



*The 3<sup>rd</sup> Indonesian Symposium on Heart Failure and Cardiometabolic Disease 2023*

## **UNPACKING DIABETES AND HEART FAILURE**

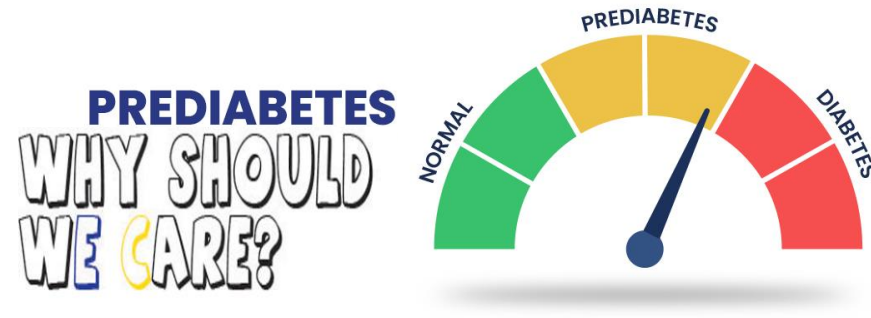
# **Prediabetes Intervention:**

*Tackling the prevalent comorbidities in heart failure*

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**Prediabetes** is associated with an **increased risk of HF**

**Prediabetes** is associated with **increased CV Death and HF hospitalizations**

**Reversion from prediabetes** is associated with a **reduction in CV Death**

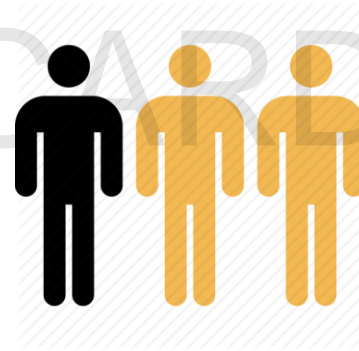


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# Cardiometabolic Risk Factors in Indonesia

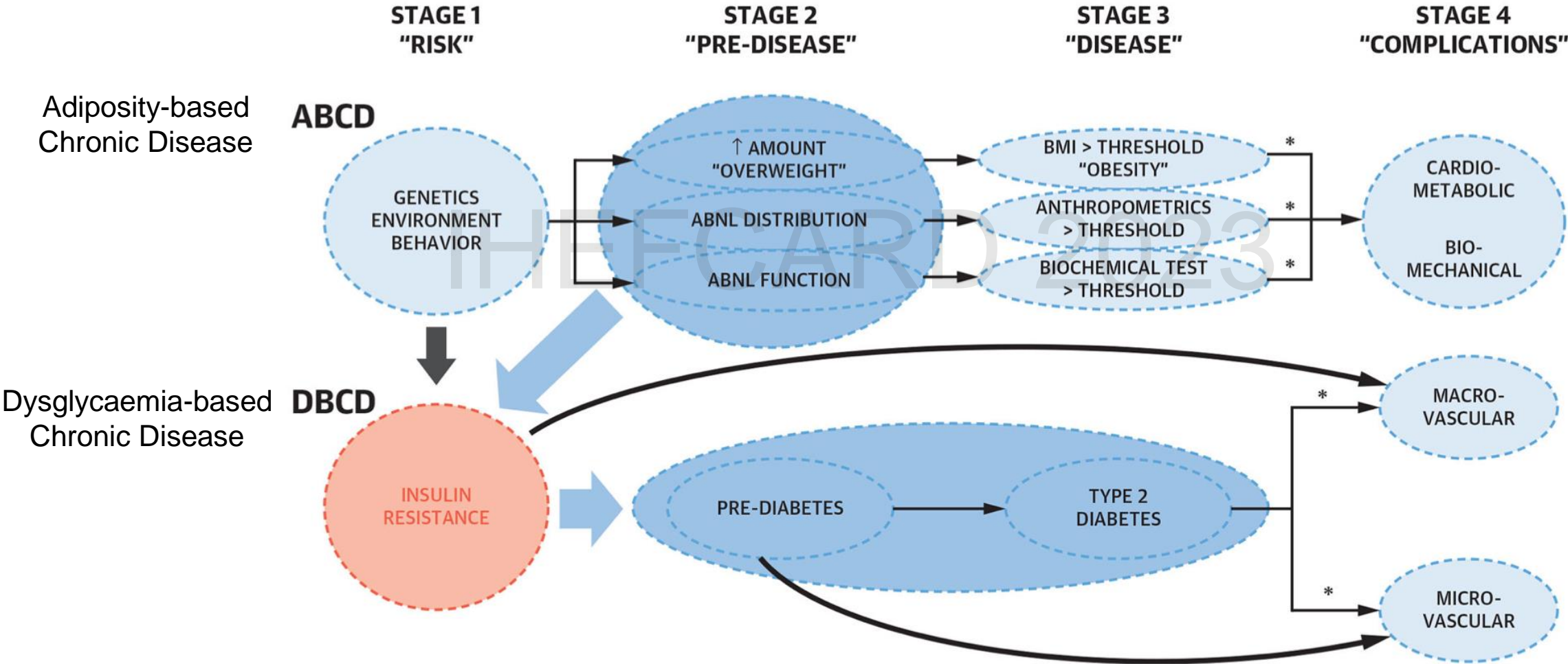


Obesity  
**Prediabetes**  
Dyslipidemia  
Hypertension

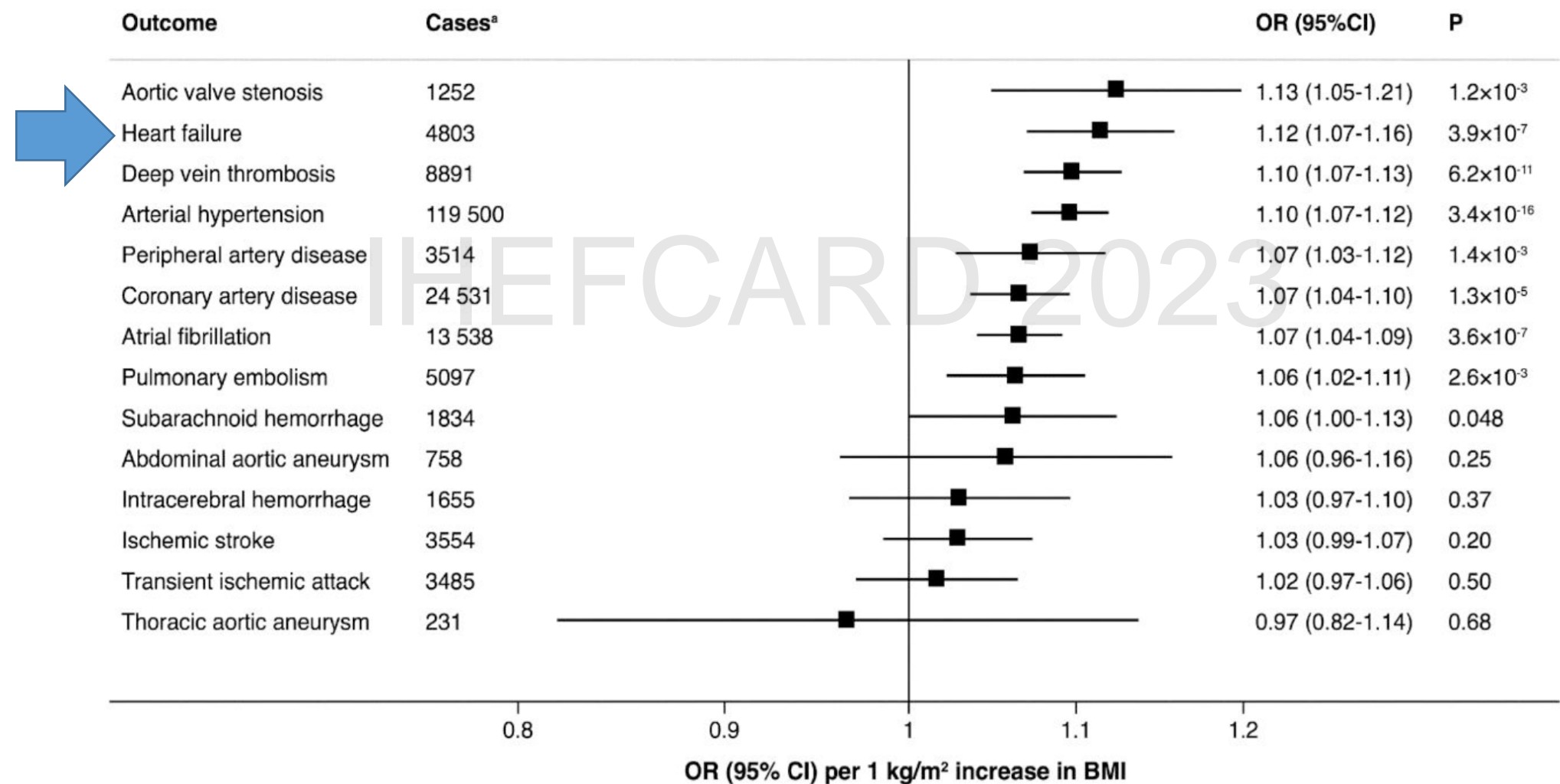
Metabolic Syndrome

IHEFOCARD 2023

# Cardiometabolic-Based Chronic Disease (CMBCD)

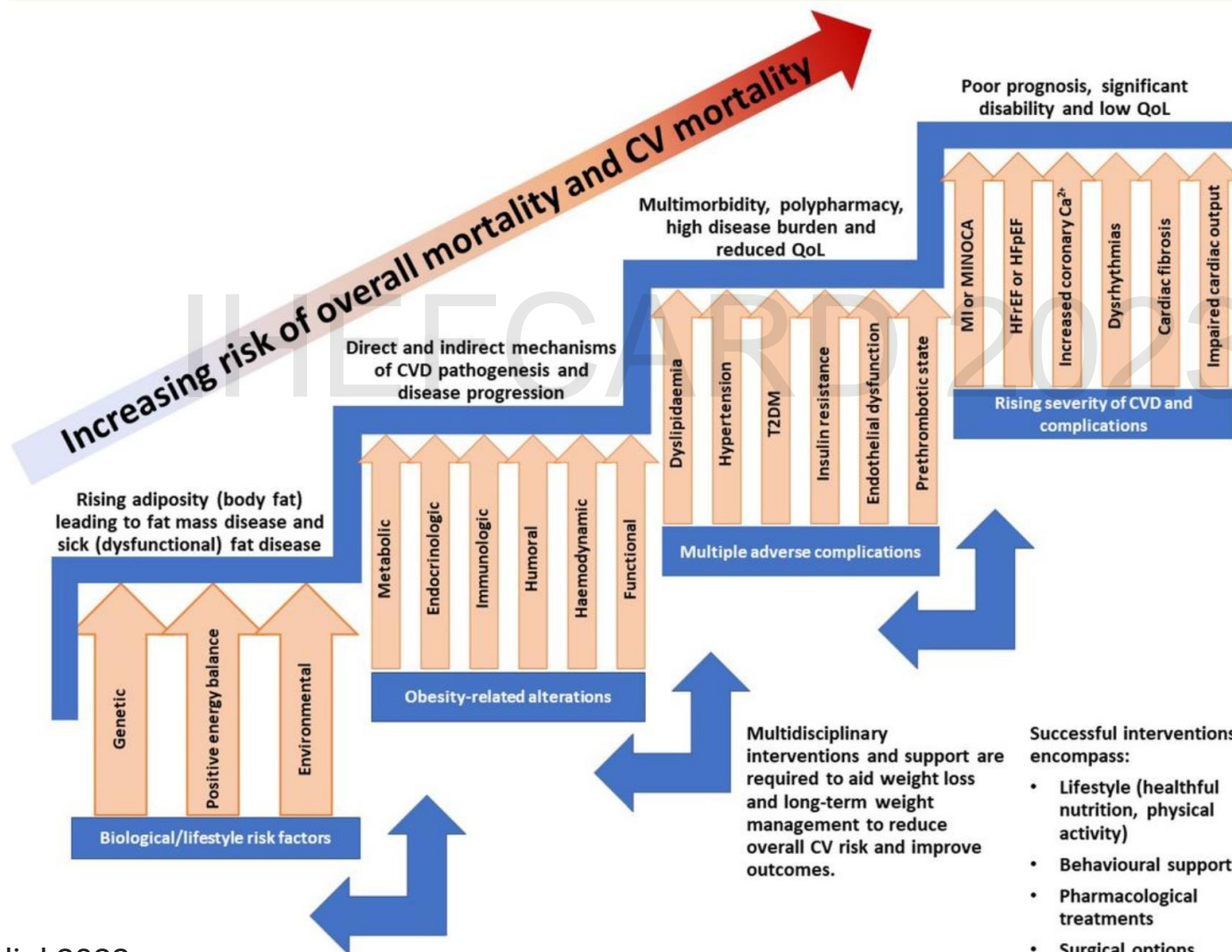


# Increasing BMI and Cardiovascular Diseases

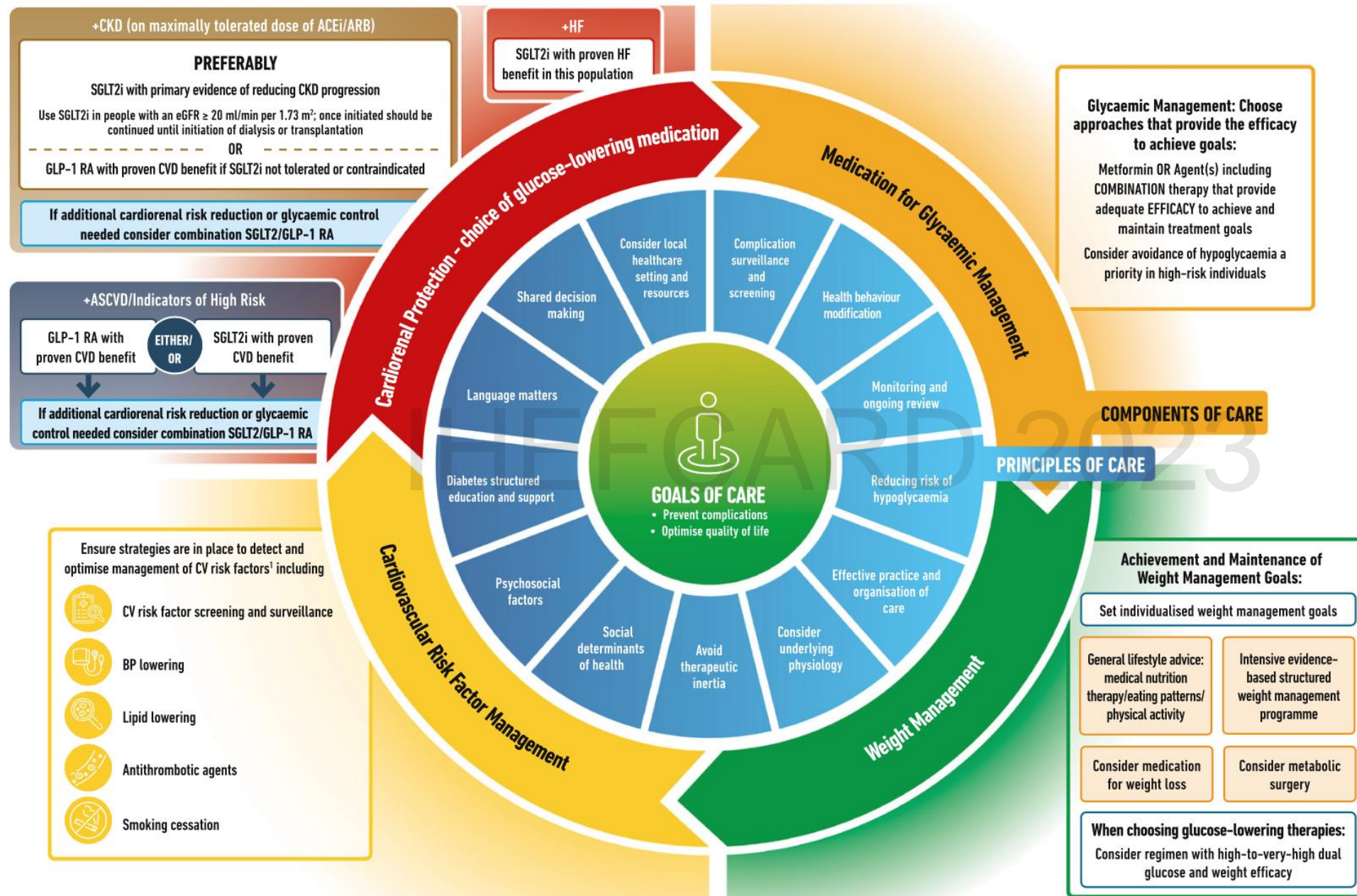




# Obesity, (Pre)Diabetes, CVD: Mechanistic Insights and Strategies

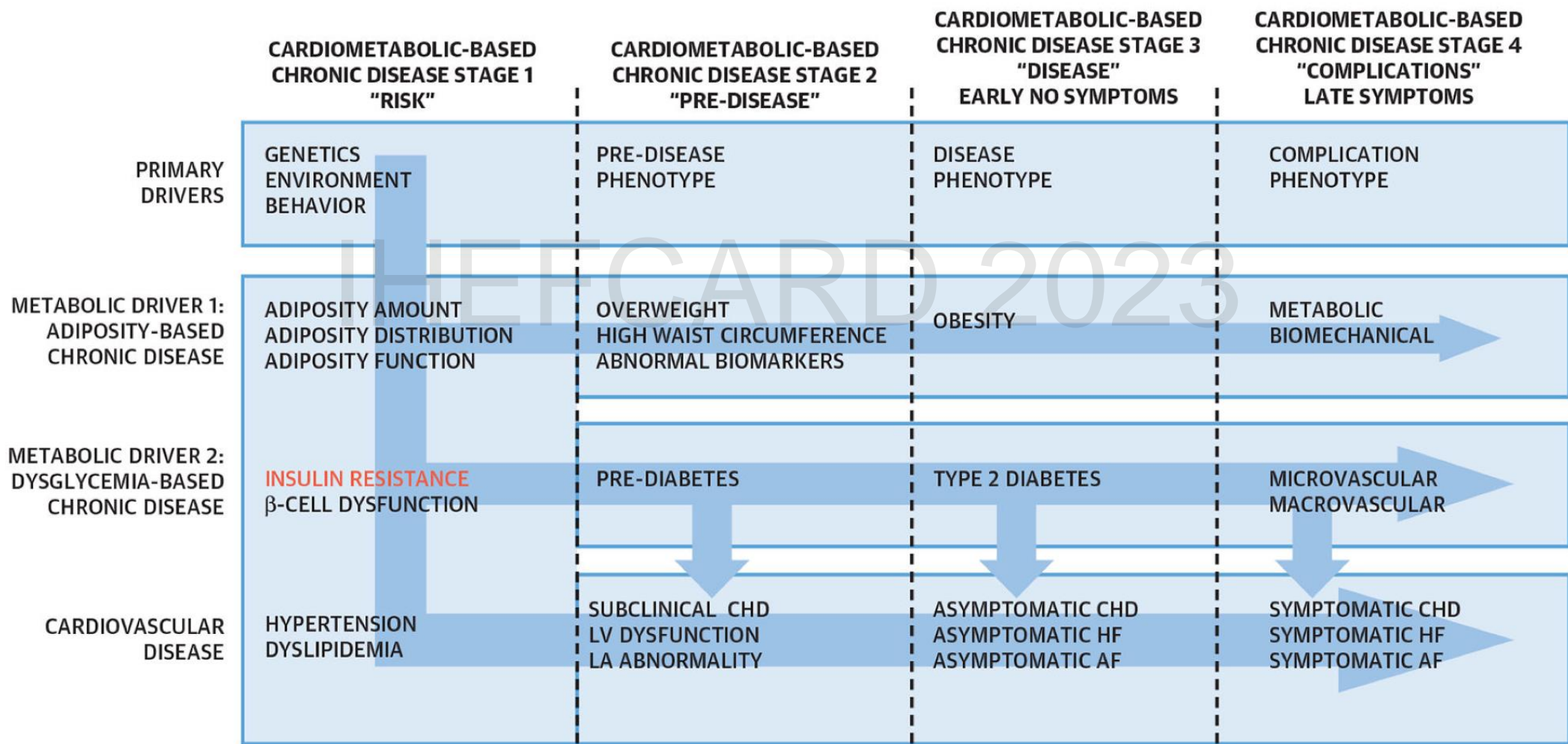


# HOLISTIC PERSON-CENTRED APPROACH TO T2DM MANAGEMENT



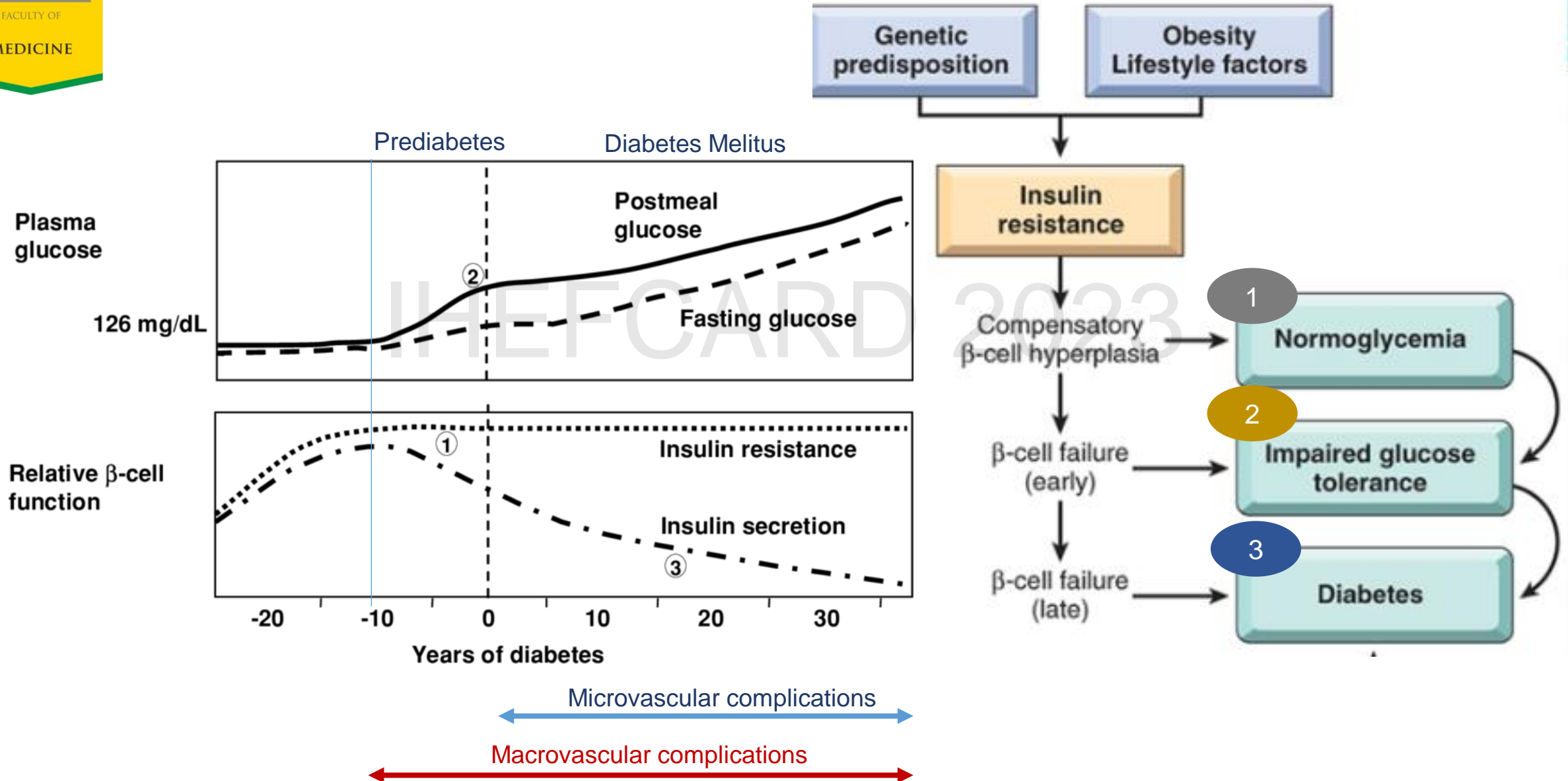


# Cardiometabolic-Based Chronic Disease (CMBCD)





# Progressive Nature of Type 2 Diabetes Mellitus





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# Prediabetes among Those with CVD

## Prediabetes and Macrovascular Disease



### Coronary Artery Disease

- 24% with prediabetes



### Stroke

- 32-34% with prediabetes



### Peripheral Artery Disease

- 26-28% with prediabetes



### Chronic Heart Failure

- 40% with prediabetes

Prediabetes

CVD



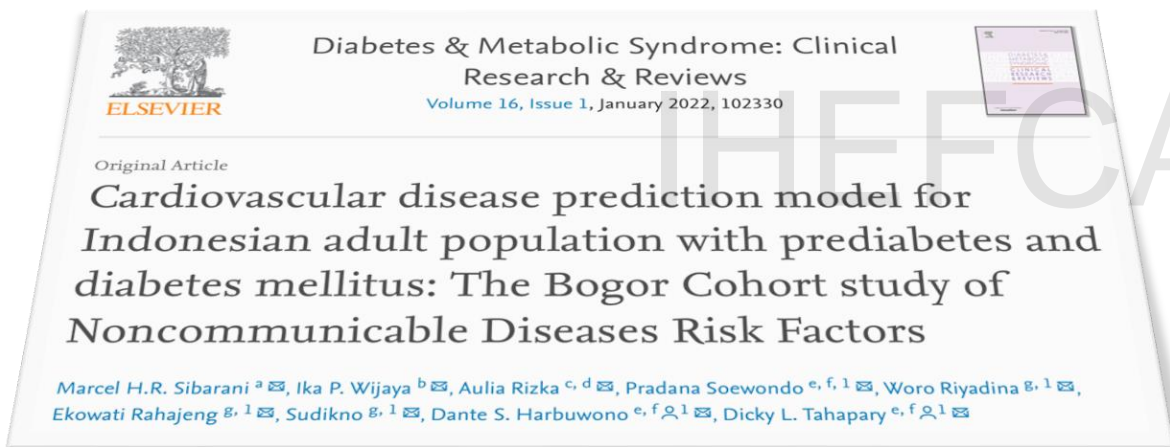
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*Veritas, Probitas, Justitia*

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## 6-Year Cardiovascular Incidences Among Prediabetes and Diabetes in Indonesia



The cumulative incidence of  
cardiovascular events in six years was 9.7%.

Predictors of cardiovascular events were  
age  $\geq 45$  years (HR = 2.737; 95% CI 1.565–4.787)  
hypertension (HR = 2.580; 95% CI 1.619–4.112).



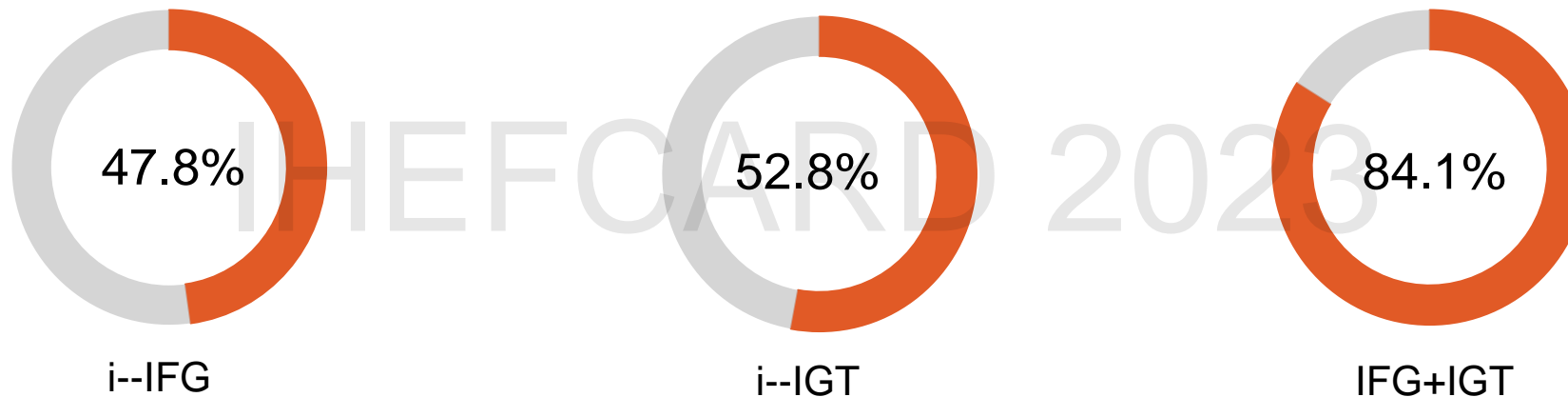
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# Prediabetes Signaled an Increased Risk of Progression to Diabetes

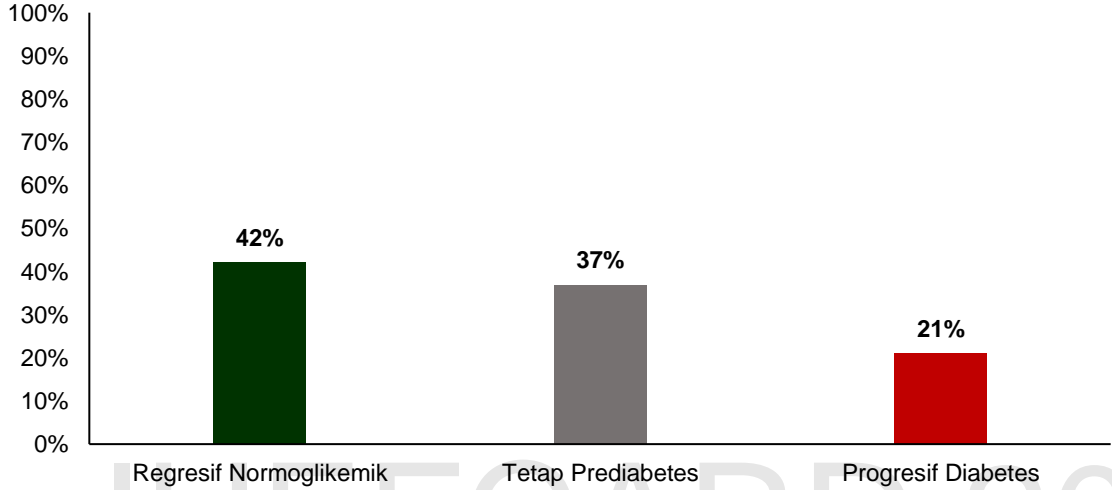
## Conversion of Pre-diabetes to Diabetes *CURES Study 10-year Follow Up*



- Incidence of Diabetes and Prediabetes and Predictors of Progression Among Asian Indians: 10-Year Follow-up of the Chennai Urban Rural Epidemiology Study (CURES): Data on progression to diabetes and prediabetes from 1,376 individuals, a subset of 2,207 of the Chennai Urban Rural Epidemiology Study (CURES) cohort (phase 3) with normal glucose tolerance (NGT) or prediabetes at baseline, who were followed for a median of 9.1 years (11,629 person-years), are presented

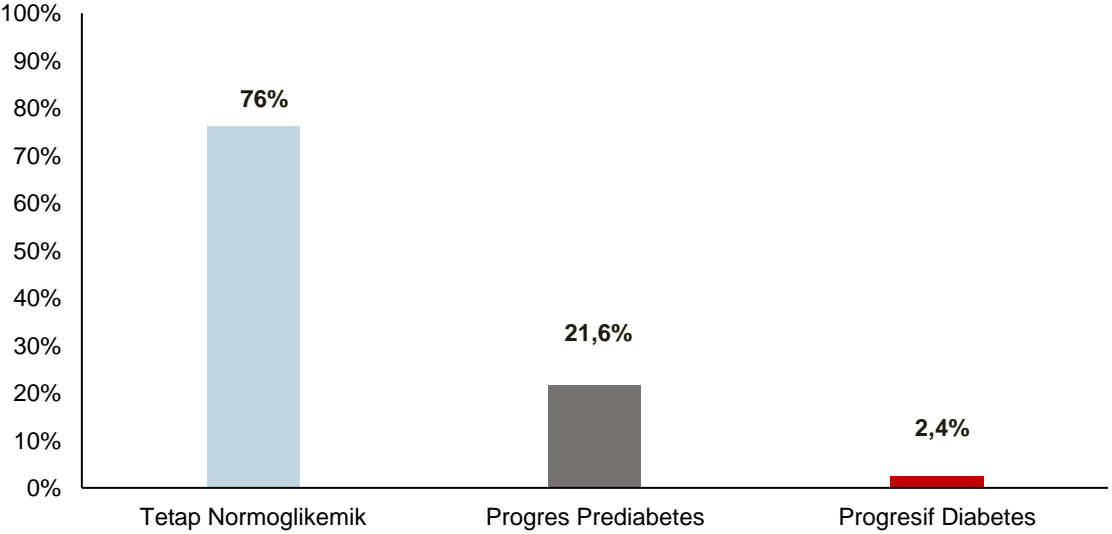


# Prediabetes Conversion in Reproductive-Age Women in Indonesia



*N=371, 5 years of follow up*

## Conversion among Normoglycemia Subjects



*N=1300, 5 years of follow up*



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# What can we do to manage prediabetes?



**1. Early Detection**

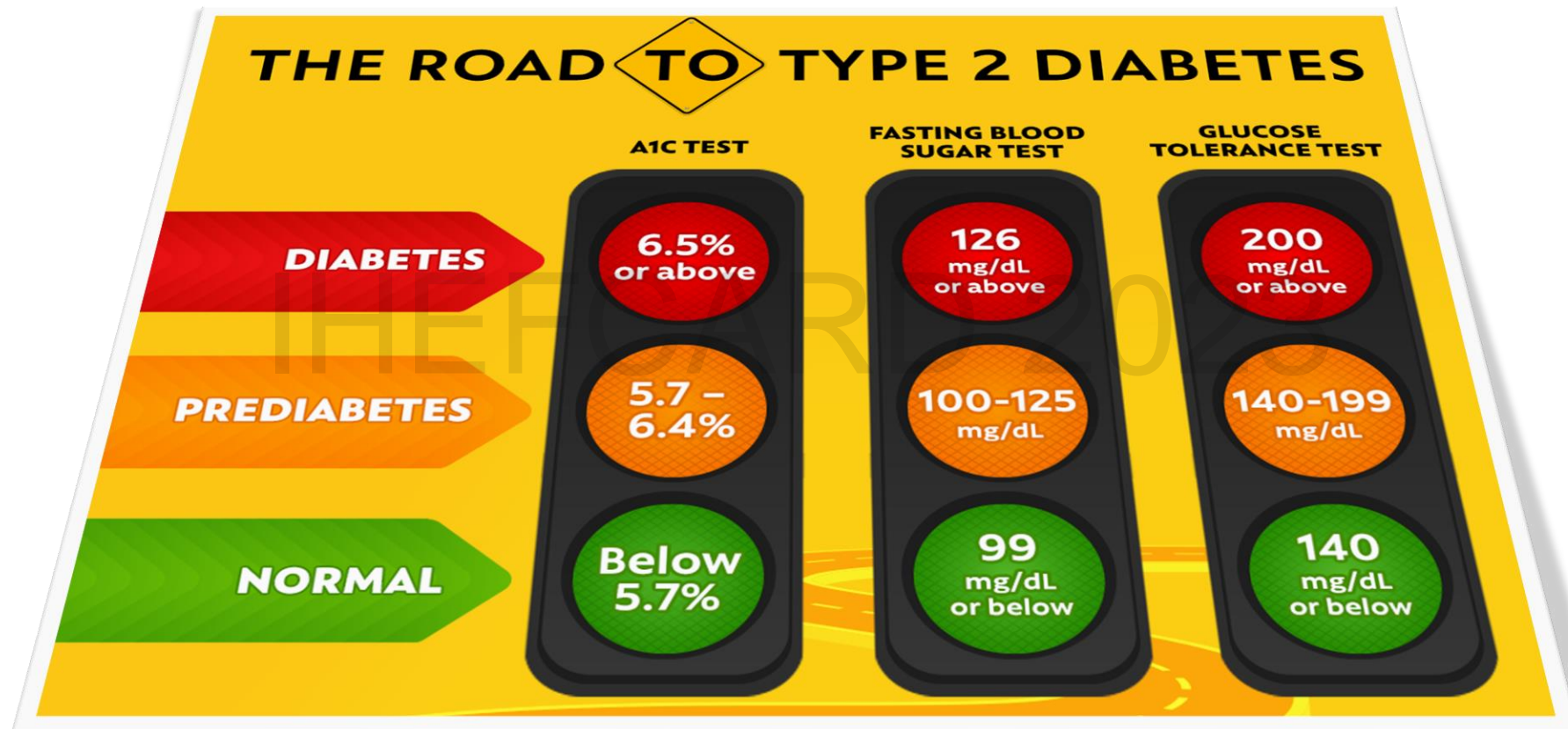
**2. Prompt Management**

# Criteria for Screening

1. Testing should be considered in adults with overweight or obesity ( $\text{BMI} \geq 25 \text{ kg/m}^2$  or  $\geq 23 \text{ kg/m}^2$  in Asian American individuals) who have one or more of the following risk factors:
  - First-degree relative with diabetes
  - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
  - History of CVD
  - Hypertension ( $\geq 130/80 \text{ mmHg}$  or on therapy for hypertension)
  - HDL cholesterol level  $< 35 \text{ mg/dL}$  ( $0.90 \text{ mmol/L}$ ) and/or a triglyceride level  $> 250 \text{ mg/dL}$  ( $2.82 \text{ mmol/L}$ )
  - Individuals with polycystic ovary syndrome
  - Physical inactivity
  - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
2. People with prediabetes ( $\text{A1C} \geq 5.7\%$  [ $39 \text{ mmol/mol}$ ], IGT, or IFG) should be tested yearly.
3. People who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other people, testing should begin at age 35 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.
6. People with HIV.

IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

# DIAGNOSTIC TEST



*OGTT is the most sensitive screening method ..*

*... however, HbA1c is relatively simple as it does not require fasting*





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## PREDIABETES ALGORITHM

IFG (100-125 mg/dL) | IGT (140-199 mg/dL) | A1C (5.7%-6.4%) | METABOLIC SYNDROME<sup>1</sup>

**GOALS:** Prevent Progression to Diabetes | Prevent Progression of NAFLD | Improve CVD Risk Factors |  
Prevent Excess Weight Gain and Promote Weight Loss | Improve Functionality and Quality of Life

### LIFESTYLE INTERVENTION<sup>2</sup>

Nutrition | Physical Activity | Sleep Hygiene | Healthy Habits

### CARDIOVASCULAR RISK REDUCTION (SIMILAR TARGETS TO T2D)

Excess Weight Reduction | Blood Pressure Control | Lipid Management

### OVERWEIGHT OR OBESITY<sup>3</sup>

YES

GOAL: WEIGHT LOSS >7%-10%

GLP-1 RA<sup>4</sup>  
PHENTERMINE / TOPIRAMATE ER

CONSIDER BARIATRIC SURGERY

NO

GOAL: TREAT DYSGLYCEMIA

METFORMIN  
PIOGLITAZONE  
ACARBOSE

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

OVERT  
DIABETES

GO TO  
GLYCEMIC CONTROL  
ALGORITHMS

<sup>1</sup>NCEP ATP III Criteria. <sup>2</sup>See COMPLICATIONS-CENTRIC MODEL FOR THE CARE OF PERSONS WITH OVERWEIGHT/OBESITY. <sup>3</sup>If no overweight or obesity, consider T1D antibody testing for LADA. <sup>4</sup>Indications for weight-loss medications are obesity or overweight BMI >27 kg/m<sup>2</sup> with ABCD complication(s) including prediabetes. Choose GLP-1 RA for approved for weight loss. Also consider other approved weight-loss medications (phentermine [short term], orlistat, naltrexone-ER/bupropion-ER). See also PROFILES OF WEIGHT-LOSS MEDICATIONS table.

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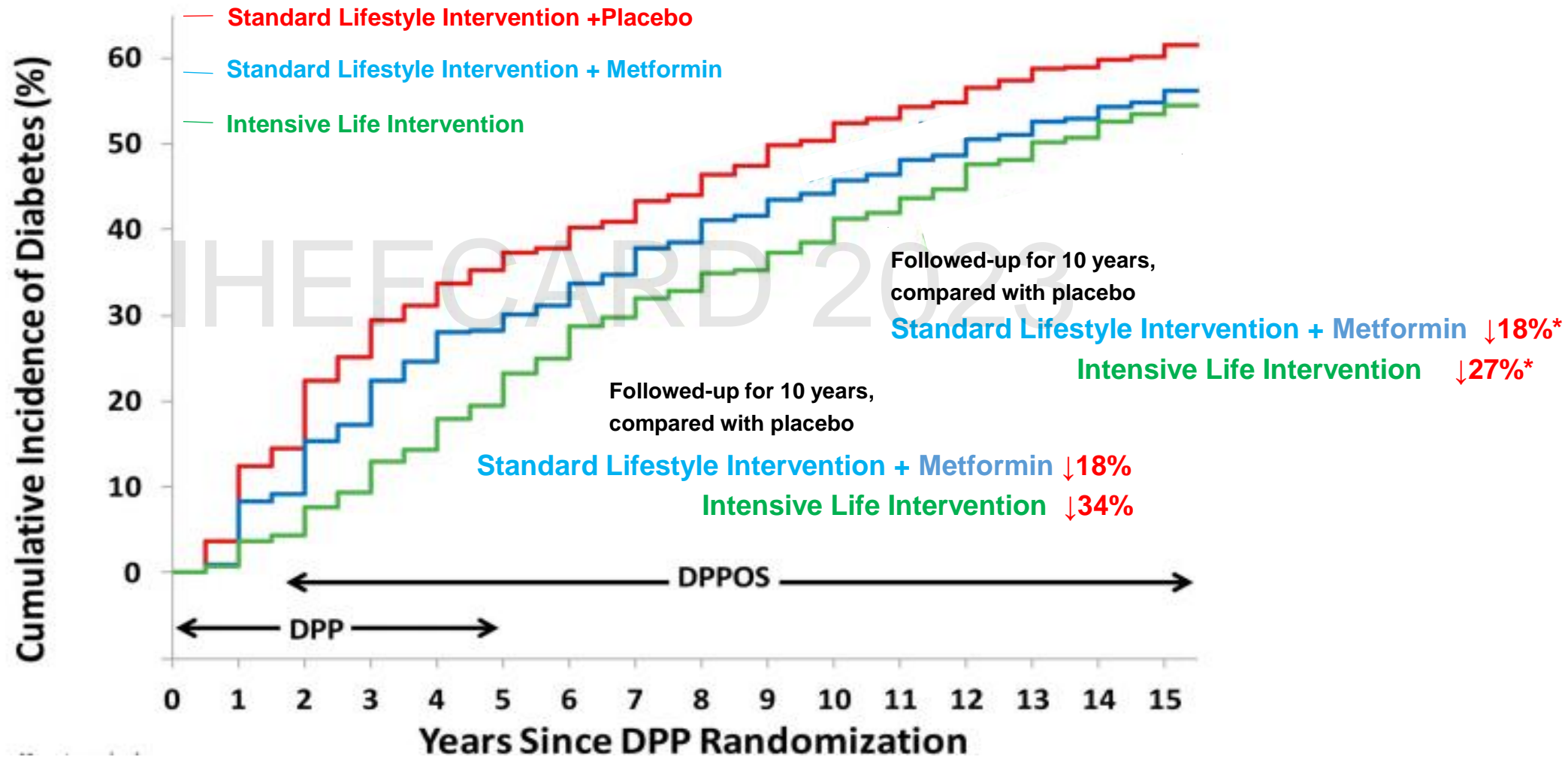
Algorithm Figure 3-Prediabetes



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# DPPOS 15 years follow-up:

Metformin and intensive lifestyle interventions reduced the incidence of diabetes





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# Pharmacologic Approaches to Glucose Management in Prediabetes



should be considered for **higher-risk patients**:  
some **combination** of IFG + IGT  
and/or the **metabolic syndrome** (ie,  $\geq 2$  of these risk factors).

Other **key considerations**:  
**worsening glycemia**,  
the presence of **CVD** and/or **nonalcoholic fatty liver disease (NAFLD)**,  
or a history of **gestational diabetes mellitus (GDM)**  
or **polycystic ovary syndrome (PCOS)**

# Metformin has widely experienced and could prevent diabetes

Trial	Subjects	N; duration (years)	Control group	Active treatments	% change in diabetes risk
DPP <sup>1</sup>	IGT	3234; 2.8	Placebo plus standard lifestyle advice	<b>Metformin plus standard lifestyle advice</b> Intensive lifestyle intervention	<b>-31</b> -58
DPPOS <sup>2</sup>	IGT	2766; 5.7	Placebo plus group-implemented lifestyle intervention	<b>Metformin 1700 mg/day+group-implemented lifestyle intervention</b> Intensive lifestyle intervention+additional lifestyle support	<b>-18</b> -34
IDPP <sup>3</sup>	IGT	531; 2.5	Standard lifestyle advice	<b>Metformin plus standard lifestyle advice</b> <b>Metformin plus intensive lifestyle intervention</b> Intensive lifestyle intervention	<b>-26.4</b> <b>-28.2</b> -28.5
Yang <sup>4</sup>	IGT	321; 3	Standard lifestyle advice	<b>Metformin</b> acarbose Intensive lifestyle intervention	<b>-76.8</b> -87.8 -43
Li <sup>5</sup>	IGT	70; 1	Placebo	<b>Metformin</b>	<b>-66</b>
Iqbal <sup>6</sup>	IGT	317; 1.5	Standard lifestyle advice	<b>Metformin</b> Intensive lifestyle intervention	<b>-76.5</b> -71
CANOE (Canada) <sup>7</sup>	IGT	207;3.9	placebo	Metformin 500mg plus rosiglitazone 2 mg twice	<b>-66</b>

1. Knowler WC, et al. N Engl J Med. 2002 Feb 7;346(6): 393-403.; 2. Diabetes Prevention Program Research Group, et al. Lancet. 2009 Nov 14;374(9702): 1677-86.; 3. Ramachandran A, et al. Diabetologia. 2006 Feb;49(2): 289-97.; 4. Yang wenying, et al. Chinese Journal of Endocrinology and Metabolism..2001,3;(17): 131-134.; 5. Li CL, et al. Diabet Med. 1999 Jun;16(6): 477-81.; 6. Iqbal Hydrie MZ, et al. J Nutr Metab. 2012;2012: 867604. 7. Zinman B, et al. Lancet. 2010 Jul 10;376(9735):103-11.



## A Consensus of Key Opinion Leaders on the Management of Pre-diabetes in the Asia-Pacific Region

Roberto Mirasol,<sup>1</sup> Ah Chuan Thai,<sup>2</sup> Aftab Ahmad Salahuddin,<sup>3</sup> Kathryn Tan,<sup>4</sup> Chaicharn Deerochanawong,<sup>5</sup> Mafauzy Mohamed,<sup>6</sup> Made Ratna Saraswati,<sup>7</sup> Bipin Kumar Sethi,<sup>8</sup> Sanjiv Shah,<sup>9</sup> Nanny Natalia Soetedjo,<sup>10</sup> Swangjit Suraamornkul,<sup>11</sup> Rima Tan,<sup>12</sup> Farid Uddin<sup>13</sup>

- Pharmacologic intervention is recommended if there is **inadequate response to lifestyle intervention after 3 to 6 months.**
- Metformin should be initiated at a **starting dose of 500 mg/day titrated up to a maximum of 2,000 mg/day as required.**
- Alternative treatment should be considered if the patient is **nonresponsive or intolerant to metformin** (e.g., acarbose), or when it is contraindicated.
- **Follow up is recommended at 3 to 6 months.**



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# Summary



**1 out of 3**  
have Prediabetes

## 1. Early Detection

- Screening: OGTT, HbA1c, FPG

## 2. Prompt Treatment

- Risk Stratification
- Intensive Lifestyle Modifications +/- Medication(s)

*Prediabetes comprehensive intervention  
will lead to prevention of cardiometabolic complications*

***“Alone we can do so little; together we can do so much.”***

*Helen Keller*



**THANK YOU**