TIME TO ACT

Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
Diabetes mellitus is a chronic disease which has been described as a state of raised blood glucose (hyperglycaemia) associated with premature mortality.

Hyperglycaemia seriously damages many of the body’s systems, especially the blood vessels and nerves.
Type 1 and type 2 diabetes

Diabetes arises when the beta cells in the pancreas fail to produce enough of the hormone insulin - type 1 diabetes

Or when the body cannot effectively use the insulin produced - type 2 diabetes.

. 90% of people with diabetes have type 2 diabetes.
The pancreas

Pancreas

Kidneys

Stomach

Type 2 diabetes, the **metabolic syndrome** and **cardiovascular disease** in Europe
Insulin is a hormone that allows cells to extract glucose from the blood and use it for energy.

- Insulin is produced by the beta cells of the pancreas.
- It regulates protein and lipid metabolism.
When a person has diabetes, either:

- their pancreas does not produce the insulin they need - **type 1 diabetes**
- or their body cannot use this insulin effectively – **type 2 diabetes**.

This leads to an increase in the amount of glucose in the blood. This high concentration of glucose or ‘high blood sugar’ is termed **hyperglycaemia**.
Hormones

- Synthesised in glands, hormones are chemical signaling molecules which have a specific regulatory effect upon the activity of body tissues.
- Hormones are transported around the body in the blood so that they can act on tissues at a distance from the gland in which they were produced.
- Hormones can only act in those tissues where they have specific receptors in the cells.
Tissue damage

- Chronic elevation of blood glucose eventually leads to tissue damage.
- The kidneys, eyes, peripheral nerves and vascular tree manifest the most significant diabetic complications.
- The mechanism for this is complex and not yet fully understood. It involves:
  - The direct toxic effects of high glucose levels
  - The impact of elevated blood pressure
  - Abnormal lipid levels
  - Functional and structural abnormalities of small blood vessels
The short term effects of diabetes

- Out-of-control diabetes, when severe, leads to the body using stored fat for energy and a subsequent build-up of acids (ketone bodies) in the blood. This is known as **ketoacidosis** and is associated with very high glucose levels. It requires emergency treatment and can lead to coma and even death.

- Recurrent or persistent **infections** (including tuberculosis).

- Both hyperglycaemia and hypoglycaemia (abnormally low blood glucose resulting from treatment) may cause **coma** and, if untreated, may be fatal.
The long term effects of diabetes can be divided into

- macrovascular complications
- microvascular complications.

- **Macrovascular complications** affect the larger blood vessels, such as those supplying blood to the heart, brain and legs. The most common macrovascular fatal complication is coronary artery disease. Strokes are also a common cause of disability and death in people with diabetes.

- **Microvascular complications** affect the small blood vessels, such as those supplying blood to the eyes and kidneys. The microvascular complications of diabetes are retinopathy, nephropathy and neuropathy.

**Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe**

**TIME TO ACT**
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
- Poor blood supply to lower limbs (peripheral vascular disease)
- Necrobiosis lipidoica
- Gangrene
- Visual impairment: diabetic retinopathy, cataract and glaucoma
- Kidney disease (diabetic nephropathy)
- Autonomic neuropathy (including slow emptying of the stomach and diarrhea)
- Sensory impairment (peripheral neuropathy)
- Ulceration

Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
Diagnosing diabetes

• If someone has the typical symptoms of diabetes the diagnosis is clear:
  - increased thirst
  - excess urine
  - weight loss
  - a clearly raised plasma glucose level

• Ketones in the urine accompanied by high plasma glucose levels is also a clear indication of diabetes.

• However, diagnosis is less straightforward for those with minor degrees of hyperglycaemia, and in the person without symptoms, two abnormal results on separate occasions are needed.
## Diagnostic criteria for diabetes and its risk states

<table>
<thead>
<tr>
<th>Condition</th>
<th>Venous Plasma*Glucose concentration, Mmol l⁻¹ (mg dl⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetes mellitus</strong></td>
<td></td>
</tr>
<tr>
<td>Fasting <em>or</em></td>
<td>≥7.0 (≥126)</td>
</tr>
<tr>
<td>2-h post glucose load</td>
<td>≥11.1 (≥200)</td>
</tr>
<tr>
<td><strong>Impaired Glucose Tolerance (IGT)</strong></td>
<td></td>
</tr>
<tr>
<td>2-h post glucose load</td>
<td>≥7.8 -&lt;11.1 (≥140 -&lt;200)</td>
</tr>
<tr>
<td><strong>Impaired Fasting Glycaemia (IFG)</strong></td>
<td></td>
</tr>
<tr>
<td>Fasting</td>
<td>≥6.1 -&lt;7 (≥110 -&lt;126)</td>
</tr>
</tbody>
</table>

*In the fasting state, the plasma glucose concentration is measured in the morning after an overnight fast of at least 12 hours.

---

**Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe**
Risk factors for type 2 diabetes

- Physical inactivity
- Overweight and obesity
- Age
- High-fat and low-fiber diet
- Urbanisation
- Family history
- Low birth weight
- Ethnicity

Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
The metabolic syndrome

- The close association of type 2 diabetes with cardiovascular disease has led to the hypothesis that they both share a common antecedent. This concept has been labeled ‘The Metabolic Syndrome’ by the World Health Organization and others.

The metabolic syndrome reflects the clustering of central obesity with several other major cardiovascular disease risk factors.

- Insulin resistance
- Hypertension
- Impaired glucose regulation or diabetes
- Central obesity
- Dyslipidaemia
A disturbing feature of diabetes has been the clustering of diabetes with other well-known cardiovascular risk factors, in particular central (abdominal) obesity.

The occurrence of central obesity, hypertension and disturbed blood lipids is dramatically increased in people with diabetes.

People with IGT and IFG also have a substantial increase in cardiovascular risk factors and, like people with diabetes, higher cardiovascular risk.
There is now broad agreement on the overall risk factors which must be taken into account when defining the metabolic syndrome. These have been called ‘the deadly quartet’.

- Impaired glucose regulation
- Hypertension
- Dyslipidaemia
- Obesity
It is suggested that **insulin resistance** and **central obesity** are the key underlying defects in the aetiology of type 2 diabetes.

A universal definition of metabolic syndrome is urgently needed to identify individuals at high risk of developing diabetes and cardiovascular disease.
In order to make a diagnosis of the metabolic syndrome a patient must present with **three or more** of the following five risk factors:

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abdominal obesity</strong></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>Waist circumference ≥ 102 cm (&gt;40 in)</td>
</tr>
<tr>
<td>Women</td>
<td>&gt;88 cm (&gt;35 in)</td>
</tr>
<tr>
<td><strong>Triglycerides</strong></td>
<td>≥150 mg/dL (1.7 mmol/L)</td>
</tr>
<tr>
<td><strong>HDL cholesterol</strong></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&lt;40 mg/dL (1.04 mmol/L)</td>
</tr>
<tr>
<td>Women</td>
<td>&lt;50 mg/dL (1.29 mmol/L)</td>
</tr>
<tr>
<td><strong>Blood pressure</strong></td>
<td>≥130/ ≥85 mmHg</td>
</tr>
<tr>
<td><strong>Fasting glucose</strong></td>
<td>≥100 mg/dL (5.6 mmol/L)</td>
</tr>
</tbody>
</table>

*2001, updated 2005*
## Metabolic syndrome: IDF consensus definition (2005)

### Central Obesity

<table>
<thead>
<tr>
<th>Waist circumference</th>
<th>- ethnicity specific*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- for Europids:</td>
</tr>
<tr>
<td></td>
<td>Male ≥ 94 cm</td>
</tr>
<tr>
<td></td>
<td>Female ≥ 80 cm</td>
</tr>
</tbody>
</table>

**plus any two of the following:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raised Triglycerides</td>
<td>≥150mg/dL (1.7mmol/L) or specific treatment for this lipid abnormality</td>
</tr>
<tr>
<td>Low HDL Cholesterol</td>
<td>&lt;40mg/dL (1.03 mmol/L) in males &lt;50mg/dL (1.29 mmol/L) in females or specific treatment for this lipid abnormality</td>
</tr>
<tr>
<td>Raised blood pressure</td>
<td>Systolic: ≥130 mmHg or Diastolic: ≥85 mmHg or Treatment of previously diagnosed hypertension</td>
</tr>
<tr>
<td>Impaired fasting glycaemia</td>
<td>Fasting plasma glucose ≥100 mg/dL (5.6 mmol/L) or previously diagnosed type 2 diabetes If above 5.6 mmol/L or 100 mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome.</td>
</tr>
</tbody>
</table>
Metabolic syndrome: Prevalence in the US as defined by NCEP ATP III

Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
**Metabolic syndrome:**
Prevalence in adults as defined by IDF criteria

<table>
<thead>
<tr>
<th>Location</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lima, Peru</td>
<td>21.6%</td>
<td>30%</td>
</tr>
<tr>
<td>Mexico City</td>
<td>55.6%</td>
<td>64%</td>
</tr>
<tr>
<td>Spain</td>
<td>27.3%</td>
<td>31.7%</td>
</tr>
<tr>
<td>Greece</td>
<td></td>
<td>24.5%</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>7.4% of Chinese men and women</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td></td>
<td>39%</td>
</tr>
<tr>
<td>Germany</td>
<td>57%</td>
<td>46%</td>
</tr>
</tbody>
</table>
Risk factors for obesity

- High fat, energy dense diet
- Sedentary lifestyle/physical inactivity
- Family history
- Ethnicity
- Age
- Stopping smoking
Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
Measuring obesity

Body Mass Index

Obesity is most commonly assessed by a single measure, the Body Mass Index (BMI), which uses a mathematical formula based on a person’s height and weight.

\[
\text{BMI} = \frac{\text{weight (kg)}}{\text{height (m}^2\text{)}}
\]

- Individuals with a BMI
  - between 25 to 29.9 are considered overweight
  - of 30 and above are considered obese.
- The risk of serious health consequences such as type 2 diabetes, coronary heart disease, hypertension, dyslipidaemia, albuminuria and a wide range of other conditions increases with BMI.
Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe

Measuring obesity up to here
The limitations of the Body Mass Index

- **BMI DOES NOT**
  - show the difference between excess fat and muscle.
  - identify whether the fat is laid down in particular sites. For example, abdominal fat has more serious health consequences than fat located elsewhere.
- The relation between fatness and BMI differs with age, race and gender.
**Measuring obesity**

**WHO classification of adult categories of BMI**

<table>
<thead>
<tr>
<th>Classification</th>
<th>BMI (kg/m²)</th>
<th>Risk of co-morbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
<td>Low (but risk of other clinical problems increased)</td>
</tr>
<tr>
<td>Normal range</td>
<td>18.5-24.9</td>
<td>Average</td>
</tr>
<tr>
<td>Overweight*</td>
<td>≥25</td>
<td></td>
</tr>
<tr>
<td>Pre-obese</td>
<td>25.0-29.9</td>
<td>Mildly increased</td>
</tr>
<tr>
<td><strong>Obese</strong></td>
<td><strong>&gt;30.0</strong></td>
<td></td>
</tr>
<tr>
<td>Class I</td>
<td>30.0-34.9</td>
<td>Moderate</td>
</tr>
<tr>
<td>Class II</td>
<td>35.0-39.9</td>
<td>Severe</td>
</tr>
<tr>
<td>Class III</td>
<td>40.0</td>
<td>Very severe</td>
</tr>
</tbody>
</table>

*Measuring obesity: WHO classification of adult categories of BMI*
## Measuring obesity

**WHO classification of BMIs for adults of Asian origin**

<table>
<thead>
<tr>
<th>Classification</th>
<th>BMI (kg/m²)</th>
<th>Risk of co-morbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>Waist circumference</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 90 cm (men) &lt; 80 cm (women)</td>
</tr>
<tr>
<td>Underweight</td>
<td>&lt; 18.5</td>
<td>Low (but risk of other clinical problems increased)</td>
</tr>
<tr>
<td></td>
<td>≥ 23</td>
<td>Average</td>
</tr>
<tr>
<td>Normal range</td>
<td>18.5-22.9</td>
<td>Average</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increased</td>
</tr>
<tr>
<td>Overweight</td>
<td>≥ 23</td>
<td></td>
</tr>
<tr>
<td>At risk</td>
<td>23.0-24.9</td>
<td>Increased</td>
</tr>
<tr>
<td>Obese I</td>
<td>25-29.9</td>
<td>Moderate</td>
</tr>
<tr>
<td>Obese II</td>
<td>≥ 30.0</td>
<td>Severe</td>
</tr>
</tbody>
</table>

**World Health Organization, 1998**

**Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe**
The relationship between BMI and the risk of developing type 2 diabetes

Body mass index (kg/m²)

Risk of type 2 diabetes

- Women
- Men

Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
The presence of abdominal obesity is more highly correlated with the metabolic risk factors than is an elevated BMI.

The new IDF consensus definition of the metabolic syndrome stipulates the following as a pre-requisite for a diagnosis of metabolic syndrome:

- ≥ 80 cm for European women
- ≥ 94 cm for European men

Waist circumference is calculated by comfortably measuring the waist halfway between the bottom of the rib cage and the top of the pelvis.
<table>
<thead>
<tr>
<th>Country/Ethnic group</th>
<th>Waist circumference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Europids</strong></td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Female</td>
</tr>
<tr>
<td><strong>South Asians</strong></td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Female</td>
</tr>
<tr>
<td><strong>Chinese</strong></td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Female</td>
</tr>
<tr>
<td><strong>Japanese</strong></td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Female</td>
</tr>
<tr>
<td><strong>Ethnic South and Central Americans</strong></td>
<td>Use South Asian recommendations until</td>
</tr>
<tr>
<td></td>
<td>more specific data are available</td>
</tr>
<tr>
<td><strong>Sub-Saharan Africans</strong></td>
<td>Use European data until more specific</td>
</tr>
<tr>
<td></td>
<td>data are available</td>
</tr>
<tr>
<td><strong>Eastern Mediterranean and Middle East</strong></td>
<td></td>
</tr>
<tr>
<td>(Arab) populations</td>
<td></td>
</tr>
</tbody>
</table>
Insulin resistance: A state in which a given level of insulin produces a less than expected biological effect.
Insulin resistance

- Insulin resistance is an underlying feature of both the metabolic syndrome and type 2 diabetes.
- It is associated with abnormalities in both glucose and lipid metabolism.
- These abnormalities are associated with an increased risk of cardiovascular disease and are often present before the onset of type 2 diabetes.
Obesity and type 2 diabetes are causally linked.

The means by which excess body fat causes type 2 diabetes is not clearly defined, but it appears that excess fat increases insulin resistance, raising blood glucose levels and the likelihood of developing diabetes.
Weight gain and insulin resistance

Weight gain leads to insulin resistance through several mechanisms:

• Fat accumulation induces insulin resistance through changes in its hormonal and other secretions. Protective hormones decline as fat cells expand, particularly in the abdomen.

• Physical inactivity, both a cause and consequence of weight gain, also contributes to insulin resistance.

• Insulin resistance places a greater demand on the pancreatic capacity to produce insulin, which also declines with age, leading to the development of clinical diabetes.
Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are not clinical entities in their own right but rather risk categories for future diabetes and/or cardiovascular disease.

The terms refer to different measurements of abnormal glucose regulation: IFG in the fasting state and IGT in the post prandial state.
Impaired glucose regulation

**IGT**: Blood levels that are higher than normal in response to an oral glucose load but below the level of someone with diabetes.

**IFG**: Raised fasting levels of glucose.
Impaired glucose regulation

- IGT and IFG are considered risk categories for developing type 2 diabetes.
- Both IFG and IGT represent a risk of 25% to 50% of developing type 2 diabetes in the next 10 years but it is not inevitable.
- IFG and IGT are particularly amenable to treatment through lifestyle interventions.
Hypertension (high blood pressure): damages the smaller vessels in the circulatory system. Over time they become scarred, hardened, narrowed and less elastic. High blood pressure can also both predispose to and accelerate the development of atherosclerosis.

Systolic blood pressure: \( \geq 130 \text{mm Hg of mercury} \)

or

Diastolic blood pressure: \( \geq 85 \text{mm Hg of mercury} \)

Component of the Metabolic Syndrome (according to the IDF consensus definition)
Dyslipidaemia: Abnormal levels of lipids (fats) in the blood.
Dyslipidaemia and cardiovascular disease

- Dyslipidaemia is a major risk factor for cardiovascular disease - for patients with metabolic syndrome as well as those with type 2 diabetes
- The dyslipidaemia observed in these high risk patients is complex, and is characterised by:
  - Normal or only slightly elevated LDL cholesterol
  - Hypertriglyceridemia (↑TG)
  - Low high-density lipoprotein cholesterol (↓HDL)
  - Small, dense LDL particles
- All these elements can be measured in the blood.
Dyslipidaemia key terms: Triglyceride and cholesterol

**Triglyceride:** The major form of fat made in the liver. Most of the fat we eat is composed of triglycerides. The rest is cholesterol.

- Raised levels of triglycerides (↑TG) are a characteristic of diabetic dyslipidaemia.

**Cholesterol:** A fat of the body. It is absorbed from animal fat we eat and is also produced by the liver. Cholesterol circulates in the blood in the form of particles called lipoproteins.
High density lipoprotein (HDL): protects against cardiovascular disease. Therefore low levels of HDL-C (↓HDL-C) increase cardiovascular disease.

Low density lipoprotein (LDL): LDL-C cholesterol promotes cardiovascular disease.
Small LDL particles are different from the larger LDL particles and may be more atherogenic. Therefore the cholesterol blood level in a patient with diabetes may be misleading.

The combination of normal or only slightly elevated levels of LDL cholesterol, low HDL (↓HDL) and the presence of small dense LDL particles are characteristic of diabetic dyslipidaemia.
Diabetic dyslipidaemia

- Diabetic dyslipidaemia and insulin resistance:
  \( \downarrow \text{HDL} \) and \( \uparrow \text{TG} \) and insulin resistance are frequently correlated (with or without type 2 diabetes).

- Diabetic dyslipidaemia and coronary artery disease:
  \( \downarrow \text{HDL} \), \( \uparrow \text{TG} \) and \( \uparrow \text{LDL} \) indicate a significant increase in the risk of coronary artery disease.
<table>
<thead>
<tr>
<th>Atherogenic dyslipidemic profile in the metabolic syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Triglycerides</strong></td>
</tr>
<tr>
<td><strong>Fasting VLDL</strong></td>
</tr>
<tr>
<td><strong>Non-HDL cholesterol</strong></td>
</tr>
<tr>
<td><strong>Apolipoprotein B</strong></td>
</tr>
<tr>
<td><strong>HDL cholesterol</strong></td>
</tr>
<tr>
<td><strong>LDL cholesterol</strong></td>
</tr>
<tr>
<td><strong>LDL small and dense particles</strong></td>
</tr>
</tbody>
</table>

**Type 2 diabetes, the metabolic syndrome and cardiovascular disease** in Europe
Cardiovascular disease

- **Cardiovascular disease (CVD):** Cardiovascular diseases are defined as diseases and injuries of the circulatory system: the heart, the blood vessels of the heart, and the system of blood vessels throughout the body, and to (and in) the brain.

- **Stroke:** Stroke is the result of a blood flow problem within, or leading to, the brain and is considered a form of cardiovascular disease.
Cardiovascular disease and type 2 diabetes

- The processes by which diabetes can lead to cardiovascular damage do not develop independently. Each may accelerate or worsen the others.
- Atherosclerosis and hypertension are the two main processes which lead to cardiovascular disease.
- Microangiopathy and autonomic neuropathy are other damaging effects which are specific to diabetes.
- In many people with diabetes these different factors co-exist, resulting in progressive damage to the heart and blood vessels.
Atherosclerosis: leads to the formation of plaques of atheroma which narrow the diameter of the large and medium sized arteries. This narrowing impairs blood flow. Plaques are also prone to rupture, or to ulcerate and then act as a site for blood clot formation. The resulting blood clots, which can block the affected vessel completely, are usually responsible for the more severe clinical manifestations of cardiovascular disease such as heart attack and stroke.
Today the most widespread forms of cardiovascular disease are those which start with damage to the blood vessels – hypertension and atherosclerosis.

**Hypertension**
- is at least twice as common in people with diabetes as in the general population.
- is also more frequent in people with impaired glucose tolerance.

**Atherosclerosis**
- Not only are people with diabetes at increased risk of developing atherosclerosis, but the process also tends to be accelerated, more severe and more widespread.
The major clinical manifestations of cardiovascular disease can be divided into three groups.

- **Brain and cerebral circulation** - cerebrovascular disease
- **Heart and coronary circulation** - coronary heart disease
- **Lower limbs** - peripheral vascular disease
The clinical consequences of diabetes and cardiovascular disease

- People with type 2 diabetes have the same risk of heart attack as people without diabetes who have already had a heart attack.
- Women with diabetes are subject to sudden death 300% more often and men with diabetes 50% more often than their counterparts without diabetes of the same age.
- Strokes occur twice as often in people with diabetes and hypertension as in those with hypertension alone.
- A person with diabetes has a two to three-fold greater risk of heart failure compared to a person without diabetes.
Heart attacks in people with and without diabetes over a period of seven years.
Cardiovascular risk factors

- Advancing age
- **Diabetes and other high blood glucose conditions**
- Dyslipidaemia
- Genetic background
- **High alcohol consumption**
- Hypertension
- **Insulin resistance**
- Left ventricular hypertrophy
- Male gender
- Menopause
- **Obesity**
- Sedentary lifestyle
- Smoking

**Bold text**: modifiable risk factor
What is a risk factor?

- **A risk factor** can be genetic or acquired.
- It may be identified as a single measurement (e.g., weight), disease (e.g., hypertension) or lifestyle characteristic (e.g., smoking).
- The condition must be associated with that disease in a manner which is beyond chance alone. A causal link is therefore implied.
- A risk factor will not necessarily always lead to the development of the disease.
- The ultimate purpose of identifying a risk factor is to modify it in order to prevent the disease.
Prevalence of cardiovascular risk factors in people with diabetes, compared to people without diabetes

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypertension</strong></td>
<td>Prevalence is at least double in people with type 2 diabetes</td>
</tr>
<tr>
<td><strong>High Blood Cholesterol</strong></td>
<td>Prevalence is similar in people with diabetes</td>
</tr>
<tr>
<td><strong>High Triglycerides with Low HDL</strong></td>
<td>Prevalence is higher in people with diabetes</td>
</tr>
<tr>
<td><strong>Left ventricular Hypertrophy</strong></td>
<td>Most commonly seen in people with long-standing high blood pressure, but is also seen in the absence of elevated blood pressure in people with diabetes</td>
</tr>
<tr>
<td><strong>Obesity</strong></td>
<td>Prevalence is stronger in people with diabetes. Weight distribution is also usually different, with more central obesity which is linked with a tendency to develop coronary heart disease.</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td>People with diabetes smoke less (presumably due to medical advice).</td>
</tr>
</tbody>
</table>
# Targets for common cardiovascular risk factors in people with diabetes

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Targets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyslipidaemia</td>
<td>Decrease LDL cholesterol levels (&lt;100 mg/dl or 2.5 mmol/l*)</td>
</tr>
<tr>
<td></td>
<td>Raise HDL cholesterol levels (&gt;46 mg/dl or 1.2 mmol/l*)</td>
</tr>
<tr>
<td></td>
<td>Lower triglycerides (&lt;150 mg/dl or 1.7 mmol/l*)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Lower blood pressure (&lt;135/85 mm Hg)</td>
</tr>
<tr>
<td>Hyperglycaemia</td>
<td>Reduce hyperglycaemia (HbA1c &lt;7%)</td>
</tr>
</tbody>
</table>
Diabetes - a growing threat

- There are currently more than 230 million people with diabetes worldwide. If nothing is done to slow the epidemic, the number will exceed 350 million by 2025.
- In 2003, the five countries with the largest numbers of persons with diabetes were
  - **India (35.5 million)**
  - **China (23.8 million)**
  - **the United States (16 million)**
  - **Russia (9.7 million)**
  - **Japan (6.7 million)**.
- By 2025, the number of people with diabetes is expected to more than double in Africa, the Eastern Mediterranean, the Middle East, and South-East Asia.
By 2025 the number of people with diabetes is expected to rise by

- 20% in Europe
- 50% in North America
- 75% in the Western Pacific
- 85% in South and Central America.

For developing countries, there will be a projected increase of a 170% of cases;

For developed countries, there will be a projected rise of 42%.

Diabetes is the fourth main cause of death in most developed countries.

Diabetes – a growing threat
The prevalence estimates of diabetes worldwide – 2003

Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe

The prevalence estimates of diabetes worldwide – 2025

The map shows the estimated prevalence of diabetes worldwide in the year 2025. The colors indicate different prevalence ranges: < 2%, 2% - 5%, 5% - 8%, 8% - 11%, 11% - 14%, 14% - 17%, 17% - 20%, and >20%.


TIME TO ACT

Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe

International Diabetes Federation
Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe

A growing threat
Diabetes in the elderly and the young

- Diabetes increased by one-third during the 1990s, due to the prevalence of obesity and an ageing population.
- Diabetes is particularly common in ageing populations, and the incidence is increasing in proportion to the number of people living longer.
- The incidence of type 2 diabetes in children and adolescents has also risen dramatically in recent years.
- Young people with diabetes will develop diabetes-related micro- and macrovascular complications at a relatively young age.
Overweight and obesity can affect as many as 30% – 35% of people under the age of 30 in some developed countries.

In Europe, the UK has demonstrated the most rapid increase in obesity which could see more than 40% of the population obese by 2025.

Worldwide the prevalence of obesity is rising to epidemic proportions at an alarming rate, with over half the world’s population already affected.
A growing threat
Diabetes and obesity

- International Obesity Task Force figures suggest that up to **1.7 billion people** are already at a heightened risk of weight related non-communicable disease such as type 2 diabetes.

- These rising levels are likely to drive the prevalence of diabetes even higher than present forecasts, which do not take into account changes in the obesity epidemic.

- It is estimated that at least half of all diabetes cases would be eliminated if weight gain in adults could be prevented.
Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
The prevalence of male and female obesity levels in selected European countries

Yugoslavia
Greece
Romania
Czech Rep.
England
Finland
Germany
Scotland
Slovakia
Portugal
Spain
Denmark
Belgium
Sweden
France
Italy
Netherlands
Norway
Hungary
Switzerland

% BMI ≥ 30

TYPE TO ACT

Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
A growing threat
The complications of diabetes

• **Diabetes is the leading cause of blindness and visual impairment in adults in developed countries.**

• **Diabetes is the most common cause of amputation which is not the result of an accident.**

• **People with diabetes are 15 to 40 times more likely to require a lower-limb amputation compared to the general population.**

• **Many people with diabetes develop severe kidney disease, which may be fatal if left untreated.**

*Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe*
A growing threat
Diabetes and cardiovascular disease

- 70%–80% of people with diabetes die of cardiovascular disease.
- For each risk factor present, the risk of cardiovascular death is about three times greater in people with diabetes as compared to people without the condition.
- Cardiovascular disease is the number one cause of death in industrialized countries. It is also set to overtake infectious diseases as the most common cause of death in many parts of the less developed world.
Changes in coronary heart disease mortality rates in the USA

- Men
- Women

Coronary heart disease mortality (%)

People without diabetes  People with diabetes

Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
The cost of diabetes

- The annual direct healthcare costs of diabetes worldwide, for people in the 20 – 79 age bracket, is estimated to be at least 153 billion international dollars.

- It is estimated that diabetes accounts for between 5% and 10% of total healthcare spending in most countries and up to 25% in some.

- If predictions of diabetes prevalence are fulfilled, total direct healthcare expenditure on diabetes worldwide will be between 213 billion and 396 billion international dollars in 2025.
Cardiovascular disease is the most important single contributor to diabetes costs.

In the industrialised world, CVD accounts for 57% of total medical care costs for people with diabetes.

The trend of escalating diabetes prevalence, with its impact on CVD, will no doubt lead to an immense financial burden in many countries, unless action is taken to prevent diabetes and its complications.
The cost of diabetes
Estimates of the cost of diabetes care by region

Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
A collaborative study of the direct costs of diabetes in eight European countries, the CODE-2 study demonstrated that type 2 diabetes is a serious and costly condition.

The study estimated that:

- The total direct medical costs for the 10 million people with type 2 diabetes in these countries were 29 billion Euros in 1998.
- Type 2 diabetes accounted for between 3% and 6% of total healthcare expenditure in the different countries.
- It also showed that diabetes-related complications are the main reason for the high costs.
Total annual direct medical costs for patients with type 2 diabetes (CODE-2 1998)

UK  2.6 billion Euros
Belgium  1.1 billion Euros
France  4.0 billion Euros
Spain  2.0 billion Euros
Sweden  0.7 billion Euros
Netherlands  0.4 billion Euros
Germany  12.4 billion Euros
Italy  5.8 billion Euros

Total for these 8 countries = 29 billion Euros

Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe

TIME TO ACT
Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
The cost of diabetes
Implications for health systems

- Direct health care costs of diabetes are high and rising
- Direct health care costs of the metabolic syndrome dominate health care budgets
- Preventing or delaying the onset of type 2 diabetes results in considerable cost reduction
- Improving metabolic control can also reduce health care resource use
Proportion of hospital bed days used for the treatment of diabetic complications

United Kingdom
- Neuropathy
- Eye disorders
- Kidney disease
- Total cardiovascular disease
- Acute complications
- Other

Argentina
- All microvascular disease
- Other acute cardiovascular disease
- Infections
- Other acute

Type 2 diabetes, the metabolic syndrome and cardiovascular disease in Europe
Managing Diabetes and Diabetic Complications

The human and economic costs of diabetes could be significantly reduced by investing in prevention, particularly early detection, in order to avoid the onset of diabetic complications.

- At least 50% of all people with diabetes are unaware of their condition.
- In some countries this figure may rise to 80%.
Managing diabetes
Blood glucose and lipids

- There is conclusive evidence that good control of blood glucose levels can substantially reduce the risk of developing complications and slow the progression in all types of diabetes.

- The management of high blood pressure and raised blood lipids (fats) is equally important.

- In all societies, better control of these parameters would contribute to a substantial improvement in quality of life.
### Recent Trials Relevant to the Primary Prevention of Type 2 Diabetes

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Interventions</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>DaQing (China)</td>
<td>1997</td>
<td>Diet, physical activity or both (control group: general)</td>
<td>Reduction in diabetes incidence 31% in diet group, 46% in physical activity and 42% in diet and physical activity compared to control group</td>
</tr>
<tr>
<td>Finnish Diabetes Prevention Study</td>
<td>2001</td>
<td>Diet and physical activity (control group: general advice)</td>
<td>Reduction by 58% of the risk of diabetes compared to control group</td>
</tr>
<tr>
<td>Diabetes Prevention Program (USA)</td>
<td>2002</td>
<td>Diet, physical activity, metformin and placebo</td>
<td>58% reduction in incidence of diabetes with lifestyle intervention, 31% with metformin</td>
</tr>
<tr>
<td>STOP-NIDDM</td>
<td>2002</td>
<td>Acarbose or placebo</td>
<td>32% patients randomised to acarbose and 42% randomised to placebo developed diabetes</td>
</tr>
</tbody>
</table>

*Diabetes and Obesity, Time to Act, p.33, IDF 2004*
Managing obesity

- Obesity is the main modifiable risk factor for type 2 diabetes.
- Small amounts of weight loss (5%–10%) can prevent or delay the development of type 2 diabetes in individuals with a high risk of the disease.
- Even a 5% weight reduction in those who are overweight or obese improves the risk of complications such as heart disease.
Lifestyle interventions, including diet and moderate physical activity (for example, walking 25 minutes per day, 6 times per week) can reduce the risk of diabetes by as much as 40–60%.

Weight loss drugs have a role in individuals in whom lifestyle changes are either insufficient to produce the required weight control or are impossible to achieve because of physical incapacity.

Weight management is the best strategy to prevent the development of type 2 diabetes.
Half or more of type 2 diabetes is undiagnosed.

Opportunistic screening during a healthcare visit for other reasons can identify undiagnosed diabetes, particularly in individuals at high risk.

Up to half of those afflicted already have signs of complications at diagnosis.

Strong scientific evidence relating good metabolic control to the prevention or delay of these complications is now available.
Microvascular complications

- Eye Problems
- Foot Problems
- Kidney Problems
The eye complications associated with diabetes (either specific to diabetes or more common in people with diabetes) are retinopathy, macular oedema, glaucoma and cataract.

- All of these complications are common, and, if left untreated, lead to deterioration of vision and ultimately, blindness.
- They are all treatable if detected early and most are potentially preventable.
Screening for eye problems

- Screening for diabetic retinopathy is cost-effective where subsequent treatment, such as laser treatment, is available and affordable.

- Where there is no access to laser treatment, good metabolic control aimed at delaying the progress of diabetic eye disease is likely to be cost-effective.
Managing eye problems

- Diabetic eye disease can be prevented or delayed by careful management of the underlying diabetes.
- If detected early, well before symptoms begin, its progress can be further delayed by photocoagulation.
- Laser treatment for diabetic retinopathy and macular oedema is highly effective.
- Laser screening is also particularly cost effective for younger patients, in whom the number of years of sight saved will be large.
- Cataract can be dealt with cheaply and effectively by surgical removal.
Foot problems

The combination of nerve damage and insufficient blood supply in the legs and feet of people with diabetes often leads to painful ulcers, infection and gangrene. This can ultimately result in amputation and even death.
Foot problems

- Foot ulceration affects some 15% of all people with diabetes some time during their lives.
- In developed countries, amputation of lower extremities is at least 10 times more common in persons with diabetes than in persons without diabetes.
- In developed countries, hospitalisation for people with diabetes-related foot ulcers is approximately 60% longer than for people without foot ulcers.
- The costs of diabetic foot problems are so high that a host of interventions are likely to be cost effective depending on the problem and the circumstances in which these interventions are carried out.
Managing foot problems

A number of interventions have been found to be effective in preventing the consequences of diabetic foot problems:

- Education
- Pressure-relieving interventions
- Multidisciplinary clinics
The cost effectiveness of managing foot problems

Although sources of cost savings vary country by country, the strategies of education, pressure-relieving interventions and multidisciplinary clinics have been judged to be cost-effective.

(Unfortunately data on cost-effectiveness comes exclusively from developed countries.)

One study identifies patient education as the most cost-effective intervention. Even if risk reduction is only half of the 50%–86% reported in the literature, the economic benefits of implementing such an approach will be substantial.
Renal problems

• The renal problems associated with diabetes are among the most costly in terms of their direct healthcare costs.

• People who develop these complications can, if left untreated, proceed to renal failure, which in turn leads to premature death if dialysis or kidney transplantation are not available.

• When they are available, long-term dialysis or the more desirable option of transplantation brings high healthcare costs to the individual and family, or to the healthcare sector or, more typically, to both.
Screening for renal problems

- Renal failure in diabetes can be detected very early by screening for ‘microalbuminuria’ (very small traces of protein in the urine).
- A number of studies suggest that when the facilities for treatment are available, screening for microalbuminuria is cost-effective.
- Treatment with ACE inhibitors (even in the absence of hypertension) is deemed, at least in the USA, to be cost-saving. When these are not available much can be done with other, less costly and more readily available anti-hypertensives (when hypertension is present). Improved blood glucose is also an important part of the response.
- However, effective treatment must be available in order to follow on from the detection of this early sign of renal failure.
Managing renal problems

- Keeping blood pressure at near-normal level in people with diabetes who also have hypertension is known to be effective in preventing or delaying renal failure.
- Maintaining a near-normal level of blood glucose also plays an important part.
- In addition, even in the absence of hypertension, the anti-hypertensive ACE-inhibitor drugs have been shown to provide protection for the kidney in people who have microalbuminuria.
The prevention of microvascular complications

Maintaining near-normal levels of blood glucose and blood pressure significantly decreases the risk of microvascular complications in people with diabetes.

- The DCCT, UKPDS and Kumamoto Studies have demonstrated this in regard to hyperglycaemia.

- The UKPDS Study and HOT Trial have shown the importance of the effective control of blood pressure.

The control of dyslipidaemia is also of vital importance, as is, if necessary, weight reduction.
The prevention of macrovascular complications

- The same basic improvements in diet and physical activity that prevent type 2 diabetes are likely to prevent CVD complications.
- Also, a wide range of drugs has now been proven to be effective in reducing the risk of CVD in people with diabetes, and in treating diabetes-associated CVD once it is present.
Each of these drugs can decrease CVD risk by 20% - 30% or more:

• **Aspirin**
  One of the world’s least expensive drugs, aspirin has been proven to be risk-beneficial in people with diabetes. However, caution is needed if the risk of strokes resulting from bleeding is high.

• **Beta Blockers, Diuretics and ACE Inhibitors**
  (angiotensin – converting enzyme inhibitors): lower blood pressure
Drug therapy

Each of these drugs can decrease CVD risk by 20% - 30% or more:

- **ACE Inhibitors**
  Also the drug of choice for preventing renal disease – the second most expensive complication of diabetes.

- **Lipid Lowering Agents such as statins**
  Statins appear to be beneficial in almost all people with diabetes and seem to be safe over the usual range of dosages used.
<table>
<thead>
<tr>
<th>Strategy</th>
<th>Complication</th>
<th>Reduction of Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid control</td>
<td>• Coronary heart disease mortality</td>
<td>↓ 36%¹</td>
</tr>
<tr>
<td></td>
<td>• Major coronary heart disease event</td>
<td>↓ 55%¹</td>
</tr>
<tr>
<td></td>
<td>• Any atherosclerotic event</td>
<td>↓ 37%¹</td>
</tr>
<tr>
<td></td>
<td>• Cerebrovascular disease event</td>
<td>↓ 62%¹</td>
</tr>
<tr>
<td>Blood Pressure Control</td>
<td>• Cardiovascular disease</td>
<td>↓ 51%²</td>
</tr>
<tr>
<td></td>
<td>• Heart failure</td>
<td>↓ 56%³</td>
</tr>
<tr>
<td></td>
<td>• Stroke</td>
<td>↓ 44%³</td>
</tr>
<tr>
<td></td>
<td>• Diabetes-related deaths</td>
<td>↓ 32%³</td>
</tr>
<tr>
<td>Blood Glucose Control</td>
<td>• Heart Attack</td>
<td>↓ 37%³</td>
</tr>
</tbody>
</table>

1 The 4S Study  
2 Hypertension Optimal Treatment (HOT) Randomised Trial  
3 UKPDS