Epidemiology of Diabetes, Impaired Glucose Homeostasis and Cardiovascular Risk

Eberhard Standl

European Heart House
Sophia Antipolis
Thursday, June 17, 2010
### IDF Diabetes Atlas 2009: Global Numbers Still Dramatically Rising

#### AT A GLANCE

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total world population (billions)</td>
<td>7.0</td>
<td>8.4</td>
</tr>
<tr>
<td>Adult population (20-79 years, billions)</td>
<td>4.3</td>
<td>5.6</td>
</tr>
</tbody>
</table>

#### DIABETES AND IGT (20-79 years)

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global prevalence [%]</td>
<td>6.6</td>
<td>7.8</td>
</tr>
<tr>
<td>Comparative prevalence [%]</td>
<td>6.4</td>
<td>7.7</td>
</tr>
<tr>
<td>Number of people with diabetes [millions]</td>
<td>285</td>
<td>438</td>
</tr>
<tr>
<td>IGT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global prevalence [%]</td>
<td>7.9</td>
<td>8.4</td>
</tr>
<tr>
<td>Comparative prevalence [%]</td>
<td>7.8</td>
<td>8.4</td>
</tr>
<tr>
<td>Number of people with IGT [millions]</td>
<td>344</td>
<td>472</td>
</tr>
</tbody>
</table>
Prevalence of diabetes and prediabetes in China

Estimated diabetes = 92.4 millions; prediabetes = 148.2 millions

N=46,239 aged ≥20 years; oral glucose tolerance test
Estimated diabetes = 92.4 million; estimated prediabetes = 148.2 million
CVD and chronic hyperglycemia (=diabetes): Some epidemiological notions

Further life expectancy reduced by 30% from diagnosis of diabetes

CVD: relative risk increased 2-3 fold in men with diabetes, some 5 fold in women with diabetes, some 70-80% of diabetic patient die from CVD, diabetes represents an equivalent of CVD, same risk for MI, but 20 years earlier, 70% of all CVD patients have diabetes or IGT

Stroke: 2 fold increased risk

QUESTION? Are glycemia related parameters predictive for CVD?
The AusDiab Study: 5.2 y CVD mortality in 10,428 participants according to baseline glycemic status
Meta-analysis: increased HbA1c associated with increased CV risk

Relative risk (RR) and 95% CIs for 1% increase in HbA1c and incident CVD (coronary heart disease + stroke) in type 2 diabetes

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Events/Persons, n/n*</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>della Rovere et al. 2003</td>
<td>22/113</td>
<td>2.56 (1.10–5.98)</td>
</tr>
<tr>
<td>Florkowski et al. 1998</td>
<td>92/422</td>
<td>1.43 (1.02–2.00)</td>
</tr>
<tr>
<td>Agewall et al. 1997</td>
<td>21/94</td>
<td>1.54 (1.14–2.09)</td>
</tr>
<tr>
<td>Kuusisto et al. 1994</td>
<td>33/229</td>
<td>1.29 (0.98–1.70)</td>
</tr>
<tr>
<td>Mattock et al. 1998</td>
<td>20/138</td>
<td>1.25 (1.01–1.55)</td>
</tr>
<tr>
<td>Gall et al. 1995</td>
<td>29/321</td>
<td>1.30 (1.10–1.60)</td>
</tr>
<tr>
<td>Standl et al. 1996</td>
<td>58/223</td>
<td>1.18 (1.02–1.35)</td>
</tr>
<tr>
<td>Lehto et al. 1997</td>
<td>256/1059</td>
<td>1.03 (0.96–1.15)</td>
</tr>
<tr>
<td>Stratton et al. 2000</td>
<td>606/3642</td>
<td>1.16 (1.09–1.27)</td>
</tr>
<tr>
<td>Moss et al. 1994</td>
<td>241/1194</td>
<td>1.10 (1.04–1.17)</td>
</tr>
<tr>
<td>Pooled</td>
<td>1378/7435</td>
<td>1.18 (1.10–1.26)</td>
</tr>
</tbody>
</table>

Predictive power of glucose related parameters for CVD risk

The relationship between glycemic parameters and CVD shows a continuum (the risk starts within the normal range)

• An increase of 1% HbA1c increases the risk of CVD by 10 to 20 %

• An increase of 1 mmol/l FPG above optimum increases CVD mortality by 20 % (40 % in the age group below 60 years)

• IGT („prediabetes“) is also predictive

• What is the effect of reducing hyperglycemia?
Europe – a „Hot Spot“ in Diabetes
The Growing Diabetes Epidemic

Statistics

- Diabetes is a leading cause of death in Europe

- Currently, there are 31 million people in the enlarged EU and 22 million outside the EU in Europe living with diabetes

- By 2025, the number of people with diabetes is expected to rise by 20% in Europe*

Complications

- Diabetes is among the leading causes of kidney failure and neuropathy

- CVD accounts for 75% of all deaths among diabetes patients in Europe

- Diabetes is the main cause of partial vision loss and blindness in people over 20 in Europe

- Diabetes stimulates various socio-psychological conditions

*WHO Report, 6 May, 2004
Diabetes is high across Europe and set to increase over the next 20 years.

International Diabetes Federation (IDF) Diabetes Atlas, 3rd Edition
Gender and Age Specific Survey of prevalent Diabetes in Germany

Basispopulation: Durchgängig Versicherte 1998 und 2004;
Studienpopulation: Definierte Diabetiker

(Köster, Schubert, Hauner 2006)
FIGURE 2.2
Number of people with diabetes by age group 2010 and 2030
Loss of Life-Years related to Diabetes mellitus

**Table 3.** Duration of Diabetes, Life-Years Lost, and Quality-Adjusted Life-Years Lost Among Males

<table>
<thead>
<tr>
<th>Age at Diagnosis, y</th>
<th>Duration</th>
<th>Life-Years Lost</th>
<th>QALYs Lost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic White</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>51.0</td>
<td>16.6</td>
<td>29.3</td>
</tr>
<tr>
<td>20</td>
<td>42.6</td>
<td>15.3</td>
<td>26.0</td>
</tr>
<tr>
<td>30</td>
<td>35.3</td>
<td>13.2</td>
<td>22.0</td>
</tr>
<tr>
<td>40</td>
<td>28.2</td>
<td>10.9</td>
<td>18.0</td>
</tr>
<tr>
<td>50</td>
<td>21.2</td>
<td>8.8</td>
<td>14.1</td>
</tr>
<tr>
<td>60</td>
<td>14.5</td>
<td>7.1</td>
<td>10.8</td>
</tr>
<tr>
<td>70</td>
<td>9.3</td>
<td>5.2</td>
<td>7.5</td>
</tr>
<tr>
<td>80</td>
<td>5.3</td>
<td>3.6</td>
<td>4.9</td>
</tr>
</tbody>
</table>

**Table 4.** Duration of Diabetes, Life-Years Lost, and Quality-Adjusted Life-Years Lost Among Females

<table>
<thead>
<tr>
<th>Age at Diagnosis, y</th>
<th>Duration</th>
<th>Life-Years Lost</th>
<th>QALYs Lost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic White</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>55.4</td>
<td>17.9</td>
<td>31.8</td>
</tr>
<tr>
<td>20</td>
<td>46.6</td>
<td>16.9</td>
<td>28.5</td>
</tr>
<tr>
<td>30</td>
<td>38.2</td>
<td>15.6</td>
<td>25.1</td>
</tr>
<tr>
<td>40</td>
<td>30.2</td>
<td>13.8</td>
<td>21.4</td>
</tr>
<tr>
<td>50</td>
<td>22.9</td>
<td>11.8</td>
<td>17.5</td>
</tr>
<tr>
<td>60</td>
<td>16.4</td>
<td>9.3</td>
<td>13.4</td>
</tr>
<tr>
<td>70</td>
<td>11.3</td>
<td>6.2</td>
<td>9.1</td>
</tr>
<tr>
<td>80</td>
<td>6.8</td>
<td>3.9</td>
<td>5.6</td>
</tr>
</tbody>
</table>

Number of deaths attributable to diabetes (20-79 years) 2010
Deaths from coronary heart disease

Civilization kills. Since 1980, more people have died from coronary heart disease than from any other cause. Unlike stroke, coronary heart disease is a comparative newcomer on the world stage. Variations in death rates are marked; they are lower in populations with short life expectancy.

Heart disease mortality rates are also affected by differences between countries in the major risk factors, especially blood pressure, blood cholesterol, smoking, physical activity and diet. While genetic factors play a part, 80% to 90% of people dying from coronary heart disease have one or more major risk factors that are influenced by lifestyle.

Death rates from coronary heart disease have decreased in North America and many western European countries. This decline has been due to improved prevention, diagnosis, and treatment, in particular reduced cigarette smoking among adults, and lower average levels of blood pressure and blood cholesterol. It is expected that 82% of the future increase in coronary heart disease mortality will occur in developing countries.

Of all coronary heart disease patients who die within 28 days after the onset of symptoms, about two-thirds die before reaching hospital. This highlights not only the need for early recognition of the warning signs of a heart attack, but also the need for prevention.

Deaths from coronary heart disease compared with other causes

Number of deaths of people aged 15 to 89 years, and 60 years and over 2002 thousands

Change of heart
Percentage change in coronary heart disease death rates, in people aged 35 to 74 years, 1990–1998 selected countries

WHO 15.05.09
Hyperglycaemia is common and often undiagnosed in patients with CAD in Europe and Asia.

In the Euro Heart Survey (n=4,961), 2/3 of patients have hyperglycaemia. The distribution is as follows:
- Normal glucose tolerance: 31%
- Prediabetes (IGT): 29%
- Prediabetes (IFG): 12%
- Newly diagnosed diabetes: 3%
- Previously known diabetes: 25%

In the China Heart Survey (n=3,513), ~3/4 of patients have hyperglycaemia. The distribution is as follows:
- Normal glucose tolerance: 33%
- Prediabetes (IGT): 23%
- Prediabetes (IFG): 24%
- Newly diagnosed diabetes: 20%
- Previously known diabetes: 29%

CAD: coronary artery disease; OGTT: oral glucose tolerance test; FPG: fasting plasma glucose; IFG: impaired fasting glucose; IGT: impaired glucose tolerance.

Total and CVD mortality during 18 years of follow-up in type 1 (T1D) diabetic, type 2 diabetic (T2D), and nondiabetic (Non-D) men (M) and women (W).

The plot for total and CVD mortality, adjusted for age, area of residence, current smoking, use of alcohol, systolic blood pressure, BMI, total and HDL cholesterol, Cockroft-Gault estimate of creatinine clearance, and urinary protein (log).

A. JUUTILAINEN, S. LEHTO, T. RÖNNEMAA, K. PYÖRÄLÄ, M. LAAKSO


© Prof. Eberhard Standl
The major diabetic complications

Stroke
(cerebrovascular disease)

Heart disease
(cardiovascular disease)
Bacterial and fungal infections of the skin
Severe hardening of the arteries (atherosclerosis)
Sexual dysfunction

Visual impairment:
diabetic retinopathy
cataract glaucoma

Kidney disease
(diabetic nephropathy)

Autonomic neuropathy
(including slow emptying of the stomach and diarrhoea)

Necrobiosis lipidoica

Sensory impairment
(peripheral neuropathy)

Gangrene

Ulceration
Relation between age and acute myocardial infarction in men and women with diabetes compared with non-diabetic people

Gillian L Booth  The Lancet 2006; 368:29-36
© Prof. Eberhard Standl
Type 2 diabetes and CHD: 7-year incidence of fatal/nonfatal MI (East West Study)

MI = myocardial infarction. * These patients had no prior MI at baseline.


© Prof. Eberhard Standl
Coronary heart disease may be present at diagnosis of Type 2 diabetes

The Munich GP-Project: Characteristics of a random cohort of recently diagnosed Type 2 diabetic patients

Standl et al 1993 Diabetologia 36: 1017-20

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (y)</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.9</td>
<td></td>
</tr>
<tr>
<td>FBG (mg/dl)</td>
<td>140</td>
<td></td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Triglycerides↑ (%)</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>Cholesterol↑ (%)</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>(Micro-)albumin. (%)</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Obesity (%)</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>CHD (ECG)</td>
<td></td>
<td>41%</td>
</tr>
<tr>
<td>PVD (Doppler)</td>
<td></td>
<td>35%</td>
</tr>
<tr>
<td>Carotissten. (Doppler)</td>
<td></td>
<td>4%</td>
</tr>
</tbody>
</table>

Standl et al 1993 Diabetologia 36: 1017-20

© Prof. Eberhard Standl
Metabolic syndrome / Insulin resistance: causes and associated disease

- Adiposity and physical inactivity
- Low birth weight
- Genetics
- Glucose toxicity
- Type 2 diabetes
- Hypertension
- Dyslipidemia
- Procoagulatory state
- Endothelial dysfunction
- Lipatrophy
- Drugs
- Age
- Chronic low grade inflammation

CARDIO-/MACRO-VASCULAR DISEASE
Abdominal adiposity – a key factor for myocardial infarction

Cardiometabolic risk factors for Western Europe

InterHeart Study

Odds Ratio
Myocardial infarction

- Abdominal adiposity: 4.50
- Hypertension: 2.22
- Dyslipidemia: 3.76
- Diabetes: 4.29

Yusuf et al. The Interheart Study, Lancet 364, 2004
app. 80% are insulin resistant
app. 80% are hypertensive
app. 70% are dyslipidemic
app. 80%: HbA1c > 6,5%,
  70% HbA1c > 7,0%
What are the clinical outcomes of the metabolic syndrome?

- **Cardiovascular disease**
  - Relative risk = 2x

- **Type 2 diabetes**
  - Relative risk = 5x

- **Fatty liver**
- **Obstructive sleep apnea**
- **Cholesterol gallstone**
- **Polycystic ovarian disease**
# 2005 ‘Global’ IDF Criteria For The Metabolic Syndrome

**Revision in Circulation 2009; online Oct 5: WC only 1 criterion among 3 out of 5**

<table>
<thead>
<tr>
<th>Central Obesity - defined by WC (in cm)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europid</td>
<td>≥ 94</td>
<td>≥ 80</td>
</tr>
<tr>
<td>S/SE Asian</td>
<td>≥ 90</td>
<td>≥ 80</td>
</tr>
</tbody>
</table>

Plus any 2 of:

- Triglycerides ≥ 1.7mmol/L
- HDL <1.03 (M); <1.29 (F) mmol/L
- BP ≥130/85 mmHg
- Fasting glucose ≥ 5.6 mmol/L or pre-existing diabetes

PREVALENCE OF THE METABOLIC SYNDROME, ACCORDING TO THE IDF DEFINITION

Australia
Germany
Korea, Republic of
Mexico
Peru
Spain
United Kingdom
United States of America
USA (Mexican-American)
USA (non-Hispanic white)

Yellow: Males
Red: Females

SOURCE: DIABETES ATLAS THIRD EDITION © INTERNATIONAL DIABETES FEDERATION, 2006
Cardiometabolic Risk (ADA MCR Initiative)

GLOBAL CARDIOMETABOLIC RISK

Diabetes → Cardiovascular disease
Blood glucose lowering therapy: Important Co-Morbidities in CAD patients with diabetes

• Impaired kidney function
• Heart failure
• Mental disorders (e.g. depression)
• Cognitive impairment
• Advanced physical and mental disablement
The first Joint ESC/EASD Guidelines in "Cardio-Diabetology": A perspective in reducing CV risk

L. Ryden & E. Standl
Co-chairs
www.easd.org
www.escardio.org
You wanted to know your future....