Highlights från EASD 2022

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Jävsdeklaration

Föreläsningsuppdrag för de flesta läkemedelsbolag i inom metabolism/diabetes: AMGEN, Astra-Zeneca, Bayer, Boehringer-Ingelheim, Lilly, MSD, Novartis, Novo Nordisk, Sanofi m.fl

Expertgruppsuppdrag för AZ, MSD, Lilly, Novo Nordisk, Sanofi

Ordförande i SBU-grupp om intensivbehandling av diabetes 2007-2009

Expert i LMVs senaste rekommendationer för T2DM-beh 2017

Honorärsekreterare EASD

EASD 2022

- Världens största internationella diabeteskongress
- Trots post-covideran deltog:
  - 8000 delegater på plats
  - 3000 delegater digitalt
- Deltagare huvudsakligen kliniskt verksamma

Wednesday, 21 September 2022

	Bernard Hall	Minkowski Hall	Golgi Hall	Nobel Hall	Doniach Hall	Peltonen Hall	Heding Hall	Jacobsohn Hall	Virchow Hall
08:30 10:00	EASD/ADA Symposium: Precision medicine in type 2 diabetes: How far can we get?	Diabetologia Symposium: Remission of type 2 diabetes – fact or fiction?	COVID-19 and diabetes	A New Hope (© Star Wars) or Strange New Worlds (© Star Trek): submerging diabetes into emerging technologies	From models to clinic: much more than just a catwalk	Cell biology for diabetologists: A piece of cake?	Overcoming challenges in obesity medicine: The SURMOUNT Clinical Development Program	UKPDS 44-year follow-up	
10:15 11:45	OP 13	OP 14	OP 15	OP 16	OP 17	OP 18			
12:00 13:00	Short Oral Discussions Event C								EASD e-Learning: Dual incretin receptor agonists: Is GIP receptor agonism the key for success?
13:15 14:15	Short Oral Discussions Event D								EASD e-Learning: Diabetic kidney disease and KDIGO guidelines
14:30 16:00	OP 19	OP 20	OP 21	OP 22	OP 23	OP 24			
16:15 17:15	EASD-Novo Nordisk Foundation Diabetes Prize for Excellence				EASD Morgagni Prize				
17:30 18:30	EFSD/Novo Nordisk Foundation Future Leaders Symposium	Modulators of gluco- and lipotoxicity	Debate: Insulin-free type 2 diabetes treatment is…	The heat is on! Diabetes and climate change	Epigenetic regulation and diabetes	EASD/JDRF Symposium: Prevention of type 1 diabetes, is it possible?			Intended self-injury and suicide amongst people with diabetes: tackling this public health challenge

Thursday, 22 September 2022

	Bernard Hall	Minkowski Hall	Golgi Hall	Nobel Hall	Doniach Hall	Peltonen Hall	Heding Hall	Jacobsohn Hall	Virchow Hall
08:30 10:00	Juggling with lipids to find new targets for managing diabetes and comorbidities	New insights to prevention of microvascular complications	Delivering the best of diabetes care in under-resourced populations – how much of the wishful thinking?	Metabolic insights from single-cell studies: clinical implications	Flexing muscle metabolism to battle diabetes: What can we learn from omics?	Cells talk in fatty liver disease	Re-inventing the insulin experience: exploring the prospects of once-weekly insulins	Mineralocorticoid receptor overactivation: novel approach to treatment of multi-organ impact with finerenone	
10:15 11:45	OP 25	OP 26	OP 27	OP 28	OP 29	OP 30	EFSD Mentorship Programme (10:15 - 11:00)		
12:00 13:00	Short Oral Discussions Event E								EASD e-Learning: ADA/EASD management of type 1 diabetes consensus report
13:15 14:15	Short Oral Discussions Event F								EASD e-Learning: Technology and type 1 diabetes
14:30 16:00	OP 31	OP 32	OP 33	OP 34	OP 35	OP 36			
16:15 17:00	Induction of Honorary Members 57th Minkowski Lecture	EASD-Lilly Centennial Anniversary Prize Lecture							
17:15 18:15	The 3 P's of large vessels in type 1 diabetes	Is it the genes or the epigenetics behind diabetic kidney disease?	Debate: "… and CGM for all"	Thermogenic activation of adipose tissue: the holy grail in the treatment of diabesity?	A clinical perspective on the Krebs cycle and insulin sensitivity	New little players in beta cell function			DELIVER Trial

Friday, 23 September 2022

	Bernard Hall	Minkowski Hall	Golgi Hall	Nobel Hall	Doniach Hall	Peltonen Hall	Heding Hall	Jacobsohn Hall	Virchow Hall
08:30 09:30	EASD/ESC Symposium: New perspectives on heart function and failure in diabetes	Diabetic nephropathy or diabetic kidney disease? In search of a phenotype	How much can people with type 1 diabetes benefit from adjunct therapies?	Diabetes in old age: myths and facts	Fasting and feeding: the most important F-words in metabolism	Three reasons for why non-coding RNAs are important in metabolic control	Hepatokines: Do they play a role in diabetes and NAFLD?	10th East-West Forum: Care through the eyes of the patient (08:30 - 10:00)	
09:45 10:45	OP 37	OP 38	OP 39	OP 40	OP 41	OP 42			
11:00 12:00	OP 43	OP 44	OP 45	OP 46	OP 47	OP 48			
12:15 13:45	Management of hyperglycaemia in type 2 diabetes: ADA/EASD Consensus Report 2022	Gut microbiome: a link between autonomic neuropathy and kidney disease in diabetes?	Targeting energy sensing to treat diabetes	The power of dietary policies: evidence from population-based studies	Lipids all over the place: Are lipid droplets friends or foe?	The Greek alphabet revisited: focus on all pancreatic islet cells	Epidemiology of diabetes and COVID-19 hospitalisation in Europe: a European Collaboration (12:15 - 13:15)	The crucial role of primary care for integrated diabetes management (12:15 - 13:15)	

Tirzepatid-SURMOUNT programmet

The NEW ENGLAND JOURNAL of MEDICINE

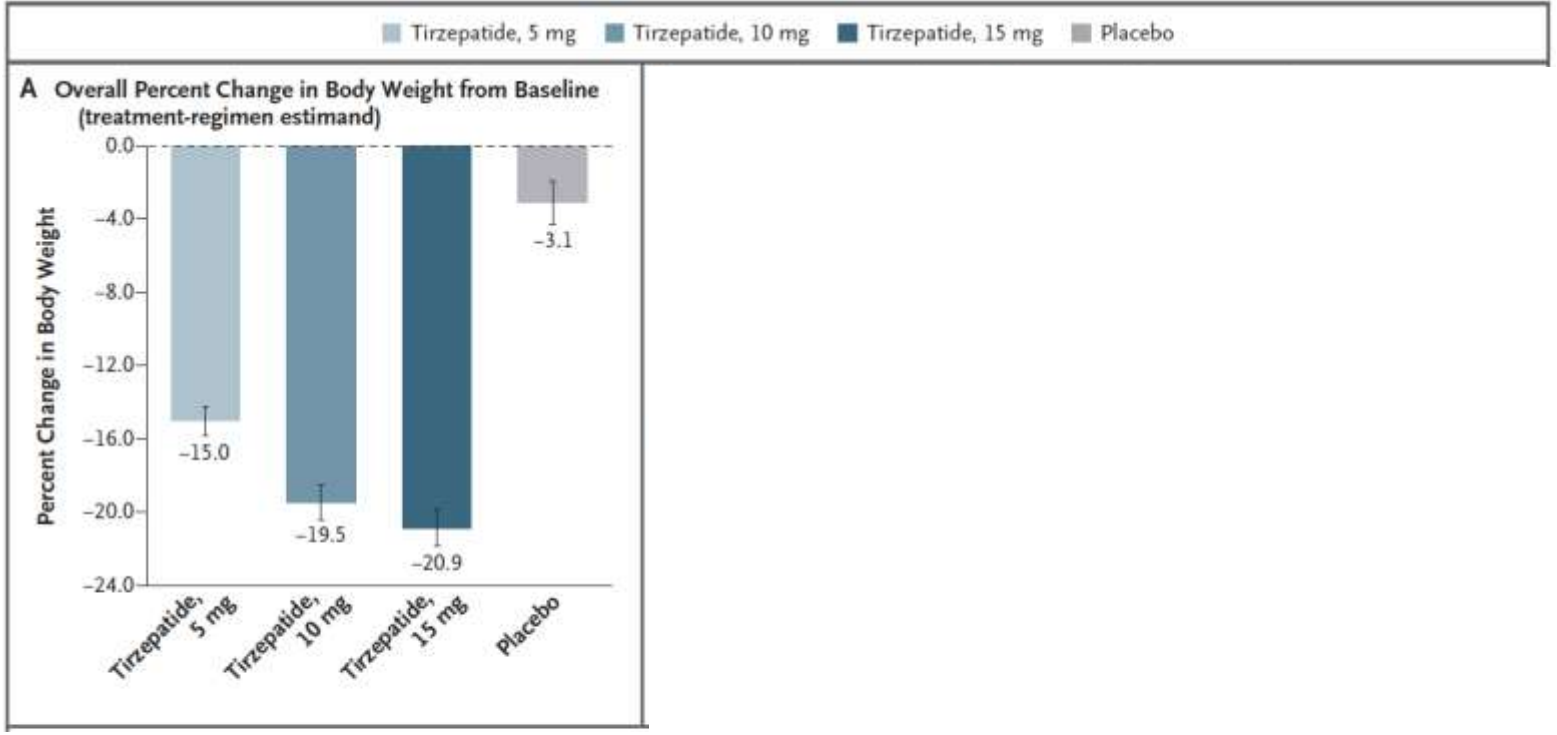
ESTABLISHED IN 1812 JULY 21, 2022 VOL. 387 NO. 3

Tirzepatide Once Weekly for the Treatment of Obesity

Ania M. Jastreboff, M.D., Ph.D., Louis J. Aronne, M.D., Nadia N. Ahmad, M.D., M.P.H., Sean Wharton, M.D., Pharm.D., Lisa Connery, M.D., Breno Alves, M.D., Arihiro Kiyosue, M.D., Ph.D., Shuyu Zhang, M.S., Bing Liu, Ph.D., Mathijs C. Bunck, M.D., Ph.D., and Adam Stefanski, M.D., Ph.D., for the SURMOUNT-1 Investigators*

Tirzepatide

- Dual GLP1R/GIPR agonist, skiljer sig från övriga inkretin-l-m
- Data från SURPASS programmet (T2DM) presenterades 2021 med
  - 27 mmol/mol sänkning av HbA1c
  - 13% viktminskning
- Data från SURMOUNT programmet på obesitas (utan T2DM)
- Tirzepatide godkänt i EU 2022-09-16
- Oklart pris och tillgänglighet


Tirzepatide, 5 mg
Tirzepatide, 10 mg
Tirzepatide, 15 mg
Placebo
A Overall Percent Change in Body Weight from Baseline
(treatment-regimen estimand)
Percent Change in Body Weight
0.0
−4.0
−8.0
−12.0
−16.0
−20.0
−24.0
−15.0
−19.5
−20.9
−3.1
Tirzepatide, 5 mg
Tirzepatide, 10 mg
Tirzepatide, 15 mg
Placebo

Vad tyckte patienterna?

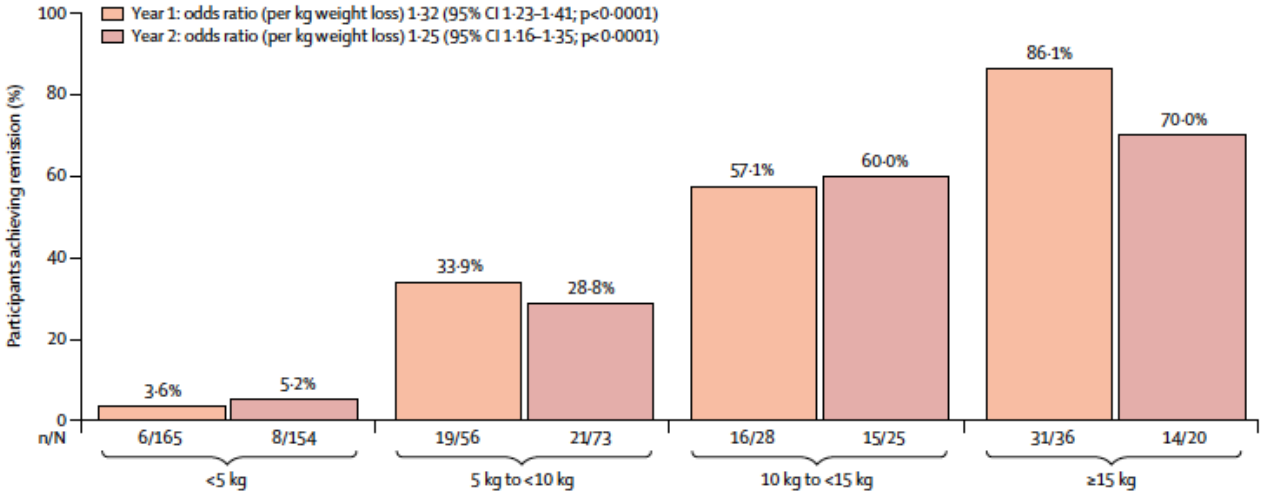
- “Det var lika lätt att gå ner i vikt som det var att gå upp i vikt”
- Vid studieavslut sågs som förväntat reboundfenomen med viktuppgång

Flera andra preparat under utveckling
presenterade under EASD

- Trippel-agonist (GLP1R, GIP och glucagon)-LY3437943
  - Sänker glukos och kroppsvikt hos personer med T2DM under 12 veckors behandling
- Non-peptid baserad liten GLP1R agonists-PF0708132
  - Sänker glukos och kroppsvikt hos personer med eller utan T2DM under 4-6 v behandling
- OBS att inga av dessa preparat, inklusive tirzepatid, ännu har några data avseende kardiovaskulär effektmått

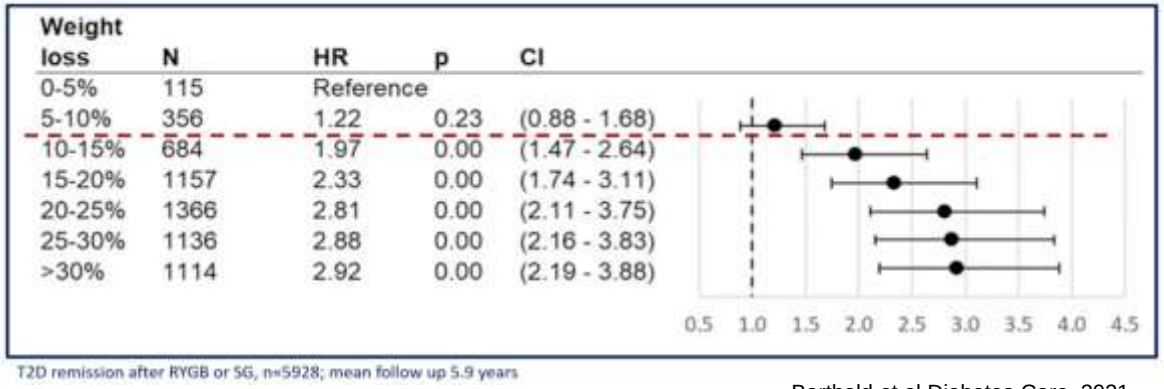
Vad behövs för diabetesremission?

Viktreduktionsprogram i primärvården (DiRECT)



Lean et al Lancet Diabetes and Endocrinology, 2019

Bariatrisk kirurgi



Weight loss	N	HR	p	CI
0-5%	115	Reference		
5-10%	356	1.22	0.23	(0.88 - 1.68)
10-15%	684	1.97	0.00	(1.47 - 2.64)
15-20%	1157	2.33	0.00	(1.74 - 3.11)
20-25%	1366	2.81	0.00	(2.11 - 3.75)
25-30%	1136	2.88	0.00	(2.16 - 3.83)
>30%	1114	2.92	0.00	(2.19 - 3.88)

T2D remission after RYGB or SG, n=5928; mean follow up 5.9 years

Barthold et al Diabetes Care, 2021

Oberoende av metod:

Minst 10-15% viktreduktion behövs för diabetesremission…

…och en relativt kort diabetesduration…

UKPDS-44 års uppföljning

- Första stora studien (n=4209) på personer med nydebuterad T2DM
- Randomiserades till intensiv beh med SU/insulin eller metformin
- Påbörjades 1977-medelålder 53 år
- Avslutades 1997-medelålder 62 år, 80% kvar
- Data publicerade 1998: UKPDS33 (SU/insullin) och 34 (metformin)-visade effekt på mikrovaskulär sjukdom men mortalitet och AMI endast i metformingruppen
- Observationsstudie till 2007-medelålder 72 år, <40% kvar (UKPDS80) visade sk “legacy effect”
- Administrativ uppföljning 2021, ca 10% kvar
- Effekten av att ha ingått i intensivarmen kvarstod över hela observationstiden, för diabetesrelaterat utfall:
  - SU/insulin (HR 0,90; 0,83-0,98, p=0,016)
  - Metformin (HR 0,81; 0,68-0,96, p=0,015)

Veckoinsuliner

- Flera preparat under utveckling
- Olika principer, koppling till antikroppsfragment (basal insulin Fc-BIF) eller fettsyror (Icodec)
- Ger långsamt upptag subkutant med jämna koncentrationer i plasma
- Testade i T1DM och T2DM men troligen mer adekvat för de senare
- Mest data vid T2DM, liknande effect på HbA1c och hypoglykemier men endast korta studier (upp till 26 veckor)
- Dock viss viktuppgång (sekundärt till högre insulindoser)?
- Vid T1DM fler allvarliga hypoglykemier

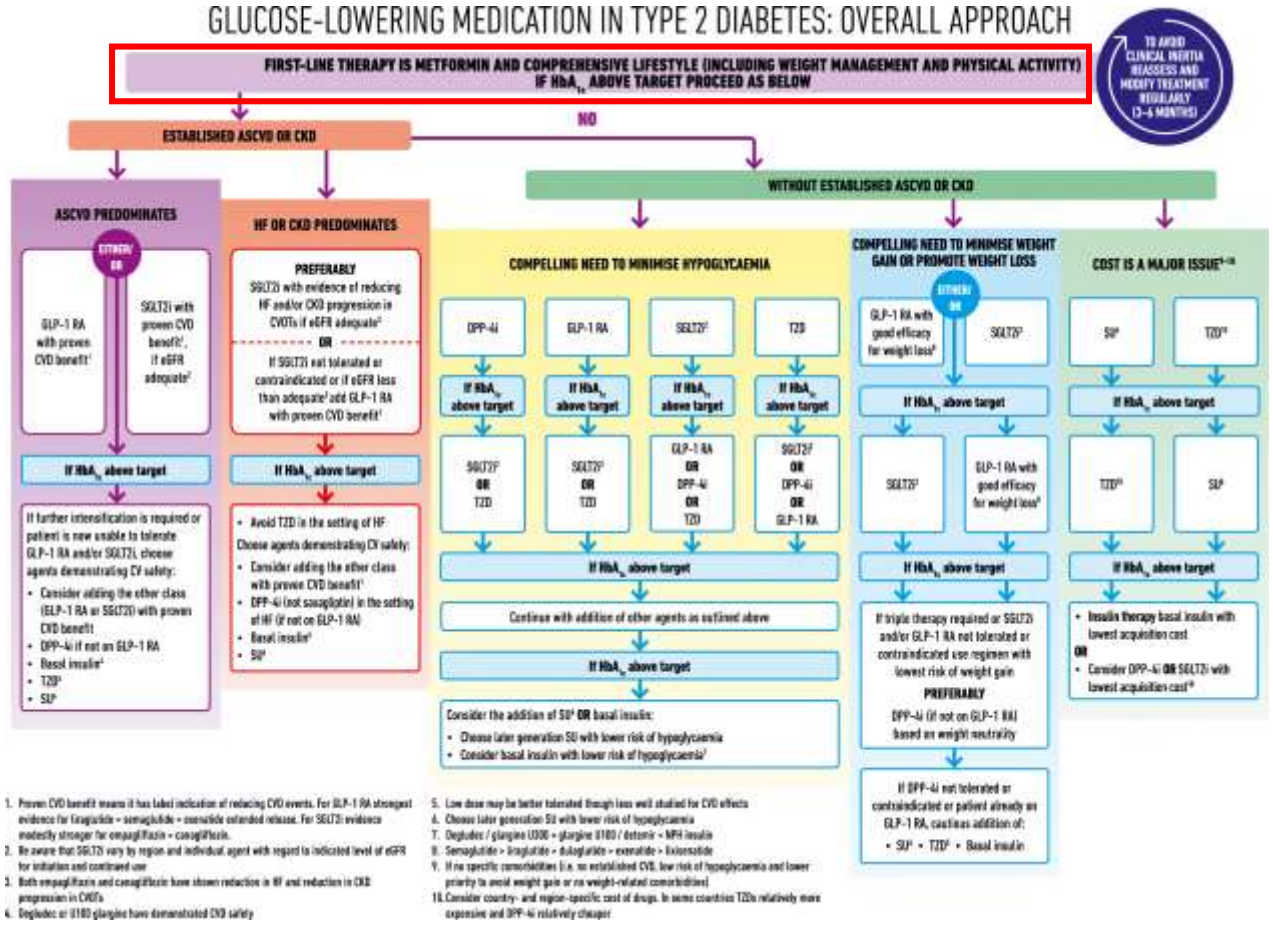
Hjärtsvikt, förmaksflimmer och diabetes

- SGLT2i och GLP1Ra har klara indikationer vid T2DM
- Här diskuterades mekanismer bakom HFpEF, HFrEF och kort om FF
- HFrEF starkt kopplad till atherosklerotisk sjukdom
- Vid DM är kopplingen starkast till HFpEF

Uppdaterade ADA/EASD riktlinjer

- Publicerade sedan 2006
- Uppdaterades senast 2019
- Nyheter:
  - Mer patientcentriskt
  - Uppdatering inkl även senaste generationen l-m såsom tirzepatide
  - Metformin inte längre det första man ska använda
  - Större fokus på viktförlust

De tidigare ADA/EASD riktlinjerna



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 hypoglycaemia
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 hypoglycaemia 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

Davies, M.J., D'Alessio, D.A., Fradkin, J. et al. Diabetologia (2018). https://doi.org/10.1007/s00125-018-4729-5

USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

HEALTHY LIFESTYLE BEHAVIOURS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

Goal: Cardiorenal Risk Reduction in High-Risk Patients with Type 2 Diabetes (In addition to comprehensive CV risk management)*

+ASCVD†

Defined differently across CVOTs but all included individuals with established CVD (e.g. MI, stroke, any revascularisation procedure). Variably included: conditions such as transient ischaemic attack, unstable angina, amputation, symptomatic or asymptomatic coronary artery disease.

+Indicators of high risk

While definitions vary, most comprise ≥ 55 years of age with two or more additional risk factors (including obesity, hypertension, smoking dyslipidaemia or albuminuria)

+ASCVD/Indicators of High Risk

GLP-1 RA# with proven CVD benefit

EITHER/OR

SGLT2i§ with proven CVD benefit

If HbA_{1c} above target

- For patients on a GLP-1 RA consider adding SGLT2i with proven CVD benefit or vice versa
- TZD^

+HF

Current or prior symptoms of HF with documented HFrEF or HFpEF

+HF

SGLT2i§ with proven HF benefit in this population

+CKD

eGFR < 60 ml/min per 1.73 m^2 OR albuminuria (ACR ≥ 3.0 mg/mmol (30mg/g)). These measurements may vary over time; thus, a repeat measure is required to document CKD.

+CKD (on maximally tolerated dose of ACEi/ARB)

PREFERABLY

SGLT2i§ with primary evidence of reducing CKD progression

Use SGLT2i in people with an eGFR ≥ 20 ml/min per 1.73 m^2; once initiated should be continued until dialysis or transplantation

OR

GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated

If HbA_{1c} above target, for patients on SGLT2i, consider incorporating a GLP-1 RA or vice versa

If additional cardiorenal risk reduction or glycaemic lowering needed

Goal: Achievement and Maintenance of Glycaemic and Weight Management Goals

Glycaemic Management: Choose approaches that provide the efficacy to achieve goals:

Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals

Consider avoidance of hypoglycaemia a priority in high-risk individuals

In general, higher efficacy approaches have greater likelihood of achieving glycaemic goals

Efficacy for glucose lowering

Very High:
Dulaglutide (high dose), Semaglutide, Tirzepatide

Insulin

Combination Oral, Combination Injectable (GLP-1 RA/Insulin)

High:
GLP-1 RA (not listed above), Metformin, SGLT2i, Sulfonylurea, TZD

Intermediate:
DPP-4i

Achievement and Maintenance of Weight Management Goals:

Set individualised weight management goals

- General lifestyle advice: medical nutrition therapy/eating patterns/physical activity
- Intensive evidence-based structured weight management programme
- Consider medication for weight loss
- Consider metabolic surgery

When choosing glucose-lowering therapies:

Consider regimen with high-to-very-high dual glucose and weight efficacy

Efficacy for weight loss

Very High:
Semaglutide, Tirzepatide

High:
Dulaglutide, Liraglutide

Intermediate:
GLP-1RA (not listed above), SGLT2i

Neutral:
DPP-4i, Metformin

If HbA_{1c} above target

Identify barriers to goals:

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

* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † 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 the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, 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.

Sammanfattning

- Det sker en mycket snabb utveckling på läkemedelssidan vid diabetes
  - inkretinläkemedel
  - insuliner
  - övriga preparat inklusive SGLT2i och Finerenone
- Nästa generation inkretinläkemedel kommer ha väsentligt starkare effekter på HbA1c och kroppsvikt
- Diabetesremission är nu inom räckhåll, åtminstone för patienter med kortvarigare diabetesduration
- Hjärtdysfunktion är starkt kopplat till diabetes-använd l-m med kardiorenal protektiv effekt tidigare
- Uppdaterade internationella guidelines foksuerar på ökad patientmedverkan samt tuff glukos- och viktkontroll

Tack för uppmärksamheten!

DECISION CYCLE FOR PERSON-CENTRED GLYCAEMIC MANAGEMENT IN TYPE 2 DIABETES

GOALS OF CARE

- Prevent complications
- Optimise quality of life

ASSESS KEY PERSON CHARACTERISTICS

- The individual's priorities
- Current lifestyle and health behaviours
- Comorbidities (i.e. CVD, CKD, HF)
- Clinical characteristics (i.e. age, HbA_{1c}, weight)
- Issues such as motivation, depression, cognition
- Social determinants of health

CONSIDER SPECIFIC FACTORS THAT IMPACT CHOICE OF TREATMENT

- Individualised glycaemic and weight goals
- Impact on weight, hypoglycaemia and cardiorenal protection
- Underlying physiological factors
- Side effect profiles of medications
- Complexity of regimen (i.e. frequency, mode of administration)
- Regimen choice to optimise medication use and reduce treatment discontinuation
- Access, cost and availability of medication

UTILISE SHARED DECISION MAKING TO CREATE A MANAGEMENT PLAN

- Ensure access to DSMES
- Involve an educated and informed person (and the individual's family/caregiver)
- Explore personal preferences
- Language matters (include person-first, strengths-based, empowering language)
- Include motivational interviewing, goal setting and shared decision making

AGREE ON MANAGEMENT PLAN

- Specify SMART goals:
  - **S**pecific
  - **M**easurable
  - **A**chievable
  - **R**ealistic
  - **T**ime limited

IMPLEMENT MANAGEMENT PLAN

- Ensure there is regular review; more frequent contact initially is often desirable for DSMES

PROVIDE ONGOING SUPPORT AND MONITORING OF:

- Emotional well-being
- Lifestyle and health behaviours
- Tolerability of medications
- Biofeedback including BGM/CGM, weight, step count, HbA_{1c}, BP, lipids

REVIEW AND AGREE ON MANAGEMENT PLAN

- Review management plan
- Mutually agree on changes
- Ensure agreed modification of therapy is implemented in a timely fashion to avoid therapeutic inertia
- Undertake decision cycle regularly (at least once/twice a year)
- Operate in an integrated system of care

IMPORTANCE OF 24-HOUR PHYSICAL BEHAVIOURS FOR TYPE 2 DIABETES

SITTING/BREAKING UP PROLONGED SITTING

Limit sitting. Breaking up prolonged sitting (every 30 min) with short regular bouts of slow walking/simple resistance exercises can improve glucose metabolism.

STEPPING

- An increase of only 500 steps/day is associated with 2-9% decreased risk of cardiovascular morbidity and all-cause mortality.
- A 5 to 6 min brisk intensity walk per day equates to ~4 years' greater life expectancy.

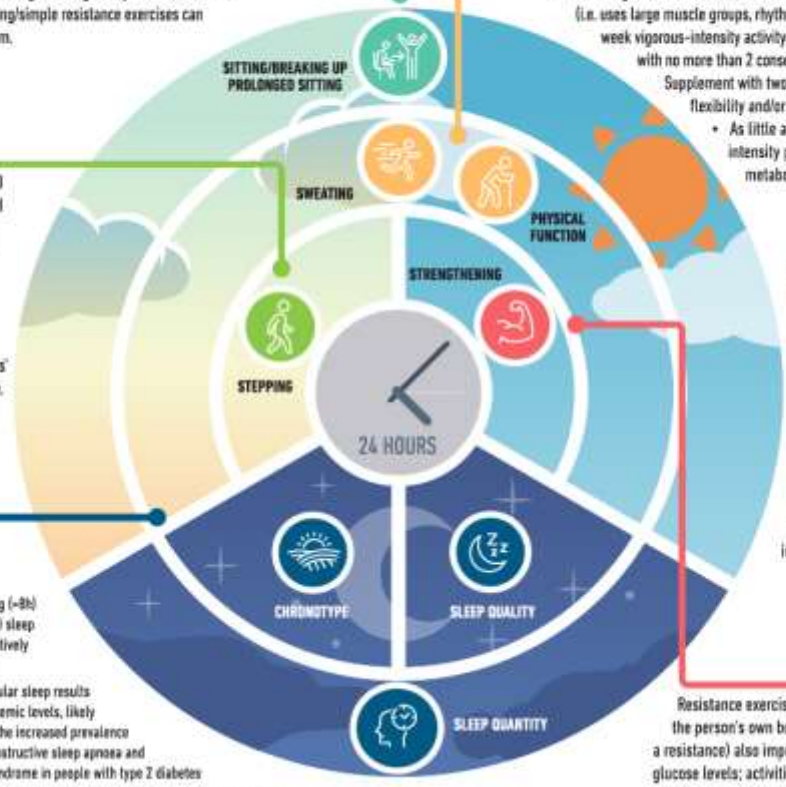
SLEEP

Aim for consistent, uninterrupted sleep, even on weekends.

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

Quality - Irregular sleep results in poorer glycaemic levels, likely influenced by the increased prevalence of insomnia, obstructive sleep apnoea 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 glycaemic levels vs morning chronotypes (i.e. early bird: go to bed early and get up early).



SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)

- Encourage ≥150 min/week of moderate-intensity physical activity (i.e. uses large muscle groups, rhythmic in nature) OR ≥75 min/week vigorous-intensity activity spread over ≥3 days/week, with no more than 2 consecutive days of inactivity. Supplement with two to three resistance, flexibility and/or balance sessions.
  - As little as 30 min/week of moderate-intensity physical activity improves metabolic profiles.

Physical function/frailty/sarcopenia

- The frailty phenotype in type 2 diabetes is unique, 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 works against a resistance) also improves insulin sensitivity and glucose levels; activities like tai chi and yoga also encompass elements of flexibility and balance.

	Glucose/insulin	Blood pressure	HbA_{1c}	Lipids	Physical function	Depression	Quality of life
SITTING/BREAKING UP PROLONGED SITTING	↓	↓	↓	↓	↑	↓	↑
STEPPING	↓	↓	↓	↓	↑	↓	↑
SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)	↓	↓	↓	↓	↑	↓	↑
STRENGTHENING	↓	↓	↓	↓	↑	↓	↑
ADEQUATE SLEEP DURATION	↓	↓	↓	↓	●	↓	↑
GOOD SLEEP QUALITY	↓	↓	↓	↓	●	↓	↑
CHRONOTYPE/CONSISTENT TIMING	↓	●	↓	●	●	↓	●

IMPACT OF PHYSICAL BEHAVIOURS 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**.

HOLISTIC PERSON-CENTRED APPROACH TO T2DM MANAGEMENT

+CKD (on maximally tolerated dose of ACEi/ARB)

PREFERABLY

SGLT2i with primary evidence of reducing CKD progression

Use SGLT2i in people with an eGFR ≥ 20 ml/min per 1.73 m²; once initiated should be continued until dialysis or transplantation

OR

GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated

If additional cardiorenal risk reduction or glycaemic control needed consider combination SGLT2/GLP-1 RA

+HF

SGLT2i with proven HF benefit in this population

+ASCVD/Indicators of High Risk

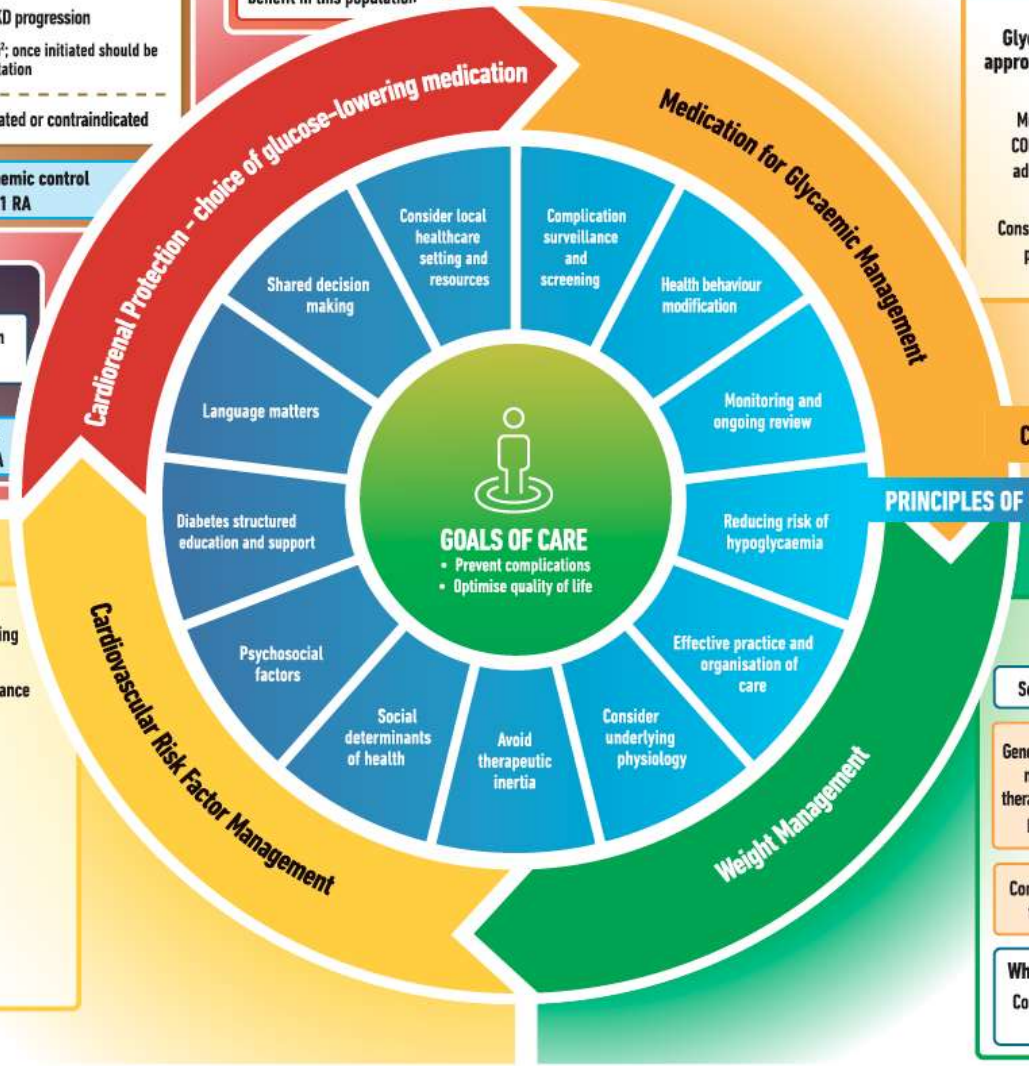
GLP-1 RA with proven CVD benefit — EITHER/OR — SGLT2i with proven CVD benefit

If additional cardiorenal risk reduction or glycaemic control needed consider combination SGLT2/GLP-1 RA

Glycaemic Management: Choose approaches that provide the efficacy to achieve goals:

Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals

Consider avoidance of hypoglycaemia a priority in high-risk individuals



COMPONENTS OF CARE

PRINCIPLES OF CARE

Ensure strategies are in place to detect and optimise management of CV risk factors[1] including

- CV risk factor screening and surveillance
- BP lowering
- Lipid lowering
- Antithrombotic agents
- Smoking cessation

Achievement and Maintenance of Weight Management Goals:

Set individualised weight management goals

General lifestyle advice: medical nutrition therapy/eating patterns/physical activity

Intensive evidence-based structured weight management programme

Consider medication for weight loss

Consider metabolic surgery

When choosing glucose-lowering therapies:

Consider regimen with high-to-very-high dual glucose and weight efficacy