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Diabetes Alliance Integration Program
Diabetes Master Class 1

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phn
HUNTER NEW ENGLAND AND CENTRAL COAST
An Australian Government Initiative

NSW GOVERNMENT Health
Hunter New England Local Health District

Master Class 1 – Type 2 diabetes mellitus

- Screening and Diagnosis
- Pathophysiology
- Management
  - Basic nutritional advice for health eating
  - Monitoring & Targets
  - Pharmacotherapy
- The National Diabetes Services Scheme (NDSS)
- Latest guidelines

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Definition

- Fasting BGL⩾7 mmol/L
- Random or 2h BGL>11.1mmol/L
- HbA1c ⩾48mmol/mol (6.5%)

Why these numbers?

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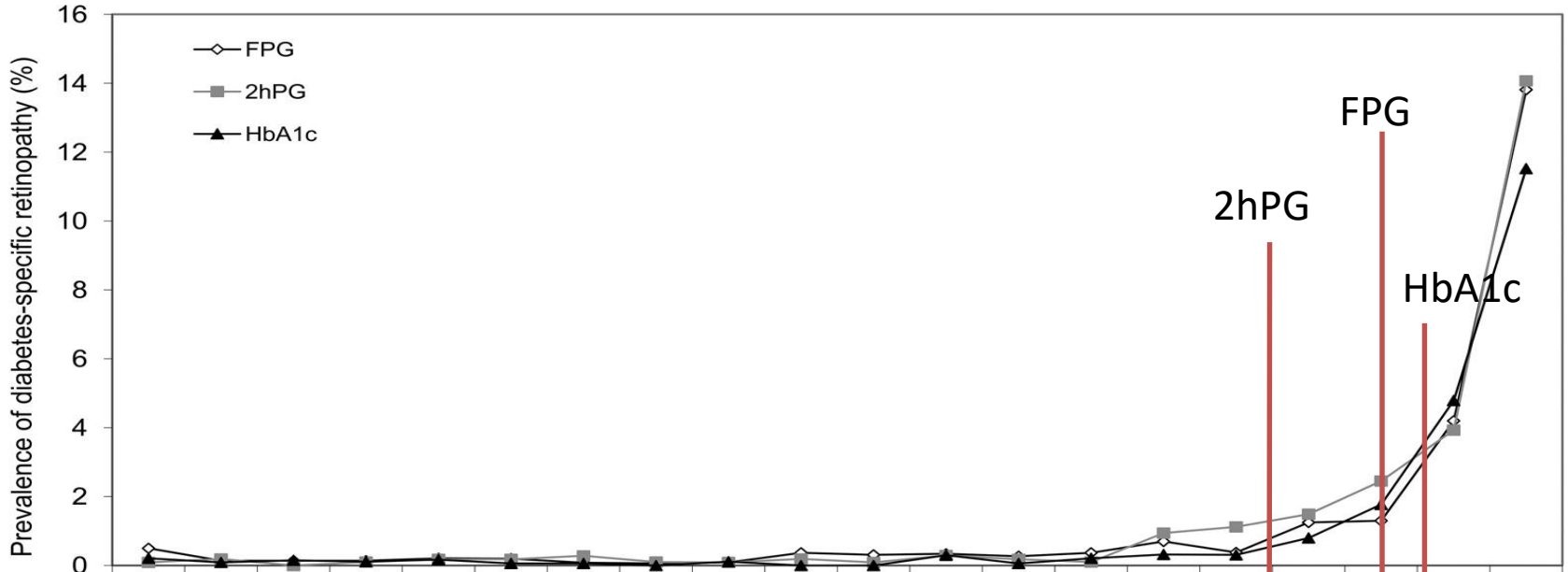
Diabetic Retinopathy

Prevalence of diabetes-specific retinopathy (moderate or more severe retinopathy) by vigintiles of the distribution of FPG, 2-h PG, and A1C.



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
FPG (mmol/L)	1.7-	4.5-	4.7-	4.8-	4.9-	5.1-	5.2-	5.2-	5.3-	5.4-	5.5-	5.6-	5.7-	5.8-	6.0-	6.2-	6.4-	6.9-	7.7-	10.1-
2-h PG (mmol/L)	1.1-	4.3-	4.9-	5.3-	5.7-	6.0-	6.3-	6.6-	6.9-	7.2-	7.7-	8.0-	8.5-	9.1-	9.8-	10.7-	11.9-	13.4-	15.9-	19.9-
HbA1c (%)	3.1-	4.6-	4.7-	4.9-	5.0-	5.0-	5.1-	5.2-	5.3-	5.3-	5.4-	5.5-	5.6-	5.7-	5.8-	5.9-	6.1-	6.3-	6.8-	7.9-

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Stephen Colagiuri et al. Dia Care 2011;34:145-150

American Diabetes Association.

Screening for Type 2 Diabetes

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Symptomatic Diabetes

- Symptoms: thirst, polyuria, weight loss, recurrent thrush/UTI, blurred vision
- Do not delay diagnostic tests
  - Check random BGL, HbA1c
  - Avoid OGTT as it may precipitate HHS
- Check POC ketones

Screening for Type 2 DM

Refer to RACGP Handbook or HNE HealthPathways

Screening for diabetes risk :

- LOW RISK: every 3 years from age 40 with AUSDRISK
- HIGH RISK: every 3 years with FBG or HbA1c
- Annual with FBG or HbA1c
  - Aboriginal and TS Islanders from age 18
  - IFG or IGT

* Fast 8 hours

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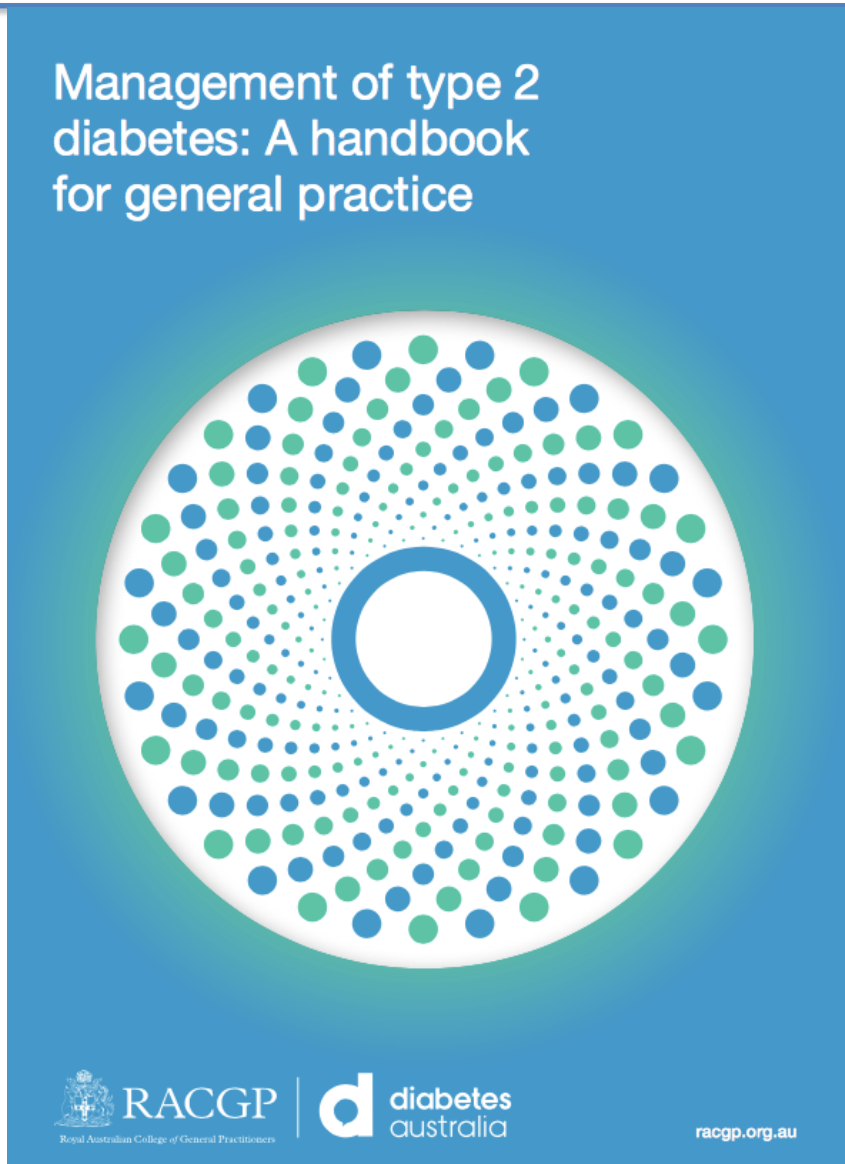

High Risk
(regardless of AUSDRISK score)

- aged ≥40 years AND overweight or obese
- any age with IGT or IFG
- 1st-degree relative with diabetes
- history of a cardiovascular event (eg. IHD, PVD, CVA)
- people of high-risk ethnicity/background
  - Aboriginal and Torres Strait island
  - Pacific Islands
  - Asian (esp subcontinent)
  - Southern European
- history of
  - Cardiovascular event
  - GDM
  - polycystic ovary syndrome (PCOS)
- taking antipsychotic medication
- Aboriginal and/or Torres Strait Islander people.

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Examples of risk factors associated with DM

Risk factor	Risk
Obesity	HR 7.37 (6.39-8.50)
Family history	HR 2.72 (2.48 – 2.99)
Both parents DM	HR 5.14 (3.73-7.07)
Ethnicity Aboriginals and Torres Strait Islanders Asian	 RR 4.7 HR 2.26 (1.70-2.99)
Sedentary lifestyle (every 2h TV watching)	RR1.20 (1.14-1.27)
Sugar sweetened beverages	RR 1.83 (1.4-2.4)
Current smokers	RR 1.4 (1.3-1.6)
Antipsychotic use (Olanzapine, Clozapine, Risperidone and Quetiapine)	

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How do you screen for asymptomatic DM?

1. Fasting glucose
2. 75g OGTT
3. POC glucose with glucose meter
4. HbA1c

Diagnostic criteria

- Diagnostic criteria for type 2 diabetes requires either:
  - symptoms and 1 qualifying result
  - no symptoms and 2 qualifying results on separate occasions:
    - FBG ≥ 7.0 mmol/L
    - Random blood glucose or 2 hour post–OGTT ≥ 11.1 mmol/L
  - no symptoms and 2 qualifying results on same day:
    - HbA1c ≥ 6.5% (48 mmol/mol)
    - AND FBG ≥ 7.0 mmol/L or random BG/2hBG ≥ 11.1 mmol/L
    - If both HbA1c and glucose levels are elevated in an individual, the diagnosis of diabetes is confirmed. If only one of the values is elevated, the abnormal test should be repeated to confirm the diagnosis

Example 1

Mr. R, overweight 58yo male, asymptomatic

- fasting glucose of 7.3mmol/L

- Are you confident with the diagnosis?
- What additional test would you use ?

  HbA1c 45 mmol/mol (6.3%)

- What tests do you recommend ?

  - repeat fasting
  - repeat HbA1c
  - 75g OGTT

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Example 2

Mr. M, fasting BGL 12mmol/L, asymptomatic

- Next option would be:

  -OGTT

  -HbA1c

  -Recheck fasting

- If FBG is clearly elevated: avoid OGTT

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Indications for an OGTT

- Universal screening for GDM
  - Diagnostic criteria: FBG > 5.1, 1hBG > 10, 2hBG >8.5mmol/l
- **Do not request OGTT for those with pre-existing DM during pregnancy – potentially harmful**

Outside pregnancy

- If fasting glucose 6.1 to 6.9mmol/l, HbA1c >6.5% (48mmol/mol)
- If fasting is 6.1-6.9mmol/l and HbA1c <6.5% (48mmol/mol) – prediabetes/early DM; OGTT rarely indicated
- There is NO NEED to measure for insulin levels

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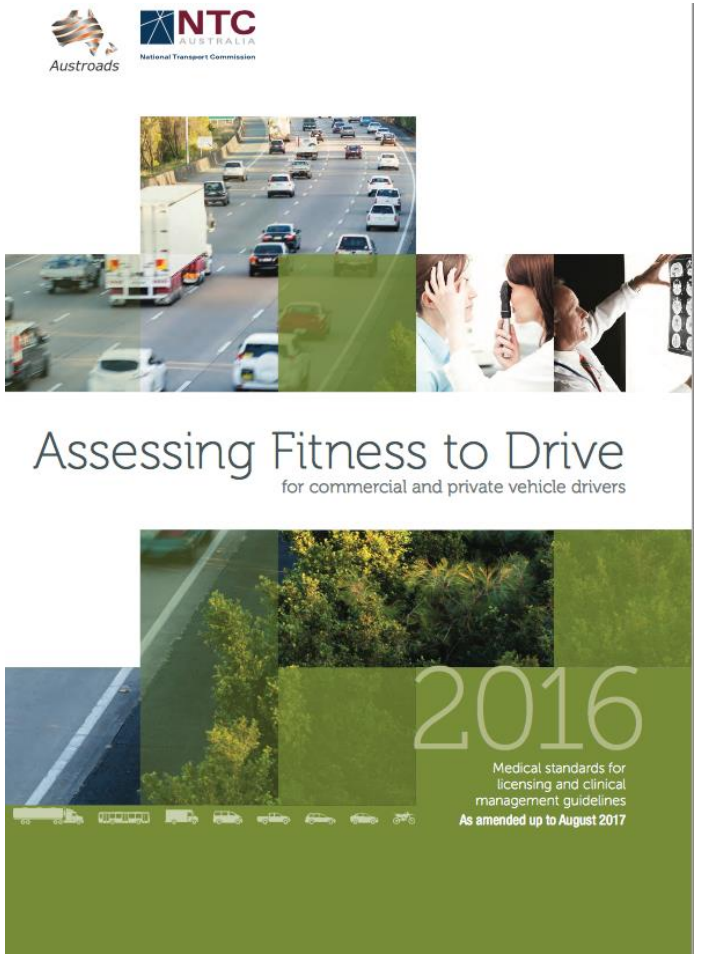
Example 4

- Mr. T, 48 yo overweight HR truck driver
- On screening with GTT
  - FPG 6.8 mmol/L, 2hPG 11.7mmol/L
  - no symptoms
  - HbA1c 5.6% (38mmol/mol)
- Do you diagnose DM?
- What are the consequences of diagnosis?



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HbA1c for diagnosis

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Beware of HbA1c limitations

	Increased HbA1c	Decreased HbA1c	Variable effect
Erythropoiesis	**Iron deficiency** **Vitamin B12 deficiency** Decreased erythropoiesis	Erythropoietin use Iron Vitamin B12 Reticulocytosis Chronic liver disease	
Altered Haemoglobin			**Haemoglobinopathies** HbF Methaemoglobin
Glycation	•Alcoholism •Chronic renal failure, Decreased intraerythrocyte pH	•Aspirin •Vitamin C and E •Certain haemoglobinopathies •Increased intra-erythrocyte pH	Genetic determinants
Erythrocyte life span	Increased erythrocyte life span: •**Splenectomy**	Decreased erythrocyte life span: •**haemoglobinopathies** •**Splenomegaly** •Rheumatoid arthritis •Drugs eg. antiretrovirals, ribavirin and dapsone	Genetic determinants
Assays	•Hyperbilirubinaemia •Carbamylated Hb •Alcoholism •Large doses of aspirin •Chronic opiate use	Hypertriglyceridaemia	Haemoglobinopathies

POC HbA1c may vary by 0.4%

Pre Diabetes

- Fasting 6.1-6.9mmol/l (IFG)
- 2h post oGTT 7.8-11mmol/l (IGT)
- HbA1c 5.7-6.4% (30 to 46mmol/mol) provided fasting/random values not in the overt diagnostic range for diabetes

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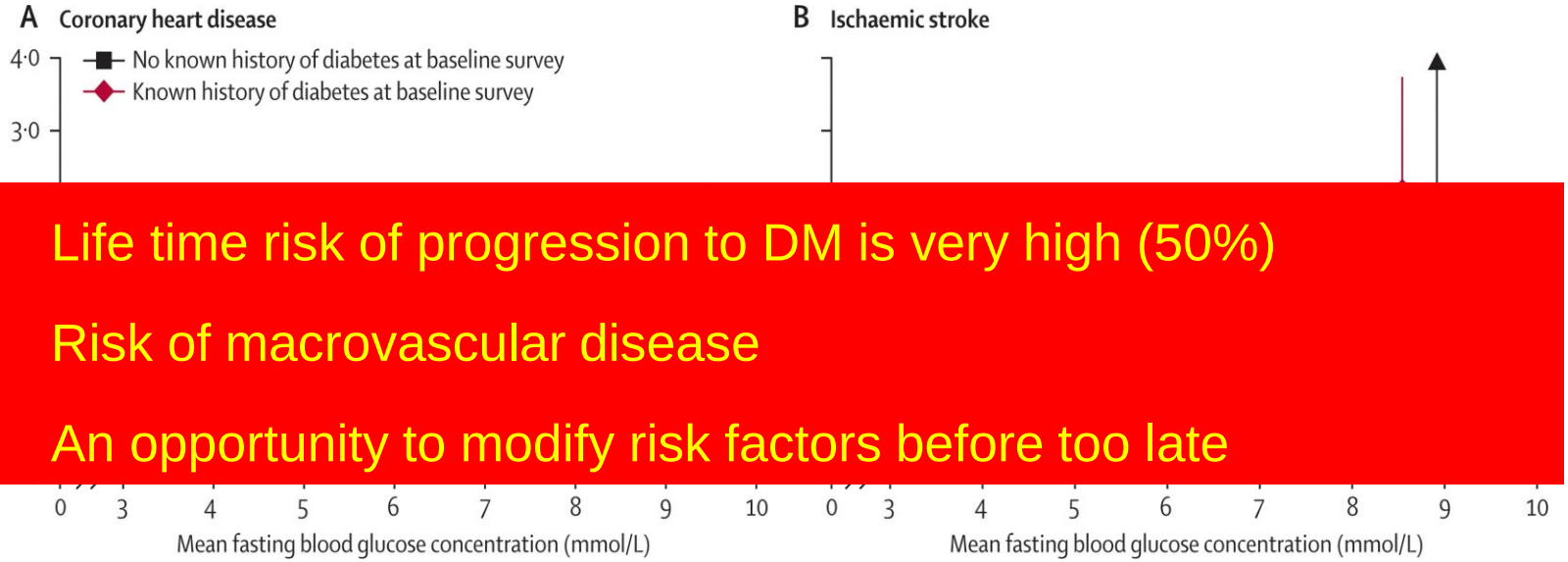
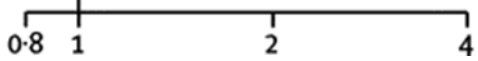
Why is pre diabetes important to diagnose?

Fasting Glucose and the CVS risk in 698782 patients in 102 studies
Emerging Risk Collaboration group **Lancet 2010; 375: 2215–22**



- Life time risk of progression to DM is very high (50%)
- Risk of macrovascular disease
- An opportunity to modify risk factors before too late

Fasting blood glucose concentration	Number of participants (%)	Number of cases	HR (95% CI)
Known diabetes at baseline			
≥7 mmol/L	13 122 (4·7%)	1186	2·36 (2·02–2·76)
<7 mmol/L	5807 (2·1%)	380	1·61 (1·42–1·82)
No known diabetes at baseline			
≥7 mmol/L	7240 (2·6%)	452	1·78 (1·56–2·03)
6·1 to <7 mmol/L	19 607 (7·0%)	1011	1·17 (1·08–1·26)
5·6 to <6·1 mmol/L	32 008 (11·5%)	1631	1·11 (1·04–1·18)
3·9 to <5·6 mmol/L*	185 590 (66·5%)	9508	1·00 (0·95–1·06)
<3·9 mmol/L	15 916 (5·7%)	646	1·07 (0·97–1·18)



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Management of Pre Diabetes

- Lifestyle promotion [exercise, nutrition, weight]
  - 7 yr follow up Finnish Diabetes study: HR 0.57, mean weight diff. 3.5kg
  - Diabetes Prevention Program: Lifestyle vs. MF bd 58% RRR vs. 31%
- Smoking cessation
- Statin therapy for those with 10yr CV risk>10%
- Consider Bariatric surgery if BMI >40kg/m^2

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PATHOPHYSIOLOGY OF TYPE 2 DIABETES

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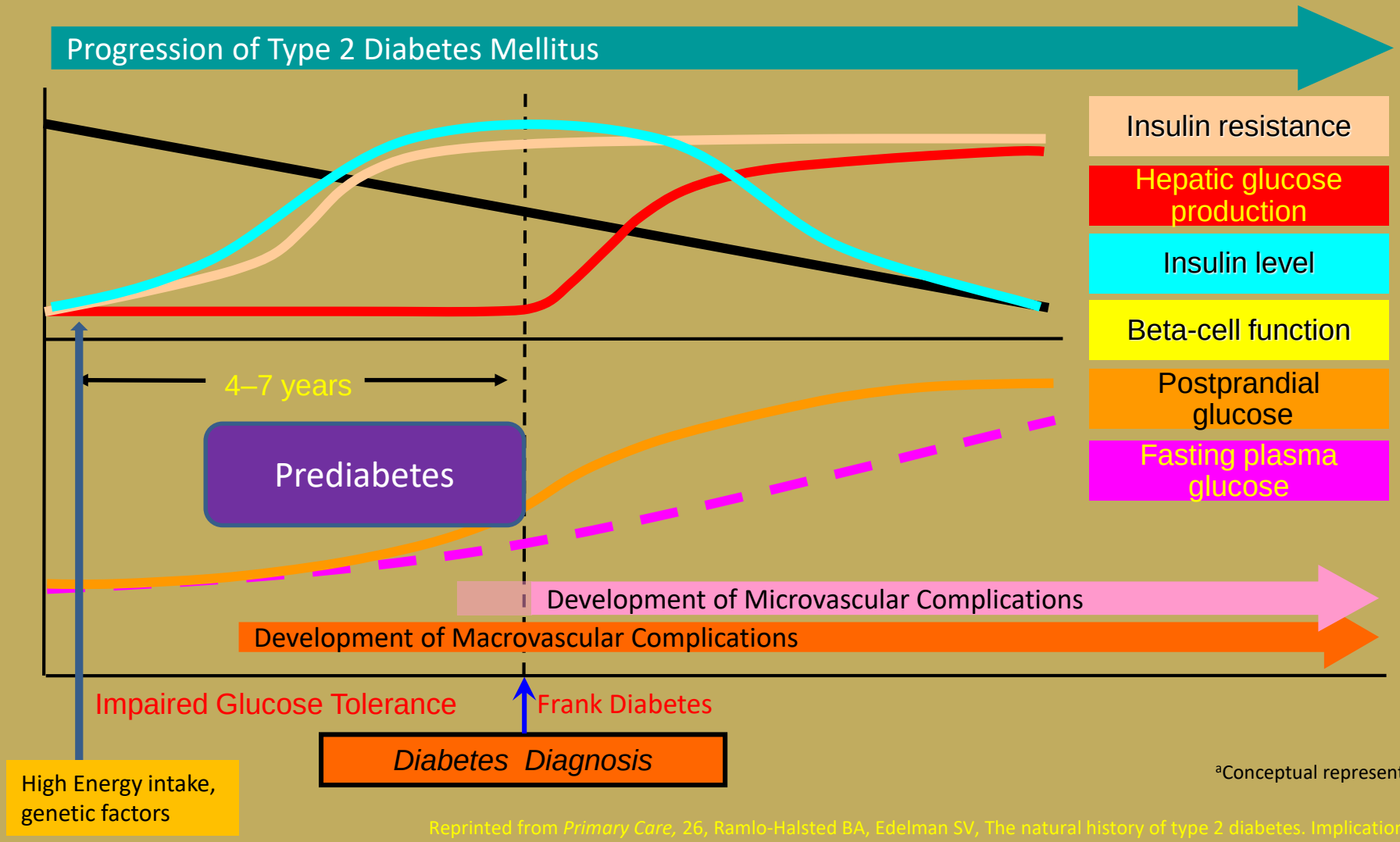
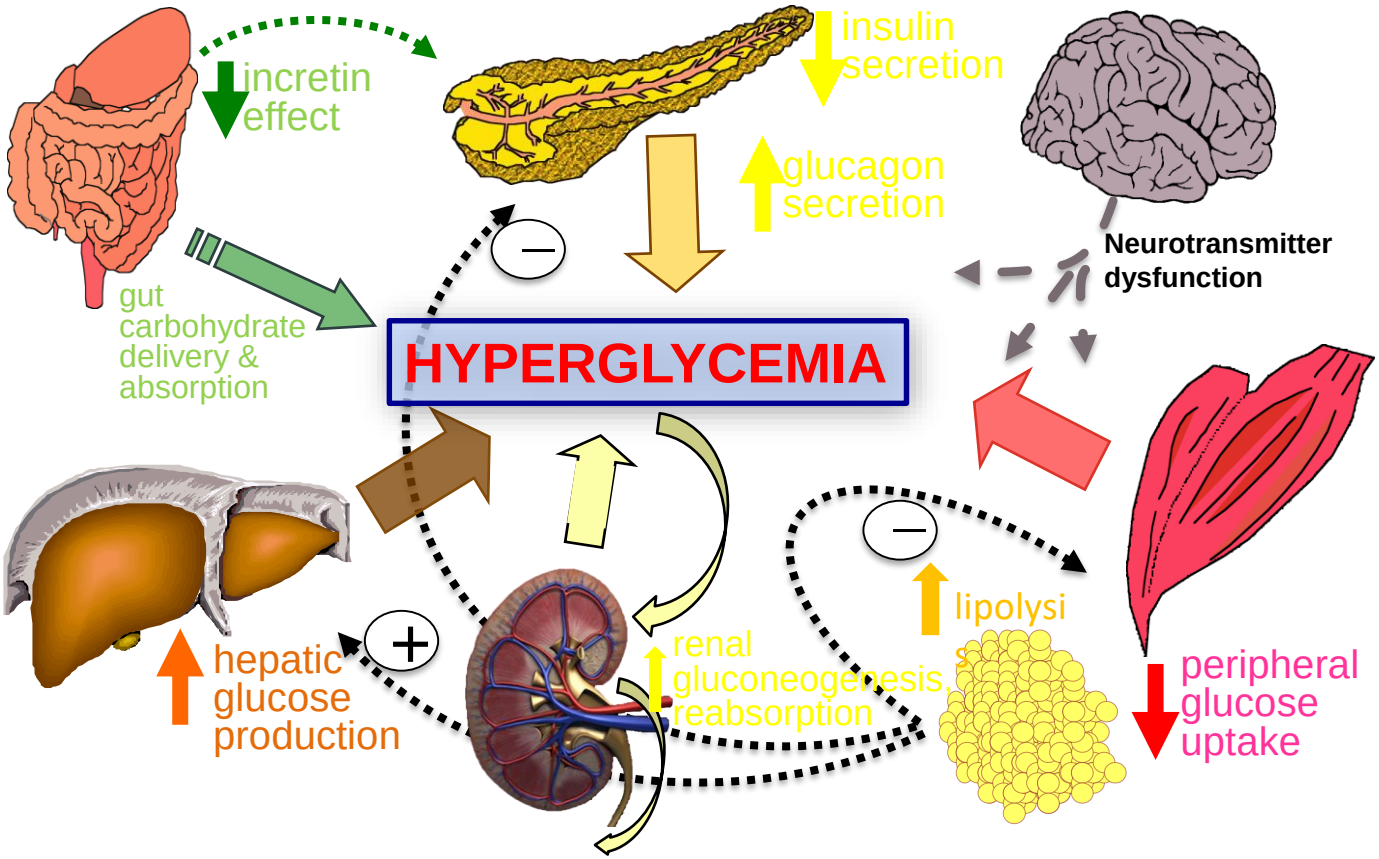
Development and Progression of Type 2 Diabetes and Related Complications[a]



[a]Conceptual representation.

Pathophysiological Abnormalities in T2DM



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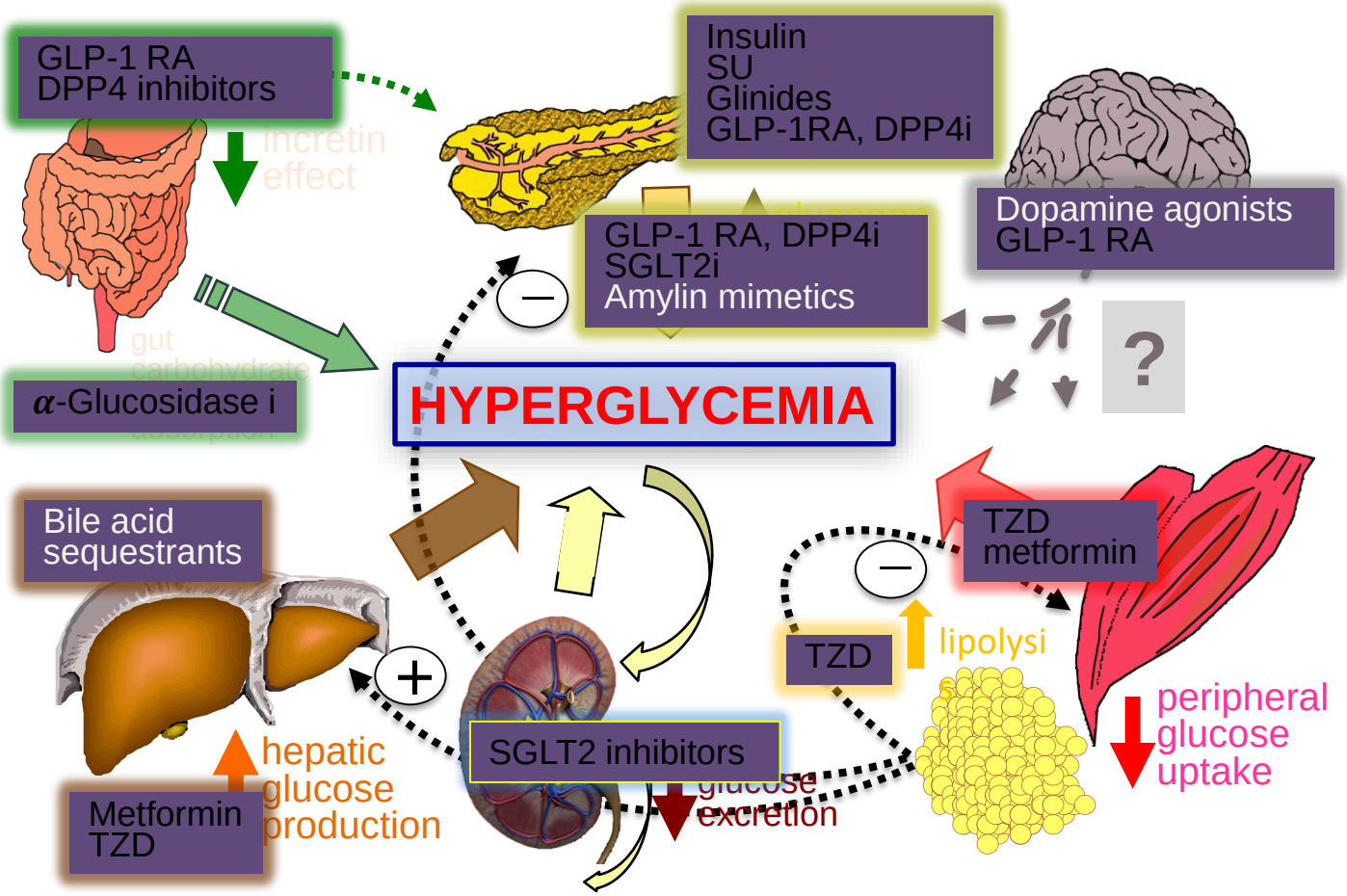
DeFronzo RA. Diabetes. 2009;58(4):773–795

Treatment Targets in T2DM

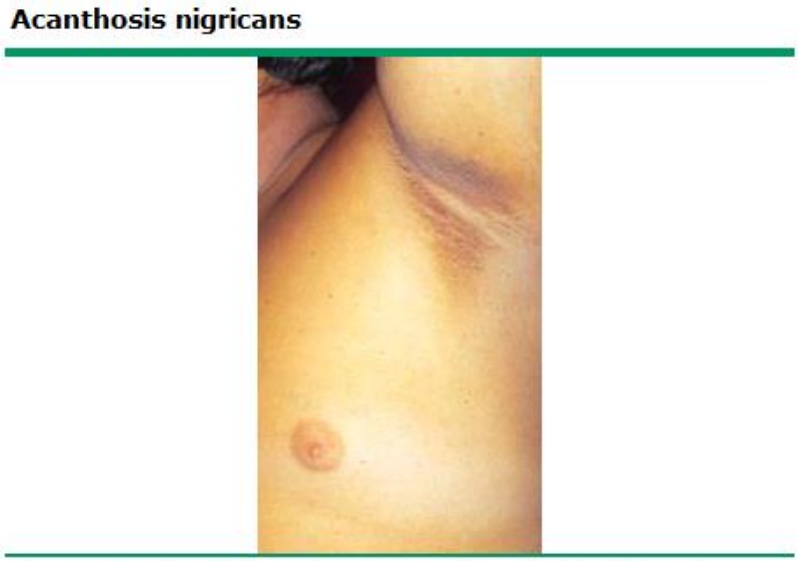


Signs of Insulin resistance

- Central obesity (waist circumference)
  - 90cm for men, 80cm for women
- Neck circumference (37cm for men, 33cm for women)
- Acanthosis
- Cutaneous skin tags
- Lipodystrophy syndromes

Insulin levels offer little additional information

– not indicated routinely



Classic hyperpigmented axillary lesion in acanthosis nigricans.
Courtesy of Jeffrey Flier, MD.

UpToDate®

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Example 3

Ms. K, 26 yo obese female

- presents with weight loss, thirst, polyuria

- POC glucose 17mmol/L

- advised to have 75 OGTT on Monday
  - What are the risks of delaying diagnosis?
  - Is an OGTT necessary ?
  - What should you do?

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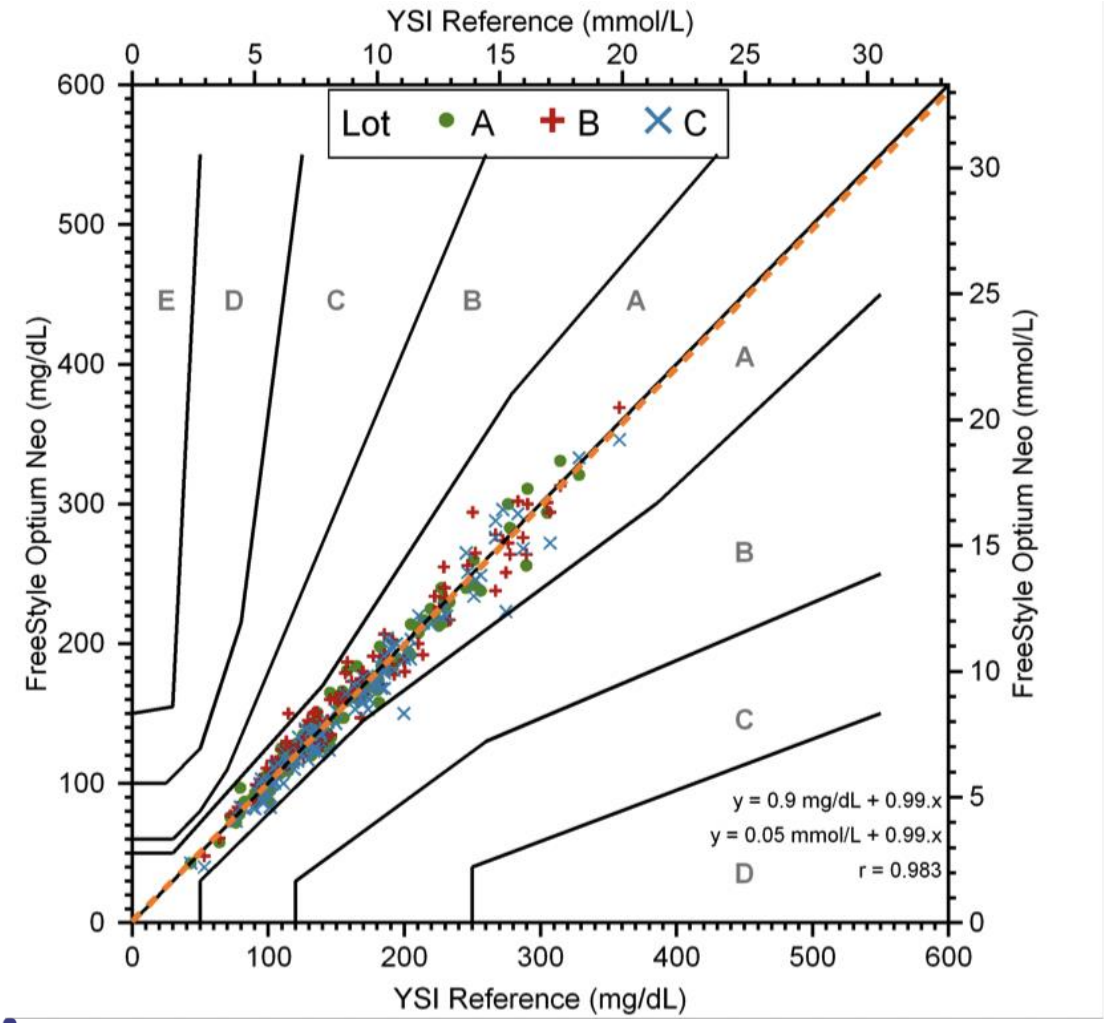
MARD



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Types of DM

- Type I (5-10%)– β cell destruction
  - 1a. Immune mediated
  - 1b. idiopathic
- Type II – (90+%)
- Type III – due to another known aetiology
  - A. Genetic defect in β cell function
  - B. Genetic defect in insulin action
  - C. Exocrine pancreatic disease
  - D. Endocrinopathies
  - E. Drug or chemical induced
  - F. Infections
  - G. Uncommon autoimmune forms
  - H. Syndrome associated
- Type IV - GDM*

American Diabetes Association Dia Care 2014;37:S81-S90

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I. Type 1 diabetes (β-cell destruction, usually leading to absolute insulin deficiency)
   A. Immune mediated
   B. Idiopathic

II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)

III. Other specific types
   A. Genetic defects of β-cell function
      1. MODY 3 (Chromosome 12, HNF-1α)
      2. MODY 1 (Chromosome 20, HNF-4α)
      3. MODY 2 (Chromosome 7, glucokinase)
      4. Other very rare forms of MODY (e.g., MODY 4: Chromosome 13, insulin promoter factor-1; MODY 6: Chromosome 2, *NeuroD1*; MODY 7: Chromosome 9, carboxyl ester lipase)
      5. Transient neonatal diabetes (most commonly ZAC/HYAMI imprinting defect on 6q24)
      6. Permanent neonatal diabetes (most commonly KCNJ11 gene encoding Kir6.2 subunit of β-cell K_{ATP} channel)
      7. Mitochondrial DNA
      8. Others
   B. Genetic defects in insulin action
      1. Type A insulin resistance
      2. Leprechaunism
      3. Rabson-Mendenhall syndrome
      4. Lipoatrophic diabetes
      5. Others
   C. Diseases of the exocrine pancreas
      1. Pancreatitis
      2. Trauma/pancreatectomy
      3. Neoplasia
      4. Cystic fibrosis
      5. Hemochromatosis
      6. Fibrocalculous pancreatopathy
      7. Others
   D. Endocrinopathies
      1. Acromegaly
      2. Cushing's syndrome
      3. Glucagonoma
      4. Pheochromocytoma
      5. Hyperthyroidism
      6. Somatostatinoma
      7. Aldosteronoma
      8. Others
   E. Drug or chemical induced
      1. Vacor
      2. Pentamidine
      3. Nicotinic acid
      4. Glucocorticoids
      5. Thyroid hormone
      6. Diazoxide
      7. β-Adrenergic agonists
      8. Thiazides
      9. Dilantin
      10. γ-Interferon
      11. Others
   F. Infections
      1. Congenital rubella
      2. Cytomegalovirus
      3. Others
   G. Uncommon forms of immune-mediated diabetes
      1. Stiff-man syndrome
      2. Anti-insulin receptor antibodies
      3. Others
   H. Other genetic syndromes sometimes associated with diabetes
      1. Down syndrome
      2. Klinefelter syndrome
      3. Turner syndrome
      4. Wolfram syndrome
      5. Friedreich ataxia
      6. Huntington chorea
      7. Laurence-Moon-Biedl syndrome
      8. Myotonic dystrophy
      9. Porphyria
      10. Prader-Willi syndrome
      11. Others

IV. Gestational diabetes mellitus

Patients with any form of diabetes may require insulin treatment at some stage of their disease. Such use of insulin does not, of itself, classify the patient.

When to consider Type 1 Diabetes ?

- T1D can occur at any age
- Typically presents with thirst, polyuria and weight loss
- If BGL >17mmol/l at presentation, check POC ketones
- If ketones +, indicative of insulin deficiency, requires urgent insulin initiation – even if obese phenotype

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When do you screen for adult onset Type 1 DM ?

Presence of 2 or more had >90% sensitivity and 70% specificity

- Age of onset <50
- Acute symptoms
- BMI <25kg/m²
- Personal history of autoimmune disease

Additional risk factors:

- Presence of ketones
- absence of family history of type 2 diabetes
- Positive f/h of type 1 diabetes or autoimmune conditions
- No signs of insulin resistance (central obesity, acanthosis)
- Labile BGL patterns despite dietary changes

Screening for Type 1 DM

- Fasting BGL, C-peptide, insulin, BOHB
- Autoantibodies:
  - Anti-GAD
  - Anti-IA2, Zn transporter 8 Ab
  - Anti-islet cell Ab, insulin Ab (not v. useful)

	Sensitivity	Specificity	AUC	SE	95% CI
GADA	64.77	96.6	0.807	0.034	0.74-0.86
IA2A	19.32	100.00	0.597	0.043	0.52-0.67
ZnT8A	31.82	97.73	0.648	0.041	0.57-0.71

AUC: Area under curve, SE: Standard error, CI: Confidence interval, ZnT8A: Zinc transporter-8 antibodies, GADA: Glutamic acid decarboxylase antibodies, IA2A: Insulinoma-2 antigen antibodies

When to seek specialist advice for newly diagnosed T2DM (please refer to HealthPathways)

- Seek urgent specialist assessment if:
  - **Persistent or severe hyperglycaemia (> 20 mmol/L)**
  - **HbA1c > 11% (> 97 mmol/mol)**
  - **Unwell or dehydrated**
  - **Presence of ketones**
  - **Recurrent hypoglycaemia on medications**

If BGL≥17mmol/l - check for ketones
- if positive may need urgent admission if unwell or consider specialist advice/insulin initiation

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Newly diagnosed type 2: summary

- If well and BGL <17mmol/l , start lifestyle changes, optimal nutrition, dietitian review and education as soon as possible
- One in 4 patients have complications at diagnosis. Complication screening should begin at diagnosis in type 2 DM
  - Check renal function, lipids, urine ACR, feet examination and fundal examination
- Arrange education and glucose meter (as appropriate)
- Review BGL records over next few visits (if significantly hyperglycaemic initially)
- Encourage regular exercise (exercise physiologist)
- Commence Metformin and titrate slowly (over 2-4 weeks)
- See HealthPathway: Newly Diagnosed Diabetes

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Australian Guide to Healthy Eating

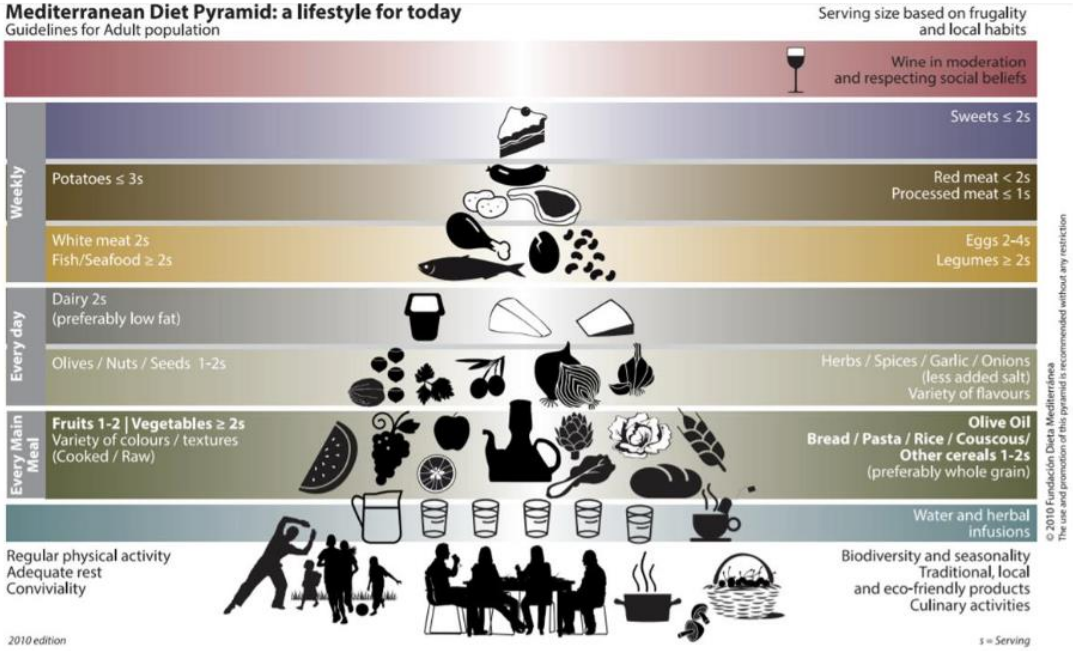
Enjoy a wide variety of nutritious foods from these five food groups every day.

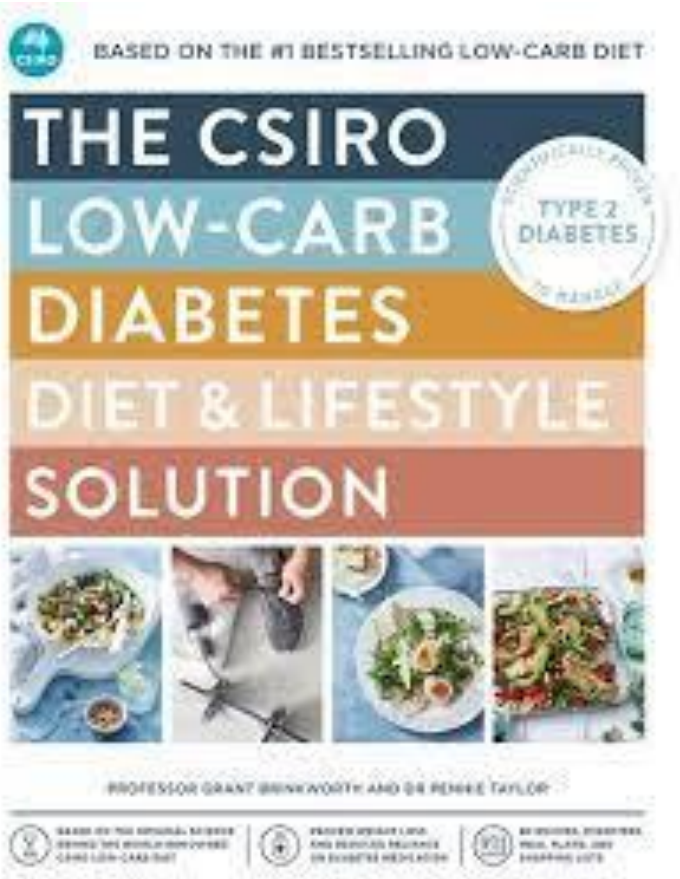
Drink plenty of water.

Use small amounts

Only sometimes and in small amounts

The Mediterranean Diet Pyramid





high ratio of MUFA:SFA, high intake of legumes, grains, fruit and nuts, vegetables, fish, low intake of meat and meat products, and moderate intake of milk and dairy products, alcohol.

Low carb diet: 14% of energy as CHO (<50g/day); 28% as protein; 58% as fat (<10% saturated fat); 24.7g fibre

https://www.youtube.com/embed/kocPaXRcPmA

BGL monitoring in type 2 DM

- Routine BGL monitoring for all type 2 DM is NOT indicated
- BGL monitoring is recommended
  - Insulin therapy
  - SU therapy at risk of hypoglycemia
  - When HbA1c unreliable
  - Occupational requirement
  - When unwell, symptomatic
  - When treatment decisions are to be made
  - To understand the impact of food and exercise on BGL profile, undertake BGL monitoring for limited period
- *NDSS: 6 months initially then a letter of clinical need can be given*

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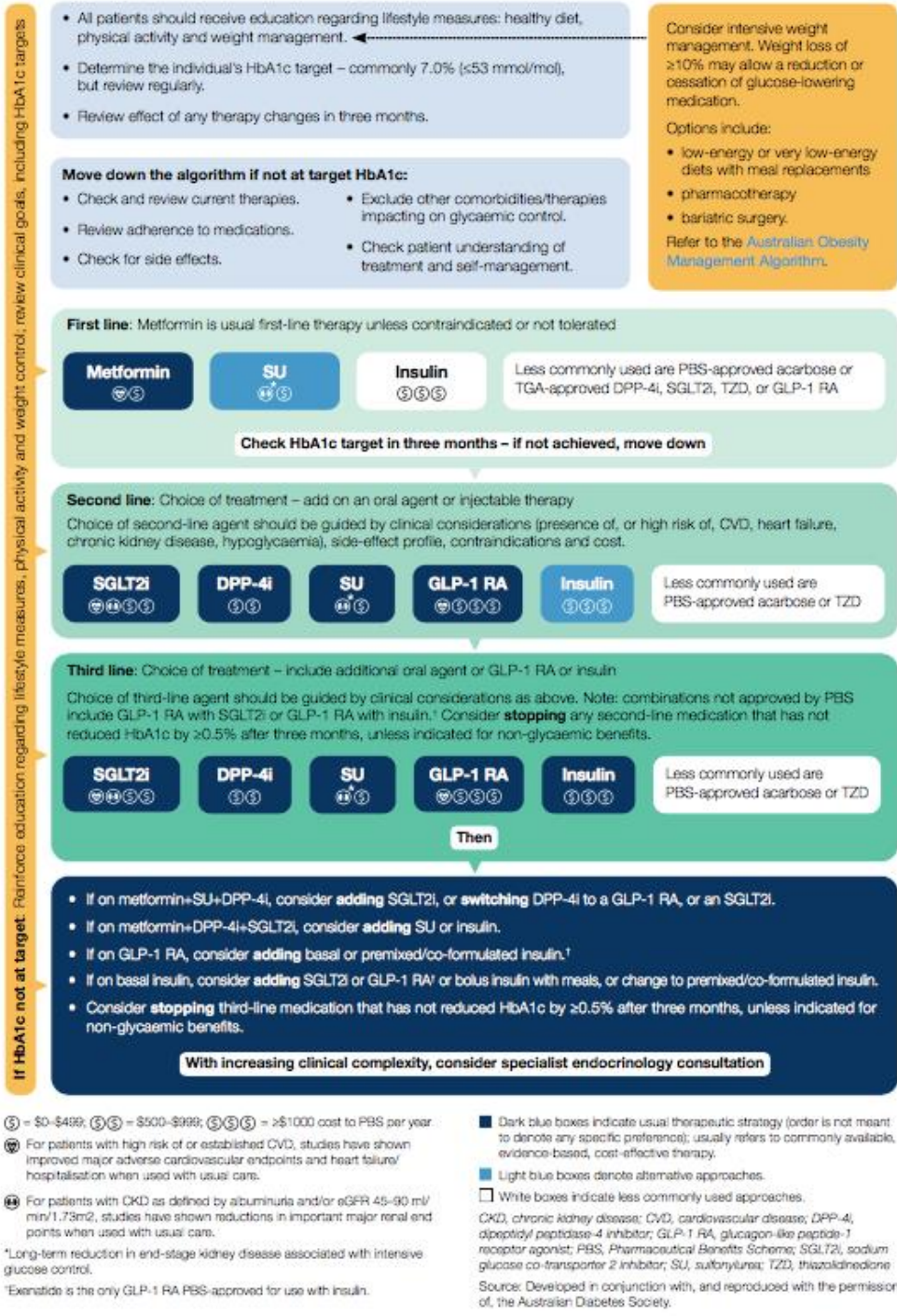
What is after Metformin? Contemporary evidence

- SU
  - Gliclazide, Glimepiride, Glibenclamide, Glipizide
- DPP4 inhibitor
  - Sitagliptin, Vildagliptin, Linagliptin, Saxagliptin, Alogliptin
- GLP-1 analogue
  - Exenatide, dulaglutide, semaglutide, Liraglutide
- SGLT2 inhibitor
  - Dapagliflozin, Empagliflozin, Ertugliflozin
- Insulin (basal, premixed, basal-bolus)
- TZD
  - pioglitazone
- Acarbose

See HealthPathways: [Diabetes Medications]



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Current oral agents

	Metformin	Sulfonylurea	Glitazone	Acarbose	Gliptins	SGLT2 inhibitor
Hypoglycaemia	no	yes	no	yes	no	no
HbA1c reduction	1-1.5%	1-1.5%	1%	0.5%	0.5-1%	1%
limitation	Renal, liver Failure	Hypos, monitoring, renal failure	IHD, macular edema, CCF Small bone fractures ca bladder?	GI side effects	??Pancreatitis Current evidence safe ?CCF	Thrush, UTI and dehydration Acute kidney injury Risk of DKA
Metabolic aspects	Weight friendly B12 deficiency	Weight gain+	Weight gain++	Weight friendly	Weight friendly	Weight friendly
Cost	$	$	$$	$	$$	$$$
Durability	+++	+	++	+	++	+?
CV SAFETY	+++	+/-?	CCF	Safe	Safe CCF signal for saxagliptin and alogliptin	Reduction in mortality (empa) Reduction in CCF

Current combination therapy and HbA1c lowering

3rd line agent when added to maximal dual agents

		Add on agent	HbA1c reduction
MF	SU	GLITAZONE	0.4-0.6%
MF	SU	GLIPTIN	0.4-0.7%
MF	SU	GLP-1	1%-1.5%
MF	SU	ACARBOSE	0.4%
MF	SU	SGLT2 inhibitor	0.6-0.9%
MF	SU +/-	INSULIN	>1.5%

INCRETIN THERAPY

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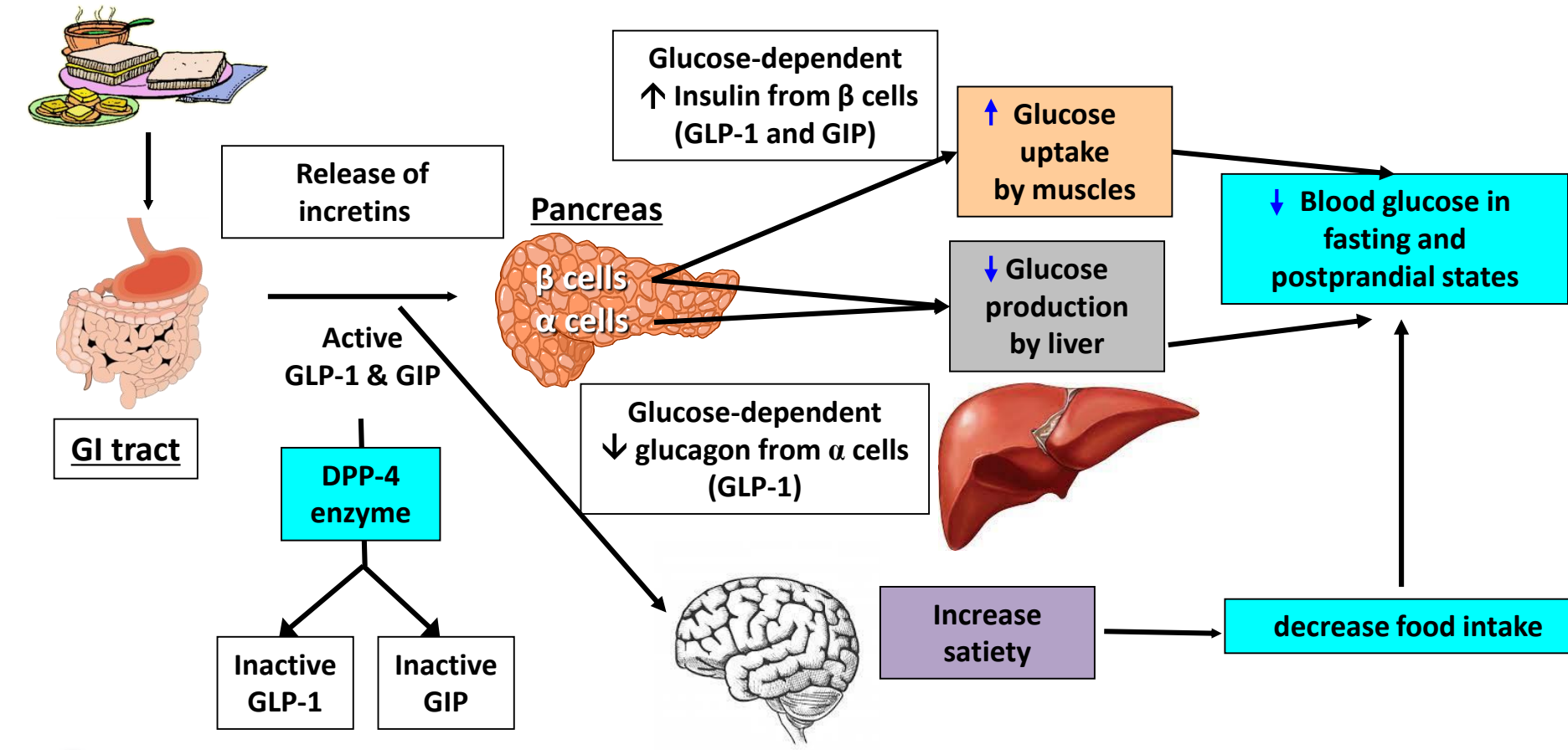
Incretins Modulate Insulin and Glucagon to Decrease Blood Glucose During Hyperglycaemia

*Incretin hormones GLP-1 and GIP are released by the intestine throughout the day; their levels increase in response to a meal.



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GLP-1=glucagon-like peptide-1; GIP=glucose-dependent insulinotropic polypeptide.

Brubaker PL et al. *Endocrinology* 2004;145:2653–2659; Zander M et al. *Lancet* 2002;359:824–930; Ahren B. *Curr Diab Rep* 2003;3:365–372; Buse JB et al. In: *Williams Textbook of Endocrinology*,11th ed. Philadelphia: Saunders; 2008:1329–1389; Drucker DJ. *Diabetes Care* 2003;26:2929–2940.

GLP-1 analogue

- At 12 months, average weight loss 3-6.5kg and 1-1.8% HbA1c reduction
- Exenatide, Dulaglutide and semaglutide available on PBS
- Byetta and dulaglutide can be prescribed with insulin on PBS
- Injectable, twice daily (Byetta) or weekly (Bydureon, Trulicity, Ozempic)
- Durability for few years
- Nausea is the main side effect
- If HbA1c is >10% (86mmol/mol) on two or 3 oral agents- unlikely to achieve target glycaemia

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DPP4I (Gliptin) or GLP-1 analogue

Gliptins

- Oral
- Prolongs action of native GLP1
- Weight neutral
- Minimal side effects
- HbA1c 0.7-1% reduction
- No hypo
- CV safe - Sitagliptin, linagliptin
- Increased CCF with saxagliptin and alogliptin, ?vildagliptin

GLP-1 analogue

- Injectable
- Short acting and long acting formulations (bd, od, wkly)
- weight loss 3-6 kg
- Nausea side effects
- HbA1c 1-1.5% reduction
- Minimal hypos
- Transient chronotropic effect (10bpm)
- CV safety +/- benefits
- Renal benefit

DO NOT COMBINE THESE TWO AGENTS

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SGLT2-INHIBITORS

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Normal glucose input and uptake[1]

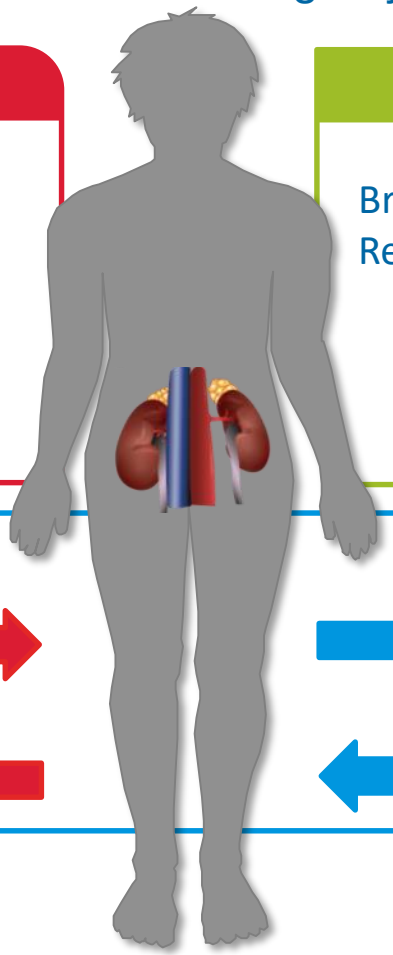
Net balance ~0 g/day

Glucose input ~250 g/day:

Dietary intake ~180 g/day
Glucose production ~70 g/day
- Gluconeogenesis
- Glycogenolysis

Glucose uptake ~250 g/day:

Brain ~125 g/day
Rest of the body ~125 g/day



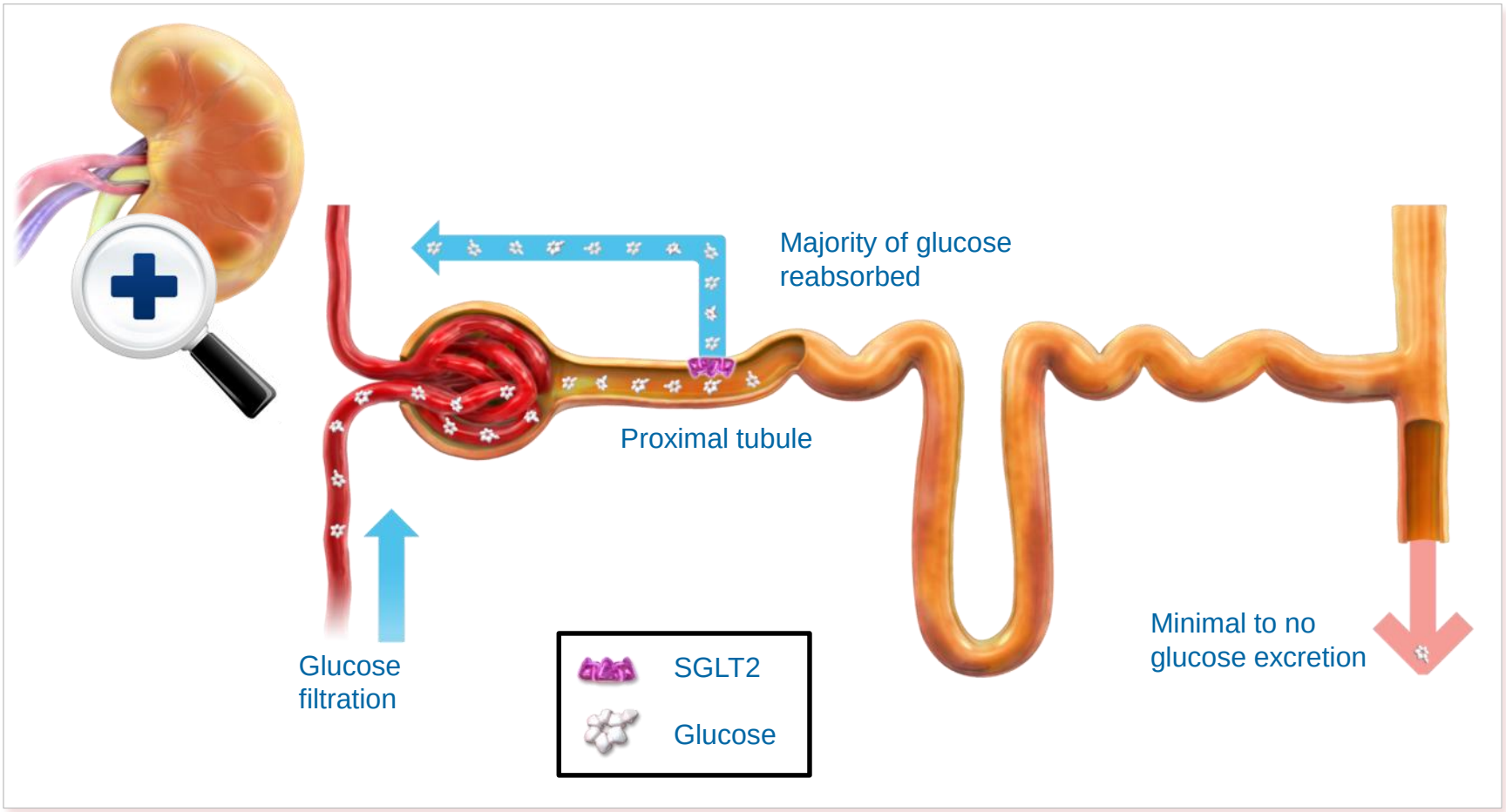
The kidney reabsorbs and recirculates glucose

Glucose reabsorbed ~ 180 g/day

Glucose filtered ~ 180 g/day

1. Wright EM, et al. J Int Med 2007;261:32–43.

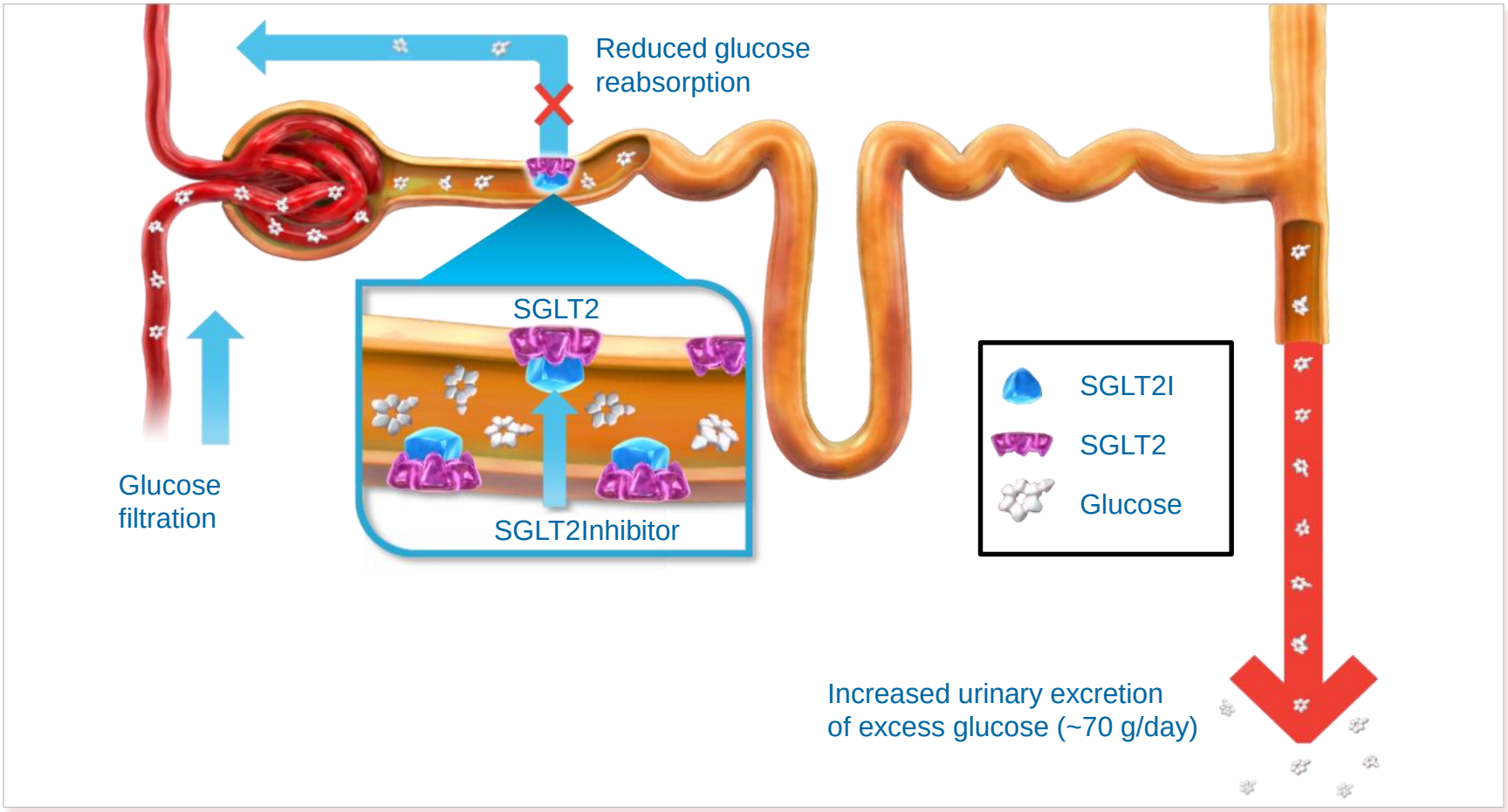
The kidney and normal glucose handling[1,2]



SGLT: sodium-glucose cotransporter

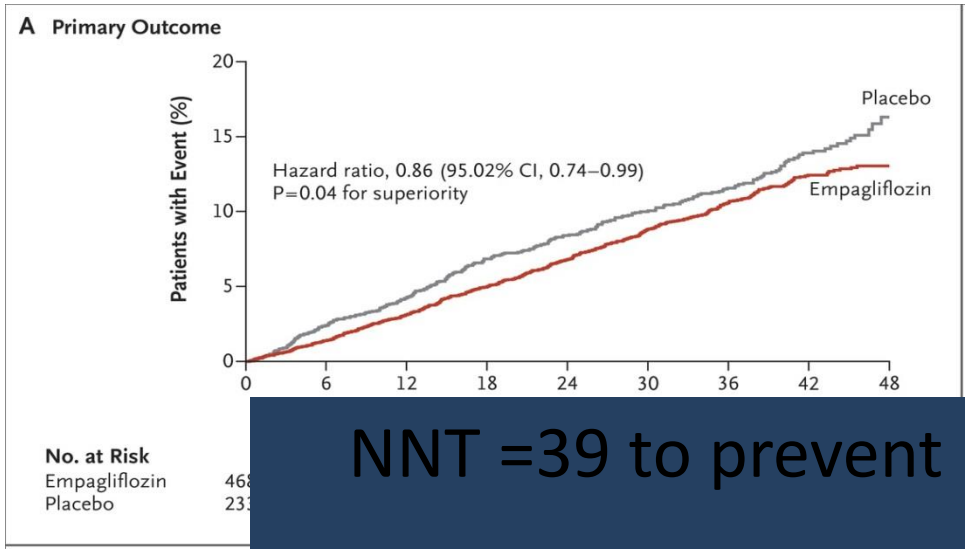
1. Wright EM, et al. J Int Med 2007;261:32–43. 2. Hummel CS, et al. Am J Physiol Cell Physiol 2011;300:C14−21.

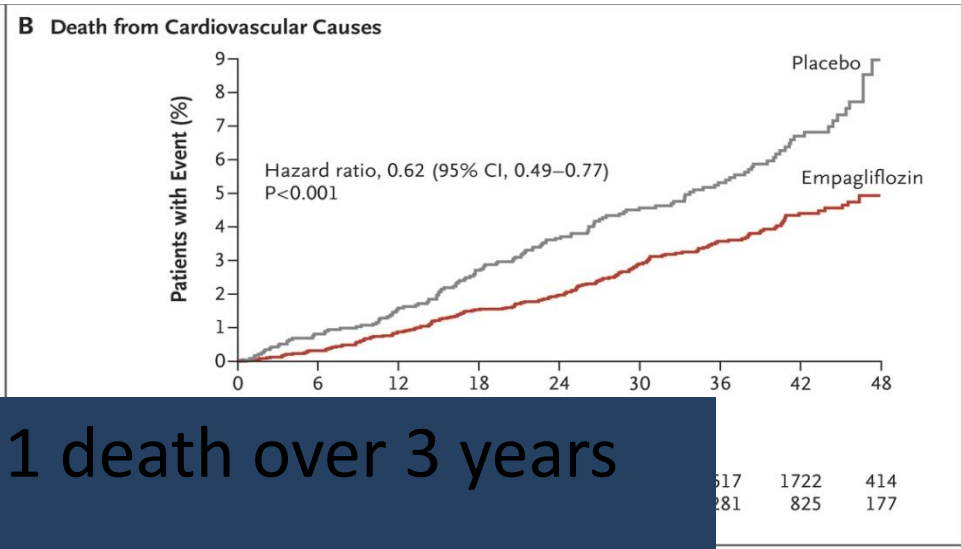
SGLT2 inhibitor removes excess glucose via the kidneys[1,2] and acts independently of insulin mechanisms



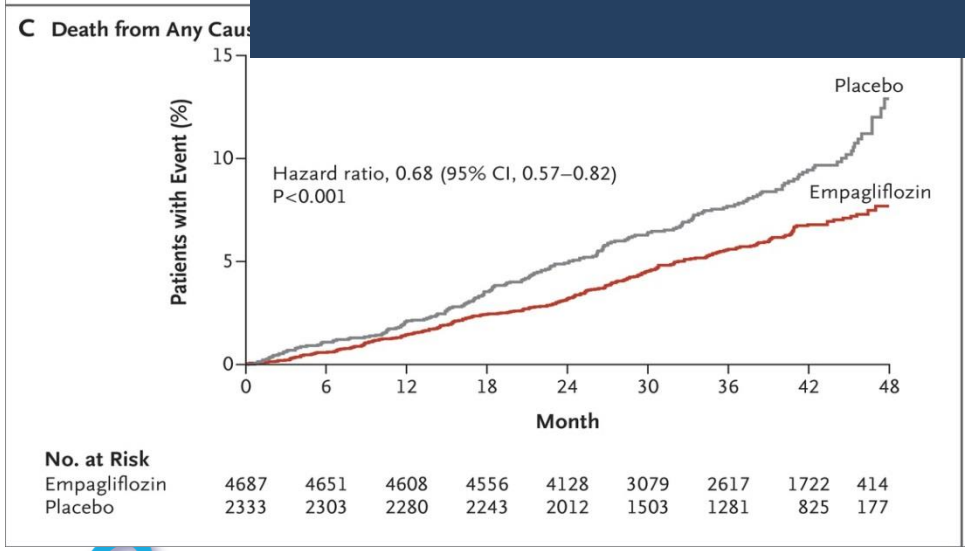
1.Gerich JE, Bastien A. Expert Rev Clin Pharmacol 2011;4:669−683.

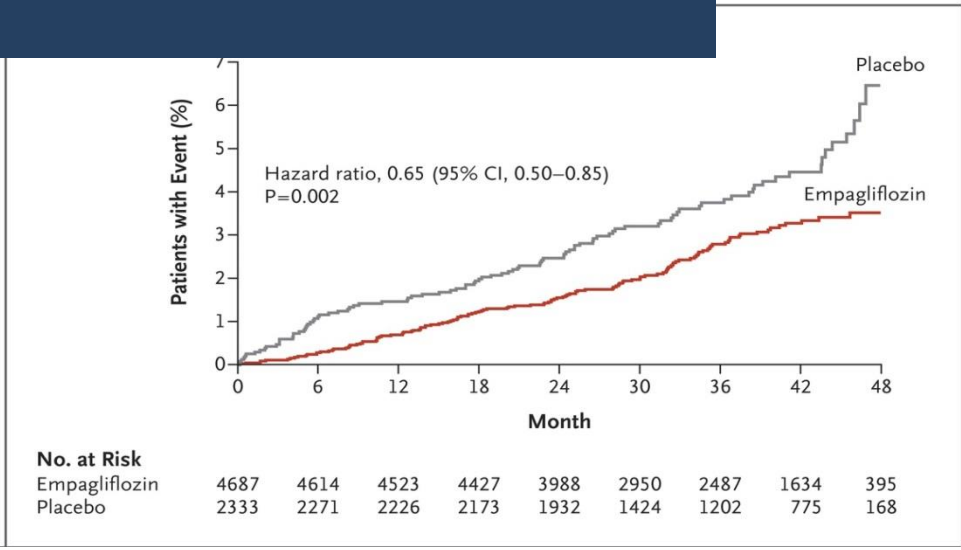
EMPA-REG: Cardiovascular Outcomes And Death From Any Cause.





NNT =39 to prevent 1 death over 3 years





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Zinman B et al. N Engl J Med 2015;373

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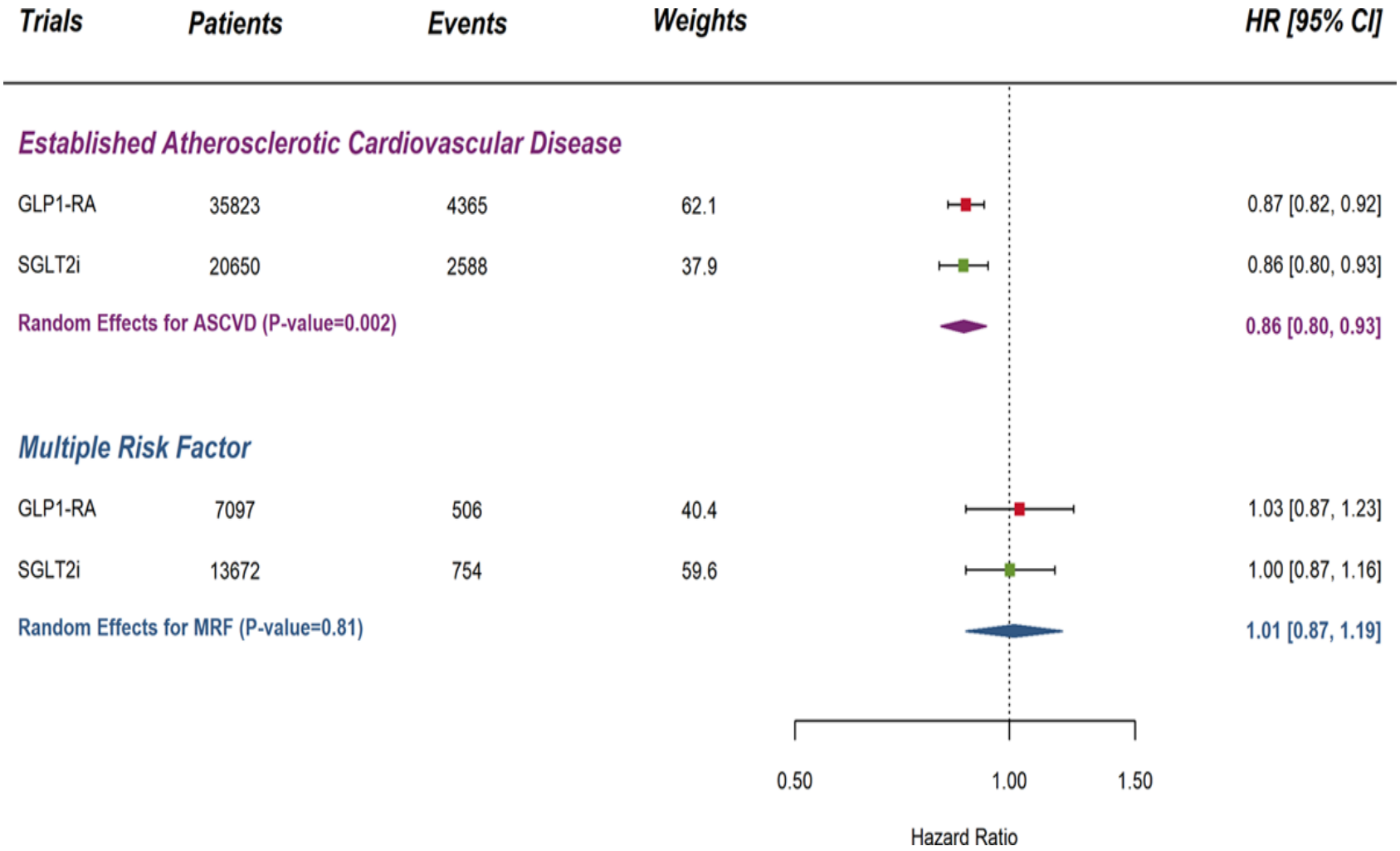
CVOT MACE/mortality



Comparison of the Effects of Glucagon-Like Peptide Receptor Agonists and Sodium-Glucose Cotransporter 2 Inhibitors for Prevention of Major Adverse Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus, Volume: 139, Issue: 17, Pages: 2022-2031, DOI: (10.1161/CIRCULATIONAHA.118.038868)

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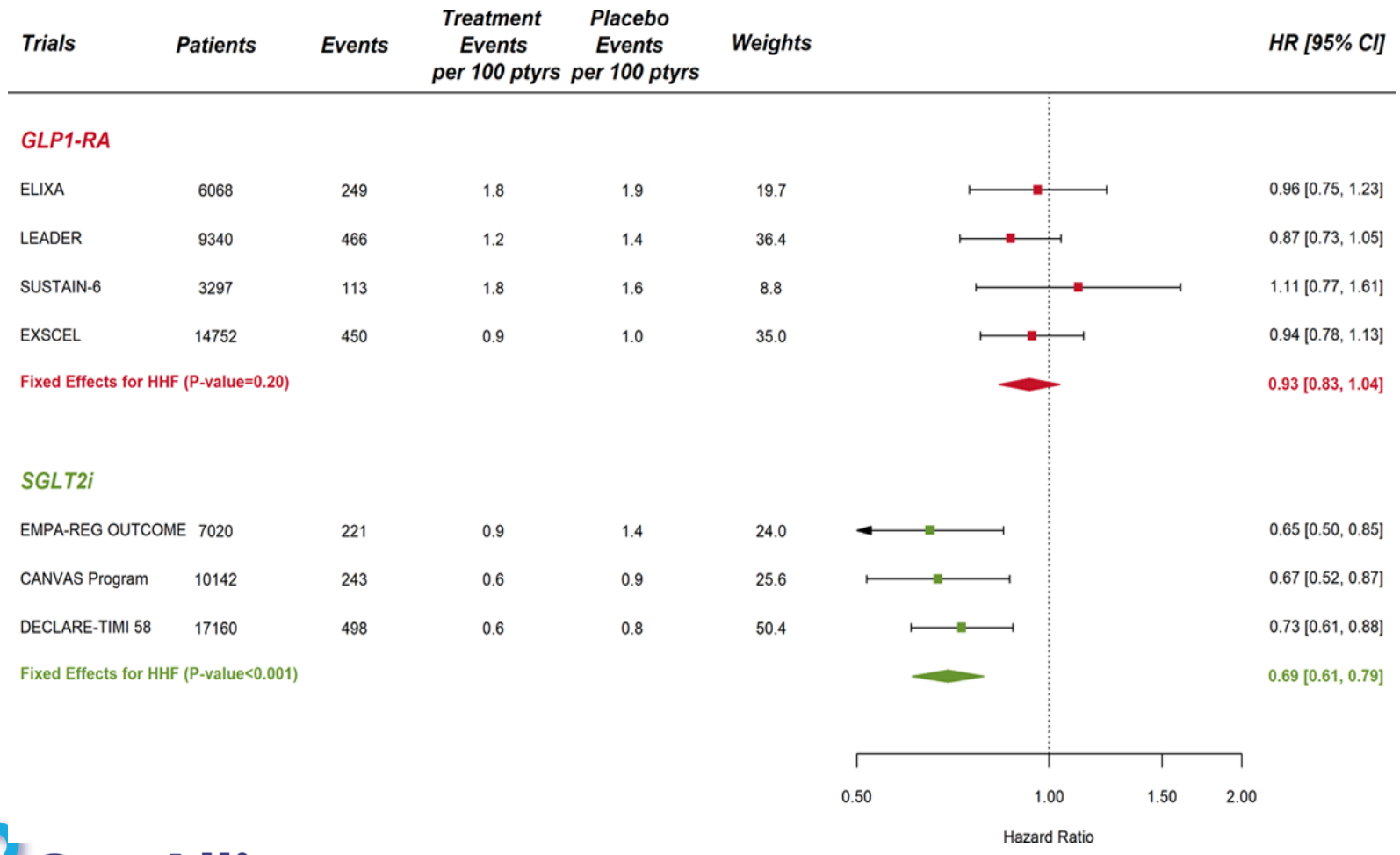
Heart Failure



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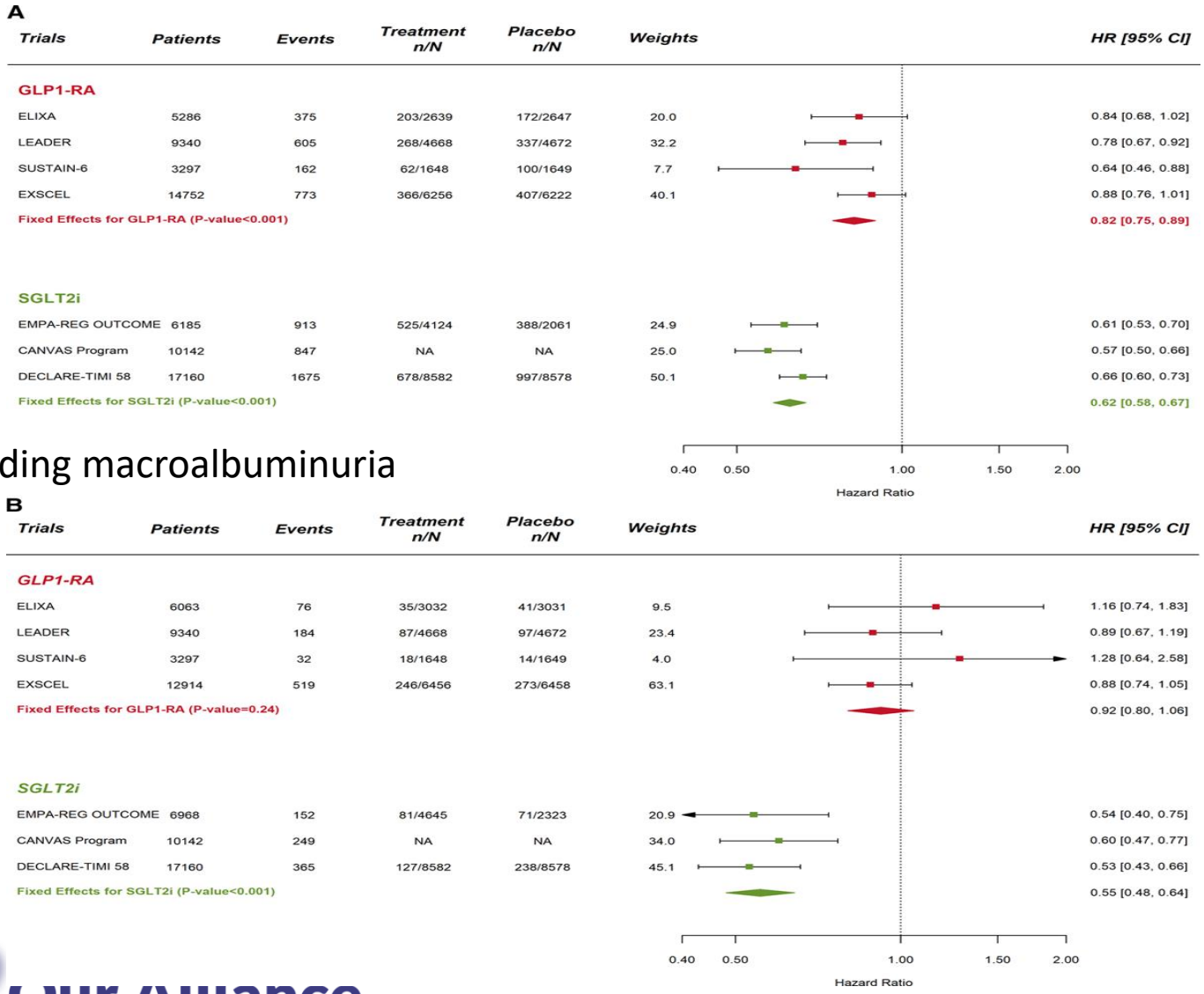
Renal outcome

Excluding macroalbuminuria



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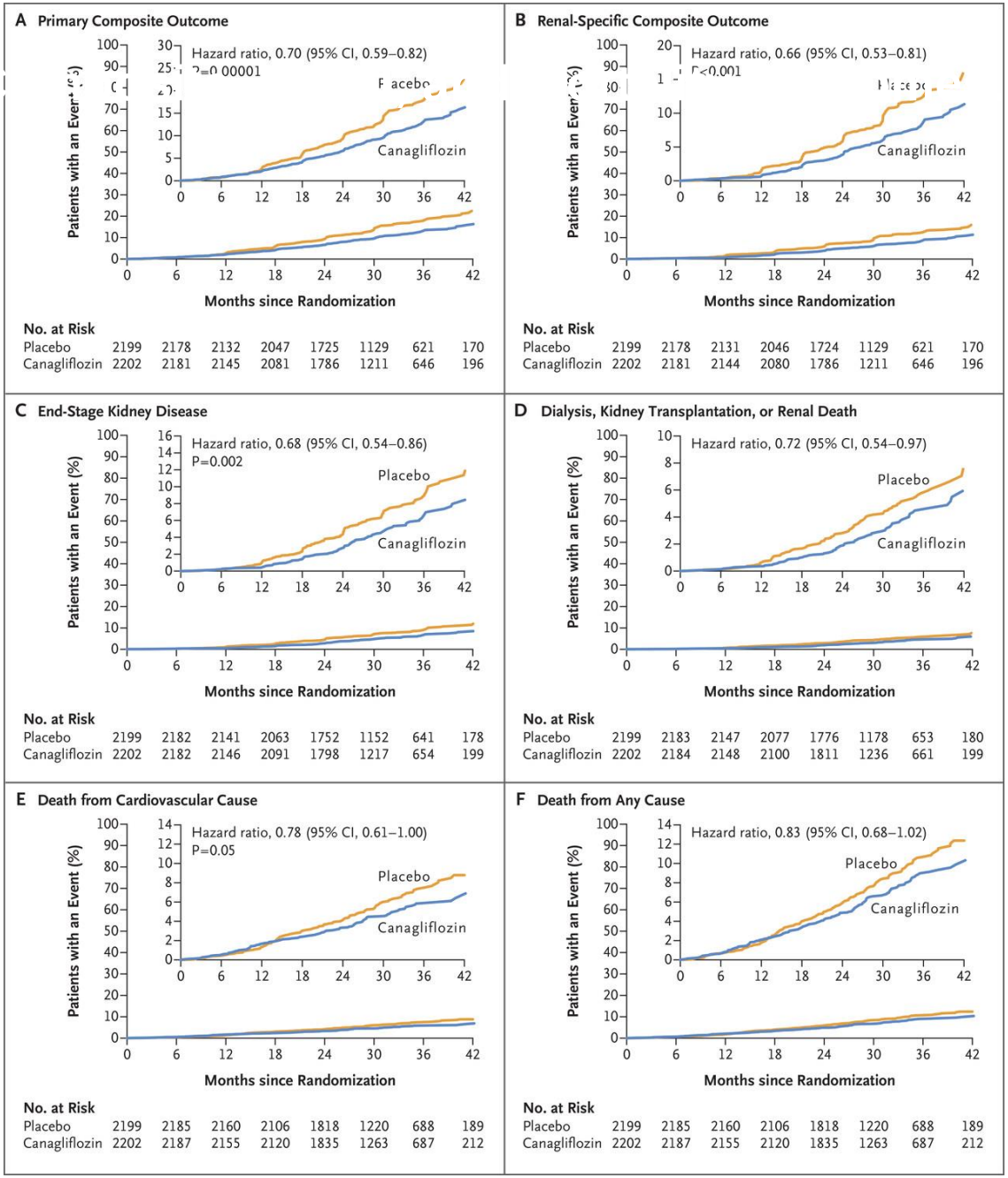
Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy

V. Perkovic, M.J. Jardine, B. Neal, S. Bompoint, H.J.L. Heerspink, D.M. Charytan, R. Edwards, R. Agarwal, G. Bakris, S. Bull, C.P. Cannon, G. Capuano, P.-L. Chu, D. de Zeeuw, T. Greene, A. Levin, C. Pollock, D.C. Wheeler, Y. Yavin, H. Zhang, B. Zinman, G. Meininger, B.M. Brenner, and K.W. Mahaffey, for the CREDENCE Trial Investigators*

A: NNT 22
B: NNT 28
C: NNT 43
HF: NNT 46
E: NNT 40



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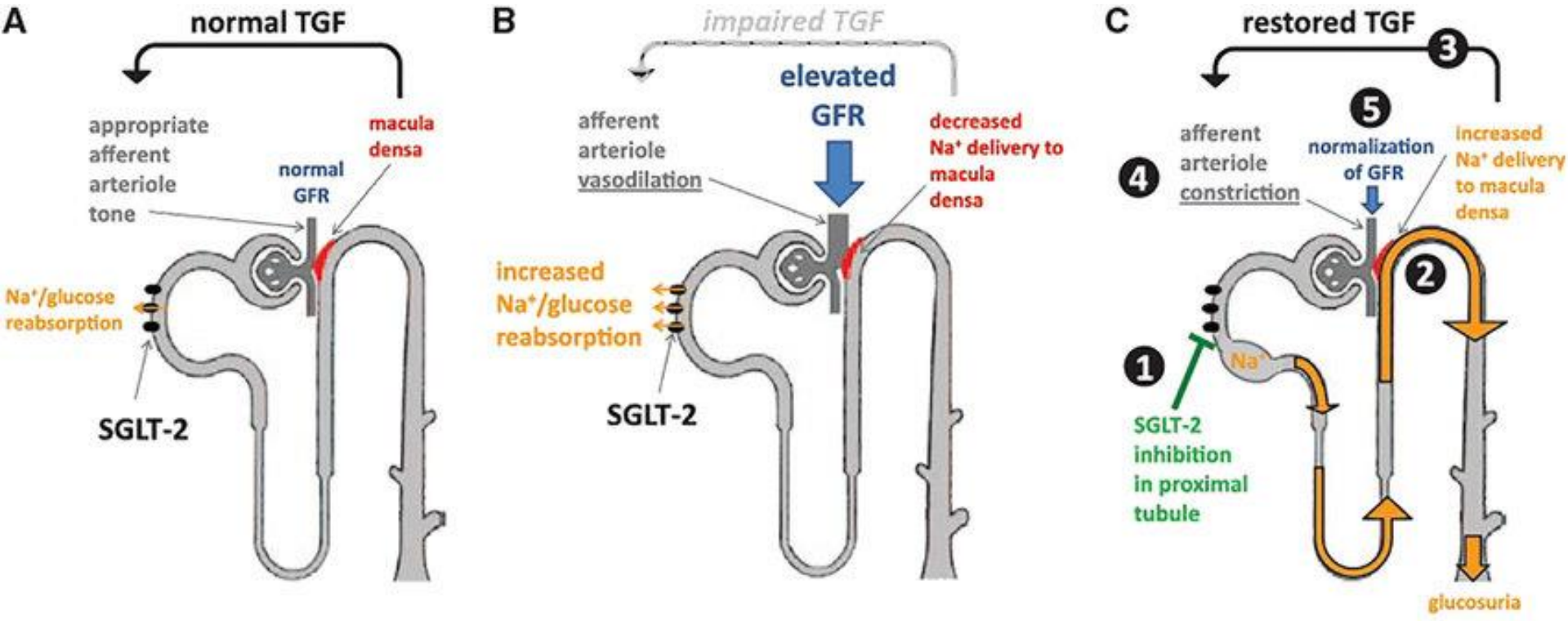

Normal physiology

Hyperfiltration in early stages of diabetic nephropathy

SGLT-2 inhibition reduces hyperfiltration via TGF

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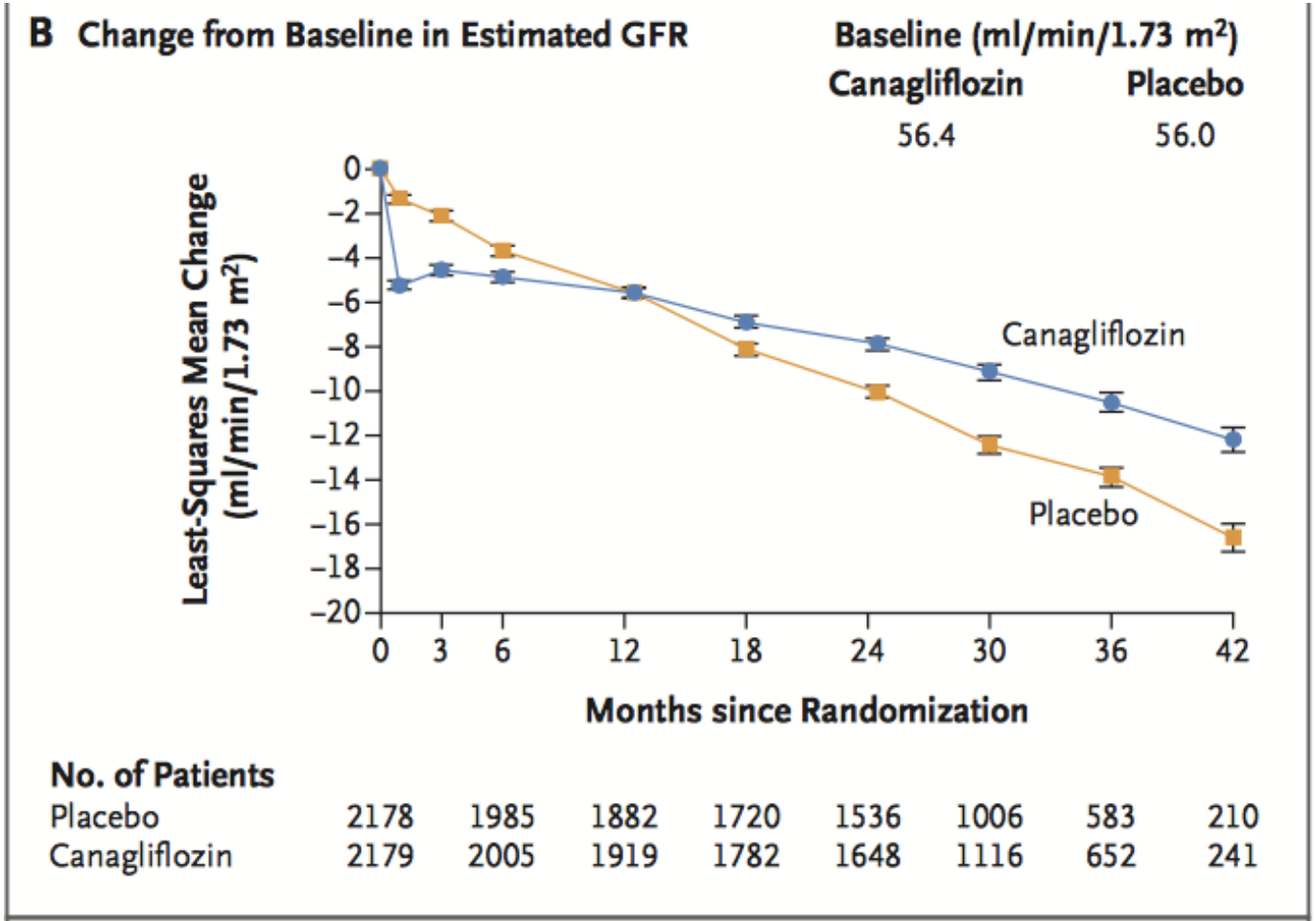

Figure 3. Effects on Albuminuria and Estimated GFR.

Panel A shows the effects of canagliflozin and placebo on the urinary albumin-to-creatinine ratio in the intention-to-treat population. Panel B shows the change from the screening level in the estimated GFR in the on-treatment population. The I bars indicate the 95% confidence interval in Panel A and the standard error in Panel B. The albumin-to-creatinine ratio was calculated with albumin measured in milligrams and creatinine measured

Renal impairment and diabetic medications

- GFR<45mL/min/1.73m^2
  - Reduce metformin dosage by 50%
  - Reduce DPP4i (except linagliptin)
  - ????? stop SGLT2 inhibitor
- GFR<30mL/min/1.73m^2
  - Stop GLP-1 RA and metformin
  - Long acting SU not recommended (Glimepiride, Glibenclamide)
  - All gliptins (except linagliptin) require dose reduction
- Insulin preferred however dosage needs regular review to avoid hypoglycaemia

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Cardiovascular risk reduction

Statins

- Secondary prevention (following MI, Stroke, PVD)
- Primary prevention
  - ACV Risk>10% – most T2DM>60
  - microalbuminuria, CKD
  - Aboriginal or Torres Strait Islander
  - Treatment goal: Cholesterol <4, LDL <2mmol/l

Fibrates

- For high triglycerides
- Uncertain benefit for primary prevention
- may reduce retinopathy progression

ACE inhibition

- Hypertension
- microalbuminuria, proteinuria
- following vascular events

Aspirin

- Secondary prevention
- Uncertain benefit in primary prevention

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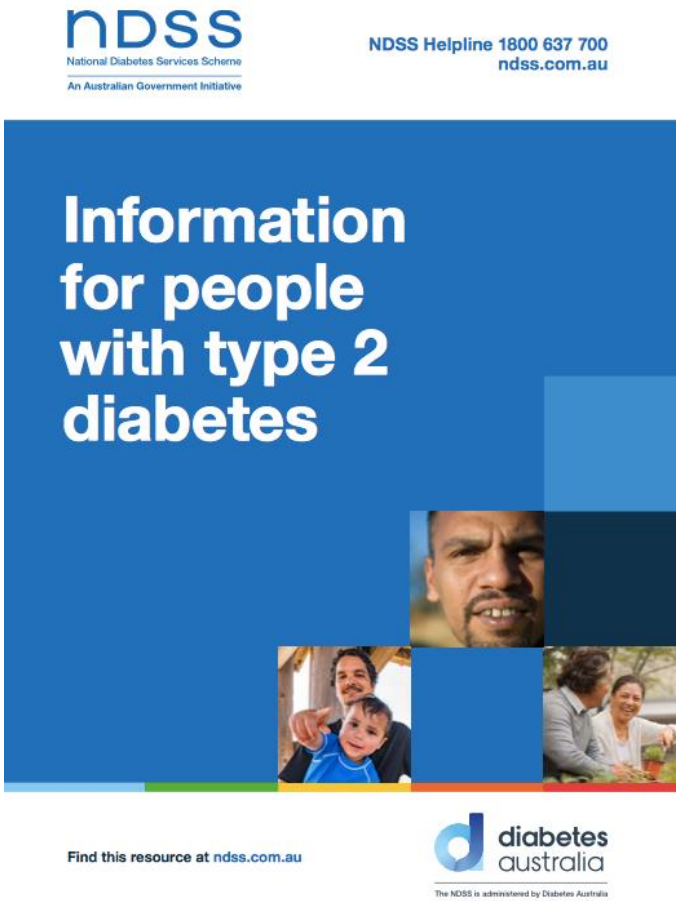
NDSS

- Registration

- Data registry
- Subsidised products
- Services and support



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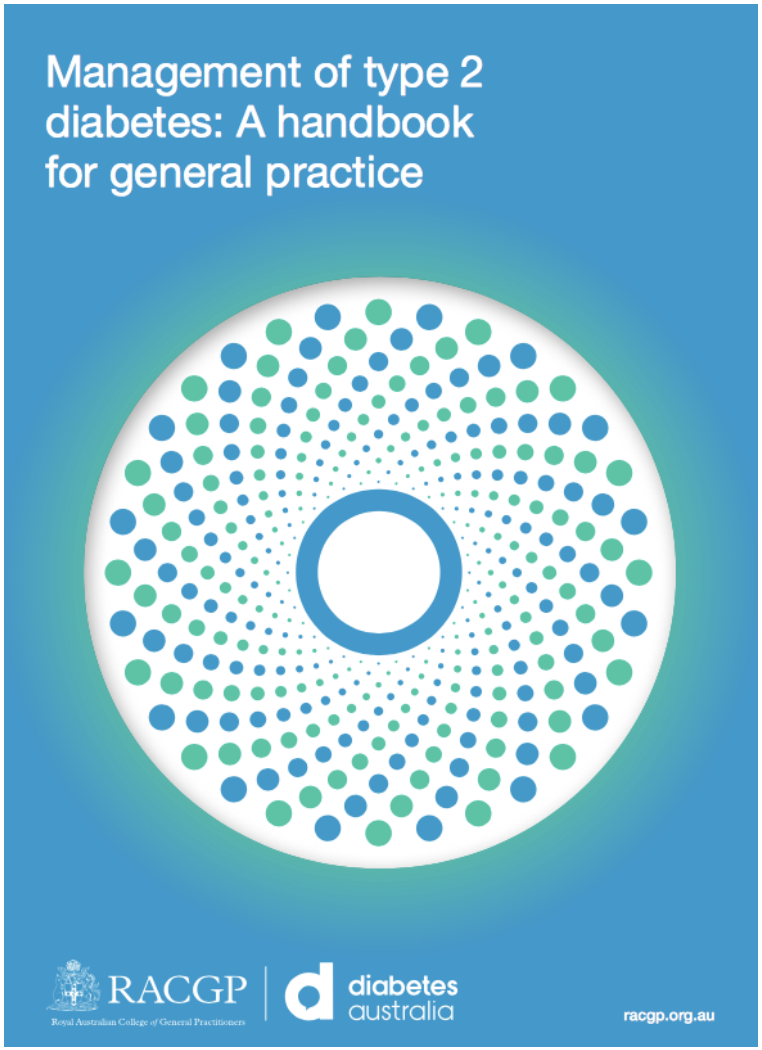
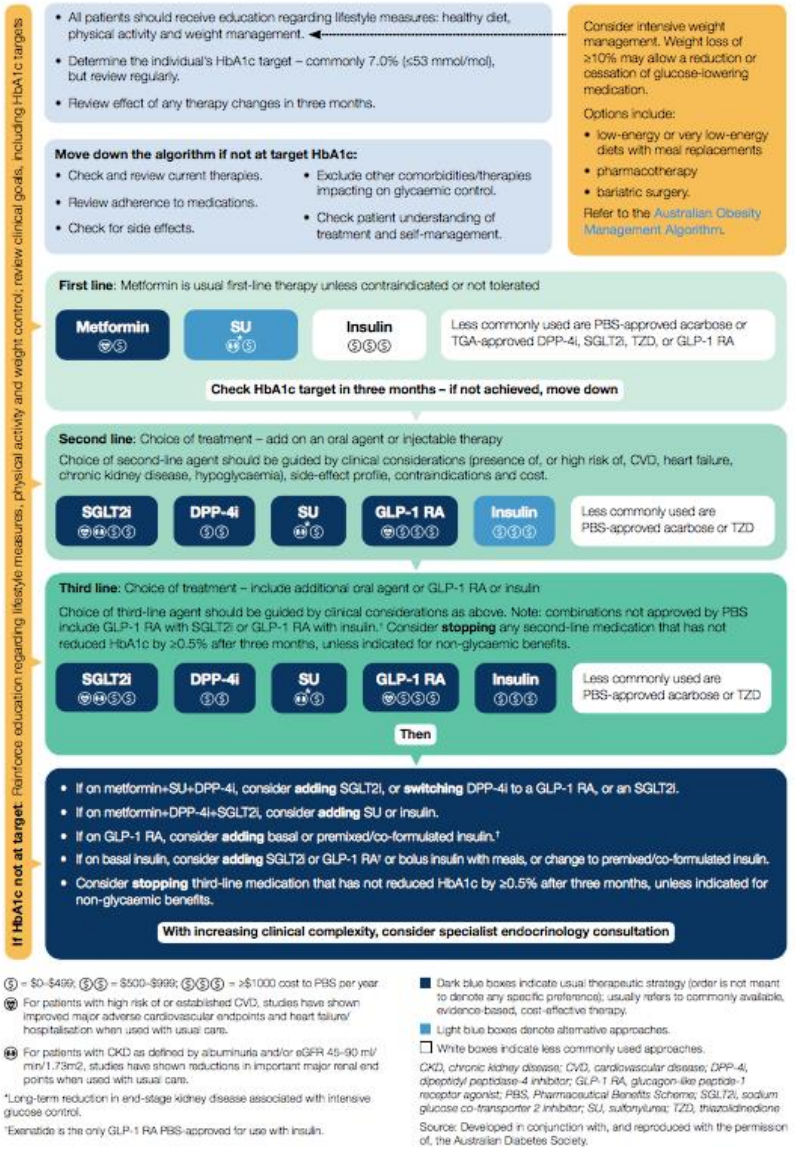
AUSTRALIAN Guidelines





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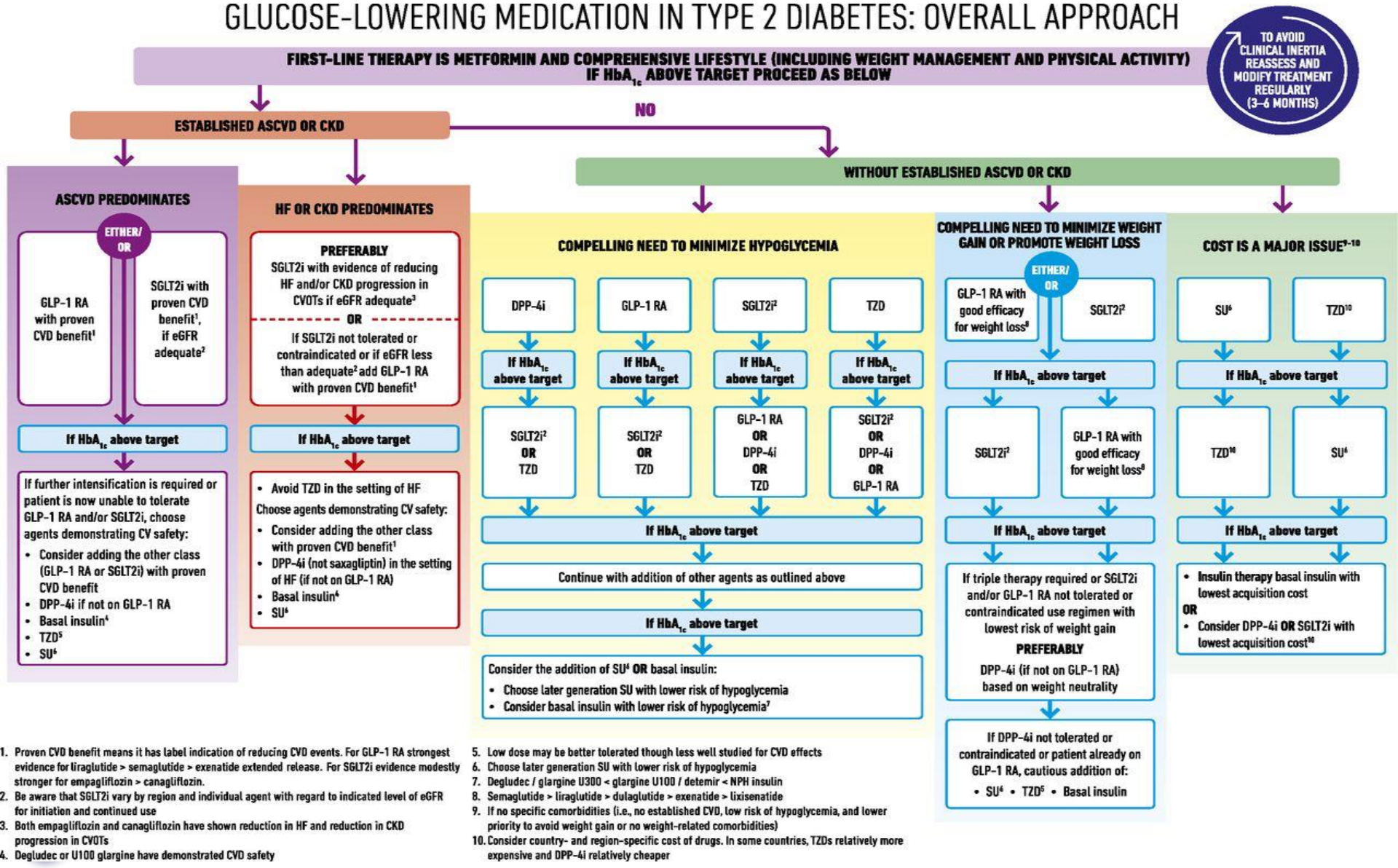
EASD/ADA CONSENSUS



1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for liraglutide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Both empagliflozin and canagliflozin have shown reduction in HF and reduction in CKD progression in CVOTs
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU with lower risk of hypoglycemia
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries, TZDs relatively more expensive and DPP-4i relatively cheaper

Case scenario 1

Dorothy is 76yrs old, had type 2 DM for 10yrs. Her co morbidities include hypertension, obesity, sleep apnoea

- normal renal function, no microalbuminuria but mild retinopathy
- BP 138/78 on ACEi, Cholesterol 4.2mmol/l on statin
- HbA1c has been 7.8-8.4%(62 -68mmol/mol) for the past 5 yrs. Currently on Metformin 2g/day
- Her diet is reasonable

- What would be your next glycaemic lowering agent of choice?

1. SU

2. Gliptin

3. SGLT2 inhibitor

4. GLP-1 analogue

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Case scenario 2

Mr. Hart is 54yrs old, ex smoker, hypertensive

- BMI 35
- Pre diabetes for 5 yrs, Type 2 DM diagnosed this year
- NSTEMI 6 months ago – treated with stent
- HbA1c at diagnosis 64mmol/mol (8%), commenced Metformin, now 2g/day
- Latest HbA1c 58mmol/mol (7.5%)

Which of the following is the most appropriate next step?

1. continue current medication

2. add gliclazide MR

3. add SGLT2 inhibitor

4. add basal insulin glargine (Lantus)

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QUESTIONS?

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