

# The Tsunami of Prediabetes: What is It, Why Do We Care?

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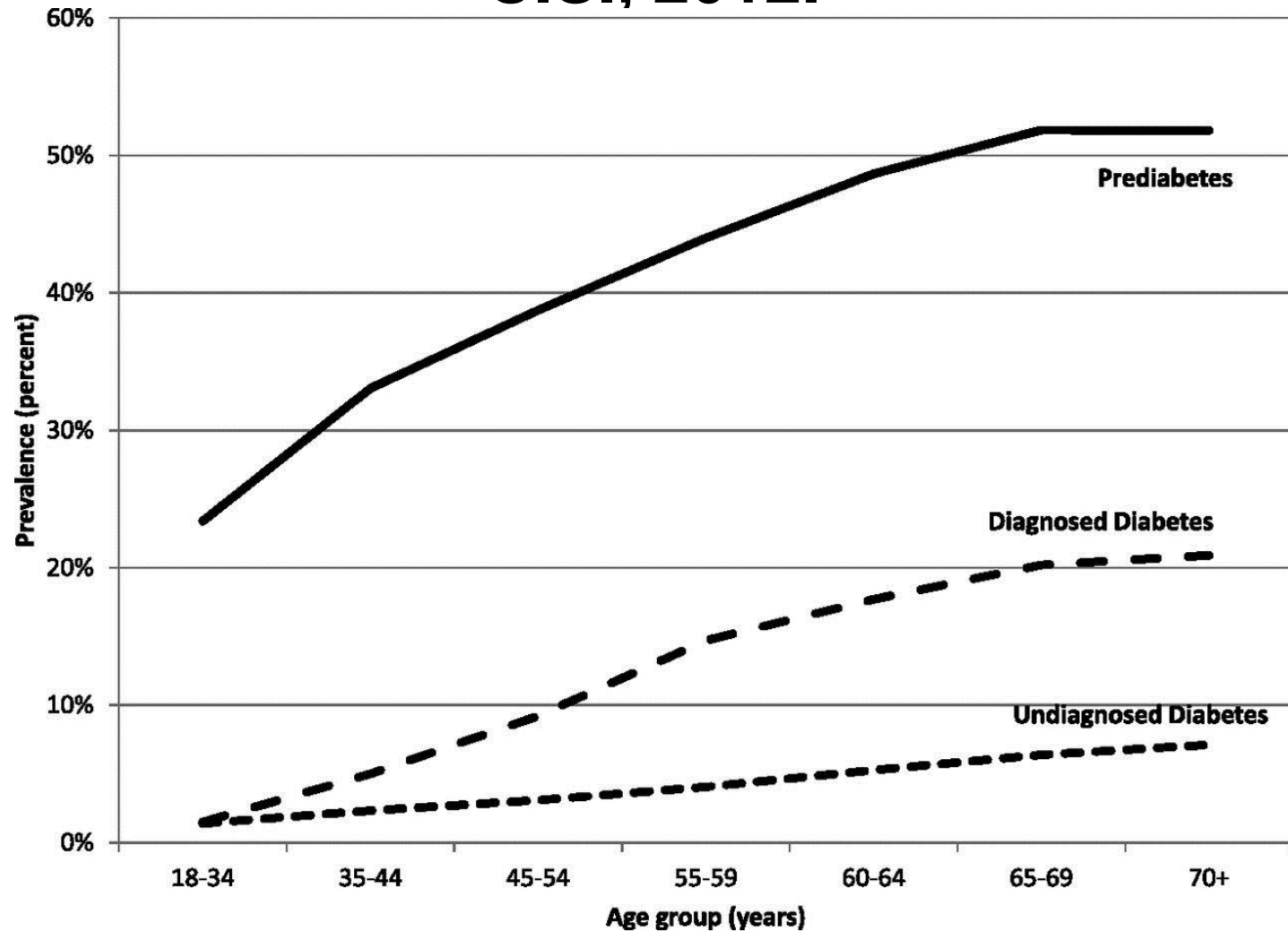
# Disclosures

- Advisor and speaker for: Astra Zeneca, Boehringer Ingelheim, Eli Lilly, Janssen, Novo Nordisk, sanofi
- Speaker for Insulet
- Advisor for Becton Dickenson

# Outline

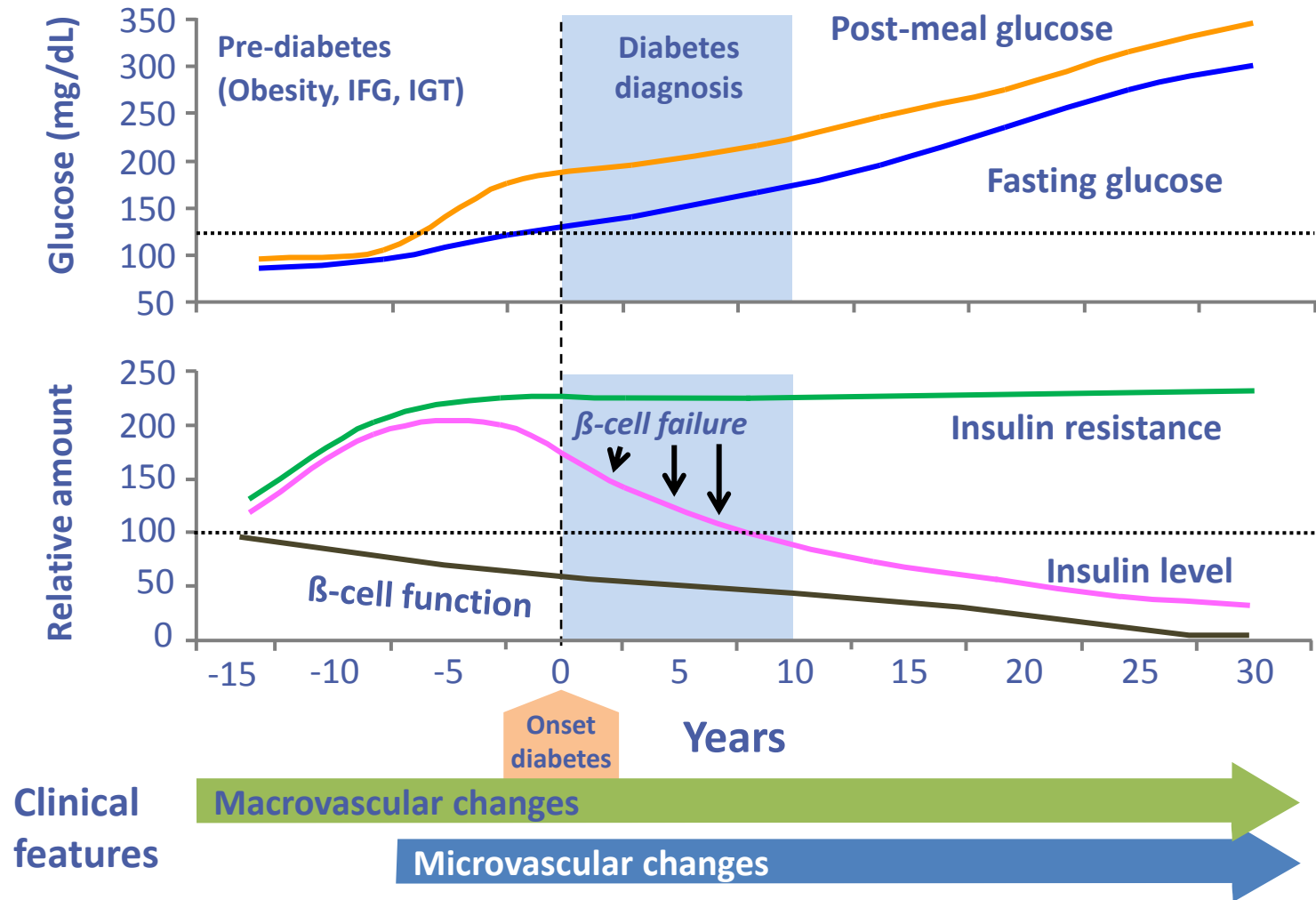
- Prevalence of diabetes and prediabetes
- Rate of progression of prediabetes to diabetes
- Risk factors for prediabetes/diabetes
- Complications of prediabetes
- Screening for prediabetes
- Prevention trials
- CVD Outcomes (CVOT, CIMT study, Acarbose study, DA Qing study, ADDITION study)
- CV risk factor treatment
- Cost effectiveness

# Prevalence of diabetes and prediabetes in the U.S., 2012.



Timothy M. Dall et al. Dia Care 2014;37:3172-3179

# T2DM is a multifaceted, progressive disease



- Assessing dysglycemia is vital in guiding treatment throughout the continuum
- Crucial to understand/apprehend the merits of new basal insulins

# Who Is At Risk for Prediabetes?

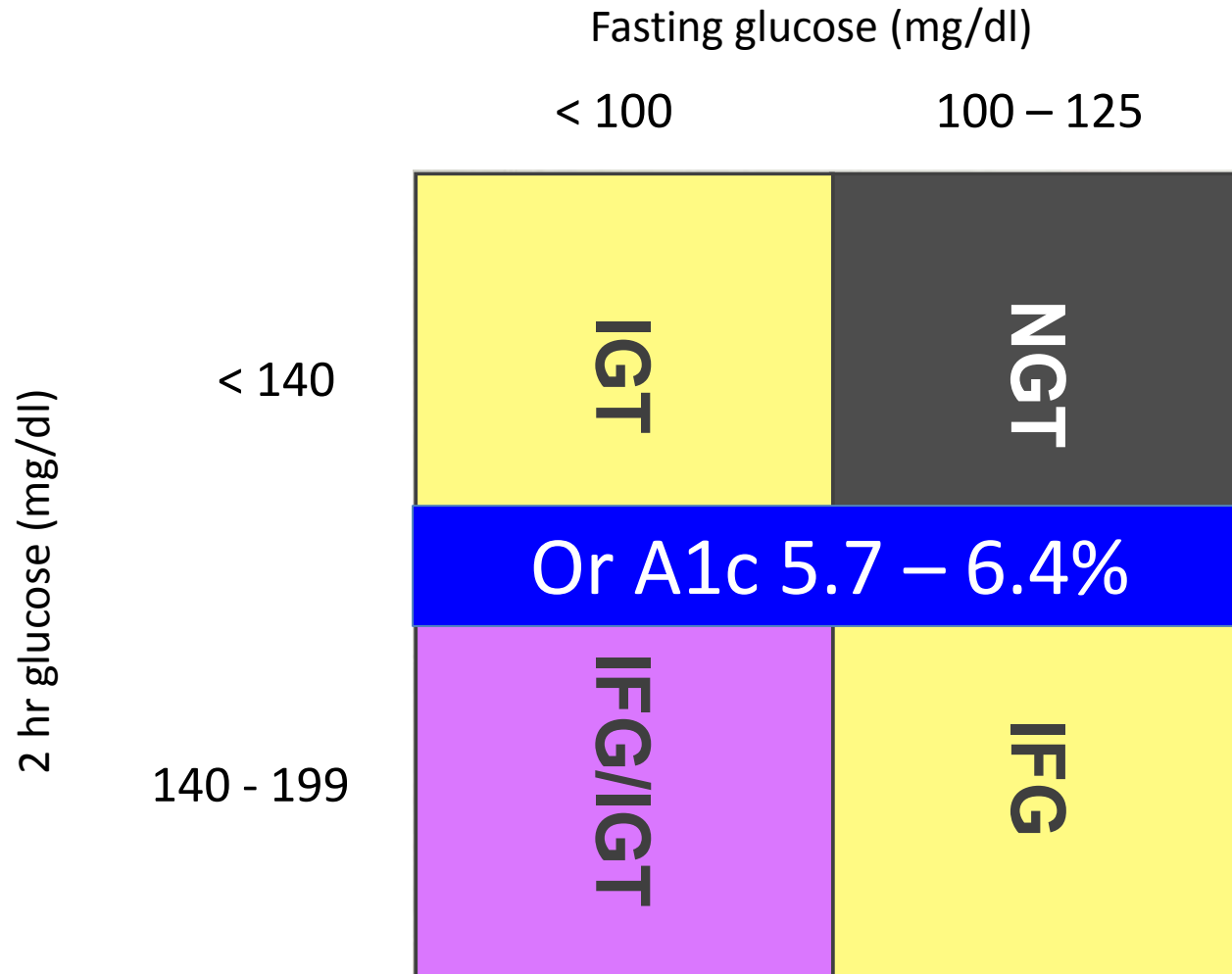
- Age 45 or older
- Overweight (BMI  $\geq$  25 (23 in Asians))
- Inactivity
- Ethnic or minority population
- Family history of diabetes
- Excess abdominal fat
- High blood pressure
- Dyslipidemia (HDL  $<$ 35 mg/dl, TG  $>$  250 mg/dl)
- Acanthosis nigricans
- Polycystic ovary syndrome
- History of gestational diabetes
- Delivery of baby  $\geq$  9 lbs

# Preferred screening test?

- Fasting glucose (100-125 mg/dl)
- 2-hour post-OGTT glucose (140-199 mg/dl)
- A1c (5.7-6.4%)

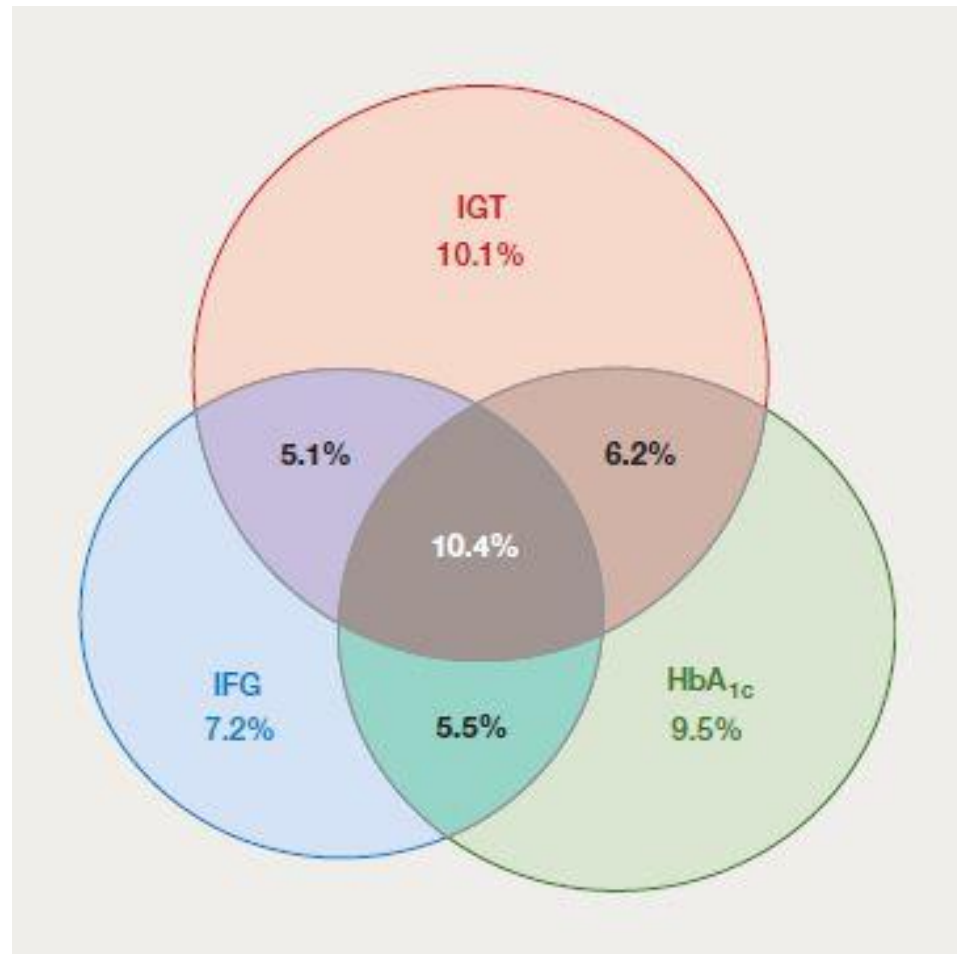
**Confirm on 2<sup>nd</sup> test**

# ADA Glucose Criteria for Prediabetes





# Classification of Prediabetes



# Systematic Review of the Incidence of Diabetes Associated with Various Categories of Glycemia

	Number of studies	Regress to normal (median %)	Progress to Diabetes (median %)	Relative Risk of Diabetes
Impaired Glucose Tolerance	26	8%	7%	6.4 (4.9 – 7.8)
IGT Isolated	3	n/a	6%	5.5 (3.1 – 7.9)
IFG	6	13 – 29%	5-20%*	4.7 (2.5 – 6.9)
IFG Isolated	3	n/a	7%	7.5 (4.6 – 10.5)
IGT and IFG	3	n/a	10-15%	12.1 (4.3 – 20)

\*extremely variable; 1-7% in European pops; 23-34% in Asian pops.

# Annual Rate of Progression from Prediabetes to Diabetes

- By A1c<sup>1</sup>
  - 5.5 – 6%: 2 – 5%
  - 6 – 6.5%: 5 - 10% (20 times higher than A1c 5%)
- These numbers may be 4-fold higher in Asians

1. Zhang X et al. Diab Care 2010;33:1665–1673

2. Gerstein HC et al. Diabetes Res Clin Pract 2007;78(3):305–12.

# ATP III Definition of the Metabolic Syndrome

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Defined by the presence of  $\geq 3$  risk factors

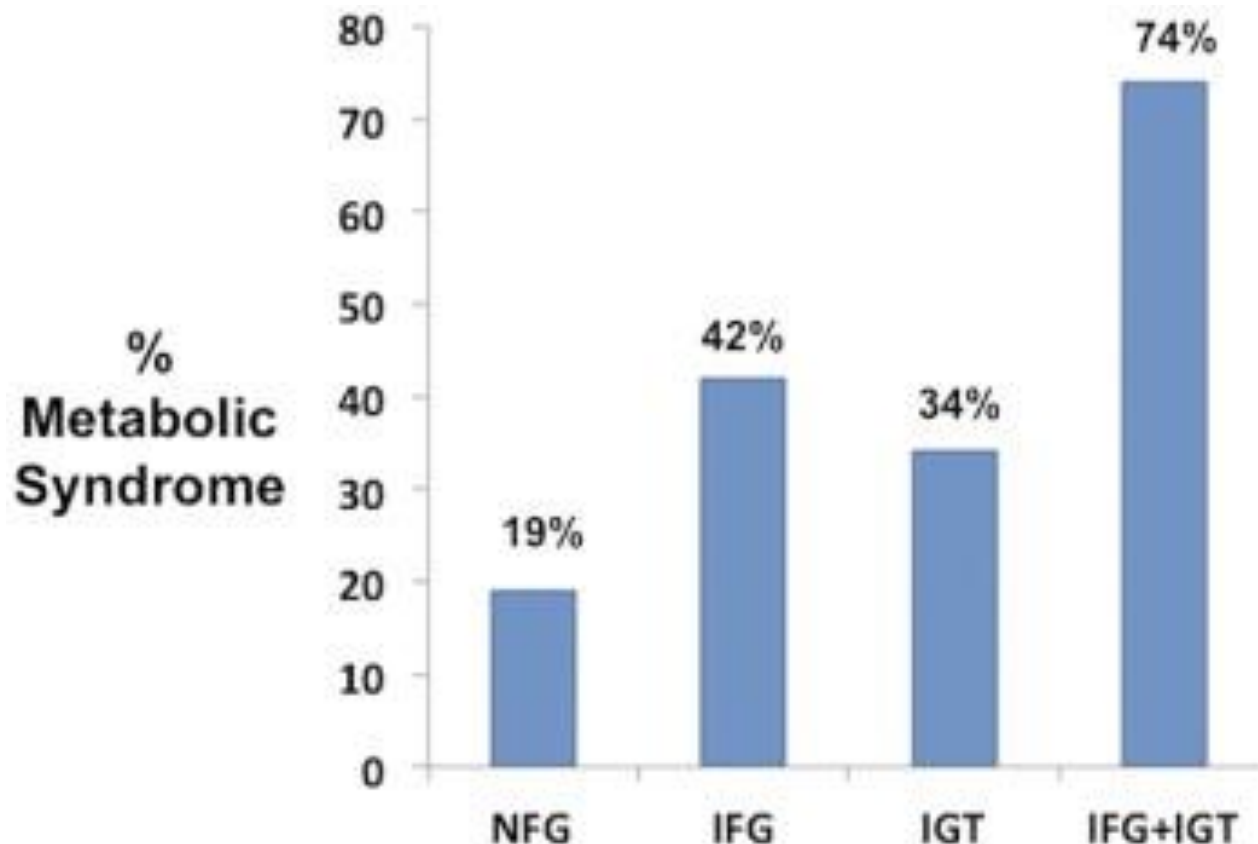
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Risk Factor	Defining Level
Waist circumference (abdominal obesity)	>40 in (>102 cm) in men >35 in (>88 cm) in women
Triglyceride level	$\geq 150$ mg/dl
HDL-C level	<40 mg/dl in men <50 mg/dl in women
Blood pressure	$\geq 130 / \geq 85$ mmHg
Fasting glucose	$\geq 100$ mg/dl

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HDL-C=High-density lipoprotein cholesterol

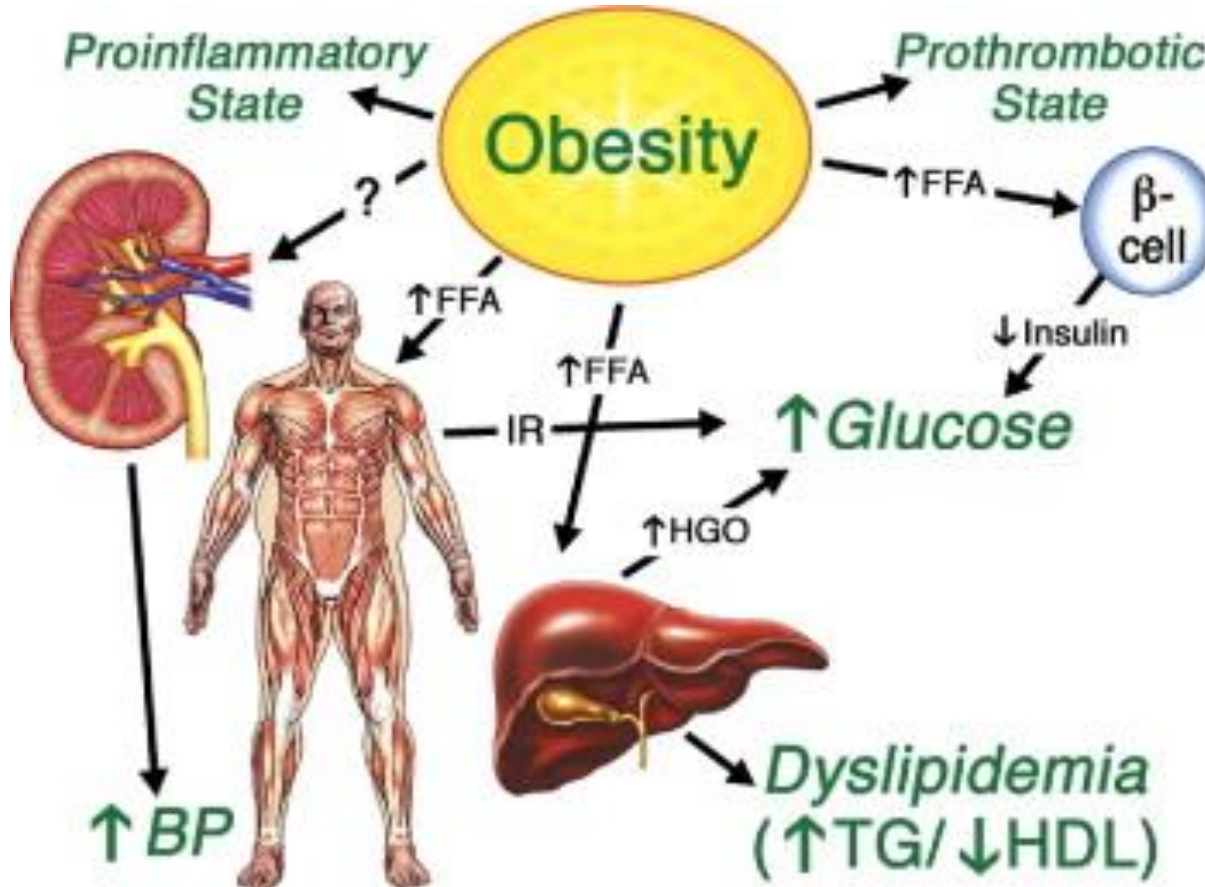
# Metabolic Syndrome is Common in Prediabetes



# Risk for Diabetes Increases with IFG and Metabolic Syndrome

Fasting glucose	Metabolic Syndrome	OR (95% CI)
Normal	No	Ref
Normal	Yes	5.03 (3.39 - 7.48)
IFG	No	7.07 (3.32 – 15.1)
IFG	Yes	21.0 (13.1 – 32.8)

# Pre-Diabetes, Metabolic Syndrome, and Cardiovascular Risk



# Hypertension Predicts Risk for Prediabetes

- OGTT performed in hypertensive patients without known diabetes
  - 54.2% impaired glucose metabolism (IGM)
    - 12.1% incidence of new diabetes
  - 48.5% metabolic syndrome (MS)
  - 36.6% had combined IGM and MS
- At least 50% of people with hypertension have insulin resistance
- Hypertension worsens the risk for complications of diabetes (? Prediabetes)



# Gestational Diabetes and the Incidence of Type 2 Diabetes: A systematic review (Kim et al., Diabetes Care, 2002)

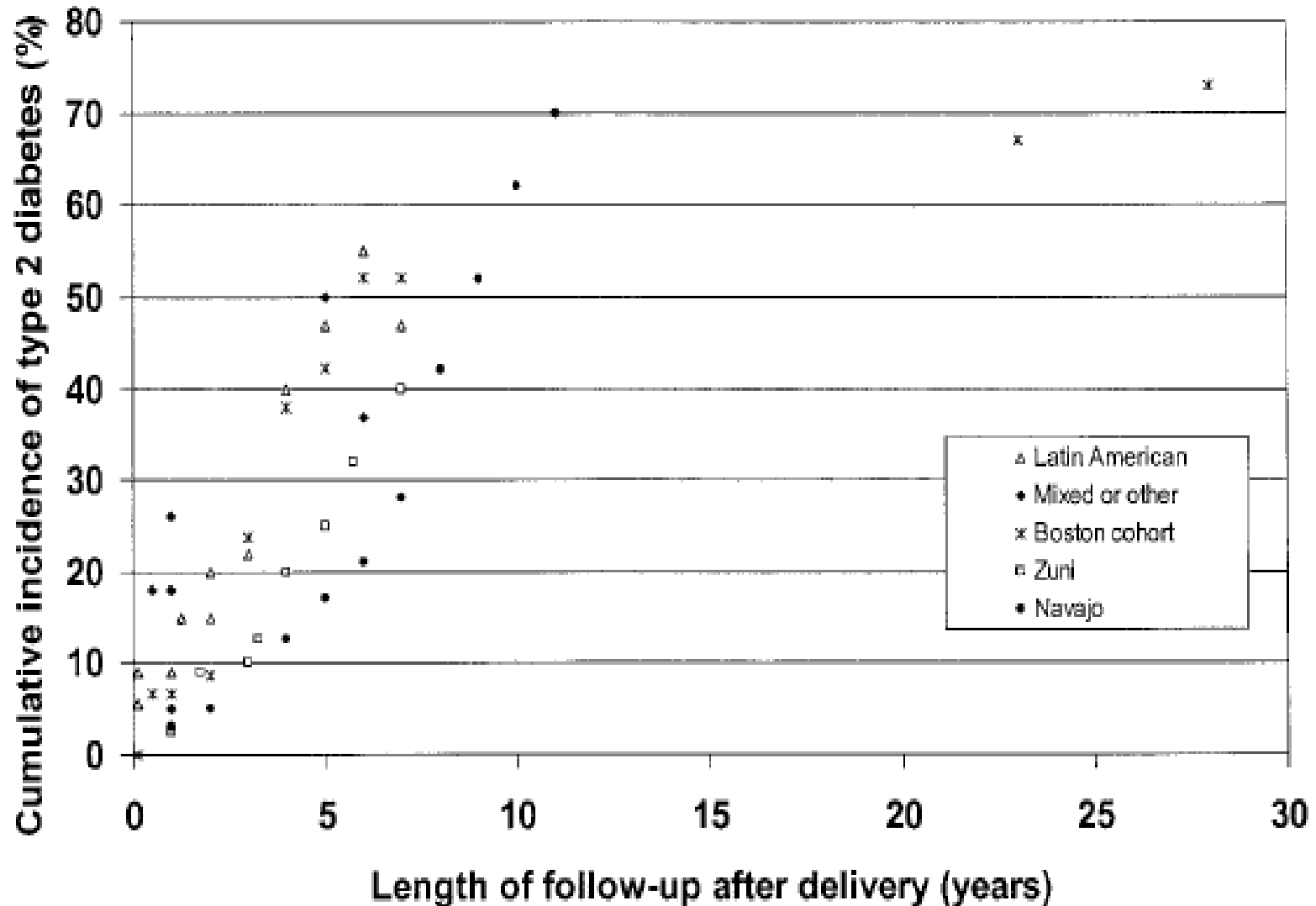


Figure 2—Cumulative incidence of type 2 diabetes by ethnicity and length of follow-up, adjusted for retention. Studies using local criteria or WHO criteria for GDM diagnosis are not illustrated.

# Prevalence of Dysglycemia in PCOS

- 30 – 40% of women with PCOS have impaired glucose tolerance
- Up to 10% have type 2 diabetes by their fourth decade
- Many have insulin resistance which is greater than that predicted by BMI alone
- Risk for development of diabetes is significantly increased, especially in those with positive FH of DM

# Prediabetes is Common in Patients with Obstructive Sleep Apnea

- Impaired glucose metabolism is 20 – 69% higher in people with obstructive sleep apnea
- OSA is present in more than 50% of people with type 2 diabetes
- Odds ratio for diagnosis of OSA is 3-fold higher in people with prediabetes

# Acanthosis Nigricans



# Prediabetes in Nonalcoholic Fatty Liver Disease

- 32 – 75% of patients with NAFLD have prediabetes<sup>1</sup>
- 14 – 16% have diabetes<sup>1</sup>
- In prediabetes, those with highest fatty liver index had an increased risk of progressing to diabetes<sup>2</sup>
  - Men: OR 2.68
  - Women: OR 10.35

1. Buysschaert M et al. Endocrine 2015;48:371-379

2. Nishi T et al. J Diabetes Invest 2015; 6: 309–316