T2DM MED 341 FEB 2016

AlMaatouq MA, MD

OBJECTIVES:

1. SCOPE OF DIABETES
2. MAKING THE DIAGNOSIS
3. PATHOPYSIOLOGY
4. DISEASE CONSEQUENCES
5. MANAGEMENT
6. CONCLUSION

The Top 10s
(prevalence %)

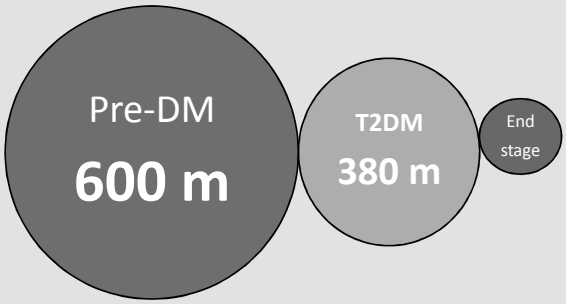
Table 2.1. Top 10 countries/territories for prevalence* (%) of diabetes (20-79 years), 2011 and 2030

	COUNTRY /TERRITORY	2011 PREVALENCE (%)		COUNTRY /TERRITORY	2030 PREVALENCE (%)
1	Kiribati	25.7	1	Kiribati	26.3
2	Marshall Islands	22.2	2	Marshall Islands	23.0
3	Kuwait	21.1	3	Kuwait	21.2
4	Nauru	20.7	4	Tuvalu	20.8
5	Lebanon	20.2	5	Nauru	20.7
6	Qatar	20.2	6	Saudi Arabia	20.6
7	Saudi Arabia	20.0	7	Lebanon	20.4
8	Bahrain	19.9	8	Qatar	20.4
9	Tuvalu	19.5	9	Bahrain	20.2
10	United Arab Emirates	19.2	10	United Arab Emirates	19.8

*comparative prevalence

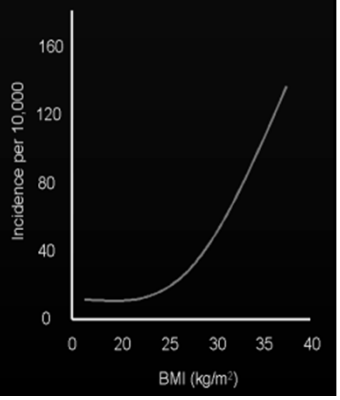
International Diabetes Federation

Global: T2DM 2030



Obesity and type 2 diabetes

- Elevated BMI (> 25) is associated with an increased risk for the development of Type 2 diabetes.
- Prevalence of Type 2 diabetes closely matches the prevalence of obesity.
- Elevated TNF-α levels may be partly responsible.



Obesity in Saudi Arabia

Mansour M. Al-Nozha, Yaqoub Y. Al-Mazrou, Mohammed A. Al-Maatouq, et al

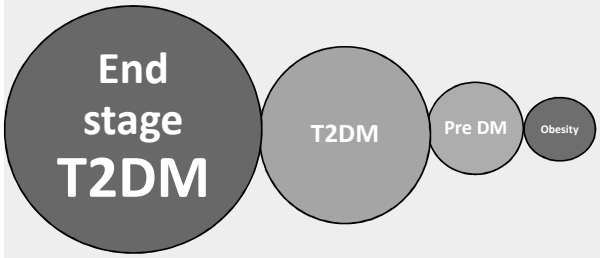
Methods: This study is a community-based national epidemiological health survey, conducted by examining Saudi subjects in the age group of 30-70 years of selected households over a 5-year period between 1995 and 2000 in KSA.

Results: Data were obtained by examining 17,232 Saudi subjects from selected households who participated in the study. The prevalence of **overweight was 36.9%.** Overweight is significantly more prevalent in males (42.4%) compared to 31.8% of females (p<0.0001). The age-adjusted **prevalence of obesity was 35.5%** in KSA with an overall prevalence of 35.6% [95% CI: 34.9-36.3], while severe (gross) obesity was 3.2%. Females are significantly more obese with a prevalence **of 44%** than males **26.4%** (p<0.0001).

Conclusion: Obesity and overweight are increasing in KSA with an overall obesity prevalence of **35.5%**.

Saudi Med J. 2007 Apr ;28 (4):559-68

Costs of T2DM 2030



Diabetes mellitus in Saudi Arabia

Al-Nozha MM, Al-Maatouq MA, Al-Mazrou YY, et al

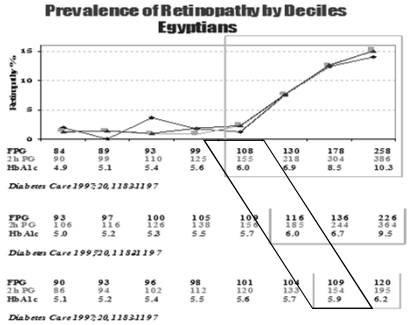
- OBJECTIVE: Diabetes mellitus (DM) is a major public health problem worldwide, and it is a known risk factor for coronary artery disease (CAD). New recommendations for the diagnosis of diabetes have changed the epidemiology of DM. Therefore, we designed this study with the objective to determine the prevalence of DM among Saudis of both sexes, between the ages of 30-70-years in rural as well as urban communities. This work is part of a major national project: Coronary Artery Disease in Saudis study (CADISS) that is designed to look at CAD and its risk factors in Saudi population.
- METHODS: This study is a community-based national epidemiological health survey, conducted by examining Saudi subjects in the age group of 30-70-years of selected households over a 5-year period between 1995 and 2000. Data were obtained from history, fasting plasma glucose levels, and body mass index. The data were analyzed to classify individuals as diabetic, impaired fasting glucose and normal, using 1997 American Diabetes Association (ADA) criteria, which was adopted by the World Health Organization (WHO) in 1998, to provide prevalence of DM in the Kingdom of Saudi Arabia (KSA).
- RESULTS: A total of 17232 Saudi subjects were selected in the study, and 16917 participated (98.2% response rate). Four thousand and four subjects (23.7%), out of 16917 were diagnosed to have DM. **Thus, the overall prevalence of DM obtained from this study is 23.7% in KSA**. The prevalence in **males and females were 26.2% and 21.5% (p<0.00001)**. The calculated age-adjusted prevalence for Saudi population for the year 2000 is 21.9%. Diabetes mellitus was more prevalent among Saudis living in **urban areas of 25.5% compared to rural Saudis of 19.5%** (p<0.00001). Despite the readily available access to healthcare facilities in KSA, a large number of diabetics 1116 **(27.9%) were unaware of having DM.**
- CONCLUSION: The overall prevalence of DM in adults in KSA is 23.7%. A national prevention program at community level targeting high risk groups should be implemented sooner to prevent DM. We further recommend a longitudinal study to demonstrate the importance of modifying risk factors for the development of DM and reducing its prevalence in KSA.

Saudi Med J. 2004 Nov;25(11):1603-10.

What is the GOLD standard for the Diagnosis of Diabetes?

Etiologic classification of diabetes mellitus

Impaired glucose tolerance IGT
Impaired fasting glucose IFG



Diagnostic criteria for T2DM

1.	8 hours fasting plasma glucose value ≥ 126 mg/dL (7 mmol/L)
	OR
2.	Polyuria, polydipsia, unexplained weight loss and random plasma glucose value ≥ 200 mg/dL (11.1 mmol/L)
	OR
3.	2 hour plasma glucose during a (75 g anhydrous glucose) OGTT ≥ 200 mg/dL (11.1 mmol/L)
	OR
4.	HbA1c ≥ 6.5 %

1, 3 & 4 to be confirmed by repeat testing on a different day if no unequivocal hyperglycemia

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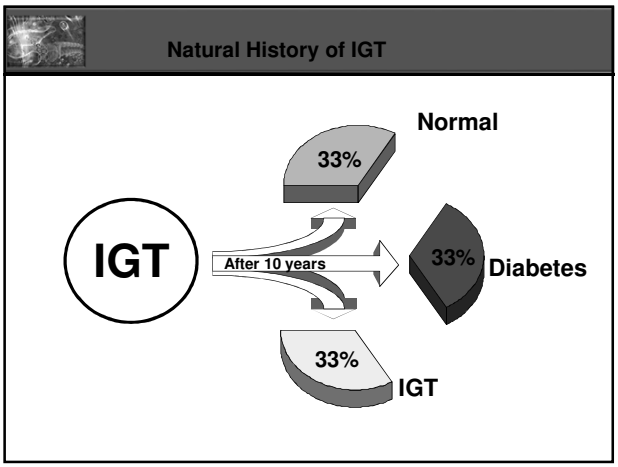
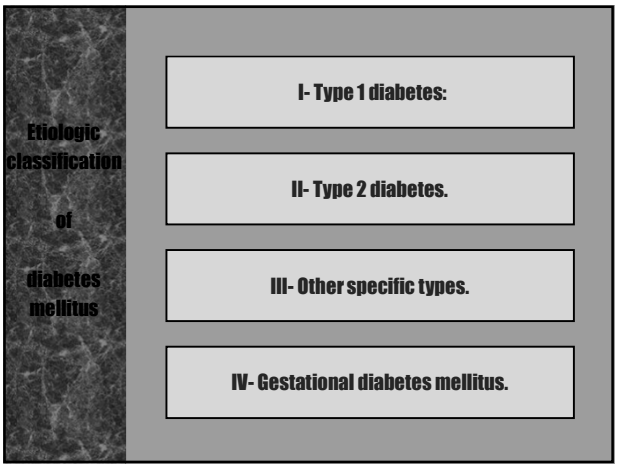
Etiologic classification of diabetes mellitus

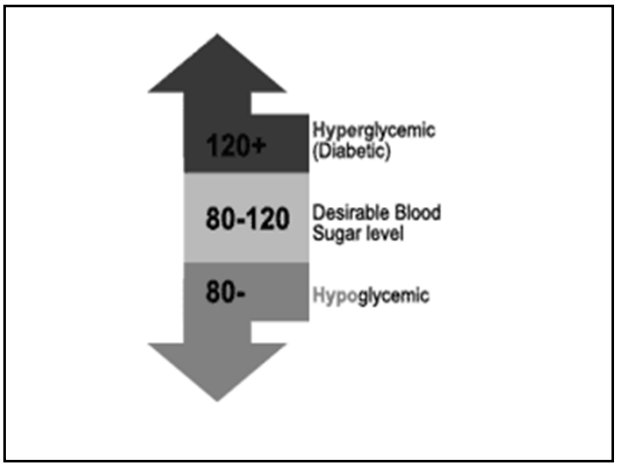
Impaired glucose tolerance IGT
Impaired fasting glucose IFG

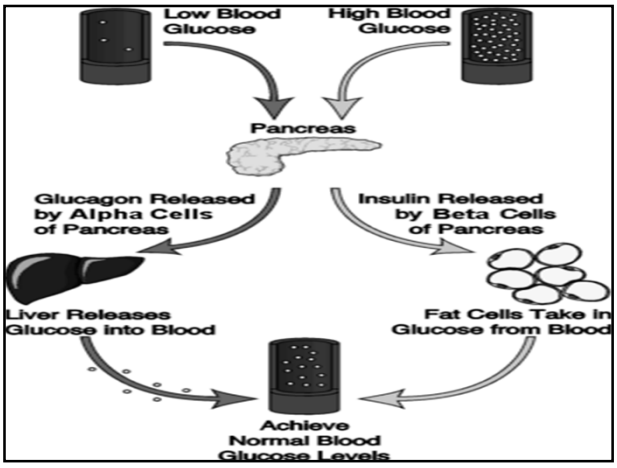
- They are known risk factors for future diabetes and cardiovascular disease.
- Intermediate stage for all types of diabetes.
- Associated with insulin resistance syndrome or :

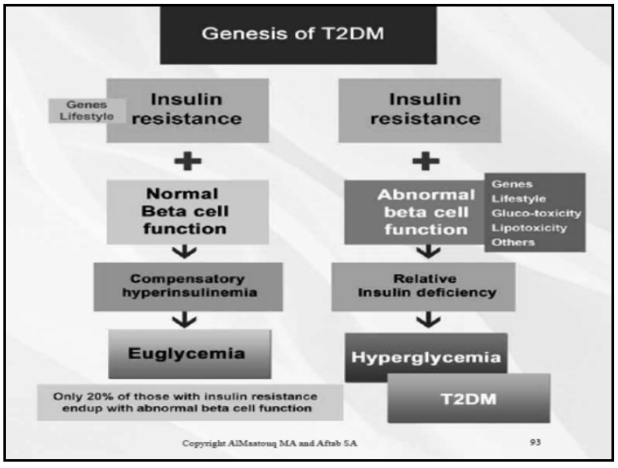
Syndrome X :
- Insulin resistance
- Hyperinsulinemia
- Obesity
- Dyslipidemia (high triglyceride and/or low HDL)
- Hypertension


Natural History of IGT
Normal
33%
IGT
After 10 years
33%
Diabetes
33%
IGT


Etiologic classification of diabetes mellitus
I- Type 1 diabetes:
II- Type 2 diabetes.
III- Other specific types.
IV- Gestational diabetes mellitus.


120+
Hyperglycemic (Diabetic)
80-120
Desirable Blood Sugar level
80-
Hypoglycemic


Low Blood Glucose
High Blood Glucose
Pancreas
Glucagon Released by Alpha Cells of Pancreas
Insulin Released by Beta Cells of Pancreas
Liver Releases Glucose into Blood
Fat Cells Take in Glucose from Blood
Achieve Normal Blood Glucose Levels


Genesis of T2DM
Genes
Lifestyle
Insulin resistance
Normal Beta cell function
Compensatory hyperinsulinemia
Euglycemia
Insulin resistance
Abnormal beta cell function
Genes
Lifestyle
Gluco-toxicity
Lipotoxicity
Others
Relative Insulin deficiency
Hyperglycemia
T2DM
Only 20% of those with insulin resistance endup with abnormal beta cell function
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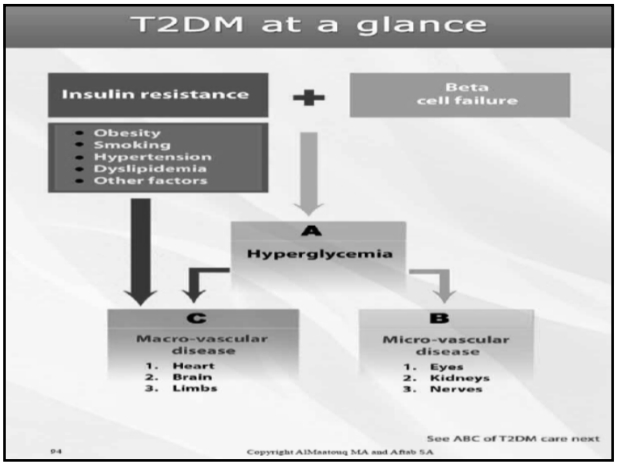
T2DM at a glance
Insulin resistance
Beta cell failure
Obesity
Smoking
Hypertension
Dyslipidemia
Other factors
A
Hyperglycemia
C
Macro-vascular disease
1. Heart
2. Brain
3. Limbs
B
Micro-vascular disease
1. Eyes
2. Kidneys
3. Nerves
See ABC of T2DM care next
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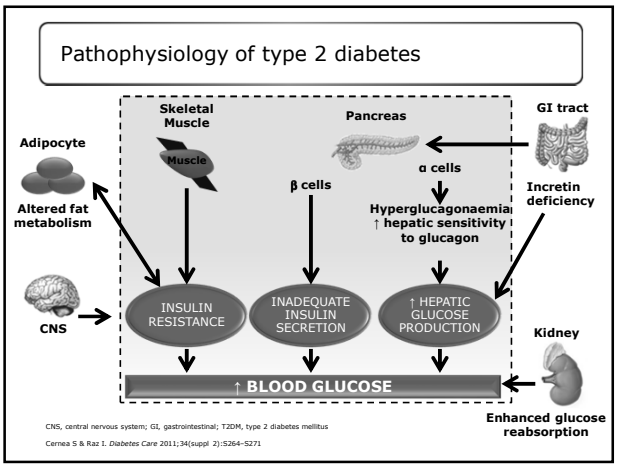
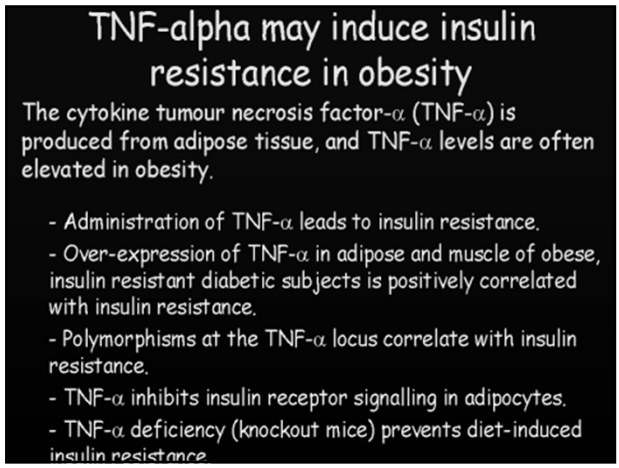
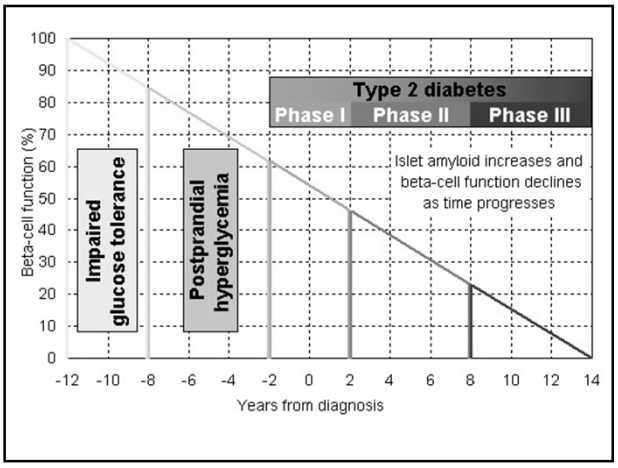
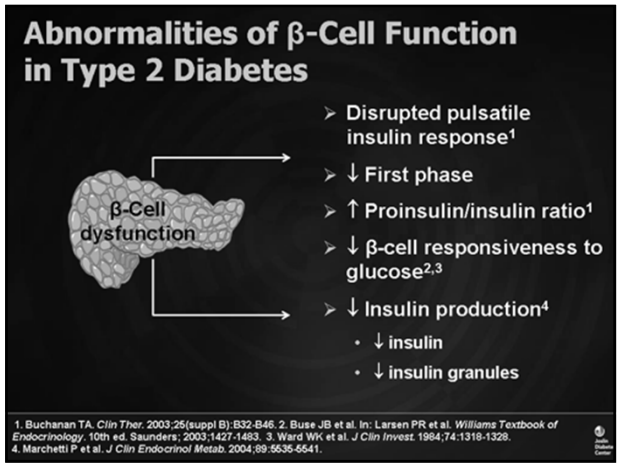
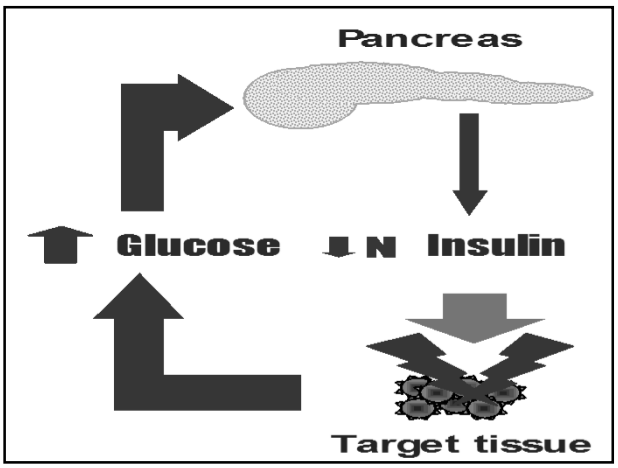
Copyright AlMaatouq MA and Alfaki SA











UKPDS: Complications at diagnosis

Microvascular disease	**Retinopathy**	**21 %**
Peripheral neuropathy	**Impotence**	**66 %***
	Impaired reflexes	**49 %**
	Reduced vibration	**51 %**
Hypertension		**65 %**
Macrovascular disease	**Stroke/TIA**	**38 %**
	Myocardial infarction	**34 %**
	Abnormal ECG	**33 %**
Peripheral vascular disease	**Absent foot pulses**	**45 %**
	Intermittent claudication	**37 %**
	Ischermic skin changes	**46 %**

* male

UKPDS Group. *Diabetes Res* 1990, 13: 1-11.

Patients with type 2 diabetes are at heightened risk of disabling complications versus non-diabetics

Complication	Relative Risk*
Blindness	20
End-stage renal disease	25
Amputation	40
Myocardial Infarction	2-5
Stroke	2-3
Lifespan	6 years

* Diabetics versus non-diabetics

Ryden L. Eur Heart J. 2007; 28: 88-136

Burden of Type 2 Diabetes

15 Years Follow-up

Complications

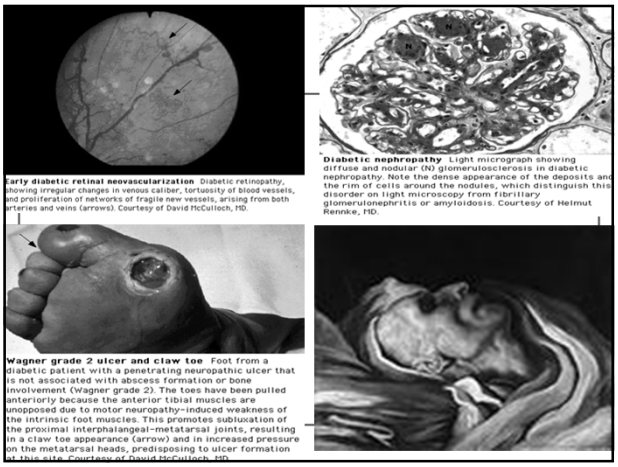
Heart attacks	27 patients
Stroke	10 patients
Retinopathy	23 patients

Premature Mortality

Diabetes deaths	28 patients
Life expectancy	5-7 years ↓

100 Patients - Age 55

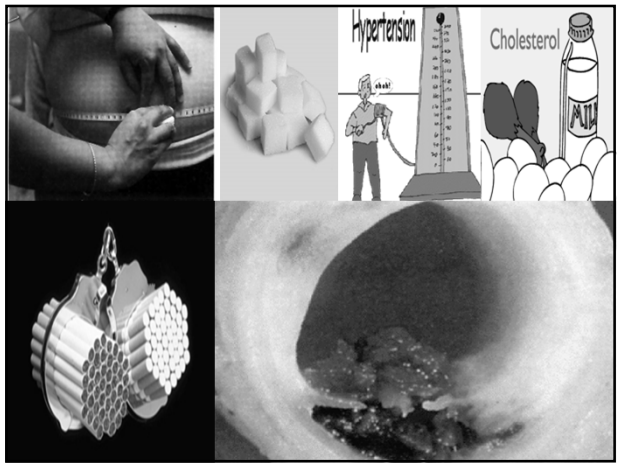
UKPDS 33. Lancet 1998; 352: 837-53

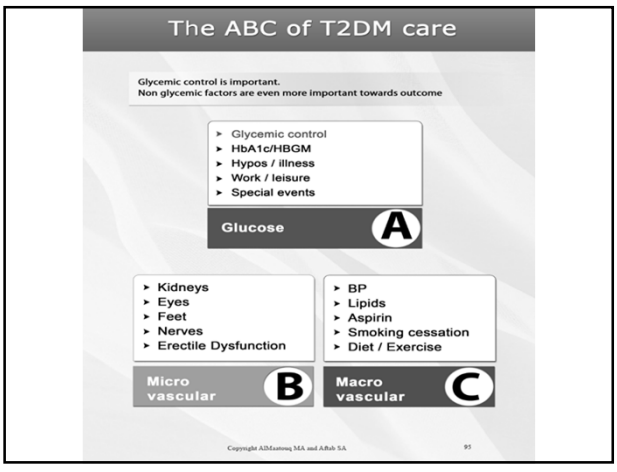


Early diabetic retinal neovascularization Diabetic retinopathy, showing irregular changes in venous caliber, tortuosity of blood vessels, and proliferation of networks of fragile new vessels, arising from both arteries and veins (arrows). Courtesy of David McCulloch, MD.

Diabetic nephropathy Light micrograph showing diffuse and nodular (N) glomerulosclerosis in diabetic nephropathy. Note the dense appearance of the deposits and the rim of cells around the nodules, which distinguish this disorder on light microscopy from fibrillary glomerulonephritis or amyloidosis. Courtesy of Helmut Rennke, MD.

Wagner grade 2 ulcer and claw toe Foot from a diabetic patient with a penetrating neuropathic ulcer that is not associated with abscess formation or bone involvement (Wagner grade 2). The toes have been pulled anteriorly because the anterior tibial muscles are unopposed due to motor neuropathy–induced weakness of the intrinsic foot muscles. This promotes subluxation of the proximal interphalangeal–metatarsal joints, resulting in a claw toe appearance (arrow) and in increased pressure on the metatarsal heads, predisposing to ulcer formation at this site. Courtesy of David McCulloch, MD.





Lessons from UKPDS: Better control means fewer complications

EVERY 1% reduction in HBA_{1C}

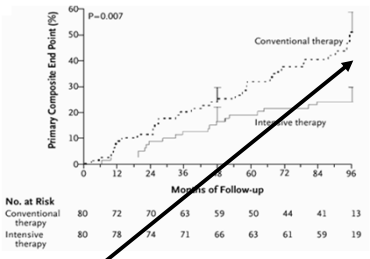
	REDUCED RISK*
Deaths from diabetes	-21%
Heart attacks	-14%
Microvascular complications	-37%
Peripheral vascular disorders	-43%

1%

*p<0.0001

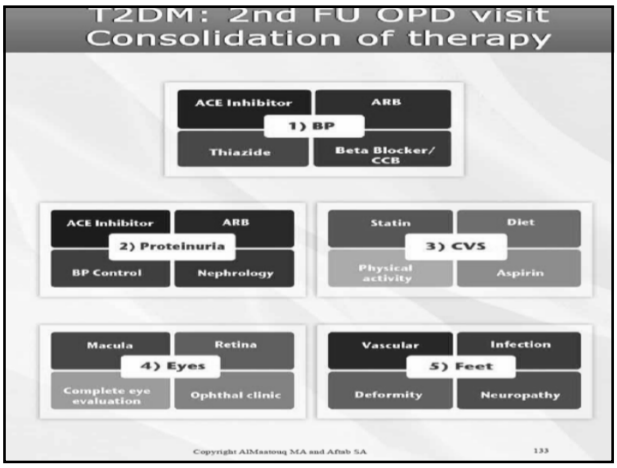
UKPDS 35. BMJ 2000; 321: 405-12

Benefits of intervention to reduce multiple risk factors – Danish Steno 2 Study



53% Risk Reduction with Intensive Therapy

Gaede P et al. NEJM 2003; 348: 383-393
Gaede P et al. NEJM 2008; 358: 580-591



Efficacy of Treatment

	Macrovascular	Microvascular
Glycemia	+	+++
BP	+++	++
Lipids	+++	++

- Multifactorial Treatment
- Lower LIMITS set by the trials (this cohort)

Ages and Stages

Lessons from major trials

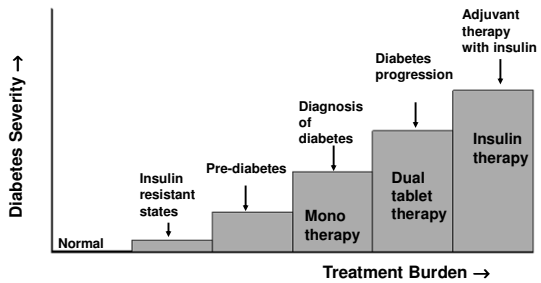
1. DM complications are present at diagnosis
2. DM complications progress with time
3. DM control predicts rate and state of complications
4. Early and sustained control limits complications
5. Management is multifaceted and complex
6. Majority of patients are NOT at target

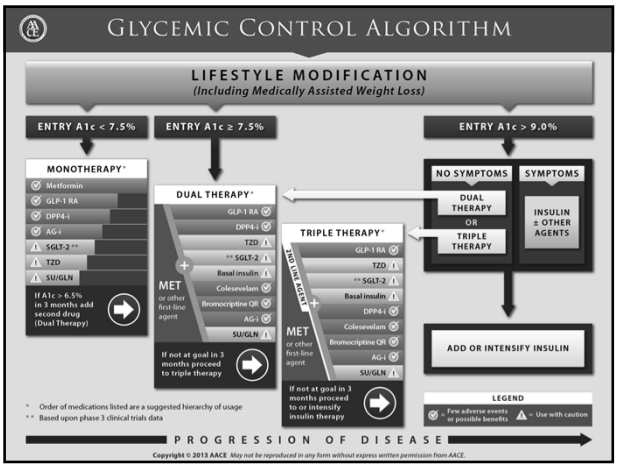
Guidelines need to address all concerns

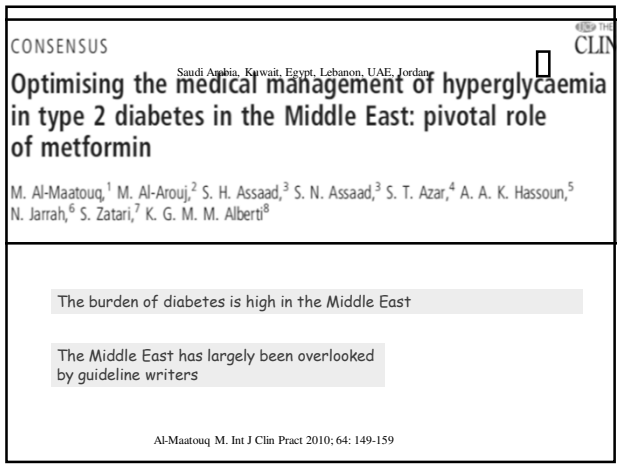
Targets

1. HgbA1c: 7% Early Young No AT
2. HgbA1c: 8% Late Old W AT

Progressive nature of diabetes means stepwise increase in therapies to achieve optimal outcomes in management






CONSENSUS

Optimising the medical management of hyperglycaemia in type 2 diabetes in the Middle East: pivotal role of metformin

Saudi Arabia, Kuwait, Egypt, Lebanon, UAE, Jordan

M. Al-Maatouq,[1] M. Al-Arouj,[2] S. H. Assaad,[3] S. N. Assaad,[3] S. T. Azar,[4] A. A. K. Hassoun,[5] N. Jarrah,[6] S. Zatari,[7] K. G. M. M. Alberti[8]

The burden of diabetes is high in the Middle East

The Middle East has largely been overlooked by guideline writers

Al-Maatouq M. Int J Clin Pract 2010; 64: 149-159

Practical dietary advice

1. Salad: 1hour BEFORE the meal

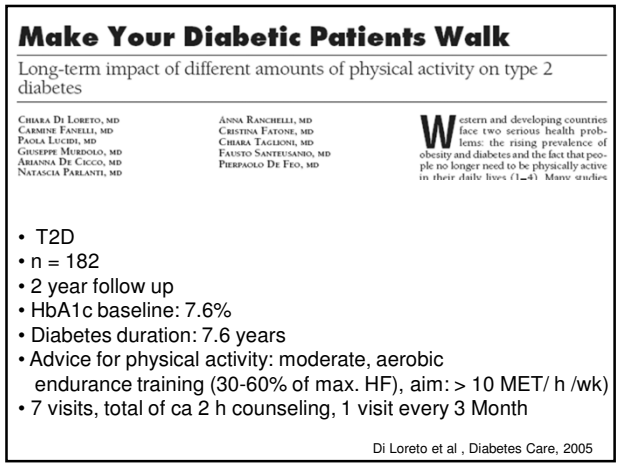
2. ¼ - ½ what you are used to. No cheating.

3. 1 Fruit per meal (juice is fruit)

4. 2 DATES BID (1 extra date BID)

5. No Communal eating

6. Avoid what you can live without.


Make Your Diabetic Patients Walk

Long-term impact of different amounts of physical activity on type 2 diabetes

Chiara Di Loreto, MD
Carmine Fanelli, MD
Paola Lucidi, MD
Giuseppe Murdolo, MD
Arianna De Cicco, MD
Natascia Parlanti, MD

Anna Ranchelli, MD
Cristina Fatone, MD
Chiara Taglioni, MD
Fausto Santeusanio, MD
Pierpaolo De Feo, MD

Western and developing countries face two serious health problems: the rising prevalence of obesity and diabetes and the fact that people no longer need to be physically active in their daily lives (1–4). Many studies

- T2D
- n = 182
- 2 year follow up
- HbA1c baseline: 7.6%
- Diabetes duration: 7.6 years
- Advice for physical activity: moderate, aerobic endurance training (30-60% of max. HF), aim: > 10 MET/ h /wk)
- 7 visits, total of ca 2 h counseling, 1 visit every 3 Month

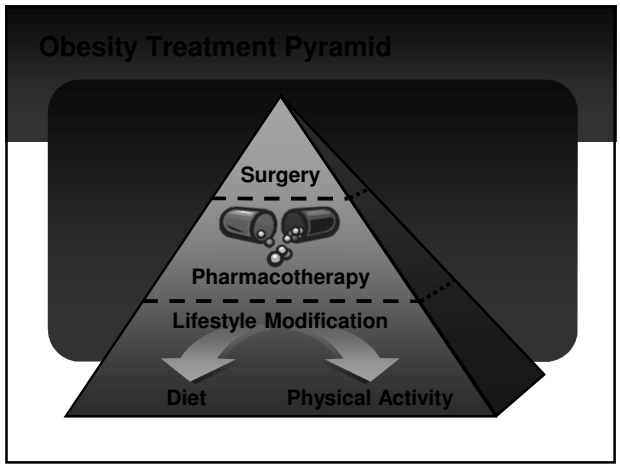
Di Loreto et al , Diabetes Care, 2005

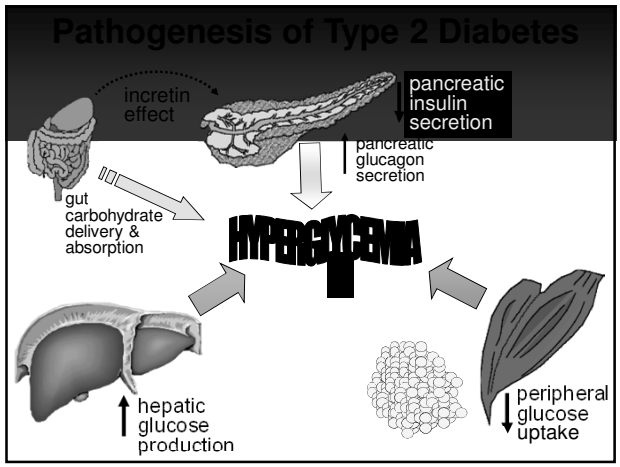
Effects of physical activity in T2DM

	Walking / Hours / Week*					
	0	1,5	4	5,5*	7,5	12
Weight (kg)	+ 0,8	+ 0,6	+ 0,1	- 2,2	-3,0	-3,2
Waist (cm)	+ 1,0	+ 1,0	- 0,9	- 3,8	- 5,5	- 7,1
HbA_{1c} (%)	+ 0,03	- 0,06	- 0,44	- 0,8	- 1,11	- 1,19
BD syst. (mmHg)	- 1,8	- 1,5	- 6,4	- 5,5	- 6,6	- 9,2
BD diast. (mmHg)	- 4,6	- 2,4	- 2,9	- 4,8	- 5,3	- 7,1
Chol. (mg/dl)	- 3,8	- 5,6	- 10,2	- 10,7	- 7,4	- 10,9
LDL-Chol. (mg/dl)	- 4,5	- 7,1	- 3,4	- 5,3	- 6,3	- 7,1

* e.g. 21-30 MET: 45 min walking (4 mph) /day, ca. 5 km/day) p <0,05

Di Loreto C. et al. Diabetes Care (2005)28:1295-1302





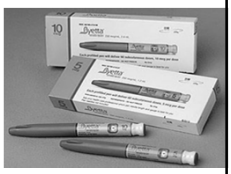
Dipeptidyl Peptidase 4 inhibitors

- Sitgliptin: Januvia
- Vildagliptin: Galvus
- Saxagliptin: Onglyza

Incretin Mimetics = GLP-1 Analougues

Exenatide:

- Twice daily
- 2 doses: 5 mcg -10 mcg
- Weight reduction



Liraglutide:

- is a once daily
- 3 doses: 0.6, 1.2, 1.8 mg
- HbA1c 0.8-1.8
- Weight reduction, Less nausea

The 'Puzzle' of Setting Glycemic Goals in T2DM