



ΔΗΜΕΡΙΔΑ
ΓΙΑ ΤΟ
ΣΑΚΧΑΡΩΔΗ
ΔΙΑΒΗΤΗ

Diabetes:
Treating the gap
6-7 ΟΚΤΩΒΡΙΟΥ 2017
ΟΛΥΜΠΙΑΚΟ ΜΟΥΣΕΙΟ
ΘΕΣΣΑΛΟΝΙΚΗ

Προδιαβήτης Νόσος ή προάγγελος εμφάνισης

Νίκη Κατσίκη MD, MSc, PhD, FRSPH

IASO/EASO Scope Member

EASD Diabetes & Cardiovascular Disease Group
Member

Μέλος ΔΣ της Ελληνικής Εταιρείας Αθηροσκλήρωσης
Ειδική Παθολόγος, Επιστημονική συνεργάτης
Β΄ Προπ. Παθολογικής Κλινικής
Α.Π.Θ.

Δήλωση συμφερόντων

- Associate Editor of ***Angiology***
- Associate Editor of ***Clinical Lipidology***
- Associate Editor of the Hellenic College of Treatment of Atherosclerosis for
The Open Cardiovascular Medicine Journal
- Section Editor of ***Archives of Medical Science***
- Book Review and News and Views Editor of ***Current Vascular Pharmacology***
- Editorial Board Member of ***Metabolism Clinical and Experimental*** and
Current Medical Research and Opinion
- Η ΝΚ έχει συμμετάσχει σε κλινικές μελέτες, συνέδρια ή/και έχει δώσει ομιλίες χρηματοδοτούμενες από Amgen, Angelini, Astra-Zeneca, Boehringer Ingelheim, Elpen, Galenica, MSD, Novartis, Novo Nordisk, Sanofi και WinMedica

ΠΡΟΔΙΑΒΗΤΗΣ: ΟΡΙΣΜΟΣ



Prediabetes*

**FPG 100–125 mg/dL
(5.6–6.9 mmol/L): IFG**

OR

**2-h plasma glucose 140–199 mg/dL
(7.8–11.0 mmol/L): IGT**

OR

A1C 5.7–6.4%

* For all three tests, risk is continuous, extending below the lower limit of a range and becoming disproportionately greater at higher ends of the range.



Κατευθυντήριες
Οδηγίες
για τη Διαχείριση
του Διαβητικού
Ασθενούς

2017

Πίνακας 1.2. Κατηγορίες αυξημένου κινδύνου ανάπτυξης ΣΔ (Προδιαβήτης)

Γλυκόζη πλάσματος νηστείας 110-125 mg/dL (IFG)¹

Γλυκόζη πλάσματος 2 ωρών (κατά τη δοκιμασία φόρτισης με γλυκόζη 75 γρ.) 140-199 mg/dL (IGT)²

¹IFG: Impaired fasting glucose (Διαταραγμένη Γλυκόζη Νηστείας).

²IGT: Impaired Glucose Tolerance (Διαταραγμένη Ανοχή στη Γλυκόζη).

*Εάν δεν γίνει OGTT δεν μπορεί να αποκλεισθεί η ύπαρξη ΣΔ ή συνύπαρξη της IFG με IGT.

Οι τιμές γλυκόζης νηστείας που έχουν καθοριστεί από την Αμερικανική Διαβητολογική Εταιρεία ως διαχωριστικό όριο για την κατηγορία της Διαταραγμένης Γλυκόζης Νηστείας (IFG) είναι 100-125 mg/dL. Η ΠΟΥ και η Ευρωπαϊκή Εταιρεία Διαβήτη (EASD) διαφοροποιούνται σε αυτό το σημείο, και δεν θεωρούν ως κατώτερο διαχωριστικό όριο την τιμή των 100 mg/dL, αλλά των 110 mg/dL. Η ΕΔΕ συντάσσεται με τις Ευρωπαϊκές κατευθυντήριες οδηγίες.

Η Ελληνική Διαβητολογική Εταιρεία δεν συνιστά τη χρησιμοποίηση της HbA1c ως μέθοδο διάγνωσης του προδιαβήτη προς το παρόν στην Ελλάδα, αλλά εμμένει στη χρήση της τιμής γλυκόζης πλάσματος (νηστείας ή με OGTT) για τον σκοπό αυτό.

ΣΥΧΝΟΤΗΤΑ ΠΡΟΔΙΑΒΗΤΗ



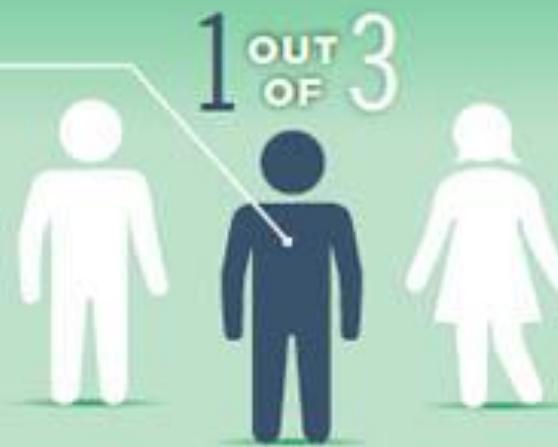
PREDIABETES

COULD IT
BE YOU?



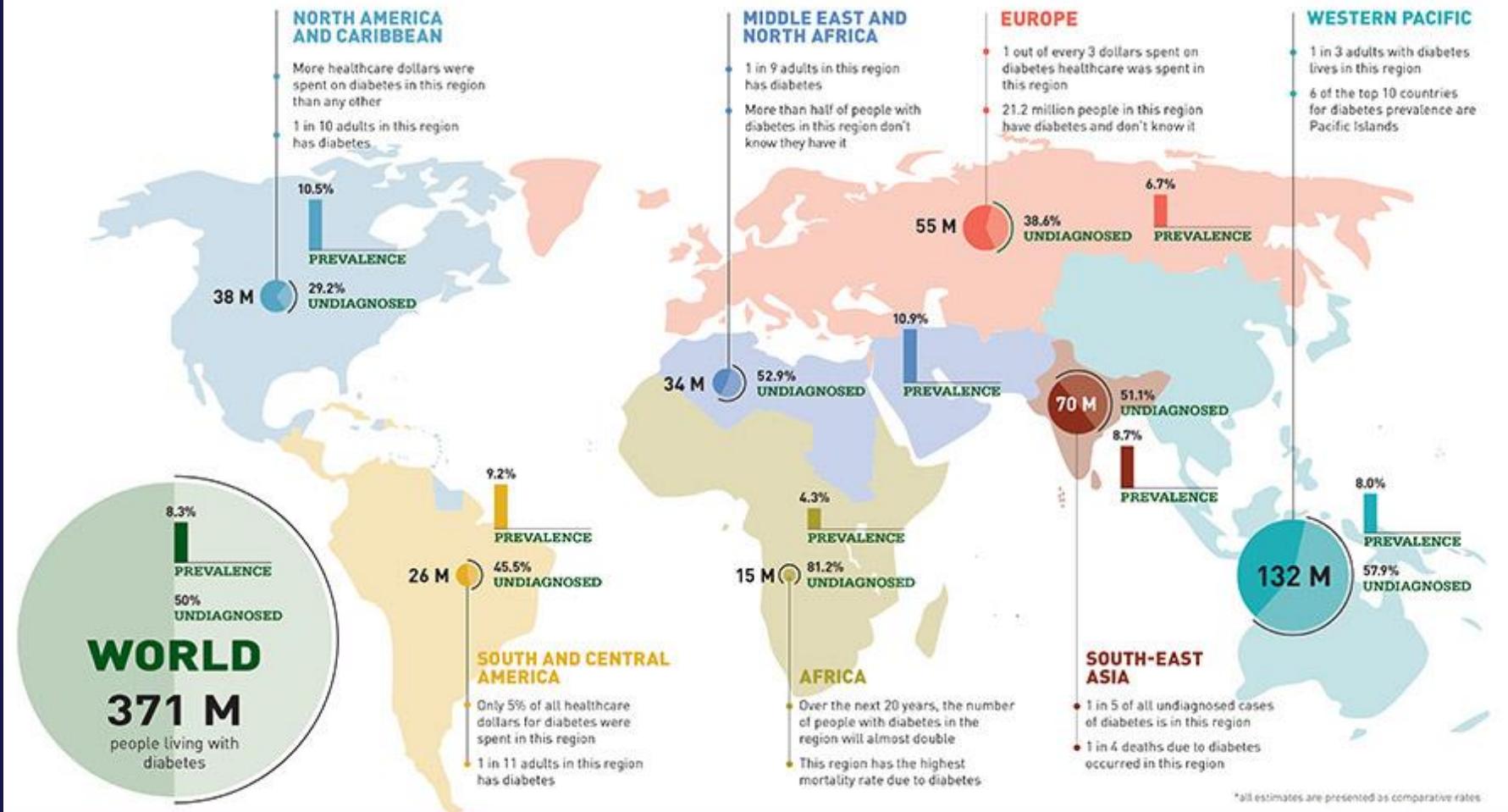
86
MILLION

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

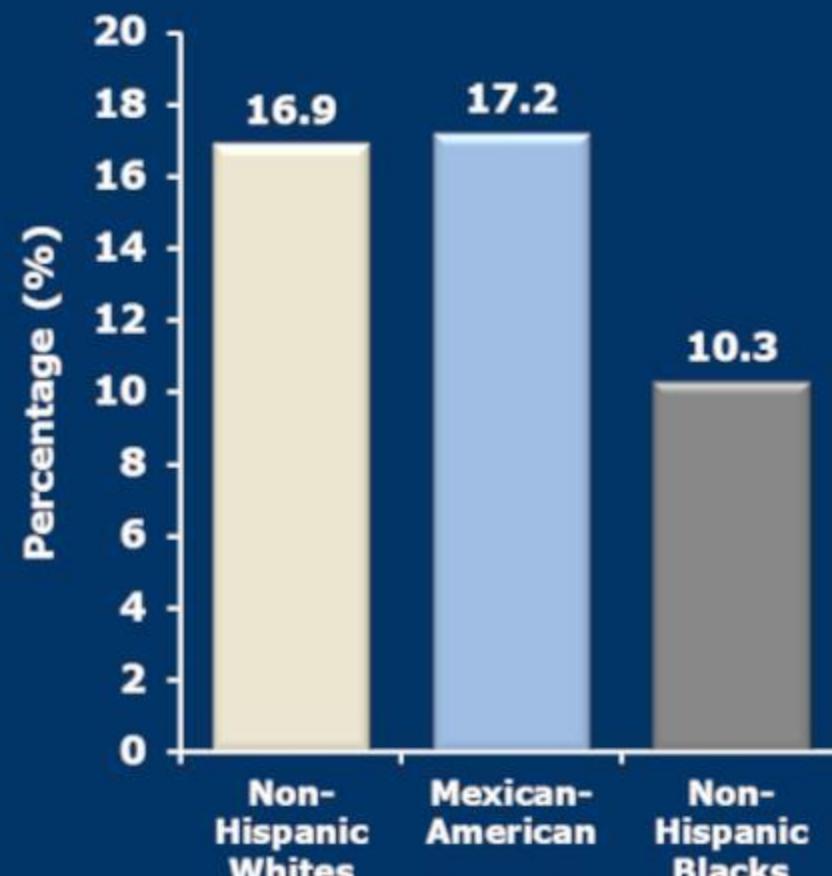
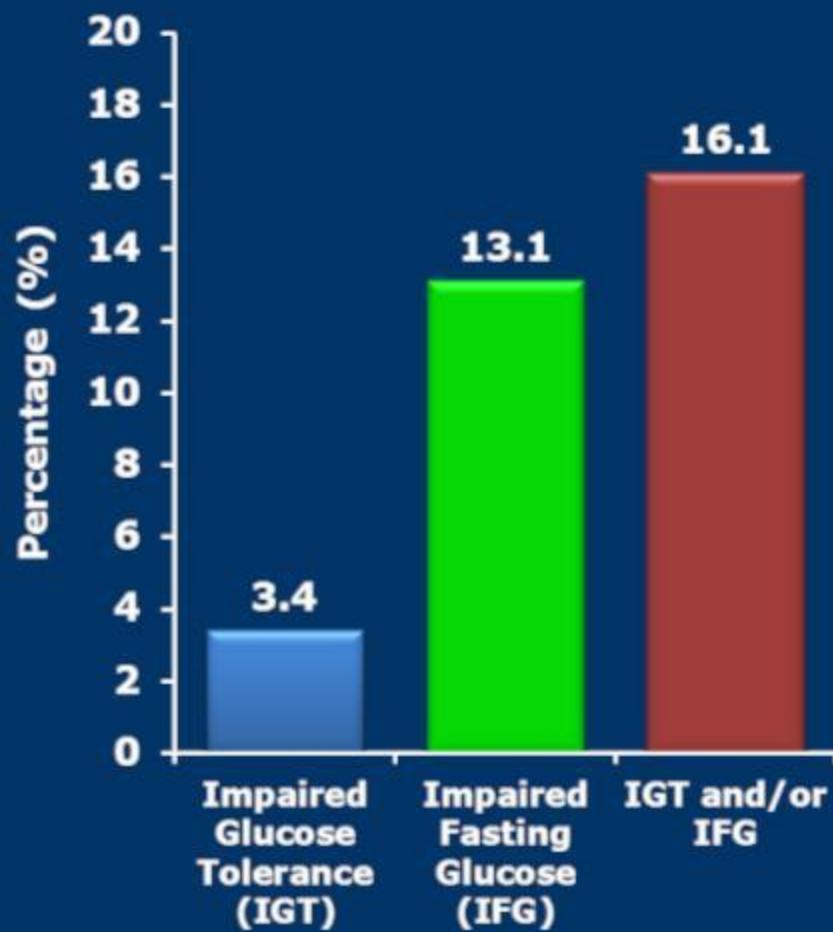


9 **OUT
OF
10**

people with prediabetes
do not know they have it



Prevalence of Prediabetes in Children/Adolescents in the U.S.



ΠΑΡΑΓΟΝΤΕΣ ΚΙΝΔΥΝΟΥ ΓΙΑ ΠΡΟΔΙΑΒΗΤΗ



ΑΥΞΗΜΕΝΟΣ ΚΙΝΔΥΝΟΣ ΓΙΑ ΠΡΟΔΙΑΒΗΤΗ

Ηλικία >45 έτη

Περιφέρεια μέσης >102 cm (άνδρες) και >88 cm (γυναίκες)

Δείκτης μάζας σώματος >30 kg/m²

Οικογενειακό ιστορικό διαβήτη σε γονείς, αδέλφια, παιδιά

Ιστορικό υπέρτασης ή καρδιοαγγειακής νόσου

Ιστορικό δυσλιπιδαιμίας (υψηλά τριγλυκερίδια, χαμηλή HDL)

Ιστορικό διαβήτη κύησης

Γέννηση παιδιών με σωματικό βάρος >4 kg

Γυναίκες με σύνδρομο πολυκυστικών ωοθηκών

Λήψη φαρμάκων από εκείνα που προδιαθέτουν σε αύξηση της γλυκόζης αίματος (π.χ. κορτικοστεροειδή, αντιψυχωσικά)

ΚΛΙΝΙΚΗ ΕΙΚΟΝΑ ΠΡΟΔΙΑΒΗΤΗ



ΣΥΜΠΤΩΜΑΤΑ ΠΡΟΔΙΑΒΗΤΗ

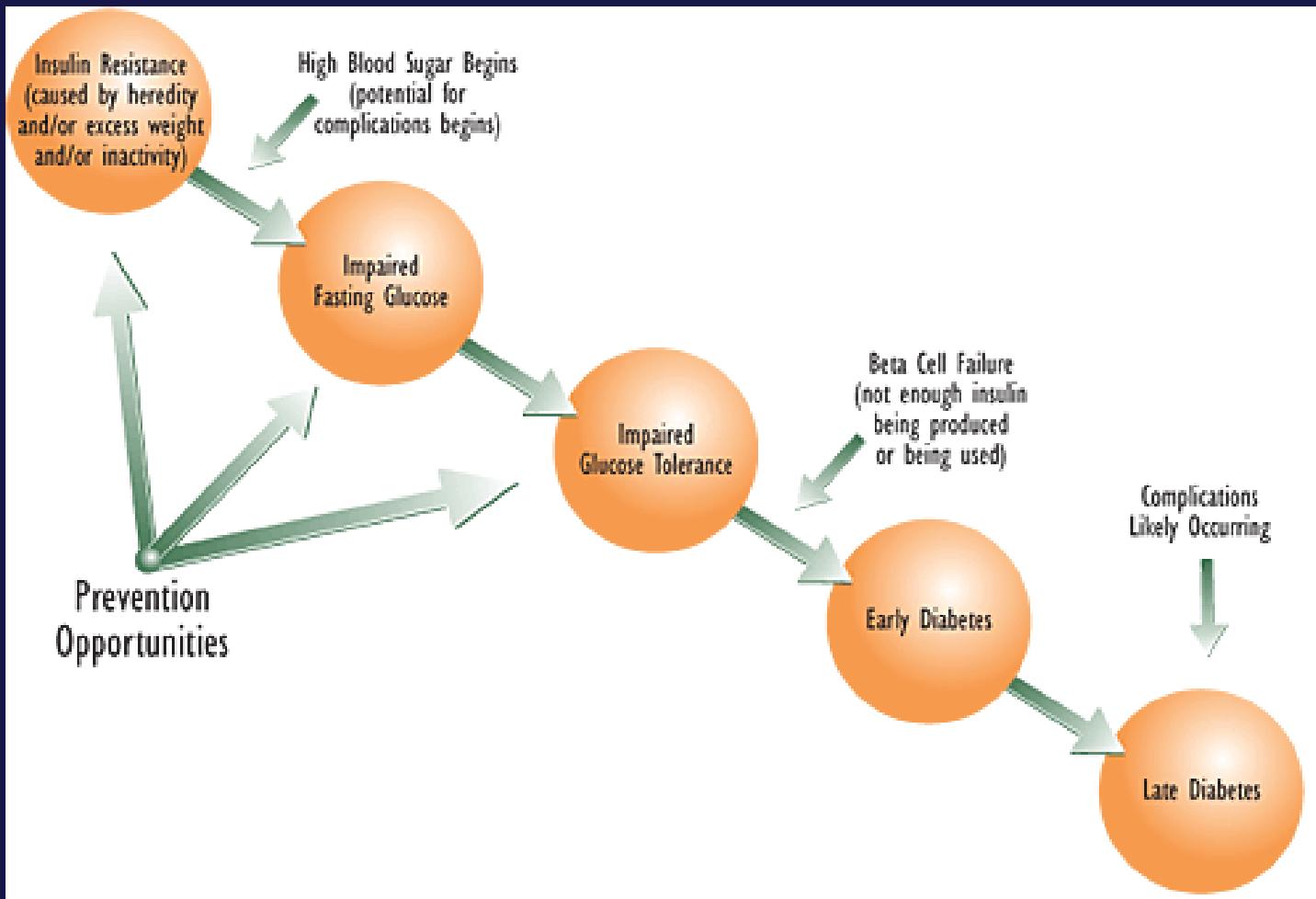
- **Συχνά ασυμπτωματικός**
- **Συνήθη συμπτώματα:**
 - Αδυναμία, κόπωση, υπνηλία
 - Πολυδιψία
 - Πολυφαγία
 - Πολυουρία
 - Απώλεια κιλών
 - Θόλωση όρασης



ΚΛΙΝΙΚΗ ΣΗΜΑΣΙΑ ΠΡΟΔΙΑΒΗΤΗ



ΕΞΕΛΙΞΗ ΠΡΟΔΙΑΒΗΤΗ ΣΕ ΔΙΑΒΗΤΗ



ΠΡΟΔΙΑΒΗΤΗΣ → ΔΙΑΒΗΤΗΣ

- Το ετήσιο ποσοστό των ατόμων με προδιαβήτη που μεταπίπτουν στην κατηγορία του ΣΔ κυμαίνεται στο 5 -10%.
- Από μετααναλύσεις κλινικών μελετών έχει εκτιμηθεί, ότι τελικά το 70% των ατόμων αυτών θα εμφανίσουν κάποια στιγμή ΣΔ.
- Ο κίνδυνος εμφάνισης ΣΔ πολλαπλασιάζεται στις περιπτώσεις όπου συνυπάρχει IGT και IFG.

Complications of Hyperglycemia in Prediabetes (1)

- **Retinopathy**
- In the Diabetes Prevention Program (DPP), diabetic retinopathy was observed in **7.9%** of patients with IGT who did not progress to diabetes, compared with **12.6%** of patients who later progressed to diabetes.
- The Blue Mountains Eye Study (BMES) revealed a **10%** retinopathy incidence among individuals with fasting plasma glucose (FPG) levels between 99 and 112 mg/dL and a **20%** retinopathy incidence among individuals with FPG levels between 113 and 126 mg/dL.

Complications of Hyperglycemia in Prediabetes (2)

- **Neuropathy**
 - Intraepidermal nerve fiber loss is an early feature of metabolic syndrome, prediabetes, and established diabetes.
 - Managing glucose may prevent worsening of neuropathy.

- **Nephropathy**
 - Patients with prediabetes may have comorbid CKD but are also at risk of developing diabetic nephropathy.
 - Appropriate management of prediabetes, along with ACE inhibitor or ARB therapy, if indicated, should be instituted.

Prediabetes and Chronic Kidney Disease

- According to data from the **National Health and Nutrition Examination Survey (NHANES)**, approximately 18% of adults with prediabetes have chronic kidney disease (CKD)
- Patients with CKD and prediabetes should receive treatment with an ACE inhibitor or an ARB to **prevent progression of CKD**

Why Primary Prevention of Diabetes?

Macrovascular complications
Microvascular complications

Macrovascular complications starts during the prediabetes phase and benefits much from primary prevention of diabetes compared to microvascular disease.

-10

Prevention

Diagnosis

10+

Years

IFG/IGT (Prediabetic phase)

Type 2 diabetes (Overt diabetic phase)

IFG: impaired fasting glucose

IGT: impaired glucose tolerance

Risk of Cardiovascular Disease Is Elevated Prior to Diagnosis of T2DM



*MI=myocardial infarction.

Adapted from: Hu F, et al. *Diabetes Care*. 2002;25:1129-1134.

Clinical Risks of Not Treating Prediabetes Are Substantial

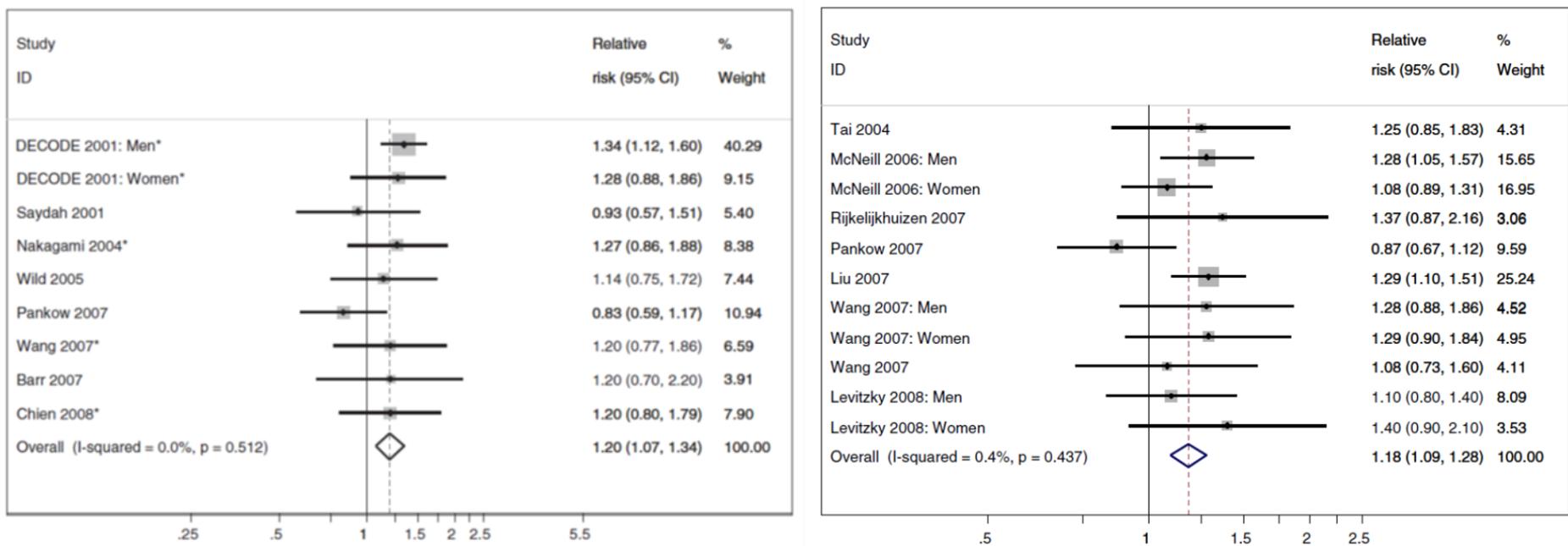
- Microvascular disease
 - Retinopathy
 - Neuropathy
 - Nephropathy
- Cardiovascular disease (CVD)
 - Heart disease
 - Stroke
 - Peripheral vascular disease



Pre-Diabetes and the Risk for Cardiovascular Disease

A Systematic Review of the Evidence

Earl S. Ford, MD, MPH, Guixiang Zhao, MD, PhD, Chaoyang Li, MD, PhD



Impaired Glucose Tolerance and Cardiovascular Outcomes

Impaired Fasting Glucose (100 to 125 mg/dl) and Cardiovascular Outcomes

Association between prediabetes and risk of cardiovascular disease and all cause mortality: systematic review and meta-analysis

BMJ 2016;355:i5953

Yuli Huang,¹ Xiaoyan Cai,² Weiyi Mai,³ Meijun Li,^{1,4} Yunzhao Hu¹

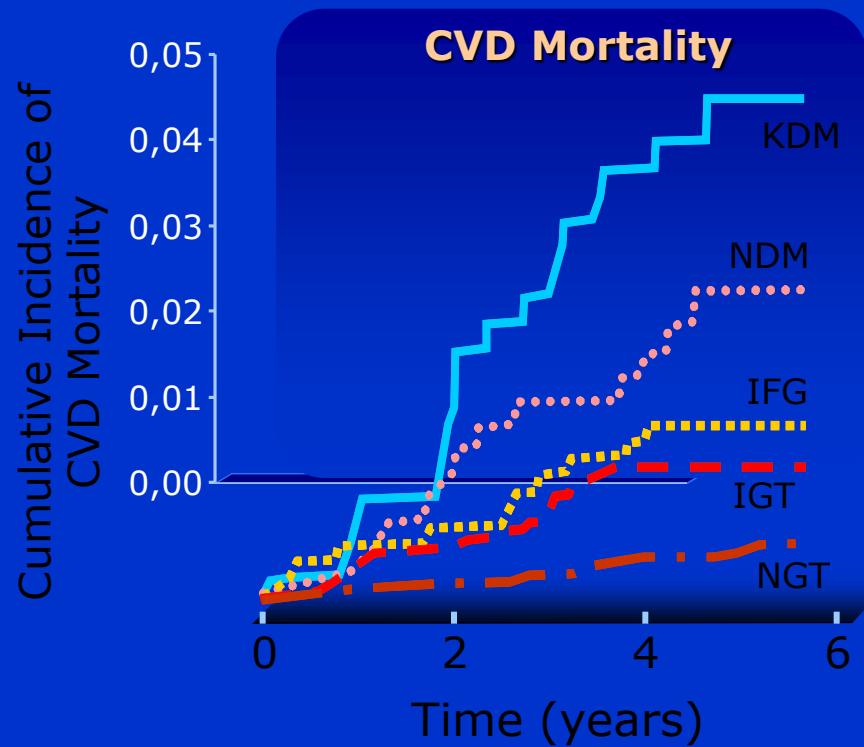
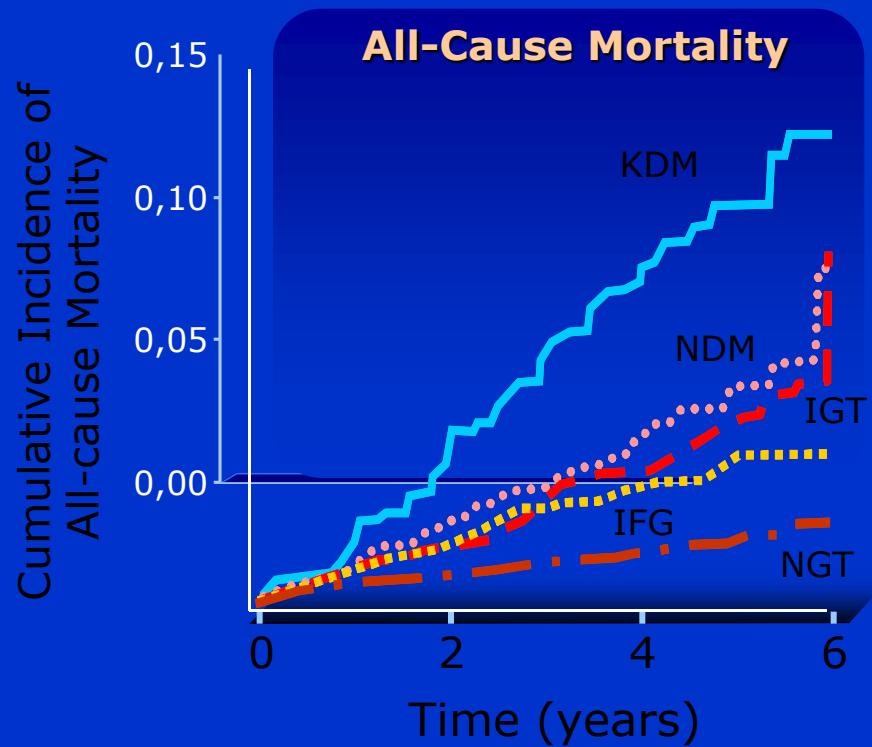
WHAT THIS STUDY ADDS

Prediabetes defined as impaired glucose tolerance or impaired fasting glucose was associated with an increased risk of cardiovascular disease and all cause mortality

The risk increased in people with a fasting glucose concentration as low as 5.55 mmol/L HbA_{1c} 39-47 mmol/mol or 42-47 mmol/mol was associated with an increased risk of composite cardiovascular disease and coronary heart disease

Lifestyle modification is the main management for people with prediabetes

Unadjusted Mortality According to Glucose Metabolism: Data from AusDiab



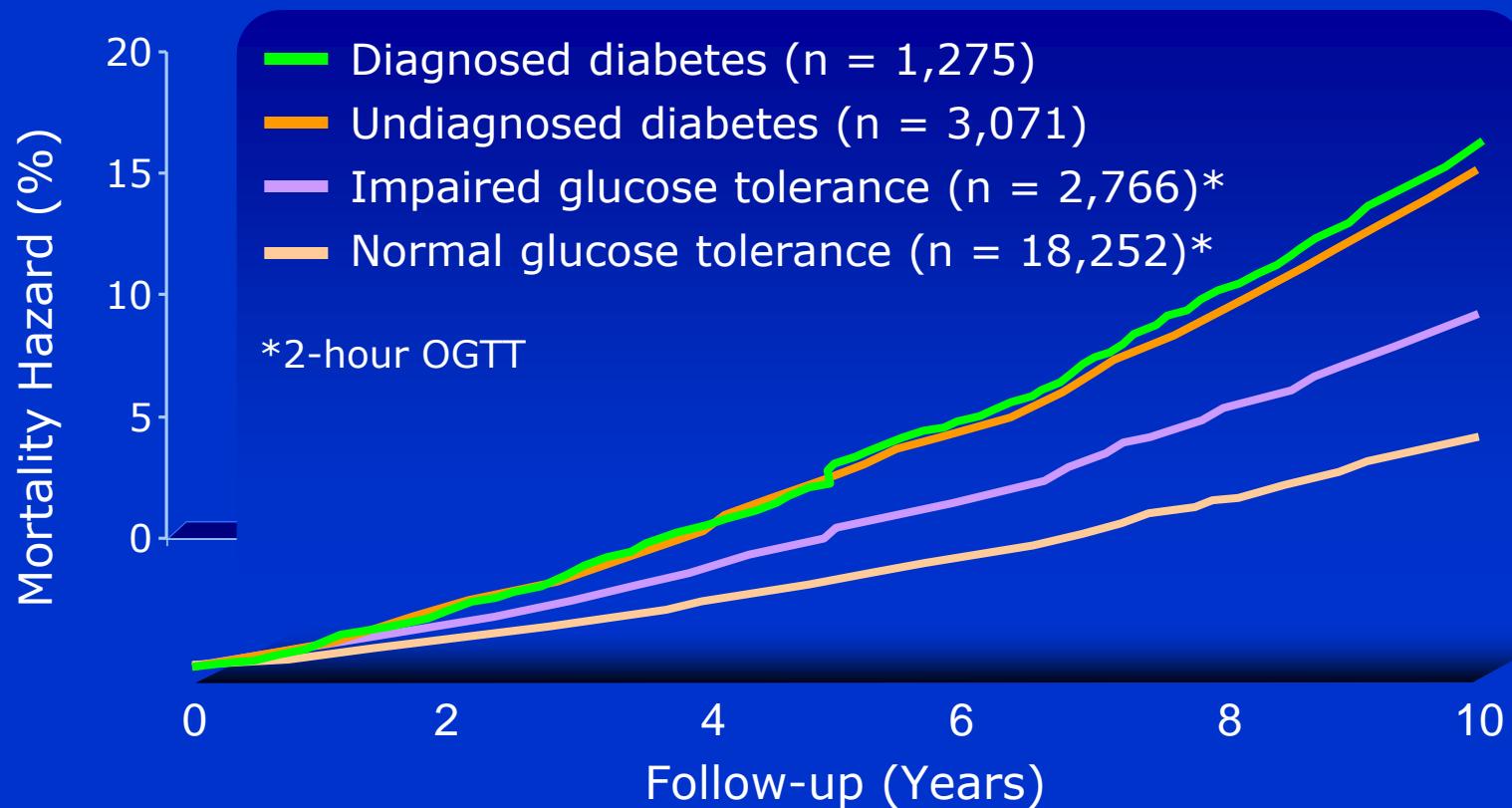
AusDiab = Australian Diabetes, Obesity, and Lifestyle Study; CVD = cardiovascular; KDM = known diabetes mellitus; NDM = newly diagnosed diabetes mellitus; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; NGT = normal glucose tolerance

Reprinted from Barr EL, et al. *Circulation*. 2007;116:151–157, with permission from Lippincott Williams & Wilkins.

Slide Source:
Lipids Online Slide Library
www.lipidsonline.org

Impaired Glucose Tolerance Increases Mortality Risk: The DECODE Study

N = 25,364 Men and Women \geq 30 Years of Age



DECODE = Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe;
OGTT = oral glucose tolerance test

Reprinted from DECODE Study Group. *Lancet*. 1999;
354:617–621, with permission from Elsevier.

Slide Source:
Lipids Online Slide Library
www.lipidsonline.org



Annals of Medicine, 2014; 46: 684–692

© 2014 Informa UK, Ltd.

ISSN 0785-3890 print/ISSN 1365-2060 online

DOI: 10.3109/07853890.2014.955051

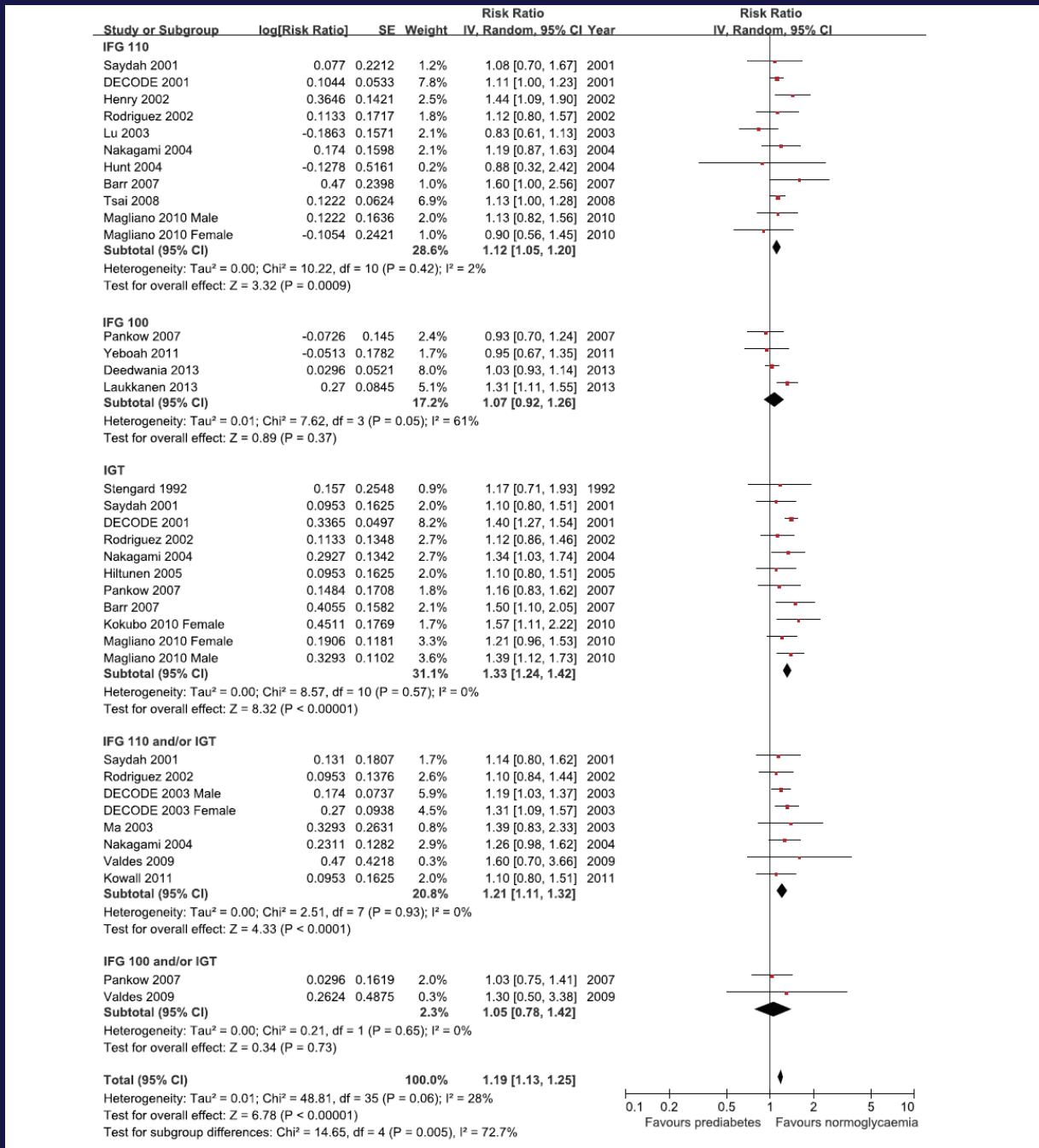


ORIGINAL ARTICLE

Associations of prediabetes with all-cause and cardiovascular mortality: A meta-analysis

Yi Huang¹, Xiaoyan Cai¹, Peisong Chen², Weiyi Mai³, Hongfeng Tang¹, Yuli Huang^{1,4} & Yunzhao Hu^{1,4}

¹Clinical Medicine Research Institute, the Affiliated Hospital at Shunde, Southern Medical University, Foshan, PR China, ²Department of Laboratory Medicine, the First Affiliated Hospital of Sun Yat-sen University, Guangzhou, PR China, ³Department of Cardiology, the First Affiliated Hospital of Sun Yat-sen University, Guangzhou, PR China, and ⁴Department of Cardiology, the First People's Hospital of Shunde, Foshan, PR China



Prediabetes

- Long-term consequences include
 - Hypertension¹
 - Cancer²
 - Risk increased by 15%
 - Stomach/colorectal, liver, pancreas, breast, endometrium
 - Alzheimer's disease³

ΕΛΕΓΧΟΣ ΓΙΑ ΠΡΟΔΙΑΒΗΤΗ



Recommendations: Prediabetes

- Testing should begin at age 45 for all patients, particularly those who are overweight or obese.
- Consider testing for prediabetes in asymptomatic adults of any age w/ BMI $\geq 25 \text{ kg/m}^2$ or $\geq 23 \text{ kg/m}^2$ (in Asian Americans) who have 1 or more additional risk factors for diabetes.
- If tests are normal, repeat at a minimum of 3-year intervals.

Recommendations: Prediabetes (2)

- FPG, 2-h PG after 75-g OGTT, and A1C, are equally appropriate for prediabetes testing.
- In patients with prediabetes, identify and, if appropriate, **treat other CVD risk factors**.
- Consider prediabetes testing in **overweight/obese children and adolescents with 2 or more additional diabetes risk factors**.

ARE YOU AT RISK FOR

TYPE 2 DIABETES?



Diabetes Risk Test

1 How old are you?

- Less than 40 years (0 points)
40–49 years (1 point)
50–59 years (2 points)
60 years or older (3 points)

Write your score
in the box.

2 Are you a man or a woman?

- Man (1 point) Woman (0 points)

3 If you are a woman, have you ever been diagnosed with gestational diabetes?

- Yes (1 point) No (0 points)

4 Do you have a mother, father, sister, or brother with diabetes?

- Yes (1 point) No (0 points)

5 Have you ever been diagnosed with high blood pressure?

- Yes (1 point) No (0 points)

6 Are you physically active?

- Yes (0 points) No (1 point)

7 What is your weight status?
(see chart at right)

If you scored 5 or higher:

You are at increased risk for having type 2 diabetes. However, only your doctor can tell for sure if you do have type 2 diabetes or prediabetes (a condition that precedes type 2 diabetes in which blood glucose levels are higher than normal). Talk to your doctor to see if additional testing is needed.

Type 2 diabetes is more common in African Americans, Hispanics/Latinos, American Indians, and Asian Americans and Pacific Islanders.

Higher body weights increase diabetes risk for everyone. Asian Americans are at increased diabetes risk at lower body weights than the rest of the general public (about 15 pounds lower).

For more information, visit us at diabetes.org or call 1-800-DIABETES (1-800-342-2383)

Add up
your score.

Height	Weight (lbs.)		
4' 10"	119-142	143-190	191+
4' 11"	124-147	148-197	198+
5' 0"	128-152	153-203	204+
5' 1"	132-157	158-210	211+
5' 2"	136-163	164-217	218+
5' 3"	141-168	169-224	225+
5' 4"	145-173	174-231	232+
5' 5"	150-179	180-239	240+
5' 6"	155-185	186-246	247+
5' 7"	159-190	191-254	255+
5' 8"	164-196	197-261	262+
5' 9"	169-202	203-269	270+
5' 10"	174-208	209-277	278+
5' 11"	179-214	215-285	286+
6' 0"	184-220	221-293	294+
6' 1"	189-226	227-301	302+
6' 2"	194-232	233-310	311+
6' 3"	200-239	240-318	319+
6' 4"	205-245	246-327	328+

(1 Point) (2 Points) (3 Points)

You weigh less than the amount
in the left column
(0 points)

Adapted from Bang et al., Ann Intern Med
151:775-783, 2009.
Original algorithm was validated without
gestational diabetes as part of the model.

Lower Your Risk

The good news is that you can manage your risk for type 2 diabetes. Small steps make a big difference and can help you live a longer, healthier life. If you are at high risk, your first step is to see your doctor to see if additional testing is needed. Visit diabetes.org or call 1-800-DIABETES (1-800-342-2383) for information, tips on getting started, and ideas for simple, small steps you can take to help lower your risk.

Visit us on Facebook
Facebook.com/AmericanDiabetesAssociation

Figure 2.1—ADA risk test.

ΘΕΡΑΠΕΙΑ ΠΡΟΔΙΑΒΗΤΗ

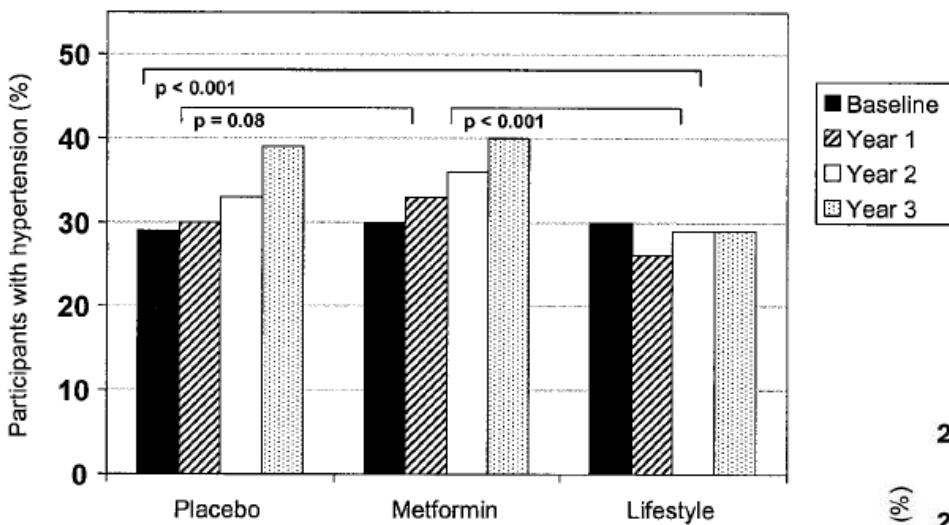


Recommendations: Prevention or Delay of T2DM

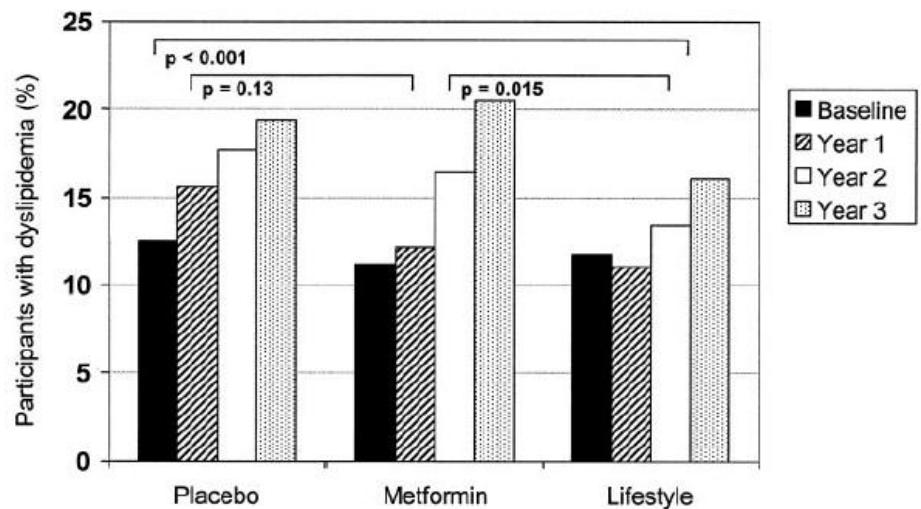
- Patients with prediabetes should be referred to an **intensive diet and physical activity behavioral counseling** program targeting a loss of 7% of body weight, and should increase their **moderate physical activity** to at least 150 min/week.
- **Metformin therapy** for prevention of type 2 diabetes should be considered in those with prediabetes, especially for those with BMI $>35 \text{ kg/m}^2$, aged $< 60 \text{ years}$, and women with prior **gestational diabetes**, those with rising A1C despite lifestyle intervention.

Impact of Intensive Lifestyle and Metformin Therapy on Cardiovascular Disease Risk Factors in the Diabetes Prevention Program

Diabetes Care 28:888–894, 2005



3,234 individuals with IGT



Risk Stratification¹ 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 $\geq 25 \text{ kg/m}^2$	✓	✓	✓
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 $\geq 40 \text{ kg/m}^2$ with no risk factors or $\geq 35 \text{ kg/m}^2$ 1 or more severe obesity-related co-morbidities and/or if no weight loss after lifestyle modification and/or metformin therapy

Lifestyle Modification Facilitating Weight Loss

- Reduce caloric intake by 500-1000 kcal/day (depending on starting weight)
- Reduce dietary fat
- Limit intake of sugar-sweetened beverages
- Dietary fiber intake of 14 grams/1000 kcal
- Whole grains are 50% of grain intake
- 5-7 servings of fruits and vegetables a day

Antiobesity drugs approved by FDA

Drug	Dosage	Mechanism of action	Common adverse events	Date of FDA approved
Lorcaserin (Belviq)	10 mg oral twice daily	5-HT _{2c} agonist	Headache, upper respiratory tract infection, dizziness, nausea, constipation, and fatigue	June 27, 2012
Phentermine/ topiramate (Qsymia)	7.5 mg of phentermine/46 mg of topiramate ER once daily	Phentermine (amphetamine that increases the release of noradrenaline, dopamine and serotonin)/ topiramate(anticonvulsant, precise mechanism of action unknown)	Dry mouth, unpleasant taste, diarrhea, constipation, vomiting, headache, insomnia	July 17, 2012
Naltrexone/ bupropion (Contrave)	8 mg of naltrexone/90 mg of bupropion 2 tablets twice daily	Naltrexone (μ -opioid receptor agonist)/ bupropion (dopamine and noradrenaline reuptake inhibitor)	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, and diarrhea	September 10, 2014
Liraglutide (Saxenda)	3 mg subcutaneous injection once daily	Long-acting GLP-1 analog	Nausea, diarrhea, constipation, hypoglycemia, headache, decreased appetite, pancreatitis, kidney failure, gallbladder problems and increased heart rate	December 23, 2014

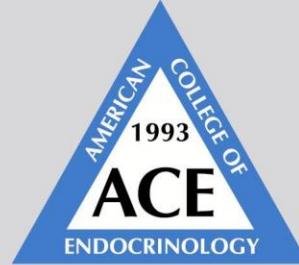


Overweight/Obesity Treatment

	Body Mass Index Category (kg/m ²)				
Treatment	23.0* or 25.0-26.9	27.0-29.9	30.0-34.9	35.0-39.9	≥40
Diet, physical activity & behavioral therapy	+	+	+	+	+
Pharmacotherapy		+	+	+	+
Bariatric surgery				+	+

* Asian-American individuals

† Treatment may be indicated for selected, motivated patients.



AACE/ACE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM

2017

TASK FORCE

Alan J. Garber, MD, PhD, FACE, *Chair*

Martin J. Abrahamson, MD

Joshua I. Barzilay, MD, FACE

Lawrence Blonde, MD, FACP, FACE

Zachary T. Bloomgarden, MD, MACE

Michael A. Bush, MD

Samuel Dagogo-Jack, MD, DM, FRCP, FACE

Ralph A. DeFronzo, MD

Daniel Einhorn, MD, FACP, FACE

Vivian A. Fonseca, MD, FACE

Jeffrey R. Garber, MD, FACP, FACE

W. Timothy Garvey, MD, FACE

George Grunberger, MD, FACP, FACE

Yehuda Handelsman, MD, FACP, FNLA, FACE

Robert R. Henry, MD, FACE

Irl B. Hirsch, MD

Paul S. Jellinger, MD, MACE

Janet B. McGill, MD, FACE

Jeffrey I. Mechanick, MD, FACP, FACE, FACN, ECNU

Paul D. Rosenblit, MD, PhD, FNLA, FACE

Guillermo Umpierrez, MD, FACP, FACE



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

1 PRE-DM
CRITERION

Intensify
Weight
Loss
Therapies

MULTIPLE PRE-DM
CRITERIA

Low-risk
Medications

Metformin
Acarbose

Consider with
Caution

TZD
GLP-1 RA

LEGEND

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

PROCEED TO
HYPERGLYCEMIA
ALGORITHM

If glycemia
not normalized

ΠΑΡΑΚΟΛΟΥΘΗΣΗ ΕΞΕΛΙΞΗΣ ΠΡΟΔΙΑΒΗΤΗ



ΕΤΗΣΙΟΣ ΕΛΕΓΧΟΣ

- Γλυκόζη
- HbA1c
- Καμπύλη σακχάρου (σε επιδείνωση)
- Προφίλ λιπιδίων
- Αρτηριακή πίεση
- Μικροαλβουμινουρία

ΣΥΜΠΕΡΑΣΜΑΤΙΚΑ....

ΠΡΟΛΗΠΤΙΚΟΣ ΕΛΕΓΧΟΣ ΣΑΚΧΑΡΟΥ: ΕΓΚΑΙΡΗ ΔΙΑΓΝΩΣΗ ΠΡΟΔΙΑΒΗΤΗ

- Ηλικία > 45 ετών
- Περιφέρεια μέσης >102 cm (άντρες) και >88 cm (γυναίκες)
- Δείκτης μάζας σώματος >30 kg/m²
- Θετικό οικογενειακό ιστορικό για ΣΔ2
- Ιστορικό αρτηριακής υπέρτασης ή άλλης καρδιαγγειακής νόσου
- Ιστορικό ΣΔ κύησης
- Γυναίκες με σύνδρομο πολυκυστικών ωοθηκών
- Λήψη φαρμάκων που ευνοούν την δυσγλυκαιμία (π.χ. κορτιζόνη)

I'm Not Diabetic...

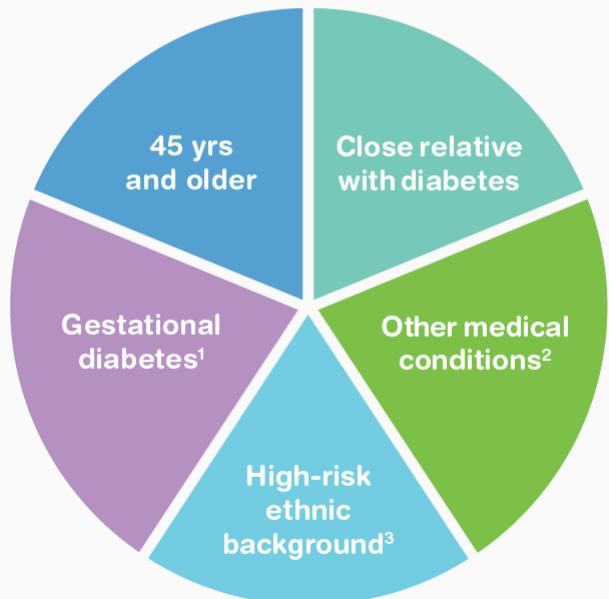


I'm Pre-diabetic...

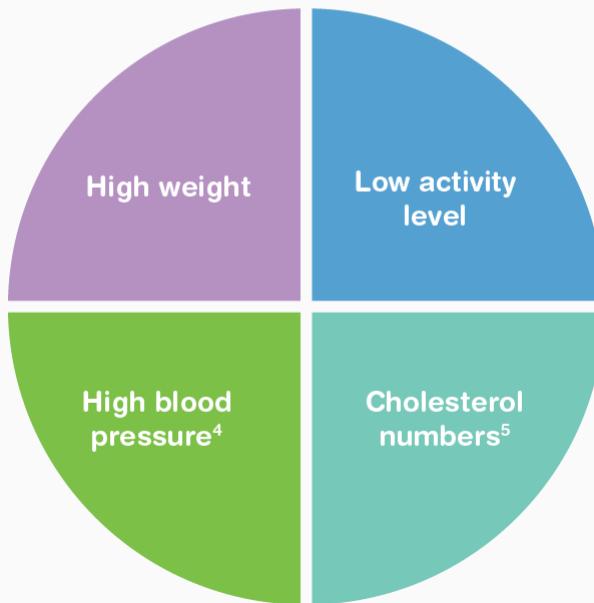
Now what can you do for me!

RISK FACTORS

FACTORS YOU CAN'T FIX

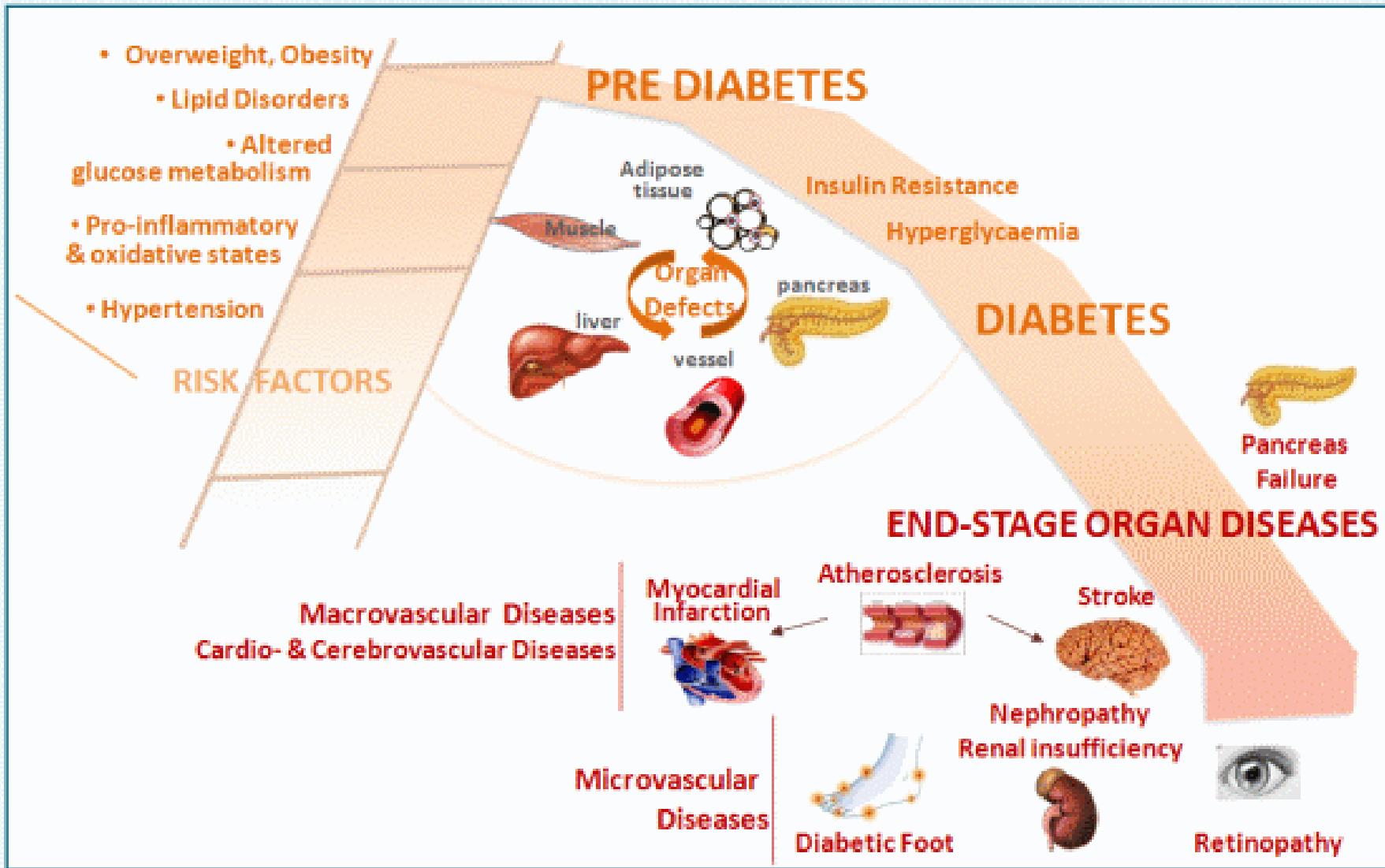


FACTORS YOU CAN IMPROVE



Prediabetes - Diabetes

A Deleterious Progression





**26 million
with Diabetes**

**79 million
with
Pre-Diabetes**



DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION



ΕΥΧΑΡΙΣΤΩ ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ ΣΑΣ!

