



Type 2 Diabetes Remission; Internist Perspective

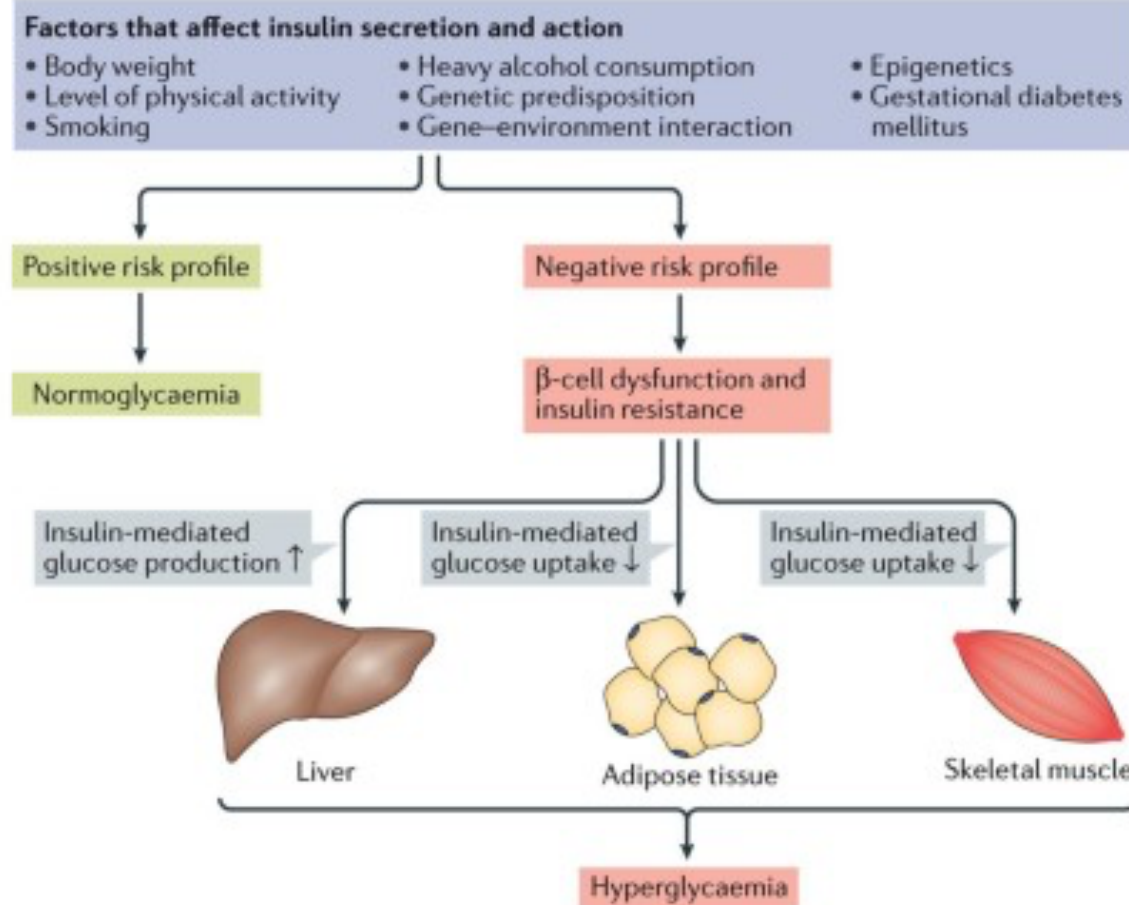
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Faculty of Medicine Siriraj Hospital, Mahidol University,
Bangkok, Thailand



Agenda

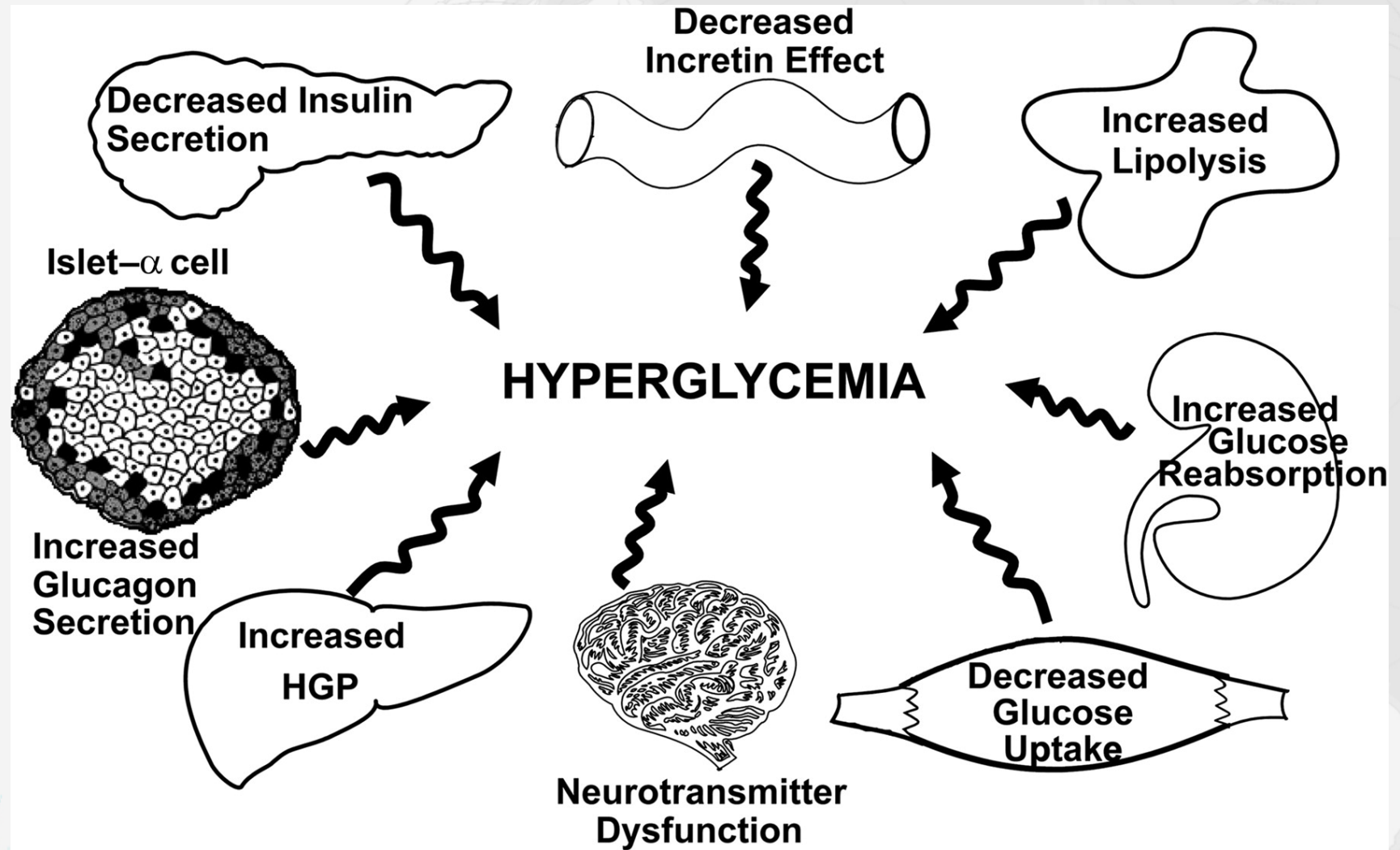
- Pathophysiology of T2DM 'old and new concepts'
- Definition of T2DM remission
- Landmark studies
- Differences between Asians and Caucasians in terms of T2DM
- Studies of T2DM remission in Asians
- Who will get the remission?
- How to get the remission?

Conventional View of Diabetes

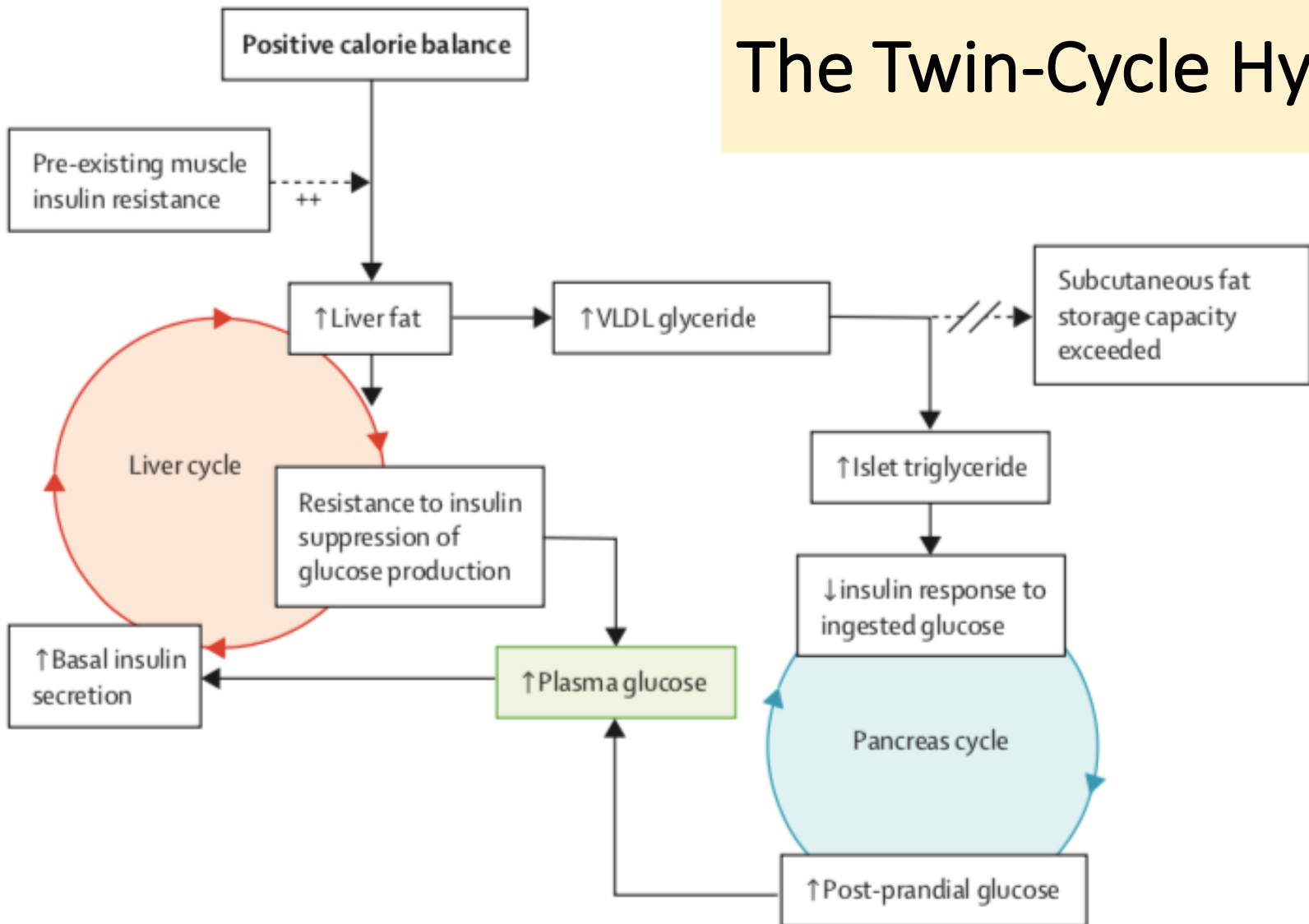




The Ominous Octet



The Twin-Cycle Hypothesis





- American Diabetes Association

- HbA_{1c} <6.5% (48 mmol/mol)
- Remains at that level for at least 3 months
- Without continuation of the usual anti-hyperglycaemic agents

Definition of T2D remission

Table 1—Interventions and temporal factors in determining remission of T2D

Intervention <i>Note: Documentation of remission should include a measurement of HbA_{1c} just prior to intervention</i>	Interval before testing of HbA _{1c} can reliably evaluate the response	Subsequent measurements of HbA _{1c} to document continuation of a remission
Pharmacotherapy	At least 3 months after cessation of this intervention	Not more often than every 3 months nor less frequent than yearly
Surgery	At least 3 months after the procedure <i>and</i> 3 months after cessation of any pharmacotherapy	
Lifestyle	At least 6 months after beginning this intervention <i>and</i> 3 months after cessation of any pharmacotherapy	



The Look AHEAD Study

- 5,145 overweight or obese patients with type 2 diabetes
- An intensive lifestyle intervention (intervention group) or to receive diabetes support and education (control group)
- Median follow-up was 9.6 years
- Weight loss was greater in the intervention group than in the control group throughout the study
 - 8.6% vs. 0.7% at 1 year
 - 6.0% vs. 3.5% at study end

T2D remission rate in intervention group

- 11.5% at 1 year
- 7.3% at 4 years
- Modest weight loss achieved
- Wide range of T2D duration

The Diabetes Remission Clinical Trial (DiRECT)

- 49 primary care practices in Scotland
- Weight management programme (intervention) or best-practice care by guidelines (control)
 - Individuals aged 20–65 years
 - Diagnosed with T2D within the past 6 years
 - BMI of 27–45 kg/m²
 - Not receiving insulin

	Intervention group (n=149)	Control group (n=149)
Sex		
Female	66 (44%)	56 (38%)
Male	83 (56%)	93 (62%)
White ethnicity	146 (98%)	147 (99%)
Age (years)	52.9 (7.6)	55.9 (7.3)
Weight (kg)	101.0 (16.7)	98.8 (16.1)
Body-mass index (kg/m ²)	35.1 (4.5)	34.2 (4.3)
Waist (cm)	107.5 (8.4)	106.5 (8.9)
Systolic blood pressure (mm Hg)	132.7 (17.5)	137.2 (16.0)
Diastolic blood pressure (mm Hg)	84.6 (10.2)	85.5 (8.8)
Time since diabetes diagnosis (years)		
Mean (SD)	3.0 (1.7)	3.0 (1.8)
Median (range)	3.1 (0.0–6.0)	2.6 (0.2–6.0)
HbA _{1c}		
%	7.7 (1.25)	7.5 (1.05)
mmol/mol	60 (13.7)	58 (11.5)
Fasting glucose (mmol/L)	9.22 (3.29)	8.82 (2.54)

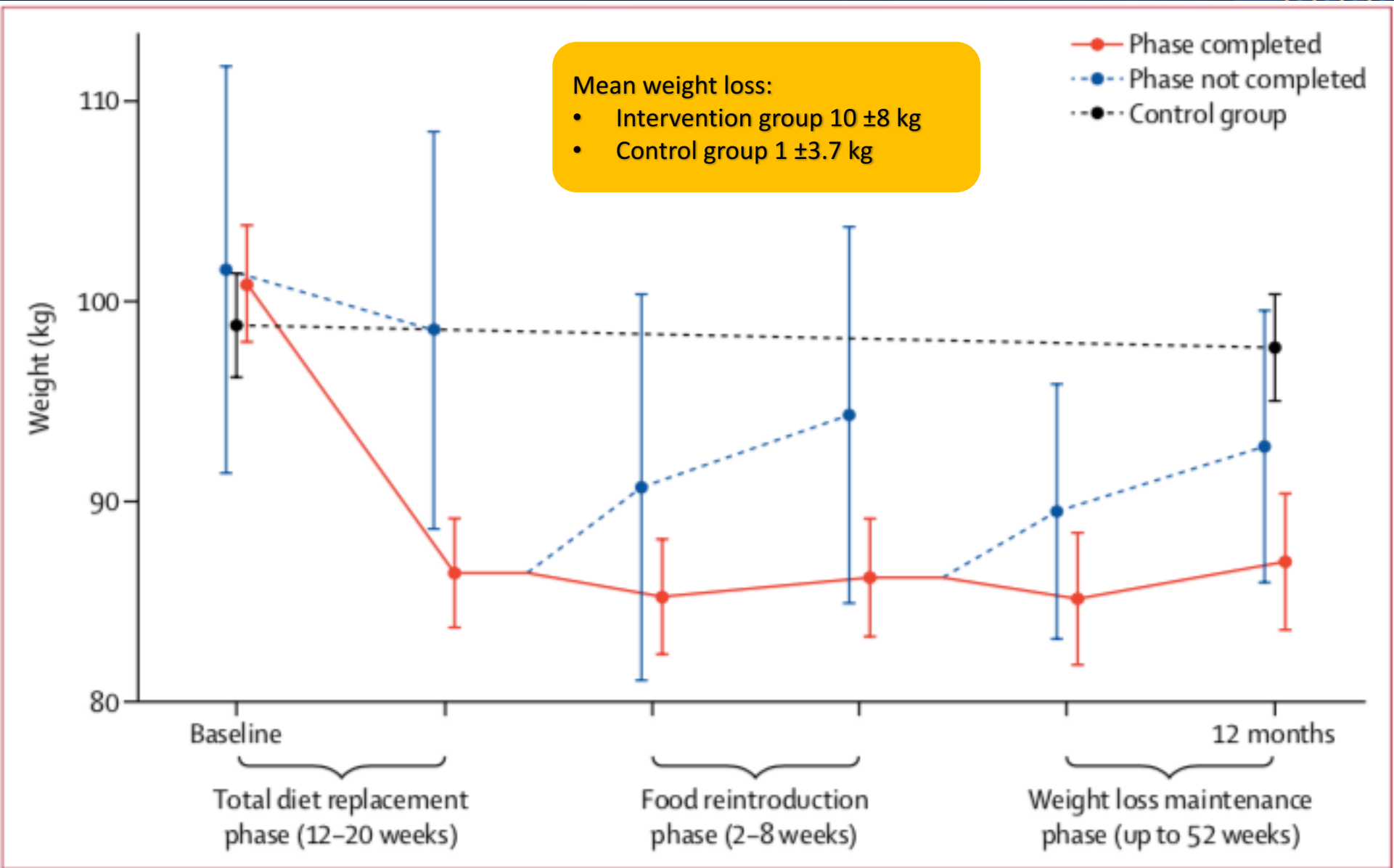
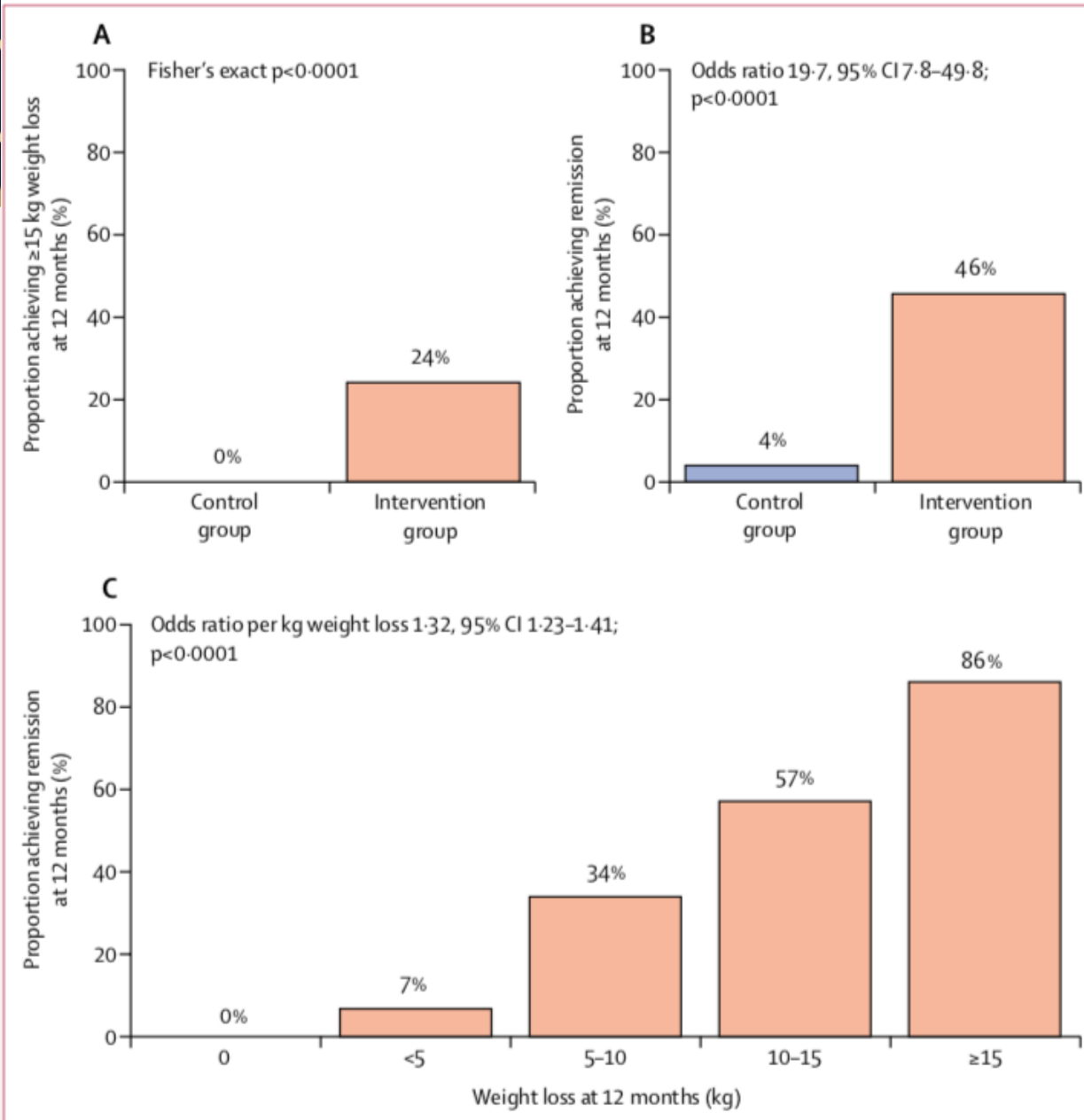


Figure 3: Change in weight of participants who remained in the trial and those who dropped out during each phase of the intervention
 Error bars represent 95% CIs.

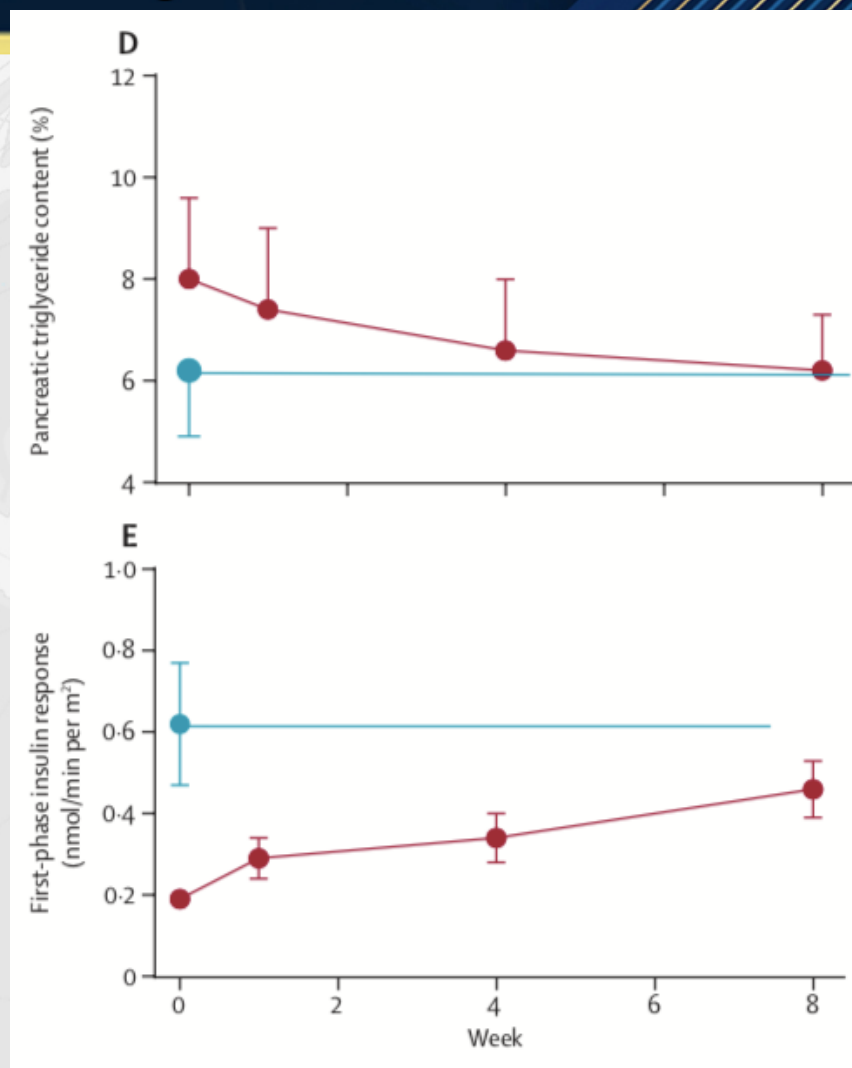
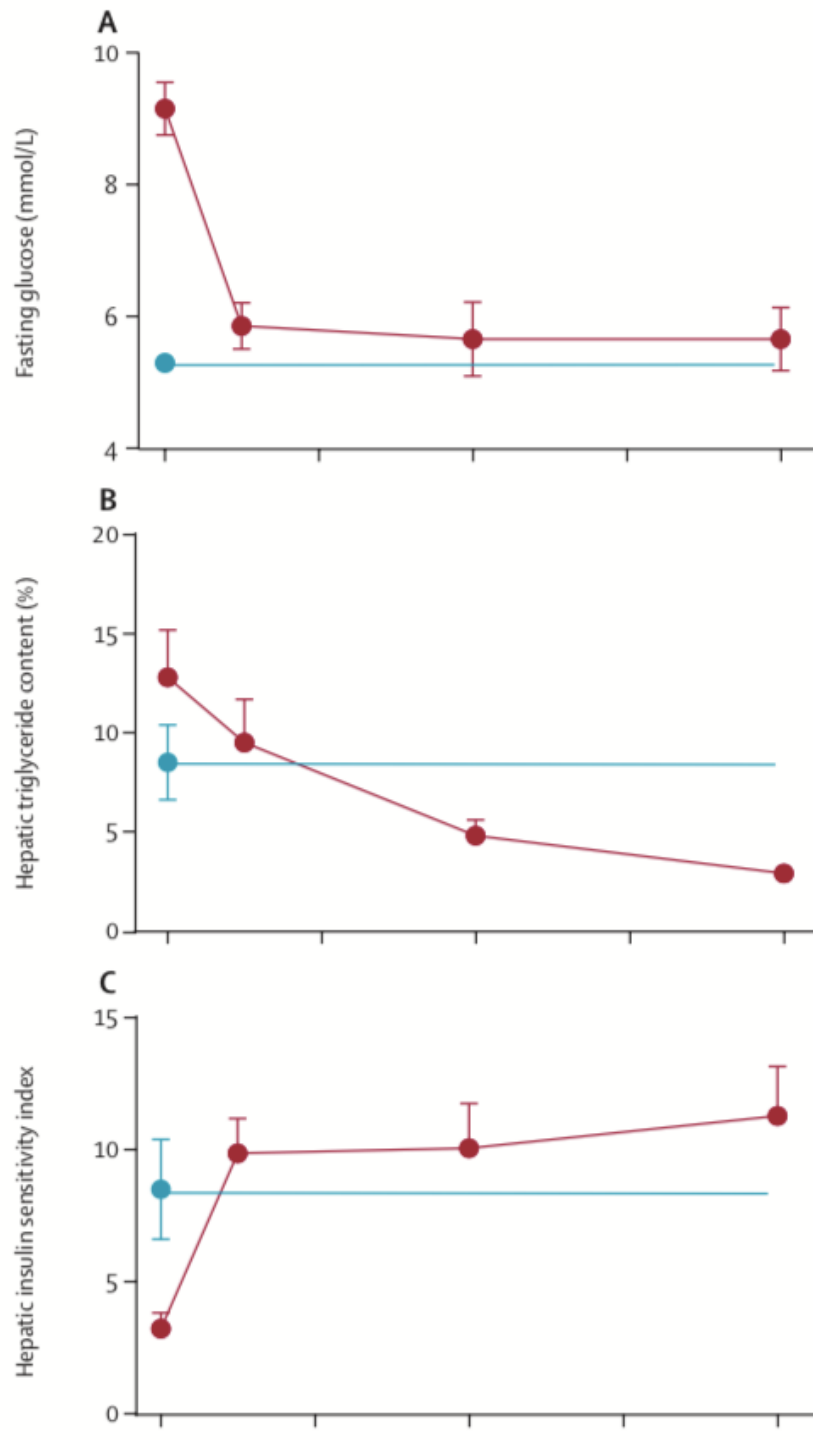


T2D remission rate

- At 1 year: 46%
- At 2 years: 36%

Figure 2: Primary outcomes and remission of diabetes in relation to weight loss at 12 months

(A) First co-primary outcome: achievement of at least 15 kg weight loss at 12 months. (B) Second co-primary outcome: remission of diabetes (glycated haemoglobin $< 6.5\%$ [48mmol/mol], off antidiabetic medication for 2 months). (C) Remission of diabetes, in relation to weight loss achieved at 12 months (both groups combined).





**What Asians differ from
Caucasians in terms of T2DM?**



Pathophysiology, phenotypes and management of type 2 diabetes mellitus in Indian and Chinese populations

Calvin Ke^{1,2,3,4,5}✉, K. M. Venkat Narayan^{6,7,8}, Juliana C. N. Chan^{4,5,9,10}, Prabhat Jha³ and Baiju R. Shah^{1,11}

- India and China account for nearly half of the global number of people with T2DM
- Compared with European people, Indian and Chinese people seem to be:
 - Generally younger ages at diagnosis
 - Lower β -cell function
 - Lower insulin resistance
 - Lower BMI



Type 2 diabetes in East Asians: similarities and differences with populations in Europe and the United States

Ronald C.W. Ma and Juliana C.N. Chan

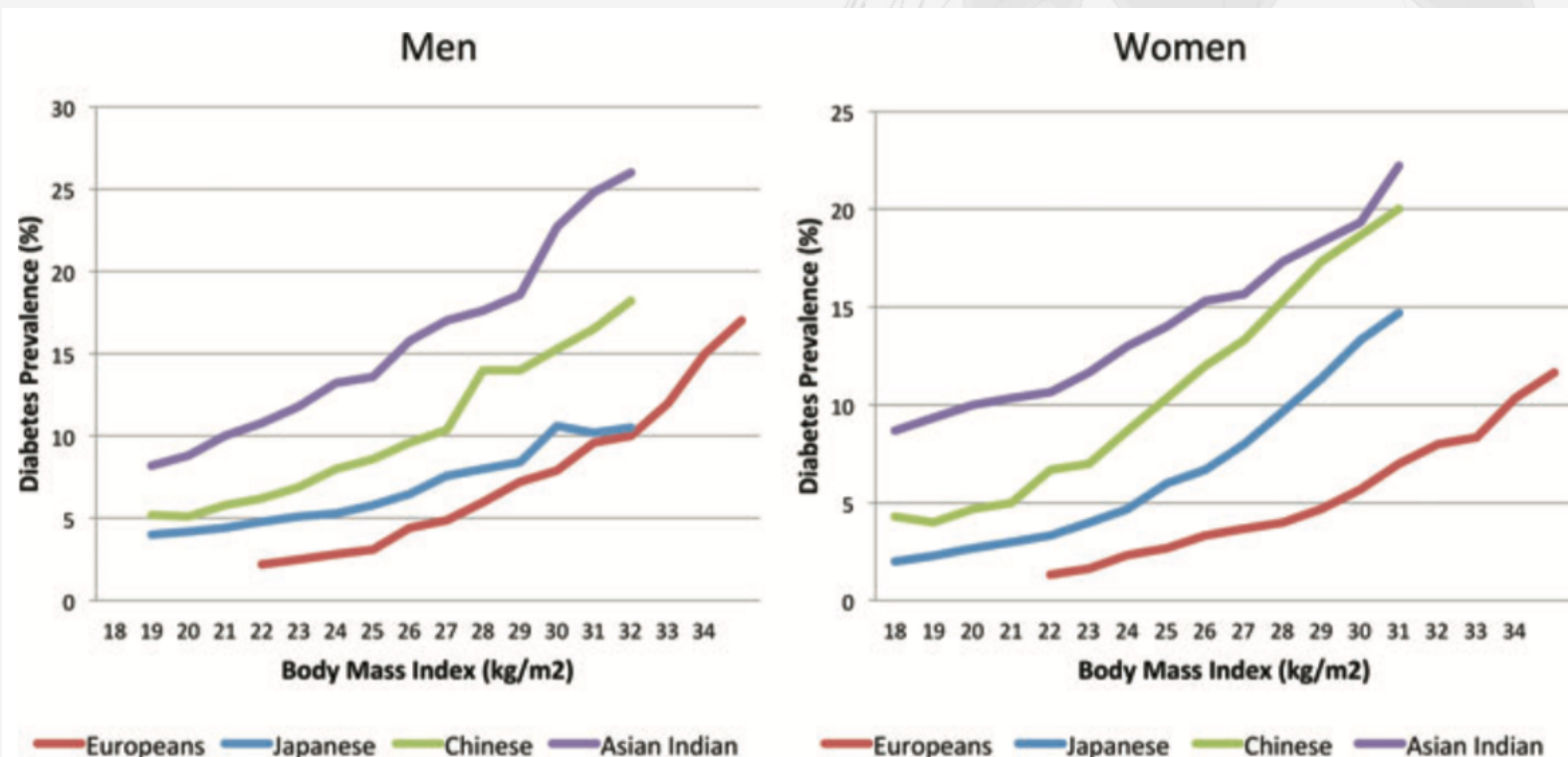


Figure 1. Relationship between BMI and diabetes prevalence in different ethnicities from the DECODA Study compared to a European population.³⁷ Adapted with permission.

- East Asians develop T2DM at much lower BMI than Caucasians
- Obesity associated T2DM risk
 - a 2.5- to 3-fold in Asians
 - A 6- to 8-fold in a U.S. population
- Younger onset (3 years lower)
- Beta-cell dysfunction
- Visceral fat
- More insulin resistance
- White rice consumption



White rice consumption and risk of type 2 diabetes: meta-analysis and systematic review

OPEN ACCESS

Emily A Hu *research assistant*¹, An Pan *research fellow*¹, Vasanti Malik *research fellow*¹, Qi Sun *instructor in medicine*^{1,2}

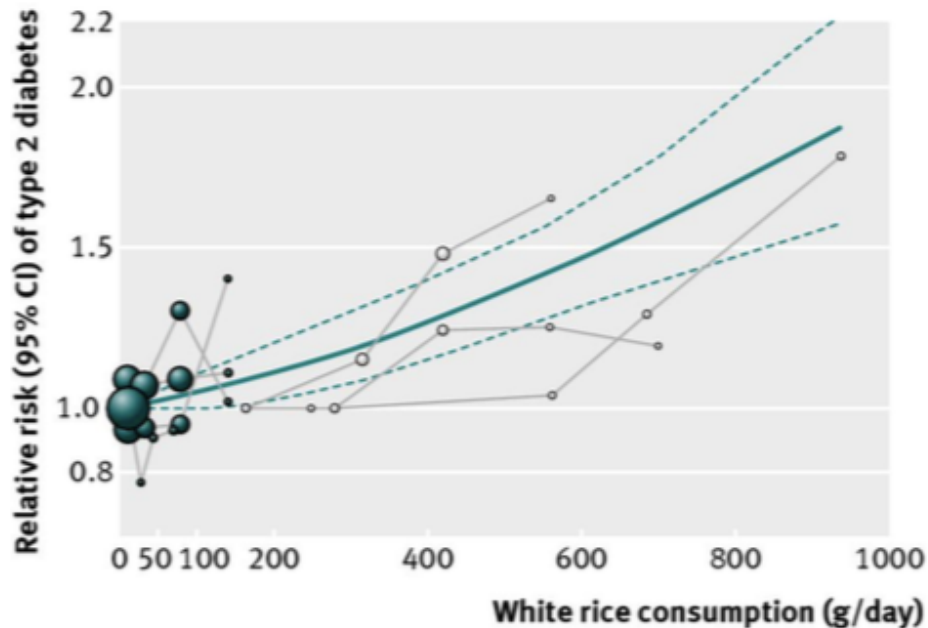


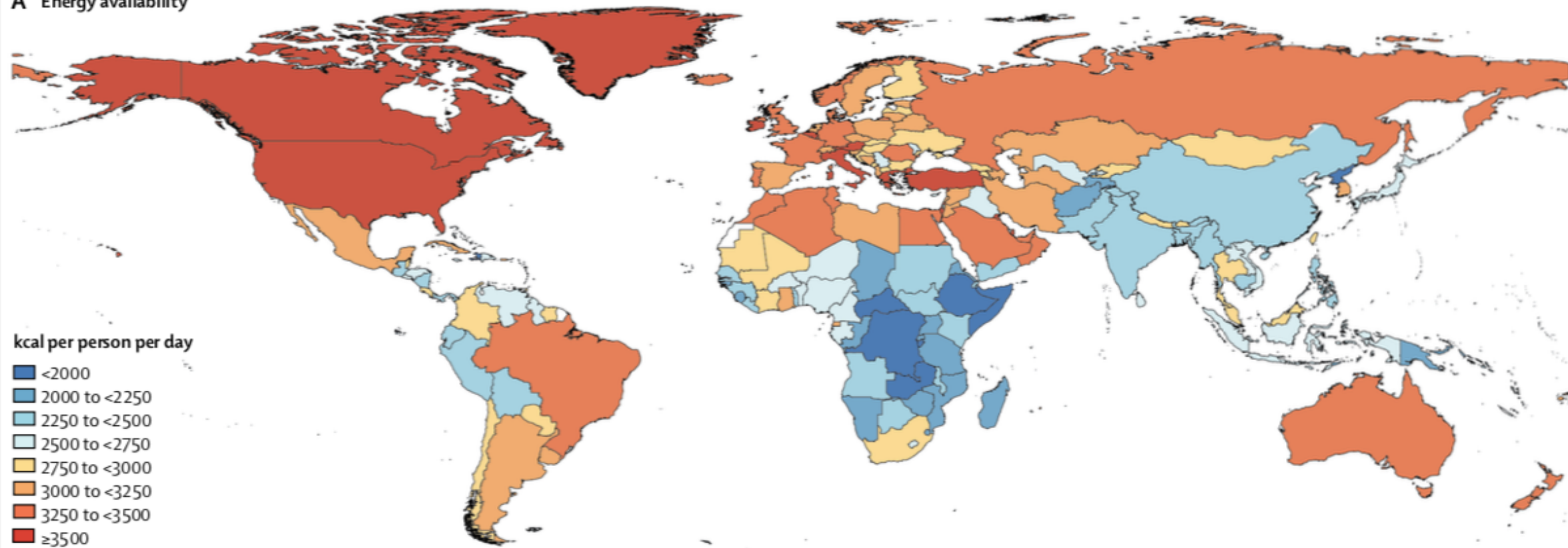
Fig 3 Dose-response relation between white rice intake and risk of type 2 diabetes.

For each serving per day increment of white rice intake, the relative risk of T2DM was **1.11** (1.08 to 1.14)

The Global Nutrient Database: availability of macronutrients and micronutrients in 195 countries from 1980 to 2013

Josef Schmidhuber, Patrick Sur, Kairsten Fay, Bethany Huntley, Joseph Salama, Alexander Lee, Leslie Cornaby, Masako Horino, Christopher Murray, Ashkan Afshin

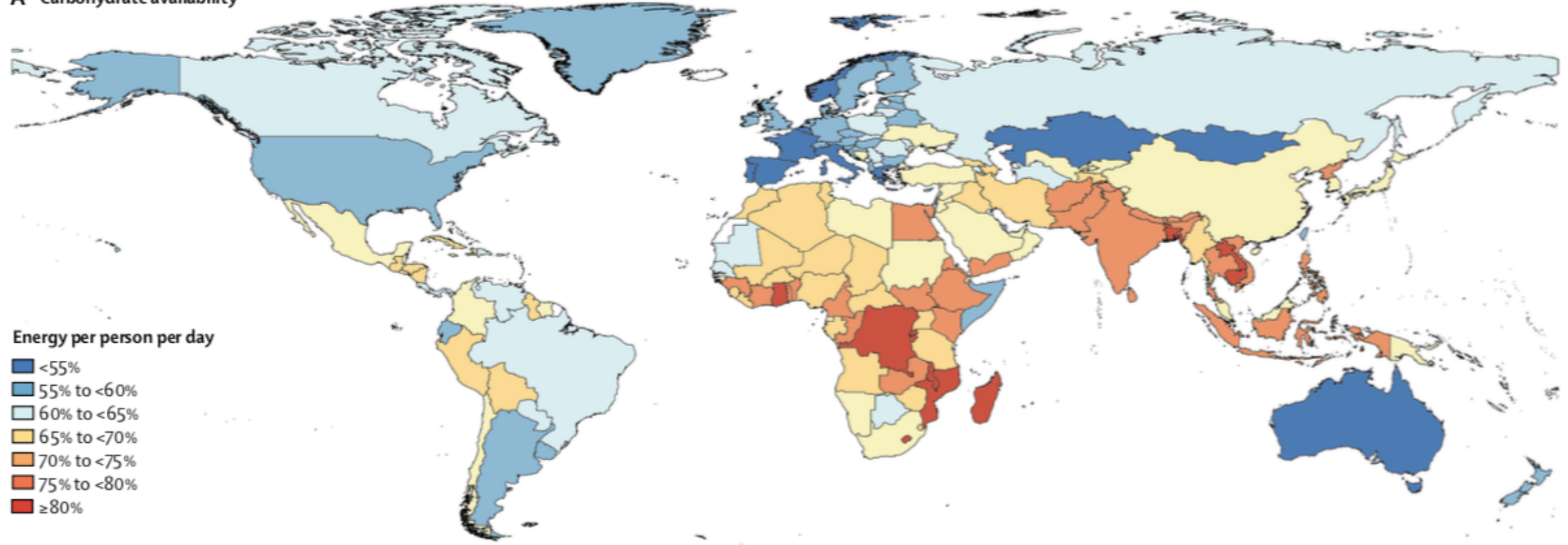
A Energy availability



The Global Nutrient Database: availability of macronutrients and micronutrients in 195 countries from 1980 to 2013

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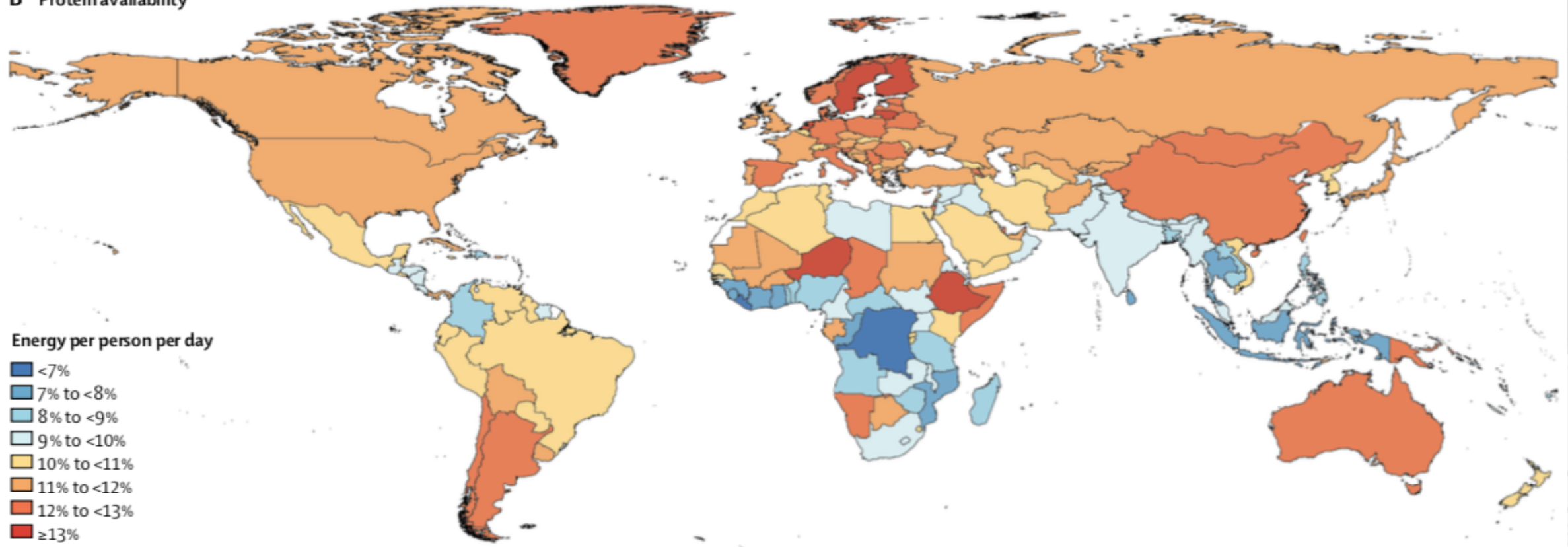
A Carbohydrate availability



The Global Nutrient Database: availability of macronutrients and micronutrients in 195 countries from 1980 to 2013

Josef Schmidhuber, Patrick Sur, Kairsten Fay, Bethany Huntley, Joseph Salama, Alexander Lee, Leslie Cornaby, Masako Horino, Christopher Murray, Ashkan Afshin

B Protein availability





What Asians differ from Caucasians in terms of T2DM?

- Younger ages at diagnosis
- Lower BMI
- More impaired β -cell function
- Different fat distribution
 - Higher visceral fat
- Dietary pattern
 - Lower energy
 - Higher CHO consumption
 - White rice
 - Lower protein

Effect of intensive lifestyle intervention on bodyweight and glycaemia in early type 2 diabetes (DIADEM-I): an open-label, parallel-group, randomised controlled trial

Shahrad Taheri, Hadeel Zaghloul, Odette Chagoury*, Sara Elhadad, Salma Hayder Ahmed, Neda El Khatib, Rasha Abou Amona, Katie El Nahas, Noor Suleiman, Abdulla Alnaama, Abdulla Al-Hamaq, Mary Charlson, Martin T Wells, Samya Al-Abdulla, Abdul Badi Abou-Samra*

18 – 50 years, Middle East and north Africa region
Diabetes duration ≤ 3 years (mean 21 months)
BMI ≥ 27 kg/m² (mean 35 kg/m²)



Intensive lifestyle
n = 79



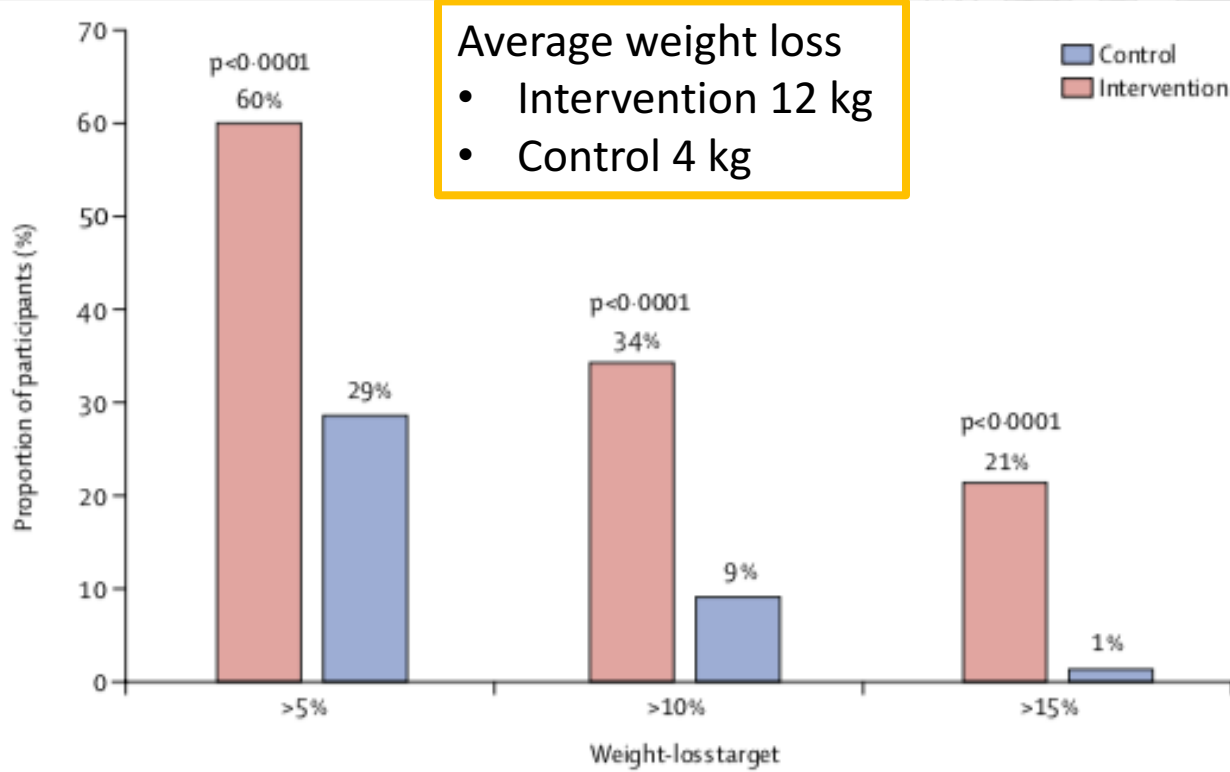
Usual care
n = 79

Intensive lifestyle intervention

- A 12-week total diet replacement phase (800 kcal/day)
- Followed by a 12-week food reintroduction phase
- All diabetes medications were discontinued

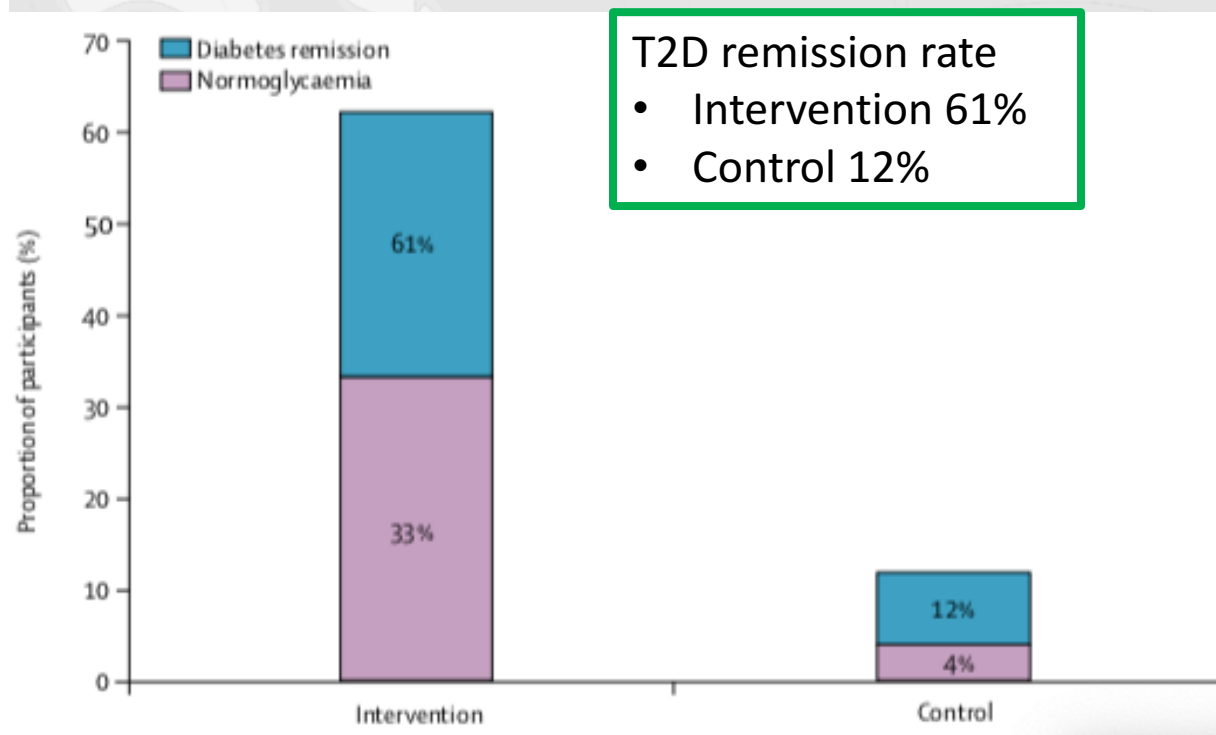
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Average weight loss


- Intervention 12 kg
- Control 4 kg



T2D remission rate

- Intervention 61%
- Control 12%

Immediate and long-term effects of a very-low-calorie diet on diabetes remission and glycemic control in obese Thai patients with type 2 diabetes mellitus

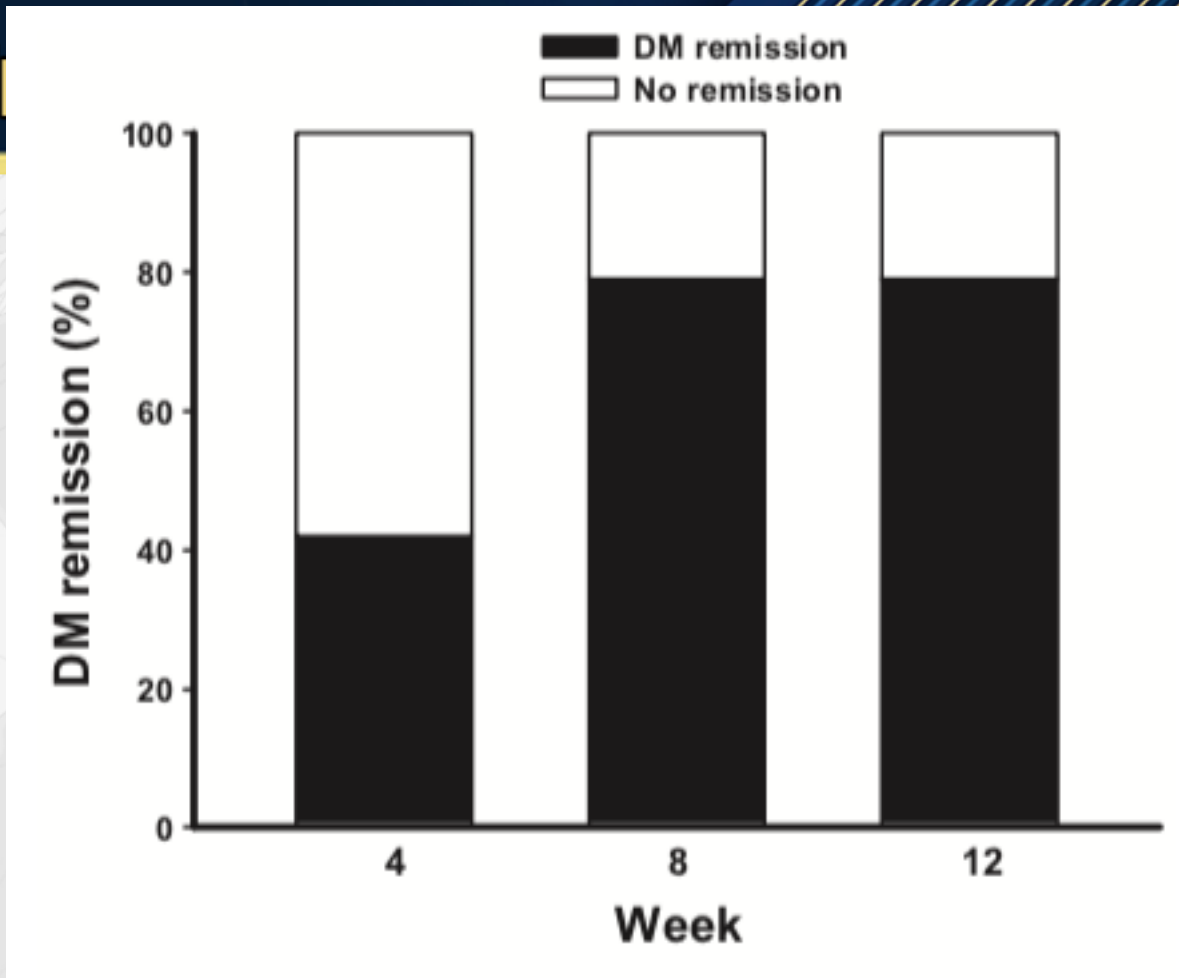
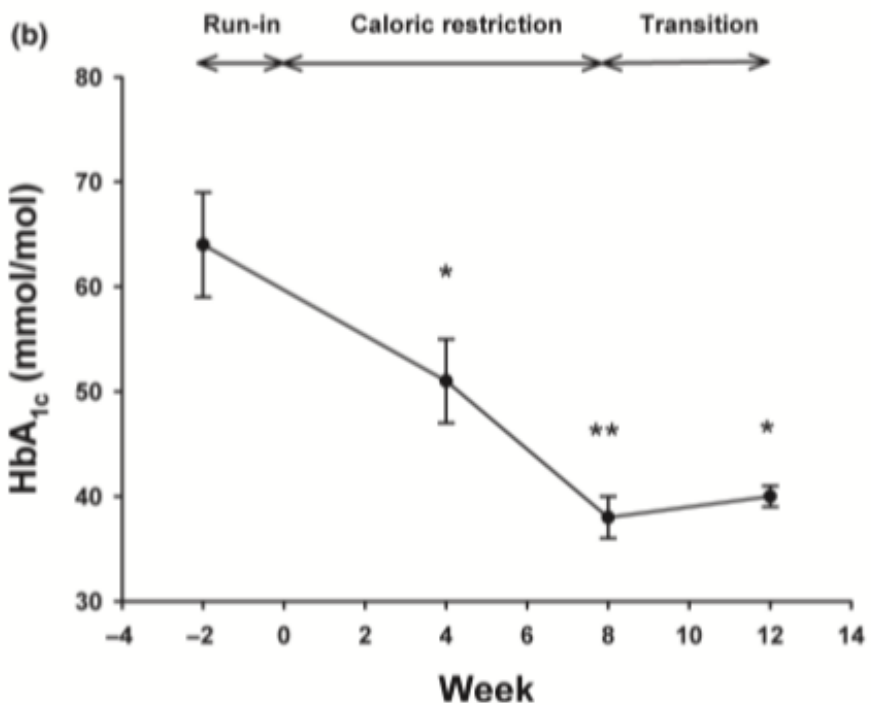
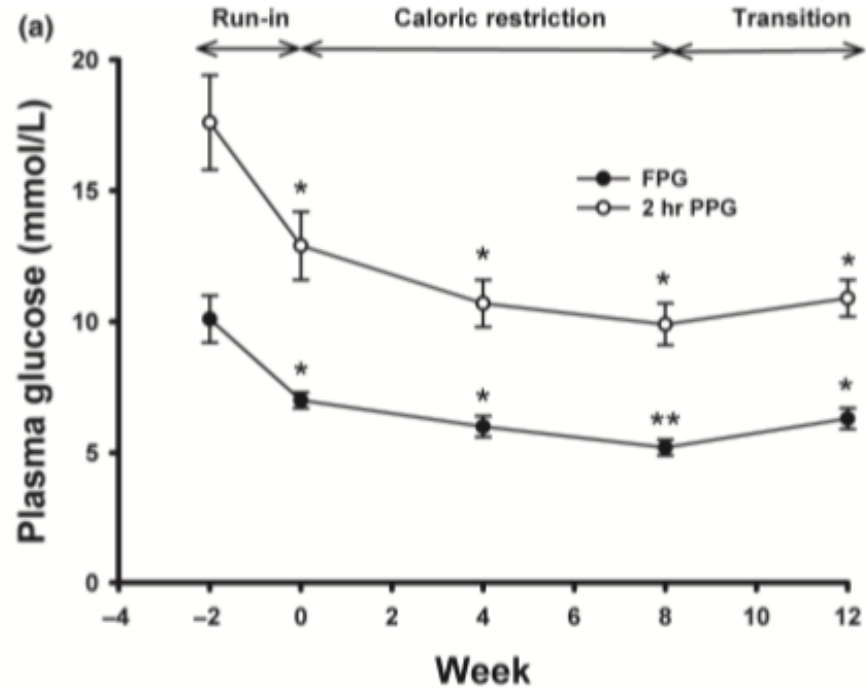
Mongkontida Umphonsathien¹  | Pornsawan Prutanopajai² | Juntagan Aiam-O-Ran² | Titiprang Thararoop² | Apaporn Karin¹ | Chanida Kanjanapha¹ | Wiroj Jiamjarasrangsri³ | Weerapan Khovidhunkit¹

Age was 48 ± 1.7 years (range, 33–59)

DM duration <10 years (median 2.0)

BMI 23–30 kg/m² (BMI 27.7 kg/m²)

Week	-2	0	4	8	12
Period	Run-in		Caloric restriction		Transition
Kcal	600/day 10 days/2 wks		600/day 7 days/wk		800–1,500/day 7 days/wk
OGTT	✓	✓	✓	✓	✓
Chemistry	✓		✓	✓	✓
Anthropometry	✓	✓	✓	✓	✓
QOL	✓		✓	✓	✓



At 12 months, DM remission was achieved in approximately 30%.

Diabetes remission after a lifestyle-medicine intervention on type 2 diabetes in lean and obese Chinese subjects: a prospective study

Wenying Zou^{1#^}, Kunyuan Luo^{2#}, Zhiyong Hu¹, Xiongchou Zhang², Cuiping Feng², Dingkang Ye², Shenghao Liu², Qiwei Zhang³, Rongshao Tan⁴, Chengbin Fu^{2,5^}

<20 years after T2DM diagnosis
≥6 months treatment with oral anti-diabetic drugs
without serious complications
no history of insulin use.



Obesity group
(BMI ≥25 kg/m²)
n = 31



Lean group
(BMI <25 kg/m²)
n = 77

Lifestyle-medicine intervention

- Withdrawal of anti-diabetic drugs
- 1st month, a low-carbohydrate diet (35–40% carbohydrate, 20–30% protein, and 30–45% fat);
 - **1,800** kcal/day for the lean group
 - **700–900** kcal/day for the obese group
- 2nd – 6th month, stepped normal construction diet **50–55% carbohydrate**, 15–20% protein, and 20–30% fat; **30–35 kcal/kg/day**

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Table 3 Remission at A1C <6.5% in participants with T2DM response to 6-month of lifestyle medicine intervention in the obese, lean, and whole groups

Baseline	Obese group (n=31)			Lean group (n=77)			Whole group (n=125)		
	6th month			6th month			6th month		
	A1C <6.5% [48 mmol/mol]	A1C ≥6.5% [48 mmol/mol]	Sum	A1C <6.5% [48 mmol/mol]	A1C ≥6.5% [48 mmol/mol]	Sum	A1C <6.5% [48 mmol/mol]	A1C ≥6.5% [48 mmol/mol]	Sum
A1C <6.5% [48 mmol/mol]	8	2	10 (32.26%)	40	4	44 (46.81%)	48	6	54 (43.20%)
A1C ≥6.5% [48 mmol/mol]	12	9	21	17	33	50	29	42	71
Sum	20 (64.52%)	11	31	57 (60.64%)	37	94	77 (61.60%)	48	125

A1C, glycated hemoglobin; T2DM, type 2 diabetes.

A reduced **visceral fat** was strongly associated with decreases in A1C levels



PENSA Interdisciplinary Webinar

Macronutrient Recommendations for Remission and Prevention of Diabetes in Asian Indians Based on a Data-Driven Optimization Model: The ICMR-INDIAB National Study

Diabetes Care 2022;45:2883–2891 | <https://doi.org/10.2337/dc22-0627>

The national Acceptable Macronutrient Distribution

Range (AMDR) for adults:

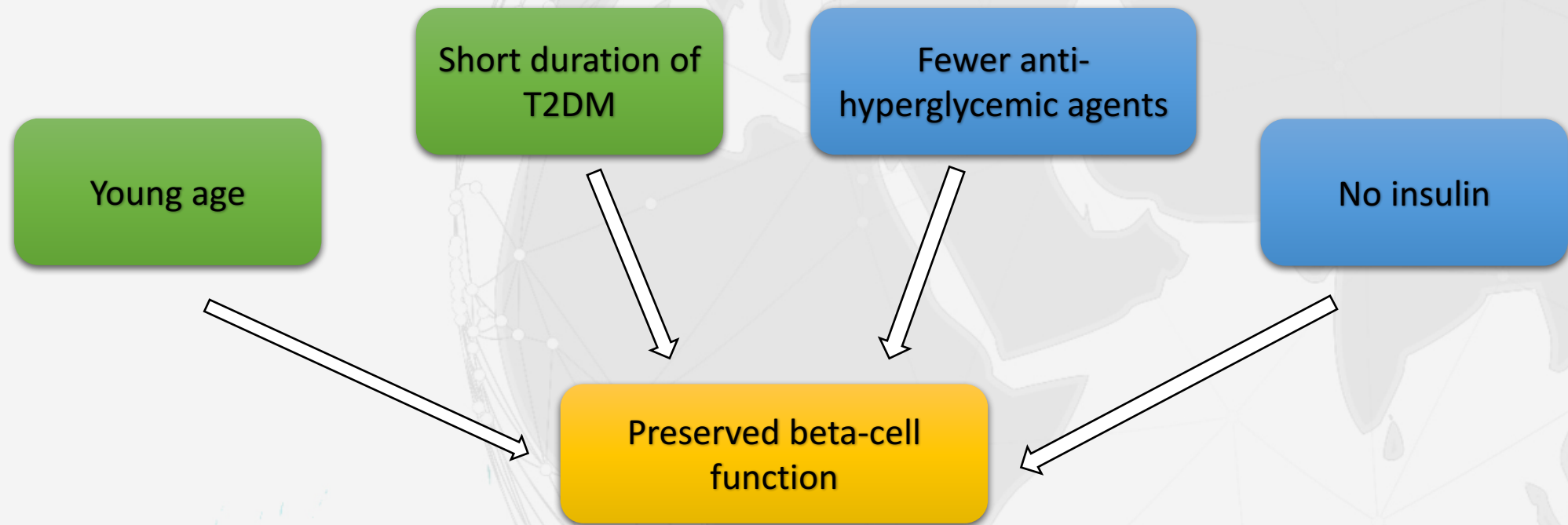
- Carbohydrates 45–65% of total calories
- Protein 5–15%
- Fat 15–35%

For remission/prevention of T2D

- A lower range of carbohydrate intake **(49–56%E)**
- A higher range of protein **(14–20%E)**
- A narrower range of fat intake **(21–27%E)**

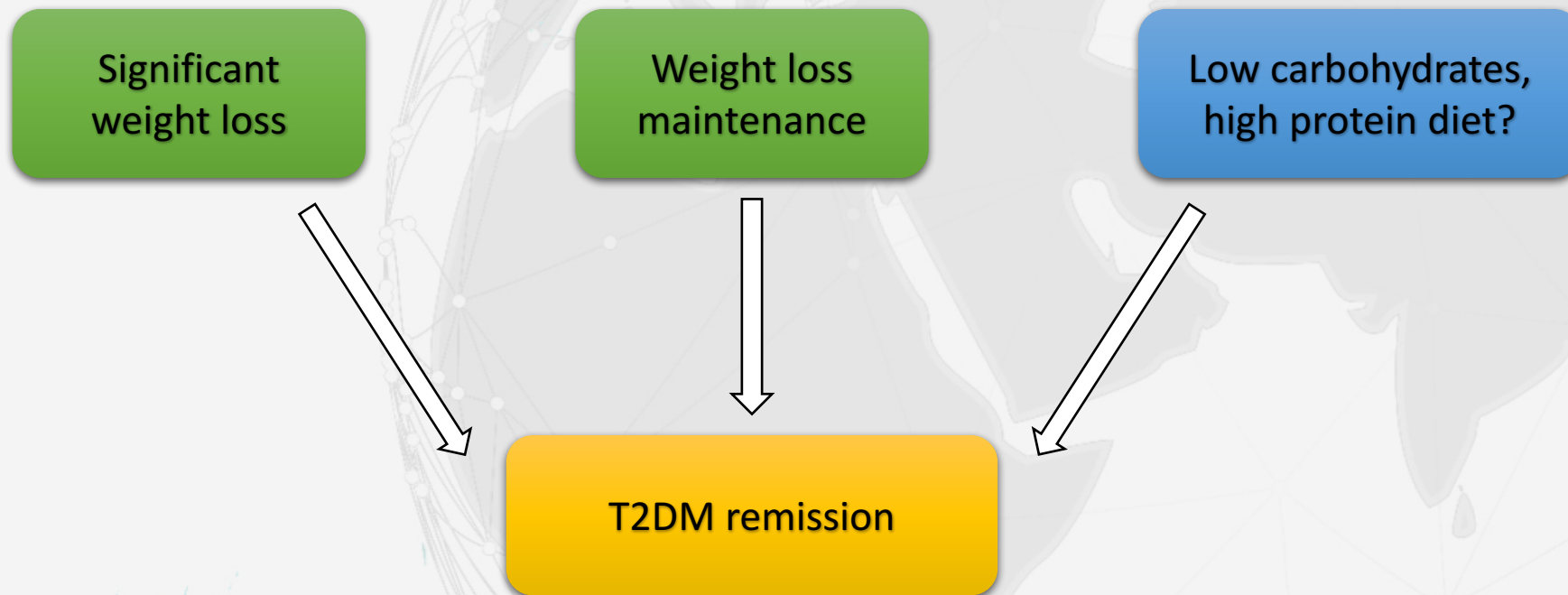


Who will get T2DM remission?





How to get T2DM remission?





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Thank you very much.