

# Dünden Bugüne Diyabet Kılavuzları

Dr.Kubilay Karşıdağ



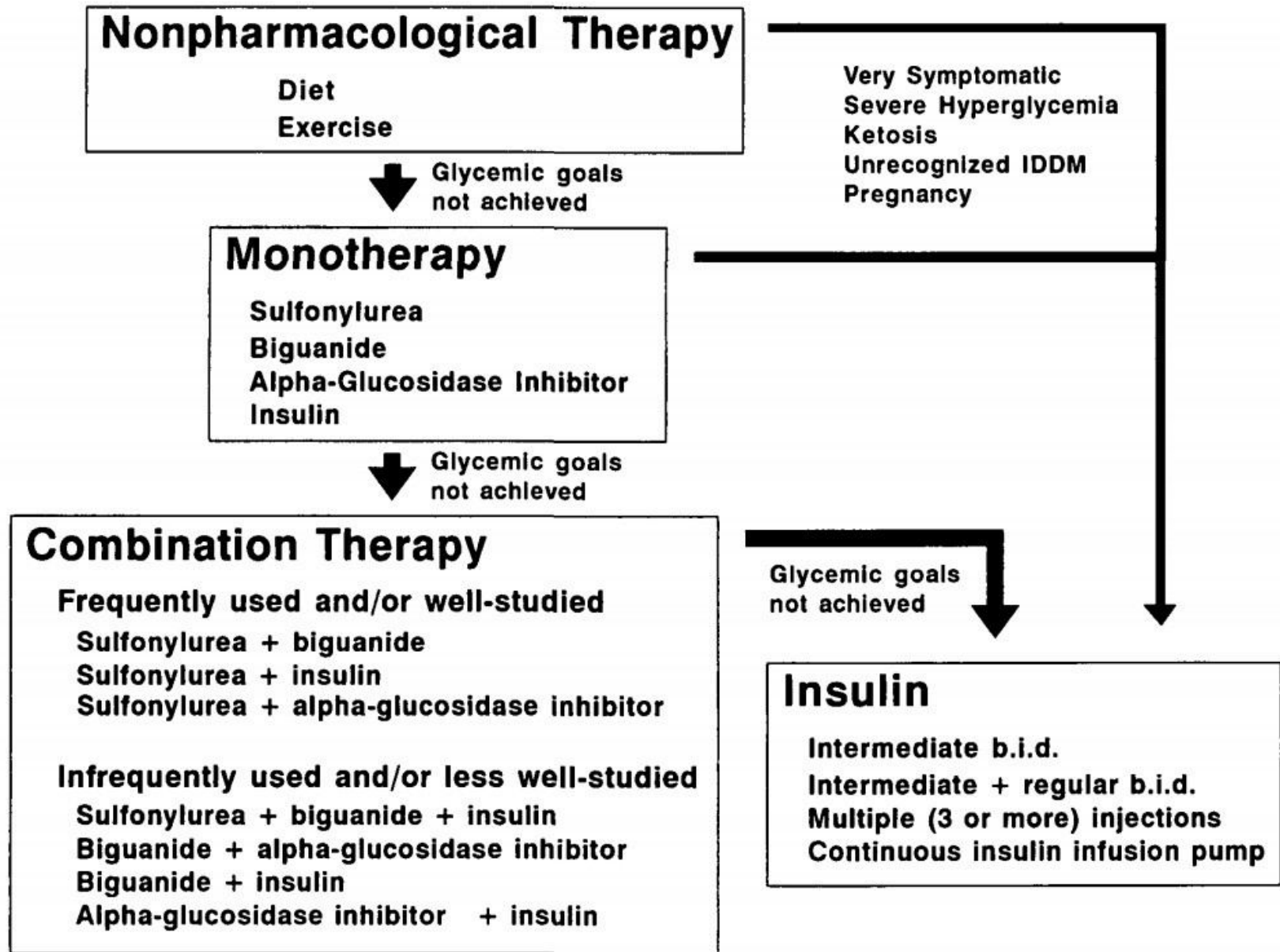


M.S. 1979



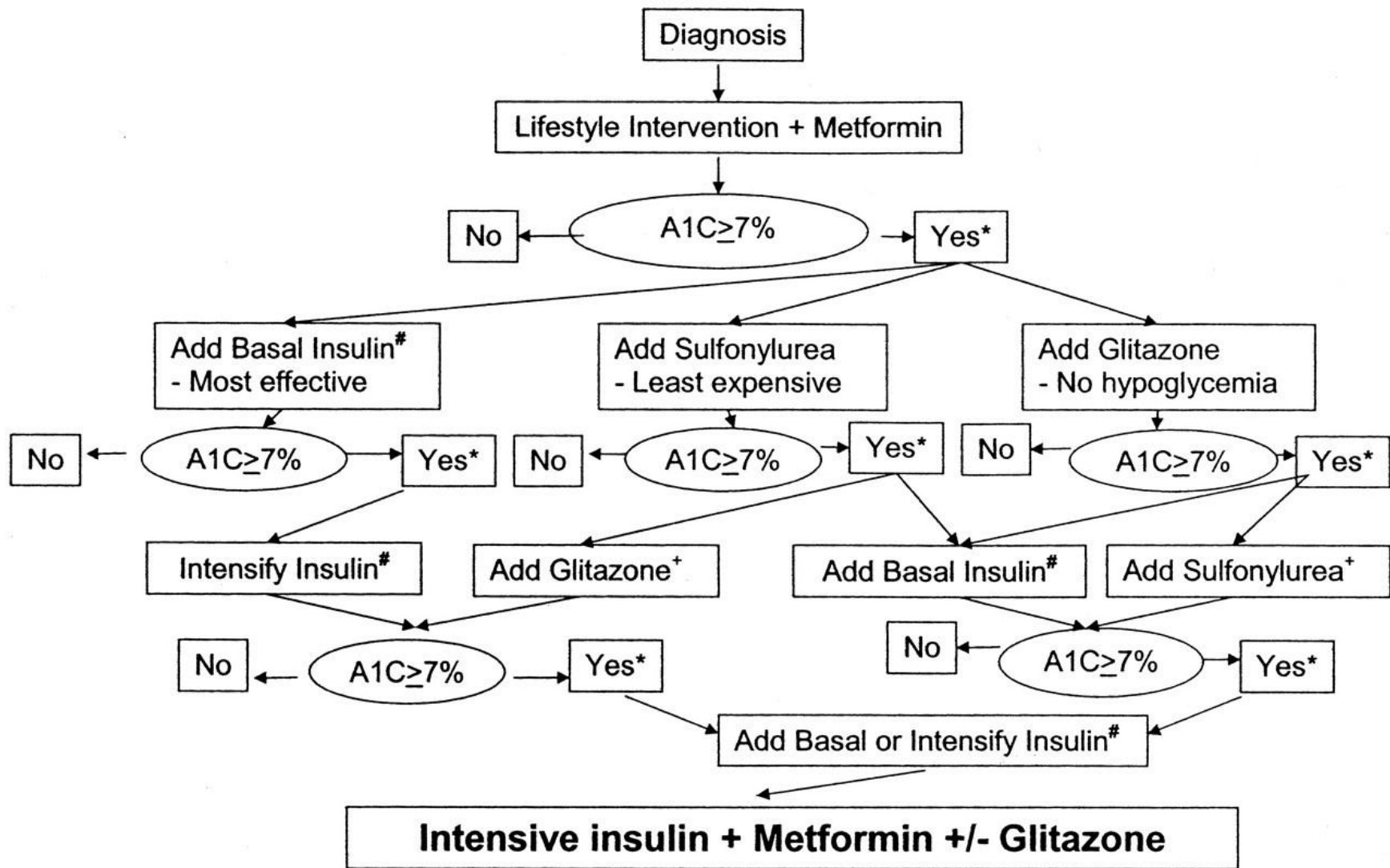
1983

1995



**Figure 1**—Pharmacological therapy of NIDDM.

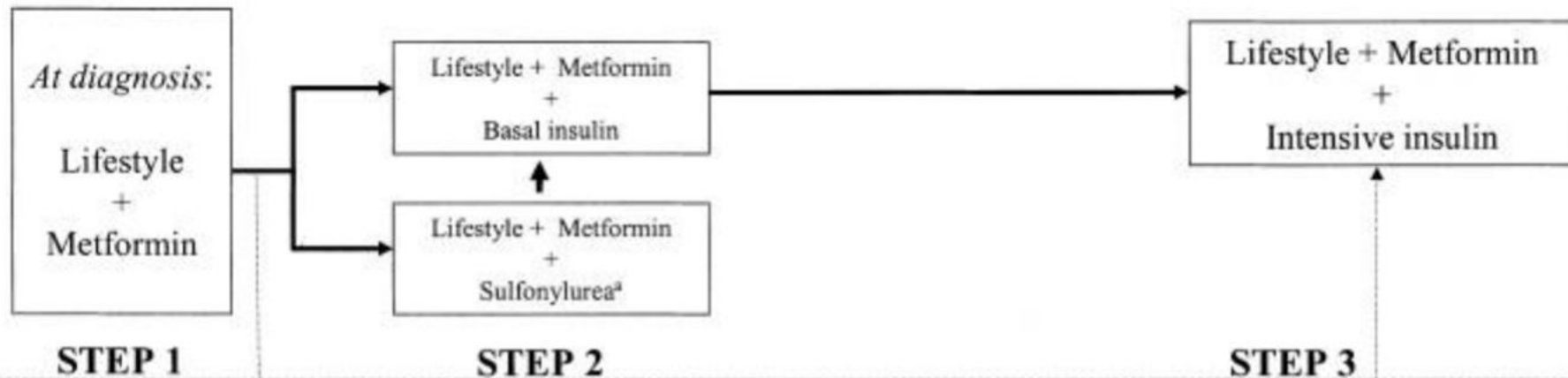
2006



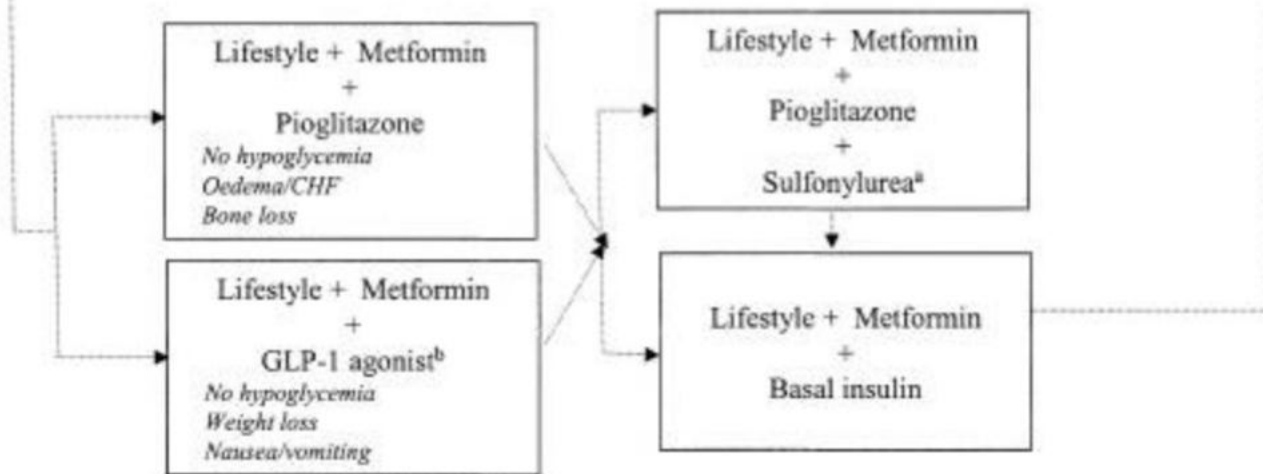
2009



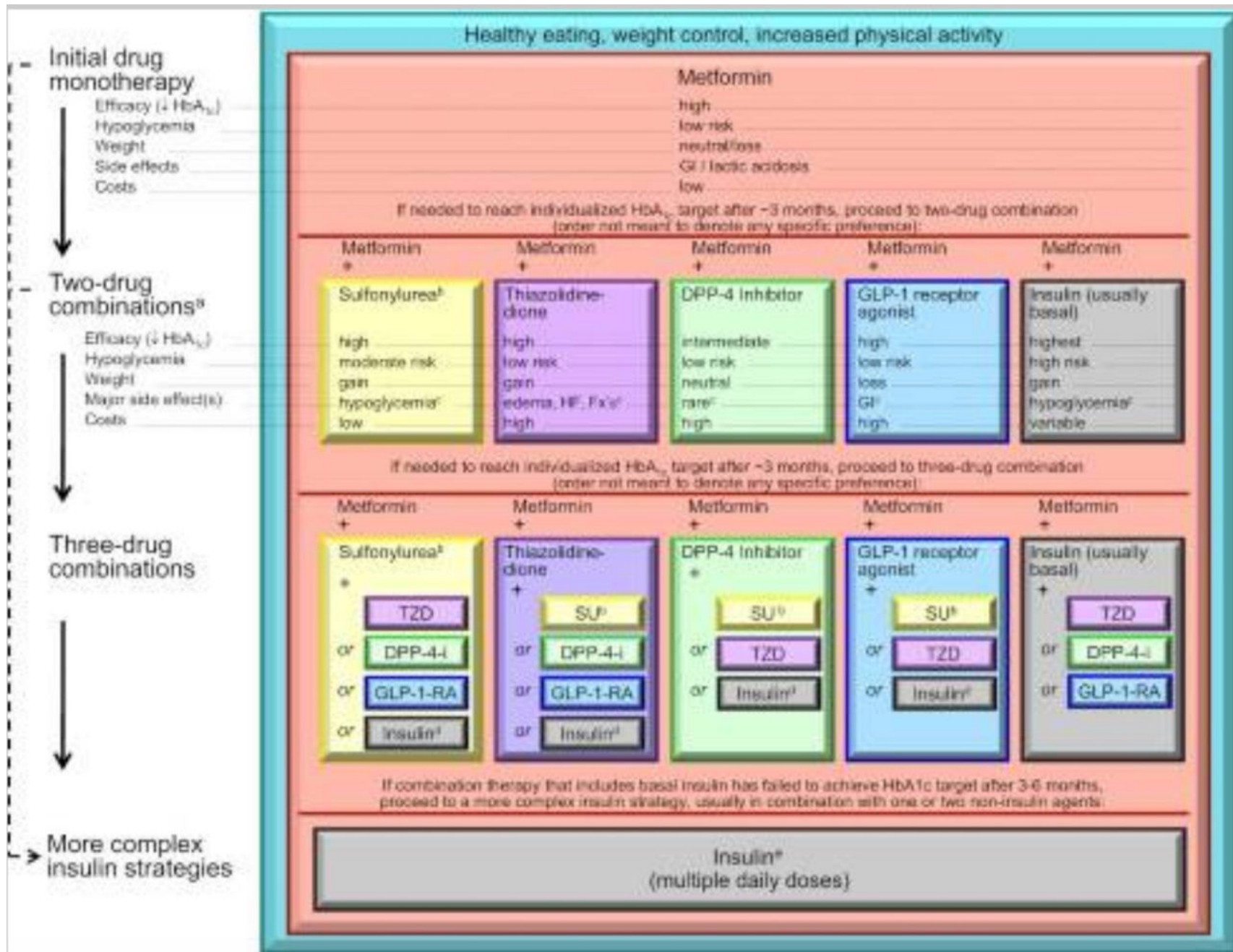
### Tier 1: Well-validated core therapies

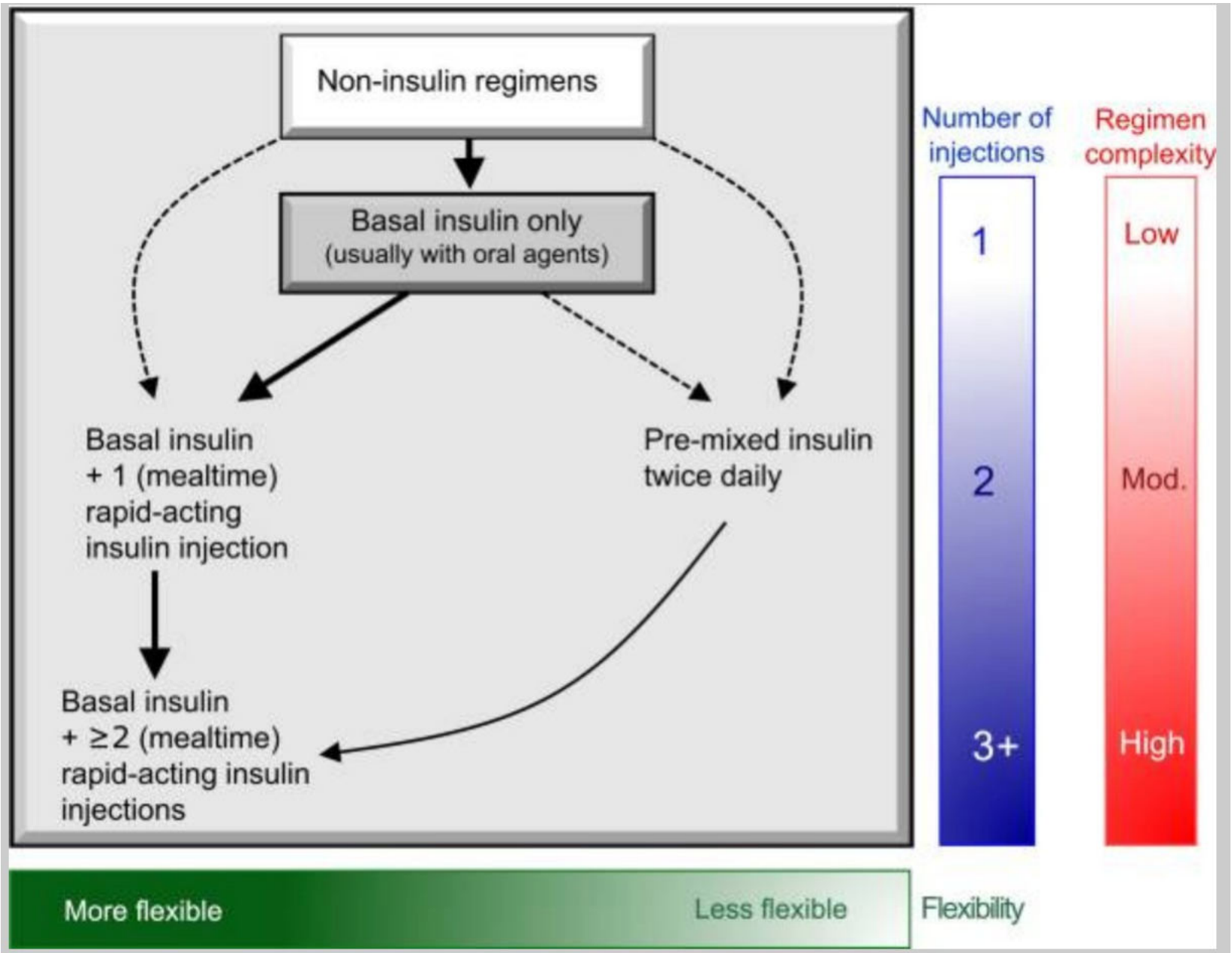


### Tier 2: Less well-validated therapies



2012





2015

**Mono-therapy**

Efficacy<sup>a</sup>  
Hypo. risk  
Weight  
Side effects  
Costs

**Dual therapy<sup>b</sup>**

Efficacy<sup>a</sup>  
Hypo. risk  
Weight  
Side effects  
Costs

**Triple therapy**

**Combination injectable therapy<sup>d</sup>**

**Healthy eating, weight control, increased physical activity and diabetes education**

**Metformin**

high  
low risk  
neutral / loss  
GI / lactic acidosis  
low

---

If HbA<sub>1c</sub> target not achieved after ~3 months of monotherapy, proceed to two-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

Metformin +	Metformin +	Metformin +	Metformin +	Metformin +	Metformin +
Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
high	high	intermediate	intermediate	high	highest
moderate risk	low risk	low risk	low risk	low risk	high risk
gain	gain	neutral	loss	loss	gain
hypoglycaemia	oedema, HF, Fxs	rare	GU, dehydration	GI	hypoglycaemia
low	low	high	high	high	variable

---

If HbA<sub>1c</sub> target not achieved after ~3 months of dual therapy, proceed to three-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

Metformin + Sulfonylurea +	Metformin + Thiazolidinedione +	Metformin + DPP-4 inhibitor +	Metformin + SGLT2 inhibitor +	Metformin + GLP-1 receptor agonist +	Metformin + Insulin (basal) +
TZD	SU	SU	SU	SU	TZD
or	or	or	or	or	or
DPP-4-i	DPP-4-i	TZD	TZD	TZD	DPP-4-i
or	or	or	or	or	or
SGLT2-i	SGLT2-i	SGLT2-i	DPP-4-i	Insulin <sup>c</sup>	SGLT2-i
or	or	or	or	or	or
GLP-1-RA	GLP-1-RA	Insulin <sup>c</sup>	Insulin <sup>c</sup>	Insulin <sup>c</sup>	GLP-1-RA
or	or				
Insulin <sup>c</sup>	Insulin <sup>c</sup>				

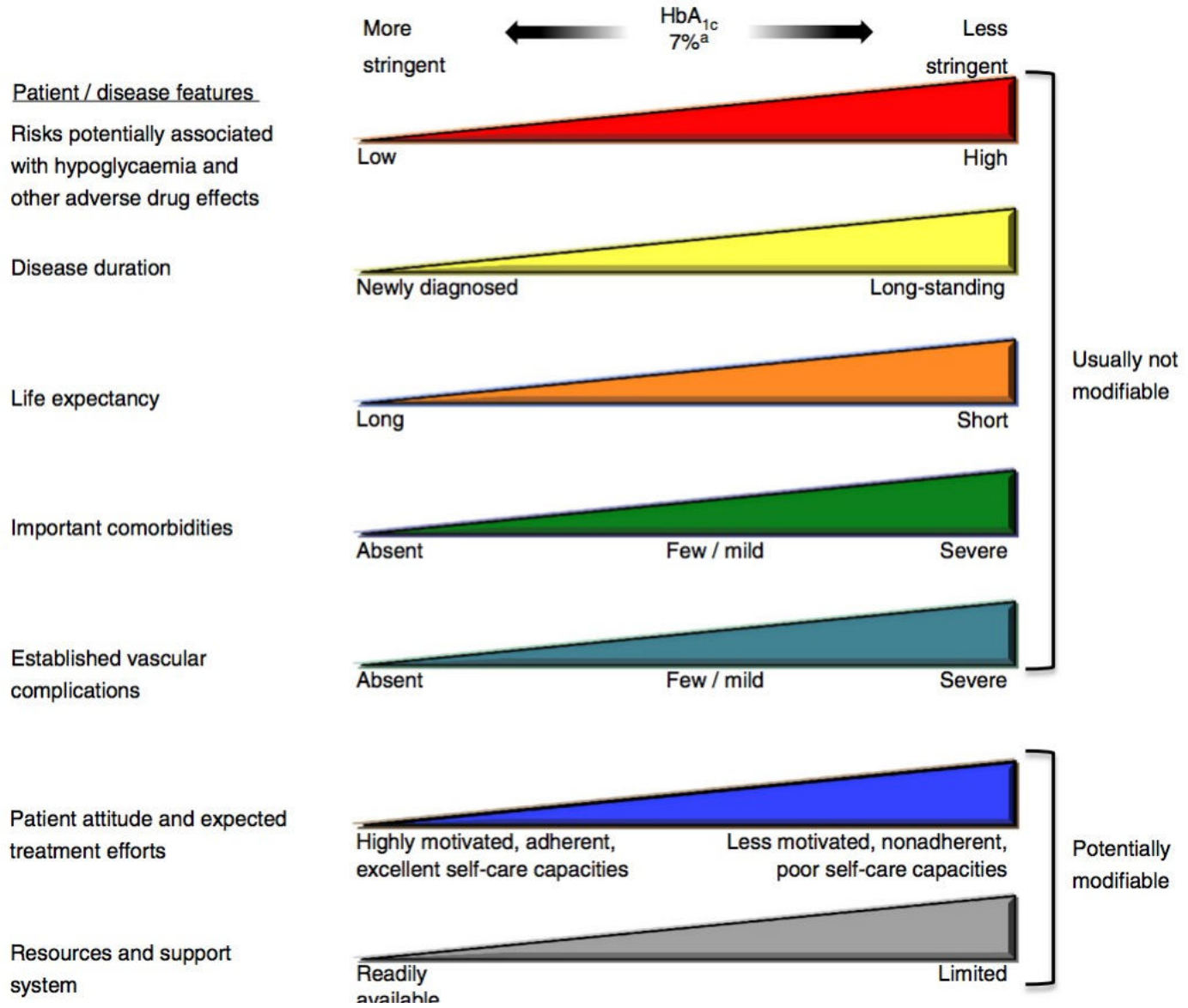
---

If HbA<sub>1c</sub> target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables; (2) on GLP-1-RA, add basal insulin; or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGLT2-i:

Metformin +

Basal insulin + Mealtime insulin or GLP-1-RA

# Approach to the management of hyperglycaemia



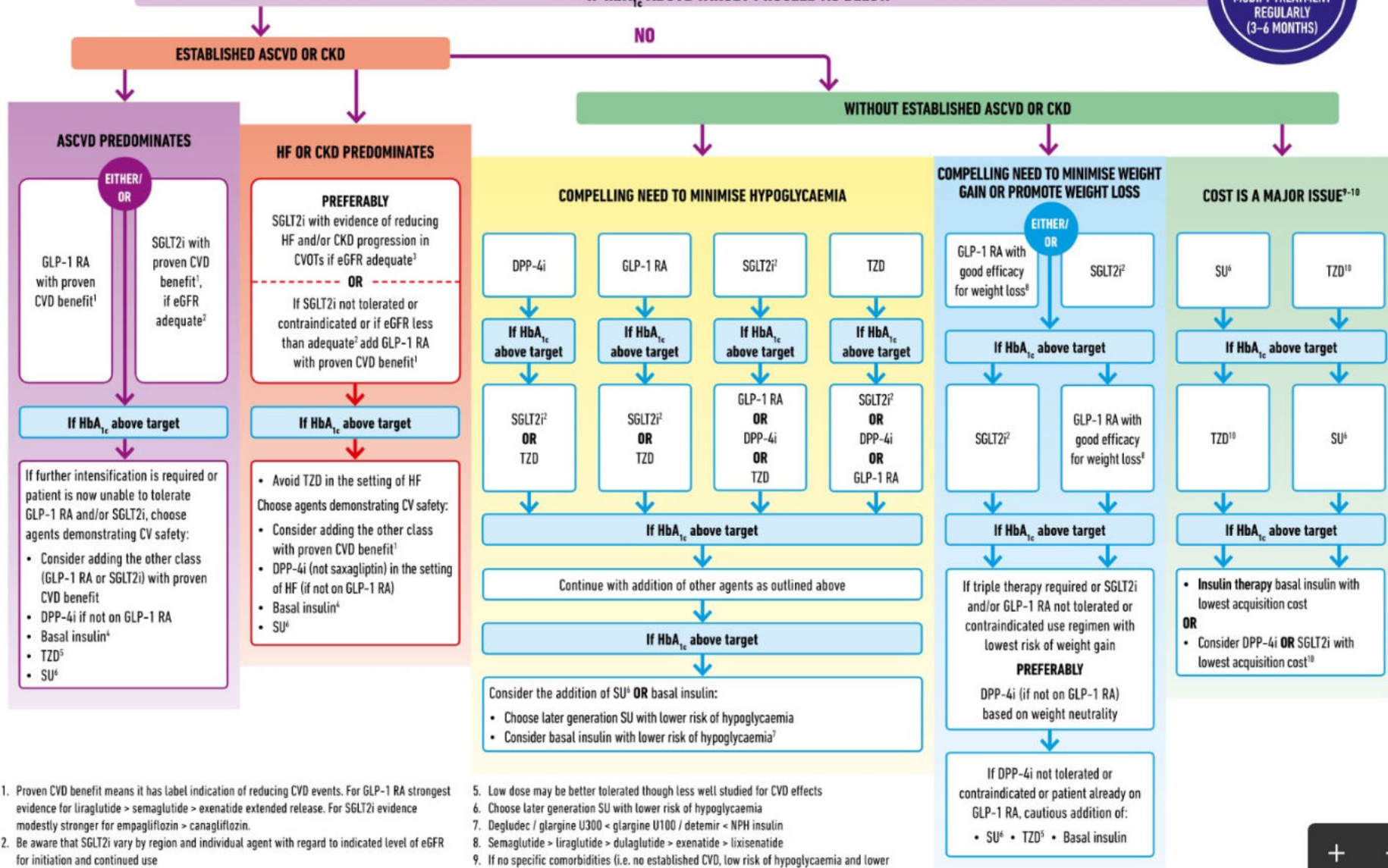
2018



# GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)

FIRST-LINE THERAPY IS METFORMIN AND COMPREHENSIVE LIFESTYLE (INCLUDING WEIGHT MANAGEMENT AND PHYSICAL ACTIVITY)  
IF HbA<sub>1c</sub> ABOVE TARGET PROCEED AS BELOW

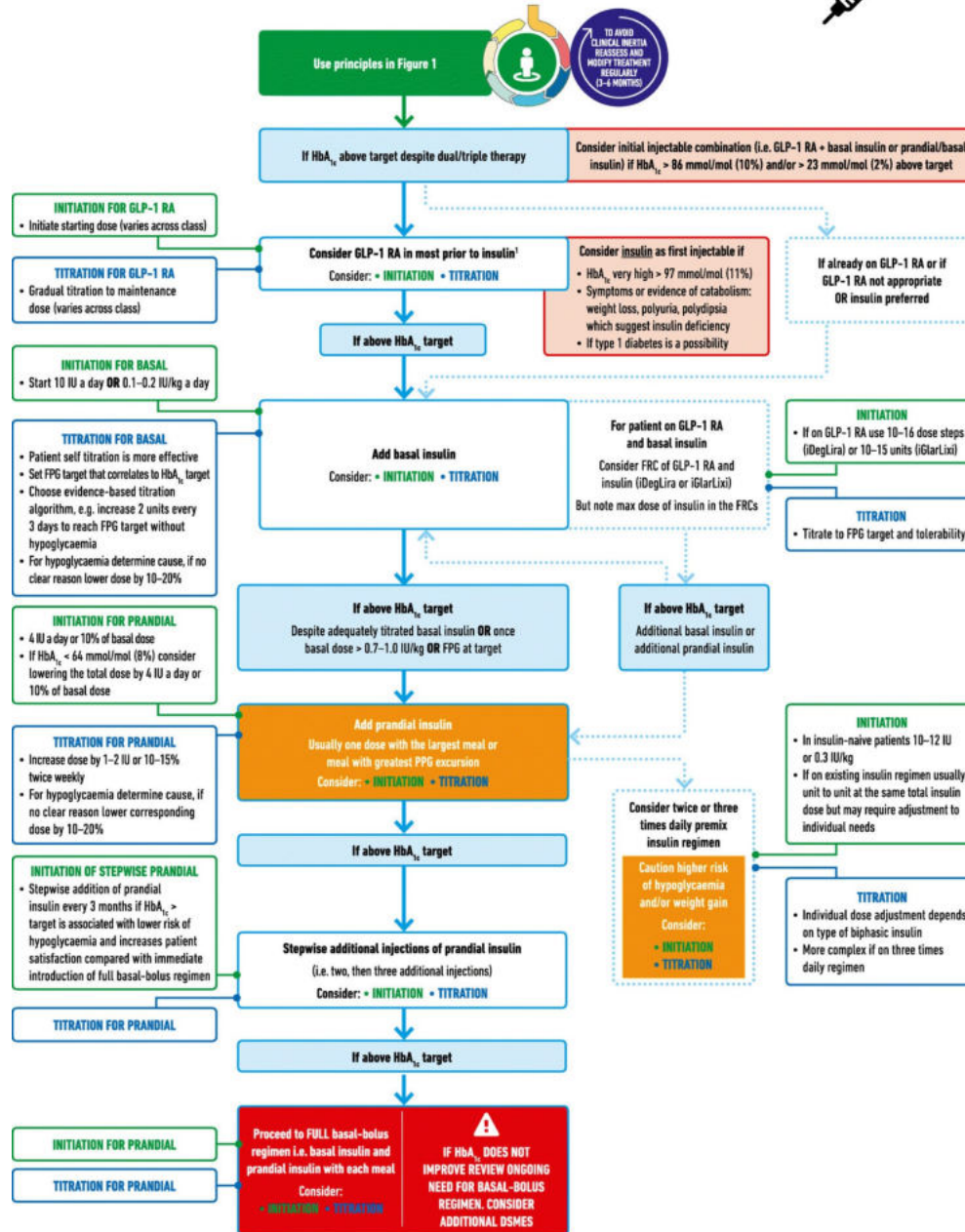


1. Proven CVD benefit means it has label indication of reducing CVD events. For GLP-1 RA strongest evidence for liraglutide > semaglutide > exenatide extended release. For SGLT2i evidence modestly stronger for empagliflozin > canagliflozin.
2. Be aware that SGLT2i vary by region and individual agent 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

Fig. 2 Glucose-lowering medication in type 2 diabetes: overall approach

# INTENSIFYING TO INJECTABLE THERAPIES



1. Consider choice of GLP-1 RA considering: patient preference, HbA<sub>1c</sub> lowering, weight-lowering effect or frequency of injection. If CVD, consider GLP-1 RA with proven CVD benefit

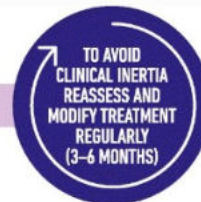
FPG = Fasting Plasma Glucose

FRC = Fixed Ratio Combination

PPG = Post Prandial Glucose

2019

# GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH



**FIRST-LINE THERAPY IS METFORMIN AND COMPREHENSIVE LIFESTYLE (INCLUDING WEIGHT MANAGEMENT AND PHYSICAL ACTIVITY)**

NO

**INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD OR HF<sup>†</sup>**

Consider independently of baseline HbA<sub>1c</sub> or individualised HbA<sub>1c</sub> target

### ASCVD PREDOMINATES

- Established ASCVD
- Indicators of high ASCVD risk (age ≥55 years + LVH or coronary, carotid, lower extremity artery stenosis >50%)

### PREFERABLY

- GLP-1 RA with proven CVD benefit<sup>1</sup>
- OR
- SGLT2i with proven CVD benefit<sup>1</sup> if eGFR adequate<sup>2</sup>

If HbA<sub>1c</sub> above target

If further intensification is required or patient is now unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety:

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit<sup>1</sup>
- DPP-4i if not on GLP-1 RA
- Basal insulin<sup>4</sup>
- TZD<sup>5</sup>
- SU<sup>6</sup>

### HF OR CKD PREDOMINATES

- Particularly HFrEF (LVEF <45%)
- CKD: Specifically eGFR 30-60 ml min<sup>-1</sup> [1.73m]<sup>-2</sup> or UACR >30 mg/g, particularly UACR >300 mg/g

### PREFERABLY

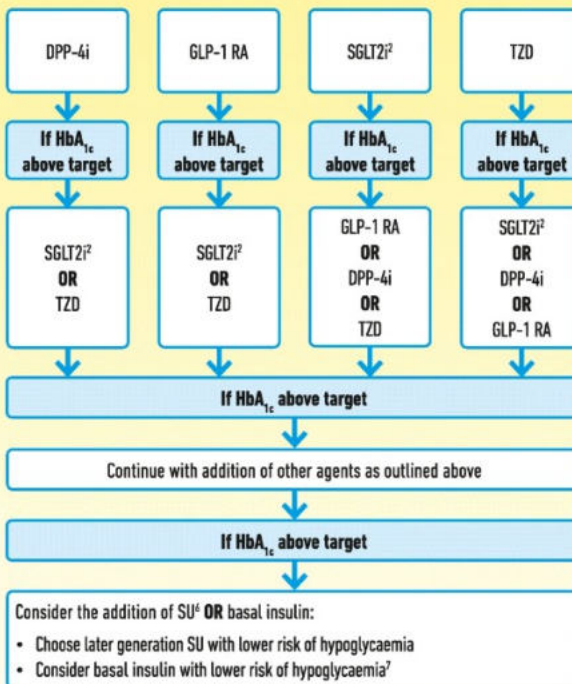
- SGLT2i with evidence of reducing HF and/or CKD progression in CVDts if eGFR adequate<sup>3</sup>
- OR
- If SGLT2i not tolerated or contraindicated or if eGFR less than adequate<sup>2</sup> add GLP-1 RA with proven CVD benefit<sup>1</sup>

If HbA<sub>1c</sub> above target

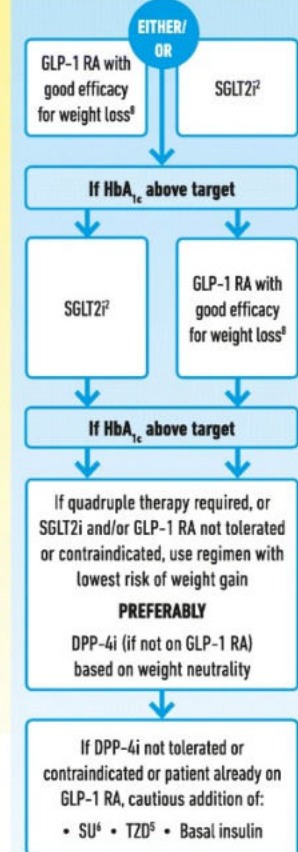
- Avoid TZD in the setting of HF
- Choose agents demonstrating CV safety:
- For patients on a SGLT2i, consider adding GLP-1 RA with proven CVD benefit<sup>1</sup>
- DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA)
- Basal insulin<sup>4</sup>
- SU<sup>6</sup>

If HbA<sub>1c</sub> above individualised target proceed as below

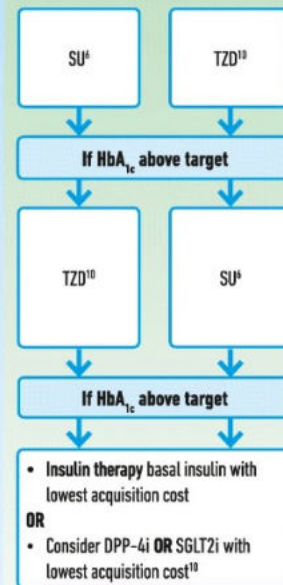
### COMPELLING NEED TO MINIMISE HYPOGLYCAEMIA



### COMPELLING NEED TO MINIMISE WEIGHT GAIN OR PROMOTE WEIGHT LOSS



### COST IS A MAJOR ISSUE<sup>9-10</sup>



1. Proven CVD benefit means it has label indication of reducing CVD events.  
2. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use  
3. Empagliflozin, canagliflozin and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVDts. Canagliflozin has primary renal outcome data from CREDENCE, Dapagliflozin has primary heart failure outcome data from DAPA-HF  
4. Degludec and U100 glargine have demonstrated CVD safety  
5. Low dose may be better tolerated though less well studied for CVD effects  
† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

6. Choose later generation SU to lower risk of hypoglycaemia. Gliclazide has shown similar CV safety to DPP-4i  
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

Updates to the 2018 consensus report are indicated in magenta font

LVH = Left Ventricular Hypertrophy; HFrEF = Heart Failure reduced Ejection Fraction  
UACR = Urine Albumin-to-Creatinine Ratio; LVEF = Left Ventricular Ejection Fraction

2021

# Özetle Bu Kılavuz

- Kalb Yetersizliği, ASKVH ve Renal yetersizlik olup olmadığını araştır
- Eğer tolere edebilirse Metformin başla. Daha sonra,



ASKVH var ise GLP-1 RA veya SGLT2-i



ASKVH ve KY varsa SGLT2-i



ASKVH olsun olmasın KBY varsa SGLT2-i



Fakirse SU / TSZ

# Kronik Bakım Modelinin Uygulanması

- Kiři merkezli ekip bakım anlayışı,
- Diyabet ve komorbiditelere yönelik uzun vadeli entegre tedavi yaklaşımlar
- Tüm ekip üyeleri arasında işbirlikçi iletişim ve hedef belirleme

# Vaka Bazında Yaklaşım

- Öz bakım kapasitelerinin ne olduğu,
- Amaçlarının ve tedavilerinin ne olduğu,
- Glisemik hedeflerinin ne olması gerektiği
- Bakıcı desteğinin olup olmadığı
- Teknolojiden ne kadar yararlanacak?



# Glisemiye Yaklaşım

- Başlangıç HbA1c veya bireysel hedefe ulaşılmış HbA1c'den bağımsız kardiyak-renal sonuçlarda etkin yeni tedavilerin kullanımı (mevcut A1C düzeyleri ne olursa olsun, KVH bilinen tip 2 diyabetli tüm hastalar, daha yeni glikoz düşürücü tedaviler için uygun kabul edilmelidir).
- Glisemik takip
- Glisemik değişkenlik

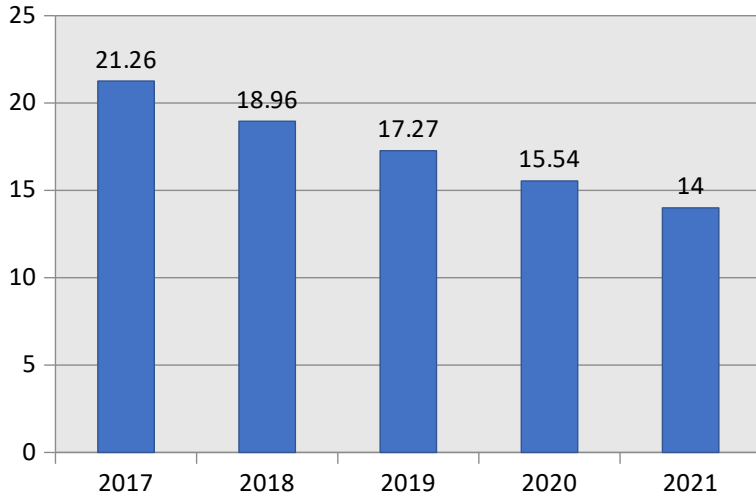
# Davranışsal Saęlıęı Yönetme

- Hastaların kendi saęlıkları üzerinde daha fazla kontrol sahibi olmaları
- Psikolojik saęlıklarını iyileştirmek

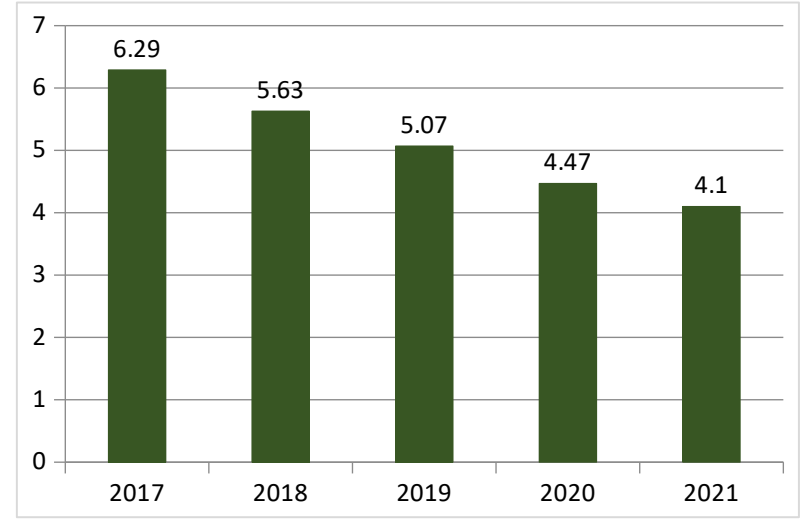
-% 34

# 2017 – 2021 Tedavi Seçimindeki Değişim: SÜLFONİLÜRE

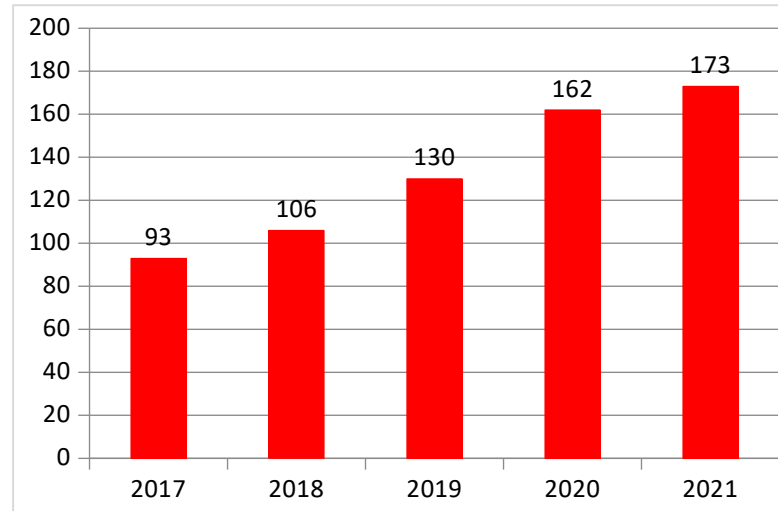
-% 34



Kullanım Oranı(%)



Toplam Maliyetteki Oranı (%)

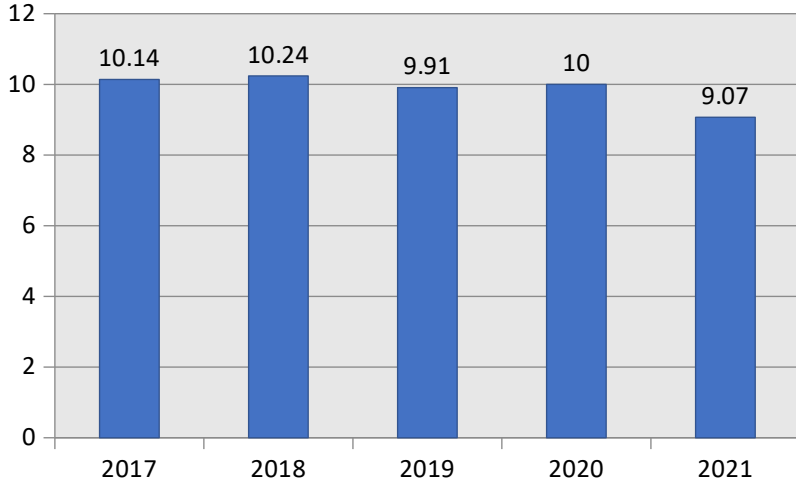


Maliyet (x Milyar TL)

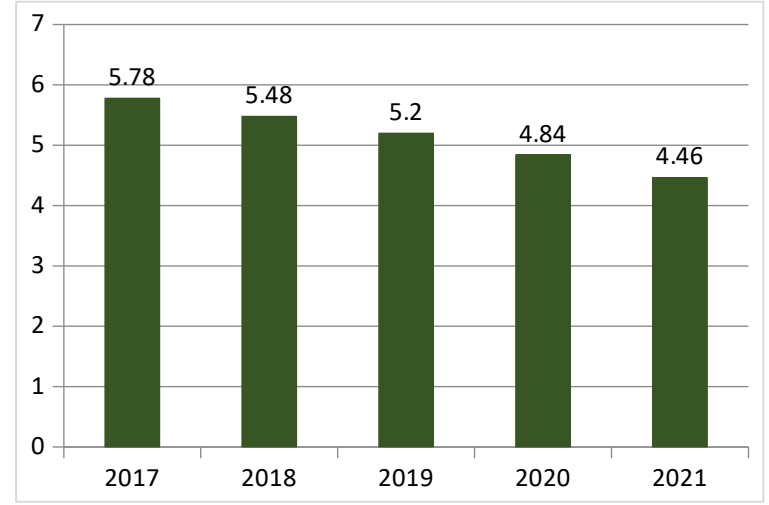
-% 11

# 2017 – 2021 Tedavi Seçimindeki Değişim: GLİTAZOL

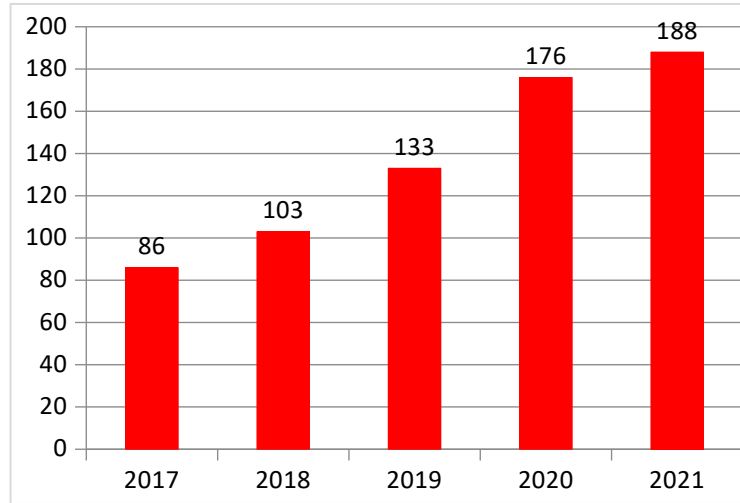
-% 23



Kullanım Oranı(%)



Toplam Maliyetteki Oranı (%)

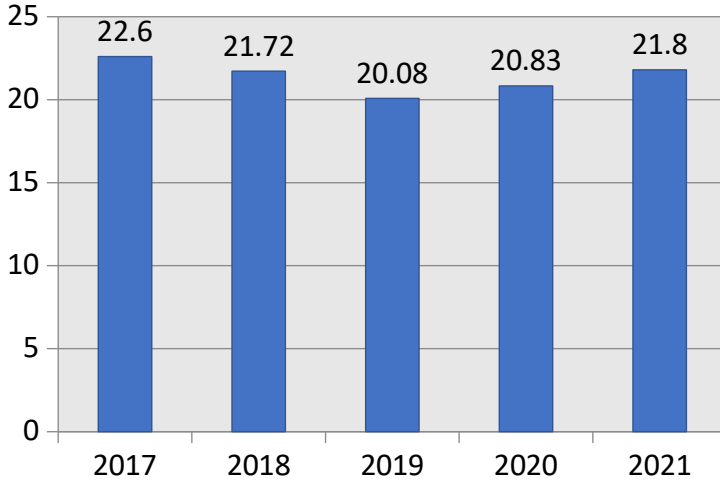


Maliyet (x Milyar TL)

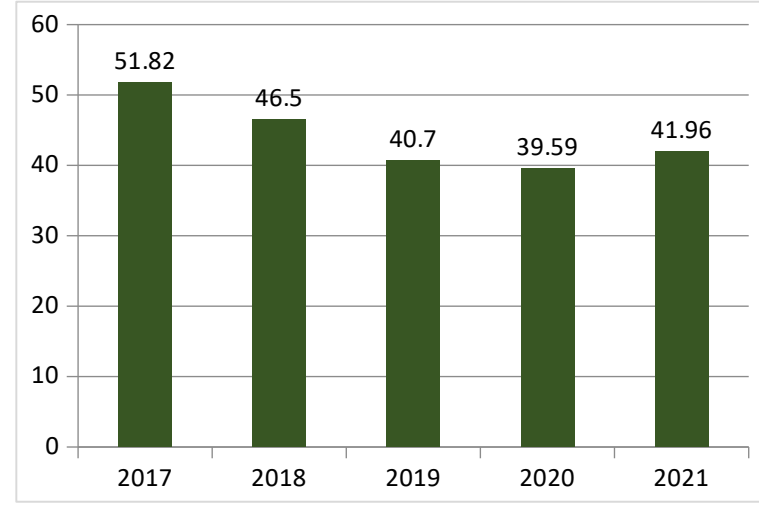
-% 4

# 2017 – 2021 Tedavi Seçimindeki Değişim: İNSULİN

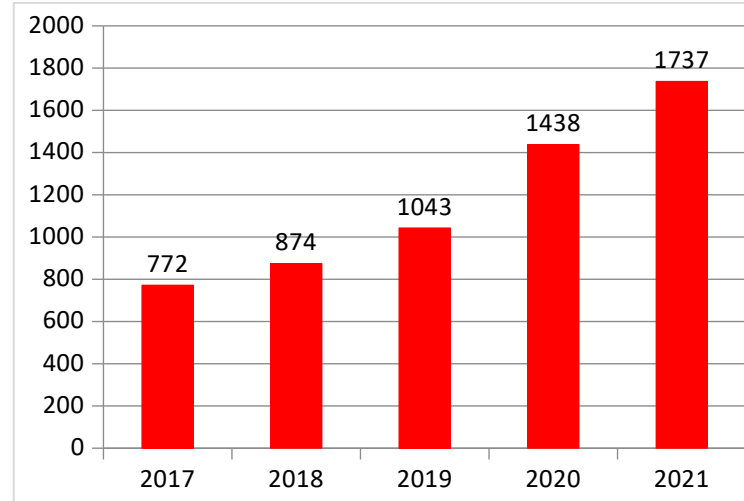
-% 20



Kullanım Oranı(%)



Toplam Maliyetteki Oranı (%)

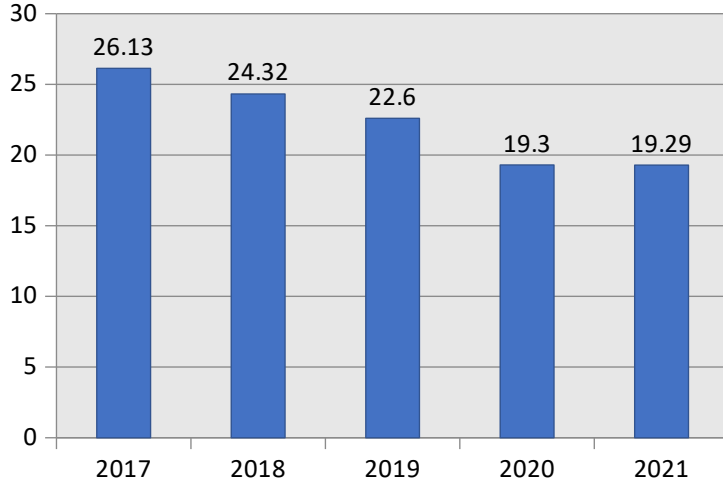


Maliyet (x Milyar TL)

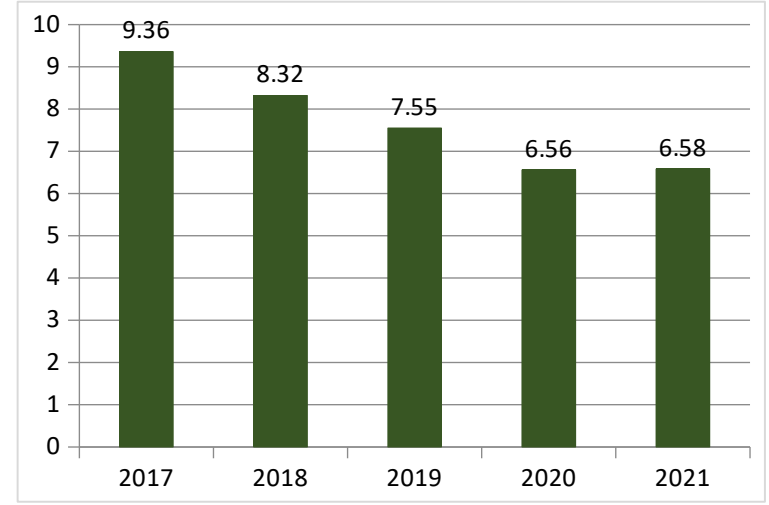
-% 27

# 2017 – 2021 Tedavi Seçimindeki Değişim: BİGUAN

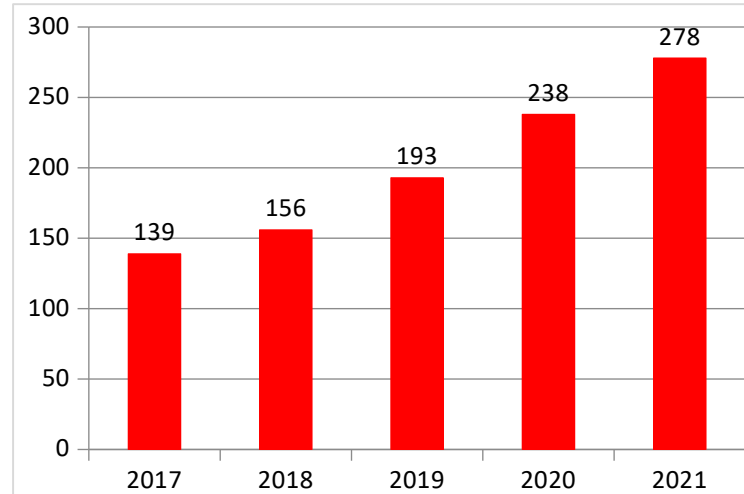
-% 30



Kullanım Oranı(%)



Toplam Maliyetteki Oranı (%)

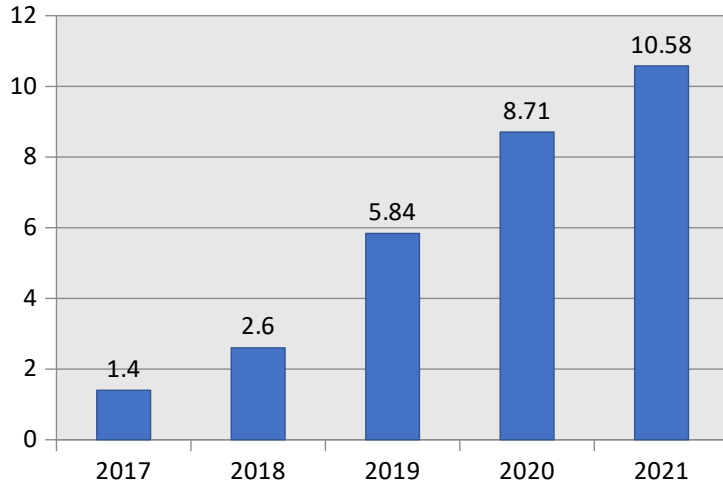


Maliyet (x Milyar TL)

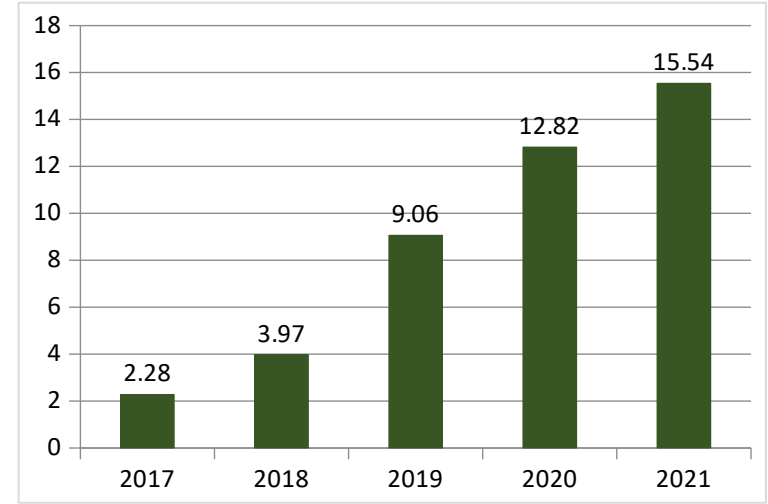
% 655

# 2017 – 2021 Tedavi Seçimindeki Değişim: SGLT-2 İNHİBİTÖRLERİ

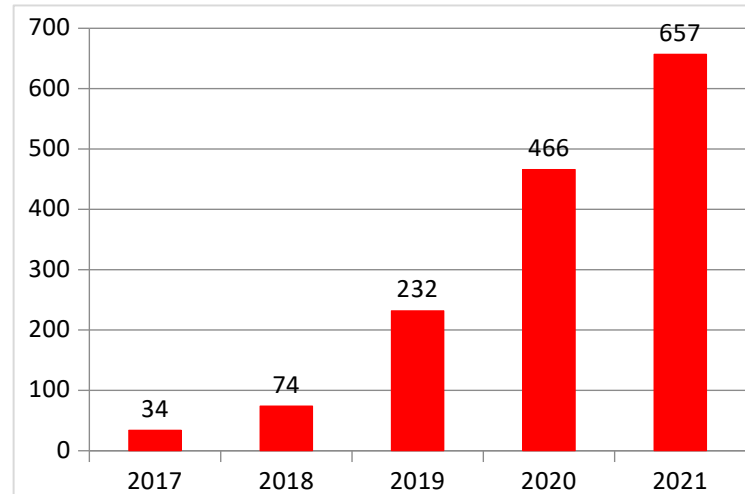
% 581



Kullanım Oranı(%)



Toplam Maliyetteki Oranı (%)

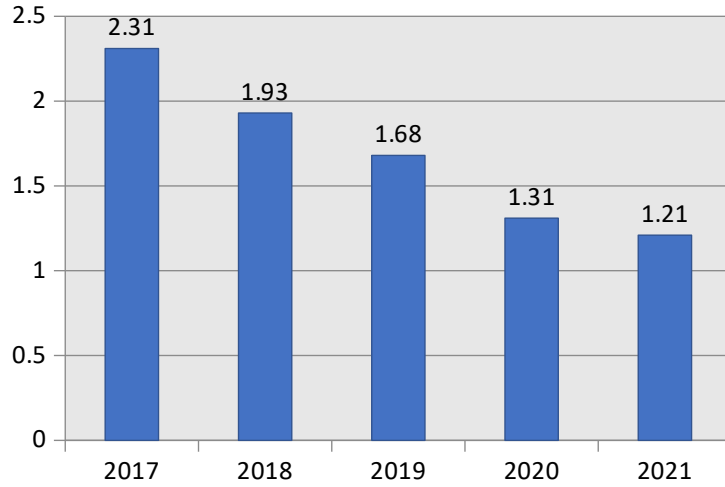


Maliyet (x Milyar TL)

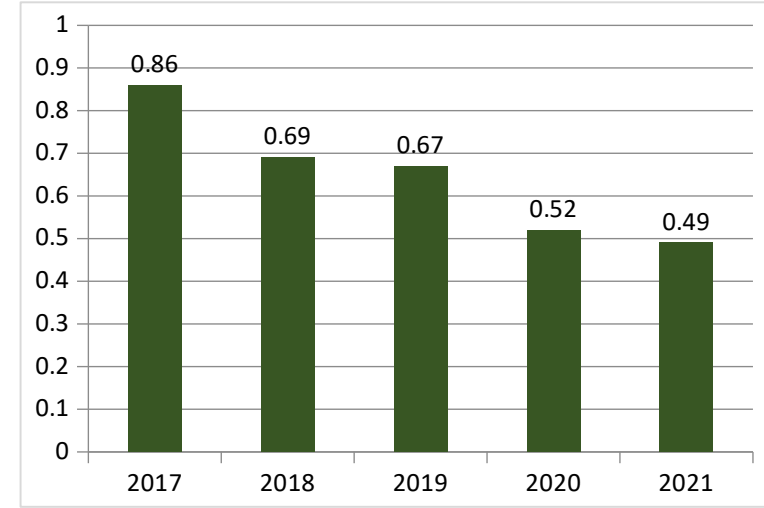
-% 47

# 2017 – 2021 Tedavi Seçimindeki Değişim: ALFA GLİKOZİDAZ İNHİBİTÖRLERİ

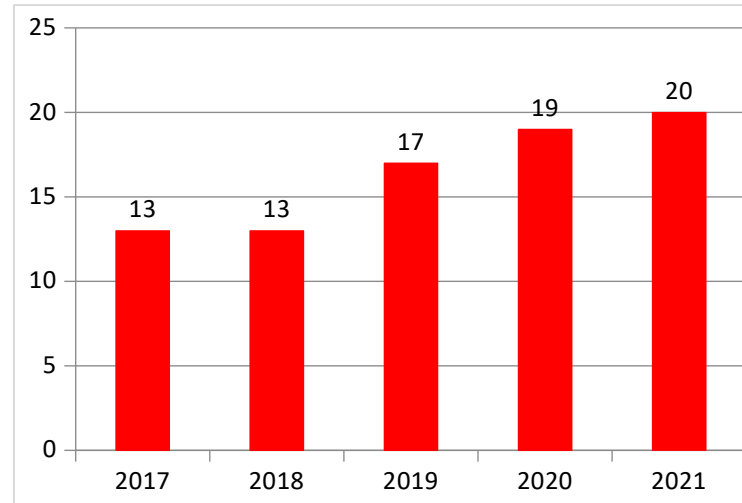
-% 43



Kullanım Oranı(%)



Toplam Maliyetteki Oranı (%)



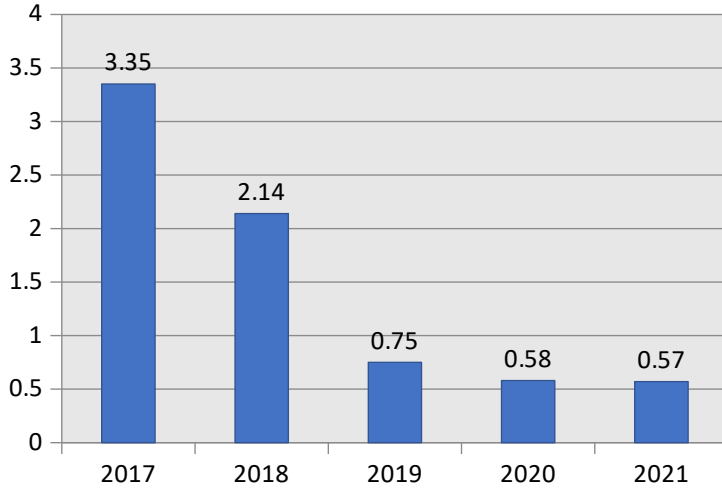
Maliyet (x Milyar TL)



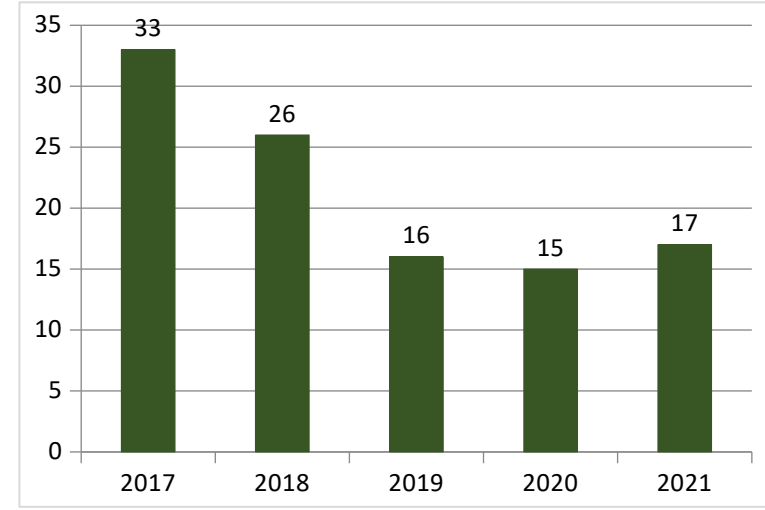
-% 83

# 2017 – 2021 Tedavi Seçimindeki Değişim: GLİNİDLE

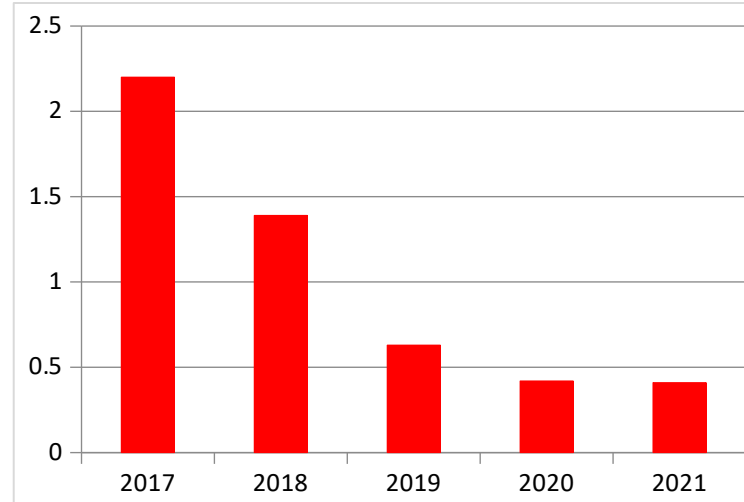
-% 49



Kullanım Oranı(%)



Toplam Maliyetteki Oranı (%)

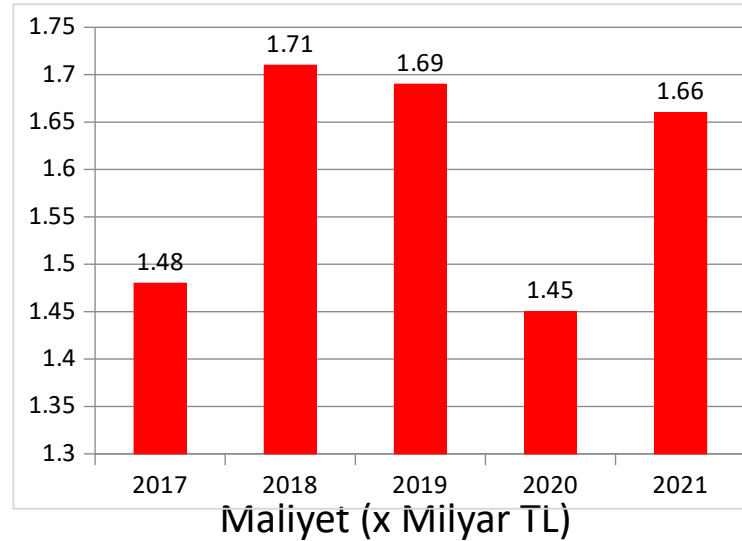
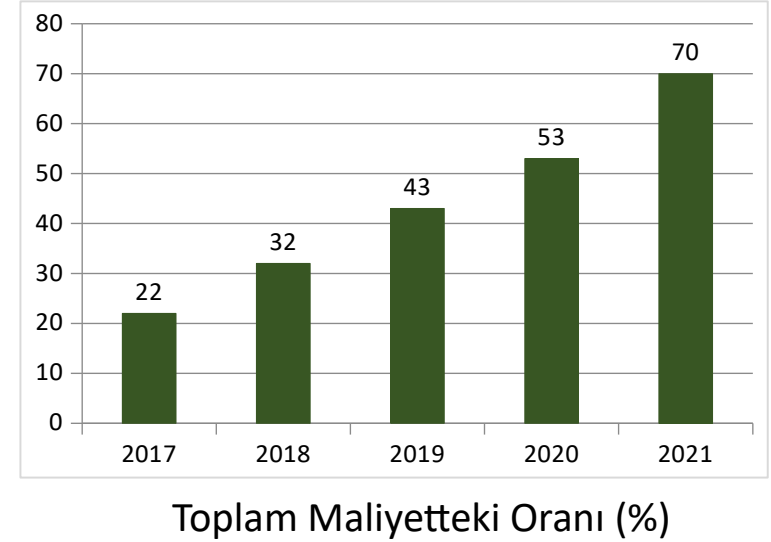
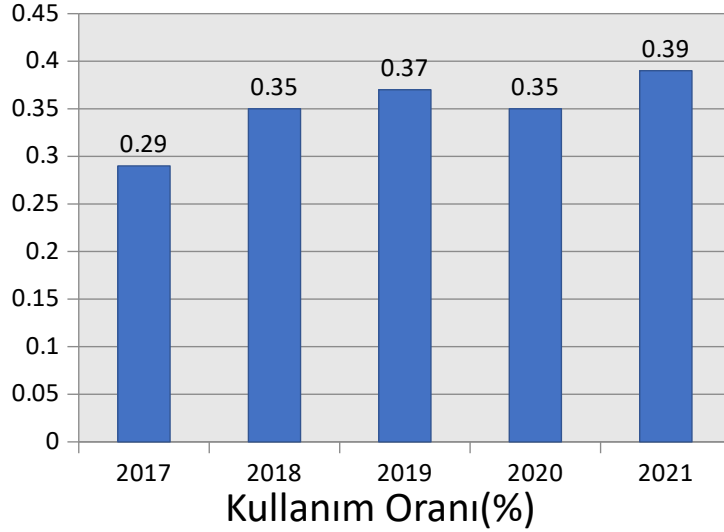


Maliyet (x Milyar TL)

% 34

# 2017 – 2021 Tedavi Seçimindeki Değişim: GLP-1 ANALOGLARI

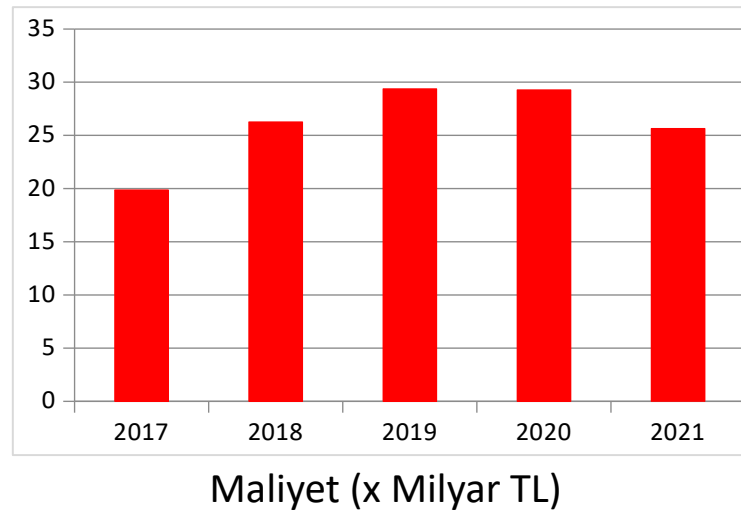
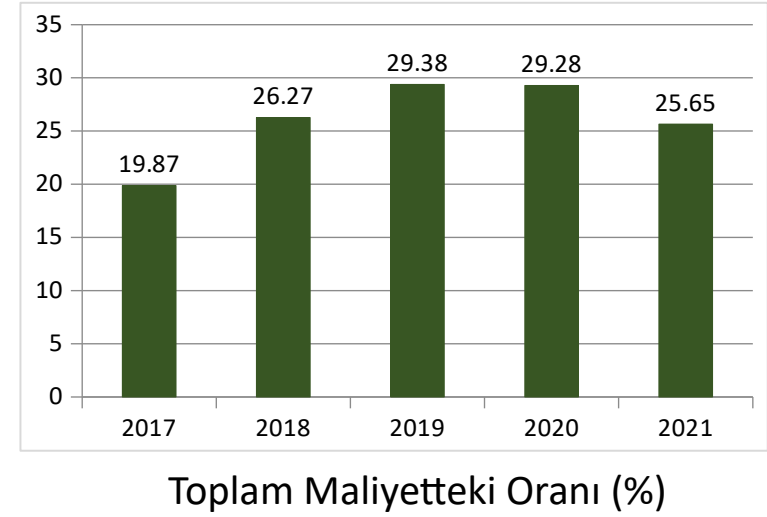
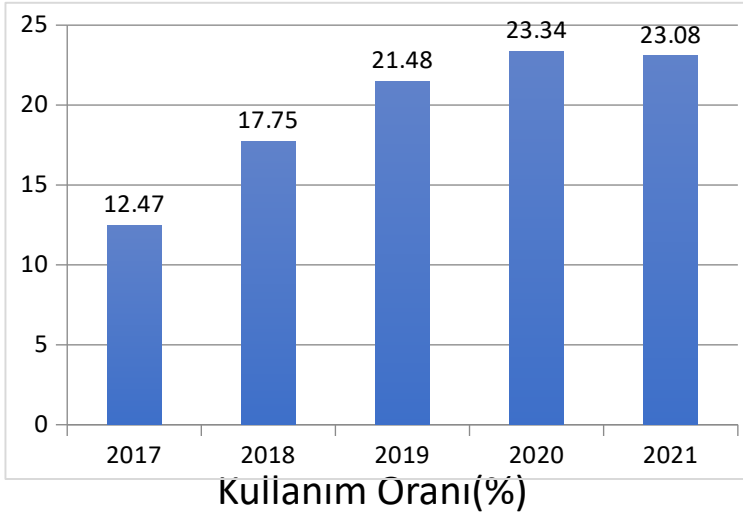
% 218



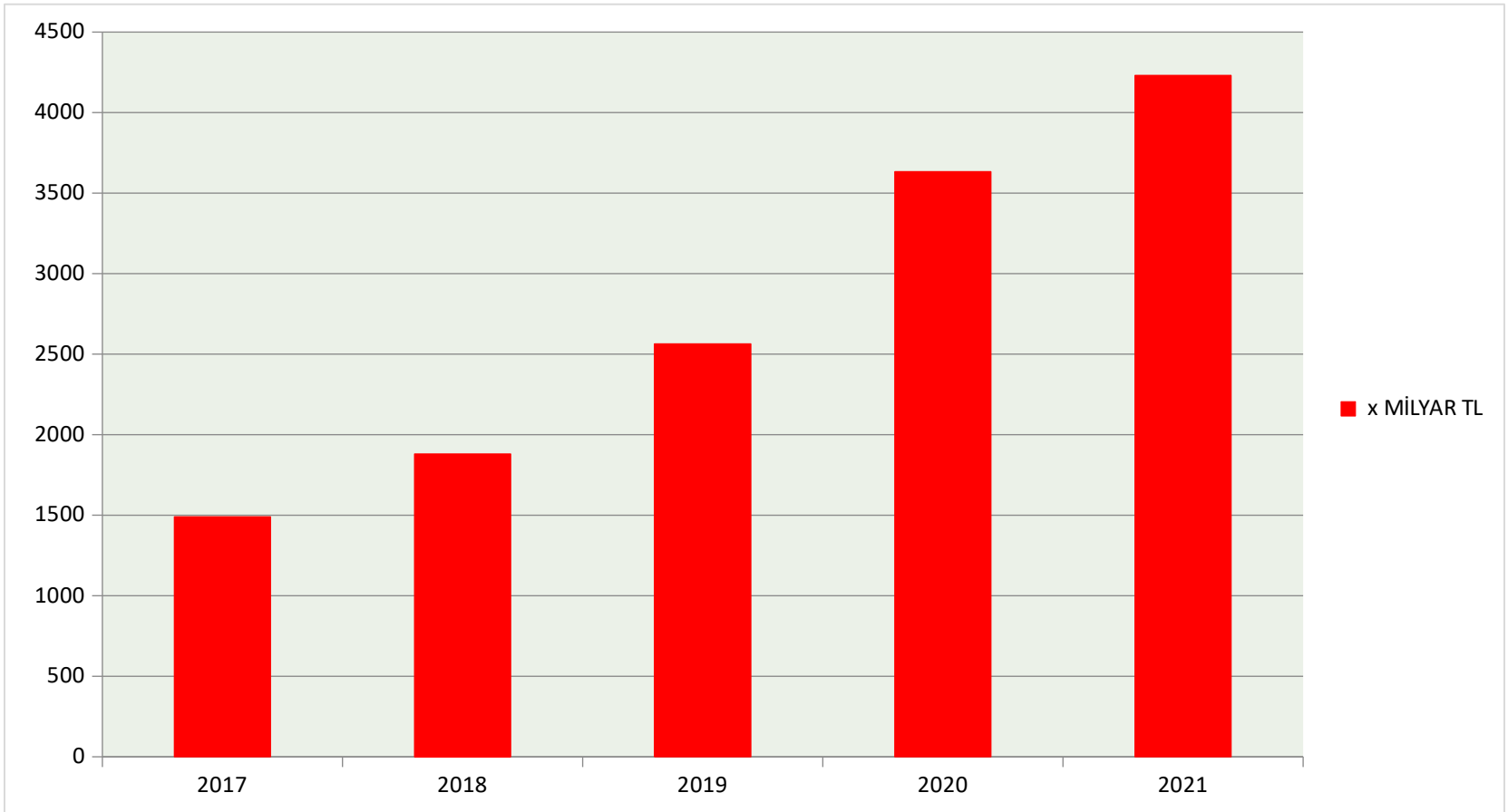
% 85

# 2017 – 2021 Tedavi Seçimindeki Değişim: DPP-IV İNHİBİTÖRLERİ

% 30



# 2017-2021 Yılları Arasında Diyabet Tedavisinde İlaç Maliyeti



Diabetologia

<https://doi.org/10.1007/s00125-022-05787-2>

## CONSENSUS REPORT



# Management of hyperglycaemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

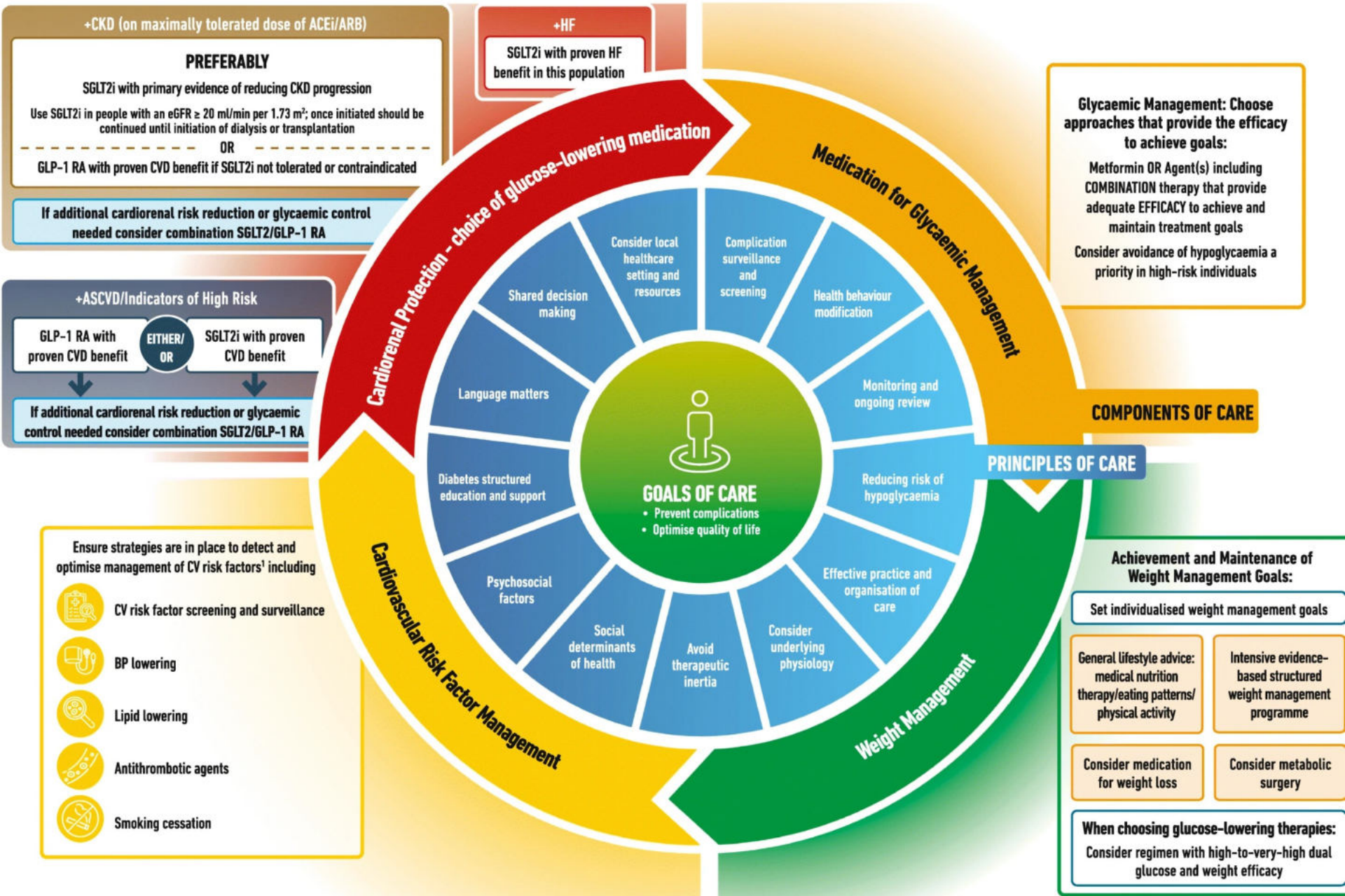
Melanie J. Davies<sup>1,2</sup> • Vanita R. Aroda<sup>3</sup> • Billy S. Collins<sup>4</sup> • Robert A. Gabbay<sup>5</sup> • Jennifer Green<sup>6</sup> •  
Nisa M. Maruthur<sup>7</sup> • Sylvia E. Rosas<sup>8</sup> • Stefano Del Prato<sup>9</sup> • Chantal Mathieu<sup>10</sup> • Geltrude Mingrone<sup>11,12,13</sup> •  
Peter Rossing<sup>14,15</sup> • Tsvetalina Tankova<sup>16</sup> • Apostolos Tsapas<sup>17,18</sup> • John B. Buse<sup>19</sup>

Received: 2 August 2022 / Accepted: 18 August 2022

© American Diabetes Association and the European Association for the Study of Diabetes 2022

- Glukoz düşürücü.....Organ koruyucu
- İletişim /Dil
- Vegan, vejeteryan, düşük karbonhidratlı diyetler en fazla 6 aya kadar etkin, sonrası bilinmiyor. Akdeniz diyeti daha uzun sürelerde etkin.
- Uyku 6 saatten az, 8 saatten fazla olmamalı
- Tüm cerrahi çalışma popülasyonlarında remisyon, kilo kaybı düzeyiyle orantılı

# HOLISTIC PERSON-CENTRED APPROACH TO T2DM MANAGEMENT



<sup>1</sup> = 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.

# 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<sub>1c</sub>.



**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  $\geq 150$  min/week of moderate-intensity physical activity (i.e. uses large muscle groups, rhythmic in nature) OR  $\geq 75$  min/week vigorous-intensity activity spread over  $\geq 3$  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.



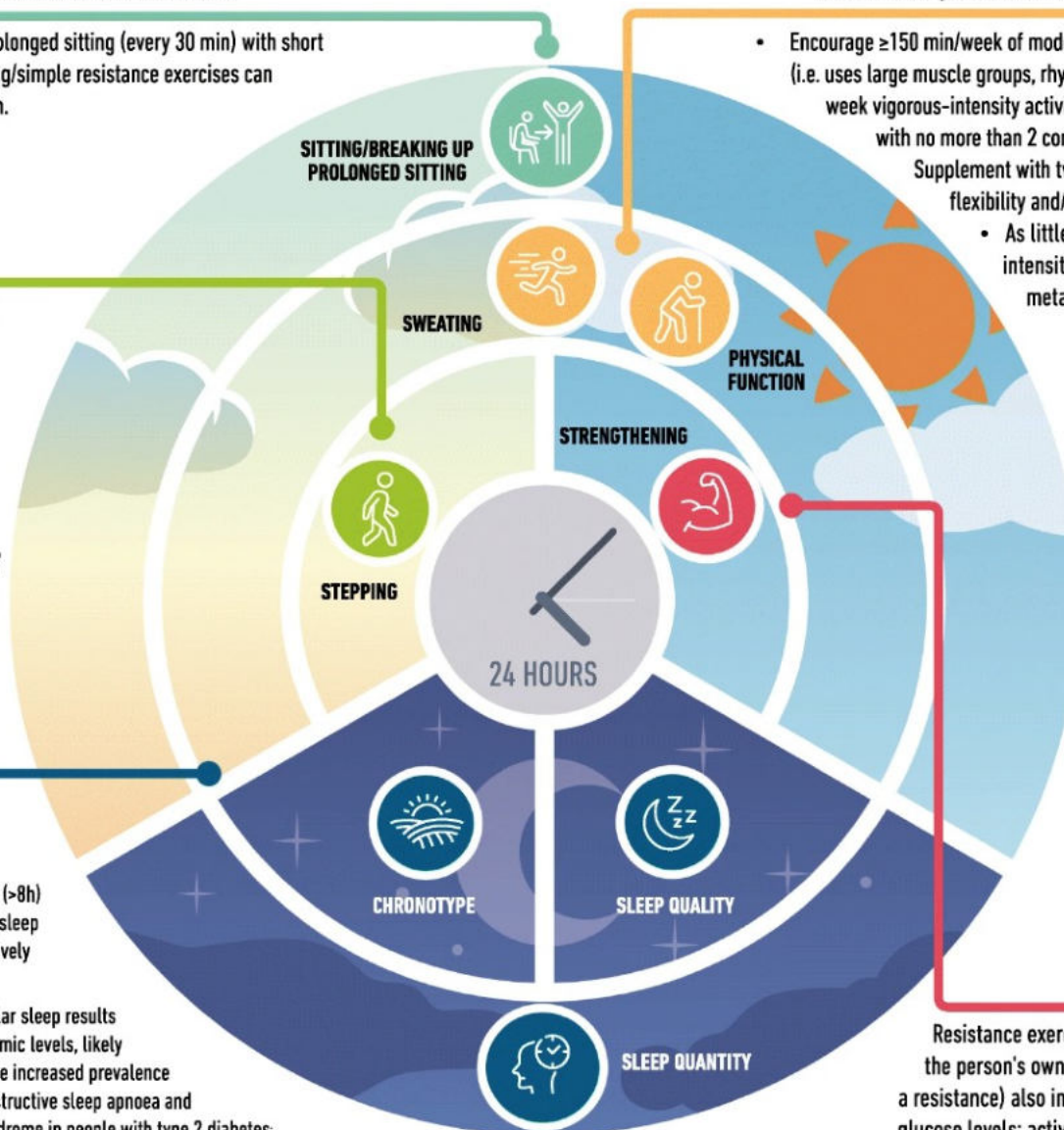
**Physical function/frailty/sarcopenia**

- 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 <sub>1c</sub>	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

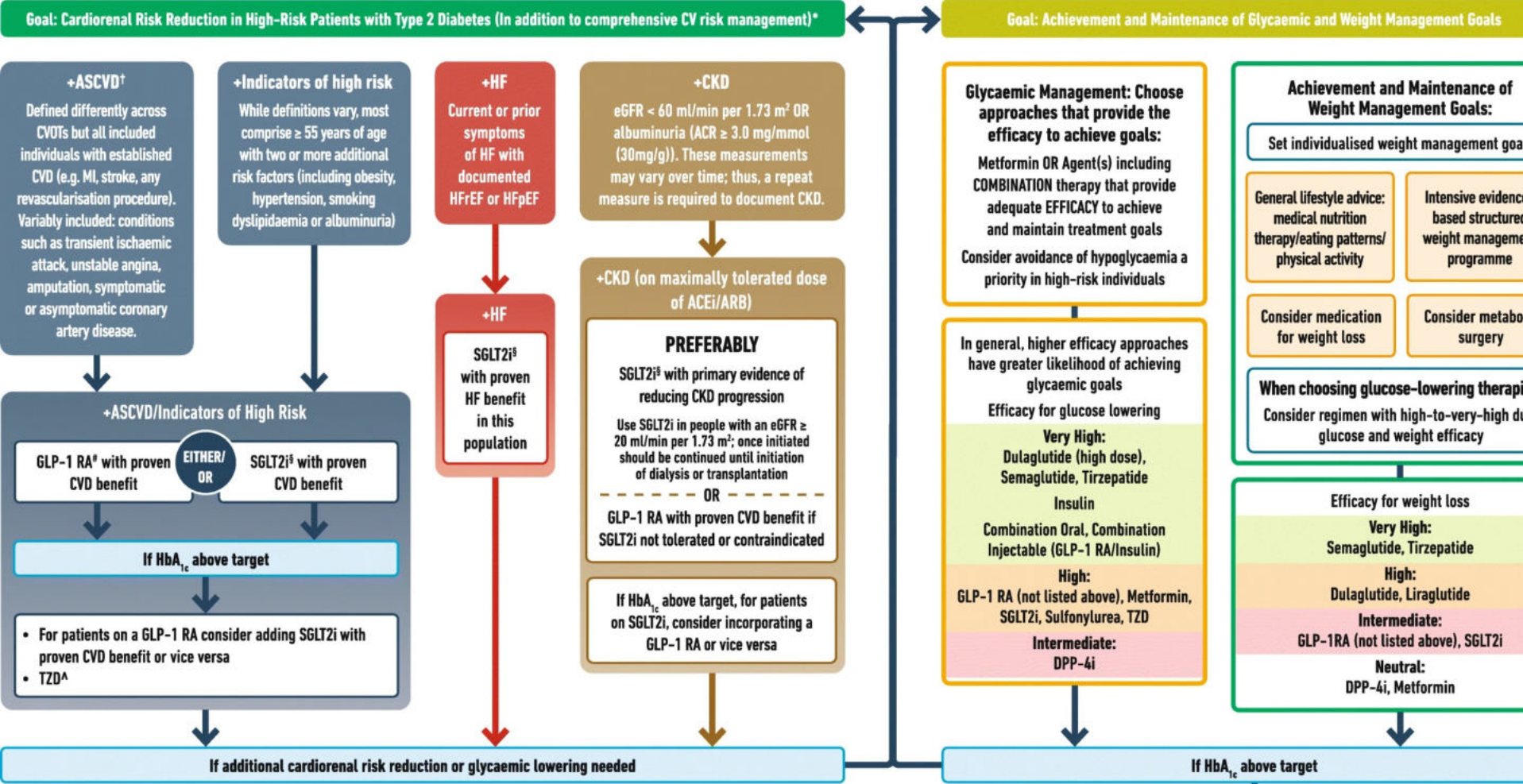
↑ Higher levels/improvement (physical function, quality of life); ↓ Lower levels/improvement (glucose/insulin, blood pressure, HbA<sub>1c</sub>, lipids, depression); ? no data available;  
 ↑ Green arrows = strong evidence; ↑ Yellow arrows = medium strength evidence; ↑ Red arrows = limited evidence.

Tip 2 diyabet için 24 saatlik fiziksel davranışların önemi

# 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)



ACEi, Angiotensin-Converting Enzyme Inhibitor; ACR, Albumin/Creatinine Ratio; ARB, Angiotensin Receptor Blocker; ASCVD, Atherosclerotic Cardiovascular Disease; CGM, Continuous Glucose Monitoring; CKD, Chronic Kidney Disease; CV, Cardiovascular; CVD, Cardiovascular Disease; CVOT, Cardiovascular Outcomes Trial; DPP-4i, Dipeptidyl Peptidase-4 Inhibitor; eGFR, Estimated Glomerular Filtration Rate; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agonist; HF, Heart Failure; HFpEF, Heart Failure with preserved Ejection Fraction; HFrEF, Heart Failure with reduced Ejection Fraction; HHF, Hospitalisation for Heart Failure; MACE, Major Adverse Cardiovascular Events; MI, Myocardial Infarction; SDOH, Social Determinants of Health; SGLT2i, Sodium-Glucose Cotransporter-2 Inhibitor; TZD, Type 2 Diabetes; TZD, Thiazolidinedione.

\* 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.

**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 the
- Identify and address SDOH that impact on achievement of goals

METFORMIN

GLP-1 / SGLT 2





Overall, for treatment of hyperglycaemia, metformin remains the agent of choice in most people with diabetes, based on its glucose-lowering efficacy, minimal risk of hypoglycaemia, lack of weight increase and affordability. Often, monotherapy with metformin will not suffice to maintain glucose levels at target. As proposed in the previous consensus report and update [5, 6], other classes of agents are useful in combination with metformin or when metformin is contraindicated or not tolerated. Selection of other glucose-lowering agents will be determined

### **Practical tips for clinicians (Supplementary Fig. 3)**

- 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 an individualised fasting glycaemic 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.

*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

SEPTEMBER 22, 2022

VOL. 387 NO. 12

Glycemia Reduction in Type 2 Diabetes — Glycemic Outcomes

The GRADE Study Research Group\*

*The* NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

Glycemia Reduction in Type 2 Diabetes —  
Microvascular and Cardiovascular Outcomes

The GRADE Study Research Group\*

ABSTRACT

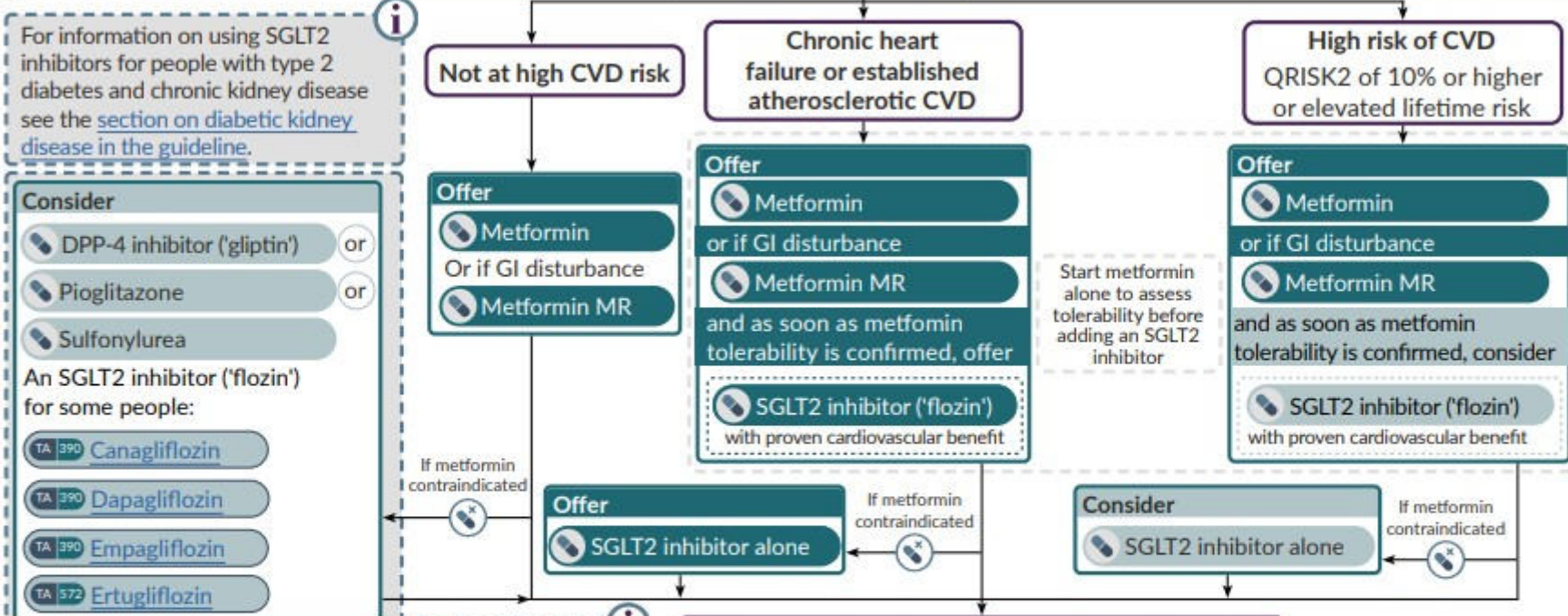
## RESULTS

During a mean 5.0 years of follow-up in 5047 participants, there were no material differences among the interventions with respect to the development of hypertension or dyslipidemia or with respect to microvascular outcomes; the mean overall rate (i.e., events per 100 participant-years) of moderately increased albuminuria levels was 2.6, of severely increased albuminuria levels 1.1, of renal impairment 2.9, and of diabetic peripheral neuropathy 16.7. The treatment groups did not differ with respect to MACE (overall rate, 1.0), hospitalization for heart failure (0.4), death from cardiovascular causes (0.3), or all deaths (0.6). There were small differences with respect to rates of any cardiovascular disease, with 1.9, 1.9, 1.4, and 2.0 in the glargine, glimepiride, liraglutide, and sitagliptin groups, respectively. When one treatment was compared with the combined results of the other three treatments, the hazard ratios for any cardiovascular disease were 1.1 (95% confidence interval [CI], 0.9 to 1.3) in the glargine group, 1.1 (95% CI, 0.9 to 1.4) in the glimepiride group, 0.7 (95% CI, 0.6 to 0.9) in the liraglutide group, and 1.2 (95% CI, 1.0 to 1.5) in the sitagliptin group.



**Rescue therapy**  
For symptomatic hyperglycaemia, consider insulin or a sulfonylurea and review when blood glucose control has been achieved.

**First-line treatment** Assess HbA1c, cardiovascular risk and kidney function



NICE technology appraisals recommend SGLT2 inhibitors as monotherapy options in people:

- who cannot have metformin
- for whom diet and exercise alone do not provide adequate glycaemic control.

The SGLT2 inhibitors are recommended only if a dipeptidyl peptidase-4 (DPP-4) inhibitor would otherwise be prescribed and a sulfonylurea or pioglitazone is not appropriate.

In February 2022, using ertugliflozin to reduce cardiovascular risk when blood glucose is well controlled was off label. See [NICE's information on prescribing medicines](#).

Person's HbA1c not controlled below individually agreed threshold, or the person develops CVD or a high risk of CVD

See [treatment options if further interventions are needed](#)

Established atherosclerotic CVD includes coronary heart disease, acute coronary syndrome, previous myocardial infarction, stable angina, prior coronary or other revascularisation, cerebrovascular disease (ischaemic stroke and transient ischaemic attack) and peripheral arterial disease.

Published date: February 2022. Last updated: August 2022. This is a summary of the advice in the [NICE guideline on type 2 diabetes in adults: management](#). © NICE 2022. All rights reserved. Subject to [Notice of rights](#).

## therapy

Asymptomatic hyperglycaemia, consider insulin or a sulfonylurea and review when blood glucose control has been achieved.

## Options if further interventions are needed

At any point  
Blood glucose not controlled below individually agreed threshold

### Switching or adding treatments

Consider:

GLP-1 inhibitor **or** Pioglitazone

Sulfonylurea

SGLT2 inhibitors may also be an option in dual

Empagliflozin **TA 288** Dapagliflozin

Empagliflozin **TA 572** Ertugliflozin

Triple therapy:

Empagliflozin **TA 418** Dapagliflozin

Empagliflozin **TA 583** Ertugliflozin

At any point

Cardiovascular risk or status change

If the person has or develops chronic heart failure or established atherosclerotic CVD

Switching or adding treatments

Offer

An SGLT2 inhibitor (if not already prescribed)

If the person has or develops a high risk of CVD (QRISK2 of 10% or higher, or elevated lifetime risk)

Switching or adding treatments

Consider

An SGLT2 inhibitor (if not already prescribed)

Established atherosclerotic CVD includes coronary heart disease, acute coronary syndrome, previous myocardial infarction, stable angina, prior coronary or other revascularisation, cerebrovascular disease (ischaemic stroke and transient ischaemic attack) and peripheral arterial disease.

At any point follow the prescribing guidance.

Consider adding treatments from different drug classes up to triple therapy (dual therapy if metformin is contraindicated).

As of July 2022, using ertugliflozin to reduce cardiovascular risk when blood glucose is well controlled was off label. See [NICE's information on prescribing medicines](#).

## therapy

If dual therapy has not continued to control HbA1c to below the person's individually agreed threshold, also consider basal-bolus therapy (with or without other

Dapagliflozin **TA 336** Empagliflozin

Dapagliflozin

## GLP-1 mimetic treatments

If triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated, consider triple therapy by switching one drug for a GLP-1 mimetic for adults with type 2 diabetes:

- have a body mass index (BMI) of 35 kg/m<sup>2</sup> or higher (adjust accordingly for people from Black, Asian and other minority ethnic groups) and specific psychological or other medical problems associated with obesity **or**
- have a BMI lower than 35 kg/m<sup>2</sup> **and**:
  - for whom insulin therapy would have significant occupational implications **or**
  - weight loss would benefit other significant obesity related comorbidities.

## AGREE II: advancing guideline development, reporting and evaluation in health care

Melissa C. Brouwers PhD, Michelle E. Kho BHSc(PT) MSc, George P. Browman MD MSc, Jako S. Burgers MD PhD, Francoise Cluzeau PhD, Gene Feder MD, Béatrice Fervers MD PhD, Ian D. Graham PhD, Jeremy Grimshaw MBChB PhD, Steven E. Hanna PhD, Peter Littlejohns MD, Julie Makarski BSc, Louise Zitzelsberger PhD, for the AGREE Next Steps Consortium

∞∞ See related research articles by Brouwers and colleagues, available at [www.cmaj.ca](http://www.cmaj.ca)

Clinical practice guidelines, which are systematically developed statements aimed at helping people make clinical, policy-related and system-related decisions,<sup>1,2</sup> frequently vary widely in quality.<sup>3,4</sup> A strategy was needed to differentiate among guidelines and ensure that those of the highest quality are implemented.

An international team of guideline developers and researchers, known as the AGREE Collaboration (Appraisal of Guidelines, Research and Evaluation), was established to create a generic instrument to assess the process of guideline development and reporting of this process in the guideline.

### Key points

- AGREE II (Appraisal of Guidelines, Research and Evaluation), which comprises 23 items and a user's manual, offers refinements of a new way to develop, report and evaluate practice guidelines.
- Key changes from the original version include a new seven-point response scale, with modifications to half of the items, and a new user's manual.
- AGREE II is available online at the AGREE Research Trust ([www.agreetrust.org](http://www.agreetrust.org)).

- 11 264 çalışma taranmış, 124 ünün tam metni incelenmiş ve bu çalışmalardan 17 rehber uygunluk sağlamıştır.
- 2008 den önce yayınlanan makaleler çalışmaya dahil edilmemiştir.
- Dahil edilen yayınlar 2012-2018 yılları arasında yayınlanan rehberlerdir.
- Rehberlerin 16 tanesi ulusal kapsamlı ve sadece bir tanesi küresel yaklaşıma sahiptir.

- AGREE PLUS platformunu ([www.agreetrust.org](http://www.agreetrust.org)) kullanılarak AGREE aracı ile kılavuzların raporlama kalitesini değerlendirilmiştir.
- AGREE aracı altı alanda 23 madde içerir:
  - ❖ **Kapsam ve amaç** (1–3. sorular);
  - ❖ **Paydaş katılımı** (soru 4-6);
  - ❖ **Geliştirmenin titizliği** (7-14. sorular),
  - ❖ **Sunumun anlaşılabilirliği** (15-17. sorular);
  - ❖ **Uygulanabilirlik** (18–21. sorular) ve
  - ❖ **Editoryal tarafsızlık** (22–23. sorular)
- Her soruyu 1'den (kesinlikle katılmıyorum) 7'ye (kesinlikle katılıyorum) kadar bir dizi seçenikle cevaplamak için yedi puanlık bir ölçek kullanılmaktadır.

- Her alan için %0 ile %100 arasında deęişen standart bir puan hesaplanmıřtır.
- Tüm alanlar deęerlendirildikten sonra her bir kılavuzdaki genel güvenilirlik üç şekilde deęerlendirilmiřtir:
  - ✓ **“Kılavuz řiddetle tavsiye edildi.”** (Altı alandan dördü  $\geq$  %60);
  - ✓ **“Kılavuz deęişikliklerle birlikte önerildi.”** (En az iki alan puanı  $>$  %60);
  - ✓ **“AGREE kriterlerine göre çok ciddi problemler nedeniyle kılavuz tavsiye edilmemektedir.”** (Altı alandan üçü  $<$  %30 veya alanların hiçbirini  $>$ %60 puan)

## **Ortalama alan puanları**

**iyi ( $\geq$  %80),**

**kabul edilebilir (%60-79),**

**orta (%40-59) veya**

**düşük (<%40) olarak**

**sınıflandırılmaktadır.**

# Tip 2 Diyabetle İlgili Kılavuzların Kalitesi (AGREE)

	Kapsam ve Amaç	Paydaş Katılım	Geliştirme Titizliği	Sunum Netliği	Uygulanabilirlik	Editoryal Bağımsızlık		
ADA, 2018	50	44	49	87	26	61	4 (2.6)	Modifikasyonla Önerilir
ICSI, 2014	46	46	40	57	61	88	3.6 (2)	Modifikasyonla Önerilir
AACE/ACE, 2015	51	29	37	66	13	52	3 (1)	Modifikasyonla Önerilir
ACP, 2017	77	50	58	79	36	75	5.3 (0.5)	Modifikasyonla Önerilir
VA/DoD, 2018	92	90	75	79	55	61	6.3 (0.5)	Kuvvetle Önerilir
NICE, 2015	92	77	88	92	84	86	6.3 (0.5)	Kuvvetle Önerilir
Canada, 2018	44	51	56	75	50	63	4.6 (1.1)	Modifikasyonla Önerilir
South Africa, 2012	25	12	4	7	0	0	1.3 (0.5)	Önerilmez
SIGN, 2013	77	61	54	81	72	69	5.6 (1.1)	Kuvvetle Önerilir
Japan, 2018	48	11	18	53	18	0	3.3 (1.5)	Önerilmez
Colombia, 2016	81	72	65	87	63	88	6.3 (0.5)	Kuvvetle Önerilir
Korea, 2017	35	25	29	57	12	47	3.6 (1.5)	Önerilmez
Pakistan, 2017	37	14	6	37	11	27	1.6 (0.5)	Önerilmez
Singapore, 2014	50	33	22	66	25	8	3.6 (1.5)	Önerilmez
Taiwan, 2018	33	22	13	40	6	55	3 (1)	Önerilmez
Malaysia, 2015	74	51	40	70	61	72	4.3 (1.52)	Kuvvetle Önerilir
WHO, 2018	90	87	92	92	51	91	6.6 (0.5)	Kuvvetle Önerilir



Kılavuzları çođu,  
yerel yargı odaklı öneriler sunmuřtur



“İşte bilimin ulaşabileceği en son nokta bu...”

