Prediabetes :Diagnosis and Management

Prof. Dr. Md. Ismail Patwary

FCPS,FACP,MD,FRCP(Glasgow, Edinburgh)
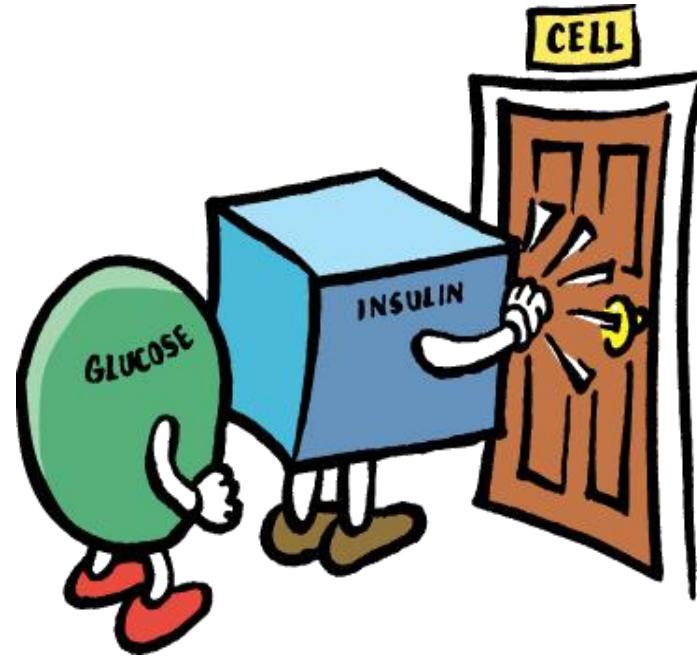
Professor , Department of Medicine
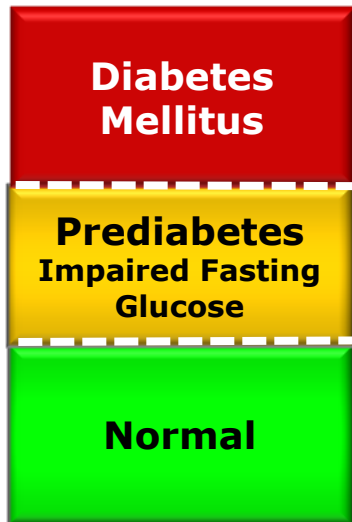
Sylhet Women's Medical College

Sylhet

Prediabetes

- Prediabetes is a condition when plasma glucose level is higher than normal but not high enough for a diagnosis of diabetes.
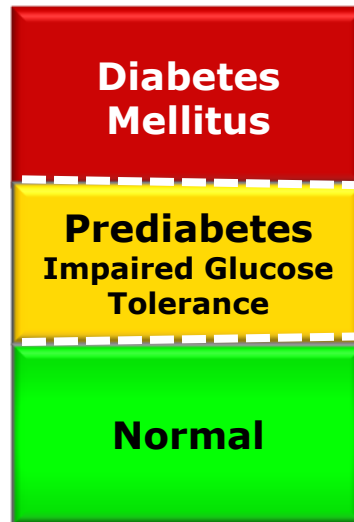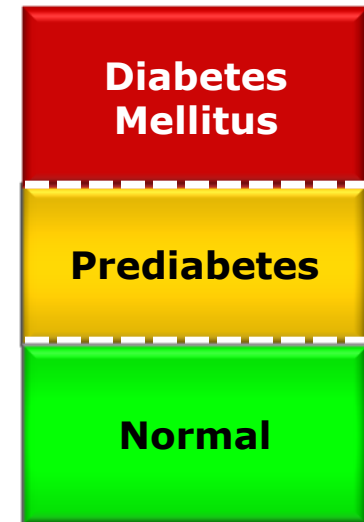
What is Prediabetes?

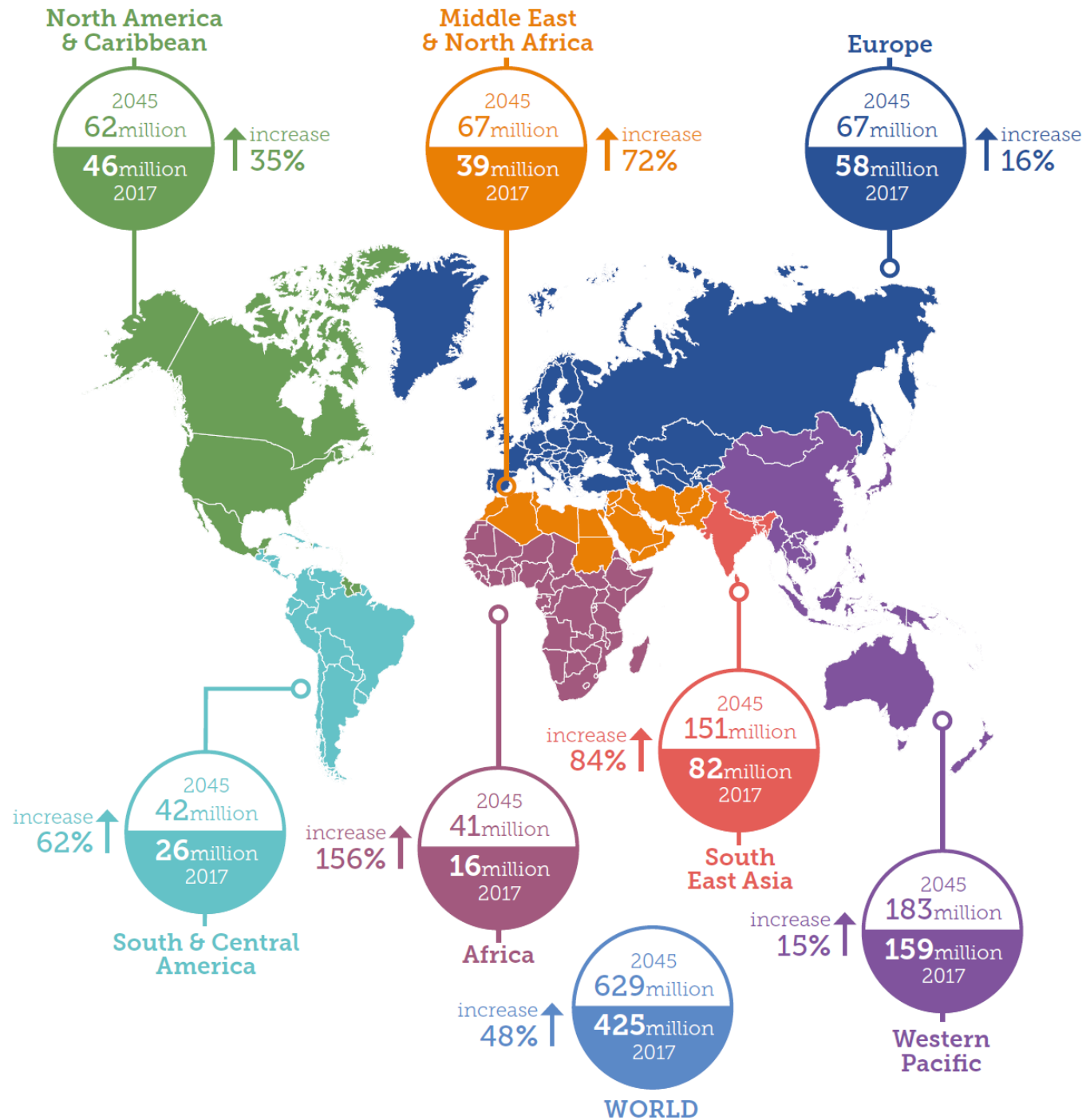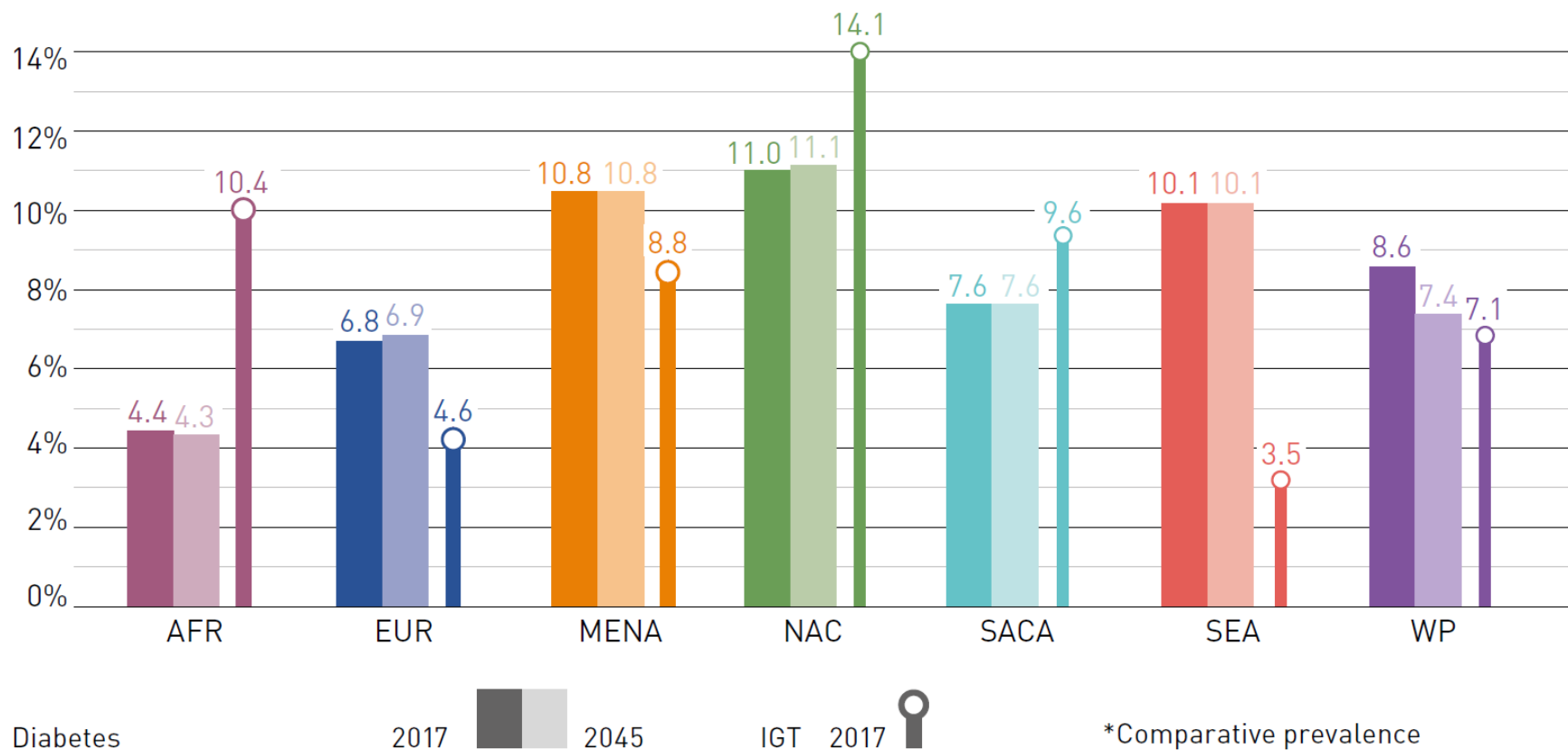| Fasting Plasma Glucose		2-hour Plasma Glucose On OGTT		Hemoglobin A1C	
Diabetes Mellitus		**Diabetes Mellitus**		**Diabetes Mellitus**	
	126 mg/dL		200 mg/dL		6.5%
Prediabetes Impaired Fasting Glucose		**Prediabetes** Impaired Glucose Tolerance		**Prediabetes**	
	100 mg/dL		140 mg/dL		5.7%
Normal		**Normal**		**Normal**	

Any abnormality must be repeated and confirmed on a separate day

The diagnosis of diabetes can also be made based on unequivocal symptoms and a random glucose >200 mg/dL

Adapted from:
American Diabetes Association. *Diabetes Care.* 2014;37 Suppl 1:S81-90.

North America & Caribbean
2045
62 million
46 million
2017
increase 35%

Middle East & North Africa
2045
67 million
39 million
2017
increase 72%

Europe
2045
67 million
58 million
2017
increase 16%

South & Central America
2045
42 million
26 million
2017
increase 62%

Africa
2045
41 million
16 million
2017
increase 156%

South East Asia
2045
151 million
82 million
2017
increase 84%

Western Pacific
2045
183 million
159 million
2017
increase 15%

WORLD
2045
629 million
425 million
2017
increase 48%

Prevalence* of diabetes and IGT (20-79 years) by IDF Region, 2017 and 2045

	AFR	EUR	MENA	NAC	SACA	SEA	WP
Diabetes 2017	4.4	6.8	10.8	11.0	7.6	10.1	8.6
Diabetes 2045	4.3	6.9	10.8	11.1	7.6	10.1	7.4
IGT 2017	10.4	4.6	8.8	14.1	9.6	3.5	7.1

Diabetes   2017   2045   IGT   2017   *Comparative prevalence

At a glance	2017	2045
Total world population	7.5 billion	9.5 billion
Adult population (20-79 years)	4.84 billion	6.37 billion
Diabetes global estimates		
Prevalence (20-79 years)	8.8% (7.2-11.3%)	9.9% (7.5-12.7%)
Number of people with diabetes (20-79 years)	424.9 million (346.4-545.4 million)	628.6 million (477.0-808.7 million)
Number of deaths due to diabetes (20-79 years)	4.0 (3.2-5.0) million	-
Total Healthcare Expenditures for Diabetes (20-79 years), R=2* 2017 USD	USD 727 billion	USD 776 billion
Hyperglycaemia in pregnancy (20-49 years)		
Proportion of live births affected	16.2%	-
Number of live births affected	21.3 million	-
Impaired glucose tolerance (IGT) Estimates		
Global prevalence (20-79 years)	7.3% (4.8-11.9%)	8.3% (5.6%-13.9%)
Number of people with IGT (20-79 years)	352.1 million (233.5 -577.3 million)	531.6 million (353.8-883.9 million)
Type 1 diabetes (0-19 years)		
Number of children and adolescents with type 1 diabetes	1,106,500	-
Number of newly diagnosed cases each year	132,600	-

*Healthcare expenditures for people with diabetes are assumed to be on average two-fold higher than people without diabetes.

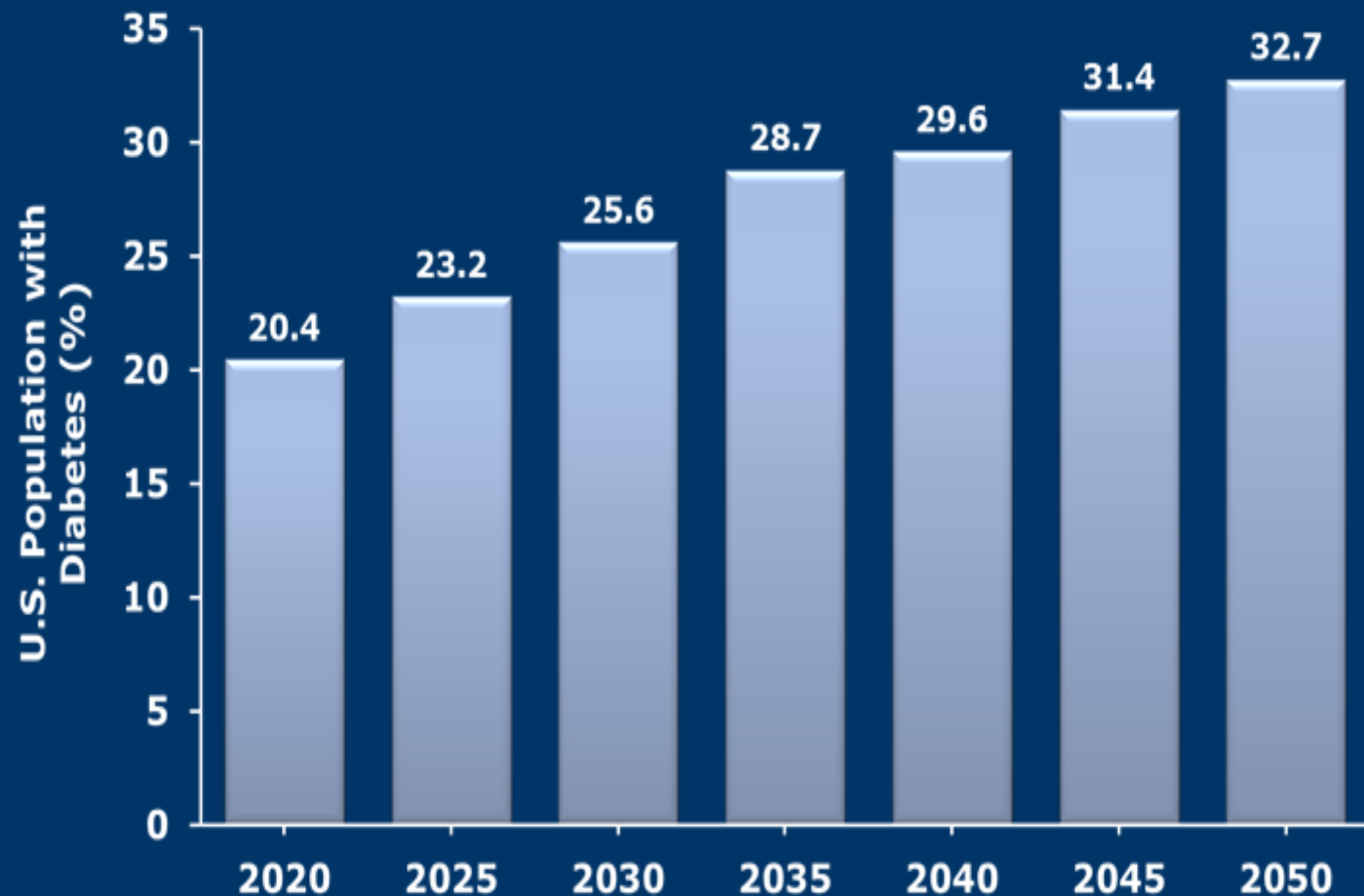# Projecting the Future Diabetes Population: It Is Growing

Bar chart titled "U.S. Population with Diabetes (%)" showing projected values:
- 2020: 20.4
- 2025: 23.2
- 2030: 25.6
- 2035: 28.7
- 2040: 29.6
- 2045: 31.4
- 2050: 32.7

Adapted from:
Boyle JP, et al. *Popul Health Metr*. 2010;8:1-12.

Table 3.9 Top ten countries/territories for the number of people with impaired glucose tolerance (20-79 years), 2017 and 2045

| 2017			2045		
Rank	Country/territory	Number of people with IGT	Rank	Country/ territory	Number of people with IGT
1	China	48.6 million (24.9-110.7)	1	China	59.9 million (29.8-136.1)
2	United States	36.8 million (31.4-42.4)	2	United States	43.2 million (35.6-49.0)
3	Indonesia	27.7 million (14.7-29.9)	3	India	41.0 million (31.1-78.6)
4	India	24.0 million (18.3-48.4)	4	Indonesia	35.6 million (22.7-37.6)
5	Brazil*	14.6 million (10.5-19.4)	5	Brazil*	20.7 million (15.7-27.0)
6	Mexico*	12.1 million (10.3-13.9)	6	Mexico*	20.6 million (17.0-23.3)
7	Japan	12.0 million (10.3-15.2)	7	Nigeria*	17.9 million (7.1-42.0)
8	Pakistan	8.3 million (4.1-11.8)	8	Pakistan	16.7 million (8.7-23.6)
9	Thailand*	8.2 million (6.8-10.3)	9	Ethiopia*	14.1 million (11.1-30.1)
10	Nigeria*	7.7 million (2.6-17.4)	10	Japan	10.3 million (8.9-13.0)

*Data was extrapolated from similar countries.
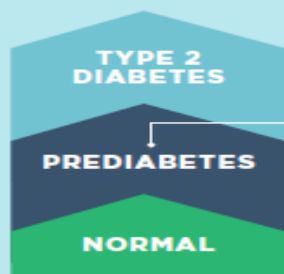
PREDIABETES

84.1 MILLION

84.1 million American adults — more than 1 out of 3 — have prediabetes

1 OUT OF 3
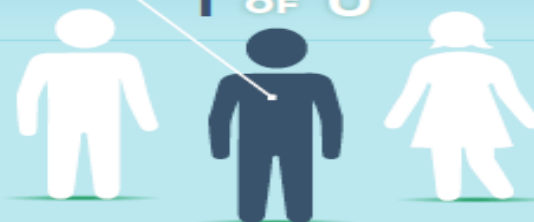
9 OUT OF 10 people with prediabetes don't know they have it

TYPE 2 DIABETES

PREDIABETES

NORMAL

Prediabetes is when your blood sugar level is higher than normal but not high enough yet to be diagnosed as type 2 diabetes

Prediabetes increases your risk of:

TYPE 2 DIABETES

HEART DISEASE

STROKE

If you have prediabetes, losing weight by:

EATING HEALTHY & **BEING MORE ACTIVE**

can cut your risk of getting type 2 diabetes in **HALF**

Ignore prediabetes and type 2 diabetes risk goes up — and so does risk for serious health complications:

BLINDNESS

KIDNEY FAILURE

HEART DISEASE

STROKE

LOSS OF TOES, FEET, OR LEGS

YOU CAN PREVENT TYPE 2 DIABETES

FIND OUT IF YOU HAVE PREDIABETES —
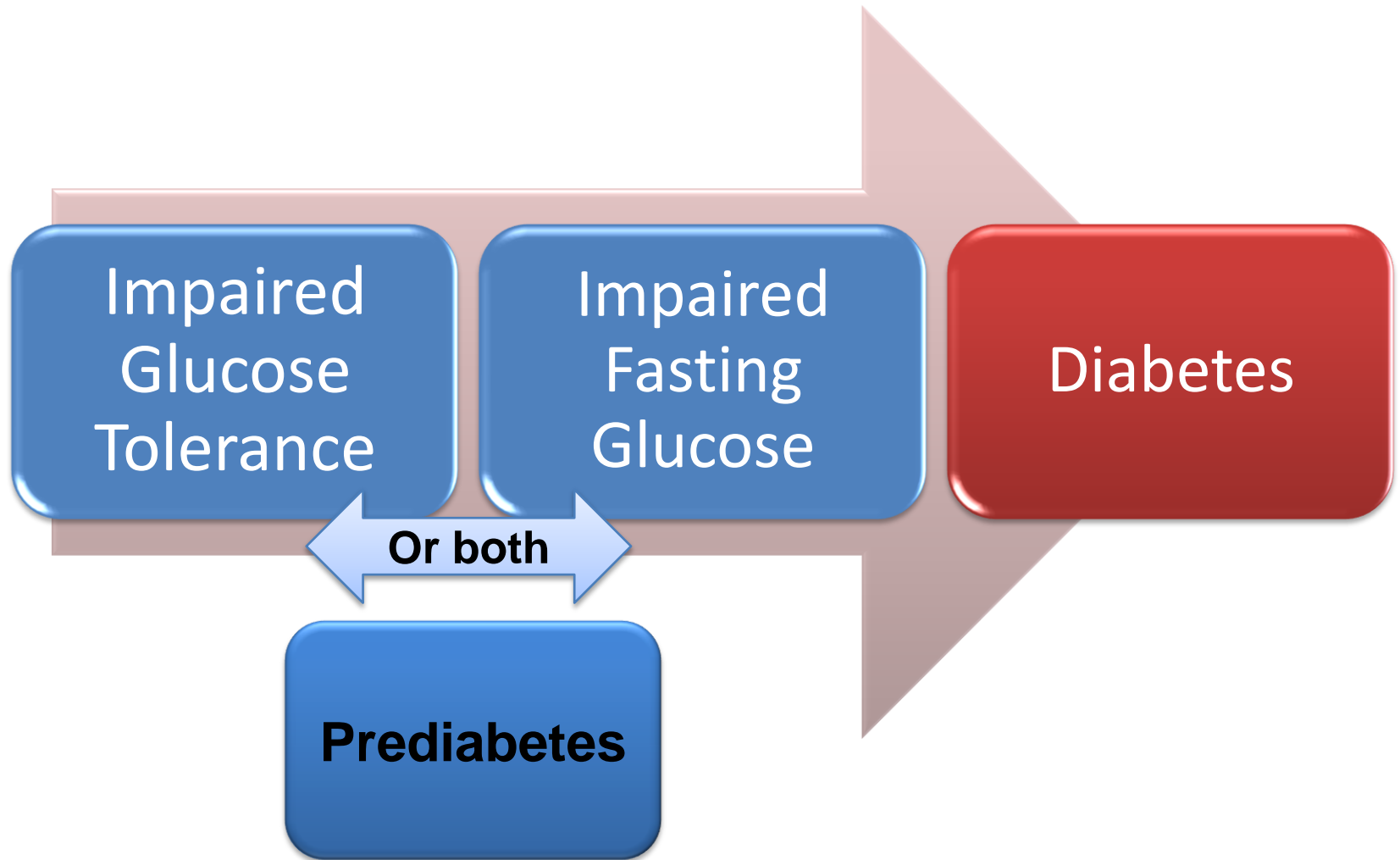See your doctor to get your blood sugar tested

✔ eat healthy
✔ be more active
✔ lose weight

JOIN A CDC-RECOGNIZED
diabetes prevention program

Progression to Type 2 Diabetes

Impaired Glucose Tolerance

Impaired Fasting Glucose

Or both

Diabetes

Prediabetes

Etiology

- Prediabetes is a state of abnormal glucose homeostasis characterized by the presence of IFG, IGT, or both. This abnormal glucose homeostasis is a result of either or both beta-cell failure and insulin resistance.

- Environmental factors such as a sedentary lifestyle and a high-fat diet can exacerbate defects in both insulin secretion from pancreatic beta-cells and insulin action in muscle and adipose tissues.

Diabetes …

Body lacks insulin or is unable to use insulin effectively

Pancreas

Cannot produce enough insulin

Muscle and fat cells

Cannot use insulin effectively

Pathophysiology

- IFG and IGT represent the transitional states of abnormal glucose regulation that occur between normal glucose homeostasis and T2D .

- Both muscular and hepatic insulin resistance are present in IFG and/or IGT.

- In isolated IFG there is hepatic insulin resistance and normal muscle insulin sensitivity, while in isolated IGT there is normal to slightly decreased hepatic insulin sensitivity and moderate to severe muscle insulin resistance.

- Isolated IFG is associated with decreased early phase (first 30 min) insulin response to oral glucose, and normal late-phase insulin response.

- In IGT, it is associated with mild decrease in early phase insulin response to oral glucose but severe deficit in late-phase (60-120 min) insulin secretion .

Impaired fasting glucose(IFG) and impaired glucose tolerance(IGT)

- **Not clinical entities but associated with:**
  - **Physical inactivity**
  - **Obesity (especially abdominal, or visceral)**
  - **Dyslipidemia**
    - **High triglycerides and/or low HDL cholesterol**
  - **Hypertension**
- **Important to identify early and begin intervention immediately to reduce further progression from prediabetes to diabetes.**

American Diabetes Association. *Diabetes Care.* 2014:37 Suppl 1:S81-90.

Rationale for Prediabetes screening

- **Epidemiologic evidence suggests the complications of diabetes begin early in the progression from normal glucose tolerance to frank type 2 diabetes**

- **Prediabetes is a condition in which early detection is appropriate, because:**
  - **Duration of hyperglycemia is a predictor of adverse outcomes**

Garber AJ, et al. *Endocr Pract*. 2008;14:933-946.

Criteria for Screening for Prediabetes/Type 2 Diabetes in Asymptomatic Adult Individuals

DIABETES RISK FACTORS →

- Physical inactivity
- First-degree relative with diabetes
- High-risk race/ethnicity
- Women who delivered a baby weighing >9 lb or were diagnosed with GDM
- Hypertension (≥140/90 mmHg or on therapy for hypertension)
- HDL-C <35 mg/dL and/or a TG >250 mg/dL
- A1C ≥5.7%, IGT, or IFG on previous testing
- Other clinical conditions associated with insulin resistance, such as severe obesity, acanthosis nigricans, PCOS
- History of CVD

- Consider testing (screening) all adults with a BMI ≥25 kg/m^2 and additional risk factors
  - If no risk factors, consider screening no later than age 45 years
- If normal results, repeat testing (screening) at ≥3-year intervals
  - More frequently depending on initial test results and risk factors
  - Test yearly if prediabetes

ADA Diabetes Risk Score

Question	Score
Age (years)	
40-49	1
50-59	2
≥60	3
Sex	
Male	1
Woman with history of gestational DM	1
Family history of T1 or T2DM	
1st degree relative	1
Hypertension diagnosis	
Yes	1

Question	Score
Physical activity	
No	1
BMI	
25-30	1
30-40	2
≥40	3
Total (maximum)	10

| Total Risk Score	Risk of developing T2DM in 10 years
≥4	High risk of having prediabetes or diabetes
≥5	High risk of having diabetes

Ban H, et al. *Ann Intern Med*. 2009;151:775-783.
American Diabetes Association. Available at: http://www.diabetes.org/assets/pdfs/at-risk/risk-test-paper-version.pdf.

Modifiable Risk Factors of Diabetes/Prediabetes for CV Disease

Non-modifiable	Modifiable
Age	Physical inactivity
Race/Ethnicity	Overweight/Obesity
Gender	Hypertension
Family history	Smoking
	Abnormal lipid metabolism
	High plasma glucose levels

American Diabetes Association. *Diabetes Care.* 2014:37:S14-80.

Effect of Metabolic Syndrome and IFG on Risk of T2D

San Antonio Heart Study
Men and Women Age 25-64 Years
(N = 2,559; 7.4 years of follow-up)
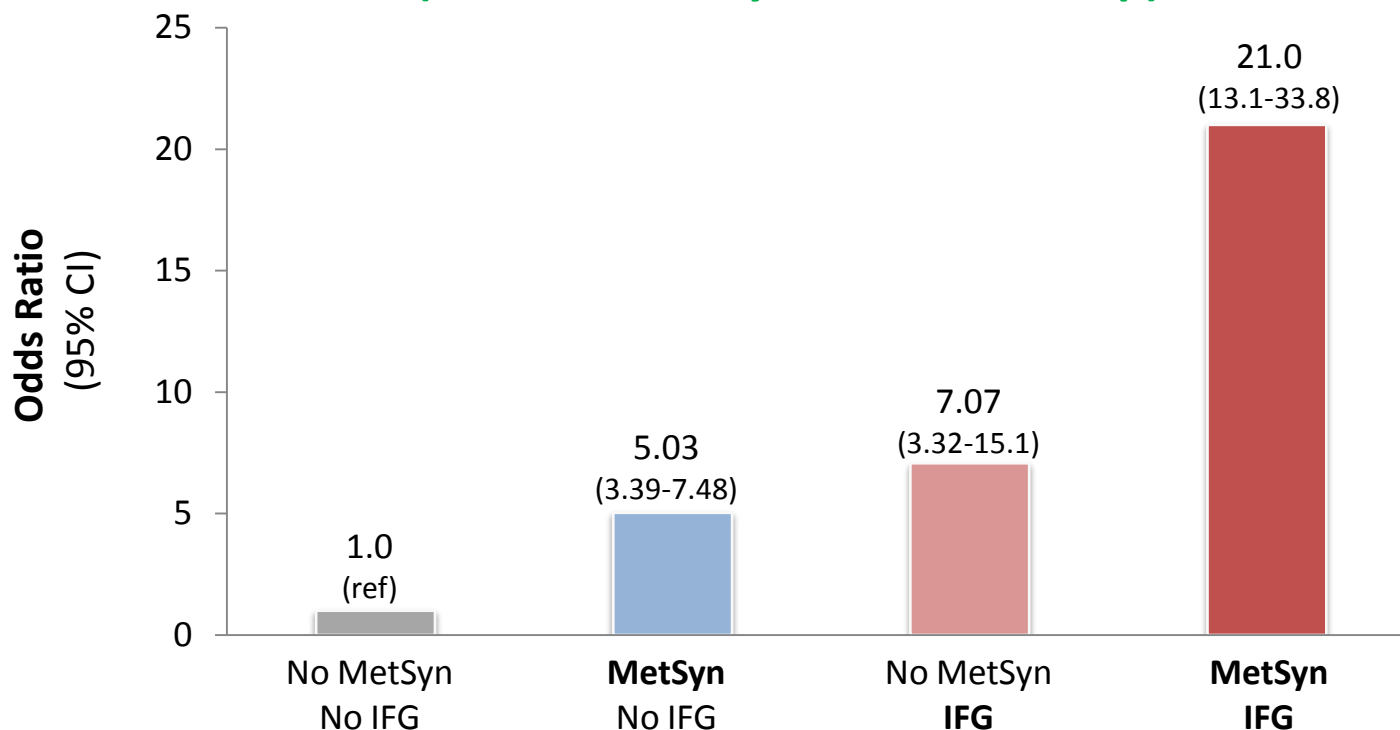
CI, confidence interval; IFG, impaired fasting glucose; MetSyn, metabolic syndrome; T2D, type 2 diabetes.

Lorenzo C, et al. *Diabetes Care*. 2007;30:8-13.

Effect of triglyceride level on risk of T2DM

Men Age 26-45 Years
(74,309 person-years of follow-up)

Effect of body mass index on risk of T2DM
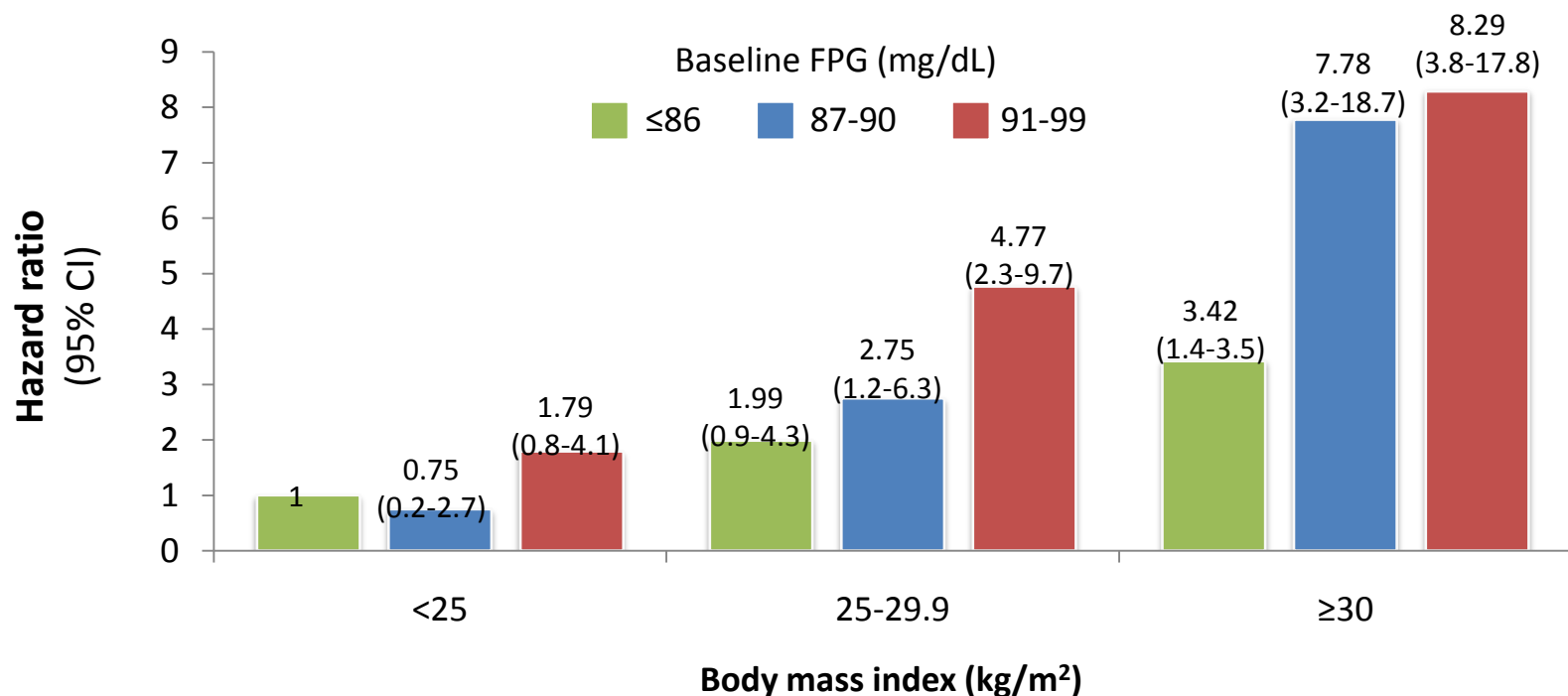
Men Age 26-45 Years
(74,309 person-years of follow-up)
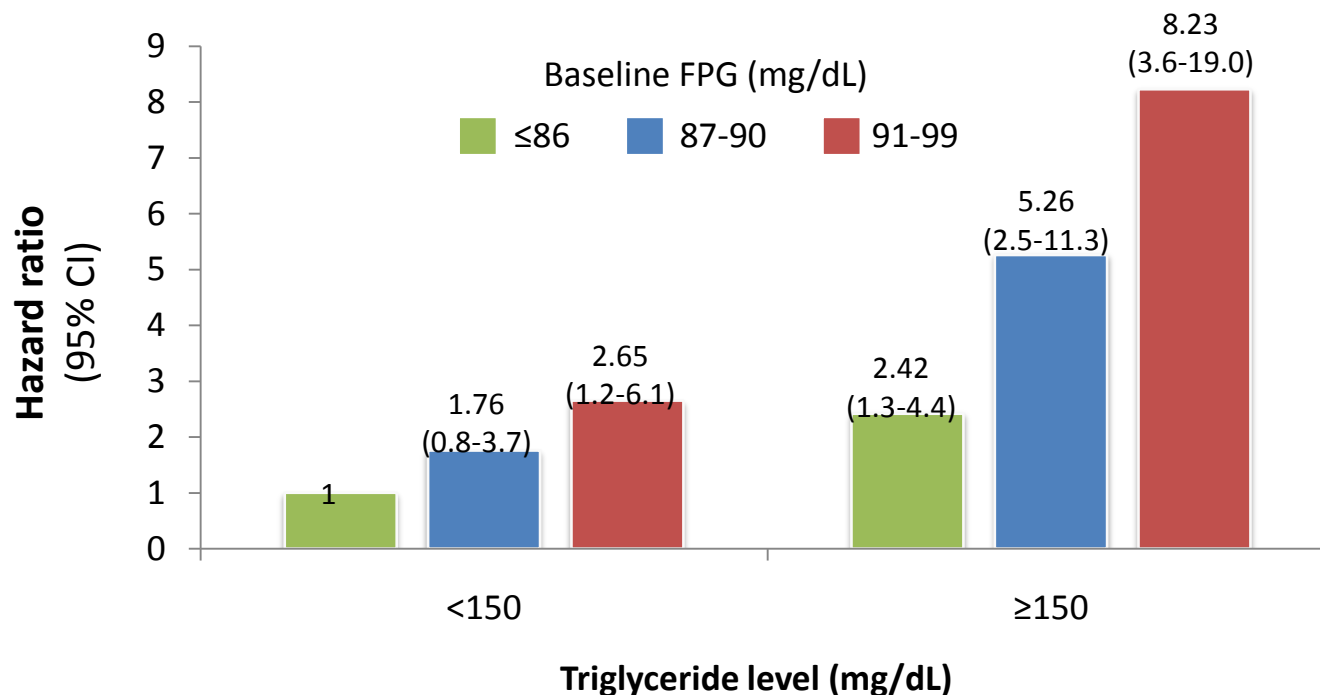
CI, confidence interval; FPG, fasting plasma glucose; T2D, type 2 diabetes.

Tirosh A, et al. *N Engl J Med.* 2005;353:1454-1462.

Clinical risks of not treating Prediabetes are substantial

- **Microvascular disease**
  - **Retinopathy**
  - **Neuropathy**
  - **Nephropathy**

- **Cardiovascular disease (CVD)**
  - **Heart disease**
  - **Stroke**
  - **Peripheral vascular disease**

Zhang Y, et al. *Population Health Management.* 2009;12:157-163.
Garber AJ, et al. *Endocr Pract*. 2008;14:933-946.

MANAGEMENT OF PREDIABETES

The good news ...

You can <u>prevent</u> or <u>delay</u> type 2 diabetes through:

More nutritious eating

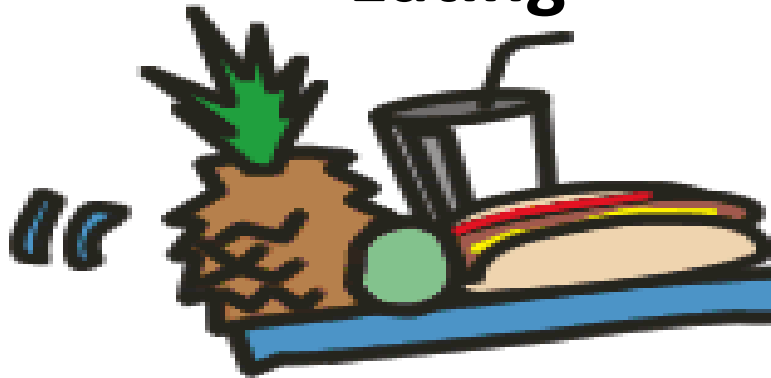*Regular physical activity*
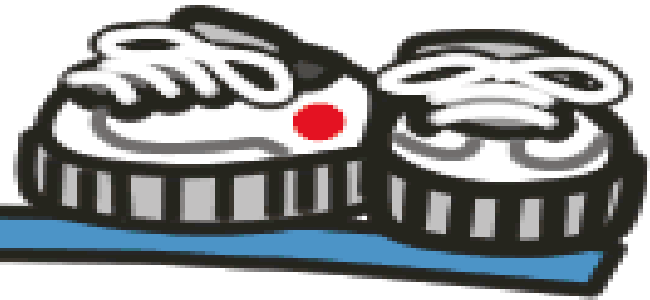(150 minutes a week)

Moderate weight loss
(7% of body weight)

Balance is the cornerstone of prevention

More Nutritious Eating

Regular Physical Activity

Moderate Weight Loss

LIFESTYLE THERAPY
RISK STRATIFICATION FOR DIABETES COMPLICATIONS

INTENSITY STRATIFIED BY BURDEN OF OBESITY AND RELATED COMPLICATIONS

Nutrition	• Maintain optimal weight • Calorie restriction (if BMI is increased) • Plant-based diet; high polyunsaturated and monounsaturated fatty acids	• Avoid *trans* fatty acids; limit saturated fatty acids	• Structured counseling • Meal replacement
Physical Activity	• 150 min/week moderate exertion (eg. walking, stair climbing) • Strength training • Increase as tolerated	• Structured program • Wearable technologies	• Medical evaluation/ clearance • Medical supervision
Sleep	• About 7 hours per night • Basic sleep hygiene	• Screen OSA • Home sleep study	• Referral to sleep lab
Behavioral Support	• Community engagement • Alcohol moderation	• Discuss mood with HCP	• Formal behavioral therapy
Smoking Cessation	• No tobacco products	• Nicotine replace-ment therapy	• Referral to structured program

PREDIABETES ALGORITHM

IFG (100–125) | IGT (140–199) | METABOLIC SYNDROME (NCEP 2001)

LIFESTYLE THERAPY
(Including Medically Assisted Weight Loss)

TREAT ASCVD RISK FACTORS

WEIGHT LOSS THERAPIES

TREAT HYPERGLYCEMIA
FPG > 100 | 2-hour PG > 140

ASCVD RISK FACTOR MODIFICATIONS ALGORITHM

- DYSLIPIDEMIA ROUTE
- HYPERTENSION ROUTE

NORMAL GLYCEMIA

Progression

OVERT DIABETES

PROCEED TO HYPERGLYCEMIA ALGORITHM

1 PRE-DM CRITERION

Intensify Weight Loss Therapies

MULTIPLE PRE-DM CRITERIA

Low-risk Medications
- Metformin
- Acarbose

Consider with Caution
- TZD
- GLP-1 RA

If glycemia not normalized

LEGEND

Orlistat, lorcaserin, phentermine/topiramate ER, naltrexone/bupropion, liraglutide 3 mg, or bariatric surgery as indicated for obesity treatment

Lifestyle intervention in Prediabetes

- **Persons with prediabetes should reduce weight by 5% to 10%, with long-term maintenance at this level**
  - **A program of regular moderate-intensity physical activity for 30-60 minutes daily, at least 5 days a week, is recommended**
  - **A diet that includes caloric restriction, increased fiber intake and carbohydrate intake limitations is advised**

Garber AJ, et al. *Endocr Pract*. 2008;14:933-946.
Garber AL, et al. *Endocr Pract*. 2017;23:207-238.

Benefits of physical activity

- Increased insulin sensitivity

- Improved lipid levels

- Lower blood pressure

- Weight control

- Improved plasma glucose control

- Reduced risk of CVD

- Prevent/delay type 2 diabetes

American Diabetes Association. *Diabetes Care.* 2014:37:S14-80.

Intensive lifestyle intervention effectively prevents progression from IGT to T2DM
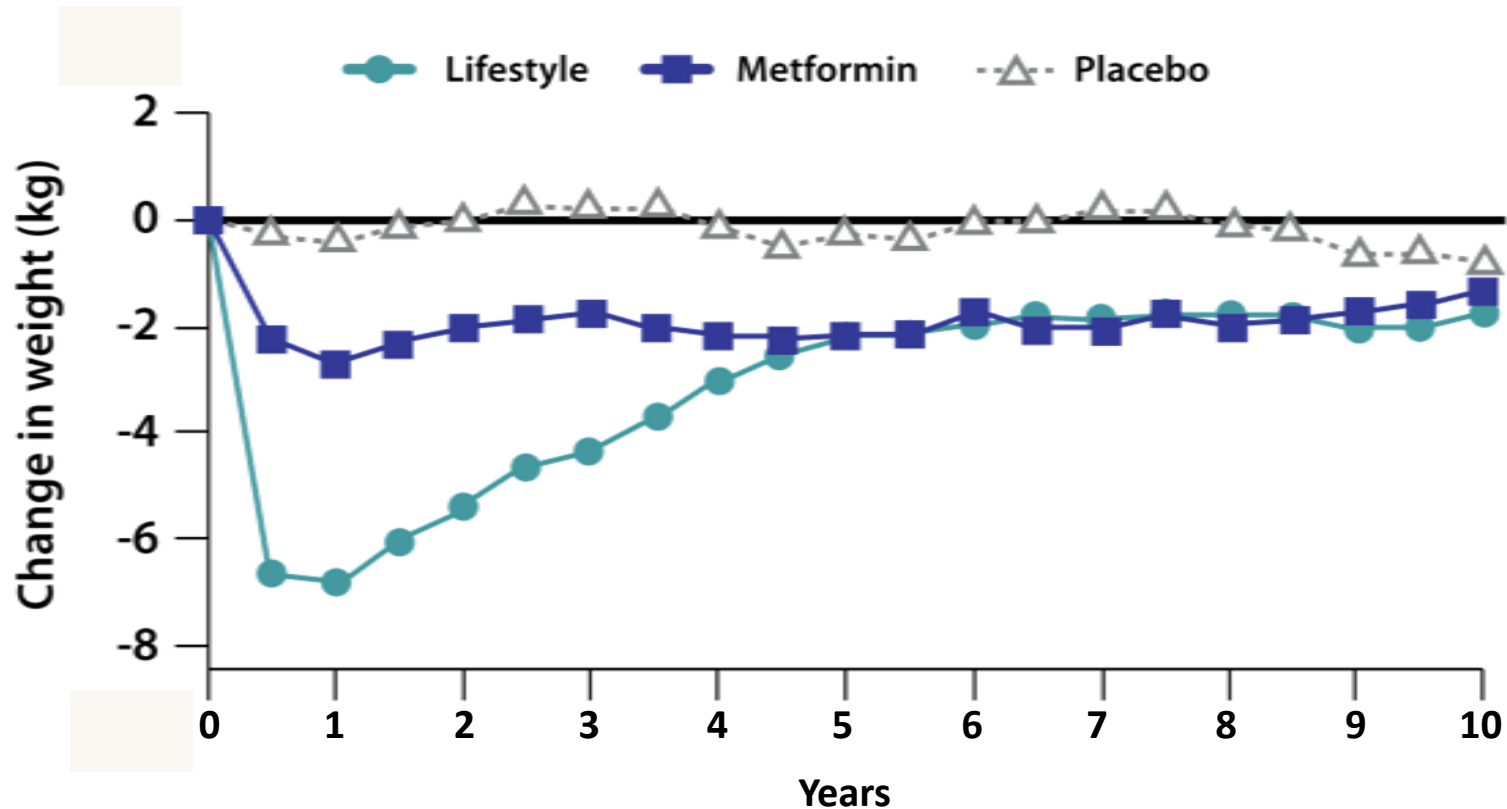
Diabetes Prevention Program
(N=3234)
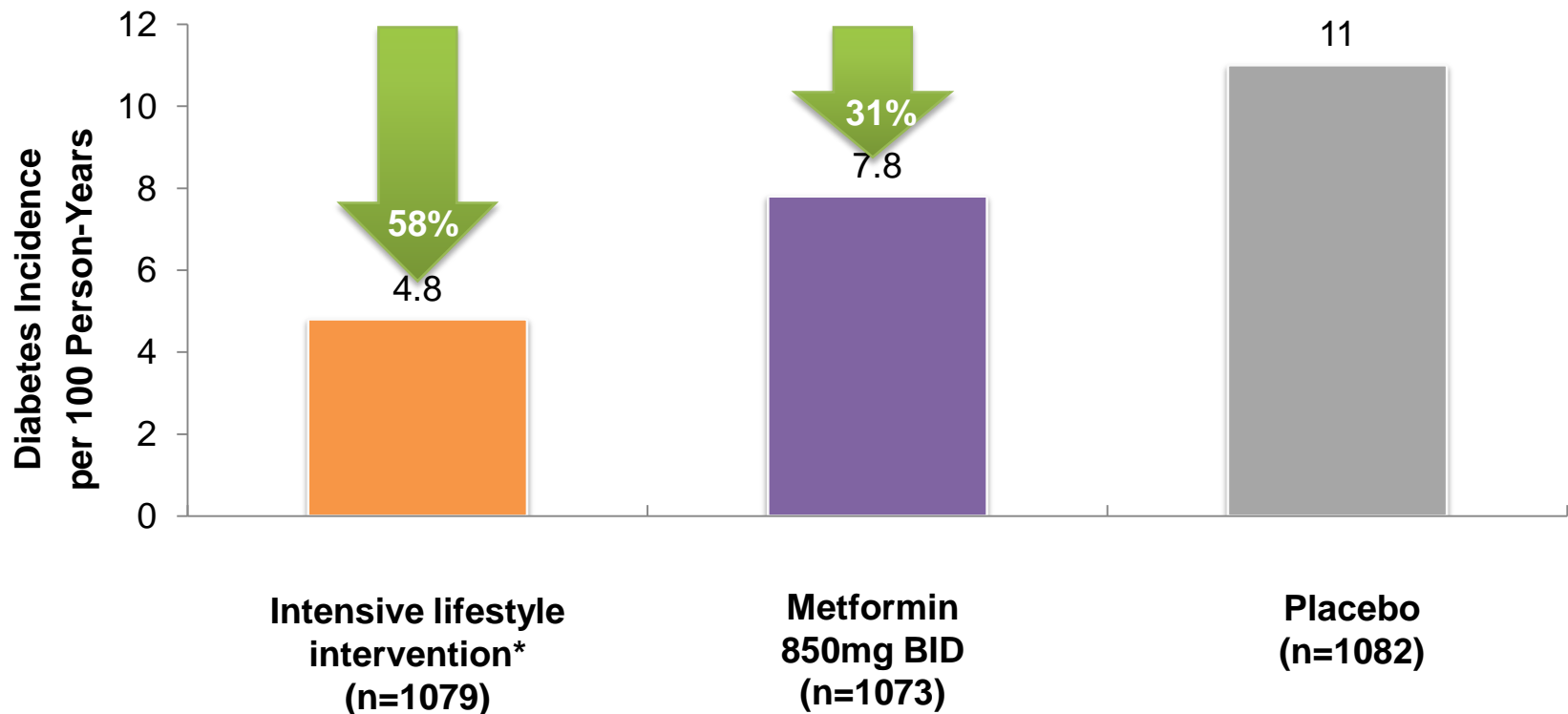
*Goal: 7% reduction in baseline body weight through low-calorie, low-fat diet and ≥150 min/week moderate intensity exercise .

IGT, impaired glucose tolerance; T2D, type 2 diabetes.

DPP Research Group. *N Engl J Med.* 2002;346:393-403.

Maintenance of long-term weight loss

DPP Outcomes Study
(N=2766)

DPP, Diabetes Prevention Program; T2D, type 2 diabetes.

DPP Research Group. *Lancet*. 2009;374:1677-1686.

T2D prevention in women with a history of GDM

- **Findings from the DPP**

  - **Progression to diabetes is more common in women with a history of GDM vs those without, despite equivalent degrees of IGT at baseline**

- **Both intensive lifestyle and metformin are highly effective in delaying or preventing diabetes in women with IGT and a history of GDM**

DPP, Diabetes Prevention Program; GDM, gestational diabetes mellitus; IGT, impaired glucose tolerance; T2D, type 2 diabetes.

Ratner RE, et al. *J Clin Endocrinol Metab*. 2008;93:4774-4779.

Risk stratification and management strategies for Prediabetes

Risks and treatments	Low	Medium	High
Hemoglobin A1C, %	5.7–5.8	5.9–6.1	6.2–6.49
Risk stratification	√	√	√
A1C target: <5.7%	√	√	√
Lifestyle modification, 16-week course	√	√	√
Lose 7% of body weight if BMI ≥25 kg/m^2	√	√	√
Physical activity ≥150 minutes/week	√	√	√
Pharmacologic therapy (e.g., metformin)*			√
Gastric bypass surgery†			√

* **Consider in low and medium risk if no weight loss after 16-week lifestyle modification course**

† **BMI ≥40 kg/m^2 with no risk factors or ≥35 kg/m^2 1 or more severe obesity-related co-morbidities and/or if no weight loss after lifestyle modification and/or metformin therapy**

Adapted from:
1. Tuso P. *Perm J*. 2014 Summer;18:88–93.

Medical and surgical interventions shown to delay or prevent T2DM

Intervention	Follow-up Period	Reduction in Risk of T2D (P value vs placebo)
Antihyperglycemic agents		
Metformin[1]	2.8 years	31% (P<0.001)
Acarbose[2]	3.3 years	25% (P=0.0015)
Pioglitazone[3]	2.4 years	72% (P<0.001)
Rosiglitazone[4]	3.0 years	60% (P<0.0001)
Weight loss interventions		
Orlistat[5]	4 years	37% (P=0.0032)
Phentermine/topiramate[6]	2 years	79% (P<0.05)
Bariatric surgery[7]	10 years	75% (P<0.001)

T2D, type 2 diabetes.

1. DPP Research Group. *N Engl J Med.* 2002;346:393-403. 2. STOP-NIDDM Trial Research Group. *Lancet.* 2002;359:2072-2077.
3. Defronzo RA, et al. *N Engl J Med.* 2011;364:1104-15. 4. DREAM Trial Investigators. *Lancet.* 2006;368:1096-1105.
5. Torgerson JS, et al. *Diabetes Care.* 2004;27:155-161. 6. Garvey WT, et al. *Diabetes Care.* 2014;37:912-921.
7. Sjostrom L, et al. *N Engl J Med.* 2004;351:2683-2693.

Follow-up counseling

- Emphasize long-term goals of treatment
  - **Monitor weight loss progress**
  - **Provide ongoing counseling for lifestyle modification**
  - **Consider pharmacologic therapy (e.g., metformin) if appropriate**
    - **IGT, IFG and/or A1C of 5.7-6.49%**
    - **Especially if BMI >35 kg/m^2**
    - **Age <60**
    - **Women with prior gestational diabetes**
- **Provide referrals to other members of the healthcare team**

American Diabetes Association. *Diabetes Care.* 2014:37, S14-80.

Follow-up counseling(Con't)

- Provide annual screenings for the development of diabetes
  - Every 12 months for those with prediabetes
  - Every 3 years if screening is negative
- On a regular basis, search EHR to determine who needs to be screened/rescreened
- Continually screen for modifiable risk factors at each interaction

American Diabetes Association. *Diabetes Care.* 2014:37, S14-80.

Take Home Messages

- **Untreated individuals with prediabetes are at increased risk for diabetes as well as for micro- and macrovascular complications**

- **Treatment goals are to prevent deterioration in glucose levels and modify other risk factors such as obesity, hypertension, and dyslipidemia**
  - The same blood pressure and lipid goals are suggested for prediabetes and diabetes

- **Intensive lifestyle management is the cornerstone of all prevention efforts; pharmacotherapy targeted at glucose may be considered in high-risk patients.**

THANK YOU