



THE EVOLVING ROLE OF INSULIN THERAPY

HISTORICAL PERSPECTIVE OF INSULIN USE OF PAST 30
YEARS

Presenter Disclosure

Relationships with commercial interests:

Grants/Research support

NOVONORDISK; SANOFI

Speaker's bureau/

honoraria:DEXCOM; ANIMAS;

MEDTRONIC; ELI LILLY NOVORDISK;

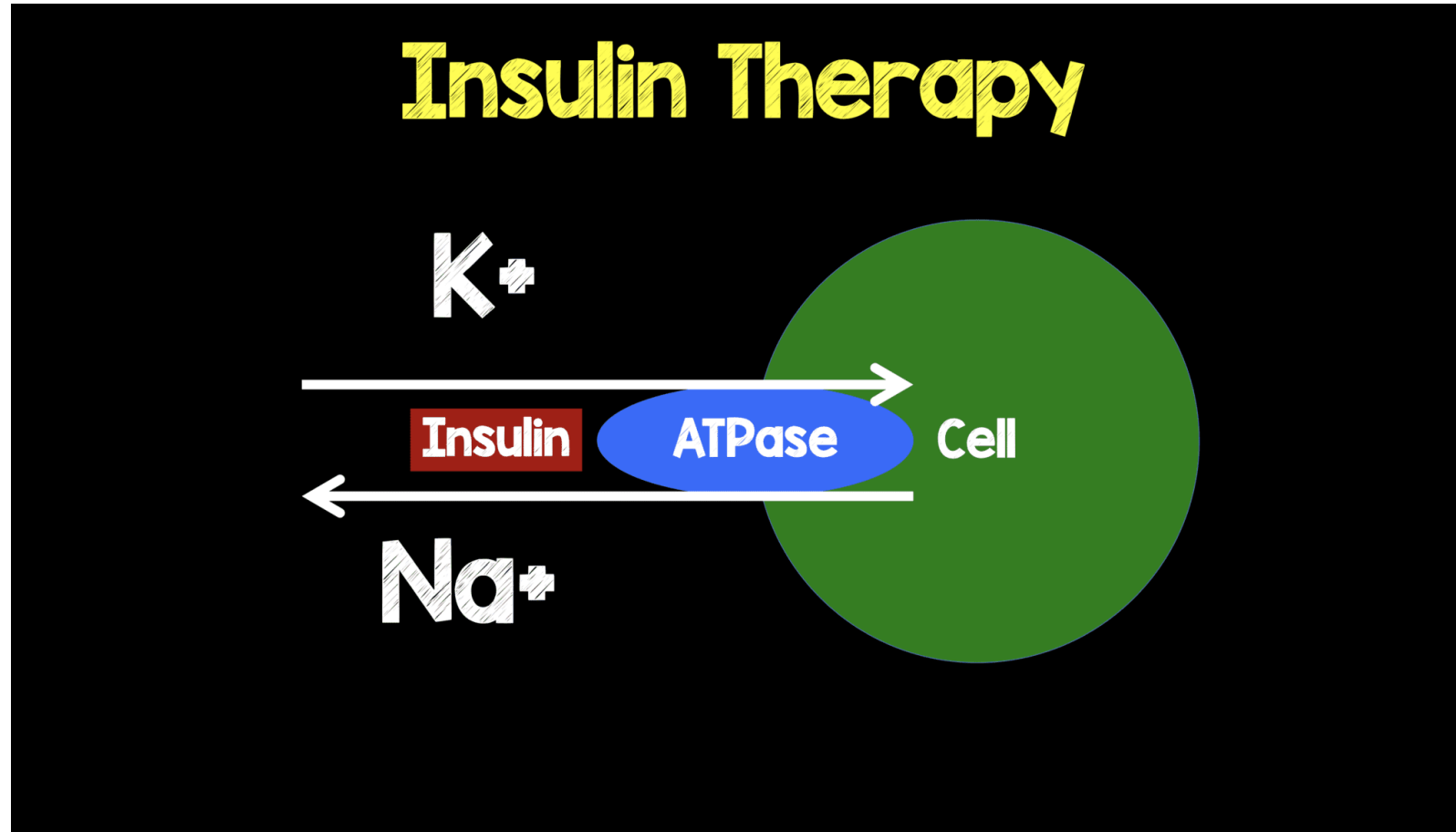
BI ; SANOFI;

Consulting/Advisory Board:SAME

AS ABOVE

Other/Patents

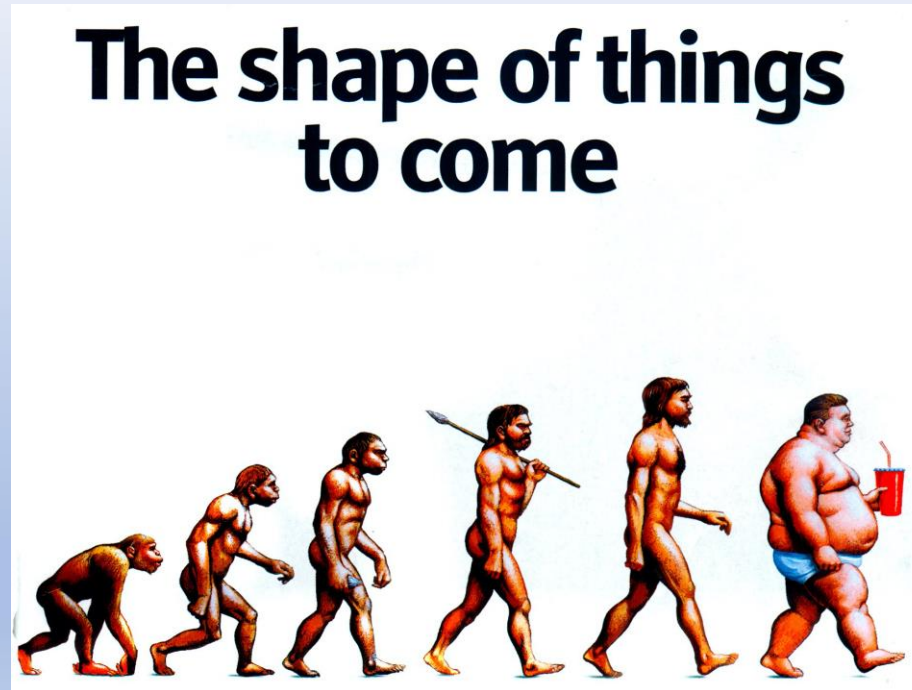
Diabetes new approaches IS IT TIME TO SAY GOODBYE TO MY DEAR FRIEND



VOTE

- A) YES
- B) NO
- C) NOT SURE

DIABETES IS CHANGING



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diabetes


*TIR: 3.9–10 mmol/L.

1. Battelino T et al. *Diabetes Care*. 2019 Aug;42(8); 2. Wright Jr. EE et al. *Clin Diabetes*. 2020 Dec;38(5):439-448.



presentation

• Case

- Historical perspective
 - Where we are in 2022
 - Who needs insulin
 - When to start
 - New guidelines 2022 sept diabetes care
- 

MRS P

- TYPE 2 DIABETES FOR ? 5 YEARS
 - NEW CONSULT
 - FEELS WELL
 - NOT CHECKING SUGARS
 - NO RECENT EYE CHECKUP
 - NO KNOWN KIDNEY ISSUES
- METFORMIN ; ACE AND STATIN
And Diamicron



EXAMINATION

- BP 140/90
- BMI 33
- FEET DECREASE MONOFILAMENT
- CVS NORMAL
- RESP CLEAR

LABS

- GFR 50
- PROTEINURIA 1 GRAM/DAY
- A1C 0.095
- LDL 1.8
- TSH NORMAL

DISCUSSION

- DISCUSSED PROS AND CONS WITH PATIENT
- GIVEN LOW GFR AND NO CAD; SGLT2 WOULD HAVE BEEN A GOOD OPTION
- PATIENT HAS RECURRENT YEAST AND UTI
- DIDN'T WANT INJECTIONS
- WENT WITH RYBELSUS

DIABETES MEDICATION

HOW DO MEDICATIONS WORK?

BIGUANIDE

GLUCOPHAGE® GLUMETZA®

- Lowers the amount of sugar produced by the liver
- Increases the sensitivity of muscle cells to insulin

TZD

ACTOS®
AVANDIA®

- Improves how the body uses insulin

INSULIN SECRETAGOGUES

DIABETA®
DIAMICRON®
AMARYL®
GLUCONORM®

- Helps the pancreas to produce more insulin

GLP1 AGONIST

VICTOZA®
TRULICITY®
BYDUREON®

- Slows down the absorption of sugar
- Increases insulin production by the pancreas when blood sugar is high
- Decreases appetite

SGLT 2 INHIBITORS

INVOKANA®
FORXIGA®
JARDIANCE®

- Increases elimination of the sugar in the urine by the kidneys

ALPHA-GLUCOSIDASE INHIBITORS

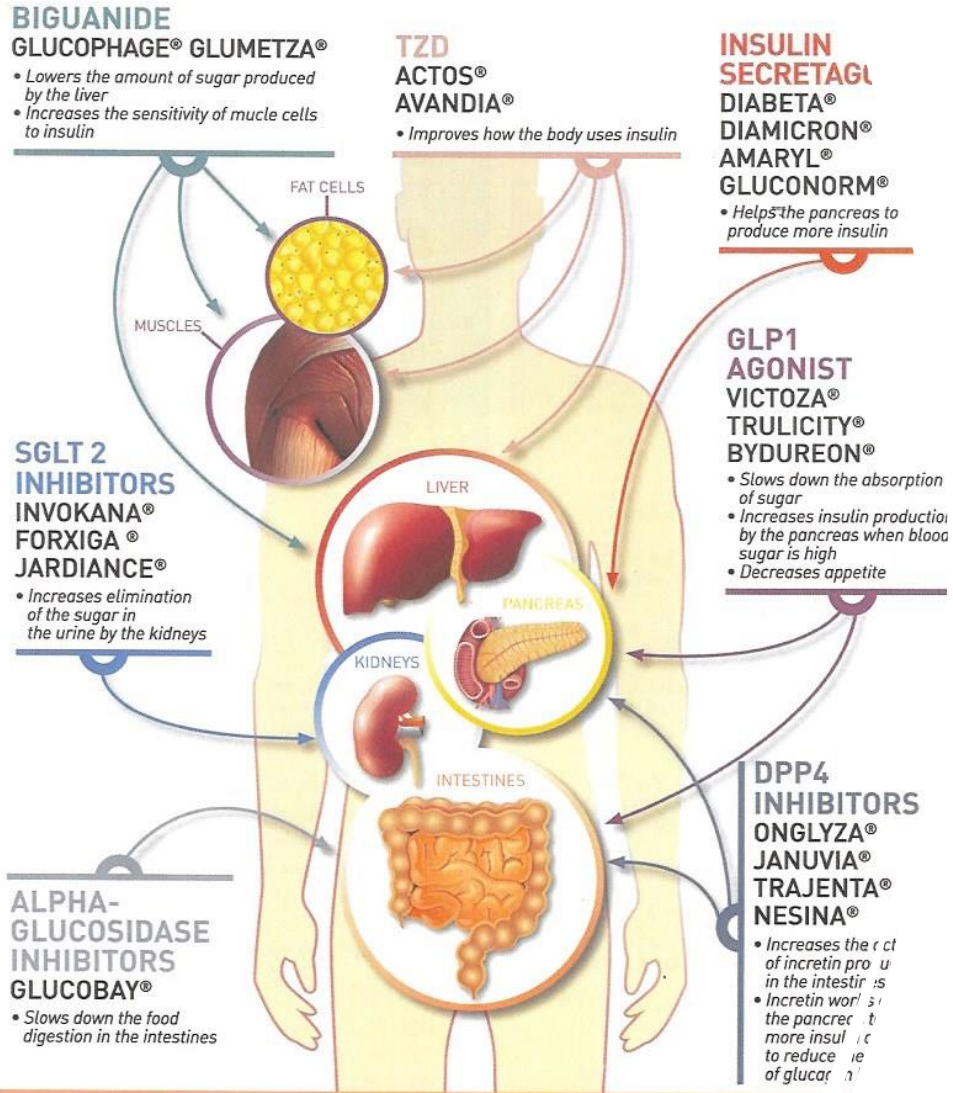
GLUCOBAY®

- Slows down the food digestion in the intestines

DPP4 INHIBITORS

ONGLYZA®
JANUVIA®
TRAJENTA®
NESINA®

- Increases the level of incretin produced in the intestines
- Incretin works with the pancreas to produce more insulin to reduce the level of glucose



RYBELSUS; OZEMPIC

COURSE

- PATIENT WAS STARTED ON 3 MG A DAY
- FOR ONE MONTH
- WAS GOING AWAY MARCH 5
- DUE TO COVID TRIP CANCELLED
- INCREASED TO 7 MG
- NO SIDE EFFECTS; TOLERATING WELL
- A1c over 7 sglt2 added
- 3 years later a1c at 8 percent on 4 agents ;what is next step


Antihyperglycemic Agents and Kidney Function

		DRUG CLASS						
		Metformin (max daily dose)	SGLT2i (Recommended daily dose*)	GLP1-RA	DPP4i (max daily dose)	All Insulins	Secretagogues	
							Glyburide	Others
eGFR (mL/min/1.73m ²)	45 – 59	2 g	No dose change	No dose change	No dose change	No dose change	Avoid Glyburide	No dose change
	30 – 44	1 g	Canagliflozin 100 mg Dapagliflozin 10 mg Empagliflozin 10 or 25 mg		No dose change			Linagliptin 5 mg Sitagliptin 50 mg (Saxagliptin 2.5 mg**)
	15 – 29	500 mg		Limited data available		Linagliptin 5 mg Sitagliptin 25 mg		
	<15 or on dialysis	Avoid	Stop on dialysis					
	Risk related to low GFR	Lactic acidosis	Cardiorenal protection preserved but less reduction in A1C with low GFR		Accumulation***	Accumulation and hypoglycemia	Prolonged and severe hypoglycemia	Hypoglycemia

*listed alphabetically, **increased risk for heart failure, ***except linagliptin



presentation

- Case
 - **Historical perspective**
 - Where we are in 2022
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History lane with dr K

- Young resident at JGH
- Started my
- endo training 1990
- We had crazy hair back then
- And Insulin was out!!!!



1992

- First clinic at jgh
- Insulin was BAD
- Caused heart disease; made you gain weight
- Made you swell
- Don't use it even if your sugars are high
- First clinic a1c 10 percent
- Don't start insulin
- He is insulin resistant he needs to lose weight and exercise

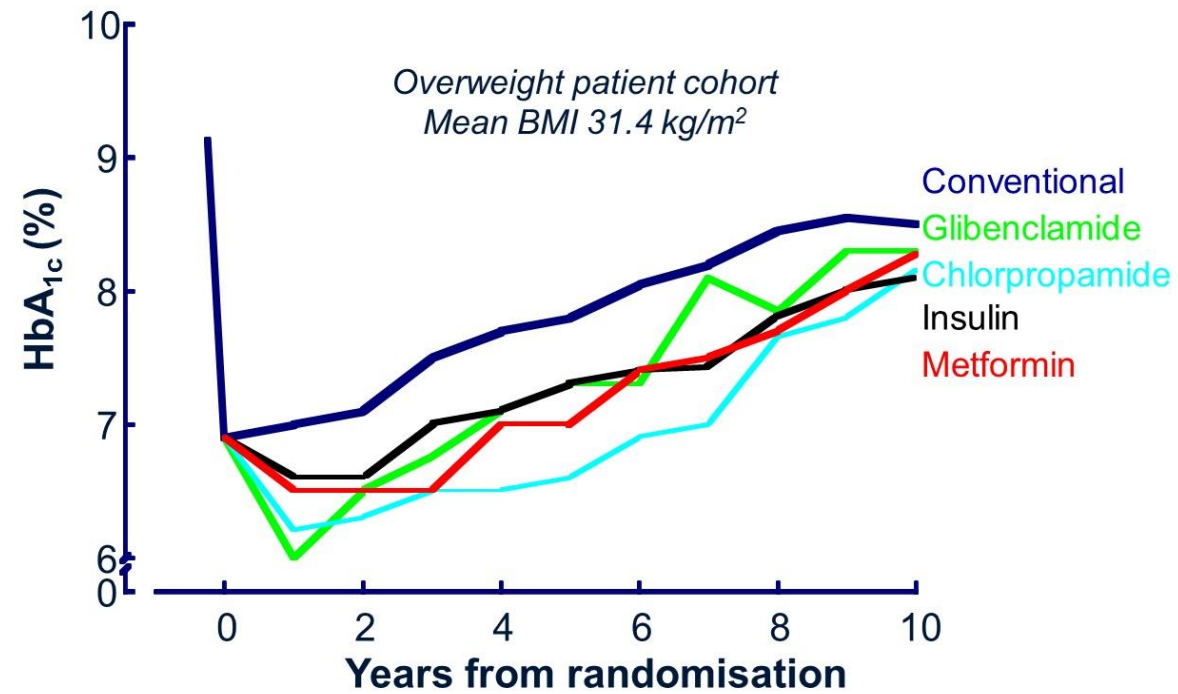
1992 to 2010

- Oral agents available
- Glyberide and its friends
- Metformin
- Dpp4
- Tzd
- Acarbose

ukpds

3

Progressive Hyperglycaemia in T2DM



UKPDS 34. *Lancet* 1998;**352**:837-853

ukpds

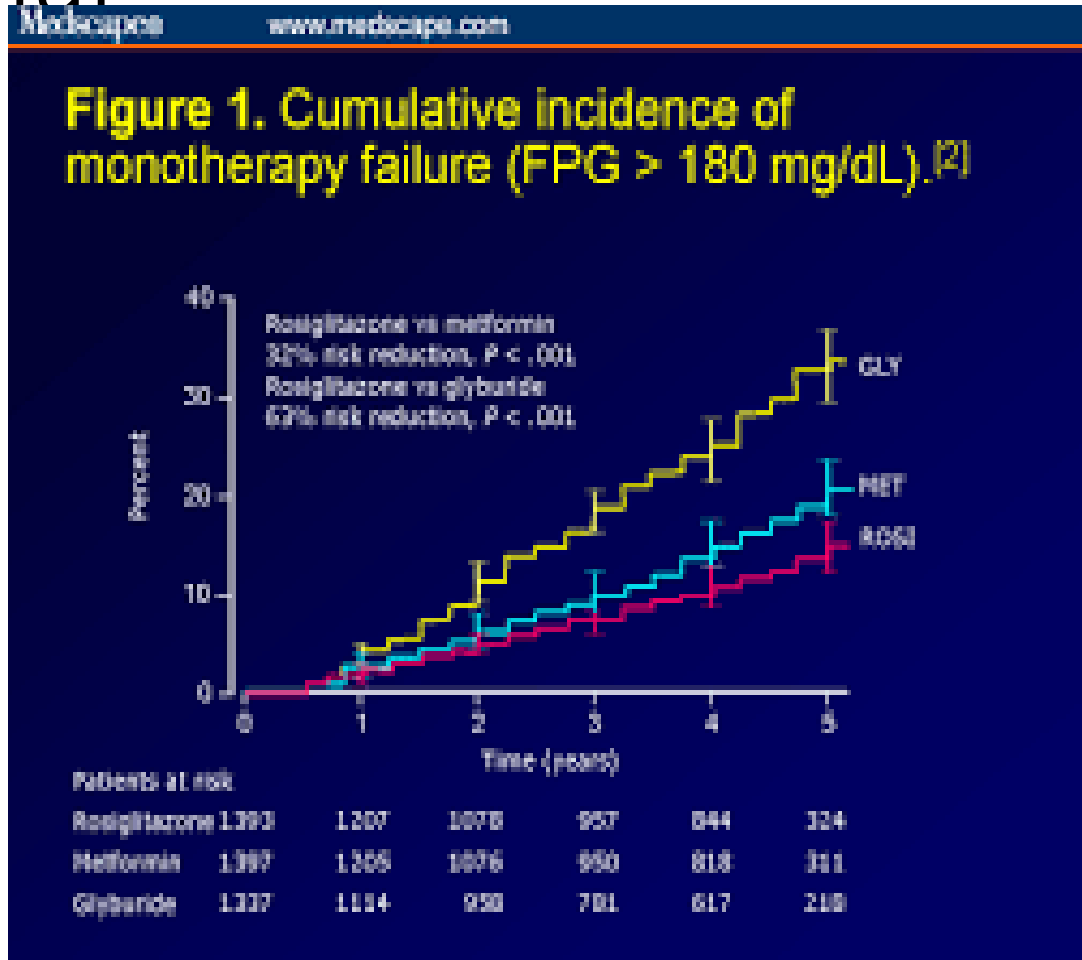
Conclusion they all work get control better and hence the following 20 years would be about glucose control; insulin was no longer evil

Glucose Control Study Summary

The intensive glucose control policy maintained a lower HbA_{1c} by mean 0.9 % over a median follow up of 10 years from diagnosis of type 2 diabetes with reduction in risk of:

12%	for any diabetes related endpoint	p=0.029
25%	for microvascular endpoints	p=0.0099
16%	for myocardial infarction	p=0.052
24%	for cataract extraction	p=0.046
21%	for retinopathy at twelve years	p=0.015
33%	for albuminuria at twelve years	p=0.000054

Adopt trial



World rocked again 2008

- Nissen published
- Linking an metanalysis
- Showing tzd high cardiac complications and death
- Gone were tzd;
- First time an agent was associated with worsening outcomes
- BUT GOING FORWARD ALL TRIALS HAD TO SHOW SAFETY OF AGENTS

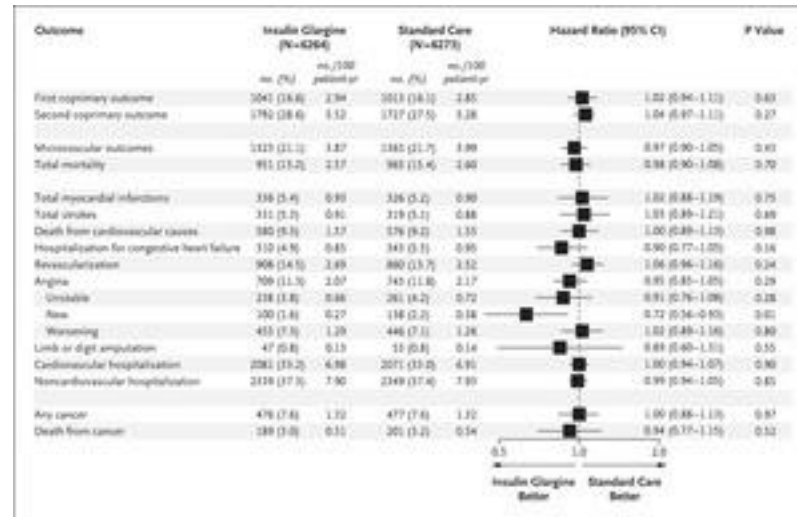
Rosiglitazone Meta-Analysis: Risk of Myocardial Infarction and Death from Cardiovascular Causes for Patients Receiving Rosiglitazone vs Several Comparator Drugs

Table 1. Risk of Myocardial Infarction and Death from Cardiovascular Causes for Patients Receiving Rosiglitazone versus Several Comparator Drugs.

Comparator Drug	Odds Ratio (95% CI)	P Value
Myocardial Infarction		
Metformin	1.14 (0.70-1.88)	0.19
Sulfonylurea	1.24 (0.78-2.00)	0.16
Insulin	2.78 (0.58-13.3)	0.20
Placebo	1.80 (0.95-3.39)	0.07
Combined comparator drugs	1.43 (0.65-3.18)	0.33
Death from cardiovascular causes		
Metformin	1.19 (0.74-1.71)	0.64
Sulfonylurea	1.40 (0.60-3.30)	0.40
Insulin	3.37 (0.31-36.52)	0.16
Placebo	1.22 (0.64-2.34)	0.15
Combined comparator drugs	1.64 (0.95-2.79)	0.06

2008 TO 2010

- INSULIN BACK IN
- TZD OUT
- ORIGIN TRIAL
- Insulin was safe but
- But didn't offer any
- Cardiac protection




2010 TO PRESENT

- DRUGS HAD TO BE TESTED FOR CARDIAC SAFETY
- AND HENCE A NEW ERA OF DIABETES



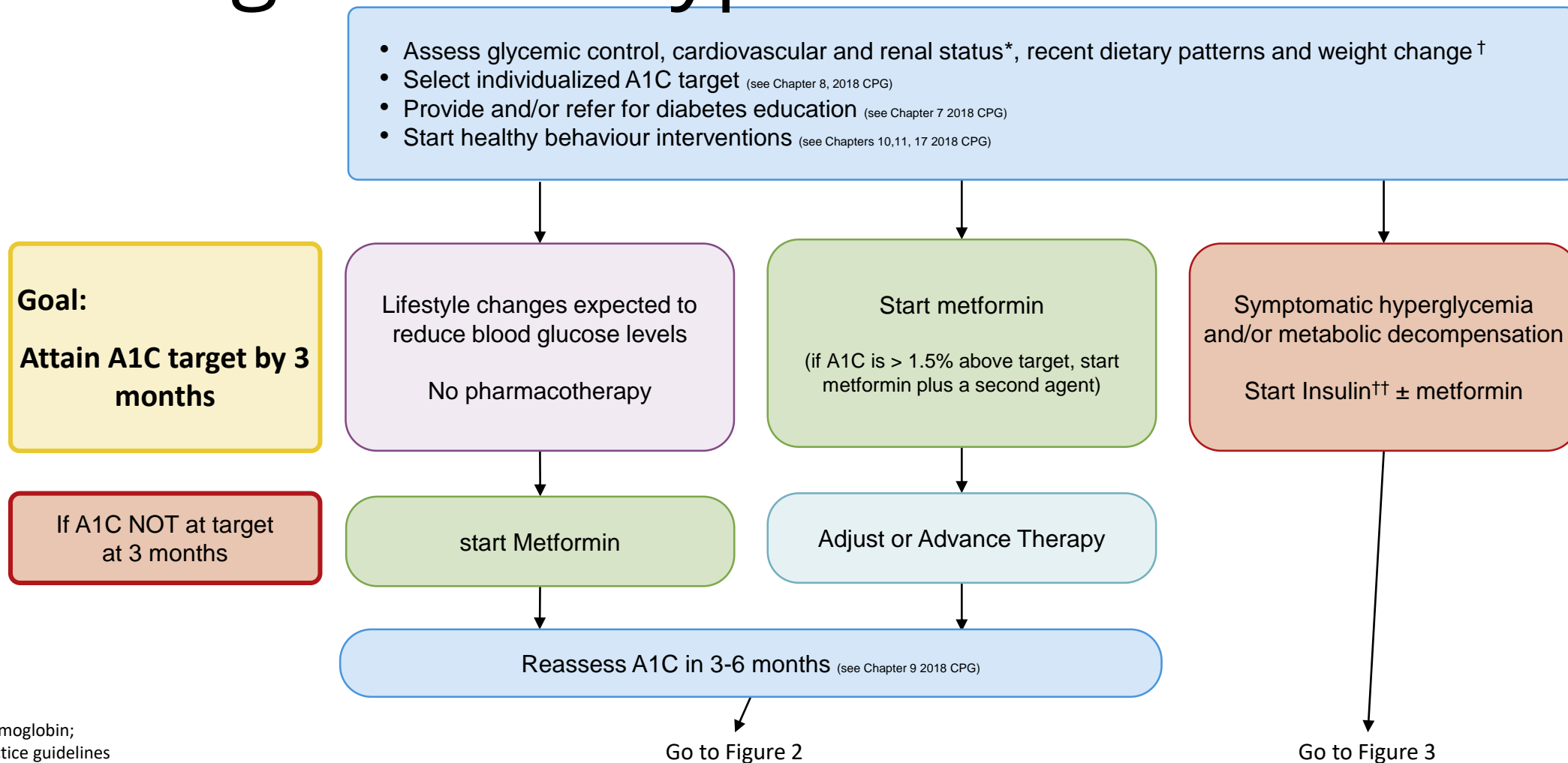
presentation

- 
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	Efficacy ¹	Hypoglycemia	Weight change ²	CV effects		Renal effects		Oral/SQ	Cost	Clinical considerations
				Effect on MACE	HF	Progression of DKD	Dosing/use considerations*			
Metformin	High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Neutral	<ul style="list-style-type: none"> Contraindicated with eGFR <30 mL/min per 1.73 m² 	Oral	Low	<ul style="list-style-type: none"> GI side effects common; to mitigate GI side effects, consider slow dose titration, release formulations, and administration with food Potential for vitamin B₁₂ deficiency; monitor at regular intervals
SGLT2 inhibitors	Intermediate to high	No	Loss (intermediate)	Benefit: canagliflozin, empagliflozin	Benefit: canagliflozin, dapagliflozin, empagliflozin, ertugliflozin	Benefit: canagliflozin, dapagliflozin, empagliflozin	<ul style="list-style-type: none"> See labels for renal dose considerations of individual agents Glucose-lowering effect is lower for SGLT2 inhibitors at lower eGFR 	Oral	High	<ul style="list-style-type: none"> DKA risk, rare in T2DM: discontinue, evaluate, and treat promptly if suspected; be aware of predisposing risk factors and clinical presentation (including euglycemic DKA); avoid before scheduled surgery (e.g., 3–4 days), during critical illness, or during prolo to mitigate potential risk Increased risk of genital mycotic infections Necrotising fasciitis of the perineum (Fournier's gangrene), rare reports: institute treatment if suspected Attention to volume status, blood pressure; adjust other volume-contracting agents
GLP-1 RAs	High to very high	No	Loss (intermediate to very high)	Benefit: dulaglutide, liraglutide, semaglutide (SQ) Neutral: exenatide once weekly, lixisenatide	Neutral	Benefit for renal endpoints in CVOTs, driven by albuminuria outcomes: dulaglutide, liraglutide, semaglutide (SQ)	<ul style="list-style-type: none"> See labels for renal dose considerations of individual agents No dose adjustment for dulaglutide, liraglutide, semaglutide Monitor renal function when initiating or escalating doses in patients with renal impairment reporting severe adverse GI reactions 	SQ; oral (semaglutide)	High	<ul style="list-style-type: none"> Risk of thyroid C-cell tumors in rodents; human relevance not determined (liraglutide, dulaglutide, exenatide extended release, semaglutide) Counsel patients on potential for GI side effects and their typically temporary nature; provide guidance on dietary modifications to mitigate GI side effects (reduction in meal eating practices [e.g., stop eating once full], decreasing intake of high-fat or spicy foods); consider slower dose titration for patients experiencing GI challenges Pancreatitis has been reported in clinical trials but causality has not been established; Discontinue if pancreatitis is suspected Evaluate for gallbladder disease if cholelithiasis or cholecystitis is suspected
GIP and GLP-1 RA	Very high	No	Loss (very high)	Under investigation	Under investigation	Under investigation	<ul style="list-style-type: none"> See label for renal dose considerations No dose adjustment Monitor renal function when initiating or escalating doses in patients with renal impairment reporting severe adverse GI reactions 	SQ	High	<ul style="list-style-type: none"> Risk of thyroid C-cell tumors in rodents; human relevance not determined Counsel patients on potential for GI side effects and their typically temporary nature; provide guidance on dietary modifications to mitigate GI side effects (reduction in meal eating practices [e.g., stop eating once full], decreasing intake of high-fat or spicy foods); consider slower dose titration for patients experiencing GI challenges Pancreatitis has been reported in clinical trials but causality has not been established; Discontinue if pancreatitis is suspected Evaluate for gallbladder disease if cholelithiasis or cholecystitis is suspected
DPP-4 inhibitors	Intermediate	No	Neutral	Neutral	Neutral (potential risk, saxagliptin)	Neutral	<ul style="list-style-type: none"> Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment 	Oral	High	<ul style="list-style-type: none"> Pancreatitis has been reported in clinical trials but causality has not been established; Discontinue if pancreatitis is suspected Joint pain Bullous pemphigoid (postmarketing): discontinue if suspected

Podcasts
adjustment required for anagapupin

At Diagnosis of Type 2 Diabetes



A1C, glycated hemoglobin;
CPG, clinical practice guidelines

Go to Figure 2

Go to Figure 3

* In individuals **with** atherosclerotic cardiovascular disease, history of heart failure (with reduced ejection fraction) or chronic kidney disease, agents with cardiorenal benefits (Fig 2a and 2b) may be considered (see 2020 Update – The Users Guide)

† Unintentional weight loss should prompt consideration of other diagnoses (e.g. type 1 diabetes or pancreatic disease) †† Reassess need for ongoing insulin therapy once type of diabetes is established and response to health behaviour interventions is assessed

Update: Reviewing, Adjusting or Advancing Therapy

Regular Review

- Assess glycemic control, cardiovascular and renal status
- Screen for complications (eyes, feet, kidneys)
- Review efficacy, side effects, safety and ability to take current medications
- Reinforce & support healthy behaviour interventions

if A1C NOT at Target
and/or
Change in Clinical Status ← **NEW**

Adjust or Advance
Therapy¹

NEW → ASCVD, **CKD** or **HF**, OR Age >60 with 2 CV risk factors²

NEW → ADD or **SUBSTITUTE** AHA
with demonstrated **cardiorenal** benefits (see Fig 2b)

A1C above target and glucose lowering required

ADD or **SUBSTITUTE** AHA³
according to clinical priorities⁴

start insulin for symptomatic hyperglycemia and/or metabolic decompensation (fig 3)

1. Changes in clinical status may necessitate adjustment of glycemic targets and/or deprescribing
2. Tobacco use; dyslipidemia (use of lipid modifying therapy or a documented untreated LDL ≥ 3.4 mmol/L, or HDL-C < 1.0 mmol/L for men and < 1.3 mmol/L for women, or triglycerides ≥ 2.3 mmol/L); or hypertension (use of blood pressure drug or untreated SBP ≥ 140 mm Hg or DBP ≥ 95 mmHg)
3. All AHA's have Grade A evidence for effectiveness to reduce blood glucose levels
4. Consider degree of hyperglycemia, costs and coverage, renal function, comorbidity, side effect profile, and potential for pregnancy

Update: For People with ASCVD, CKD or HF, OR >60yrs and 2 CV risk factors

ADD or SUBSTITUTE AHA with demonstrated cardiorenal benefits (see Figure 2B)

		POPULATION			
		ASCVD	CKD	HF	>60 yrs with CV risk factors†
OUTCOME	Lower Risks Observed in Outcome Trials	MACE	GLP1-RA or SGLT2i*	SGLT2i* or GLP1-RA	GLP1-RA
		HHF	SGLT2i*	SGLT2i*	SGLT2i* (and lower CV mortality)
		Progression of Nephropathy	SGLT2i*	SGLT2i*	SGLT2i*

Highest level of evidence:

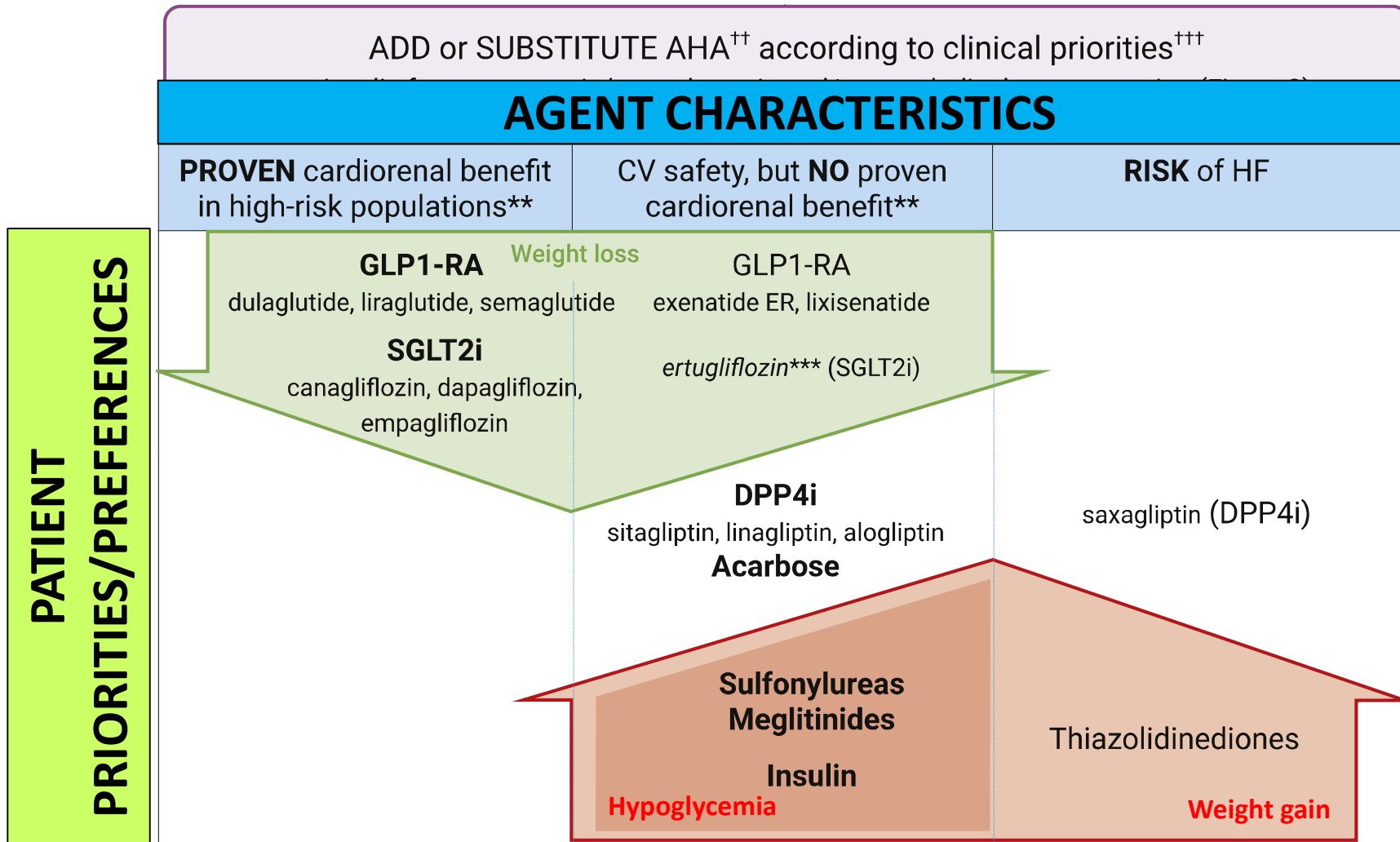
Grade A
Grade B
Grade C or D

*Initiate only if eGFR >30 ml/min/1.73m²

Where additional glucose lowering is required

†† All AHA's have Grade A evidence for effectiveness to reduce blood glucose levels

††† Consider degree of hyperglycemia, costs and coverage, renal function, comorbidity, side effect profile, and potential for pregnancy



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** In CV outcome trials performed in people with ASCVD, CKD, HF or at high CV risk

*** VERTIS (CV outcome trial for ertugliflozin) presented at ADA June 2020 showed non-inferiority for MACE. Manuscript not published at time of writing.

Summary of Outcome Trials Showing Cardiorenal Benefits

Agent (outcome trial)	Population	Clinical outcomes (HR [95% CI] vs placebo)						
		MACE	CV mortality	All-cause mortality	Fatal/ nonfatal MI	Fatal/ nonfatal stroke	Hosp HF	Progression of CKD
GLP1-RA								
Exenatide (EXSCEL)	CVD (73%) or CV risk factors	0.91* (0.83-1.00)	0.88 (0.76-1.02)	0.86 (0.77-0.97)	0.97 (0.85-1.10)	0.83 (0.70-1.03)	-	-
Liraglutide (LEADER)	CVD (72%) or CV risk factors	0.87* (0.78-0.97)	0.78 (0.66-0.93)	0.85 (0.74-0.97)	0.81 (0.7-0.93)	0.88 (0.78-0.99)	-	-
Semaglutide SC (SUSTAIN 6)	CVD (59%) or CV risk factors	0.74* (0.58-0.95)	0.98 (0.65-1.48)	1.05 (0.74-1.50)	0.74 (0.51-1.08)†	0.61 (0.38-0.99)†	-	-
Semaglutide Oral (PIONEER 6)	CVD (85%) or CV risk factors	0.79* (0.57-1.11)	0.49 (0.27-0.92)	0.50 (0.31-0.84)	1.1 (0.9-1.3)	0.74 (0.53-1.0)	-	-
Dulaglutide (REWIND)	CVD (31.5%) or CV risk factors	0.88* (0.79-0.99)	0.91 (0.78-1.06)	0.90 (0.80-1.01)	0.96 (0.79-1.15)	0.74 (0.53-1.0)	-	-
Albiglutide (HARMONY) (withdrawn from market)	CVD or PVD	0.78* (0.68-0.90)	0.93 (0.73-1.19)	0.95 (0.79-1.16)	0.96 (0.79-1.15)	0.76 (0.62-0.94)	-	-
SGLT2i								
Empagliflozin (EMPA-REG)	CVD	0.86* (0.74-0.99)	0.62 (0.49-0.77)	0.68 (0.57-0.82)	0.87 (0.70-1.09)	1.18 (0.89-1.56)	0.65 (0.50-0.85)	0.61 (0.53-0.70)
Canagliflozin (CANVAS PROGRAM)	CVD (66%) or CV risk factors	0.86* (0.75-0.97)	0.87 (0.72-1.06)	0.87 (0.74-1.01)	0.89 (0.73-1.09)	0.87 (0.69-1.09)	0.67 (0.52-0.87)	0.73 (0.67-0.79)
Canagliflozin (CREDENCE)	CKD (eGFR 30-90 + proteinuria)	0.80 (0.67-0.95)	0.78 (0.61-1.00)	0.83 (0.68-1.02)	-	-	0.61 (0.47-0.80)	0.70* ² (0.59-0.82)
Dapagliflozin (DECLARE-TIMI)	CVD (41%) or CV risk factors	0.93* (0.84-1.03)	0.98 (0.82-1.17)	0.93 (0.82-1.04)	0.89 (0.77-1.01)	1.01 (0.84-1.21)	0.73 (0.61-0.88)	0.76 (0.67-0.87)
Dapagliflozin (DAPA-HF)	CHF (reduced EF) ± DM (42%)	- ¹	0.82 (0.69-0.98)	0.83 (0.71-0.97)	-	-	0.70 (0.59-0.83)	0.71 (0.44-1.16)

For People with
T2D and ASCVD

Both GLP1-RA & SGLT2i reduce
risk of MACE

presentation

- Case
- Historical perspective
- Where we are in 2022
- ***Who needs insulin***
 - *When to start*
- New guidelines 2022 sept diabetes care

Unchanged: Initial choice of therapy

Symptomatic
Hyperglycemia
and/or
Metabolic
Decompensation

- Polyuria
- Polydipsia
- Weight loss
- Volume depletion



Start INSULIN +/- metformin

When to start insulin

1) Metabolic decompensation

2) Preconception

If a1c not at target

3) Evidence of ketoacidosis

4) Poor control despite oral agents and glp1 agonist

5) All of the above

Q10: When should initiation of insulin be considered?

- Symptomatic hyperglycemia and/or metabolic decompensation (e.g. unintentional weight loss)
- Relative insulin deficiency with severely elevated A1C and fasting glucose, even without symptomatic hyperglycemia and/or metabolic decompensation
- Unclear diagnosis (i.e. type 1 diabetes or latent autoimmune diabetes in adults [LADA] are being considered)
- Conception planning or during pregnancy
- When noninsulin AHA are unable to achieve target glycemic control

If starting insulin

- 1) Best to start with mealtime insulin
- 2) Best to start with basal insulin only
- 3) Best to start with multiple daily injections
- 4) Insulin pump is the best way to go

Clinical Practice Guidelines 2020 Updates: Initiating Insulin Treatment in Patients With T2D



What are the recommendations for patients with T2D who need to initiate insulin?

**DIABETES
CANADA**



Therapeutic considerations

- Potentially greatest A1C reduction and (theoretically) no maximum dose
- Dose escalation may be limited by hypoglycemia
- Numerous formulations and delivery systems allow for regimen flexibility



Cautions

- Education required regarding blood glucose monitoring and preventing, detecting and treating hypoglycemia
- Numerous formulations and delivery systems increases complexity and risk for errors

In people not achieving glycemic targets on existing noninsulin antihyperglycemic medication(s), the addition of a basal insulin regimen should be considered over premixed insulin or bolus-only regimens, if lower risk of hypoglycemia and/or preventing weight gain are priorities

Clinical Advantages of Second-Generation



What are the clinically meaningful benefits of second-generation basal insulin analogues compared to first-generation?

Second-generation basal analogues have advantages over previous generations

- Extended action profiles
- Comparable glycemic control
- Reduced risk of hypoglycemia
- Reduced number of injections
- Smaller injection volumes



Newer second-generation basal insulin analogues Gla-300 and IDeg have demonstrated increased stability, which translates to:

Increased convenience and flexibility in timing of administration

Potential for morning dosing, without adversely impacting efficacy or safety



Reduced risk of severe and nocturnal hypoglycemia

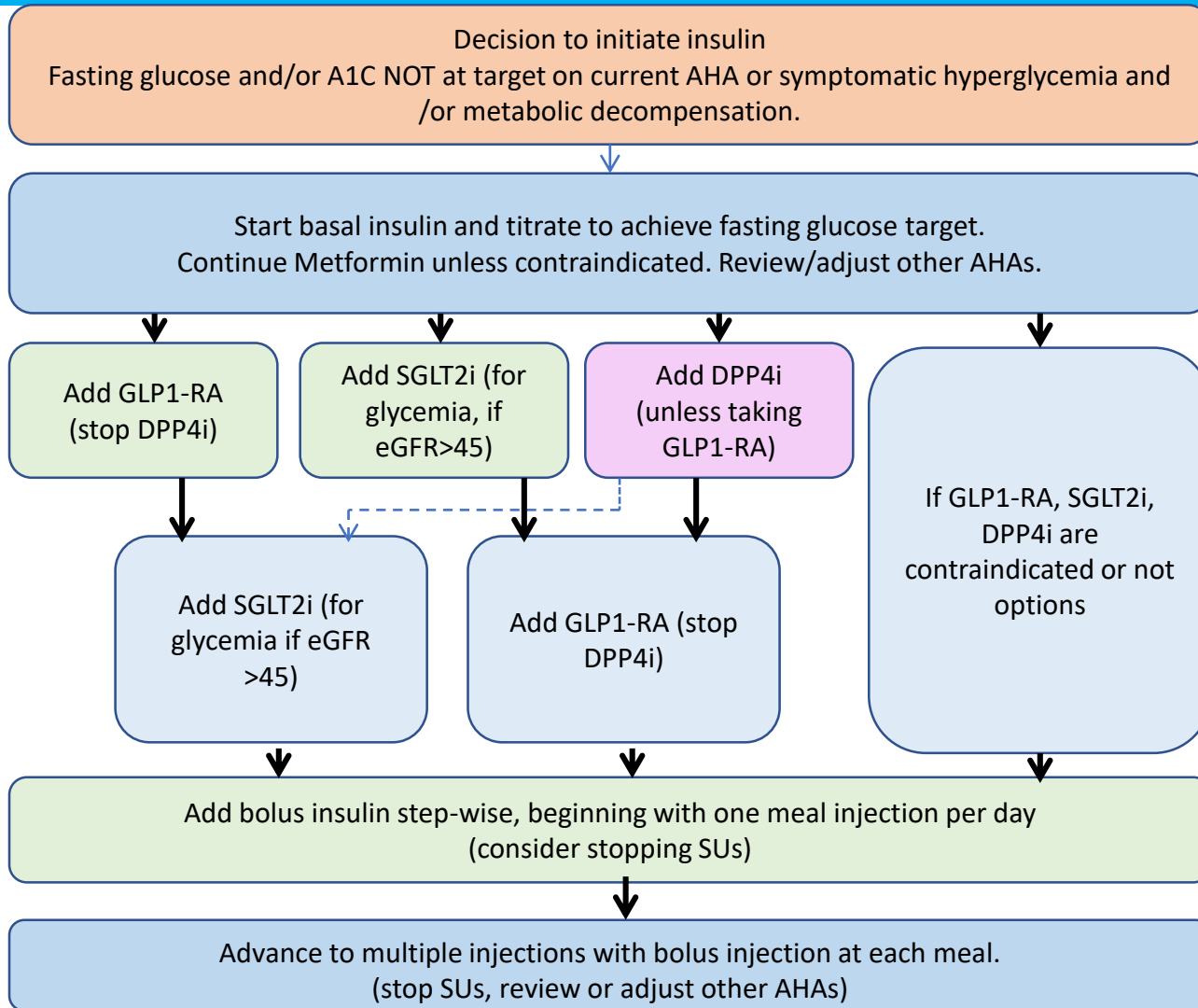
Potentially overcoming key barriers to insulin initiation and titration



Dose titration and use of combination products Starting or Advancing Insulin in Type 2 Diabetes

Regular Review

- Assess glycemic control, cardiovascular and renal status
- Screen for complications (eyes, feet, kidneys)
- Review efficacy, side effects, safety and ability to take current medications
- Reinforce and support healthy behaviour interventions



Advance therapy if A1C not at target within 3-6 months despite adequate titration* and supports for lifestyle and pharmacotherapy

Highest level of evidence:


- Grade A
- Grade B
- Grade C or D

* Titration of basal insulin to achieve target FPG without hypoglycemia
 † And titrate dose of GLP1-RA as tolerated
 †† Or fixed ratio combination
 ††† If eGFR >30ml/min/1.73m², may be used for cardiorenal benefit
 ** Sulfonylureas or meglitinides



Real-World Burden of Hypoglycemia in

Incidence of hypoglycemia among adults with diabetes taking insulin may be higher than previously thought

 InHypo-DMPQ Study
(Canada)



N=552

T1D patients
n=94

T2D patients
n=456



Total hypoglycemia:

65% experienced ≥ 1 hypoglycemia event
95% CI: 61.0 to 69.0

Overall hypoglycemia rate:
35.1 events/person-year
95% CI: 34.6 to 35.6



66%

95% CI: 58.2 to 66.3

Daytime hypoglycemia
(22.7 events/person-year)
95% CI: 22.2 to 23.0



41%

95% CI: 36.9 to 45.1

Nocturnal hypoglycemia
(12.6 events/person-year)
95% CI: 12.3 to 12.9

Severe hypoglycemia:

40% experienced ≥ 1 hypoglycemia event
95% CI: 36.5 to 44.7

Overall hypoglycemia rate:
2.5 events/person-year
95% CI: 2.3 to 2.6



38%

95% CI: 34.0 to 42.1

Daytime hypoglycemia
(1.5 events/person-year)
95% CI: 1.4 to 1.6



27%

95% CI: 23.4 to 30.8

Nocturnal hypoglycemia
(1.0 events/person-year)
95% CI: 0.9 to 1.0

InHypo-DMPQ & InHypo-DMPQ Person with Diabetes Interview

Questionnaire. CI: confidence interval.

Ratzki-Leewing A et al. *BMJ Open Diab Res Care*

2018;6:e000503.

presentation

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PLACE OF INSULIN IN TYPE 2 DIABETES



The use of a GLP-1 RA should be considered prior to initiation of insulin.



When initiating insulin, start with a basal insulin and intensify the dose in a timely fashion, titrating to achieve the individualised fasting glycaemia target set for every person.

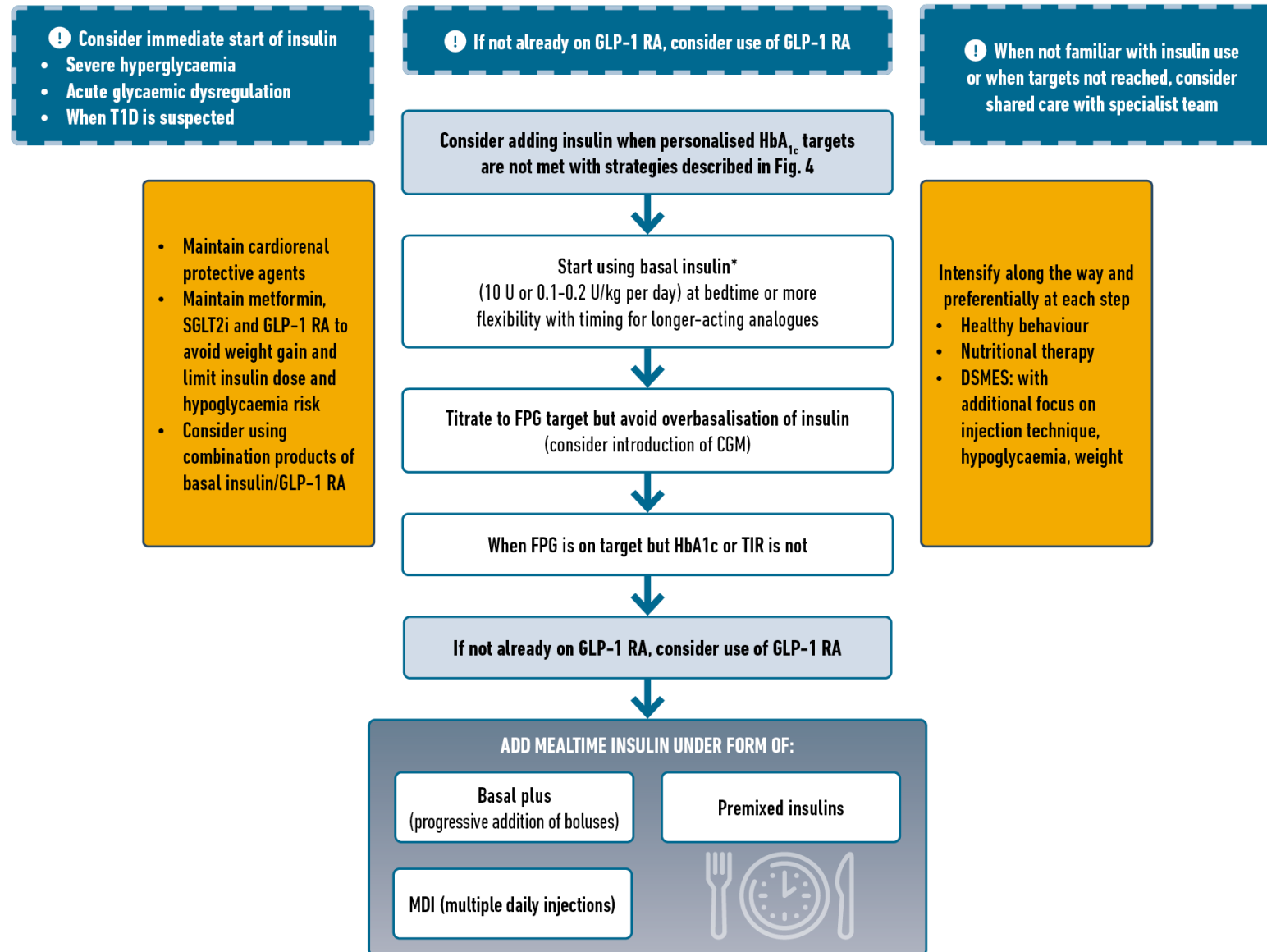


When insulin is initiated, continue organ-protective glucose-lowering medications and metformin.



Refer for DSMES when initiating insulin or advancing to basal-bolus therapy.

FIGURE 5: PLACE OF INSULIN¹



*NPH Insulin or preferably analogue to reduce nocturnal hypoglycaemia risk

CGM, Continuous Glucose Monitoring; DSMES, Diabetes Self-Management Education and Support; FPG, Fasting Plasma Glucose; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agonist; SGLT2i, Sodium-Glucose Cotransporter-2 Inhibitor; T1D, Type 1 Diabetes; TIR, Time in Range.

1. More details can be found in Davies M, D'Alessio DA, Fradkin J et al. Management of Hyperglycaemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia* 2018 61(12):2461-2498, and American Diabetes Association Professional Practice Committee, Draznin B, Aroda VR et al. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2022. *Diabetes Care*. 2022 Jan 1;45(Suppl 1):S125-43.

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

Diabetes Care 2022; <https://doi.org/10.2337/dci22-0034>. *Diabetologia* 2022; <https://doi.org/10.1007/s00125-022-05787-2>.

Time in Range Targets for People With Diabetes

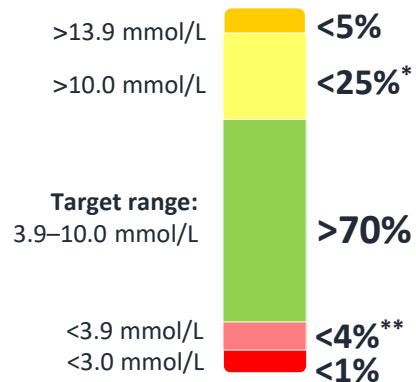


What time in range goals should my patients aim for?

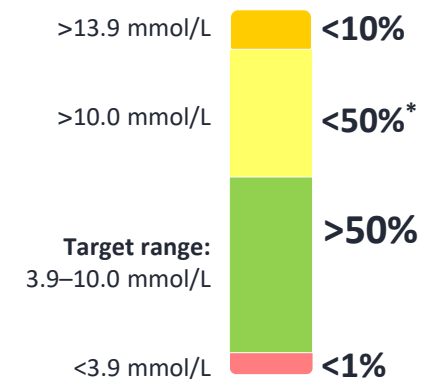
Time in range goals will be different for every person and may depend on medication, diabetes type, diet, age, general health, and hypoglycemia risk. Thus, targets can be personalized to meet individual needs.



Most people with diabetes:



Older/high-risk people with diabetes:



Click for information on factors that impact the daily life of people with type 2 diabetes



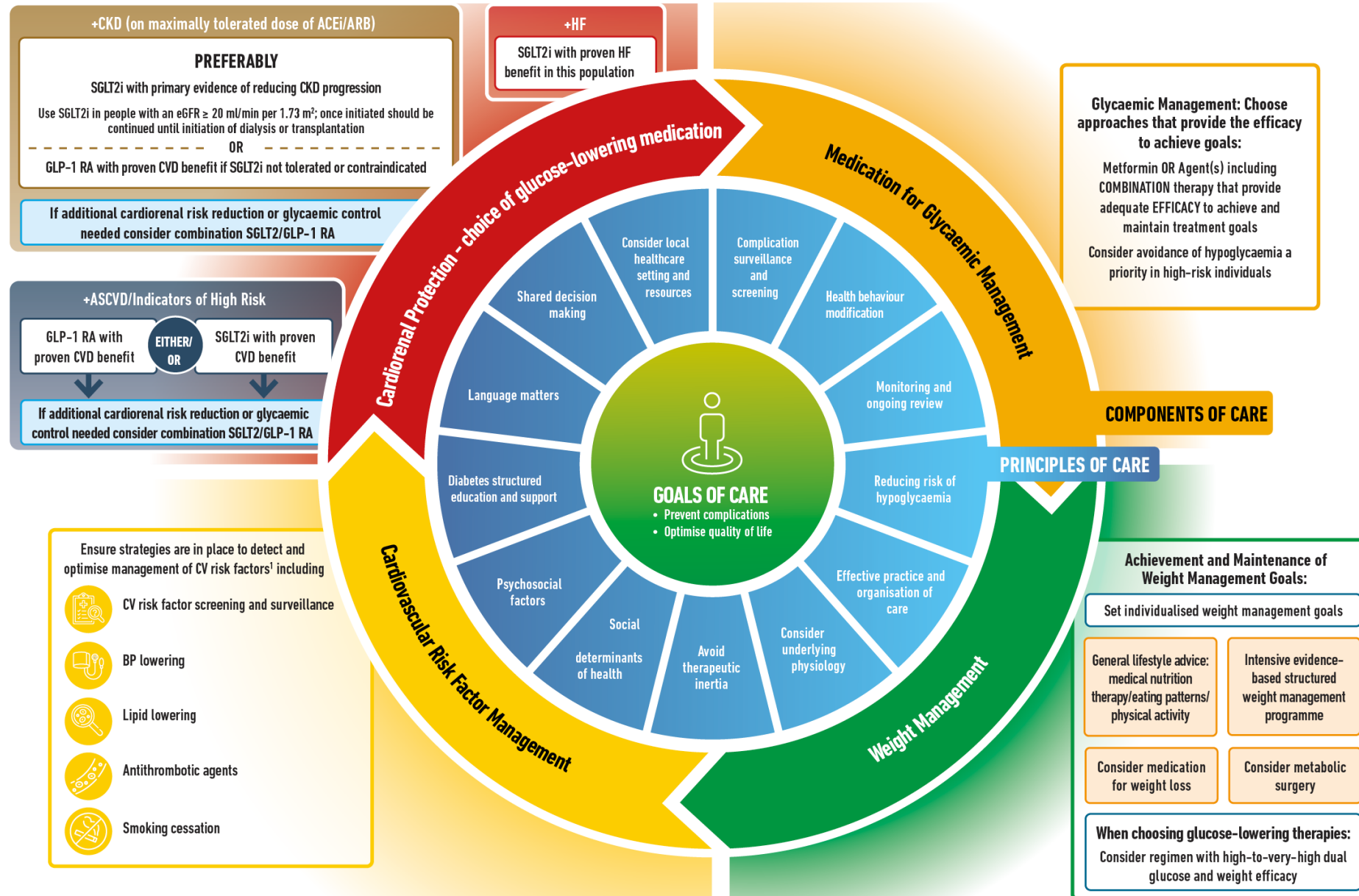
Primary goal for effective and safe glucose control is to **↑** time in range and **↓** time below range

*Includes percentage of values >13.9 mmol/L; **includes percentage of values <3.0 mmol/L.

Note: Targets are tighter for pregnancy.

Image adapted from: Battelino T et al. *Diabetes Care*. 2019 Aug;42(8):1593-1603.

FIGURE 4: HOLISTIC PERSON-CENTRED APPROACH TO T2DM MANAGEMENT



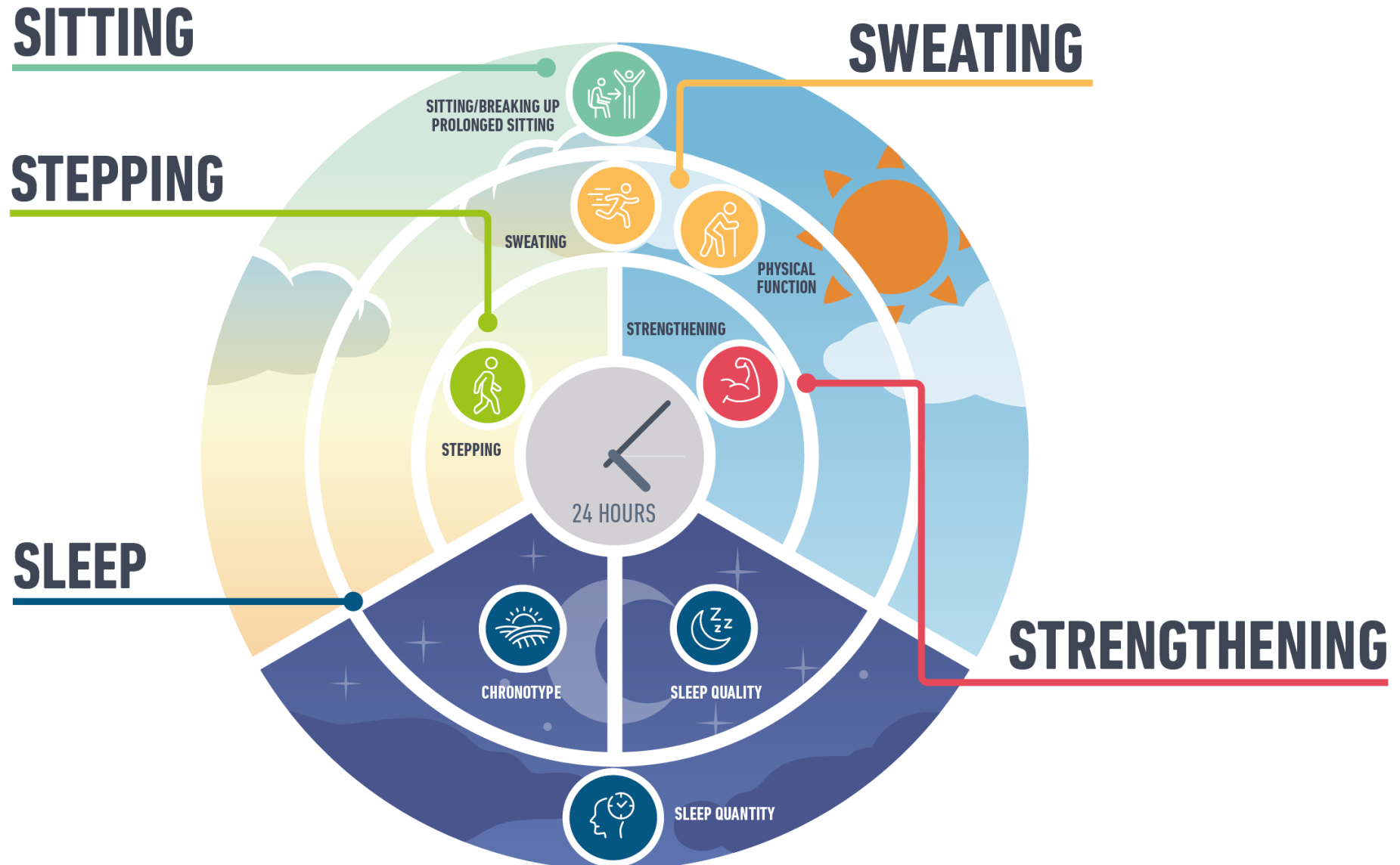
Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

Diabetes Care 2022; <https://doi.org/10.2337/dci22-0034>. Diabetologia 2022; <https://doi.org/10.1007/s00125-022-05787-2>.

1 = American Diabetes Association Professional Practice Committee. 10. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes-2022. Diabetes Care. 2022 Jan 1;45(Suppl 1):S144–74.

ACEi, Angiotensin-Converting Enzyme Inhibitor; ARB, Angiotensin Receptor Blockers; ASCVD, Atherosclerotic Cardiovascular Disease; BP, Blood Pressure; CKD, Chronic Kidney Disease; CV, Cardiovascular; eGFR, Estimated Glomerular Filtration Rate; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agonist; HF, Heart Failure; SGLT2i, Sodium-Glucose Cotransporter-2 Inhibitor; T2D, Type 2 Diabetes.

FIGURE 2: IMPORTANCE OF 24-HOUR PHYSICAL BEHAVIOURS FOR TYPE 2 DIABETES

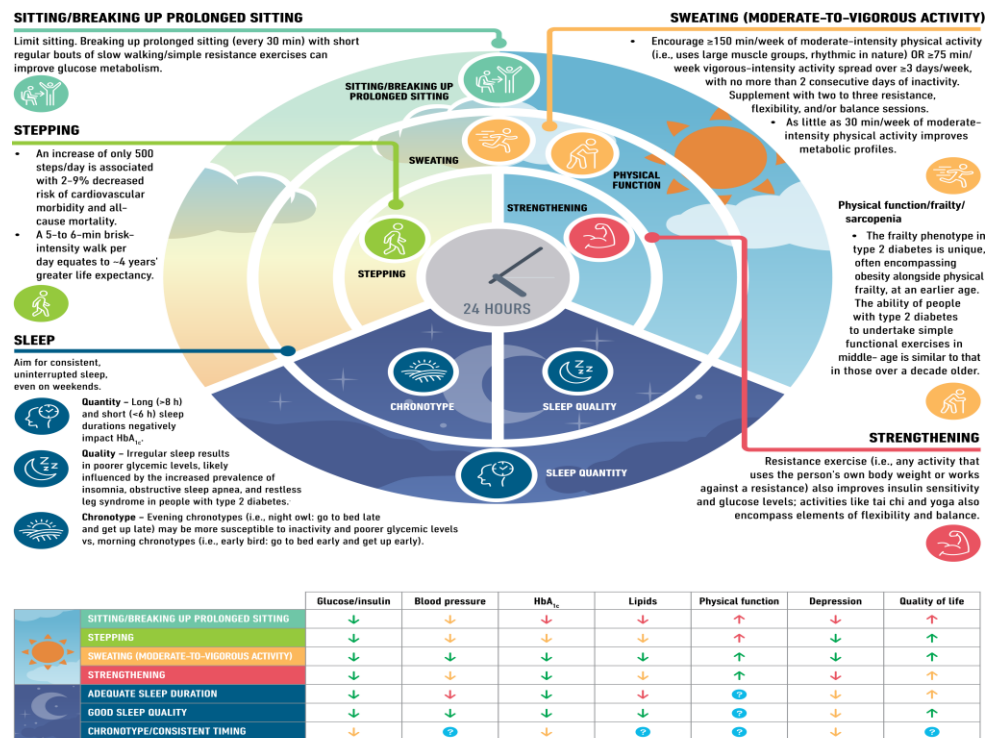


Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

Diabetes Care 2022; <https://doi.org/10.2337/dci22-0034>. *Diabetologia* 2022; <https://doi.org/10.1007/s00125-022-05787-2>.

Diabetes Care.

IMPORTANCE OF 24-HOUR PHYSICAL BEHAVIORS FOR TYPE 2 DIABETES



IMPACT OF PHYSICAL BEHAVIORS ON CARDIOMETABOLIC HEALTH IN PEOPLE WITH TYPE 2 DIABETES

↑ Higher levels/improvement (physical function, quality of life); ↓ Lower levels/improvement (glucose/insulin, blood pressure, HbA_{1c}, lipids, depression); ↔ no data available;
↑ Green arrows = strong evidence; ↑ Yellow arrows = medium strength evidence; ↑ Red arrows = limited evidence.

Figure Legend:

Importance of 24-h physical behaviors for type 2 diabetes.

only 500
associated
decreased
cardiovascular
mortality and all-
cause mortality.
15- to 6-min brisk-
intensity walk per
day equates to ~4 years'
greater life expectancy.



SLEEP

Aim for consistent, uninterrupted sleep, even on weekends.

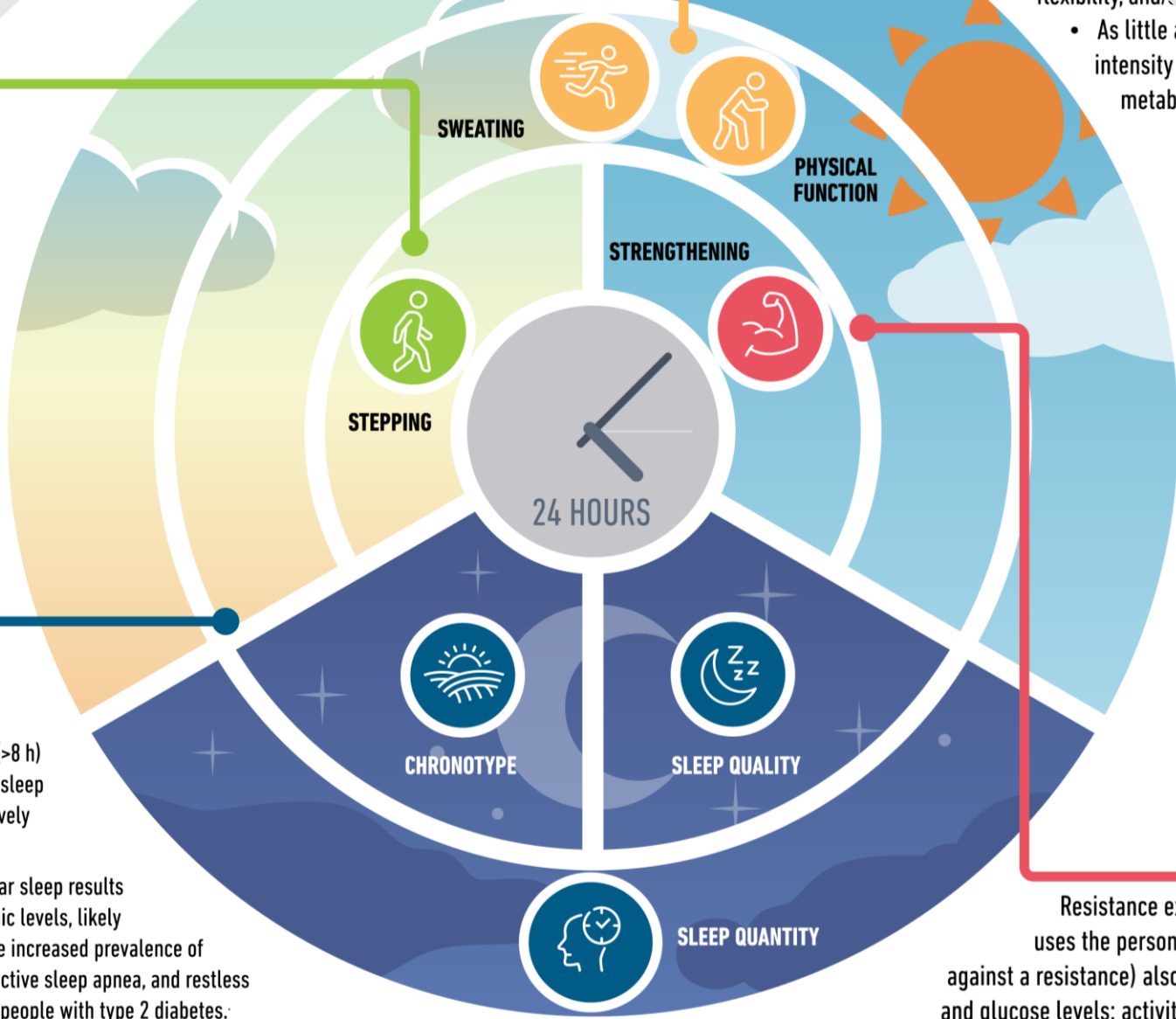


Quantity - Long (>8 h) and short (<6 h) sleep durations negatively impact HbA_{1c}.



Quality - Irregular sleep results in poorer glycemic levels, likely influenced by the increased prevalence of insomnia, obstructive sleep apnea, and restless leg syndrome in people with type 2 diabetes.

Chronotype - Evening chronotypes (i.e., night owl: go to bed late and get up late) may be more susceptible to inactivity and poorer glycemic levels than morning chronotypes (i.e., early bird: go to bed early and get up early).



- As little as 150 min of moderate intensity physical activity per week improves metabolic profile

Physical function/sarcopenia

- The frailty phenotype in type 2 diabetes is often encompassing obesity alongside physical frailty, at an earlier age. The ability of people with type 2 diabetes to undertake simple functional exercises in middle-age is similar to that in those over a decade older.

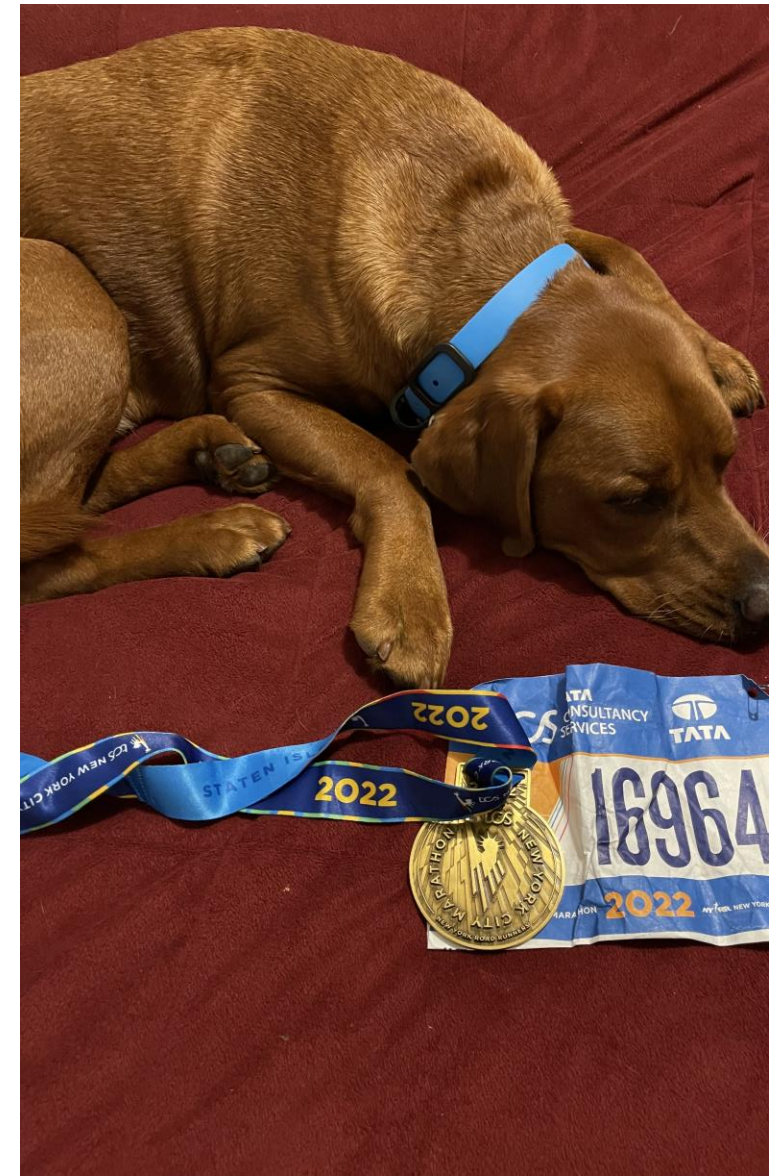


STRENGTHENING

Resistance exercise (i.e., any activity that uses the person's own body weight or an external weight against a resistance) also improves insulin sensitivity and glucose levels; activities like tai chi and yoga also encompass elements of flexibility and balance.

AND GUESS WHAT
EXERCISE IS IN

er Look



Thank you ;Any Questions

