Epidemiology and prevention of Diabetes Mellitus

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Preventive Medicine

- Prevention was defined by Last as:

"Actions aimed at eradicating, eliminating, or minimizing the impact of disease or disability, or if none of these is feasible, retarding the progress of disease and disability".

Definitions

- **Prevalence:** number of cases of particular condition present in a defined population at a specified time

- Incidence (rate): number of new cases of particular condition that occur in a population during a given time period

- **Cause:** Factor that is necessary or sufficient for the occurance of the disease

- (something that alters the frequency of the disease, health status, or associated factors in the population)

- **Risk factor:** an attribute or exposure that is associated with an increased probability of a specified outcome, such as the occurrence of a disease. Not necessarily a causal factor

Primary Prevention

aims to prevent the occurrence of the disease/health care problem. Vaccination programme during the first years of life against different infectious diseases such DtaP/IPV/HiB (Diphtheria, tetanus and Pertusis, polio and haemophilus influenzae type B) vaccines is the best example for this category.

Secondary prevention

- aims to detect disease or health care problem at early stages and to provide treatment, which cure the disease or prevent its progression. For example screening for breast and cervical cancers has reduced the incidence of invasive cervical and breast cancers and has decreased mortality and morbidity from these two diseases.

Tertiary prevention

- aims to improve the quality of life of the patients by decreasing disabilities and prevent further complications. For example tight control of blood pressure of diabetics has be shown as an effective steps to reduce the risk of diabetic microvascular and macrovascular complications.

Spectrum of health and disease with the main strategies for prevention at each level

Intervention strategies	Health	Stages		Outcomes		
		Asymptomatic	Symptomatic	Disability	Recovery	Death

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Levels of prevention	Primary $\longrightarrow$	Secondary and Quaternary	$\longrightarrow$	Tertiary
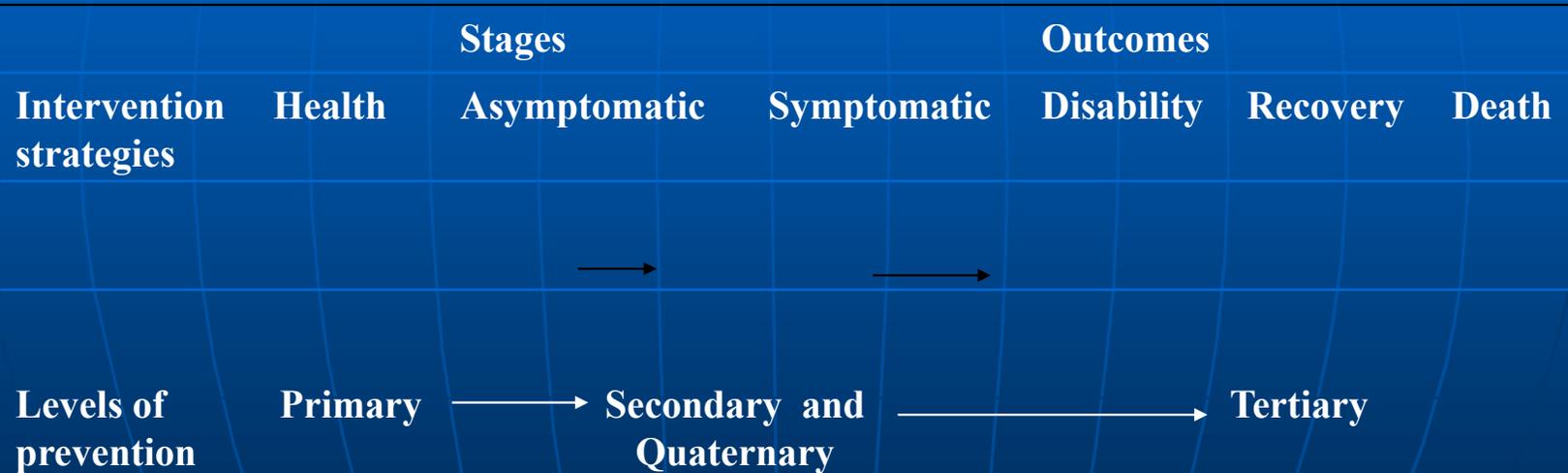
Diagnosis of diabetes mellitus (DM)

- World Health Organization criteria for the diagnosis of DM: fasting plasma glucose > or =7.8 mmol/ L (125mg/d;) or plasma glucose of > or =11.1 mmol/L (200mg/dl), 2 h after an oral anhydrous glucose load of 75 g)

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Prediabetes

- broadly refers to an intermediate stage between completely normal glucose levels and the clinical entity of type 2 diabetes.

- At this stage, fasting glucose, glucose tolerance test or glycated haemoglobin (HbA1c) will be impaired.

			Category
Definition of diabetes and prediabetes based on the American Diabetes Association guidelines for 2012			
Glycated haemoglobin	2 hour glucose (mg/dl)	Fasting glucose (mg/dl)	
<5.7%	<140	70 to 99	Normal
Prediabetes			
<6.4%	<140	100 to 125	Impaired fasting glucose (IFG)
<6.4%	140-199	<126	Impaired glucose tolerance (IGT)
5.7%-6.4%	<200	<126	Impaired glycated heamoglobin
≥6.5%	≥200	≥126	Diabetes*

*Any of the readings

Prediabetes

- Prediabetes is not only a significant risk factor for progression to type 2 diabetes but is also considered a risk factor for macrovascular diseases and for retinopathy

Criteria for Medical Screening: Presence of presymptomatic or early stage

- **Is there an evidence from a randomised controlled trial that an earlier intervention would work?**

- Detecting the disorder at this stage should help in getting better outcomes when compared with the situation without screening.

- Randomised controlled clinical trials could be needed to evaluate the impact of treatment on those detected from screening programmes as they could be different from those seeking medical attention for their conditions.

Trial	Design	Subjects	N; duration (years)	Control group	Active treatments	% change in diabetes risk
Principal diabetes prevention trials that evaluated metformin						
DPP (US) [19]	RCT	IGT and high–normal glucose	3234; 3	Placebo plus standard lifestyle advice	Metformin plus standard lifestyle advice	−31
					Intensive lifestyle intervention	−58
DPP Outcome Study (US) [69]	O	Epidemiological follow-up to DPP	2766; 5.7	Placebo plus intensive lifestyle advice	Metformin 1700 mg/day + intensive lifestyle advice	−13
					Intensive lifestyle advice	+5
IDPP (India) [20, 65]	RCT	IGT	531; 2.5	Standard lifestyle advice	Metformin plus standard lifestyle advice	−26
					Metformin plus intensive lifestyle intervention	−28
					Intensive lifestyle intervention	−29
Wenying et al. (China) [68]	NR	IGT	321; 3	Standard lifestyle advice	Metformin	−88
					Acarbose	−87
					Intensive lifestyle intervention	−43
Li et al. (China) [66]	RCT	IGT	70; 1	Placebo	Metformin	−66[a]
Iqbal Hydrie et al. (Pakistan) [67]	RCT	IGT	317; 1.5	Standard lifestyle advice	Metformin	−76.5
					Intensive lifestyle intervention	−71
CANOE (Canada) [64]	RCT	IGT	207; 3.9	Placebo	Metformin 500 mg plus rosiglitazone 2 mg twice daily	−66
Principal diabetes prevention trials that did not evaluate metformin						
Diabetes Prevention Study (Finland) [70]	RCT	IGT	522; 3.2	Standard lifestyle advice	Intensive, multifactorial lifestyle intervention	−58
Da Qing study (China) [71]	RBS	IGT	577; 6	Standard lifestyle advice	Diet, exercise, or both together	−31 to −46
STOP-NIDDM (International[b]) [72, 73]	RCT	IGT	1429; 3.3	Placebo	Acarbose	−25
XENDOS (Sween) [74]	RCT	IGT and obesity	694; 4[c]	Placebo	Orlistat	−45
DREAM (21 countries[d]) [75, 76]	RCT	IGT ± IFG	5269; 3	Placebo	Rosiglitazone	−62[e]
				Placebo	Ramipril	−9[f] (NS)
IDPP–2 (India) [77]	NR[f]	IGT	407; 3	Placebo + lifestyle intervention	Pioglitazone + lifestyle intervention	+8 (NS)
SOS study (Sweden) [78]	RCT	Obese, non-diabetic	3429; 10	No surgery[g]	Bariatric surgery	−83

Impaired glucose tolerance

- two-hour glucose levels of 140 to 199 mg per dL (7.8 to 11.0 mmol) on the 75-g <u>oral glucose tolerance test</u>.

- A patient is said to be under the condition of IGT when he/she has an intermediately raised <u>glucose</u> level after 2 hours, but less than would qualify for type 2 diabetes mellitus. The <u>fasting</u> glucose may be either normal or mildly elevated.

Impaired fasting glucose

- fasting blood glucose level is consistently elevated above what is considered normal levels; however, it is not high enough to be diagnosed as diabetes mellitus.

- This pre-diabetic state is associated with insulin resistance and increased risk of cardiovascular pathology, although of lesser risk than <u>impaired glucose tolerance</u> (IGT).

Impaired fasting glucose

- There is a 50% risk over 10 years of progressing to overt diabetes.

- A recent study cited the average time for progression as less than three years

Type I and Type II DM

	Type I	Type II
Age at onset	<25 years	>40 years
Genetics	<10% of first degree relatives are affected; 50% concordance in identical twins	>20% of first degree relatives affected; 90-100% concordance in identical twins.
HLA	Associated with HLA-DR3, HLA-DR4, HLA-DQ	None
Autoimmunity*	Increased prevalence of autoantibodies to islet cells and other tissues	None
Body build	Usually lean	Usually obese
Metabolism	Ketosis prone; insulin production is absent	Ketosis-resistant; insulin production is variable

Type I DM

- Rare causes
- Autoimmune polyendocrine syndrome type I (APS-I)
- X-linked polyendocrinopathy, immune dysfunction, and diarrhoea

Type I DM

- Seasonal variations in incidence has been observed (more in autumn and winter)
- Antibodies against other tissues:
- anti-thyroid and parietal cells antibodies
- other autoimmune disorders such as lupus erythematosus, rheumatoid arthritis, pernicious anaemia mellitus celiac disease , and Addison's disease

Type I DM

- The mechanism of damage is autoimmune, however other factors may be involved, including viruses and environmental factors:
- Viruses, e.g.mumps virus, coxsackie virus, cytomegalovirus, and hepatitis viruses
- Dietary factors: diets high in dairy products are associated with increased risk; possible risk in diets high in nitrosamines
- Environmental toxins
- Emotional and physical stress

type I diabetes mellitus risk factors

- **A family history.** Anyone with a parent or sibling with type 1 diabetes has a slightly increased risk of developing the condition.

- **Genetics.** The presence of certain genes indicates an increased risk of developing type 1 diabetes.

- **Geography.** The incidence of type 1 diabetes tends to increase as you travel away from the equator. People living in Finland and Sardinia have the highest incidence of type 1 diabetes — about two to three times higher than rates in the United States and 400 times that of people living in Venezuela.

Possible risk factors for type 1 diabetes

- **Viral exposure.** Exposure to Epstein-Barr virus, hepatitis viruses,coxsackievirus, mumps virus or cytomegalovirus may trigger the autoimmune destruction of the islet cells, or the virus may directly infect the islet cells.

- **Low vitamin D levels.** Research suggests that vitamin D may be protective against type 1 diabetes. **However, early drinking of cow's milk — a common source of vitamin D — has been linked to an increased risk of type 1 diabetes.**

- **Other dietary factors:**
  A. Omega-3 fatty acids may offer some protection against type 1 diabetes.
  B. Drinking water that contains nitrates may increase the risk.
  C. Additionally, the timing of the introduction of cereal into a baby's diet may affect his or her risk of type 1 diabetes. One clinical trial found that between ages 3 and 7 months appears to be the optimal time for introducing cereal

Type II diabetes Mellitus risk factors

• Age	• family history of type II DM,	• ethnicity (Asians, Hispanics, and blacks),
• obesity or being overweight	• sedentary lifestyle and poor dietary patterns (lack of physical activity, high-calorie, high-fat, high-carbohydrate and low fiber diet)	• impaired glucose tolerance or impaired fasting glucose
• history of gestational diabetes	• insulin resistance	• hypertension or high blood pressure (140/90 mm Hg or higher)
• low levels of HDL cholesterol (35 mg/dL) and high triglyceride	• history of polycystic ovary syndrome	• given birth to a baby weighing more than4.1kg (9 pounds)
• acanthosis nigricans	• history of vascular disease	• quantity and quality of sleep
• history of gallstones	• pancreatitis	• excessive alcohol use.

Type II diabetes risk factors

- **Family history.** The risk of type 2 diabetes increases if your parent or sibling has type 2 diabetes.

- **Race.** Although it's unclear why, people of certain races — including blacks, Hispanics, American Indians and Asian-Americans — are more likely to develop type 2 diabetes than whites are.

- **Age.** The risk of type 2 diabetes increases as you get older, especially after age 45. That's probably because people tend to exercise less, lose muscle mass and gain weight as they age. But type 2 diabetes is also increasing dramatically among children, adolescents and younger adults.

Type II diabetes risk factors

- **Weight.** Being overweight is a primary risk factor for type 2 diabetes. The more fatty tissue you have, the more resistant your cells become to insulin.

- **Fat distribution.** If your body stores fat primarily in your abdomen, your risk of type 2 diabetes is greater than if your body stores fat elsewhere, such as your hips and thighs.

- **Physical Inactivity.** The less active you are, the greater your risk of type 2 diabetes. Physical activity helps you control your weight, uses up glucose as energy and makes your cells more sensitive to insulin.

Type II DM genetics

- The strongest evidence supporting genetic factors in type 2 DM comes from twin studies which have shown almost complete concordance for type 2 DM in monozygotic twins

Genetics of type II DM

- Direct evidence for a genetic factor comes from identification of mutations in specific genes that result in a type 2 diabetic phenotype.

- There are several monogenic forms of MODY (Maturity Onset Diabetes in the Young) that have been described, resulting from point mutations in the glucokinase gene as well as in transcription factors involved primarily in beta-cell function65

Worldwide Statistics

- 6% of the world's population
- Type 2 diabetes affects approximately 8 percent of adults in the United States.

Global Incidence of type I DM
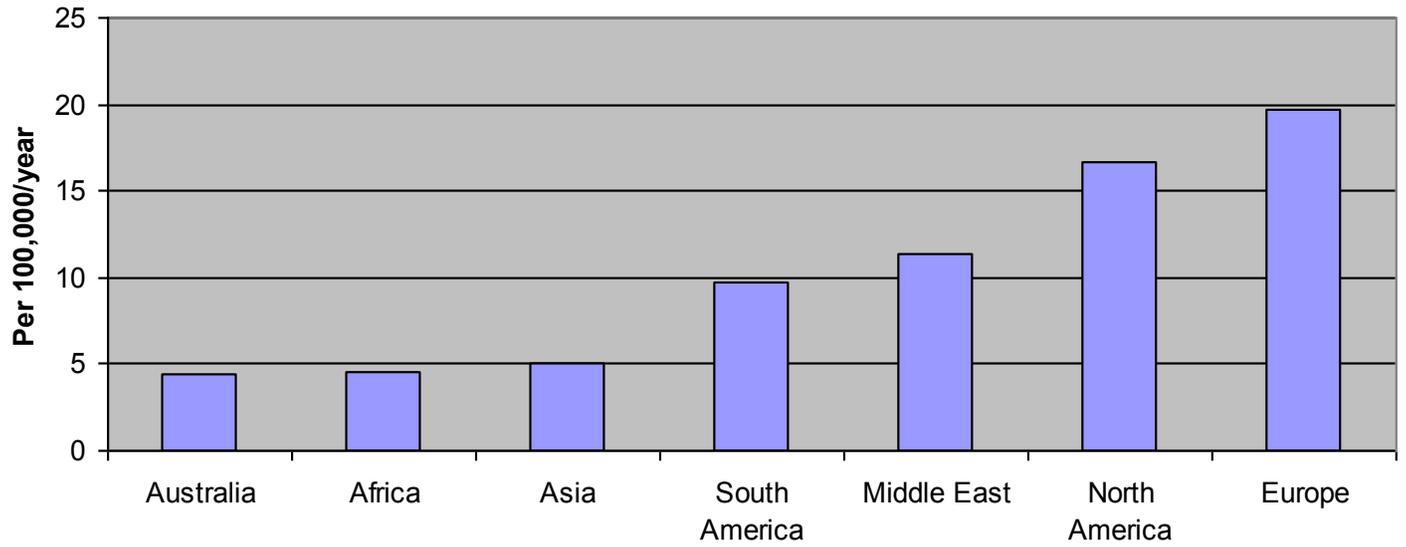
Global prevalence of type II DM
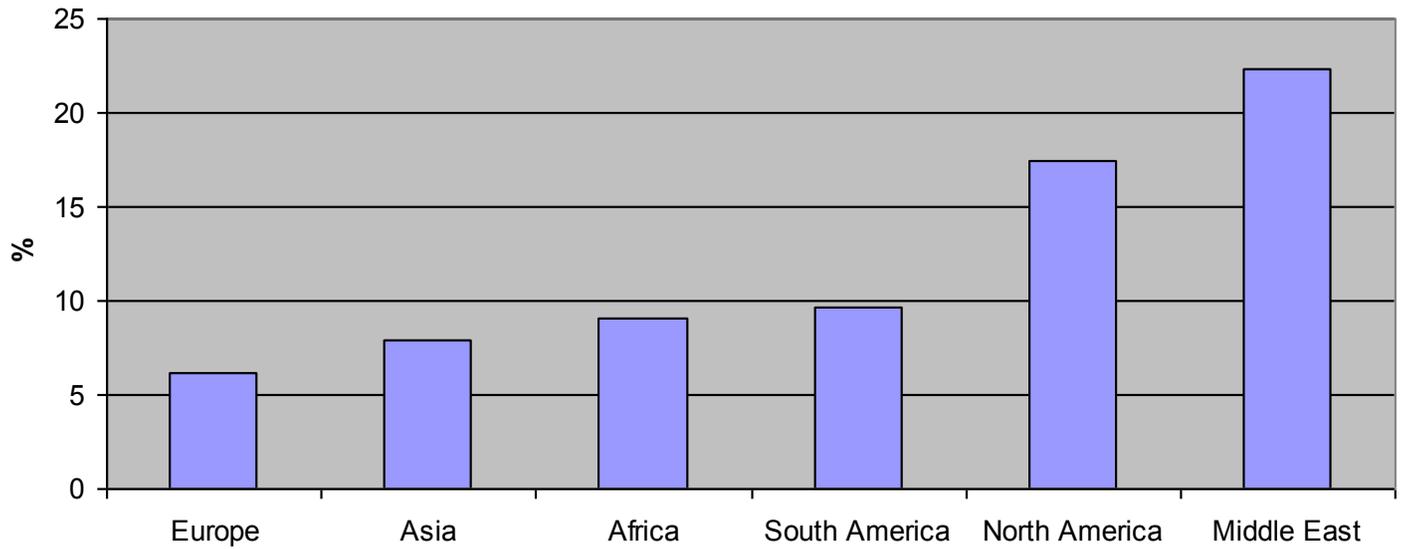
Worldwide Statistics

- Diabetes mellitus is highly prevalence in the Middle East.

- Six of the top ten countries in the world in the prevalence of this disease are located in this region (Kuwait, Lebanon, Qatar, Saudi Arabia, Bahrain, and United Arab Emirates).

Worldwide Statistics

- Several epidemiological studies were conducted in Saudi Arabia to assess the prevalence of type II diabetes and prediabetes.

- Al-Nozha and colleagues conducted a large study on prevalence of type II DM.

- 16917 adults aged 30-70 from representative regions of Saudi Arabia participated in this study.

- Results of this study showed an overall prevalence of type II DM of 23.7% and impaired fasting glycaemia of 14.1%.

Al-Nozha study

- Prevalence of newly diagnosed cases with type II DM or prediabetes was not specified in this study.
- This limits its use in the assessment of the value of screening for type II DM in Saudi Arabia.

- Another limitation of this study is that diagnosis of diabetes and prediabetes was based on fasting blood glucose tests only.

- Neither glycated haemoglobin nor glucose tolerance tests were conducted for study participants.

Statistics from Jordan

- This disease is also highly prevalent in other middle east countries mainly in Jordan. Two published studies assessed the prevalence of this disease in Jordan.

Prevalence of type II DM in Jordan

- The most recent study, published in 2008, by Ajlouni and colleagues, showed that for people older than 25, the overall prevalence of type II DM in Jordan is 17.1%(n=1121) and prevalence of impaired fasting glycaemia is 7.8%.

- The previous study, published in 1998 by Ajlouni and colleagues, showed a prevalence of 13.4% for type II DM and 9.8% for impaired glucose tolerance amongst people older than 25 (n=2836).

- Increase in age, increase in body mass index, and having a family history of diabetes were associated with increased odds of diabetes and IFG

Ajlouni and colleagues studies on prevalence of type II DM in Jordan, 1998 and 2008

- The main limitation of these two studies is that they were conducted in semiurban and rural areas and, therefore, are not representative of Jordan.

- The study published in 2008 was conducted in small semiurban town in the northern part of the country with a sample size of only 1121participants.

- Also choosing the age of 25 as reference age was not justified.

- Not based on new definitions of prediabetes

Incidence of type I DM in Jordan

- The incidence of type 1 diabetes mellitus in Jordanian children aged 0-14y was calculated as the number of cases per 100000 population, according to the national census of 1994.

- The incidence rate for these years (1992 through 1996) was 2.8, 2.9, 3.2, 3.6 and 3.6 per 100000 population, respectively. The male:female ratio was (1: 1.03).

- Seasonal variation at clinical onset was noticed, with maximum incidence in the winter months and minimum incidence in the summer months.
- the incidence of type 1 diabetes mellitus in Jordanian children aged 0-14y is among the lowest in the region, but is rising

Screening markers for type II DM

- The most sensitive screening marker for pre-diabetes and type II diabetes mellitus is a combination of fasting plasma glucose and glycated haemoglobin A1c.

- This combination has a sensitivity of 97% and 88% and specificity of 96% and 82% for detecting diabetes and pre-diabetes, respectively.

Presentations of DM

- Polyuria and polydipsia
- Weight loss
- Infections of skin vulva and urinary tract
- Blurring of vision (hyperglycaemic related osmotic alternations
- **Diabetic ketoacidosis: (DKA) (in type I):** hyperglycaemia, acidosis, dehydation. common causes: omission of insulin doses, infections, injuries, emotional stress, and intercurrent illnesses

Time of diagnosis

- Traditional form of clinical care involves awaiting until the development of symptoms and problems severe enough to lead the person with undiagnosed diabetes to present for the first time to clinical care with complications such as infections, organ failure, or even coma.

Preventive measures in type I DM

- Tight control of blood glucose and control of factors precipitating DKA
- Counselling
- Immune intervention at diagnosis of type 1 diabetes (T1D)

  aims to prevent or reverse the disease by blocking autoimmunity, thereby preserving/restoring beta-cell mass and function

- Mental and social factors

Type II DM

Chronic complications:

- Macrovascular disorders. Atherosclerosis leading to coronary, cerebrovascular or peripheral vascular disease

- Microvascular disorders: retinopathy, nephropathy and neuropathy and neuropathy
- 20% of new cases of adult blindness are caused by diabetes

Prevention of type II DM

- as obesity, physical inactivity and consumption of dietary fat, appear to contribute.

- **The ideal Body Mass Index (BMI) for patients with type II diabetes mellitus is 20-22.5**

- Some of these risk factors for the development of type 2 DM (obesity, physical inactivity, high-fat diet) can potentially be modified.

- In addition, some of the metabolic abnormalities that precede type 2 DM, such as insulin resistance or prediabetes an be improved by lifestyle changes and possibly drug treatment.

Prevention of diabetes mellitus

- Key step is the primary prevention through control of lifestyle
- The second most important step in prevention is the detection of cases at the prediabetes stage
- For secondary prevention: the key objectives are:
- Early detection and diagnosis
- Optimal glycemic control
- Control of symptoms
- Prevention of acute complications

Advice your patients on physical activities
Advice patients to be active a total of 30 minutes most days.
Always advise type II DM patients to exercise against resistance

Advice your patients to check their feet every day for cuts, blisters, sores, swelling, redness, or sore toenails.

Advice your patients to brush and floss their teeth regularly

Control their blood pressure and cholesterol.

- Advice them not to smoke.

Prevention of type II DM

- Encourages people with pre-diabetes to make lifestyle changes that could delay and possibly prevent the onset of the disease.

- By losing 5 to 7 percent of their body weight and getting 150 minutes of physical activity a week, people with pre-diabetes can cut their risk of developing type 2 diabetes by more than half.

Prevention of type II DM clinical trial

- **Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin.**

- 3234 nondiabetic persons with elevated fasting and post-load plasma glucose concentrations were randomly assigned to placebo, metformin (850 mg twice daily), or a lifestyle-modification program with the goals of at least a 7 percent weight loss and at least 150 minutes of physical activity per week.

Prevention of type II DM clinical trial

- The mean age of the participants was 51 years, and the mean body-mass index (the weight in kilograms divided by the square of the height in meters) was 34.0
- 68% were women

Prevention of type II DM clinical trial

- The incidence of diabetes was 11.0, 7.8, and 4.8 cases per 100 person-years in the placebo, metformin, and lifestyle groups, respectively.

- The lifestyle intervention reduced the incidence by 58% (95% confidence interval, 48 to 66%) and metformin by 31% (95% confidence interval, 17 to 43%), as compared with placebo

- The lifestyle intervention was significantly more effective than metformin.

Diabetes Prevention Trial

i.e. subjects with impaired glucose tolerance (IGT) or impaired fasting glucose (IFG). *Cumulative incidence of diabetes according to study group. The incidence of diabetes differed significantly among the three groups (p< 0.001 for each comparison).*
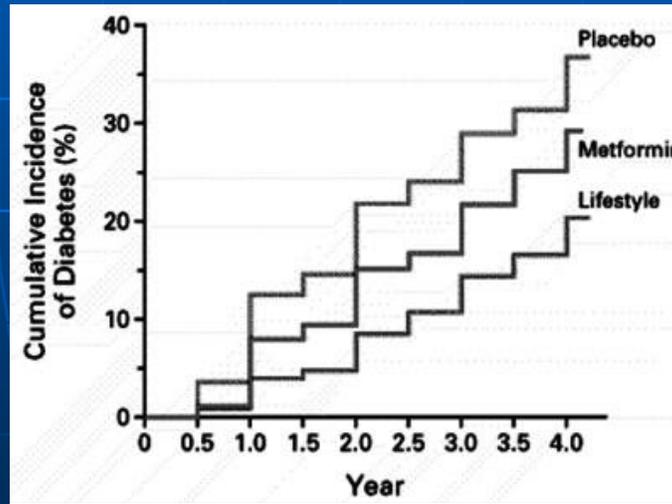
Diabetes Prevention Trial

Key two steps for prevention of type II diabetes amongst prediabetes patients:
Lifestyle modifications with focus on >10% body weight loss
Metformin SR750 starting with one tablet daily

Smoking and diabetes

- **Cigarette Smoking:** Several large prospective studies have raised the possibility that cigarette smoking increases the risk of type 2 DM.
- The relative risk of developing diabetes for individuals who smoked more than 20-25 cigarettes per day in these reports ranged from 1.4 to 3.6, compared to non-smokers.
- The risk appears to be graded, with increasing risk as the number of cigarettes smoked per day and pack-year history rises.

Gestational diabetes (GDM)

- Women who have had GDM have a 20 to 50 percent chance of developing diabetes in the next five to 10 years following pregnancy.
- The children of women with a history of GDM are at an increased risk for obesity and diabetes compared to other children.
- GDM occurs more frequently among obese women and women with a family history of diabetes
- If a lady gives birth to a baby weighing more than 9 pounds (4.1 kilograms), they are also at risk of type 2 diabetes.

Conclusion

- Type 2 diabetes is a major public health problem and the resultant enormous personal and social costs in terms of complications, patient quality of life and health care system resources are now widely recognised.
- The current system of reactive, acute episode focused disease care, practiced in most (if not all) countries, does not adequately address this public health problem.

- Without an adequate approach to the prevention of type 2 diabetes, the current type of curative medicine, by simply reducing or delaying mortality without preventing morbidity, is creating the predicted "global burden of type 2 diabetes"2.