlamydia – antibodies. The high –titered heart-attacked patients were threated with big doses of antibiotics and the number of new heart attacked patients related to the not threated group of patients has fallen to th ¼!

–Rheumatic heart disease
− caused by streptococcal bacteria (rheumatic fever) damages the heart muscle and heart valves
–Deep vein thrombosis and pulmonary embolism
− blood clots in the leg veins, which can dislodge and move to the heart and lungs

5.HEART INSUFFICIENCIES

Heart Failure

Heart failure is a sequela of various heart diseases. It is a heart "condition," not a heart "disease," and is more common as a contributing rather than an underlying cause of death. Thus, it is imprecise to classify heart failure as an underlying cause of death. The condition, however, is increasingly prevalent and common in the reporting of hospitalizations and mortality

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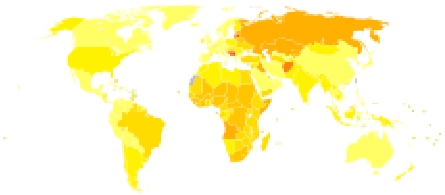
6.CARDIOMYOPATHIAS

Cardiomyopathy

In 2008, 23,932 deaths were attributed to cardiomyopathy, although no consensus exists on classification and diagnostic criteria for the disease. This limitation has little effect on any mortality differences influenced by age, race, or sex.

7.CONGENITAL HEART DISEASE– this is a heart defect present at birth. While congenital heart disease can be caused by genetic factors or by adverse exposures during pregnancy, the cause of most cases is unknown. Examples include holes in the heart (such as atrial septal defect or ventricular septal defect), abnormal valves, and abnormal heart chambers



Disability-adjusted life year for inflammatory heart diseases per 100,000 inhabitants in 2004.[8]

- **no data**
- **less than 70**
- **70-140**
- **140-210**
- **210-280**
- **280-350**
- **350-420**
- **420-490**
- **490-560**
- **560-630**
- **630-700**
- **700-770**
- **more than 770**

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Atrial Fibrillation

In 2008, 15,383 deaths were attributed to atrial fibrillation as the underlying cause. Normally, the disorder is not intrinsically a fatal condition, although it does predispose individuals to potentially fatal conditions such as stroke.

2.6.3.2. Mortality data

cvdglobalatlaswho_eng.pdf
GENERAL SITUATION IN 2011 (5-6-16-23-31-35TH PAGES)

- **Coronary artery disease (also known as coronary heart disease and ischaemic heart disease)**
- **Cardiomyopathy - diseases of cardiac muscle**
- **Hypertensive heart disease - diseases of the heart secondary to high blood pressure**
- **Heart failure**
- **Cor pulmonale - a failure at the right side of the heart with respiratory system involvement**
- **Cardiac dysrhythmias - abnormalities of heart rhythm**
- **Inflammatory heart disease**
    - **Endocarditis – inflammation of the inner layer of the heart, the endocardium. The structures most commonly involved are the heart valves.**
    - **Inflammatory cardiomegaly**
    - **Myocarditis – inflammation of the myocardium, the muscular part of the heart.**
- **Valvular heart disease**
- **Cerebrovascular disease - disease of blood vessels that supplies to the brain such as stroke**
- **Peripheral arterial disease - disease of blood vessels that supplies to the arms and legs**
- **Congenital heart disease - heart structure malformations existing at birth**
- **Rheumatic heart disease - heart muscles and valves damage due to rheumatic fever caused by streptococcal bacteria infections**

2.6.4.1.

Risk factors of cardiovascular diseases

2.6.4.2. Contributing factors

A person's genetic make-up is likely to be important in the probability of developing certain diseases, including cardiovascular disease.

The foundations of adult health are laid in early life, even before birth, and a good start in life is fundamental to later development. Young mothers, poor mothers and those of low educational achievement are more likely to produce a low-birth-weight baby and less likely to breastfeed; in turn, low birth weight is associated with increased risk of developing coronary heart disease, stroke and high blood pressure. Good health-related habits, such as eating sensibly, exercising and not smoking, are learnt early in life and associated with parental and peer group examples.

Socioeconomic group

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.

Mental health

Harmful stress is associated with cardiovascular diseases, and the prevalence of depression is a predictor of poor life expectancy among those who suffer from cardiovascular diseases.

Diet

A high intake of salt leads to hypertension. Most Europeans' daily intake of sodium exceeds the WHO recommended limit, and in an important number of Member States the main source of sodium in the diet is processed foods. According to the WHO Global Health Report 2010, convincing evidence suggests that saturated fat and trans-fat increase the risk of coronary heart disease and that replacement with monosaturated and polyunsaturated fat reduces the risk.

guidelines-CVD-prevention.pdf

E:\The DASH Diet to lower high blood pressure.doc

Overweight and obesity

Obese adults are especially likely to develop cardiovascular diseases and other health problems. Obesity is associated with some of the major risk factors for cardiovascular diseases, such as hypertension and low concentrations of HDL cholesterol.

Inactivity

Participation in 150 minutes of moderate physical activity each week (or equivalent) is estimated to reduce the risk of ischaemic heart disease by approximately 30%, as well as reducing the risk of stroke and hypertension.

Tobacco

Smoking is estimated to cause about 10% of cardiovascular disease worldwide. Of the six WHO regions, the highest overall prevalence for smoking in 2008 was estimated to be in the European Region, at nearly 29%.

Alcohol

There is a direct relationship between higher levels of alcohol consumption and rising risk of cardiovascular diseases. The relationship is complex, however, and depends on

both the amount and the pattern of alcohol consumption. Of the six WHO regions, adult per capita consumption of alcohol in 2008 was highest in the European Region (at 12.2 litres).

Diabetes

Diabetes is a major risk factor and trigger for cardiovascular disease.

Globalization and urbanization

Globalization and urbanization are associated with the trend for populations to consume unhealthy diets high in energy, saturated fats, salt and sugar, and become less physically active. This trend started in western Europe and is now seen in parts of eastern Europe. This has serious implications for obesity levels, particularly among children.

Hypertension

Well-known risk factors for CVD include:

-hypertension,

-dyslipidemia,

-diabetes mellitus,

-cigarette smoking,

-obesity, and

-physical inactivity.[33]

Prevention or control of these risk factors through

lifestyle modification (eg, diet, exercise, and smoking cessation) is a key element of preventive cardiology.

Many studies investigating lifestyle changes were not designed to quantify benefit on hard clinical end points but instead relied on surrogate end points such as reduced blood pressure and lipid changes and their epidemiological link to decreased CVD risk. Although the present review focuses on specific interventions that have yielded direct benefit on morbidity and mortality, the authors strongly endorse lifestyle modification as a component of optimizing health and effectively managing CVD.

2.6.4.3. Hypertension

Evidence from numerous clinical trials[53–65] **supports the beneficial effects of various classes of blood pressure–lowering regimens on CVD morbidity and mortality in hypertensive patients with and without evidence of LVH. Only a few of these trials are**

discussed in this article for the purposes of illustration, but detailed summaries of these and other hypertension trials are provided in Table II of the online data supplement.

Thiazide and thiazide-like diuretics have been the basis of antihypertensive therapy in numerous trials in which 1 or more of the complications of hypertension have been reduced by blood pressure lowering.[33] For example, the Systolic Hypertension in the Elderly Program (SHEP)[53] found that treatment of isolated systolic hypertension with chlorthalidone significantly reduced the 5-year incidence of fatal and nonfatal stoke by 36% (95% CI 18% to 50%) compared with placebo (P=0.0003) in patients aged 60 years or older. Isolated systolic hypertension, a condition in which systolic blood pressure is elevated but diastolic blood pressure is <90 or 95 mm Hg, is the most common form of hypertension among older individuals and greatly increases their risk of CVD events.

Similarly, the second Swedish Trial in Old Patients with Hypertension (STOP-Hypertension-2)[60] confirmed the benefits of antihypertensive therapy in subjects 70 to 84 years of age at enrollment. STOP-2 reported that antihypertensive therapy with so-called conventional drugs (eg, atenolol, metoprolol, pindolol, or hydrochlorothiazide plus amiloride) and newer drugs (eg, enalapril, lisinopril, felodipine, or isradipine) similarly lowered blood pressure and prevented CVD mortality or major events to the same degree.[60] Decreases in blood pressure were of major importance in preventing CVD events in this population. More recently, the Antihypertensive and Lipid Lowering to Prevent Heart Attack Trial (ALLHAT)[66] confirmed the benefits of thiazide-like diuretic therapy. ALLHAT is discussed in detail later, under "Multiple Risk Factors."

Other trials involving newer classes of agents, including calcium channel blockers, ACE inhibitors, and ARBs, have also shown benefit in reducing CVD events. The Hypertension Optimal Treatment (HOT) study[58] provides evidence of an optimal blood pressure level and of the frequent need for more than 1 agent to achieve target levels of blood pressure. HOT randomized >18 000 men and women aged 50 to 80 years with diastolic hypertension (100 to 115 mm Hg) to 1 of 3 target diastolic blood pressure groups: ≤90 mm Hg, ≤85 mm Hg, and ≤80 mm Hg. Felodipine 5 mg was administered to all patients; if adequate blood pressure control was not achieved, investigators followed a 5-step program of dosage increases or addition of further agents. Follow up was conducted for an average of 3.8 years. The investigators calculated that the lowest rate of cardiovascular events occurred with a mean blood pressure of 138.5/82.6 mm Hg.[58]

The Captopril Prevention Project (CAPPP)[59] compared the effects of ACE inhibition (captopril) with conventional therapy (diuretics or β-blockers) on CVD morbidity and mortality in >10 000 hypertensive patients 25 to 66 years of age. At study end, the rates of fatal and nonfatal MI were similar in the 2 treatment groups. Mortality from CVD was lower with captopril than with conventional treatment, but fatal and nonfatal stroke was more common. The difference in stroke risk may have been due to the lower levels of blood pressure obtained initially in previously treated patients randomized to conventional therapy.[59] The Heart Outcomes Prevention Evaluation (HOPE)[67] and other large trials of ACE inhibitor therapy in high-risk patients are discussed later in the section on stable CAD.

The Losartan Intervention For Endpoint reduction in hypertension (LIFE) study,[63] a randomized trial of a regimen that began with losartan versus one that began with atenolol in patients with hypertension and LVH, showed that the losartan-based

regimen was associated with a greater reduction than the atenolol-based regimen in the composite end point of death, MI, and stroke for a similar reduction in blood pressure. Only ≈10% of the subjects enrolled in LIFE received only 1 antihypertensive drug; most were also given hydrochlorothiazide and other agents.[63] Most of the significance in reduction of the composite end point was driven by a greater reduction in stroke with losartan. The absence of a greater reduction in heart failure events with losartan may be because both atenolol and losartan likely prevented heart failure and did so comparably.[68]

Another study of an ARB, the VALsartan Long-term Use Evaluation (VALUE),[69] was conducted in hypertensive patients at high risk for cardiac events and is discussed under "Multiple Risk Factors

Background: the greatest to our days health-protective screening program in Hungary has been launched in 2010 and was prepared on the basis of EU-principles and directives .It was worked with cooperation of more than 40 special organizations having main goals as :
-health –protection, disease-prevention and improve the health status of people. Life – style advices,education of methods of healthy nutrition and the formation of health-conscious life-style propagation are the main methodes to prevent the cardiovascular diseases.
Participants and methods: in a special screening-camion is realised the cardiovascular investigation related to the cardiological and hypertonia- areas. Data-procession of results of participants is collected continously .
In 2010-2011 were 10444 (women:52,7%) and 9370 men(47,3%) represented on these screenings in 332 scenes. Represented people in age group with:26-55 years : the average age at the female were:42 at the males:40 years.This %-al distribution was not modified significantly with the age, buit the 3-rd stadied hypertonia has occured more and more frequent,over 56 years the frequency overhead the 11%.
The 28% of answers signed high blood-pressure . the measures ralised with real instruments,by valid med.personal and instruments

<u>Data-processing</u>
On the basis of data was investigated high amount of hypertonics among the younger males .The average systolic blod-pressure values of men was overhead the normal values in all age –groups ,the most frequent stadium was the 1-st stadium of hypertonia among them, from 18-th years were measured values over 140/90 Hgmm in 39%.
At the women to 55 years is characteral normotonia , over 55 years the I-st stadied hypertonia has occured more. The average diastolic value is in normal range at both sexes (except of men with 46-55 years where the upper limit of normal values were overhead in minimal measures)
At the women aged 26 years occured in highest proportion(and in 1,7%) over 46 years this stadium of hypertonia has 6% frequency. Connection of blood-cholesterol level,blood-glucose and size of abdominal circumference was evidently prooved.
. The hypertension (over 140/90Hgmm) was 2-3 times more frequent in both sex at the coincidenced diabetes with high blood pressure(women: n=344,men:n=303) than without the diabetes.

cvd hypertensin hungarykeywords.doc

Evidence suggests a number of risk factors for heart disease: age, gender, high blood pressure, high serum cholesterol levels, tobacco smoking, excessive alcohol consumption, sugar consumption,[9][10] family history, obesity, lack of physical activity, psychosocial factors, diabetes mellitus, air pollution.[2] While the individual contribution of each risk factor varies between different communities or ethnic groups the consistency of the overall contribution of these risk factors to epidemiological studies is remarkably strong.[11] Some of these risk factors, such as age, gender or family history, are immutable; however, many important cardiovascular risk factors are modifiable by lifestyle change, drug treatment or social change.

Prospective studies suggest that hyperinsulinemia may be an important risk factor for ischemic heart disease. However, it has not been determined whether plasma insulin levels are independently related to ischemic heart disease after adjustment for other risk factors, including plasma lipoprotein levels.

2.6.4.4. Age

Calcified heart of older woman with Cardiomegaly taken at the Instituto Nacional de Cardiología, Mexico.

Age is by far the most important risk factor in developing cardiovascular diseases, with approximately a tripling of risk with each decade of life.[6] It is estimated that 87 percent of people who die of coronary heart disease are 60 and older.[12] At the same time, the risk of stroke doubles every decade after age 55.[13]

Multiple explanations have been proposed to explain why age increases the risk of cardiovascular diseases. One of them is related to serum cholesterol level.[14] In most populations, the serum total cholesterol level increases as age increases. In men, this increase levels off around age 45 to 50 years. In women, the increase continues sharply until age 60 to 65 years.[14]

Aging is also associated with changes in the mechanical and structural properties of the vascular wall, which leads to the loss of arterial elasticity and reduced arterial compliance and may subsequently lead to coronary artery disease.[15]

2.6.4.5. Sex

Men are at greater risk of heart disease than pre-menopausal women.[6][16] Once past menopause, it has been argued that a woman's risk is similar to a man's[16] although more recent data from the WHO and UN disputes this.[6]

There are many misconceptions about CVDs in women. In reality, CVDs affect as many men as women. However, women loose less years of life due to CVDs as the disease

develops about 7-10 years later in women compared to men (4, 6) (Figure 53). Risk factors of CVDs are similar for men and women.
Every year, 3.3 million women die of heart attacks and 3.2 million die of strokes globally.
Gender norms and roles influence these risk factors as women, in some contexts, do not have access to and control over resources that can diminish their exposure to the risk factors.

For example, women's multiple roles in the household and workplace community may diminish their ability to engage in meaningful physical activity. Social expectations relating to mobility and norms about permitted clothing influence the ability of girls and women to participate in sports and developing a lifelong habit that values physical activity.
In the developing world, tobacco use rates for adult females remain relatively low, but could rise quickly among teenage females (25). Aggressive campaigns by the tobacco industry, which targeted women and girls increasingly over the years, have contributed to such increases and are of great public health concern. The risk of heart disease and stroke in women are often underestimated because of the mistaken notion that females are protected from CVDs. There may be certain differences in the clinical presentation of CVD in women leading to inadequate diagnostic and treatment interventions (82). Better self-awareness in women regarding identification of their cardiovascular risk factors and symptoms can improve early detection.
There is evidence that CVD is underdetected in women and that there are delays in referral, hospitalization, diagnosis and invasive treatment compared to men (83–86).
Women with CVD living in developing countries experience specific challenges in accessing cost-effective prevention, early detection and treatment due to gender inequality, family responsibilities and the costs of seeking care. These factors are made worse by health systems that fail to respond to specific needs of women. Women, although responsible for household food procurement and preparation in most societies, may not have access to the requisite information about healthy food. Women are responsible for rearing children, including how time is used and development of health promoting habits. Such habits are often not passed along if women are not specifically targeted as both beneficiaries and significant gatekeepers for health promotion to other members of their families. Their potential role as "change agents" of families and communities with respect to healthy behaviorsis often underutilized.

Among middle-aged people, coronary heart disease is 2 to 5 times more common in men than in women.[14] In a study done by the World Health Organization, sex contributes to approximately 40% of the variation in the sex ratios of coronary heart disease mortality.[17] Another study reports similar results that gender difference explains nearly half of the risk associated with cardiovascular diseases[14] One of the proposed explanations for the gender difference in cardiovascular disease is hormonal difference.[14] Among women, estrogen is the predominant sex hormone. Estrogen may have protective effects through glucose metabolism and hemostatic system, and it may have a direct effect on improving endothelial cell function.[14] The production of estrogen decreases after menopause, and may change the female lipid metabolism toward a more atherogenic form by decreasing the HDL cholesterol level and by increasing LDL and

total cholesterol levels.[14] Women who have experienced early menopause, either naturally or because they have had a hysterectomy, are twice as likely to develop heart disease as women of the same age group who have not yet gone through menopause.[citation needed]

Among men and women, there are differences in body weight, height, body fat distribution, heart rate, stroke volume, and arterial compliance.[15] In the very elderly, age related large artery pulsatility and stiffness is more pronounced in women.[15] This may be caused by the smaller body size and arterial dimensions independent of menopause.[15]

2.6.4.6. Air pollution

Particulate matter has been studied for its short- and long-term exposure effects on cardiovascular disease. Currently, $PM_{2.5}$ is the major focus, in which gradients are used to determine CVD risk. For every 10 µg/m^3 of $PM_{2.5}$ long-term exposure, there was an estimated 8-18% CVD mortality risk.[18] Women had a higher relative risk (RR) (1.42) for $PM_{2.5}$ induced coronary artery disease than men (0.90) did.[18] Overall, long-term PM exposure increased rate of atherosclerosis and inflammation. In regards to short-term exposure (2 hours), every 25 µg/m^3 of $PM_{2.5}$ resulted in a 48% increase of CVD mortality risk.[19] Additionally, after only 5 days of exposure, a rise in systolic (2.8 mmHg) and diastolic (2.7 mmHg) blood pressure occurred for every 10.5 µg/m^3 of $PM_{2.5}$.[19] Other research has implicated $PM_{2.5}$ in irregular heart rhythm, reduced heart rate variability (decreased vagal tone), and most notably heart failure.[19][20] $PM_{2.5}$ is also linked to carotid artery thickening and increased risk of acute myocardial infarction.[19][20]

2.6.4.7. Dyslipidaemia

Lipoproteins are lipoprotein –complexes and by their physico-chemical properties may distributed on:

-VLDL-s: very low-density lipoproteins
-LDL-s: low-density lipoproteins
-HDL-s: high-density lipoproteins

HDL produced by the liver with main task to bind the circulating in blood free fatty acids and transport them to the liver
The high HDL-level has protective effect against the atherosclerosis (-function)

VLDL
by the enzymatic effect of lipoprotein-lipase from the VLDL-jointed fats disrupted fatty-acids are penetrating into the blood served as energy –resources for the metabolitic processes.

LDL

LDL-cholesterol transported to the liver has intaken by the LDL-receptors and get into the hepatocytes for recirculational(recycling) purposes .The unused part is conjugated to bile-acids and excreated with the produced bile.

The problem appears with the impossibility of recycling of LDL-cholesterol in the liver it could serve as a iniciative process of atheroslerotic alterations.
There are 2 main causes of this phenomenon:
1.genetic alterations: will be inherited in 50% from the parents -85 % of ill males and 65% of ill females will dye before the 40-th year in a cardiovascular disease.
2.structural alteration of LDL-cholesterol (more frequent)
a, by the binding of glucose to them in diabetes(LOX-receptors)
b,injuries by the effects of cell-toxins,O-radicals,free-radicals:transformed into the oxidated LDL-cholesterol.
this modified,injured LDL-cholesterol (oxi-cholesterol) cannot be recognised by the LDL-receptors of liver (maybe by the injury of hepatocellular receptors which cannot be expressed)
Lipoprotein-molecules containing the harmed (injured) LDL will be phaged by the big pathological cells existing in the endothelium (everywhere on the periphery because of the impotence of the hepatocellular membrane)
the level of LDL-bound cholesterol-level is an important risk-factor in the pathological development of atherosclerosis.
During the process of atherosclerosis the native LDL-phagocytosis won't be realised really fast: foam-cell production from them won't be appeared immediately.
The LDL-modification has in here great importance and named lipidoxidation.The most important modification is the reactive O-radicals caused modification:- appears a minimally-oxidated LDL having inflammatory properties in the early phase of atherosclerosis ,but the macrophages cannot recognise it yet.
This minimum-oxidized LDL activates the production of addhesive molecules,chemoattractive proteins(monocyte-attractive proteins) int he endothelium,causing immigration and collection of monocytes in here and decreases the NO-production (antiatherogen effect!)where will be increased production of reactive-O-radicalsleading to the strogly oxidized LDL-production which can be adapted and intaken by the macrophages already (activation of foam-cell-production)The strongly-oxidized LDL-intake realises through thescavenger-receptors:
-SR-A,
-CLA1/BI-SR
-CD-36, CD38
-phosphatidyl-serin
-SR-PSOX:oxidized lipoprotein scavenger receptors
The minimally modified LDL-intake realises through the CD14/toll-like (TLR-4) and the LOX-1 (new oxidized LDL-)receptors.

The problems of statins could be the impossibility to block of oxidized LDL-intake into the macrophages-the atherosclerotic process cannot be stopped.
The one of the main roles of LOX-receptors is the translation of intake of some presclerotic materials and the oxidized LDL into the endothelium.The LOX-receptor expresses in increases amount at
-hypercholesterinaemia
-abdominal obesity
-preeclampsya
-diabethic vasculopathias
-nephropathia
-coronaria-diseases

Int he process of sepsis plays role in thrombocyte-addhesion and int he connection of bacterial proteins to the endothelium.

The largest body of data on lipid-modifying therapy involves 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, known as statins. Large-scale, well-controlled primary prevention and secondary prevention clinical trials have demonstrated unequivocally that statin therapy reduces morbidity and mortality from major CVD events across a spectrum of risk.[70–75] Major statin trials are summarized in Table III of the online data supplement. Given this significant advance in knowledge, target lipid levels have been continually redefined by the National Cholesterol Education Program and its guidelines.[10] Treatment with statins is the standard of care and usual first line of therapy. Nevertheless, other agents, such as fibric acid derivatives (fibrates), nicotinic acid (niacin), cholesterol absorption inhibitors, and bile acid sequestrants (resins), may also prove useful in certain patients.[10] For example, treatment with fibrates can reduce cardiovascular end points in both primary and secondary prevention of CHD.[76,77] In the Helsinki Heart Study,[77,78] which included 4081 men with an average LDL cholesterol level of 188 mg/dL, 5 years of treatment with gemfibrozil resulted in a 34% relative reduction in cardiac deaths and fatal and nonfatal MI (95% CI 8.2% to 52.6%; P<0.02). Findings from the Veterans Affairs Cooperative Studies Program High-Density Lipoprotein Cholesterol Intervention Trial (VA-HIT)[76] demonstrated that secondary prevention patients (2531 men) with low HDL and average LDL levels experienced a significant CHD risk reduction with gemfibrozil, which lowers triglycerides, reduces the proportion of small, dense LDL particles, and enhances the clearance of very-low-density lipoprotein. A substantial percentage of the VA-HIT patients had type 2 diabetes mellitus and/or insulin resistance, a common setting in which combination therapy may be useful. Other patients cannot achieve the increasingly lower target LDL cholesterol levels identified as optimal for their risk status or cannot tolerate statin therapy or the dose of statin required to achieve their LDL goal. For all such patients, ezetimibe, either alone or in combination with a statin, has become a commonly used alternative.

Endothelial Dysfunction in Cardiovascular Diseases: The Role of Oxidant Stress

—Accumulating evidence suggests that oxidant stress alters many functions of the

endothelium, including modulation of vasomotor tone. Inactivation of nitric oxide ($NO^{\cdot}$) by superoxide and other reactive oxygen species (ROS) seems to occur in conditions such as hypertension, hypercholesterolemia, diabetes, and cigarette smoking. Loss of $NO^{\cdot}$ associated with these traditional risk factors may in part explain why they predispose to atherosclerosis. Among many enzymatic systems that are capable of producing ROS, xanthine oxidase, NADH/NADPH oxidase, and uncoupled endothelial nitric oxide synthase have been extensively studied in vascular cells. As the role of these various enzyme sources of ROS become clear, it will perhaps be possible to use more specific therapies to prevent their production and ultimately correct endothelial dysfunction.

Key Words:

- superoxide
- nitric oxide
- endothelium
- NADH/NADPH oxidase
- xanthine oxidase

Oxidative Stress and Endothelial Dysfunction

Advances in pathophysiological research suggest that the CVD continuum begins with risk factors that initiate the process that leads to tissue damage. The pathophysiological continuum includes oxidative stress, endothelial dysfunction, inflammatory processes, and vascular remodeling in the initiation and continuation of atherosclerotic disease. An understanding of these processes has enabled the development of therapeutic strategies targeting individual factors along the CVD continuum.

Normal endothelial function appears to depend greatly on the homeostatic balance between nitric oxide (NO) and reactive oxygen species, such as superoxide anion and hydrogen peroxide.[3] Oxidative stress results when an increase in reactive oxygen species generation leads to a reduction in NO activity and subsequent endothelial dysfunction. This imbalance is a known effect of established CVD risk factors such as cigarette smoking, diabetes mellitus, and obesity. In addition, oxidative stress induces the expression of proinflammatory mediators such as vascular cell adhesion molecule, intracellular adhesion molecule, and chemoattractant proteins that play a role in early atherogenesis.[3]

Through receptor-mediated and non–receptor-mediated mechanisms, endothelial cells regulate vascular tone, inflammation, lipid metabolism, cell growth and migration, and interactions with the extracellular matrix.[4] Any disruption of normal endothelial function can induce pathological vascular responses, such as smooth muscle cell proliferation, vasoconstriction, inflammation, and thrombosis. For example, endothelial dysfunction may shift relative concentrations of tissue-type plasminogen activator and plasminogen activator inhibitor type 1 toward thrombosis. Plasminogen activator inhibitor-1 is the primary inhibitor of tissue-type plasminogen activator, and elevated levels of plasminogen activator inhibitor-1 relative to tissue-type plasminogen activator lead to inhibition of the fibrinolytic system.[5] Endothelial dysfunction is also associated with changes in concentrations of important local inflammatory mediators, such as chemokines, adhesion molecules, and cytokines.

Role of Risk Factors in Oxidative Stress and Endothelial Dysfunction

Oxidized low-density lipoprotein (LDL) inactivates NO, which results in increased oxidative stress and enhanced expression of cellular adhesion molecules.[6] Higher oxidized LDL content in the lipid core of atherosclerotic plaques may also promote plaque instability.[7] Small, dense LDL particles are highly atherogenic and are associated with increased triglyceride levels. The structure of small, dense LDL particles

contributes to their atherogenicity, with increased susceptibility to oxidation, easier penetration into the arterial wall, and altered interactions with the LDL receptor.

Elevated blood pressure promotes the development of atherosclerotic plaques and increases the risk of CVD complications.[8] Endothelial dysfunction in chronic hypertension is associated with decreased endothelium-dependent relaxation. In hypertensive vessels, increased expression of matrix proteins, matrix proteinases, and growth factors leads to structural changes, such as decreased lumen diameter, increased extracellular matrix, and thickened media.[4] In addition, hypertension is associated with increased production of free radicals and oxidative stress that may promote an inflammatory state and enhance the atherosclerotic process.[8] Indeed, results from the Women's Health Study[9] and other epidemiological studies demonstrate that levels of C-reactive protein, a marker of systemic inflammation, correlate significantly with future risk of developing hypertension.

The metabolic syndrome comprises a group of lipid and nonlipid risk factors, such as insulin resistance and its associated hyperinsulinemia, atherogenic dyslipidemia, central obesity, and hypertension.[10] Metabolic syndrome is associated with increased CVD risk.[10] Specifically, insulin resistance and subsequent hyperinsulinemia appear to contribute to endothelial dysfunction and impaired NO responses.[11,12] Furthermore, the chronic exposure of vascular smooth muscle to hyperinsulinemia may promote intimal hyperplasia. In addition, the excess adipose tissue characteristic of the metabolic syndrome secretes prothrombotic factors and proinflammatory cytokines, which may contribute to vascular disease.[12,13] Changes in the distribution of adipose tissue, namely, a shift from subcutaneous to visceral locations, may also be associated with a loss of antiinflammatory mediators such as adiponectin.

Endothelial Chlamydia pneumoniae infection promotes oxidation of LDL

The bacterium Chlamydia pneumoniae chronically infects atheromatous lesions and is linked to atherosclerosis by modifying inflammation, proliferation, and the lipid metabolism of blood monocytes. As continuous LDL modification in the vascular intima is crucial for atherogenesis we investigated the impact of endothelial infection on LDL oxidation. HUVEC were infected with a vascular C. pneumoniae strain.

Supernatants of infected cells but not cell lysates increased lipid peroxidation products (6.44 vs 6.14 nmol/ml, $p<0.05$) as determined by thiobarbituric acid reacting substances assay. Moreover, supernatants rendered human LDL more susceptible to oxidation as shown in a copper-ion catalysed LDL oxidation assay by a 16% reduction of LDL resistance against pro-oxidative stimuli ($p<0.05$). Chlamydial infection of vascular endothelial cells releases acellular components that convert LDL to its proatherogenic form and reduce its resistance against oxidation. Foci of chronic endothelial chlamydial infection may thus continuously contribute to the dysregulated lipid metabolism that promotes atherogenesis.

This is extremely important considering that 1 in 3 people will die from complications attributable to atherosclerosis. In order to stem the tide education and awareness that

cardiovascular disease poses the greatest threat and measures to prevent or reverse this disease must be taken.

Obesity and diabetes mellitus are often linked to cardiovascular disease,[22] as are a history of chronic kidney disease and hypercholesterolaemia.[23] In fact, cardiovascular disease is the most life threatening of the diabetic complications and diabetics are two- to four-fold more likely to die of cardiovascular-related causes than nondiabetics.[24][25][26]

2.6.4.8. Diabetes Mellitus

Deaths from CVD and diabetes

Situation

In 2008, CVDs were the leading cause of NCD deaths (17 million deaths). Diabetes caused 1.3 million deaths.

View interactive graph –static maps also

Epidemiology of diabetes mellitus

CVDglobal atlas9789241564373_eng.pdf-CONNECTED DIABETES MELLITUS 2011 PAGES:

Globally, as of 2010, an estimated 285 million people had diabetes, with type 2 making up about 90% of the cases.[4] Its incidence is increasing rapidly, and by 2030, this number is estimated to almost double.[38] Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in the more developed countries. The greatest increase in prevalence is, however, expected to occur in Asia and Africa, where most patients will probably be found by 2030.[38] The increase in incidence in developing countries follows the trend of urbanization and lifestyle changes, perhaps most importantly a "Western-style" diet. This has suggested an environmental (i.e., dietary) effect, but there is little understanding of the mechanism(s) at present, though there is much speculation, some of it most compellingly presented.[38]

Diabetes is an important chronic disease which incidence is globally increasing and though considered as an epidemic. The World Health Organization (WHO) estimated there were 30 million people who had diabetes worldwide in 1985. This number increased to 135 million by 1995 and reached 217 million in 2005. By the year 2030 WHO predicts this number will increase to at least 366 million. This growth in diabetes prevalence, driven principally by an increased prevalence of type 2 diabetes (T2D), is occurring in both developing and developed countries. The incidence of type 1 diabetes (T1D) is also increasing in parallel to that of T2D worldwide.

Cardiovascular diseases (CVD) are the most prevalent cause of mortality and morbidity among people with T2D and T1D [8–10]. In 2004, in the USA the presence of CVD and stroke was found in 68% and 16% of deaths related to diabetes among people older than 65 years, respectively [11]. Adult people with diabetes present rates of mortality due to heart disease and stroke from two to four times higher than those without diabetes [11]. It has been stated that patients with T2D without a previous history of myocardial infarction have the same risk of coronary artery disease (CADs) as nondiabetic subjects with a history of myocardial infarction [12]; this has led the National Cholesterol Education Program to consider diabetes as a coronary heart disease risk equivalent [13]. However, there is still some uncertainty as to whether the cardiovascular risk conferred by diabetes is truly equivalent to that of a previous myocardial infarction [14]. In general, patients with diabetes aggregate other comorbidities such as obesity, hypertension, and dyslipidemia which also contribute to increase the risk for CVD [15]. In the period of 2005 to 2008, the American Diabetes Association (ADA) estimated that 67% of people with diabetes older than 20 years presented blood pressure levels ≥140/90 mmHg or were using antihypertensive drugs [16]. Although there is strong evidence that supports both the efficacy and cost effectiveness of programs directed towards an improvement of glycemic control and other cardiovascular risk factors in patients with T2D [17] and T1D [18], the majority of these patients [19, 20] never achieve the goals established by guidelines issued by diabetes societies [16, 21].

Diabetes mellitus is now considered a "cardiovascular risk equivalent" that confers to diabetic persons a risk of future CVD events equivalent to that of persons who have survived a prior MI.[83]

Approximately 50% to 75% of all deaths among patients with diabetes mellitus are CVD related, and type 2 diabetes mellitus increases the risk of death from CHD by 2- to 4-fold.[84]

Patients with diabetes are prone to a number of cardiovascular risk factors beyond hyperglycemia, including hypertension and dyslipidemia. Owing to the high risk associated with diabetes, the aggressive control of all risk factors is especially important and includes both lifestyle changes and pharmacological intervention. Clinical trials in diabetes mellitus have examined cardiovascular risk reduction in patients with existing disease and the prevention of new-onset diabetes mellitus in patients with no evidence of diabetes at baseline.[41,59,67,69,85–105] Major trials are summarized in Table IV of the online data supplement.

Achieving and maintaining glycemic control in patients with type 1 and type 2 diabetes mellitus can delay the onset or prevent the progression of microvascular disease and, to a lesser extent, macrovascular disease. For example, intensive glucose control with metformin in the United Kingdom Prospective Diabetes Study (UKPDS) 34 decreased all-cause mortality, primarily due to fewer cardiovascular deaths, particularly deaths due to MI, in a subgroup of overweight subjects with type 2 diabetes mellitus.[85] Despite the relatively disappointing impact on cardiovascular events of tighter blood glucose control in patients with diabetes, the Steno-2 trial showed that aggressive intervention to manage the multiple risk factors present in diabetes does have a favorable impact on outcomes.[41] The effects of the insulin-sensitizing thiazolidinediones on cardiovascular

events are being evaluated in several clinical trials. The first to be reported, the PROspective pioglitAzone Clinical Trial In macroVascular Events (PROACTIVE) trial,[86] showed a nonsignificant reduction in the primary composite end point; however, pioglitazone significantly reduced the composite secondary end point of all-cause mortality, MI, or stroke.

More aggressive control of hypertension (to a blood pressure level <150/85 mm Hg) in patients with diabetes mellitus, with a β-blocker or an ACE inhibitor as the main treatment, decreases both macrovascular and microvascular event rates compared with less aggressive control (<180/105 mm Hg).[89,90] The STOP Hypertension-2 trial[92] found that treatment of elderly diabetic patients with diuretics, β-blockers, or both was comparable in efficacy to treatment with calcium channel blockers or ACE inhibitors in reducing cardiovascular mortality. In the HOPE study, 37.5% of participants had diabetes at study entry, and ramipril significantly reduced rates of MI, death, or stroke compared with placebo among these high-risk patients.[93] Ramipril also decreased the risk of diabetic complications, such as nephropathy and the need for dialysis.

Inhibition of the RAAS also appears to delay the onset of diabetes in hypertensive patients and in those with congestive heart failure.[106] Findings from the CAPPP[102] demonstrated that the risk of developing diabetes was 14% (95% CI 1% to 26%) lower among patients with hypertension treated with captopril than among those treated with diuretics or β-blockers (*P*=0.039). Among subjects in the HOPE study who were not diabetic at study initiation, those who received ramipril were significantly less likely to develop diabetes during the 5-year study than those who received placebo.[67] Among ALLHAT participants who were classified as nondiabetic at baseline, the incidence of diabetes at 4 years was 8.1% in the lisinopril group compared with 9.8% in the amlodipine group and 11.6% in the chlorthalidone group.[66]

Treatment with an ARB also appears to reduce the risk of developing diabetes. Among hypertensive patients with evidence of LVH in the LIFE study,[103] those in the losartan group had a 25% lower risk (95% CI 12% to 37%; *P*=0.001) of developing diabetes than those in the atenolol group.

Similar results were reported in the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) study,[104] in which candesartan reduced the risk of new-onset diabetes by 22% versus placebo (95% CI 4% to 36%; *P*=0.02) in patients with heart failure. The Valsartan Antihypertensive Long-term Use Evaluation (VALUE)[69] reported a significant 23% (95% CI 14% to 31%) lower rate of new-onset diabetes in the valsartan arm compared with the amlodipine arm (*P*<0.0001). A meta-analysis[106] examined the development of new-onset type 2 diabetes mellitus in 10 randomized controlled trials in which RAAS inhibitors (5 ACE inhibitor trials and 5 ARB trials) were compared with placebo or other antihypertensive agents. Overall, there was a mean weighted RR reduction of 22% (95% CI 18% to 26%; *P*<0.00001) after RAAS inhibition. The beneficial effect was similar with ACE inhibitors and ARBs and in patients with hypertension and in those with heart failure. The type of comparator (placebo or active) did not affect the results.

Statin drugs also reduce the risk of major coronary events in patients with diabetes and impaired fasting glucose.[97,98] For example, the HPS study[99] reported that diabetic patients treated with simvastatin 40 mg/d experienced a 27% reduction in risk of major

coronary events (95% CI 15% to 38%; *P*<0.0001) and a 22% reduction in major vascular events (95% CI 13% to 30%; *P*<0.0001) compared with placebo. The reduction in risk extended to patients with no diagnosed occlusive arterial disease at entry and those with pretreatment LDL cholesterol levels <3.0 mmol/L (116 mg/dL).[99] It is now recommended that patients with diabetes achieve LDL cholesterol levels of <100 mg/dL regardless of their cardiovascular history.

2.6.4.9. Multiple Risk Factors

Cardiovascular risk factors rarely occur in isolation but rather tend to cluster, which confers high risk in individual persons. A well-known example of this phenomenon is the metabolic syndrome, which is characterized by a group of risk factors including central obesity, dyslipidemia, hypertension, and impaired glucose/insulin homeostasis. Intervention in such patients may influence the ultimate development of diabetes, CVD, or both. Although trials have targeted individual components of this syndrome, no end-point trials have specifically targeted the syndrome in its entirety. However, a number of trials have been conducted in patients with >1 risk factor for CVD.[66,69,80,107–109] Results of these trials are summarized in Table V of the online data supplement.

Two large trials of patients with multiple risk factors included both a hypertension arm and a lipid-lowering arm: ALLHAT and ASCOT. ALLHAT is the largest randomized, double-blind, controlled clinical trial with CVD end points in hypertensive patients conducted to date (>42 000 patients originally enrolled). In the hypertension arm, patients were initially randomized to chlorthalidone 12.5 to 25 mg/d, amlodipine 2.5 to 10 mg/d, lisinopril 10 to 40 mg/d, or doxazosin 2 to 8 mg/d.[110] (The doxazosin arm of the trial was terminated early because of an increased risk of congestive heart failure compared with chlorthalidone.[111]) The target blood pressure in ALLHAT was <140/90 mm Hg. Patients who did not achieve the blood pressure goal with the primary double-blinded treatment could receive additional, open-label treatment with other antihypertensive agents.[110] After a mean follow-up of 4.9 years, there was no significant difference between treatments in the primary outcome measure of fatal CHD or nonfatal MI.[66]

The ASCOT study[112] had 2 primary objectives: first, to assess whether combination therapy with newer antihypertensive agents (ie, amlodipine, plus the ACE inhibitor perindopril if needed to achieve goal blood pressure) is more effective in reducing nonfatal MI and fatal CHD (combined primary end point) than traditional combination therapy with a β-blocker (atenolol) followed by a diuretic (bendroflumethiazide), if needed; and second, to assess whether the addition of atorvastatin to these combinations would provide greater benefits in a subgroup of patients with normal to mildly elevated total cholesterol levels (≤6.5 mmol/L [≤251 mg/dL]). Eligible patients had at least 3 CVD risk factors, such as smoking, LVH, type 2 diabetes mellitus, or peripheral vascular disease.[112]

The ASCOT blood pressure-lowering arm (ASCOT-BPLA)[108] was terminated in December 2004 because of a significantly lower incidence of all-cause mortality with amlodipine-based therapy (11% RR reduction, 95% CI 1% to 19%; P=0.025). Although final results showed no significant difference in the primary end point (RR 0.90, 95% CI 0.79 to 1.02; P=0.1052) with amlodipine-based treatment versus atenolol-based treatment, significant differences in favor of amlodipine plus perindopril therapy were

observed for several secondary end points, including fatal and nonfatal stroke (23% RR reduction, 95% CI 11% to 34%; P=0.0003) and total cardiovascular events and procedures (16% RR reduction, 95% CI 10% to 22%; P<0.0001). Amlodipine plus perindopril therapy was also associated with a significant 30% reduction in the incidence of new-onset diabetes (95% CI 22% to 37%; P<0.0001).[108]

The VALUE trial[69] examined whether regimens based on valsartan or amlodipine would have different effects on cardiovascular outcomes in hypertensive patients at high risk for cardiac events if the same blood pressures were achieved.

The unintended unequal reductions in blood pressure in favor of amlodipine, especially early in the study, made it difficult to arrive at definitive conclusions or to prove the primary hypothesis of the trial (that an RAAS-based regimen would be superior to another regimen at reducing cardiac morbidity and mortality, the primary trial end point), because it was assumed that the 2 regimens would achieve equal blood pressure lowering results. Nevertheless, there was no difference in the primary end point between the 2 treatment groups, although there were differences in cause-specific outcomes (eg, significantly [P=0.02] lower incidence of MI in the amlodipine arm but a positive trend in favor of valsartan for heart failure).[69] The investigators noted that 79% of the excess MIs in the valsartan group occurred during the first 2 years of the study, when there was a greater discrepancy in blood pressure control between the 2 treatment groups; this emphasizes the importance of early reductions in blood pressure for decreasing the risk of subsequent CVD events.

Numerous trials have examined the role of statins in patients with multiple cardiovascular risk factors. A subset (10 355 patients aged ≥55 years) of the total ALLHAT cohort was assigned to the open-label, lipid-lowering arm of the trial (ALLHAT-LLT).[109] In addition to the assigned antihypertensive therapy, patients with moderate hypercholesterolemia received pravastatin and a lipid-lowering diet or the lipid-lowering diet plus "usual care" as determined by primary care physicians.[110] In addition to hypertension and moderate hypercholesterolemia, all patients in the lipid-lowering arm had at least 1 additional CHD risk factor. The primary end point was all-cause mortality, and mean follow-up was 4.8 years. Among the subset of patients who had LDL cholesterol levels calculated, pravastatin lowered LDL cholesterol by 28% compared with an 11% reduction in the usual-care group. (During the trial, 32% of usual-care patients with CHD and 29% of those without CHD started taking lipid-lowering drugs.) The differences in reductions in total and LDL cholesterol were not statistically significant. Perhaps because of the lack of a significant difference in cholesterol lowering, all-cause mortality was similar in the 2 treatment groups, as were CHD event rates (fatal CHD or nonfatal MI).[109]

Of the 19 342 patients who were randomized to the antihypertensive treatment arms of ASCOT, 10 305 were also eligible for the lipid-lowering arm and were further assigned to treatment with atorvastatin 10 mg/d or placebo.[80] After a median follow-up of 3.3 years, the primary end point was significantly lowered in the atorvastatin group compared with the placebo group (RR reduction 36%, 95% CI 17% to 50%; P=0.0005). The significant benefits of atorvastatin therapy were observed for a number of secondary end points, including total cardiovascular events and revascularization procedures, total coronary events, and nonfatal MI (excluding silent MIs) plus fatal

CHD. Atorvastatin also caused a significant 27% RR reduction (95% CI 4% to 44%; P=0.024) in fatal and nonfatal strokes.[80]

Left Ventricular Hypertrophy

LVH is the characteristic pathophysiological mechanism underlying the natural course of heart failure and is a strong predictor of CVD morbidity and mortality. LVH is most commonly caused by elevated blood pressure. Several classes of antihypertensive drugs have been shown to interrupt the progression of LVH. A meta-analysis[113] of 80 double-blind clinical trials that assessed the effects of antihypertensive therapy on left ventricular mass found that ARBs produced the greatest reduction in left ventricular mass, followed by calcium channel blockers, ACE inhibitors, diuretics, and β-blockers. Some evidence also suggests that interventions to reduce left ventricular mass may decrease the risk of events, which provides further support for the existence of a CVD continuum. A meta-analysis was performed of studies that reported left ventricular mass before and during antihypertensive therapy with subsequent assessment of cardiovascular events. Compared with persistence or new development of LVH, regression of LVH was associated with a marked reduction in risk for subsequent cardiovascular events, including heart failure.[114] Evidence from the LIFE trial also supports the premise that interventions targeted to high-risk hypertensive patients with LVH can reduce the risk of cardiovascular events.

Atherosclerosis and Stable CAD

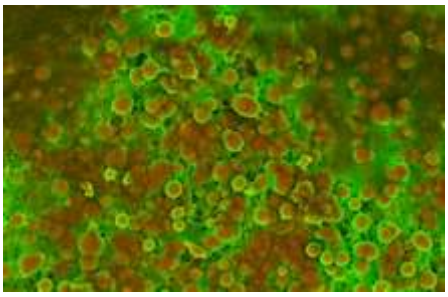
Atherosclerosis is the major underlying condition in patients who develop myocardial ischemia, CAD, MI, heart failure, peripheral arterial disease, and stroke. A number of trials have used angiography and other imaging techniques to measure changes in the diameter of the arterial lumen.[115–127] Results indicate that aggressive lipid modification may retard progression or cause regression of coronary plaques, decrease the need for revascularization, and reduce the risk of major coronary events.

2.6.5.1. Screening

Screening ECGs (either at rest or with exercise) are not recommended in those without symptoms who are at low risk.[27] In those at higher risk the evidence for screening with ECGs is inconclusive.[27]

Some biomarkers may add to conventional cardiovascular risk factors in predicting the risk of future cardiovascular disease; however, the clinical value of some biomarkers is still questionable.[28][29] Currently, biomarkers which may reflect a higher risk of cardiovascular disease include:

- **Coronary artery calcification[30]**



Density-Dependent Colour Scanning Electron Micrograph SEM (DDC-SEM) of cardiovascular calcification, showing in orange calcium phosphate spherical particles (denser material) and, in green, the extracellular matrix (less dense material).[30]

- **Carotid intima-media thickness**
- **Carotid total plaque area [31]**
- **Higher fibrinogen and PAI-1 blood concentrations**
- **Elevated homocysteine**
- **Elevated blood levels of asymmetric dimethylarginine**
- **Inflammation as measured by C-reactive protein**
- **Elevated Low-density lipoprotein-p[32]**
- **Elevated blood levels of brain natriuretic peptide (also known as B-type) (BNP)[33]**

2.6.6.1. Medication

Aspirin has not been found to be of benefit overall in those at low risk of heart disease as the risk of serious bleeding is equal to the benefit with respect to cardiovascular problems.[74]

Statins are effective in preventing further cardiovascular disease in those with a history of cardiovascular disease.[75] As the event rate is higher in men than in women, the decrease in events is more easily seen in men than women.[75] In those without cardiovascular disease but risk factors statins appear to also be beneficial with a decrease in mortality and further heart disease.[76] The time course over which statins provide preventation against death appears to be long, of the order of one year, which is much longer than the duration of their effect on lipids.[77]

Pharmacological Interventions

Clinical trials of pharmacological therapy have shown unequivocally that risk factor reduction decreases the risk of morbidity and mortality. Evidence accumulated over the

past several decades indicates that antihypertensive treatment with several classes of agents, including diuretics, ACE inhibitors, angiotensin II receptor blockers (ARBs), β-blockers, and calcium channel blockers, effectively lowers blood pressure in a broad range of patients, while also reducing CVD morbidity and mortality.[49,50] In clinical trials, antihypertensive treatment has been associated with reductions averaging 35% to 40% in stroke, 20% to 25% in MI, and >50% in heart failure.[33] A meta-analysis[51] of 58 randomized trials of cholesterol lowering by any means (fibrates, resins, niacin, statins, or dietary change) showed that for an LDL cholesterol reduction of 1.0 mmol/L (39 mg/dL), the risk of ischemic heart disease events was reduced by 11% the first year, 24% in the second year, 33% in years 3 to 5, and 36% thereafter. After several years, a reduction of 1.8 mmol/L (70 mg/dL) would reduce ischemic events by an estimated 61%.[51] Similar results were reported from a more recent, prospective meta-analysis that examined the efficacy and safety of cholesterol lowering with statins in 14 randomized trials involving >90 000 participants.[52] Each 1-mmol/L reduction in LDL cholesterol was associated with a 23% decrease in RR of first major coronary events and a 21% reduction in major cardiovascular events, largely irrespective of the baseline lipid profile or other presenting patient characteristics.

By interrupting the underlying pathophysiology of CVD, risk factor modification reduces subsequent events, thereby providing substantiating evidence of a CVD continuum.

The largest body of data on lipid-modifying therapy involves 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, known as statins. Large-scale, well-controlled primary prevention and secondary prevention clinical trials have demonstrated unequivocally that statin therapy reduces morbidity and mortality from major CVD events across a spectrum of risk.[70–75] Major statin trials are summarized in Table III of the online data supplement. Given this significant advance in knowledge, target lipid levels have been continually redefined by the National Cholesterol Education Program and its guidelines.[10] Treatment with statins is the standard of care and usual first line of therapy. Nevertheless, other agents, such as fibric acid derivatives (fibrates), nicotinic acid (niacin), cholesterol absorption inhibitors, and bile acid sequestrants (resins), may also prove useful in certain patients.[10] For example, treatment with fibrates can reduce cardiovascular end points in both primary and secondary prevention of CHD.[76,77]

In the Helsinki Heart Study,[77,78] which included 4081 men with an average LDL cholesterol level of 188 mg/dL, 5 years of treatment with gemfibrozil resulted in a 34% relative reduction in cardiac deaths and fatal and nonfatal MI (95% CI 8.2% to 52.6%; P<0.02). Findings from the Veterans Affairs Cooperative Studies Program High-Density Lipoprotein Cholesterol Intervention Trial (VA-HIT)[76] demonstrated that secondary prevention patients (2531 men) with low HDL and average LDL levels experienced a significant CHD risk reduction with gemfibrozil, which lowers triglycerides, reduces the proportion of small, dense LDL particles, and enhances the clearance of very-low-density lipoprotein. A substantial percentage of the VA-HIT patients had type 2 diabetes mellitus and/or insulin resistance, a common setting in which combination therapy may be useful. Other patients cannot achieve the increasingly lower target LDL cholesterol levels identified as optimal for their risk status or cannot tolerate statin therapy or the dose of statin required to achieve their LDL goal. For all such patients, ezetimibe, either alone or in combination with a statin, has become a commonly used alternative.

Pharmacological Therapy

Long-term medical therapy with a variety of agents has been evaluated in patients with stable CAD.[67,81,129–136] Important clinical trials are summarized in Table VII of the online data supplement. Aspirin decreases the risk of cardiovascular events and is the mainstay of antiplatelet therapy for patients who have chronic stable CAD, with or without prior MI.[137] In the Swedish Angina Pectoris Angina Trial (SAPAT),[130] the first prospective study of aspirin in stable angina, the addition of a low dose of aspirin to sotalol showed significant benefit compared with placebo in decreasing the risk of primary outcome events (MI and sudden cardiac death). The newer antiplatelet agent clopidogrel can be used as an alternative for patients who cannot tolerate aspirin. The combination of aspirin and clopidogrel has also been investigated, and some of the relevant clinical trials are discussed under "Acute Coronary Syndromes" in part II.

The management of dyslipidemia, hypertension, and diabetes mellitus plays a pivotal role in patients with CAD. If lifestyle modifications alone do not control these risk factors, then drug treatment is warranted. As shown by the 4S,[70] CARE,[71] LIPID,[72] and HPS[75] trials discussed earlier, the use of statins in persons with known CAD or at high risk for the development of CAD, including persons with normal or only slightly elevated levels of LDL cholesterol, results in significant decreases in all-cause and cardiovascular mortality and coronary/cardiovascular events. Other trials that have added to the experience of intensive lipid lowering in patients with stable CAD include the Atorvastatin VErsus Revascularization Therapy (AVERT)[134] and Treating to New Targets (TNT)[135] trials. In AVERT, patients with stable CAD who had been recommended for PCI were randomized to either atorvastatin 80 mg/d or to angioplasty followed by usual care (which could include lipid-lowering therapy).

After 18 months, atorvastatin had decreased the RR of any ischemic event by 36% (P=0.048) versus revascularization.[134] This result did not reach the level for statistical significance after adjustment for interim analyses (a probability value of 0.045). The reduction was primarily due to a decreased incidence of revascularization procedures and worsening angina that required hospitalization. Atorvastatin also significantly (P=0.03) prolonged the time to first ischemic event.[134]

The hypothesis of the TNT trial was that aggressively lowering LDL cholesterol to levels well below currently recommended treatment targets (ie, 100 mg/dL) with atorvastatin 80 mg/d would reduce the occurrence of major cardiovascular events compared with therapy that achieved lesser reductions (with atorvastatin 10 mg/d).[135] More than 10 000 patients with clinically evident CHD and LDL cholesterol levels <130 mg/dL were followed up for a mean 4.9 years. The LDL cholesterol levels achieved were 77 mg/dL in the intensive therapy group compared with 101 mg/dL in the more moderate therapy group. The greater LDL cholesterol reduction with atorvastatin 80 mg/d was associated with a 22% RR reduction (95% CI 11% to 31%; P<0.001) for the composite end point of CHD death, nonfatal MI, resuscitated cardiac arrest, and fatal or nonfatal stroke.[135] There was no difference between the 2 groups in overall mortality. The incidence of persistent elevations in liver aminotransferase levels was 0.2% in the 10-mg group and 1.2% in the 80-mg group (P<0.001).[135]

Another trial of high-dose versus usual-dose statin therapy in patients with stable CHD was the Incremental Decrease in End points through Aggressive Lipid lowering

(IDEAL) study,[81] which compared atorvastatin 80 mg/d with simvastatin 40 mg/d over a median 4.8 years of follow-up. Although the absolute difference in LDL cholesterol levels achieved at 1 year (22.9 mg/dL) was similar to that observed at the end of the TNT trial (24 mg/dL), the 11% (95% CI −1% to 22%) proportional reduction in risk of the primary composite end point (time to first major coronary event) with aggressive therapy was not significantly different from more moderate therapy. Atorvastatin 80 mg/d significantly (P=0.02) decreased the RR of nonfatal acute MI compared with simvastatin 40 mg/d (hazard ratio 0.83, 95% CI 0.71 to 0.98), but no difference was observed in cardiovascular or all-cause mortality.[81]

Antihypertensive therapy in patients with CAD also lowers the incidence of subsequent cardiovascular events. In the large-scale HOPE study,[67] treatment with ramipril for a mean of 4.5 years significantly reduced rates of cardiovascular death, MI, or stroke among patients at high risk for or with confirmed CAD but with no left ventricular dysfunction or heart failure. The HOPE study had a 2×2 factorial design and also randomized patients to receive either 400 IU of vitamin E daily or matching placebo. Dietary supplementation with vitamin E had no apparent effect on cardiovascular outcomes.[131] Longer-term (median 7 years) follow-up confirmed the lack of benefit for the prevention of major cardiovascular events and cancer and suggested that vitamin E supplementation may have increased the risk of heart failure.[138]

Two subsequently completed trials in patients with stable CAD but no symptomatic heart failure provide evidence that the benefit of ACE inhibitor therapy may depend on the patient's overall level of risk, thus explaining a "gradient" of results. The EURopean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease (EUROPA),[132] which enrolled patients who were considered at lower risk than those in HOPE, showed significant reductions in a combined primary end point (cardiovascular mortality, MI, or cardiac arrest) with perindopril compared with placebo. By contrast, the Prevention of Events with Angiotensin Converting Enzyme inhibition (PEACE) trial[133] reported that trandolapril did not significantly reduce the incidence of combined cardiovascular death, MI, or coronary revascularization compared with placebo. The investigators noted that patients enrolled in PEACE had an average baseline left ventricular ejection fraction of 58% and normal cholesterol concentrations; in addition, the baseline mean blood pressure was equivalent to the on-treatment levels achieved with ACE inhibitor therapy in both the HOPE and EUROPA trials.[133] Moreover, the patients in PEACE also received more intensive management of risk factors than those in HOPE and EUROPA.

CABG Surgery

Much of the clinical trial information comparing surgery with medical treatment was published before the 1990s. Three major randomized trials of CABG compared with medical therapy were begun in the 1970s and examined survival in patients with mild to moderate angina pectoris: the Veterans Affairs (VA) Cooperative Study, the European Cardiac Society Study (ECSS), and the National Institutes of Health–supported Coronary Artery Surgery Study (CASS).[139–141] Limitations exist in generalizing the results of these trials to current practice, because the risk profile of patients referred for surgery and the available surgical techniques and medical interventions have evolved considerably since the time those studies were conducted. Nonetheless, the basic findings of these and other trials, synthesized in a meta-analysis,[142] continue to influence current

practice guidelines.[143] The meta-analysis found that CABG improves long-term survival in a range of patients at moderate to high risk compared with medical therapy. The absolute benefit of CABG is greatest in certain anatomic subsets of patients, such as those with left main disease and 3-vessel CAD.[142]

Percutaneous Coronary Intervention

PCI, which includes conventional balloon angioplasty, coronary atherectomy, and stent implantation, is performed in more than 2 million patients worldwide annually.[144,145] The large number of clinical trials that have investigated PCI in patients with stable CAD include comparisons of conventional balloon angioplasty and/or stenting with CABG, drug-eluting versus bare-metal stents, and pharmacological therapy to enhance the success of the PCI procedure and to decrease postprocedure complications.[145–190] These trials are summarized in Table VIII of the online data supplement.

In patients with stable CAD, PCI effectively relieves the signs and symptoms of myocardial ischemia due to coronary artery obstructions and improves the quality of life in symptomatic patients. However, some evidence suggests that PCI may be less useful in stable CAD patients than intensive medical therapy for the prevention of new ischemic events, such as death and MI due to plaque rupture in less significant (<50%) coronary stenoses.[134] In contrast to the outcomes with PCI in patients with stable CAD, PCI reduces the frequency of death, recurrent MI, and recurrent ischemia in patients who present with an acute coronary syndrome, including ST-segment elevation MI (compared with fibrinolytic therapy)[191] and non–ST-segment elevation MI.[192,193]

Although the timing of PCI and the intensity of anticoagulation therapy may depend on the clinical presentation, the methods used to perform coronary revascularization are similar regardless of the particular clinical scenario. In addition, in patients with both stable and unstable CAD, PCI should be coupled with aggressive risk factor modification and lipid management to prevent further ischemic events.

Coronary Stenting

Early types of PCI procedure, that is, conventional balloon angioplasty and coronary atherectomy, were limited by clinical restenosis rates that approached 30% to 40% over the first year after the procedure.[146] Recurrent narrowing within the treated lesion was due to arterial remodeling and vessel constriction rather than intimal hyperplasia.[194] Balloon-expandable coronary stents provided sufficient arterial scaffolding to prevent the unfavorable vessel constriction that occurred after angioplasty. However, varying degrees of intimal hyperplasia developed within the stent struts, which resulted in clinical recurrence in ≈20% of patients.[195]

Numerous randomized trials that compared coronary stents with balloon angioplasty have shown a marked benefit with coronary stents on clinical and angiographic recurrence in patients with de novo and restenotic[146] lesions, on the number of total occlusions, and in patients with saphenous vein graft stenoses. An additional benefit of coronary stenting is that coronary stents “tack up” coronary dissections induced by balloon angioplasty that often (in 5% of cases) used to necessitate emergency CABG.[196,197]

Since the introduction of coronary stents in the early and mid-1990s, coronary stenting has become the default therapy for patients with stable CAD undergoing PCI procedures. More experience with coronary stents has demonstrated that recurrence rates after stenting are higher in patients with long lesions, in those with lesions in smaller vessels, and in those with diabetes mellitus.[149] Although the use of γ-radiation[148] and β-radiation[149,150] therapy reduced recurrence rates in patients treated for in-stent restenosis by 30% to 40%, these methods have been limited by the occurrence of edge restenosis and late (up to 2 years) stent thrombosis, which mandates the use of extended antiplatelet therapy, particularly if additional stents are required. Because of the limitations of these alternative therapies, newer stent designs and drug-delivery systems that would provide a more durable result in patients undergoing PCI were developed.

Drug-Eluting Stents

Drug-eluting stents include a polymer coating and an antiproliferative agent that reduces the magnitude of intimal hyperplasia after stent placement. The first clinically available drug-eluting stent was the sirolimus-eluting stent (SES; CYPHER, Cordis Corporation, Warren, NJ), which provided controlled release of sirolimus for 30 days after the procedure using a "Topcoat" durable polymer coating. Several randomized studies have demonstrated dramatic (60% to 80%) reductions in clinical and angiographic restenosis using coated compared with bare-metal stents, resulting from a profound reduction in the magnitude of intimal hyperplasia within the stent.[151–153] Another stent available for clinical use, the paclitaxel-eluting stent (PES; TAXUS, Boston Scientific, Natick, Mass), releases the antimicrotubule agent paclitaxel from the Translute polymer for 30 days after the procedure.[154] In contrast to the SES, 92% of the paclitaxel remains within the polymer after the initial elution. The slow-release formulations of the PES are associated with reduced in-stent neointimal formation and restenosis compared with the bare-metal stent. These effects have been sustained for up to 2 years after the procedure.[155]

A number of studies have compared the outcomes of patients treated with SES and PES, with varying results depending on the complexity of the lesions treated. In patients with complex coronary disease, such as those with in-stent restenosis, there appears to be an advantage with the SES. For example, the SES and PES were compared with angioplasty in 300 patients with angiographically significant in-stent restenosis.[156]

Both stents significantly decreased the rate of restenosis compared with balloon angioplasty and significantly reduced the need for target-vessel revascularization, but a secondary analysis found a trend or a significant difference in favor of the SES for all angiographic parameters and a significant reduction in target-vessel revascularizations versus the PES (8% versus 19%; P=0.02). Additional studies have demonstrated a similar effect in patients with long lesions, uncontrolled diabetes,[157] and "all comers."[158] Importantly, in patients with less complicated CAD, the SES and PES appear to result in similar clinical outcomes.[159]

Stent Thrombosis

A major limitation of early studies of bare-metal stents was subacute stent thrombosis, which often occurred despite aggressive anticoagulation treatment after patient discharge. The addition of a thienopyridine derivative, such as ticlopidine or clopidogrel,

to aspirin results in a dramatic reduction in the occurrence of subacute stent thrombosis.[186] Because of its more favorable side-effect profile, clopidogrel is preferred over ticlopidine, and therapy has been continued for 1 month after bare-metal stent placement to prevent this complication.

More prolonged dual-antiplatelet therapy has been recommended with the SES (3 months) and PES (6 months) owing to delays in endothelialization that may occur with these stents. The rate of occurrence of stent thrombosis appears similar in patients receiving drug-eluting and bare-metal stents provided that the antiplatelet therapy is given for the recommended duration. The importance of antiplatelet therapy was emphasized in a "real world" registry of patients undergoing drug-eluting stenting for complex CAD.[198] This prospective, observational cohort study of 2229 consecutive patients who had successful implantation of SES (1062 patients) or PES (1167 patients) suggested that the rate of stent thrombosis may be higher in actual clinical practice than the rates reported in controlled clinical trials.[198] This study reported a 29% incidence of stent thrombosis if the dual-antiplatelet therapy (aspirin plus clopidogrel or ticlopidine) was discontinued prematurely.

Angioplasty Versus CABG

Twenty-five years ago, percutaneous balloon angioplasty was reserved for patients with single-vessel CAD. With dramatic technical advances and improved early and late outcomes, it is now used in multivessel disease as well. Numerous randomized clinical trials comparing balloon angioplasty with CABG in patients with both single-vessel and multivessel disease found no significant difference in survival.[162–165,199] The Bypass Angioplasty Revascularization Investigation (BARI),[166] which compared CABG with conventional balloon angioplasty in patients with multivessel CAD, showed that initial angioplasty did not significantly compromise 5-year survival, although subsequent revascularization was required more often with angioplasty. However, by 7 years follow-up, CABG conferred a significant survival advantage, primarily owing to a benefit in patients with diabetes.[200]

In contrast to the information available on the relative effectiveness of angioplasty versus CABG, more limited data are available on angioplasty compared with medical therapy. It is worth noting that the outcomes of these early PCI studies may not reflect current PCI practice, because none capitalized on the most recent treatment advances with anticoagulation therapy and drug-eluting stents during PCI.

Stenting Versus CABG

Several trials have compared stent implantation with CABG in patients with single-vessel or multivessel CAD. In general, outcomes have been similar in terms of mortality and morbidity, although the need for repeated revascularization has been greater with stents.[167–174] The largest of these trials, the Arterial Revascularization Therapies Study (ARTS)[168] of 1205 patients with multivessel disease, found no difference at 1 year in the combined rate of death, MI, and stroke between the 2 strategies; however, the need for repeat revascularization was higher with stenting, and this difference was even more pronounced in diabetic patients. Outcomes at 5 years confirmed the higher rate of major adverse cardiac or cerebrovascular events with PCI, driven by the increased need for repeat revascularization (30.3% versus 8.8%; $P<0.001$).[169] The Stent or Surgery (SoS)

trial[173] showed increased mortality in the stent arm, a difference that was not attributable to diabetes. The rate of revascularization was also higher with stenting. Neither of the stent arms of ARTS and SoS used concomitant platelet glycoprotein IIb/IIIa inhibitors, which current treatment guidelines consider a reasonable drug option for patients undergoing elective PCI with stent placement.[201]

Drugs to Improve the Performance and Safety of PCI

Periprocedural use of platelet inhibitors (eg, aspirin, clopidogrel, and glycoprotein IIb/IIIa inhibitors) and anticoagulants (eg, unfractionated heparin and direct thrombin inhibitors) decreases the frequency of early ischemic complications after PCI. Long-term synergistic antiplatelet use may also reduce the occurrence of late events. Aspirin is an essential treatment before PCI, whereas the addition of a thienopyridine derivative to aspirin confers additional benefit (see "Stent Thrombosis," above). The Clopidogrel for the Reduction of Events During Observation (CREDO) trial[188] did not demonstrate an overall benefit at 28 days from administration of a loading dose of clopidogrel (along with aspirin) compared with no loading dose before the PCI procedure. A prespecified subgroup analysis, however, showed that patients pretreated with clopidogrel at least 6 hours before PCI experienced an RR reduction of 38.6% versus placebo (95% CI −1.6% to 62.9%; P=0.051) for the combined end point of death, MI, or target-vessel revascularization at 28 days compared with no risk reduction versus placebo with treatment <6 hours before the PCI. Long-term use of dual-antiplatelet therapy (aspirin and clopidogrel) in CREDO resulted in a 26.9% (95% CI 3.9% to 44.4%; P=0.02) reduction in combined death, MI, or stroke at 1 year after the procedure.[188]

Treatment with glycoprotein IIb/IIIa inhibitors before stent implantation lowers the incidence of ischemic complications within 48 hours of the procedure and at 1-month follow-up[187] and substantially reduces (by 38%) the risk of death or nonfatal MI at 30-day follow-up.[145] These agents are frequently administered with unfractionated heparin, but the risk of major bleeding with this combination remains a concern.[189] Evidence from the Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events (REPLACE-2) trial suggested that direct thrombin inhibitors, such as bivalirudin, may be used instead of heparin with glycoprotein IIb/IIIa inhibitors in stable CAD patients undergoing elective, but not urgent, PCI.[189] The benefits of bivalirudin were confirmed in unstable angina/non–ST-segment elevation MI patients by the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial,[202] which will be discussed in part II of this article under "Treatment of UA/NSTEMI."

Previous SectionNext Section

2.6.7.1. Prevention

guidelines-CVD-prevention.pdf
risk-estimation: guidelines-CVD-prevention-report1998.pdf
-Prevention of coronary heart disease in clinical practice
-Primary prevention
Individuals at high risk of developing coronary heart disease or other major atherosclerotic disease
-Secondary prevention

Patients with coronary heart disease or other atherosclerotic disease

-a very useful document for beeing aware of this topic

see below some important data:

1. What is cardiovascular disease prevention?

Atherosclerotic cardiovascular disease (CVD) is a chronic disorder developing insidiously throughout life and usually progressing to an advanced stage by the time symptoms occur. It remains the major cause of premature death in Europe, even though CVD mortality has fallen considerably over recent decades in many European countries. It is estimated that .80% of all CVD mortality now occurs in developing countries. CVD causes mass disability: within the coming decades the disability-adjusted life years (DALYs) estimate is expected to rise from a loss of 85 million DALYs in 1990 to a loss of _150 million DALYs globally in 2020, thereby remaining the leading somatic cause of loss of productivity.1 1638 Joint ESC Guidelines CVD is strongly connected to lifestyle, especially the use of tobacco, unhealthy diet habits, physical inactivity, and psychosocial stress.2 The World Health Organization (WHO) has stated that over three-quarters of all CVD mortality may be prevented with adequate changes in lifestyle. CVD prevention, remaining a major challenge for the general population, politicians, and healthcare workers alike, is defined as a co-ordinated set of actions, at public and individual level, aimed at eradicating, eliminating, or minimizing the impact of CVDs and their related disability. The bases of prevention are rooted in cardiovascular epidemiology andevidence-based medicine.

2. Why is prevention of cardiovascular disease needed?

† Atherosclerotic CVD, especially CHD, remains the leading cause of premature death worldwide.
† CVD affects both men and women; of all deaths that occur before the age of 75 years in Europe, 42% are due to CVD in women and 38% in men.
† CVD mortality is changing, with declining age-standardized rates in most European countries, which remain high in Eastern Europe.
† Prevention works: .50% of the reductions seen in CHD mortality relate to changes in risk factors, and 40% to improved treatments.
† Preventive efforts should be lifelong, from birth (if not before) to old age.
† Population and high-risk preventive strategies should be complementary; an approach limited to high-risk persons will be less effective; population education programmes are still needed.
† Despite gaps in our understanding, there is ample evidence to justify intensive public health and individual preventive efforts.
† There is still substantial room for improvement in risk factor control, even in individuals at very high risk.

2.1 Scope of the problem

‘Coronary heart disease (CHD) is now the leading cause of death worldwide; it is on the rise and has become a true pandemic that respects no borders’. This statement from 2009 on the website of the WHO11 does not differ much from the warning issued in 1969 by its Executive Board: ‘Mankind’s greatest epidemic: CHD has reached enormous proportions striking more and more at younger subjects. It will result in coming years in the greatest epidemic mankind has faced unless we are able to reverse the trend by concentrated research into its cause and prevention’.12 The second major CVD—stroke—is another substantial cause of death and disability. For these reasons, the fifth JTF guidelines refer to the total burden of atherosclerotic CVD. The choice of total burden of atherosclerotic CVD may give the impression that nothing has changed over the past 40 years, but this is not true. On the contrary, the epidemic has been and still is extremely dynamic and is influenced by both changes in cardiovascular risk factors and in increased opportunities for targeted interventions to prevent and treat CVD. This results in ups and downs of cardiovascular morbidity and mortality over relatively short periods with wide variability across the globe, including developing countries where the major proportion of all events occurs nowadays. In different parts of the world, the dynamics of the epidemic vary greatly in pattern, magnitude, and timing.13 In Europe, the burden remains high: CVD remains a major cause of premature deaths and loss of DALYs—a composite of premature death and living with the disease.

It is not widely appreciated that

CVD is the main cause of premature death in women: CVD was responsible for 42% of all deaths below 75 years of age in European women and for 38% of all deaths at ,75 years in men

Fact sheet on CVDs
cvdglobalatlaswho_eng.pdf
guidelines-CVD-prevention.pdf

However, a decline in age-standardized CHD and CVD mortality has been observed in many European countries between the 1970s and 1990s, with the earliest and most prominent decrease in the more affluent countries, illustrating the potential for prevention of premature deaths and for prolonging healthy life expectancy. In several eastern European countries, however, CVD and CHD mortality remains high.

Policy makers need to know whether major contributors to morbidity and mortality such as CVD are tracking up or down.A valid and actual description of the epidemic by place, time, and personal characteristics is continuously needed to guide and support health policies. At present there is no standardized source of Europe-wide CVD morbidity data.

Results from the Multinational MONItoring of trends and determinants in CArdiovascular disease (MONICA) project indicated a heterogeneous trend in CHD incidence in the 1980s to 1990s in Europe.16 This pattern may have changed, and results from recent reports do suggest that mortality and morbidity from CHD is levelling, especially in younger adults.17,18 One should also realize that because of an ageing population and a reduced case fatality of acute coronary events, the total number of people living with CHD increases. The majority of these patients develop the disease at

an advanced age, leading to a compression of morbidity in the very old of the community and to a prolonged life expectancy in good health. The Global Health Observatory database of the WHO (http://apps.who.int/ghodata/?vid=2510) provides data on present mortality rates from CVD in the world.

2.2 Prevention of cardiovascular disease: a lifelong approach

Prevention of CVD ideally starts during pregnancy and lasts until the end of life. In daily practice, prevention efforts are typically targeted at middle-aged or older men and women with established CVD (i.e. secondary prevention) or those at high risk of developing a first cardiovascular event [e.g. men and women with combinations of smoking, elevated blood pressure (BP), diabetes or dyslipidaemia (i.e. primary prevention)]; CVD prevention in the young, the very old, or those with just a moderate or mild risk is still limited, but can result in substantial benefit. Prevention is typically categorized as primary or secondary prevention, although in CVD the distinction between the two is arbitrary in view of the underlying, gradually developing atherosclerotic process. Since the instruction by Geoffrey Rose decades ago, two approaches towards prevention of CVD are considered: the population strategy and the high-risk strategy. The population strategy aims at reducing the CVD incidence at the population level through lifestyle and environmental changes targeted at the population at large. This strategy is primarily achieved by establishing ad-hoc policies and community interventions. Examples include measures to ban smoking and reduce the salt content of food. The advantage is that it may bring large benefits to the population although it may offer little to the individual. The impact of such an approach on the total number of cardiovascular events in the population may be large, because all subjects are targeted and a majority of events occur in the substantial group of people at only modest risk.

In the high-risk approach, preventive measures are aimed at reducing risk factor levels in those at the highest risk, either individuals without CVD at the upper part of the total cardiovascular risk distribution or those with established CVD. Although individuals targeted in this strategy are more likely to benefit from the preventive interventions, the impact on the population level is limited, because people at such high risk are few. For a long time the population strategy has been considered to be more costeffective than the high-risk approach but since the introduction of highly effective lipid lowering drugs, improvement in smoking cessation programmes and lower costs of antihypertensive drugs, the effectiveness of the high risk approach has increased.20 There is consensus that the largest preventive effect is achieved when these are combined.

Importantly, evidence that increased cardiovascular risk starts developing at a (very) young age has accumulated over past decades. Even exposure to risk factors before birth may influence the lifetime risk of CVD,21 as has been illustrated from studies in the offspring of women who were pregnant during the Dutch famine in the Second World War.22 Although children are at very low absolute risk of developing CVD, those at a relatively high risk compared with their peers remain at increased risk of experiencing a cardiovascular event later in life because of 'tracking' of risk factors (i.e. those at the high end of the distribution of a risk factor in early life tend to stay in the upper part of the distribution). 23 Thus a healthy lifestyle in the young is crucial, although ethical and other reasons prohibit the provision of strong

levels of evidence based on randomized trials for the benefits in terms of reduced incidence of CVD from, for example, school programmes on health education or smoking cessation actions. Also, the limited attention on CVD prevention in the elderly has proven unjustified. Studies have shown that preventive measures (i.e. BP lowering and smoking cessation) are beneficial up to advanced age.24,25 These facts exemplify that prevention of CVD should be a lifelong effort, albeit that the beneficial effects in terms of, for example, a lower incidence of fatal or non-fatal cardiovascular events or improvement in quality of life, should always be weighed against the potential harm that specific measures may cause (including side effects of drugs and psychological effects of labelling healthy subjects as patients) and against related costs.

2.3 Prevention of cardiovascular disease pays off

In order to interpret the dynamics of the CVD epidemic, it is important to differentiate the effect of a reduced case fatality and changes related to preventing clinical events. Some authors credit the greater use of evidence-based medical therapies such as thrombolysis, aspirin, angiotensin-converting enzyme (ACE) inhibitors, percutaneous coronary intervention (PCI), and coronary artery bypass graft (CABG) surgery,26,27 while others credit improved management of major risk factors such as smoking, hypertension, and dyslipidaemia.28 The MONICA project, performed during the 1980s and 1990s, showed that only part of the variation in the time trends of coronary event rates could be predicted by trends in risk factors.16 The relationship between changes in risk factor scores and changes in event rates was substantial. and the changes in risk factors explained almost half the variation in event rates in men but less in women. Moreover, there was a significant association between treatment change and case fatality. Thus it was concluded that both primary 1642 Joint ESC Guidelines prevention and treatment of cardiovascular events influence mortality. In many MONICA centres there were quite substantial changes, up or down, in CVD events within time periods as small as 10 years. The only reasonable explanation is that both environmental changes, especially related to lifestyle, and improved management are important. Another approach to understanding the changes in CVD mortality and incidence rates is by applying models such as the IMPACT mortality model.29 Based on information on changes in coronary risk factors and in treatment as obtained from the results of RCTs regarding the effectiveness of different treatment modalities, it estimates the expected influence on CHD mortality by age and gender. This model has been applied in different countries; the results from these studies are rather consistent and similar to what has been observed in other studies of the same subject, as summarized in Figure 1. Beneficial reductions in major risk factors—in particular smoking, BP, and cholesterol—accounted for more than half of the decrease in CHD deaths, although they were counteracted by an increase in the prevalence of obesity and type 2 diabetes; _40% of the decline in CHD death rates is attributed to better treatments of acute myocardial infarction, heart failure, and other cardiac conditions. Results from clinical trials and natural experiments also show that a decline in CHD mortality can happen rapidly after individual or population-wide changes in diet or smoking.30

The potential for prevention based on healthy lifestyles, appropriate management of classical risk factors, and selective use of cardioprotective drugs is obvious. The human and economic arguments in favour of CVD prevention were recently estimated by the

National Institute for Health and Clinical Excellence (NICE)32 as overwhelmingly positive, and many committees from other countries have almost the same views.33 According to the reportof NICE, implementation of the population approach may bring numerous benefits and savings:

† Narrowing the gap in health inequalities.
† Cost savings from the number of CVD events avoided.
† Preventing other conditions such as cancer, pulmonary diseases, and type 2 diabetes.
† Cost savings associated with CVD such as medications, primary care visits, and outpatient attendances.
† Cost savings to the wider economy as a result of reduced loss of production due of illness in those of working age, reduced benefit payments, and reduced pension costs from people retiring early from ill health.
† Improving the quality and length of people's lives.

2.4 Ample room for improvement

Within the scope of the comprehensive programme on CVD prevention of the ESC, surveys are carried out to document how well the guidelines are implemented in clinical practice. These surveys are called EUROASPIRE; the results from the hospital arm of EUROASPIRE III33 (2006–2007) in 8966 patients with established CHD from 22 European countries show that large proportions of patients still do not achieve the lifestyles, risk factor levels, and therapeutic targets set in 2003 by the third JTF. The proportions of patients who were at goal for the different recommendations and for risk factor management are given in Table 4; ideally, 100% of patients should reach the goals, but in practice fewer than half tend to reach the targets.

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Guidelines for the assessment and management of absolute CVD risk

Guidelines and tools

- **Guidelines for the Management of Absolute Cardiovascular Disease Risk (4.45MB)**

• Calculation of an individual's 'risk age' may also be of use in this situation.

High CVD risk countries are all those not listed under the low risk chart (Figure 4). Of these, some are at very high risk, and the high-risk chart may underestimate risk in these.
These countries are Armenia, Azerbaijan, Belarus, Bulgaria, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Macedonia FYR, Moldova, Russia, Ukraine, and Uzbekistan.

Figure 3 SCORE chart: 10-year risk of fatal cardiovascular disease (CVD) in countries at high CVD risk based on the following risk factors:

age, sex, smoking, systolic blood pressure, and total cholesterol.

The SCORE risk charts are shown in Figures 3–5, including a chart of relative risks. Instructions on their use and qualifiers follow. Please note that the chart in Figure 5 shows relative and not absolute risk. Thus a person in the top right-hand box has a risk that is 12 times higher than a person in the bottom left. This may be helpful when advising a young person with a low absolute but high relative risk of the need for lifestyle change.

Cardiovascular risk age
The risk age of a person with several cardiovascular risk factors is the age of a person with the same level of risk but with ideal levels of risk factors. high-risk 40 year old may have a risk age

Primary Prevention With Statins

The establishment of the benefits of statin therapy in secondary prevention was followed by large-scale, well-controlled primary prevention trials that demonstrated that statin therapy also significantly decreases morbidity and mortality from major CVD events in patients without prior CHD. The West of Scotland Coronary Prevention Study (WOSCOPS)[73] demonstrated that pravastatin therapy in patients with elevated total cholesterol (mean 272 mg/dL) with no history of MI is effective in reducing the risk of nonfatal MI and death due to CHD, with no associated increase in death due to noncardiovascular causes. The Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS)[74] showed that cholesterol-lowering therapy with lovastatin 40 mg/d significantly decreased the risk of a first acute coronary event in subjects with no clinically evident CHD and average LDL levels. Of note, AFCAPS/TexCAPS was the first large-scale statin trial to exclude patients on the basis of HDL measurements above predefined levels. After ≈5 years of treatment, lovastatin was associated with a 37% reduction in risk of first coronary events versus placebo (95% CI 21% to 50%; P<0.001).[74] These findings are particularly relevant to clinical practice because the participants were generally healthy and at lower CHD risk, and benefits were observed in both younger and older age groups.

Secondary Prevention With Statins

The Scandinavian Simvastatin Survival Study (4S),[70] which evaluated the effect of cholesterol lowering with simvastatin on morbidity and mortality in CHD patients with elevated cholesterol, was the first major secondary prevention trial to show a significant survival benefit with statin treatment. After ≈5 years of treatment, the risk of all-cause death was reduced by 30% (95% CI 15% to 42%; P<0.001) and the risk of coronary death was reduced by 42% (95% CI 27% to 54%) in the simvastatin group compared with placebo. Major coronary events and revascularization procedures were also significantly reduced.[70] The Cholesterol and Recurrent Events (CARE) trial[71] was designed to determine whether post-MI patients with so-called average cholesterol levels

would benefit from long-term statin therapy. Patients with mean total cholesterol levels of 209 mg/dL and mean LDL cholesterol levels of 139 mg/dL were treated with pravastatin or placebo for an average of 5 years. Results showed that the incidence of a fatal coronary event or nonfatal MI was significantly reduced by 24% in the pravastatin group compared with placebo (95% CI 9% to 36%; P=0.003). The incidence rates of both coronary bypass surgery and angioplasty were also significantly reduced with pravastatin.[71]

The Long-Term Intervention with Pravastatin in Ischemic Disease (LIPID) study[72] examined the potential benefits of cholesterol-lowering therapy with pravastatin on survival in patients with previous MI or unstable angina pectoris who had a range of moderately elevated total cholesterol levels (155 to 271 mg/dL). After a follow-up of ≈6 years, pravastatin treatment significantly reduced the RR of death due to CHD by 24% (95% CI 12% to 35%; P<0.001) and of overall mortality by 22% (95% CI 13% to 31%; P<0.001) compared with placebo.[72]

Primary/Secondary Prevention

The Heart Protection Study (HPS)[75] provided evidence that the benefits of statin therapy extend to patients not included in previous statin clinical trials. The HPS allowed enrollment of the elderly, women, and patients with hypertension, diabetes mellitus, or peripheral atherosclerosis, which is a patient population more representative of the general population.[75] Additionally, the trial enrolled patients both with and without CHD, so that it can be regarded as a combined primary and secondary prevention trial. The HPS showed that treatment with simvastatin for 5 years in a very large cohort of ≈20 000 patients significantly reduced the risk of all-cause mortality (primary end point) by 13% (95% CI 6% to 19%; P=0.0003) and of any vascular death by 17% (95% CI 9% to 25%; P<0.0001) compared with placebo. An important finding from HPS was that lipid-modifying therapy with a statin decreased the risk of cardiovascular events by approximately one quarter in subjects with baseline LDL cholesterol levels <116 mg/dL[75]; this result provided support for the "lower is better" hypothesis. The HPS had a 2×2 factorial design by which patients were also randomized to receive antioxidant vitamin supplementation or matching placebo. Results showed no benefit of antioxidant supplementation on reducing the risk of all-cause mortality or of any cardiovascular deaths and events.[79]

Other major trials that further extended the benefits of statin therapy to a broad range of patients include the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT),[80] which is discussed below under "Multiple Risk Factors"; the Incremental Decrease in End Points Through Aggressive Lipid Lowering (IDEAL) trial,[81] discussed in the section on stable CAD; and the PRavastatin Or atorVastatin Evaluation and Infection Therapy–Thrombolysis In Myocardial Infarction 22 (PROVE IT–TIMI 22) trial

Cardiovascular diseaes are the most frequent diseases almost in all countries of the world and give the leading cause of death in them. The pathophysiological basis of them is the atheroscerosis developing for years and symptomes of the disease appears only at the devloped stadiums and in high proportions become fatal,mainly the cases of ischemic

heart diseases as AMI and stenocardial attacks and at people diagnosed with high risk-factor influence.

The main health-advices to prevent the disease and the fatal outcomes are:
-avoid smoking
-healthy nutrition
-enough physical activity
-decrease the BMI and the waist/hip ratio to the healthy levels
-hold on the healthy level also the blood pressure,blood-cholesterol and the LDL-levels ,and the blood-glucose level

The World Heart Federation, of the which the ESC is a member, has described the forecasted trend in rising CVD incidence as "unacceptable" and has urged a global response which puts CVD prevention at the centre of national development initiatives.

The Chronic Disease Alliance, an association of ten science-based European organisations of which the ESC is a founding member, has also declared its objective in reversing the rise in chronic non-communicable diseases by urging political action against tobacco use, poor nutrition, lack of physical activity and alcohol.

Guide to Primary Prevention of Cardiovascular Diseases

- **AHA Medical/Scientific Statements**
- **prevention**
- **cardiovascular diseases**
- **risk factors**

The clinical and public health approaches to primary prevention are complementary. Primary prevention refers to guidance given to persons with no known cardiovascular disease. Physicians can contribute to the public health approach through patient education. The first goal of prevention is to prevent the development of risk factors. Physicians should instruct all patients about adopting healthy life habits that will prevent intensification of risk factors. Patient education should be family oriented. Ideally, risk factor prevention begins in childhood. Preventing cigarette smoking by children and adolescents is a prime goal. Another major goal is prevention of overweight and obesity in children and weight gain in adults; overweight lies at the heart of several risk factors. Encouraging life habits that incorporate regular physical activity, especially walking, and active recreational sports likewise will decrease intensity of risk factors. Patients and their families should be encouraged to reduce their intake of cholesterol and saturated fats by using unsaturated vegetable oils instead of animal-based saturated fats and adopting the habit of eating smaller portions. Evaluation of the family history may reveal that other family members need intervention to avoid developing cardiovascular disease. Adoption of healthy life habits and early intervention will mitigate the severity of risk factors that are the result of aging and genetic factors.

In addition to complementing public health efforts, a clinical approach is needed to detect the presence of established risk factors and to effectively modify them. The physician should regularly check for established risk factors: smoking, physical inactivity, elevated lipid levels, and high blood pressure. In the case of the latter two, the

physician should seek the causes (ie, diet and lack of exercise). The recommendations presented in the chart are consistent with the American Heart Association position on risk factor control[1] [2] [3] and the 27th Bethesda Conference, "Matching the Intensity of Risk Factor Management With the Hazard for Coronary Disease Events."[4] These recommendations are also in accord with the recommendations of the Fifth Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure[5] and the National Cholesterol Education Program (NCEP).[6] The AHA, the Joint National Committee, and the NCEP recommend testing for risk factors, beginning in early adulthood. The NCEP has identified low-density lipoprotein cholesterol as the primary target for cholesterol modification. The AHA Task Force on Risk Reduction further recognizes low levels of high-density lipoprotein cholesterol and high levels of triglycerides as secondary targets for lipid modification.

Successful implementation of these recommendations entails a multistep process including assessment, intervention, planning for change, and long-term maintenance and follow-up. These steps can be carried out directly by primary care physicians or through referrals to consultants or specialized programs. Implementation usually requires a team approach involving physicians and other healthcare professionals, including registered dietitians. The physician must commit the time to make a proper assessment and initiate preventive efforts. Patients should be involved in developing an effective plan for change and strategies for altering behavior. A long-term physician-patient relationship is usually needed for successful prevention and modification of risk factors. Physicians must establish office practices consistent with sound prevention strategies.

Introduction of healthy life habits should be universal. These habits include avoidance or cessation of smoking, healthy eating, weight control, and appropriate exercise. The decision to use drug therapy to control risk factors depends on a balanced assessment of absolute risk and the efficacy, safety, and cost-effectiveness of the intervention. Medication for control of blood pressure is used to prevent both stroke and coronary heart disease. Use of cholesterol-lowering drugs for prevention of coronary heart disease depends heavily on assessment of absolute risk; drug therapy should be used cautiously for primary prevention in young adults who are otherwise at low risk. Use of cholesterol-lowering drug therapy in special groups was reviewed in detail in the NCEP report

Heart Disease and Stroke Statistics—2011 Update A Report From the American Heart Association

Each year, the American Heart Association (AHA), in conjunction with the Centers for Disease Control and Prevention, the National Institutes of Health, and other government agencies, brings together the most up-to-date statistics on heart disease, stroke, other

vascular diseases, and their risk factors and presents them in its Heart Disease and Stroke Statistical Update. The Statistical Update is a valuable resource for researchers, clinicians, healthcare policy makers, media professionals, the lay public, and many others who seek the best national data available on disease morbidity and mortality and the risks, quality of care, medical procedures and operations, and costs associated with the management of these diseases in a single document. Indeed, since 1999, the Statistical Update has been cited more than 8700 times in the literature (including citations of all annual versions). In 2009 alone, the various Statistical Updates were cited ≈1600 times (data from ISI Web of Science). In recent years, the Statistical Update has undergone some major changes with the addition of new chapters and major updates across multiple areas. For this year's edition, the Statistics Committee, which produces the document for the AHA, updated all of the current chapters with the most recent nationally representative data and inclusion of relevant articles from the literature over the past year and added a new chapter detailing how family history and genetics play a role in cardiovascular disease (CVD) risk. Also, the 2011 Statistical Update is a major source for monitoring both cardiovascular health and disease in the population, with a focus on progress toward achievement of the AHA's 2020 Impact Goals. Below are a few highlights from this year's Update. Death Rates From CVD Have Declined, Yet the Burden of Disease Remains High

- **The 2007 overall death rate from CVD (International Classification of Diseases 10, I00–I99) was 251.2 per 100 000. The rates were 294.0 per 100 000 for white males, 405.9 per 100 000 for black males, 205.7 per 100 000 for white females, and 286.1 per 100 000 for black females. From 1997 to 2007, the death rate from CVD declined 27.8%. Mortality data for 2007 show that CVD (I00–I99; Q20–Q28) accounted for 33.6% (813 804) of all 2 243 712 deaths in 2007, or 1 of every 2.9 deaths in the United States.**
- **On the basis of 2007 mortality rate data, more than 2200 Americans die of CVD each day, an average of 1 death every 39 seconds. More than 150 000 Americans killed by CVD (I00–I99) in 2007 were <65 years of age. In 2007, nearly 33% of deaths due to CVD occurred before the age of 75 years, which is well before the average life expectancy of 77.9 years.**
- **Coronary heart disease caused ≈1 of every 6 deaths in the United States in 2007. Coronary heart disease mortality in 2007 was 406 351. Each year, an estimated 785 000 Americans will have a new coronary attack, and ≈470 000 will have a recurrent attack. It is estimated that an additional 195 000 silent first myocardial infarctions occur each year. Approximately every 25 seconds, an American will have a coronary event, and approximately every minute, someone will die of one.**
- **Each year, ≈795 000 people experience a new or recurrent stroke. Approximately 610 000 of these are first attacks, and 185 000 are recurrent attacks.**
- **Mortality data from 2007 indicate that stroke accounted for ≈1 of every 18 deaths in the United States. On average, every 40 seconds, someone in the United States has a stroke. From 1997 to 2007, the stroke death rate fell 44.8%, and the actual number of stroke deaths declined 14.7%.**
- **In 2007, 1 in 9 death certificates (277 193 deaths) in the United States mentioned heart failure.**

Prevalence and Control of Traditional Risk Factors Remains an Issue for Many Americans

- **Data from the National Health and Nutrition Examination Survey (NHANES) 2005–2008 indicate that 33.5% of US adults ≥20 years of age have hypertension (Table 7-1). This amounts to an estimated 76 400 000 US adults with hypertension. The prevalence of hypertension is nearly equal between men and women. African American adults have among the highest rates of hypertension in the world, at 44%. Among hypertensive adults, ≈80% are aware of their condition, 71% are using antihypertensive medication, and only 48% of those aware that they have hypertension have their condition controlled.**
- **Despite 4 decades of progress, in 2008, among Americans ≥18 years of age, 23.1% of men and 18.3% of women continued to be cigarette smokers. In 2009, 19.5% of students in grades 9 through 12 reported current tobacco use. The percentage of the nonsmoking population with detectable serum cotinine (indicating exposure to secondhand smoke) was 46.4% in 1999 to 2004, with declines occurring, and was highest for those 4 to 11 years of age (60.5%) and those 12 to 19 years of age (55.4%).**
- **An estimated 33 600 000 adults ≥20 years of age have total serum cholesterol levels ≥240 mg/dL, with a prevalence of 15.0% (Table 13-1).**
- **In 2008, an estimated 18 300 000 Americans had diagnosed diabetes mellitus, representing 8.0% of the adult population. An additional 7 100 000 had undiagnosed diabetes mellitus, and 36.8% had prediabetes, with abnormal fasting glucose levels. African Americans, Mexican Americans, Hispanic/Latino individuals, and other ethnic minorities bear a strikingly disproportionate burden of diabetes mellitus in the United States (Table 16-1).**

The 2011 Update Expands Data Coverage of the Obesity Epidemic and Its Antecedents and Consequences

- **The estimated prevalence of overweight and obesity in US adults (≥20 years of age) is 149 300 000, which represents 67.3% of this group in 2008. Fully 33.7% of US adults are obese (body mass index ≥30 kg/m^2). Men and women of all race/ethnic groups in the population are affected by the epidemic of overweight and obesity (Table 15-1).**
- **Among children 2 to 19 years of age, 31.9% are overweight and obese (which represents 23 500 000 children), and 16.3% are obese (12 000 000 children). Mexican American boys and girls and African American girls are disproportionately affected. Over the past 3 decades, the prevalence of obesity in children 6 to 11 years of age has increased from ≈4% to more than 20%.**
- **Obesity (body mass index ≥30 kg/m^2) is associated with marked excess mortality in the US population. Even more notable is the excess morbidity associated with overweight and obesity in terms of risk factor development and incidence of diabetes mellitus, CVD end points (including coronary heart disease, stroke, and heart failure), and numerous other health conditions, including asthma, cancer, degenerative joint disease, and many others.**
- **The prevalence of diabetes mellitus is increasing dramatically over time, in parallel with the increases in prevalence of overweight and obesity.**
- **On the basis of NHANES 2003–2006 data, the age-adjusted prevalence of metabolic syndrome, a cluster of major cardiovascular risk factors related to**

overweight/obesity and insulin resistance, is 34% (35.1% among men and 32.6% among women).

- **The proportion of youth (≤18 years of age) who report engaging in no regular physical activity is high, and the proportion increases with age. In 2007, among adolescents in grades 9 through 12, 29.9% of girls and 17.0% of boys reported that they had not engaged in 60 minutes of moderate-to-vigorous physical activity, defined as any activity that increased heart rate or breathing rate, even once in the previous 7 days, despite recommendations that children engage in such activity ≥5 days per week.**
- **Thirty-six percent of adults reported engaging in no vigorous activity (activity that causes heavy sweating and a large increase in breathing or heart rate).**
- **Data from NHANES indicate that between 1971 and 2004, average total energy consumption among US adults increased by 22% in women (from 1542 to 1886 kcal/d) and by 10% in men (from 2450 to 2693 kcal/d; see Chart 19-1).**
- **The increases in calories consumed during this time period are attributable primarily to greater average carbohydrate intake, in particular, of starches, refined grains, and sugars. Other specific changes related to increased caloric intake in the United States include larger portion sizes, greater food quantity and calories per meal, and increased consumption of sugar-sweetened beverages, snacks, commercially prepared (especially fast food) meals, and higher energy-density foods.**

The 2011 Update Provides Critical Data Regarding Cardiovascular Quality of Care, Procedure Utilization, and Costs

In light of the current national focus on healthcare utilization, costs, and quality, it is critical to monitor and understand the magnitude of healthcare delivery and costs, as well as the quality of healthcare delivery, related to CVDs. The Update provides these critical data in several sections.

Quality-of-Care Metrics for CVDs

Chapter 20 reviews many metrics related to the quality of care delivered to patients with CVDs, as well as healthcare disparities. In particular, quality data are available from the AHA's "Get With The Guidelines" programs for coronary artery disease and heart failure and the American Stroke Association/ AHA's "Get With the Guidelines" program for acute stroke. Similar data from the Veterans Healthcare Administration, national Medicare and Medicaid data and National Cardiovascular Data Registry Acute Coronary Treatment and Intervention Outcomes Network - "Get With The Guidelines" Registry data are also reviewed. These data show impressive adherence with guideline recommendations for many, but not all, metrics of quality of care for these hospitalized patients. Data are also reviewed on screening for cardiovascular risk factor levels and control.

1. **Véronique L. Roger, MD, MPH, FAHA;**
2. **Melanie B. Turner, MPH On behalf of the American Heart Association Heart Disease and Stroke Statistics Writing Group**

Cardiovascular Procedure Utilization and Costs

Chapter 21 provides data on trends and current usage of cardiovascular surgical and invasive procedures. For example, the total number of inpatient cardiovascular operations and procedures increased 27%, from 5 382 000 in 1997 to 6 846 000 in 2007 (National Heart, Lung, and Blood Institute computation based on National Center for Health Statistics annual data).

Chapter 22 reviews current estimates of direct and indirect healthcare costs related to CVDs, stroke, and related conditions using Medical Expenditure Panel Survey data. The total direct and indirect cost of CVD and stroke in the United States for 2007 is estimated to be $286 billion. This figure includes health expenditures (direct costs, which include the cost of physicians and other professionals, hospital services, prescribed medications, home health care, and other medical durables) and lost productivity resulting from mortality (indirect costs). By comparison, in 2008, the estimated cost of all cancer and benign neoplasms was $228 billion ($93 billion in direct costs, $19 billion in morbidity indirect costs, and $116 billion in mortality indirect costs). CVD costs more than any other diagnostic group.

The AHA, through its Statistics Committee, continuously monitors and evaluates sources of data on heart disease and stroke in the United States to provide the most current data available in the Statistics Update.

The 2007 mortality data have been released. More information can be found at the National Center for Health Statistics Web site,http://www.cdc.gov/nchs/data/nvsr/nvsr58/nvsr58_01.pdf.

Finally, it must be noted that this annual Statistical Update is the product of an entire year's worth of effort by dedicated professionals, volunteer physicians and scientists, and outstanding AHA staff members, without whom publication of this valuable resource would be impossible. Their contributions are gratefully acknowledged.

Note: Population data used in the compilation of NHANES prevalence estimates is for the latest year of the NHANES survey being used. Extrapolations for NHANES prevalence estimates are based on the census resident population for 2008 because this is the most recent year of NHANES data used in the Statistical Update.

Currently practiced measures to prevent cardiovascular disease include:

- **A low-fat, high-fiber diet including whole grains and plenty of fresh fruit and vegetables (at least five portions a day)[34][35]**
- **Tobacco cessation and avoidance of second-hand smoke;[34]**
- **Limit alcohol consumption to the recommended daily limits;[34] consumption of 1-2 standard alcoholic drinks per day may reduce risk by 30%[36][37] However excessive alcohol intake increases the risk of cardiovascular disease.[38]**
- **Lower blood pressures, if elevated;**
- **Decrease body fat (BMI) if overweight or obese;[39]**

- **Increase daily activity to 30 minutes of vigorous exercise per day at least five times per week;[34]**
- **Reduce sugar consumptions;**
- **Decrease psychosocial stress.[40] Stress however plays a relatively minor role in hypertension.[41] Specific relaxation therapies are not supported by the evidence.[42]**

For adults without a known diagnosis of hypertension, diabetes, hyperlipidemia, or cardiovascular disease, routine counseling to advise them to improve their diet and increase their physical activity has not been found to significantly alter behaviour, and thus is not recommended.[43]

1. World Health Organization. Global status report on noncommunicable disease 2010.

Notes to editor
ESC Press Office
+ 33 4 92 94 77 56
press@escardio.org

European Chronic Disease Alliance
-Chronic non-communicable diseases kill 86% of all people in the WHO European Region.

-Cardiovascular diseases, cancer, respiratory diseases, diabetes, kidney and liver diseases account for more than 40% the disease burden in Europe.

-Heart disease, stroke and diabetes alone are projected to lead to loss of national income in the billions, e.g. almost $33 billion in the United Kingdom (from 2005 to 2015).

The Chronic Disease alliance consists of the organisations mentioned below:

About the European Association for the Study of the Liver
EASL is the leading European scientific society involved in promoting research and education in hepatology. EASL attracts the foremost hepatology experts as members and has an impressive track record in promoting research in liver disease, supporting wider education and promoting changes in European liver policy.
http://www.easl.eu/

About the European CanCer Organisation
Following the philosophy that every cancer patient deserves the best, ECCO focuses on creating awareness of patients' needs and wishes, stimulating progressive thinking in Cancer policy, training and education, and encouraging European cancer research and its application through the organisation of international multidisciplinary conferences including the premier European cancer meetings: the ECCO – ESMO Multidisciplinary Cancer Congresses.
http://www.ecco-org.eu/

About the European Heart Network
The European Heart Network (EHN) is a Brussels-based alliance of heart foundations and like-minded nongovernmental organisations throughout Europe. EHN has member organisations in 26 countries. EHN plays a leading role in the prevention and reduction of cardiovascular diseases, in particular heart disease and stroke, through advocacy, networking, education and patient support, so that they are no longer a major cause of premature death and disability throughout Europe.
http://www.ehnheart.org/

About the European Kidney Health Alliance
The European Kidney Health Alliance (EKHA) is an Alliance of not-for-profit organisations who represent the key stakeholders in kidney health issues in Europe. EKHA takes a multidisciplinary approach involving patients and their families, doctors and nurses, researchers and other healthcare professionals who work cooperatively for a European health environment in which there is a sustained decrease in kidney disease and its consequences.
http://www.ekha.eu/

About the European Respiratory Society
The ERS, European Respiratory Society, is a professional, medical organisation with more than 10,000 members in over 100 countries representing medical and scientific experts in the field of respiratory medicine and lung science. Its mission is to promote lung health through research, knowledge sharing, and medical education.
http://www.ersnet.org/

About the European Society of Cardiology
The ESC unites over 62,000 cardiology professionals from across Europe and the Mediterranean, with the mission of reducing the burden of cardiovascular disease in Europe through education, congresses, surveys on cardiovascular diseases and the publishing of scientific materials, including journals and Clinical Practice Guidelines.
http://authors.escardio.org/

About the European Society of Hypertension
The main purpose of the European Society of Hypertension (ESH) is to provide a stable and organised European platform for scientific exchange in hypertension. The objectives of ESH are to promote, endorse and organise activities involved with the continuing medical education in the field of hypertension and associated cardiovascular diseases.
http://www.eshonline.org/

About the European Society for Medical Oncology
The European Society for Medical Oncology (ESMO) is the leading European professional organisation committed to advancing the specialty of medical oncology and promoting a multidisciplinary approach to cancer treatment and care. ESMO's mission is to advance cancer care and cure through fostering and disseminating good science that leads to better medicine and determines best practice.
http://www.esmo.org/

About the Federation of European Nurses in Diabetes
FEND has established a unique voice for nurses working in the field of diabetes care,

research and education in Europe. Its mission statement is to promote the delivery of evidence based care for people with diabetes throughout Europe.
http://www.fend.org/

About the International Diabetes Federation - Europe
IDF-Europe is the European Regional section of the International Diabetes Federation. Its constituents are the member associations of the national diabetes organisations (representing both health care professionals and patients & carers) from 45 European countries. Within the EU there are over 30 million people with diabetes, it is increasing at an alarming rate and this number is predicted to exceed 50 million by 2030. IDF-Europe aims to encourage the prevention, the earlier diagnosis, better management and education of diabetes.
www.idf.org/idf-european-region

References 1. World Health Organization. Global status report on noncommunicable disease 2010.
http://www.who.int/nmh/publications/ncd_report_full_en.pdf

2.6.8.1. PREVENTION AND TREATMENT:

Diet –THE DASH-DIET

Evidence suggests that the

Mediterranean diet improves cardiovascular outcomes.[44] This may be by "about 30 percent" in those at high risk.[45] There is also evidence that a Mediterranean diet may be more effective than a low-fat diet in bringing about long-term changes to cardiovascular risk factors (e.g., lower cholesterol level and blood pressure).[46]

In clinical trials the DASH diet (high in nuts, fish, fruits and vegetables, and low in sweets, red meat and fat) has been shown to reduce blood pressure,[47] lower total and low density lipoprotein cholesterol [48] and improve metabolic syndrome;[49] but the long term benefits outside the context of a clinical trial have been questioned.[50]

Total fat intake does not appear to be an important risk factor.[51] A diet high in trans fatty acids however does appear to increase rates of cardiovascular disease.[51][52]

Worldwide, dietary guidelines recommend a reduction in saturated fat.[53] There however is some questions around the effect of saturated fat on cardiovascular disease in the medical literature.[54][55]

A 2012 Cochrane review found suggestive evidence of a small benefit from replacing dietary saturated fat by unsaturated fat.[56] A 2013 meta analysis concludes that substitution with omega 6 linoleic acid (a type of unsaturated fat) may increase cardiovascular risk.[53] Replacement of saturated fats with carbohydrates does not change or may increase risk.[57][58] Benefits from replacement with polyunsaturated fat appears greatest[51][59] however supplementation with omega-3 fatty acids (a type of polysaturated fat) does not appear have an effect.[60]

The effect of a low salt diet is unclear. A Cochrane review concluded that any benefit in either hypertensive or normal tensive people is small if present.[61] Additionally, the review suggested a low salt diet may be harmful in those with congestive heart failure.[61] However, the review was criticized particularly for not excluding a trial in heart failure where people had low salt and water levels due to diuretics.[62] When this study is left out the rest of the trials show a trend to benefit.[62][63]

Another review of dietary salt[64] concluded that there is strong evidence that high dietary salt intake increases blood pressure and worsens hypertension, and that it increases the number of cardiovascular disease events; the latter happens both through the increased blood pressure and, quite likely, through other mechanisms.[64][65] Moderate evidence was found that high salt intake increased cardiovascular mortality; and some evidence was found for an increase in overall mortality, strokes and left-ventricular hypertrophy.[64]

The DASH Diet to lower high blood pressure

The Heart and Stroke Foundation encourages Canadians to eat a healthy diet, control salt intake, and be physically active to lower blood pressure. The latest results from the DASH study – Dietary Approaches to Stopping Hypertension – has confirmed these recommendations, providing more encouragement for people to choose a healthier diet. Research has shown that following a plan for healthy eating can reduce the risk of developing high blood pressure and lower already elevated blood pressure.

What are the DASH studies?
The DASH Diet is based on two studies, DASH and DASH-Sodium, that looked at ways of reducing blood pressure through changes in diet. In the DASH study, people were given one of three eating plans: a plan similar in nutrients to what most North Americans eat; the same plan but with extra vegetables and fruit; or the DASH diet, which is rich in vegetables, fruit and low-fat dairy foods and lower in saturated fat, total fat and cholesterol.

The results were compelling. The diet higher in vegetables and fruit and the DASH diet both reduced blood pressure. The DASH diet had the greatest effect on blood pressure, lowering levels within two weeks of starting the plan. Not only was blood pressure reduced, but total cholesterol and low-density lipoprotein (LDL) or "bad cholesterol" were lower, too.

In the DASH-Sodium study, participants were given one of three sodium plans: the DASH diet with 3,300 mg of sodium per day (a normal amount for many North Americans); 2,300 mg of sodium (a moderately restricted amount); or 1,500 mg of sodium (a more restricted amount, about 2/3 of a teaspoon of salt). Blood pressure was lower for everyone on the DASH diet. However, the less salt people consumed, the greater the decrease in blood pressure. People who already had high blood pressure had the largest decrease in blood pressure.

Why is a healthy blood pressure important?
High blood pressure causes the heart to work harder to pump nutrient- and oxygen-rich blood to the body. The arteries that deliver the blood become scarred and less elastic. Although these changes happen to everyone as they age, they happen more quickly in people with high blood pressure. As the arteries stiffen, the heart has to work even harder, causing the heart muscle to become thicker, weaker and less able to pump blood. When high blood pressure damages arteries, they are not able to deliver enough blood to organs for their proper functioning. As a result, organs may become damaged, too. For example, this type of damage can affect the heart, causing a heart attack, the brain, causing a stroke, and the kidneys, leading to kidney failure.

How is DASH different from Canadian recommendations?
The DASH diet isn't unique – it is very similar to Canada's Food Guide produced by Health Canada and endorsed by the Heart and Stroke Foundation.

Canada's Food Guide has a greater range in the number of servings than the DASH diet, which also recommends a higher level of vegetable and fruit intake.

The DASH eating plan

DASH Food Groups	DASH Daily Servings (except as noted)	DASH Serving Sizes
Vegetables	4-5	250 mL (1 cup) raw leafy vegetables 125 mL (½ cup) cooked vegetables 170 ml (6 oz) juice
Fruit	4-5	1 medium piece of fruit 63 mL (¼ cup) dried fruit 125 mL (½ cup) fresh, frozen or canned fruit
Grains (mainly whole grains)	7-8	1 slice bread 250 mL (1 cup) ready to eat cereal 125 mL (½ cup) cooked rice, pasta or cereal
Low Fat or No-Fat Dairy Foods	2-3	250 mL (1 cup) milk 250 ml (1 cup) yogurt 50 g (1½ oz) cheese
Lean meats, poultry and fish	2 or less	3 ounces cooked lean meats, skinless poultry, or fish

Nuts, seeds and dry beans	**4-5 per week**	**1/3 cup (1.5 oz.) nuts** **30 mL (2 tbsp) peanut butter** **2 tbsp (1/2 oz.) seeds** **1/2 cup cooked dry beans or peas**
Fats and Oils	**2-3**	**5 ml (1 tsp) soft margarine** **15mL (1 tbsp) low-fat mayonnaise** **30 mL (2 tbsp) light salad dressing** **5 ml (1 tsp) vegetable oil**

What about medication?
High blood pressure affects approximately a quarter of Canadian adults. Many people require medication to control their blood pressure. Lifestyle modification, which includes healthy eating and regular physical activity, may be the only treatment needed in those with mild high blood pressure. In those that require medication to control their blood pressure, following a healthy lifestyle may reduce the need for, or the amount of, medication required.

What next?
A full healthy lifestyle, including healthy eating, is part of the Canadian recommendations for the management of high blood pressure. The Heart and Stroke Foundation is involved in developing blood pressure guidelines, which are updated every year. To control your blood pressure and reduce the risk of heart disease, the guidelines recommend that you:

- **Be active 30 to 60 minutes most days of the week.**
- **Choose the following more often: vegetables, fruit, low-fat dairy products, foods lower in saturated and trans fat and salt, whole grains and fish, poultry and lean meat. Limit fast foods, canned or prepared foods, as they usually contain higher levels of sodium.**
- **If you are overweight, losing about 10 lb (5 kg) will lower your blood pressure. Reducing your weight to within a healthy range for your age and gender will lower your blood pressure even more.**
- **Eat less salt by:**
    - **limiting your use of salt in cooking and at the table**
    - **avoiding salty foods**
    - **choosing fresh or plain frozen food**
    - **avoiding canned or prepared foods that are high in salt**
    - **reading the Nutrition Facts table on food packages for sodium content**
    - **using other seasonings such as herbs, spices, lemon juice and garlic during food preparation**

- **If you drink alcohol, limit yourself to no more than 2 drinks a day, to a weekly maximum of 10 for women and 3 drinks a day to a weekly maximum of 15 for men. (Do not drink when you are driving a vehicle, taking medications or other drugs that interact with alcohol, pregnant or are planning to be pregnant, making important decisions, doing any kind of dangerous physical activity, living with alcohol dependence or mental or physical health problems, or responsible for the safety of others. If you are concerned about how drinking may affect your health, talk to your doctor.)**

- **Be smoke-free. It is important to stop smoking if you have high blood pressure. Smoking increases the risk of developing heart problems and other diseases. Your home and workplace should also be smoke-free.**
- **Take your medication as prescribed.**
- **Monitor your blood pressure regularly.**

Changing your diet means a life-long commitment to healthier lifestyle choices. People who make small changes in their diet over a longer period of time, rather than a dramatic change all at once, are more likely to stay committed to a healthier diet.

If you are considering starting on the DASH diet, discuss it with your healthcare provider first.

How much salt?
The Heart and Stroke Foundation recommends Canadians consume

no more than 2,300 mg of sodium (about 1 teaspoon/5 mL of table salt) a day. The amount of salt you eat isn't just what you shake onto your food – it is already added in large quantities to prepared foods, canned products, snack foods and restaurant meals.

Easy ways to get started on the DASH diet

Change gradually

- **If you now eat one or two vegetables a day, add another serving at lunch and dinner.**
- **If you don't eat fruit now or have only juice at breakfast, add a serving to your meals or have it as a snack.**

Treat meat as one part of the whole meal, instead of the main focus.

- **Limit meat and alternatives to about 6 oz (170 g) a day, over two meals (two servings). Each serving is about the size of a deck of cards or the palm of your hand.**

Choose fruit or low-fat foods as desserts and snacks.

- **Fruit and low-fat foods offer great taste and variety. Fresh fruit require little or no preparation. Dried fruit is easy to carry with you.**

If you would like to create a personalized action plan for healthier living, take the Heart&Stroke Risk Assessment.

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Supplements

While a healthy diet is beneficial, the effect of antioxidant supplementation (vitamin E, vitamin C, etc.) or vitamins generally has not been shown to improve protection against cardiovascular disease and in some cases may possibly result in harm.[66][67] Niacin, a type of vitamin B3, may be an exception with a modest decrease in the risk of cardiovascular events in those at high risk.[68][69] Magnesium supplementation lowers high blood pressure in a dose dependent manner.[70] Magnesium therapy is recommended for patients with ventricular arrhythmia associated with torsade de pointes who present with long QT syndrome as well as for the treatment of patients with digoxin intoxication-induced arrhythmias.[71] Results from an observational study conducted in the general Japanese population demonstrated that lower serum magnesium levels were associated with a greater average intima-media thickness and the risk of at least two carotid plaques.[72] Evidence to support omega-3 fatty acid supplementation is lacking.[73]

2.6.9.1 Management

Cardiovascular disease is treatable with initial treatment primarily focused on diet and lifestyle interventions.[78][79][80]

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2.6.10.2. Epidemiology

CARDIOVASCULAR DISEASES

Cardiovascular diseaes are the most frequent diseases almost in all countries of the world and give the leading cause of death in them. The pathophysiological basis is the atheroscerosis developing for years and symptomes appears only at the late stadiums and in high proportions become fatal,mainly the cases of ischemic heart diseases as AMI and stenocardial attacks and at people diagnosed with high risk-factor influence.

The main health-advices to prevent the disease and the fatal outcomes are:

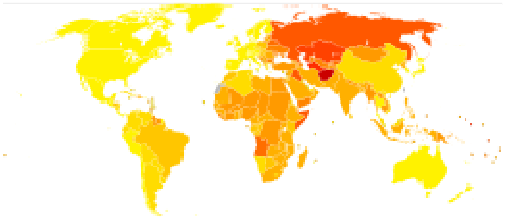
-avoid smoking

-healthy nutrition

-enough physical activity

-decrease the BMI and the waist/hip ratio to the healthy levels

-hold on the healthy level also the blood pressure,blood-cholesterol and the LDL-levels, and the blood-sugar level



Disability-adjusted life year for cardiovascular diseases per 100,000 inhabitants in 2004.[81]

Cardiovascular diseases are the leading cause of death. In 2008, 30% of all global death is attributed to cardiovascular diseases. Death caused by cardiovascular diseases are also higher in low and middle-income countries as over 80% of all global death caused by cardiovascular diseases occurred in those countries. It is also estimated that by 2030, over 23 million people will die from cardiovascular diseases annually.

THE CASE-SPECIFIC MORTALITY TRENDS IN 2012 HUNGARY

(by Katalin Kovacs,Central Statistical Office,Hungary)

Cardiovascular diseases belongs to the main leading causes among the diseases in Hungary also ,but the last years the cardiovascular mortality shows much more decreasing trend sin the european countries than here.In the '70-es years of last century the european and the hungarian cardiovascular death-indicators had very similar values but this situation have changed radically in our days: hungarian indicators show very sad results compared with the west-european data,so consequently while int he West-European countries appeared a great improvement in the life-expectancy-values,in Hungary –contrary to it- detected tendencies with worse indicators.Only in last years was shown a small emelioration in them. Consequently in Hungary the life-expectancy at birth became worse with 6 years than for the west-european people (for children also).

Main establishments

Hungary showes important mortality-surplus not only related to the other developed countries of the European union ,but in relation to the countries connected to the EU at the same time or later.

The mortality at males under 65 years is 2,5 times higher than the average mortality of the same age –group in the most developed european union's countries and is 1,2 times higher to the mortality level of connected in 2004 or in 2007 countries.

The handicap in mortality of young middle-aged males shows very slow moderation. At males over 65 years the relative handicaps in mortality-data are more restrained but also important : their mortality is 1,5 times higher than the suitable level of most developed countries exceeding with some % only the values of connected in 2004 or 2007 countries.

Related mortality data of females under 65 years is 1,7 times overhead the most developed union's country-values and have 1,2 times higher mortality levels related to the lsuitable data of connected to the EU later. The older hungarian women's mortality is equalized with the averages suitable to the less developed european countries .
The hungarian cause –specified mortality represents propitiousness picture only in relation of communicable diseases or the last years in cases of traffic accidents .The hungarian high mortality levels caused primary by the cardiovascular death. Within them the dyamism of ischemic heart diseases show extreme high levels .The dynamism of mortality in cerebrovascular diseases shows warning levels but has extremely decreasing tendenciesin Hungary so the connecting mortalites to the similar causes (seizures,insults,cerebrovascular infarcts) are small –csaled lower than in the connected to the EU countries in 2004 or 2007.
the mortality level in our days is very similar to the 1990's union's death-averages. The malignant tumour –related mortality in Hungary is higher to the union averages with 39-50% , having far less differences in this connections as in case of cardiovascular death. The tumorous death differnces of males in some last years – related to other countries mainly in the lung cancer and colorectal tumour.mortality –shows increases because of the underdeveloped moderation in them . The femal tumorous mortality in Hungary is higher the average EU levels with 28-37 % and overhead with 12-23 % the average data of connected to EU countries in 2004 or 2007. The relative handicap related to the other countries increases in this case as in the last some years did it.
In summary:
the mortality data of 1-64 years old people is significantly higher than the siutable EU-member's average data
The mortality levels of 1-64 males increased in extraordinary ranges
The risk ofearly death -mainly in case of males – has increased in significant
Among the leading causes of death the main causatives are the cardiovascular diseases ,the tumorous diseases and the diseases of digestive system. These are responsible for the ¾ part of early death in Hungary.
The relative mortality risk shows general increases in relation of early deaths of EU countries.

2.6.11.1.

Research

The first studies on cardiovascular health were performed in 1949 by Jerry Morris using occupational health data and were published in 1958.[82] The causes, prevention, and/or treatment of all forms of cardiovascular disease remain active fields of biomedical research, with hundreds of scientific studies being published on a weekly basis.

A fairly recent emphasis is on the link between low-grade inflammation that hallmarks atherosclerosis and its possible interventions. C-reactive protein (CRP) is a common inflammatory marker that has been found to be present in increased levels in patients at risk for cardiovascular disease.[83] Also osteoprotegerin which involved with regulation of a key inflammatory transcription factor called NF-κB has been found to be a risk factor of cardiovascular disease and mortality.[84][85]

Some areas currently being researched include possible links between infection with Chlamydophila pneumoniae (a major cause of pneumonia) and coronary artery disease. The Chlamydia link has become less plausible with the absence of improvement after antibiotic use.[86]

Several research also investigated the benefits of melatonin on cardiovascular diseases prevention and cure. Melatonin is a pineal gland secretion and it is shown to be able to lower total cholesterol, very low density and low density lipoprotein cholesterol levels in the blood plasma of rats. Reduction of blood pressure is also observed when pharmacological doses are applied. Thus, it is deemed to be a plausible treatment for hypertension. However, further research needs to be conducted to investigate the side effects, optimal dosage and etc. before it can be licensed for use.

2.6.12.1. References

References –you can find in a world document

References

1. **World Health Organization. Global status report on noncommunicable disease 2010.**
2. **. World Health Organization. Global status report on noncommunicable disease 2010.**
   http://www.who.int/nmh/publications/ncd_report_full_en.pdf
3. **European Chronic Disease Alliance**

4. **Chronic non-communicable diseases kill 86% of all people in the WHO European Region. Cardiovascular diseases, cancer, respiratory diseases, diabetes, kidney and liver diseases account for more than 40% the disease burden in Europe. Heart disease, stroke and diabetes alone are projected to lead to loss of national income in the billions, e.g. almost $33 billion in the United Kingdom (from 2005 to 2015).**
5. **The Chronic Disease alliance consists of the organisations mentioned below:**
6. **About the European Association for the Study of the Liver**
   EASL is the leading European scientific society involved in promoting research and education in hepatology. EASL attracts the foremost hepatology experts as members and has an impressive track record in promoting research in liver disease, supporting wider education and promoting changes in European liver policy.
   http://www.easl.eu/
7. **About the European CanCer Organisation**
   Following the philosophy that every cancer patient deserves the best, ECCO focuses on creating awareness of patients' needs and wishes, stimulating progressive thinking in Cancer policy, training and education, and encouraging European cancer research and its application through the organisation of international multidisciplinary conferences including the premier European cancer meetings: the ECCO – ESMO Multidisciplinary Cancer Congresses.
   http://www.ecco-org.eu/
8. **About the European Heart Network**
   The European Heart Network (EHN) is a Brussels-based alliance of heart

foundations and like-minded nongovernmental organisations throughout Europe. EHN has member organisations in 26 countries. EHN plays a leading role in the prevention and reduction of cardiovascular diseases, in particular heart disease and stroke, through advocacy, networking, education and patient support, so that they are no longer a major cause of premature death and disability throughout Europe.
http://www.ehnheart.org/

9. **About the European Kidney Health Alliance**
   The European Kidney Health Alliance (EKHA) is an Alliance of not-for-profit organisations who represent the key stakeholders in kidney health issues in Europe. EKHA takes a multidisciplinary approach involving patients and their families, doctors and nurses, researchers and other healthcare professionals who work cooperatively for a European health environment in which there is a sustained decrease in kidney disease and its consequences.
   http://www.ekha.eu/
10. **About the European Respiratory Society**
    The ERS, European Respiratory Society, is a professional, medical organisation with more than 10,000 members in over 100 countries representing medical and scientific experts in the field of respiratory medicine and lung science. Its mission is to promote lung health through research, knowledge sharing, and medical education.
    http://www.ersnet.org/
11. **About the European Society of Cardiology**
    The ESC unites over 62,000 cardiology professionals from across Europe and the Mediterranean, with the mission of reducing the burden of cardiovascular disease in Europe through education, congresses, surveys on cardiovascular diseases and the publishing of scientific materials, including journals and Clinical Practice Guidelines.
    http://authors.escardio.org/
12. **About the European Society of Hypertension**
    The main purpose of the European Society of Hypertension (ESH) is to provide a stable and organised European platform for scientific exchange in hypertension. The objectives of ESH are to promote, endorse and organise activities involved with the continuing medical education in the field of hypertension and associated cardiovascular diseases.
    http://www.eshonline.org/
13. **About the European Society for Medical Oncology**
    The European Society for Medical Oncology (ESMO) is the leading European professional organisation committed to advancing the specialty of medical oncology and promoting a multidisciplinary approach to cancer treatment and care. ESMO's mission is to advance cancer care and cure through fostering and disseminating good science that leads to better medicine and determines best practice.
    http://www.esmo.org/
14. **About the Federation of European Nurses in Diabetes**
    FEND has established a unique voice for nurses working in the field of diabetes care, research and education in Europe. Its mission statement is to promote the delivery of evidence based care for people with diabetes throughout Europe.
    http://www.fend.org/

15. **About the International Diabetes Federation - Europe**
    IDF-Europe is the European Regional section of the International Diabetes Federation. Its constituents are the member associations of the national diabetes organisations (representing both health care professionals and patients & carers) from 45 European countries. Within the EU there are over 30 million people with diabetes, it is increasing at an alarming rate and this number is predicted to exceed 50 million by 2030. IDF-Europe aims to encourage the prevention, the earlier diagnosis, better management and education of diabetes.
    www.idf.org/idf-european-region

10 External links
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