



# Tailoring Therapy for Dual Glycemic and Cardiovascular Benefit

Wismandari





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# Disclosure

**This presentation is meant to offer a medical education, however I have received honorarium as speaker/consultant, support for research/attendance at educational meetings from:**

Novo Nordisk, Zuellig Pharma-Boehringer  
Ingelheim, Kalventis, Merck Serono, MSD,  
Astra Zeneca, Eli Lilly, Servier, Novartis, Bayer  
AG, Kalbe Farma, Dexa Medica, Infion, Hetero







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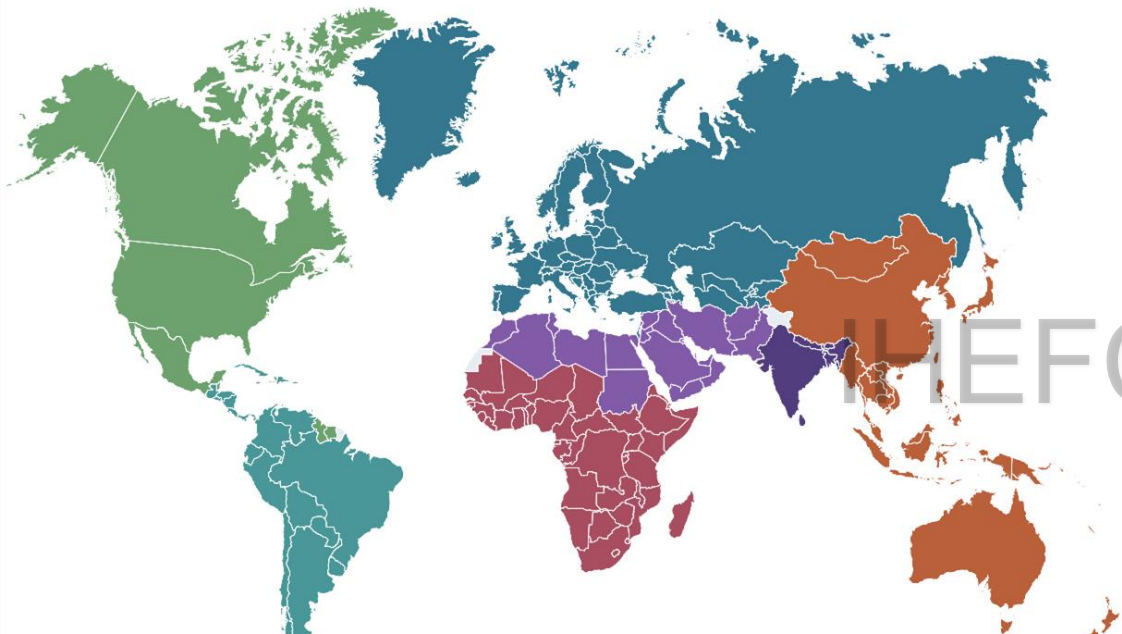
# Unmet needs in T2D

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THEFCARD 2025



# Number of people with diabetes worldwide and per IDF Region, in 2024–2050 (20–79 years)



Western Pacific (WP)

2050	253.8 Million
2024	215.4 Million

↑ 18% increase

World

2050	852.5 Million
2024	588.7 Million

↑ 45% increase

Europe (EUR)

2050	72.4 Million
2024	65.6 Million

↑ 10% increase

North America and Caribbean (NAC)

2050	68.1 Million
2024	56.2 Million

↑ 21% increase

South-East Asia (SEA)

2050	184.5 Million
2024	106.9 Million

↑ 73% increase

Africa (AFR)

2050	59.5 Million
2024	24.6 Million

↑ 142% increase

Middle-East and North Africa (MENA)

2050	162.6 Million
2024	84.7 Million

↑ 92% increase

South and Central America (SACA)

2050	51.5 Million
2024	35.4 Million

↑ 45% increase

Western Pacific (WP)

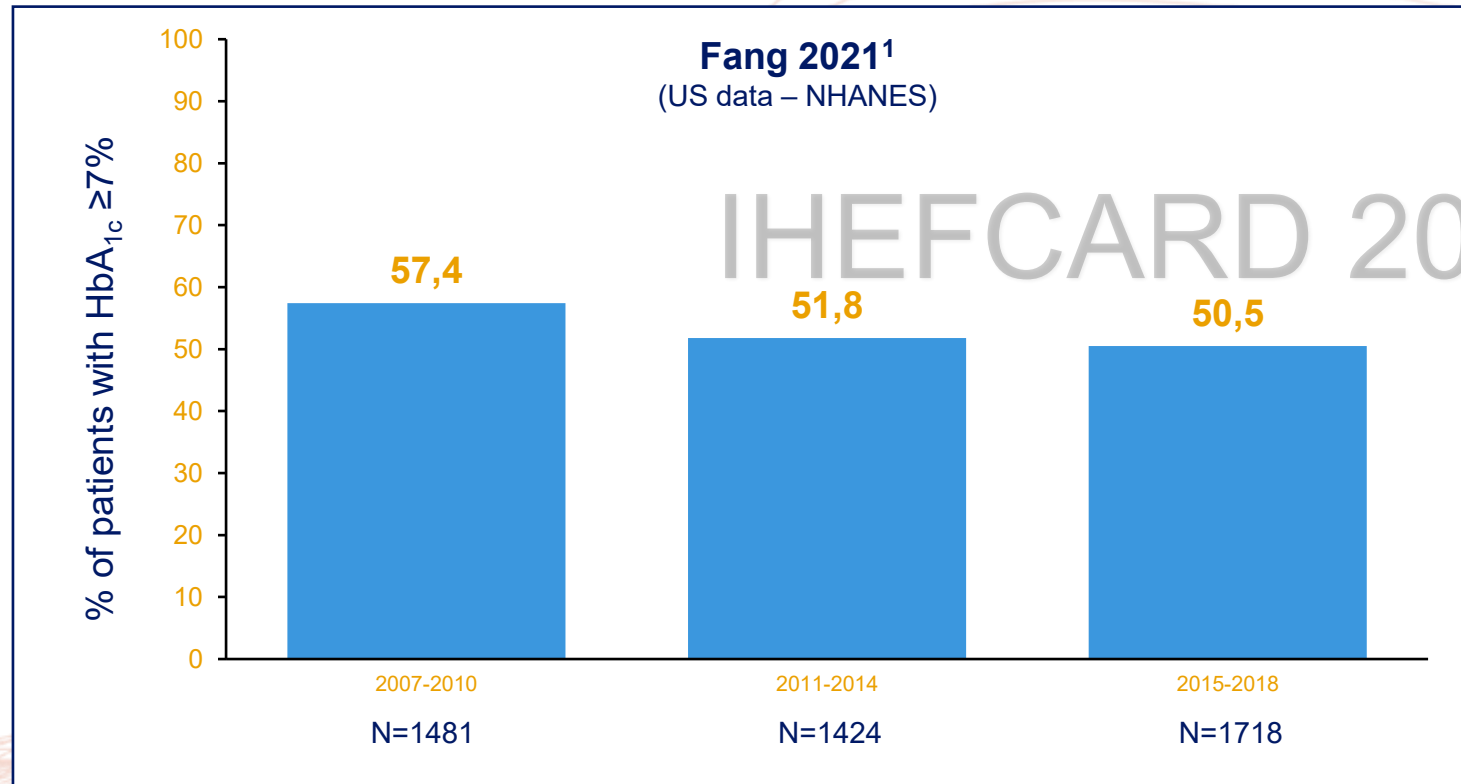
2050	253.8 Million
2024	215.4 Million

↑ 18% increase



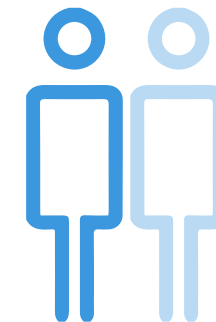
# Glycaemic control remains suboptimal in T2D

Despite the benefits of good glycaemic control and several treatment options, target HbA<sub>1c</sub> levels are often not met



## CDC 2022 National Diabetes Statistics Report<sup>2</sup>

~1 in 2 people living with diabetes achieve HbA<sub>1c</sub> ≤ 7% and may benefit from further optimisation of glycaemic control

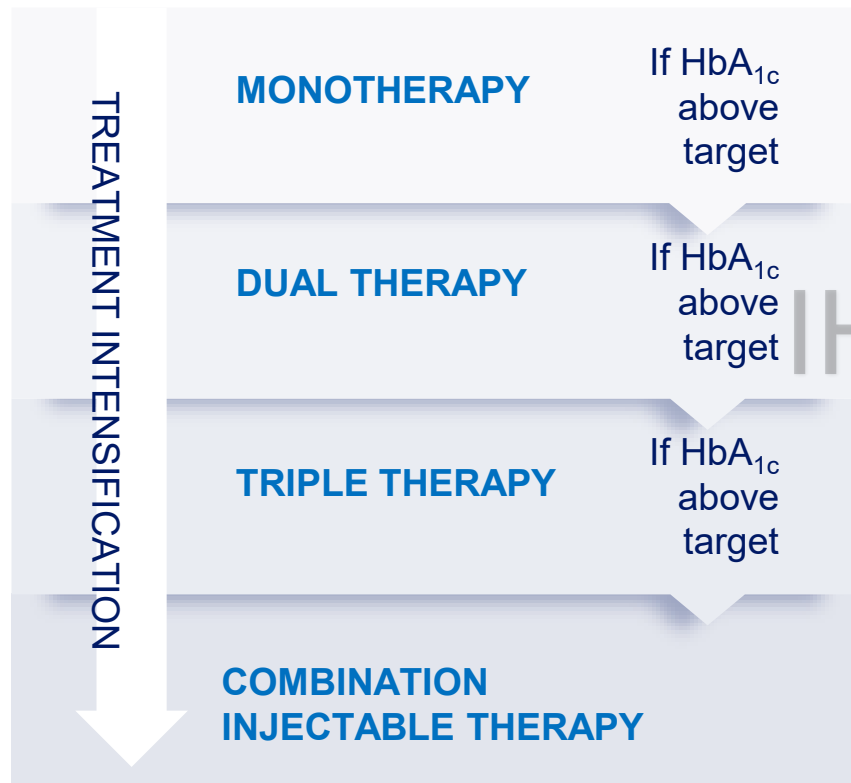


CDC, Centers for Disease Control and Prevention; NHANES, National Health and Nutrition Examination Survey; T2D, type 2 diabetes; US, United States



# The Challenge of Poor Glycaemic Control in Indonesia

Patients progress through a sequence of medications over several years<sup>1\*</sup>



Despite clinical guideline recommendations and the benefits of good glycaemic control, target HbA<sub>1c</sub> levels are **often not met**<sup>2-3</sup>



1. Davies et al. Diabetes Care 2018;41(12):2669-2701. 2. de Pablos-Velasco et al. Clin Endocrinol. 2014 ;80(1):47-56. 3. Stratton IM et al. BMJ 2000 ;321(7258):405-12. Soetedjo et al, Trop Med and Int Health. 2018 (23): 1118-1128 4. Soetedjo et al, Trop Med and Int Health. 2018 (23): 1118-1128



# Most people with diabetes have overlapping cardiometabolic risk factors

Multiple comorbidities increase CVD risk<sup>1</sup>

## Hyperlipidaemia

Of people with hyperlipidaemia:<sup>3,5†,§</sup>

- 9–16% have diabetes
- 24–54% have hypertension

## Obesity

Of people with obesity:<sup>4,‡</sup>

- 17% have diabetes
- 39% have hypertension
- 60% have hyperlipidaemia

## Diabetes

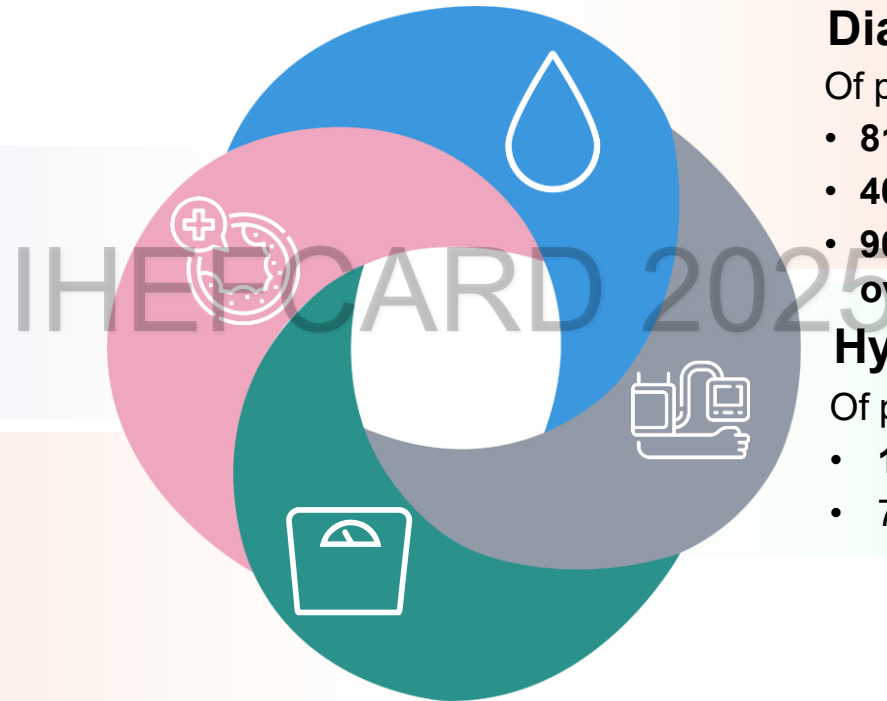
Of people with diabetes:<sup>2,\*</sup>

- 81% have hypertension
- 40% have hyperlipidaemia
- 90% live with overweight/obesity

## Hypertension

Of people with hypertension:<sup>3,†</sup>

- 19% have diabetes
- 71% have hyperlipidaemia



CDC, Centers for Disease Control and Prevention; CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; T2D, type 2 diabetes; US, United States.

\*Among US adults aged 18 years or older with diagnosed diabetes, crude estimates for 2017–2020.<sup>2</sup> †Among Taiwanese adults aged 20–79 years, using data from the MJ Health Check-up Database (2002–2017), linked with the National Health Insurance Research Database (2000–2017).<sup>3</sup> ‡Among US adults in a non-institutionalized population aged 20 years or older, using NHANES data (2011–2020); patients with abdominal obesity (defined as having a waist circumference >102 cm in men and >88 cm in women) were assessed.<sup>4</sup> §Among US adults aged ≥21–79 years with diagnosed hyperlipidaemia using NHANES data.<sup>5</sup>



# Poorly controlled diabetes leads to increased risk of developing diabetes-related complications

## Microvascular

### Diabetic retinopathy<sup>1</sup>

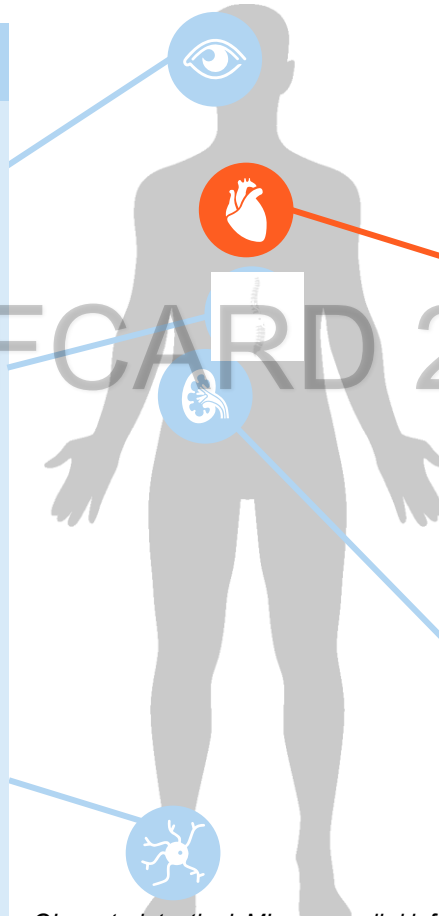
- Estimated to affect **35%** of all people with diabetes and is **one of the leading** causes of vision loss in the working age population

### Autonomic neuropathy<sup>2</sup>

- Cardiovascular impairment affects **20%** of all people with diabetes and can lead to tachycardia and high blood pressure
- Other manifestations include GI disturbances and genitourinary dysfunction

### Diabetic neuropathy<sup>1</sup>

- Nerve damage can lead to ulceration and lower-limb amputations
- **60%** of lower-limb amputations in adults are caused by type 2 diabetes



## Macrovascular

### Cardiovascular disease<sup>1</sup>

- Includes angina, CAD, MI, stroke, PAD and CHF
- People with diabetes are **two to three times** more likely to have CVD

## Microvascular

### Diabetic nephropathy<sup>1</sup>

- Diabetes is a **leading** cause of chronic kidney disease and both conditions are interlinked

CAD, coronary artery disease; CHF, congestive heart failure; CVD, cardiovascular disease; GI, gastrointestinal; MI, myocardial infarction; PAD, peripheral artery disease.



# T2D in the context of the cardio-kidney-metabolic disease spectrum

Chronic cardiometabolic diseases share underlying risk factors<sup>1-3</sup>



Hypertension



Hyperglycaemia



Pro-inflammatory state

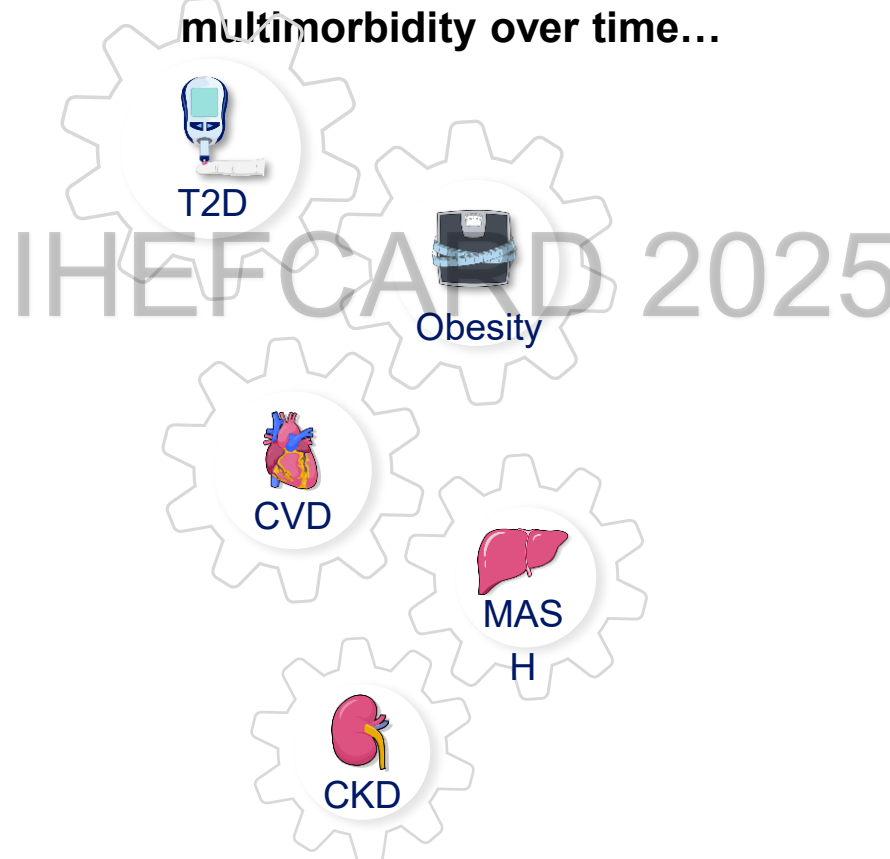


Dyslipidaemia



Abdominal adiposity

These risk factors can increase multimorbidity over time...



...leading to severe outcomes such as **heart attack** and **stroke**<sup>4-6</sup>

Management of patients with cardio-kidney-metabolic diseases requires a **holistic, multifactorial, person-centric approach** as suggested by treatment guidelines<sup>7</sup>

CKD, chronic kidney disease; CVD, cardiovascular disease; MASH, metabolic dysfunction-associated steatohepatitis; T2D, type 2 diabetes.

1. Mendrick DL, et al. Toxicol Sci. 2018;162(1):36–42. 2. Musunuru K. Lipids. 2010;45(10):907–14. 3. Schönknecht YB, et al. Eur J Nutr. 2022; doi: 10.1007/s00394-022-02870-7. Online ahead of print. 4. Kadowaki T et al. Diabetes Obes Metab. 2022;24:2283-96. 5. Targher G, et al. Lancet Gastroenterol Hepatol. 2021;6:578-88. 6. Lingvay I, et al. Lancet. 2022;399:394-405; 7. American Diabetes Association Professional Practice Committee. Diabetes Care 2024;48(suppl1):S181–S206.



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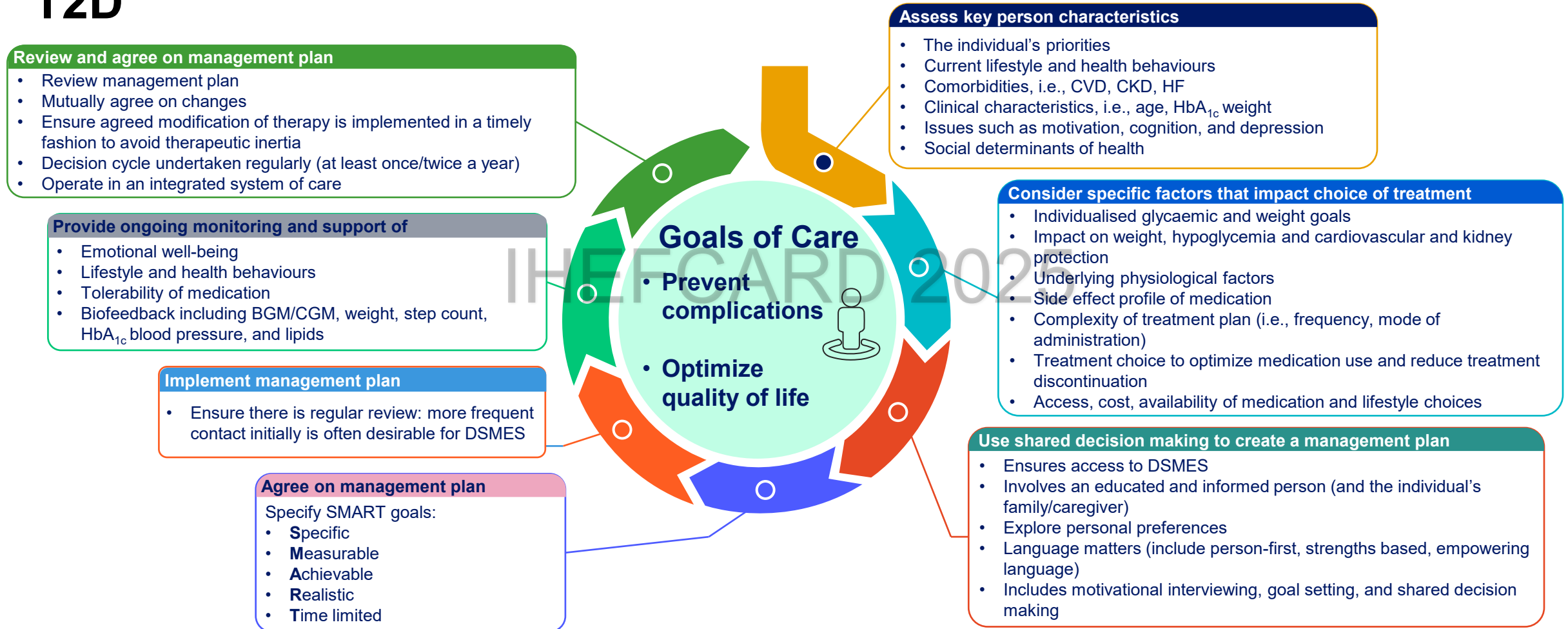
# Importance of holistic and person-centered management of T2D

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# Decision cycle for person-centered glycaemic management in T2D



BGM, blood glucose monitoring; CGM, continuous glucose monitoring; CKD, chronic kidney disease; CVD, cardiovascular disease; DSMES, Diabetes Self-Management Education and Support; HbA<sub>1c</sub>, glycated haemoglobin; HF, heart failure; T2D, type 2 diabetes.

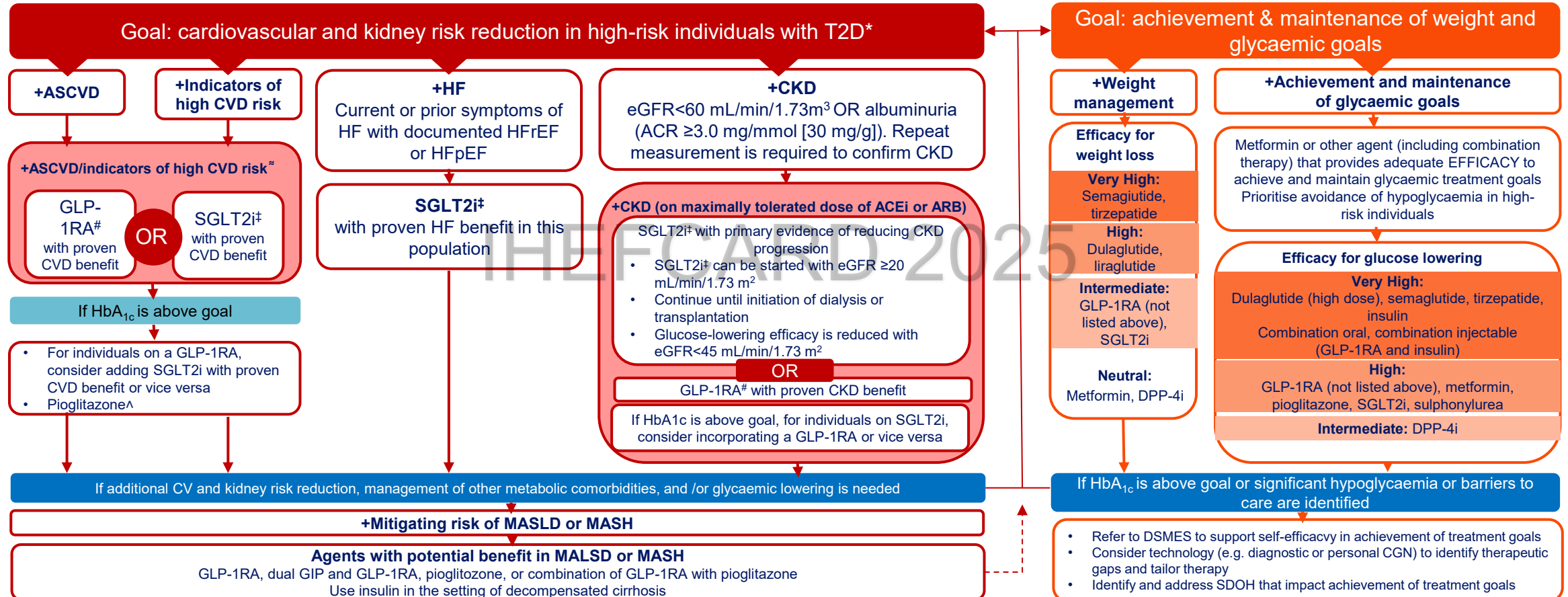


# ADA Standard of Care 2025

## Use of glucose-lowering medications in the management of T2D

To avoid therapeutic inertia, reassess and modify treatment regularly (3–6 months)

HEALTHY LIFESTYLE BEHAVIOURS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT; SOCIAL DETERMINANTS OF HEALTH



\*In people with HF, CKD and established CVD or multiple risk factors for CVD, the decision to use a GLP-1RA or SGLT2i with proven benefit should be independent of background use of metformin; <sup>‡</sup>A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into shared decision-making process. <sup>Δ</sup>Low-dose T2D may be better tolerated and similarly effective; <sup>§</sup>For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, stroke and renal endpoints in individuals with T2D with established/high risk of CVD; <sup>#</sup>For GLP-1RAs, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke and renal endpoints in individuals with T2D with established/high risk of CVD. ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin/creatinine ratio; ADA, American Diabetes Association; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; CGM, continuous glucose monitoring; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; CVOT, cardiovascular outcomes trial; DPP-4i, dipeptidyl peptidase 4 inhibitor; DSMES, diabetes self-management education and support; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalization for heart failure; MACE, major adverse cardiovascular events; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; MI, myocardial infarction; SDOH, social determinants of health; SGLT2i, sodium-glucose cotransporter 2 inhibitor; T2D, type 2 diabetes. American Diabetes Association Professional Practice Committee. Diabetes Care 2024;48(suppl1):S181–S206.

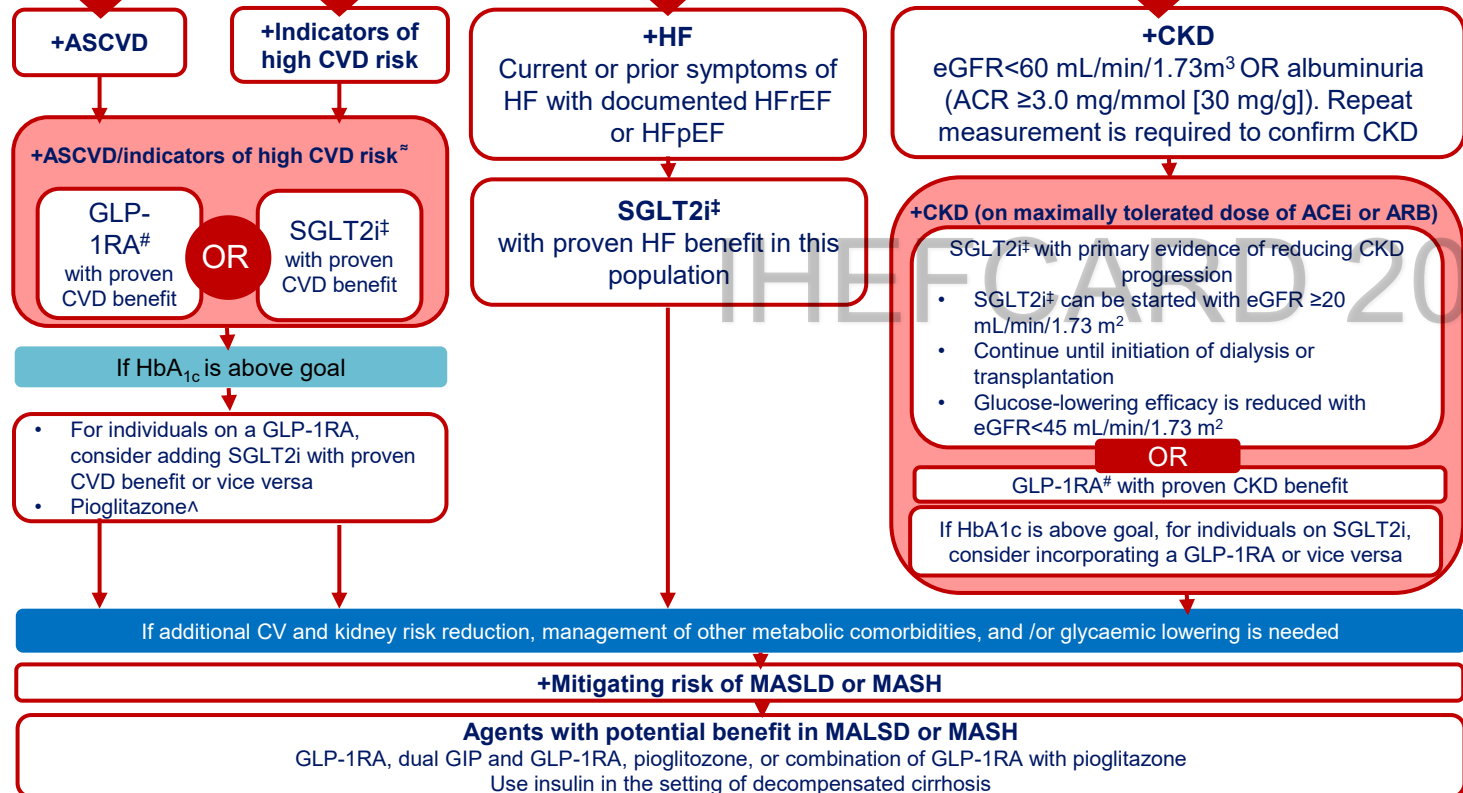


# ADA Standard of Care 2025

## Use of glucose-lowering medications in the management of T2D

HEALTHY LIFESTYLE BEHAVIOURS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT

Goal: cardiovascular and kidney risk reduction in high-risk individuals with T2D\*

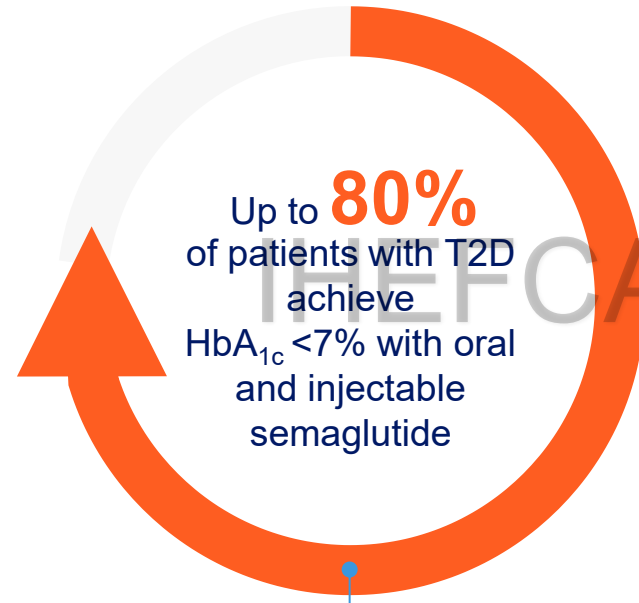


\*In people with HF, CKD and established CVD or multiple risk factors for CVD, the decision to use a GLP-1RA or SGLT2i with proven benefit should be independent of background use of metformin; <sup>‡</sup>A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into shared decision-making process. <sup>Δ</sup>Low-dose T2D may be better tolerated and similarly effective; <sup>§</sup>For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HFrEF and renal outcomes in individuals with T2D with established/high risk of CVD; <sup>#</sup>For GLP-1RAs, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke and renal endpoints in individuals with T2D with established/high risk of CVD. ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin/creatinine ratio; ADA, American Diabetes Association; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; CGM, continuous glucose monitoring; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; CVOT, cardiovascular outcomes trial; DPP-4i, dipeptidyl peptidase 4 inhibitor; DSMES, diabetes self-management education and support; eGFR, estimated glomerular filtration rate; GLP-1RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalization for heart failure; MACE, major adverse cardiovascular events; MASLD, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; MI, myocardial infarction; SDOH, social determinants of health; SGLT2i, sodium-glucose cotransporter 2 inhibitor; T2D, type 2 diabetes. American Diabetes Association Professional Practice Committee. Diabetes Care 2024;48(suppl1):S181–S206.



# Semaglutide is the first GLP-1 RA designated as 'very high' efficacy for both glucose control and body-weight reduction in the ADA/EASD consensus report<sup>1</sup>

Semaglutide helps the **majority** of patients achieve their **glycaemic target**<sup>2-11</sup>



Controlling  $HbA_{1c}$  reduces risk of **microvascular complications**<sup>12</sup>

Glycaemic control is shown to be **early** and **sustained** over **104 weeks**<sup>13</sup>

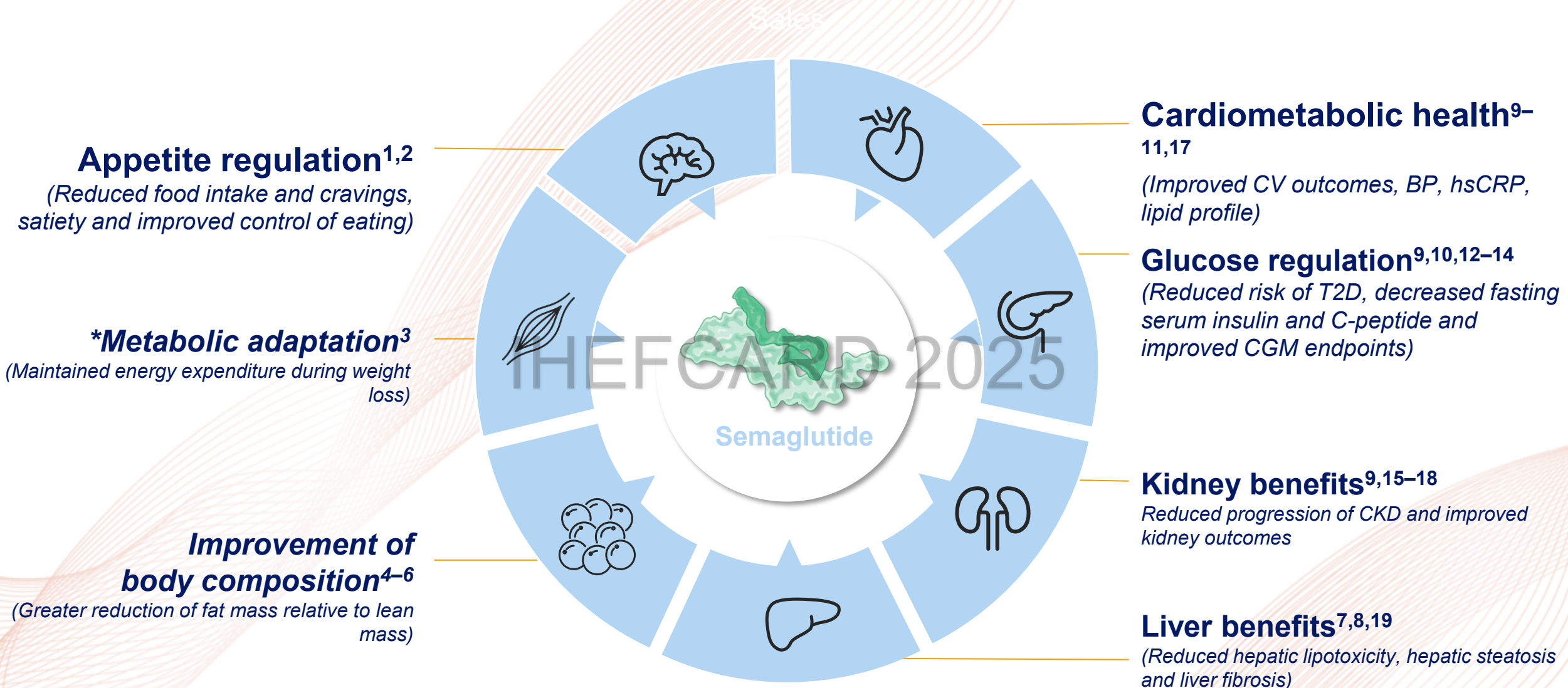


These benefits have been **confirmed in real-world settings**<sup>14</sup>

- ADA, American Diabetes Association; EASD, European Association for the Study of Diabetes; GLP-1 RA, glucagon-like peptide-1 receptor agonist;  $HbA_{1c}$ , haemoglobin  $A_{1c}$
- 1. Davies M, et al. Diabetes Care. 2022;45:2753-86. 2. Aroda VR, et al. Diabetes Care. 2019;42:1724-32. 3. Ahrén B, et al. Lancet Diabetes Endocrinol. 2017;5:341-54. 4. Pratley RE, et al. Lancet Diabetes Endocrinol. 2018;6:275-86. 5. Ahmann AJ, et al. Diabetes Care. 2018;4:258-66. 6. Lingvay I, et al. Lancet Diabetes Endocrinol. 2019;7:834-44 (Article & Suppl.). 7. Capehorn MS, et al. Diabetes Metab. 2020;46(2):100-9. 8. Aroda VR, et al. Lancet Diabetes Endocrinol. 2017;5:355-66. 9. Sorli C, et al. Lancet Diabetes Endocrinol. 2017;5:251-60. 10. Rodbard HW, et al. J Clin Endocrinol Metab. 2018;103:2291-301. 11. Zinman B, et al. Lancet Diabetes Endocrinol. 2019;7:356-67. 12. Pozzilli P, et al. J Diabetes Investig. 2014. 23;5:134-41. 13. Marso SP, et al. N Engl J Med. 2016;375:1834-44. 14. Yale J, et al. BMJ Open Diab Res Care. 2022;10:e002619.



# Semaglutide's mechanistic effects



\*Data is derived from preclinical models.

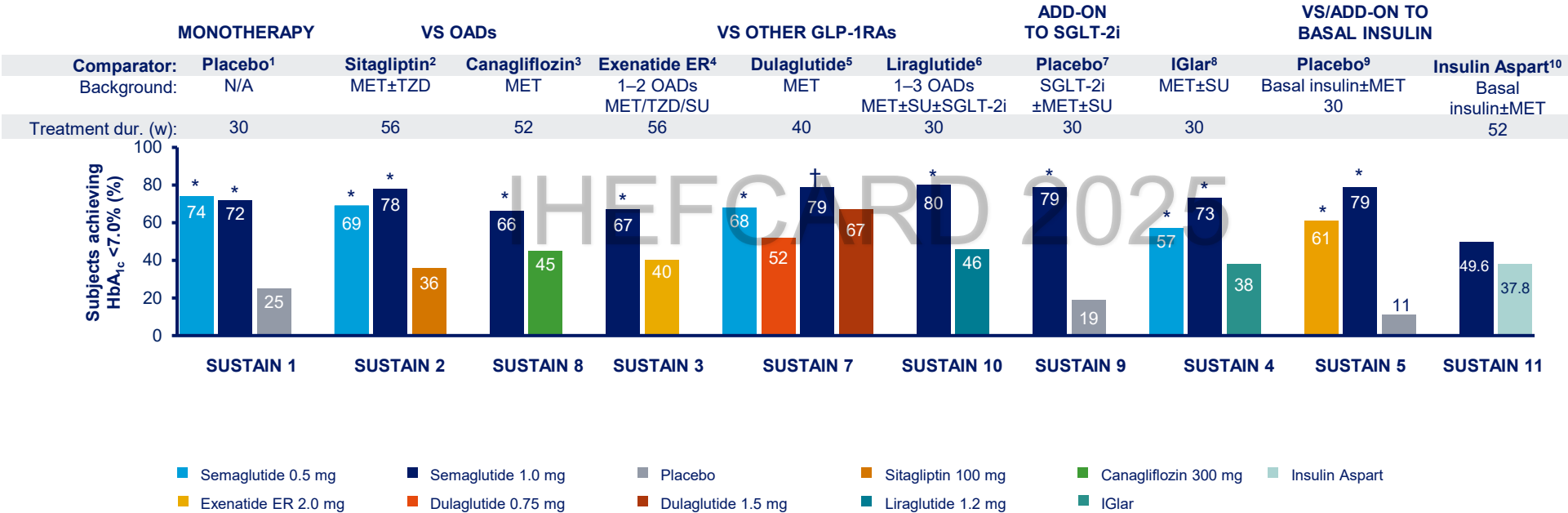
BP, blood pressure; CGM, continuous glucose monitoring; eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin; hsCRP, high-sensitivity C-reactive protein; MASH, metabolic dysfunction-associated steatohepatitis; T2D, type 2 diabetes; UACR, urinary albumin-to-creatinine ratio.

1. Friedrichsen M et al. Diabetes Obes Metab 2021;23(3):754-62; 2. Blundell J et al. Diabetes Obes Metab 2017;19:1242-5; 3. Kuhre R et al. Abstract #73: CagriSema-driven weight loss in diet-induced obese rats depends on counter-regulation of weight loss-associated reduction in energy expenditure. Presented at EASD 2024; 4. Wilding JP et al. J Endocr Soc. 2021 May 3; 5(Suppl 1): A16-A17; 5. Uchiyama S et al. J Clin Med Res 2023;15(7):377-83; 6. Volpe S et al. Nutrients 2022;14(12):2414; 7. Soto-Catalan M et al. Int J Mol Sci 2024; 25(5):2961; 8. Newsome PN et al. N Engl J Med 2021;384:1113-24; 9. Lincoff AM et al. N Engl J Med 2023;389(24):2221-32; 10. Frias JP et al. Lancet (Lond) 2023;402(10403):720-30; 11. Rakipovski G et al. JACC Basic Transl Sci 2018;3(6):844-57; 12. Lingvay I et al. Lancet Diabetes Endocrinol 2019;7(11):834-44; 13. Kapitzka C et al. Diabetologia 2017;60(8):1390-99; 14. Korsatko S et al. Diabetes Obes Metab 2018;20(11):2565-73; 15. Colhoun HM et al. Nat Med 2024;30:2058-2066 doi: 10.1038/s41591-024-03015-5; 16. Perkovic V et al. N Engl J Med 2024;391:109-121 doi: 10.1056/NEJMoa2403347; 17. Marso SP et al. N Engl J Med 2016;375:1834-44; 18. Heerspink HJL et al. Diabetes Care 2023;46(4):801-10; 19. Newsome PN et al. Phase 3 ESSENCE Trial: Semaglutide in metabolic dysfunction-associated steatohepatitis (MASH). Presented at The Liver Meeting®, American Association for the Study of Liver Diseases 2024, Nov 19, 2024.



# Glycemic Control: SUSTAIN TRIAL PROGRAM

## Upto 80% of people with T2D achieve HbA<sub>1c</sub><7% with OW semaglutide



\*p<0.0001 vs comparator; †p<0.005 vs comparator. dur., duration; exenatide ER, exenatide extended release; GLP-1RA, glucagon-like peptide-1 receptor agonist; IGlar, insulin glargine; MET, metformin; N/A, not applicable; OAD, oral antidiabetic drug; SGLT-2i, sodium–glucose cotransporter-2 inhibitor; SU, sulphonylurea; TZD, thiazolidinedione; w, weeks.



## Use of glucose-lowering medications in the management of T2D

Emphasises the importance of weight loss

HEALTHY LIFESTYLE BEHAVIOURS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT; SOCIAL DETERMINANTS OF HEALTH

Goal: achievement & maintenance of **weight** and **glycaemic goals**

**+Weight management**

**Efficacy for weight loss**

**Very High:**

Semaglutide, tirzepatide

**High:**

Dulaglutide, liraglutide

**Intermediate:**

GLP-1RA (not listed above), SGLT2i

**Neutral:**

Metformin, DPP-4i

**+Achievement and maintenance of glycaemic goals**

Metformin or other agent (including combination therapy) that provides adequate EFFICACY to achieve and maintain glycaemic treatment goals

Prioritise avoidance of hypoglycaemia in high-risk individuals

**Efficacy for glucose lowering**

**Very High:**

Dulaglutide (high dose), semaglutide, tirzepatide, insulin  
Combination oral, combination injectable (GLP-1RA and insulin)

**High:**

GLP-1RA (not listed above), metformin, pioglitazone, SGLT2i, sulphonylurea

**Intermediate:** DPP-4i

To avoid therapeutic inertia, reassess and modify treatment regularly (3–6 months)

If HbA<sub>1c</sub> is above goal or significant hypoglycaemia or barriers to care are identified

- Refer to DSMES to support self-efficacy in achievement of treatment goals
- Consider technology (e.g. diagnostic or personal CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact achievement of treatment goals

Part of figure 9.3, unchanged except for minor graphical changes such as colours.

ADA, American Diabetes Association; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; CGM, continuous glucose monitoring; DPP-4i, dipeptidyl peptidase 4 inhibitor; DSMES, diabetes self-management education and support; EASD, European Association for the Study of Diabetes; GLP-1RA, glucagon-like peptide 1 receptor agonist; SDOH, social determinants of health; SGLT-2i, sodium-glucose cotransporter 2 inhibitor; T2D, type 2 diabetes.

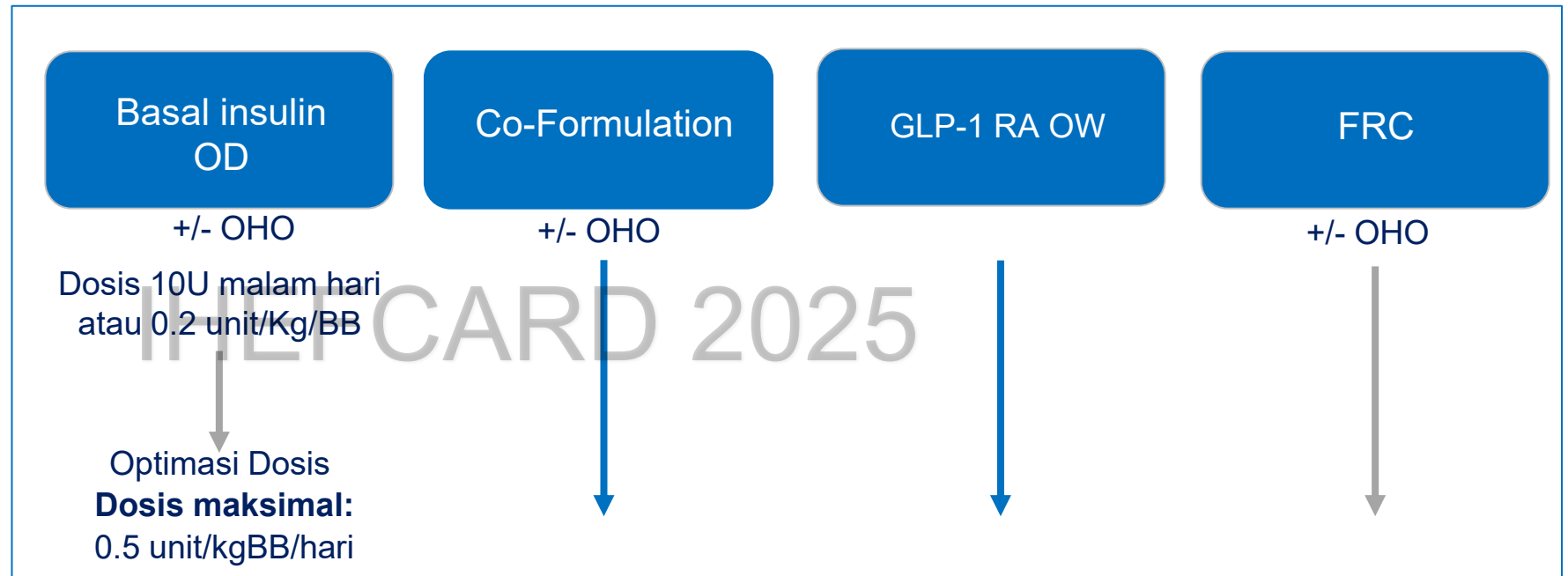
American Diabetes Association Professional Practice Committee. Diabetes Care 2024;48(suppl1):S181–S206.



## Treatment algorithm and criteria for therapy initiation

HbA1C  
 **$\geq 7.5\%$**

**Pasien DM lama + OHO**  
(dual/triple)  
Dengan HbA1C  $>7.5\%$  -  
 $<9\%$



### Target:

GDP/Pre-prandial: 80-130 mg/dL  
GD 1 – 2 PP :  $<180$  mg/dL  
HbA1C :  $<7\%$  (evaluasi 3  
bulan)

### Titrasi:

(Jika nilai GDP atau pre-prandial)  
 $> 180$  mg/dL : +4 Unit  
 $130 - 180$  mg/dL : +2 Unit  
 $< 130$  mg/dL : dosis tetap



HbA1C

$\geq 9\%$

### Pasien DM Baru

Dengan HbA1C  $>9\%$  atau  
GDP  $>250$  mg/dL  
Atau GDS  $>300$  mg/dL

Atau disertai **gejala  
dekompensasi  
Metabolik**

Co-Formulation

Mulai dosis 10 Unit

Optimasi dosis  
**OD** □ **BID**

FRC

10 Unit

Optimasi dosis  
**OD**

GLP-1 RA OW

Basal Plus

+ Prandial pada jadwal  
makan terbesar.  
Basal malam hari  
Dosis prandial mulai  
4U/hari atau 10%  
dosis basal

Optimasi dosis

Basal Bolus

+ Prandial pada ke3  
jadwal makan. Basal  
malam hari  
Basal 10U (bedtime)  
Prandial 4U

### Target:

GDP/Pre-prandial: 80-130 mg/dL  
GD 1 – 2 PP :  $<180$  mg/dL  
HbA1C :  $<7\%$  (evaluasi 3  
bulan)

### Titrasi:

(Jika nilai GDP atau pre-prandial)  
 $> 180$  mg/dL : +4 Unit  
 $130 - 180$  mg/dL : +2 Unit  
 $< 130$  mg/dL : dosis tetap



# Indonesian Realities in T2D:

will addressing basal only will be enough?

$10.5 \pm 1.9\%$   
Mean HbA1c

$230 \pm 69$   
mg/dl  
Mean FPG

**Delay Insulin Use**



**High Carbohydrate Consumption**

Asian populations generally shown a high-carbohydrate consumption, it leads to **high insulin resistance** and **PPG levels**.



# Clinical profiles of patients who can benefit from IDegAsp



## Uncontrolled patient

OAD, Basal Insulin, Premix or Basal Bolus



## High HbA1C

With High PPG Excursion



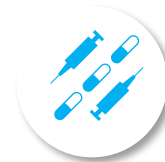
## Hypoglycemia

Increase risk of Hypoglycaemia



## Lifestyle

Patient with Irregular lifestyle and looking for flexibility in dosing



## Complex treatment

Patient who struggle to complex treatment, requiring multiple daily injection



## Special populations

Elderly patients/hepatic or renal impairment

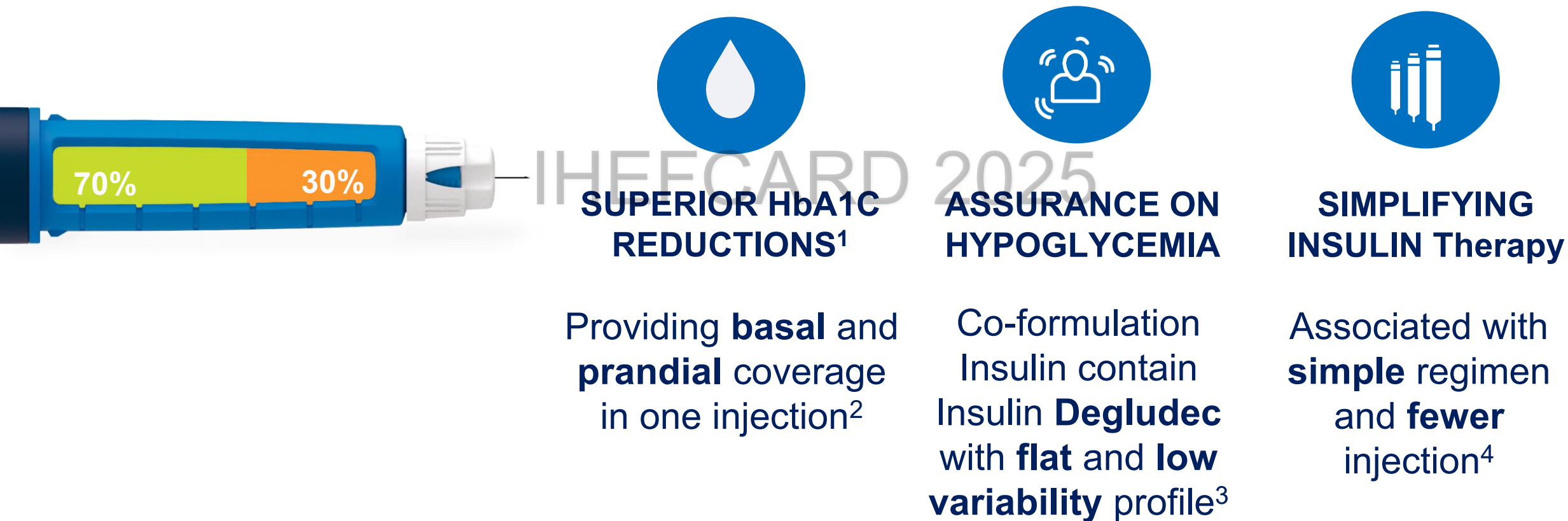


## Diet

Patient with high carbohydrate intake



# ***Co-Formulation Insulin*** have the potential to address our key challenges





# Summary

- Management of patients with **cardio-kidney-metabolic** diseases requires a **holistic, multifactorial, person-centric** approach as suggested by treatment guidelines
- **Pharmacotherapy** decision must be made to **prevent complication** and to optimize **quality of life**
- T2D patients with **ASCVD** risk and other **metabolic comorbidities** such as obesity and CKD, **GLP1 RA** might be more beneficial
- Patients with **uncontrolled** T2D who have high HbA1c levels, consume a **carbohydrate-rich** diet, and require a straightforward intensification option can benefit from **IDegAsp**, which offers flexible dosing schedules compared to traditional basal-bolus regimens.
- **Semaglutide** and **co-formulation** insulin are recommended in **guidelines** and has a well-established **efficacy, safety** and **tolerability** profile.





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*Thank You*



## Disclosure

- **Once-weekly Semaglutide 0.25 – 1 mg available in Indonesia** under the brand name of **Ozempic®**, which is indicated for the treatment of adults with insufficiently controlled **type 2 diabetes mellitus** as an adjunct to diet and exercise in addition to metformin, metformin and sulphonylurea, metformin and basal insulin, or sodium-glucose cotransporter 2 (SGLT2) inhibitor.
- This is only for educational purpose and no off-label promotion is intended