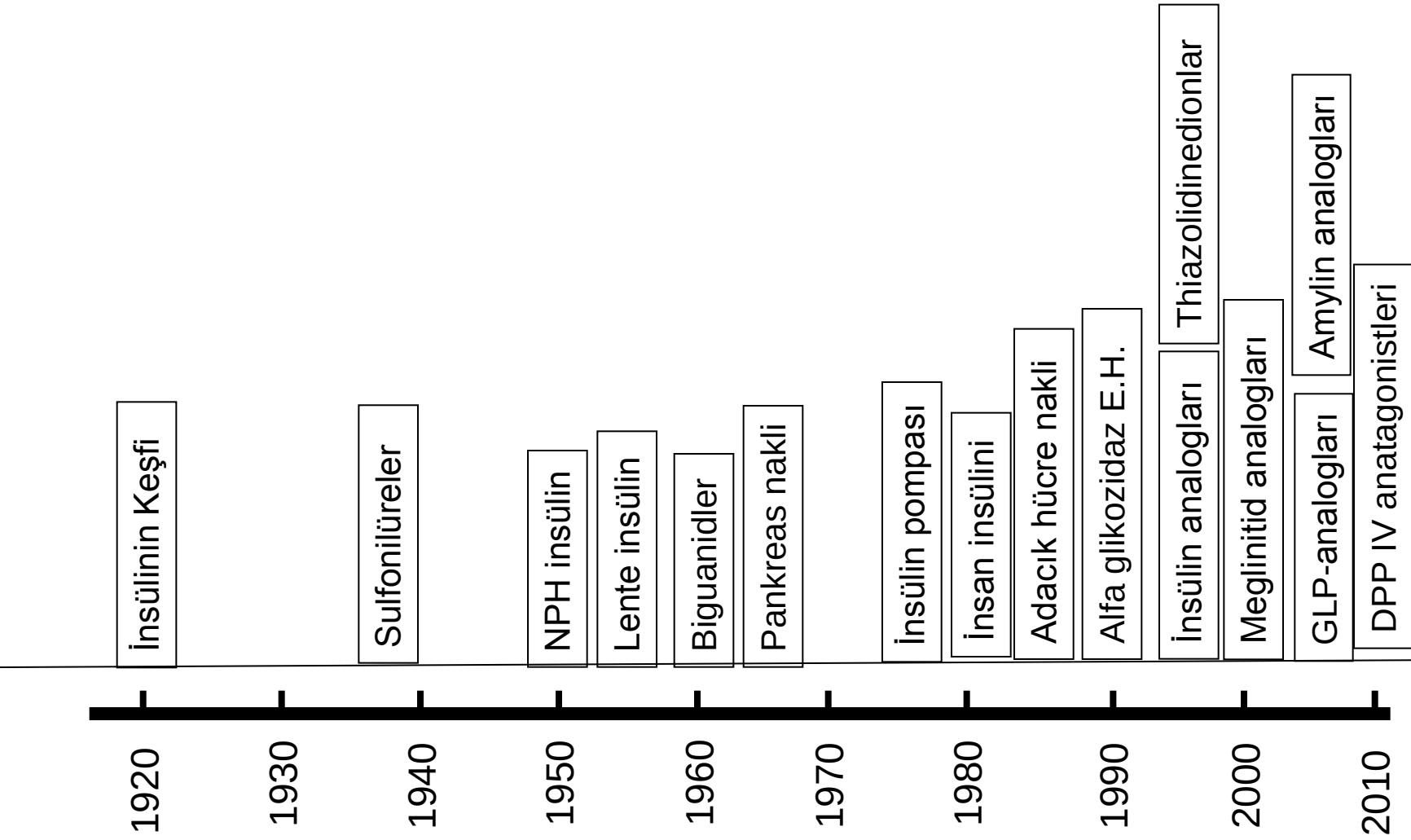
Güncel algoritmalar ışığında Tip 2 DM tedavisi

İnsülin Duyarlılaştırıcılar

Prof. Dr. Erdinç Ertürk
Uludağ Üniversitesi Tıp Fakültesi

Diyabete Bakış Kongresi
25-28 Mart 2010 Kıbrıs

DM tedavisinde gelişmeler: Tarih çizgisi



Glisemi kontrolünde farmakolojik tedavi

- Biguanidler
- Thiazolidinedonlar (Glitazonlar)
- Sulfonilüreler
- Glinidler
- Alfaglikozidaz enzim inhibitörleri
- DPP4 inhibitörleri
- İnkretin analogları
- Amylin analogları
- İnsülinler ve analogları

Farmakolojik tedavide tercih kriterleri

- Kan şekerini düşürme potansiyeli
- Hipoglisemi yapma potansiyeli
- Kontrendikasyonları
- Yan etkileri- toleransı
- Vücut ağırlığı üzerine etkisi
- Lipid profili üzerine etkisi
- Ateroskleroz proses üzerine etkisi
- Sık görülen komorbiditerlerde kullanılabilirliği

- Uzun dönem sonlanım noktaları

Metformin avantajları

- Esas olarak karaciğere etki ile insülin direncini azaltarak hepatik glukoz çıkışını azaltır
- Hem açlık, hem tokluk KŞ üzerine etkilidir
- HbA1c düzeyinde % 1.5-2 düzeyinde azalma sağlar
- Kilo artışına neden olmaz
- Hipoglisemiye neden olmaz
- Lipid profiline olumlu etkisi vardır
- Fibrinolitik aktivite gösterilmiştir
- Pankreas beta hücresini uyarmaz
- Tüm diğer ajanlarla kombine edilebilir
- Yaklaşık 50 yıldır klinik kullanımdadır

Metformin avantajları

- Mikrovasküler komplikasyonlara etkilidir
- Makrovasküler komplikasyonlara da etkilidir
- Uzun süreli randomize kontrollü çalışmalarda sonlanım noktaları üzerine olumlu etkisi gösterilmiştir

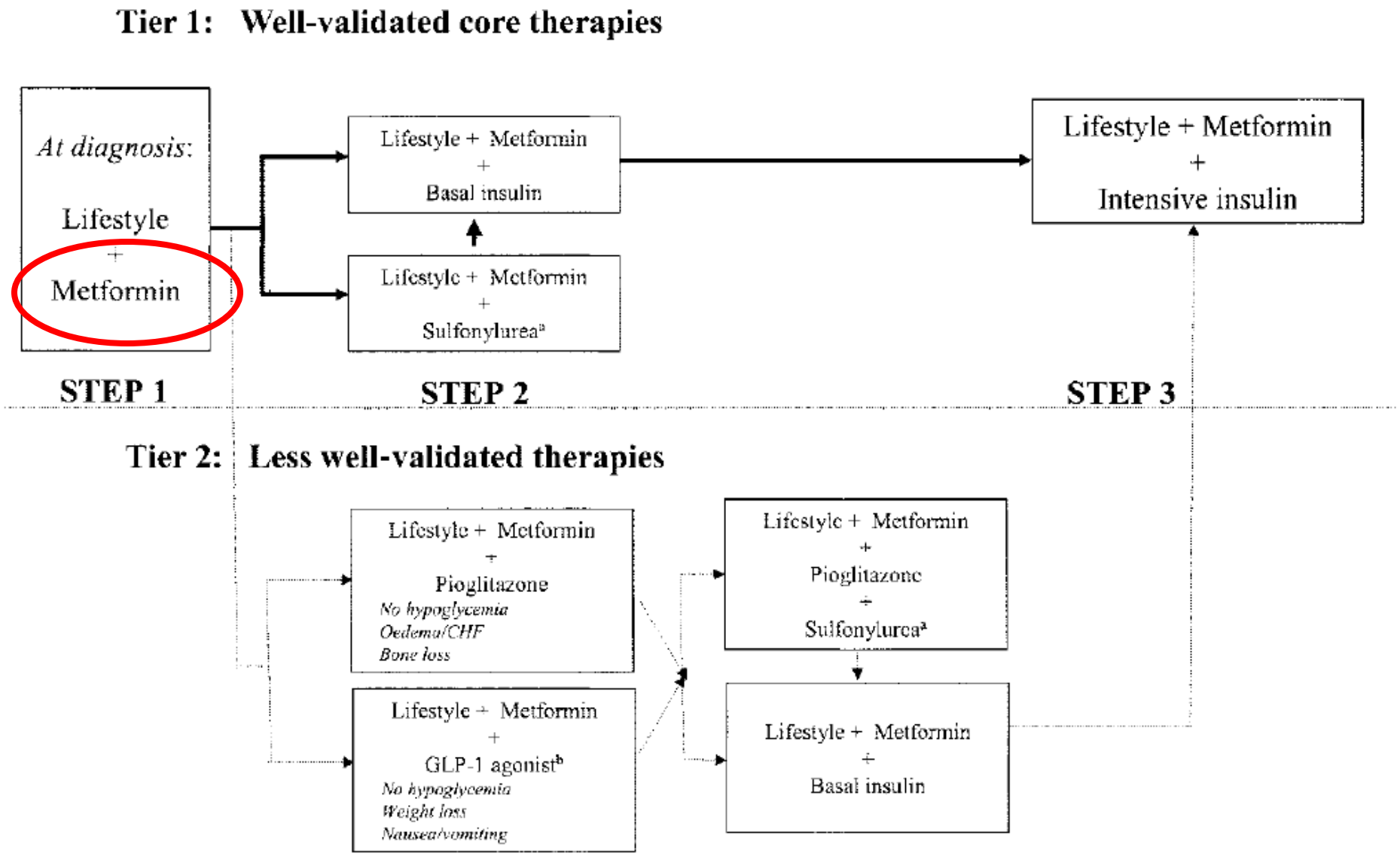
Metformin

- Günlük doz 500-2000 mg arasında
- Max doz 3000 mg
- Çok düşük doz ile başlanıp titre edilerek artırılmalıdır
- Yemek arasında veya sonunda tok karnına alınmalıdır

Metformin dezavantajları

- Kontrendikasyonları
  - Renal yetmezlik
    - Cr E > 1.5 mg/dl, K > 1.4 mg/dl
    - Cr Cl < 60 ml/dak
  - İleri derecede kalp yetmezliği
  - İleri yaş (> 80 ?)
  - Alkolizm
  - Peroperatif
  - İlaç intoleransı
  - Karaciğer toksisitesi
- Gastrointestinal yan etkileri sıktır
  - Titre edilmelidir

T2DM tedavisinde ADA-EASD konsensus algoritmi



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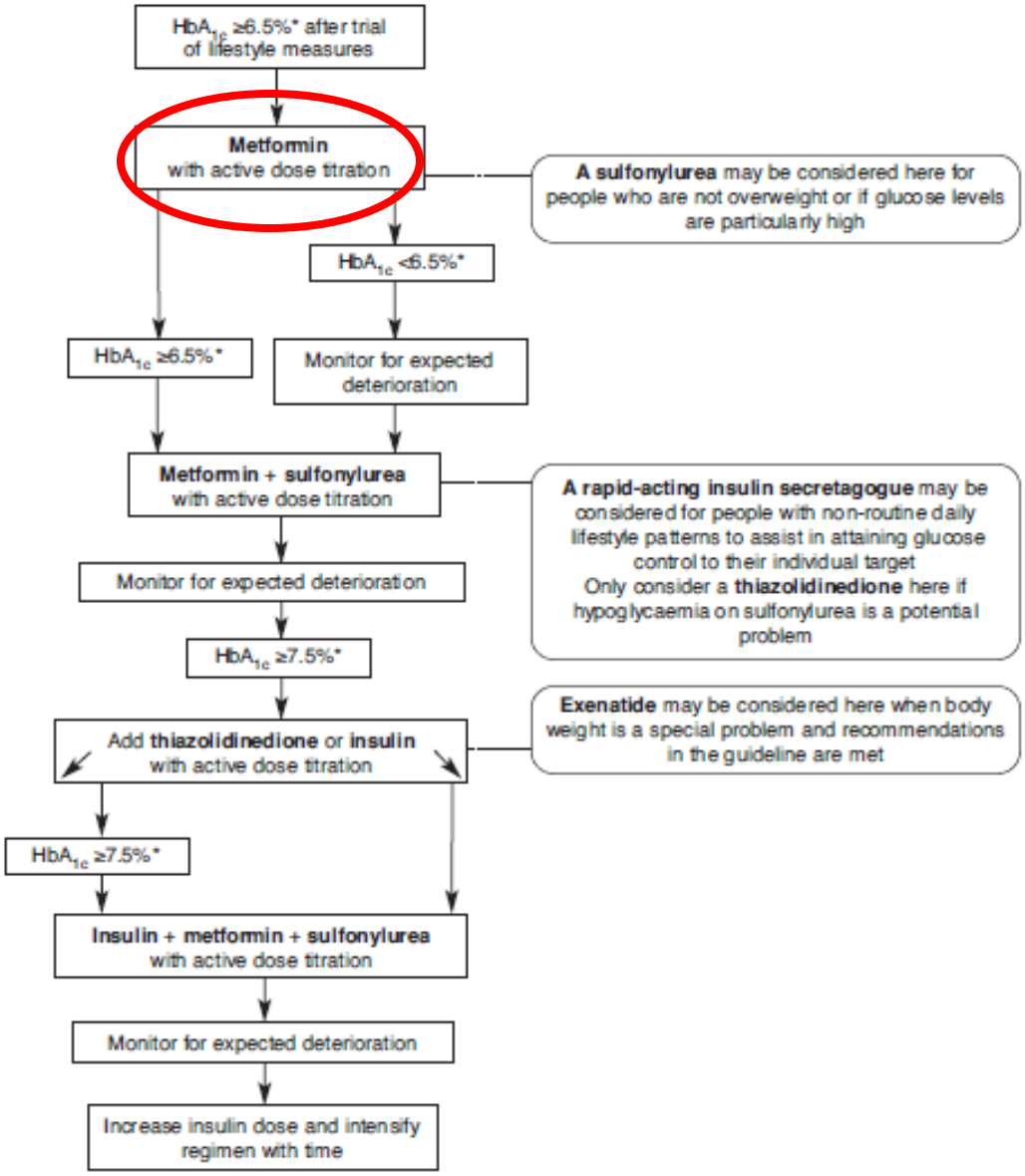

Figure 3.1 Scheme for the pharmacotherapy of glucose lowering in people with Type 2 diabetes
For details see recommendations on glucose lowering targets, clinical monitoring, use of oral agents, and use of insulin
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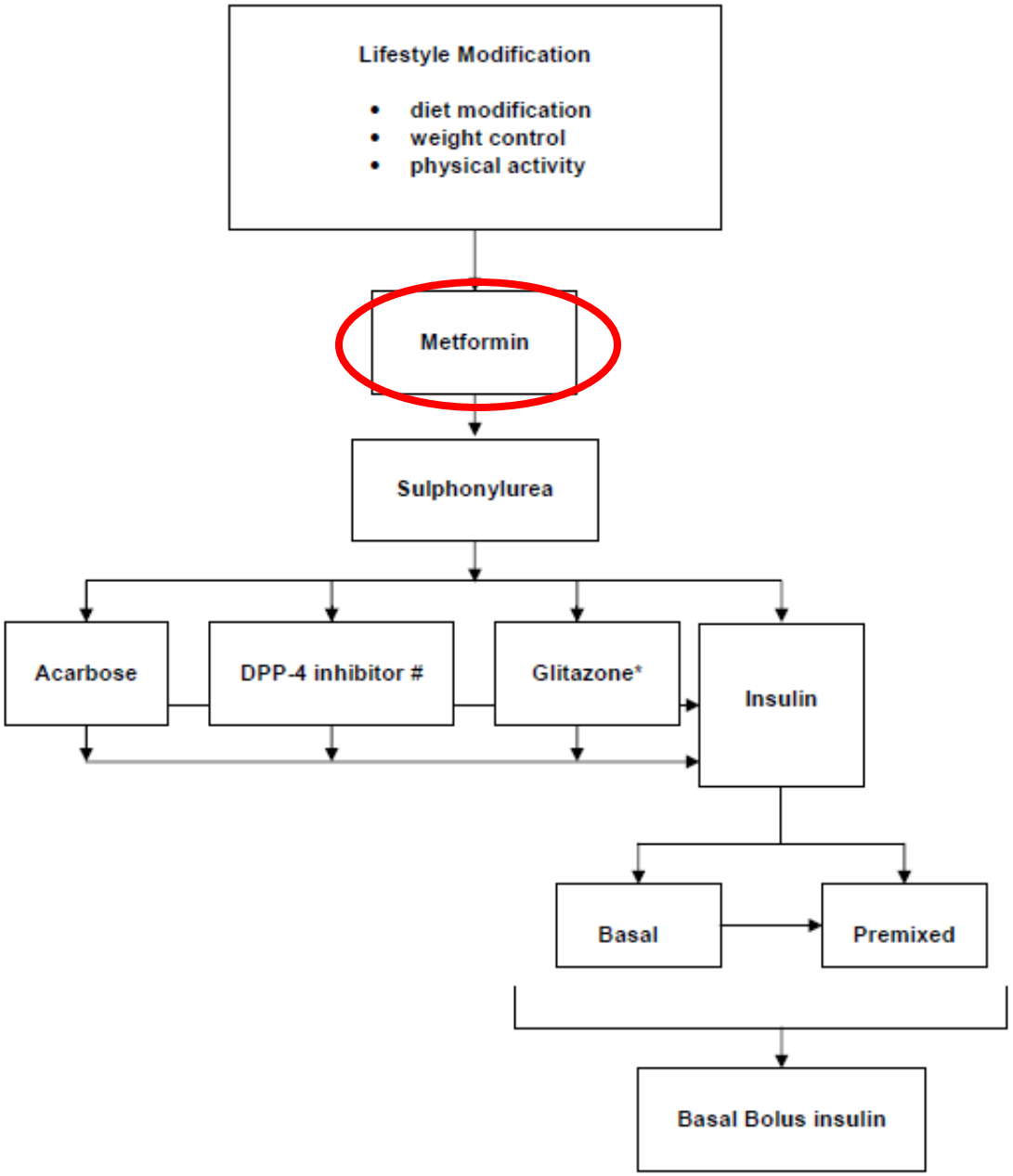
Management algorithm for blood glucose control in type 2 diabetes



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2. Flowchart: Antihyperglycaemic therapy of type 2 diabetes

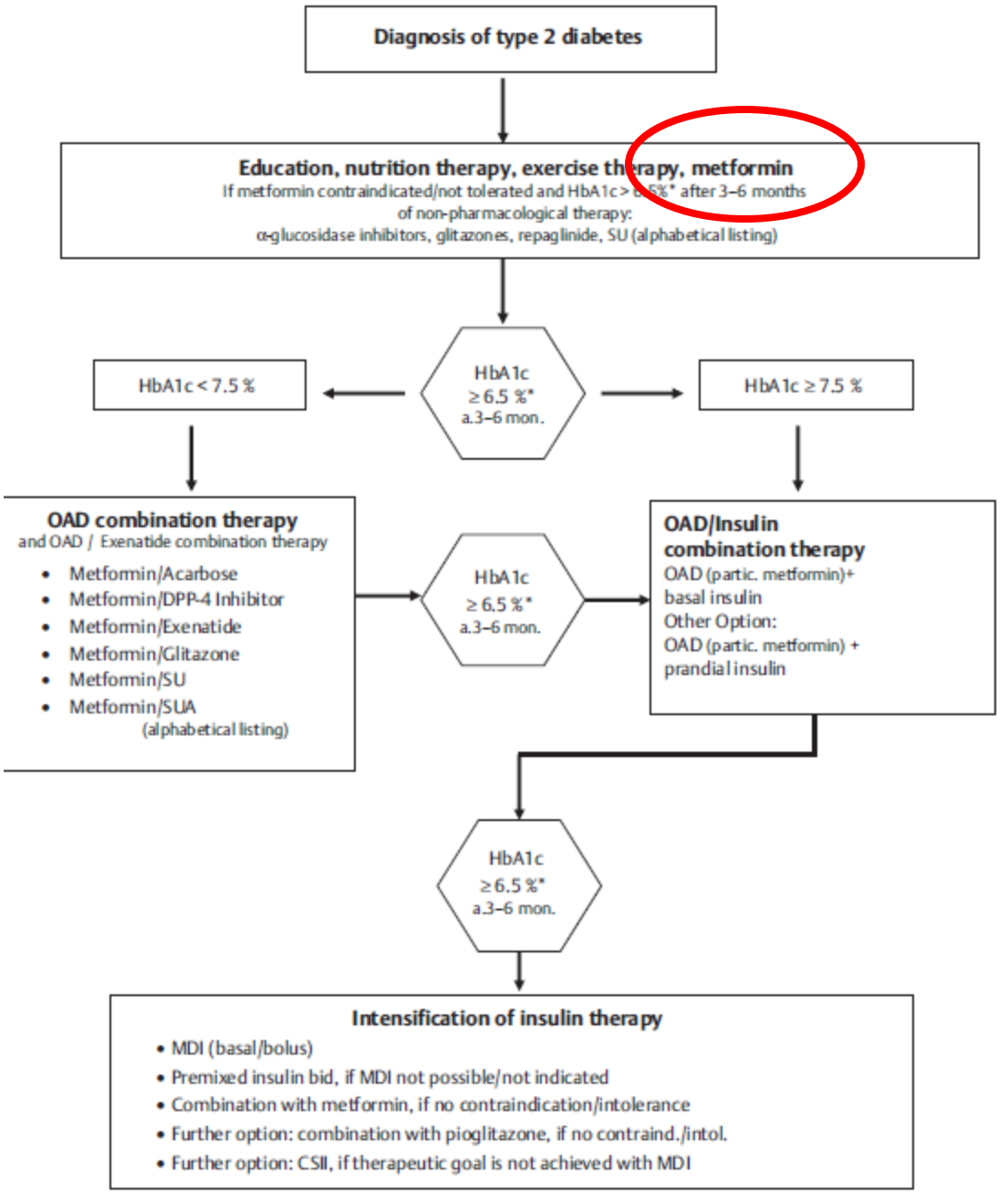

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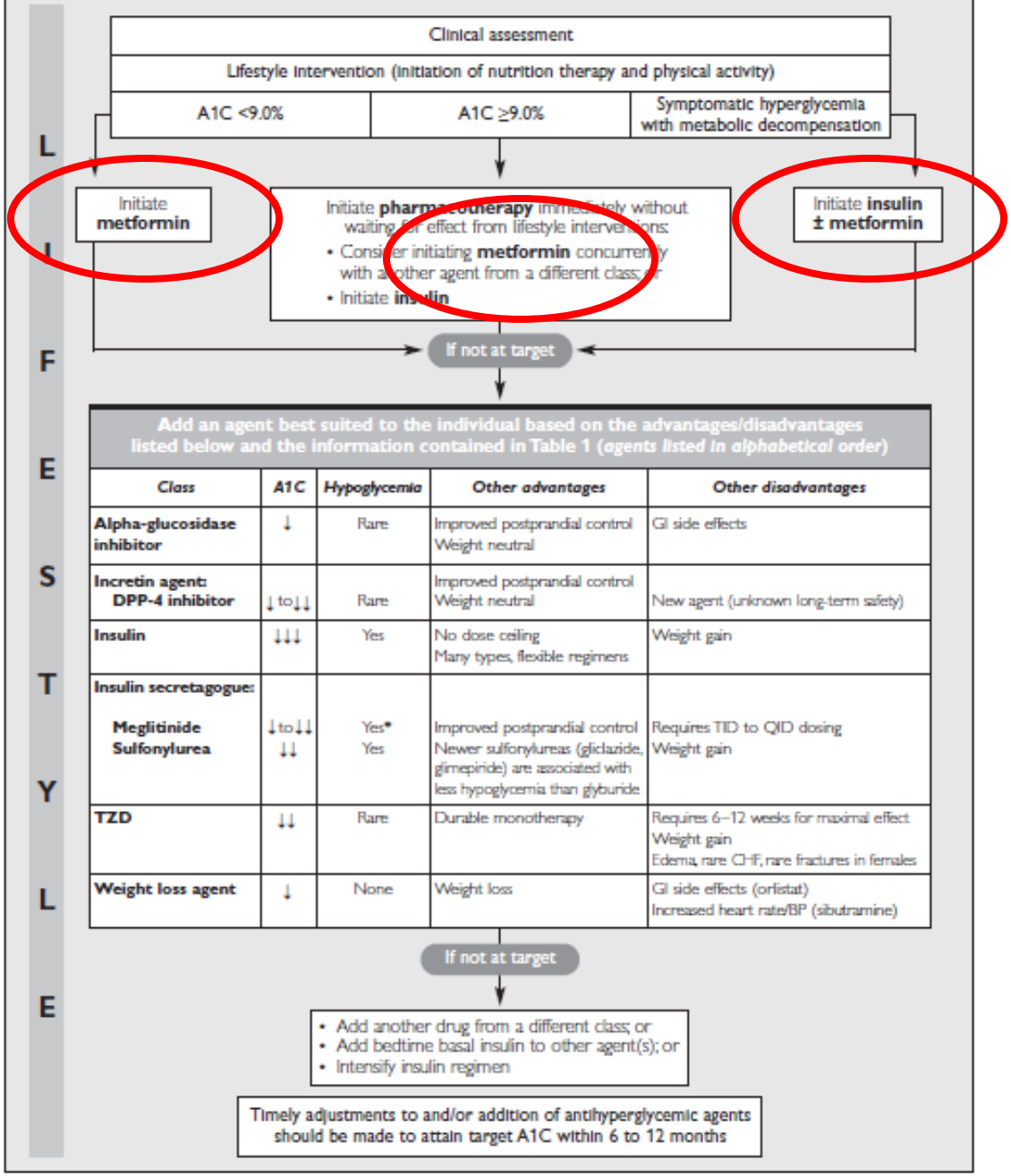
Figure 1. Management of hyperglycemia in type 2 diabetes



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Incretin agent: DPP-4 inhibitor	↓ to ↓↓	Rare	Improved postprandial control Weight neutral	New agent (unknown long-term safety)
Insulin	↓↓↓	Yes	No dose ceiling Many types, flexible regimens	Weight gain
Insulin secretagogue:				
Meglitinide	↓ to ↓↓	Yes*	Improved postprandial control	Requires TID to QID dosing
Sulfonylurea	↓↓	Yes	Newer sulfonylureas (gliclazide, glimepiride) are associated with less hypoglycemia than glyburide	Weight gain
TZD	↓↓	Rare	Durable monotherapy	Requires 6–12 weeks for maximal effect Weight gain Edema, rare CHF, rare fractures in females
Weight loss agent	↓	None	Weight loss	GI side effects (orlistat) Increased heart rate/BP (sibutramine)

AACE/ACE Diabetes Algorithm *For Glycemic Control*

A1C Goal ≤ 6.5%*

LIFESTYLE MODIFICATION

A1C 6.5 – 7.5%**

Monotherapy

MET	TZD [2]	DPP4 [1]	AGI [3]

↓ *2 - 3 Mos.****

Dual Therapy

MET	+	GLP-1 or DPP4 [1]
		TZD [2]
		Glinide or SU [5]
TZD	+	GLP-1 or DPP4 [1]
MET	+	Colesevelam
		AGI [3]

↓ *2 - 3 Mos.****

Triple Therapy

MET + GLP-1 or DPP4 [1]	+	TZD [2]
		Glinide or SU [4,7]

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INSULIN ± Other Agent(s) [6]

A1C 7.6 – 9.0%

Dual Therapy [8]

MET	+	GLP-1 or DPP4 [1,10] or TZD [2]
		SU or Glinide [4,5]

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Triple Therapy [9]

MET	+	GLP-1 or DPP4 [1] + TZD [2]
		GLP-1 or DPP4 [1] + SU [7]
		TZD [2]

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INSULIN ± Other Agent(s) [6]

A1C > 9.0%

Drug Naive | *Under Treatment*

Symptoms | *No Symptoms*

INSULIN ± Other Agent(s) [6]

MET	+	GLP-1 or DPP4 [1]	± SU [7]
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** For patients with diabetes and A1C ≤ 5.5%, pharmacologic Rx may be considered

*** If A1C goal not achieved safely

[1] DPP4 if ↑ PPG and ↑ FPG or GLP-1 if ↑↑ PPG

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[3] AGI if ↑ PPG

[4] Glinide if ↑ PPG or SU if ↑ FPG

[5] Low-dose secretagogue recommended

[6] a) Discontinue insulin secretagogue with sulfonylurea insulin
b) Can use pramlintide with prandial insulin

[7] Decrease secretagogue by 50% when added to GLP-1 or DPP-4

[8] If A1C <8.5%, combination Rx with agents that cause hypoglycemia should be used with caution

[9] If A1C > 9.5%, in patients on Dual Therapy, insulin should be considered

[10] GLP-1 not approved for initial combination Rx

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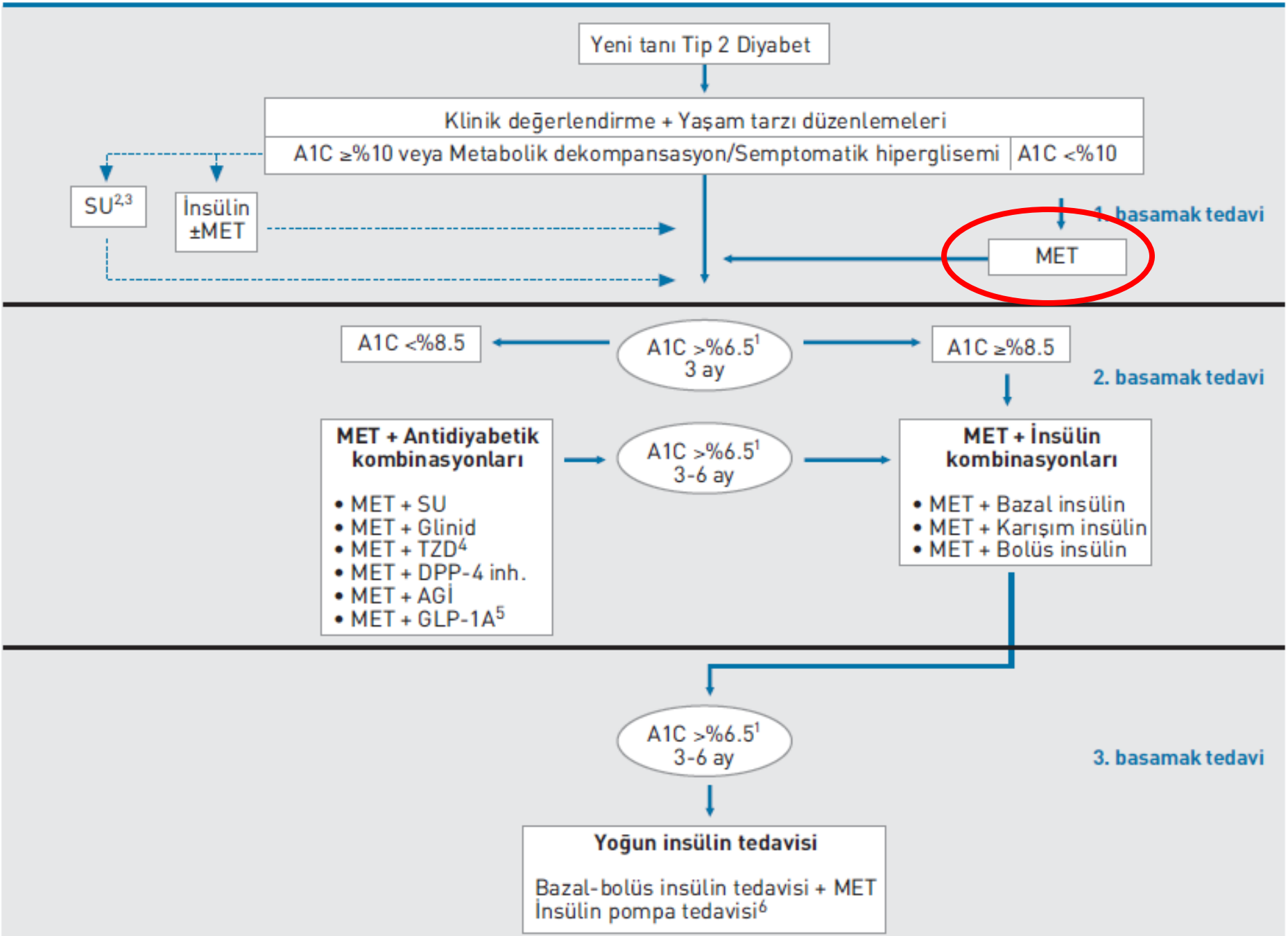
ŞEKİL 9.1 | **Tip 2 diyabetli hastalarda tedavi algoritması**



Metforminin algoritmlerdeki yeri

- Tüm algoritmlerde ilk seçenektir
  - Zayıf hastalarda da etkinliği gösterilmiştir
  - Yaşam biçimi değişiklikleri ile birlikte tanı konur konmaz tedaviye başlanmasını öneren algoritmler vardır
  - HbA1c seviyesine göre dual tedavinin bir ajanı olarak tedaviye başlanmasını öneren algoritmler vardır

Table IV. Clinical trials of dual metformin (MET) therapy.

Authors	No. of Patients	Duration	Treatment Arms	Change in HbA_{1c} from Baseline (percentage points)

Authors	No. of Patients	Duration	Treatment Arms	Change in HbA_{1c} from Baseline (percentage points)

Blonde et al[97]	639	16 wk	MET	0.18 and 0.39*
			GLY	0.10 and –0.11*
			MET/GLY 500/2.5 mg	–1.33 and –1.64*
			MET/GLY 500/5 mg	–1.76 and –1.38*
Garber et al[98]	806	20 wk	MET	–1.03
			GLY	–1.24
			MET/GLY 250/1.25 mg	–1.48
			MET/GLY 500/2.5 mg	–1.53
			PLA	–0.21
Marre et al[99]	411	16 wk	MET	–0.19
			GLIB	–0.33
			MET/GLIB 500/2.5 mg	–1.20
			MET/GLIB 500/5 mg	–0.91
Goldstein et al[100]	247	18 wk	MET	–0.2
			GLIP	–0.4
			MET/GLIP	–1.3

Table IV. Clinical trials of dual metformin (MET) therapy.

Authors	No. of Patients	Duration	Treatment Arms	Change in HbA_{1c} from Baseline (percentage points)
Metformin plus a "glitinide"				
Moses at al[81]	83	16–20 wk	MET	–0.33
			REPAG	–0.38
			MET + REPAG	–1.41
Horton et al[82]	701	24 wk	MET	–0.8
			NAT	–0.5
			MET + NAT	–1.4
			PLA	0.5
Furlong et al[91]	80	13 wk	MET + insulin	–0.3
			REPAG + insulin	0.5
Raskin et al[92]	192	16 wk	MET + REPAG	–1.28
			MET + NAT	–0.67

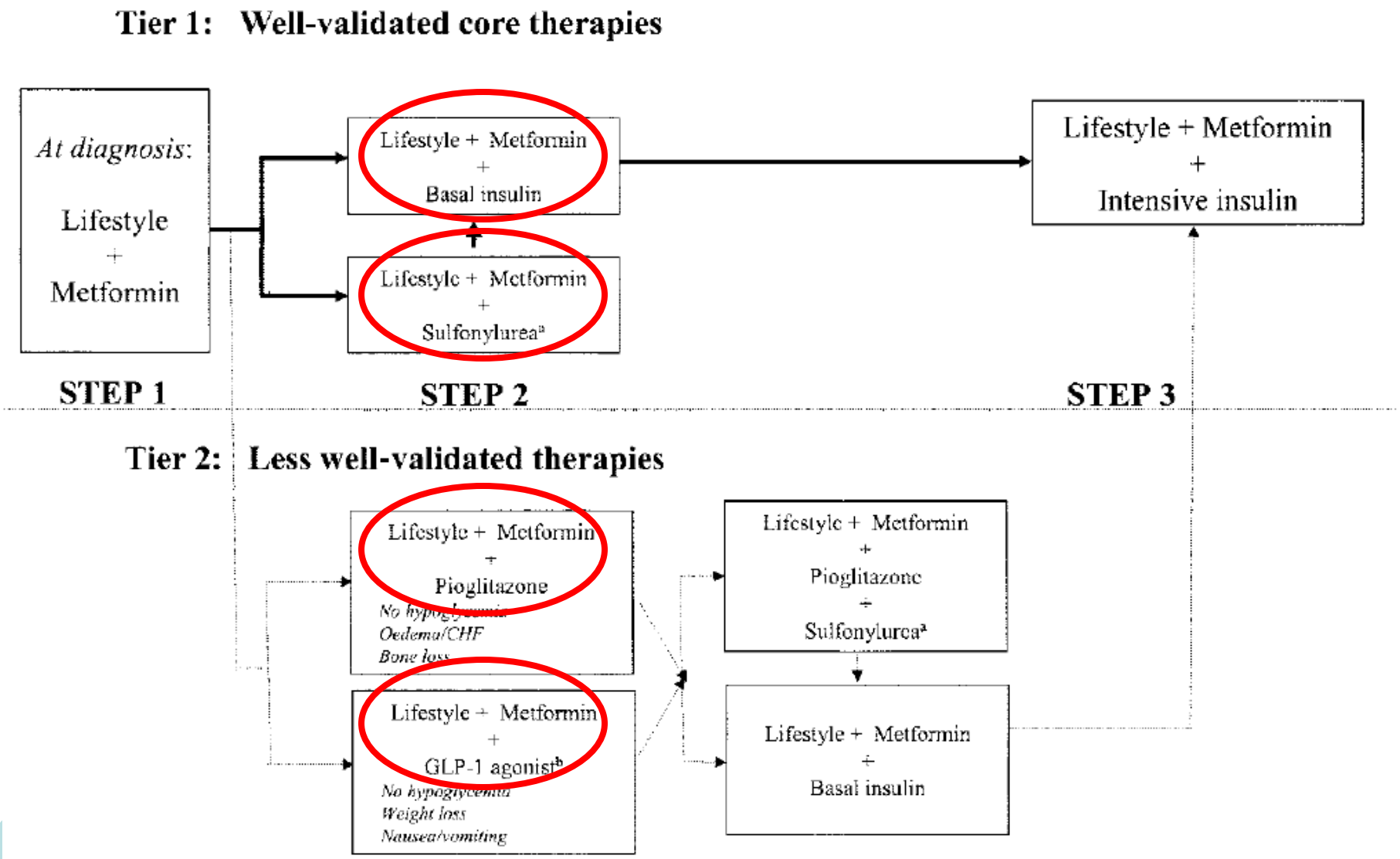
Table IV. Clinical trials of dual metformin (MET) therapy.

Authors	No. of Patients	Duration	Treatment Arms	Change in HbA_{1c} from Baseline (percentage points)
Metformin plus a thiazolidinedione				
Einhorn et al[88]	328	16 wk	MET + PIO	–0.63
			MET + PLA	0.2
Fonseca et al[89]	348	26 wk	MET + ROSI 4 mg	0.56
			MET + ROSI 8 mg	0.78
			MET + PLA	0.45
Gomez-Perez et al[90]	116	26 wk	MET + ROSI 4 mg	–0.7
			MET + ROSI 8 mg	–1.2
			MET + PLA	0.3

Table IV. Clinical trials of dual metformin (MET) therapy.

Authors	No. of Patients	Duration	Treatment Arms	Change in HbA_{1c} from Baseline (percentage points)
Metformin plus an alpha-glucosidase inhibitor				
Rosenstock et al[93]	168	24 wk	MET + ACAR	–0.57
			MET + PLA	0.08
Willms and Ruge[94]	89	12 wk	MET + ACAR + SU	–2.5
			ACAR + SU	–2.3
			PLA + SU	–1.3
Chiasson and Naditch[95]	324	36 wk	MET	–0.85
			MIG	0.02
			MET + MIG	–1.39
			PLA	0.38

T2DM tedavisinde ADA-EASD konsensus algoritmi



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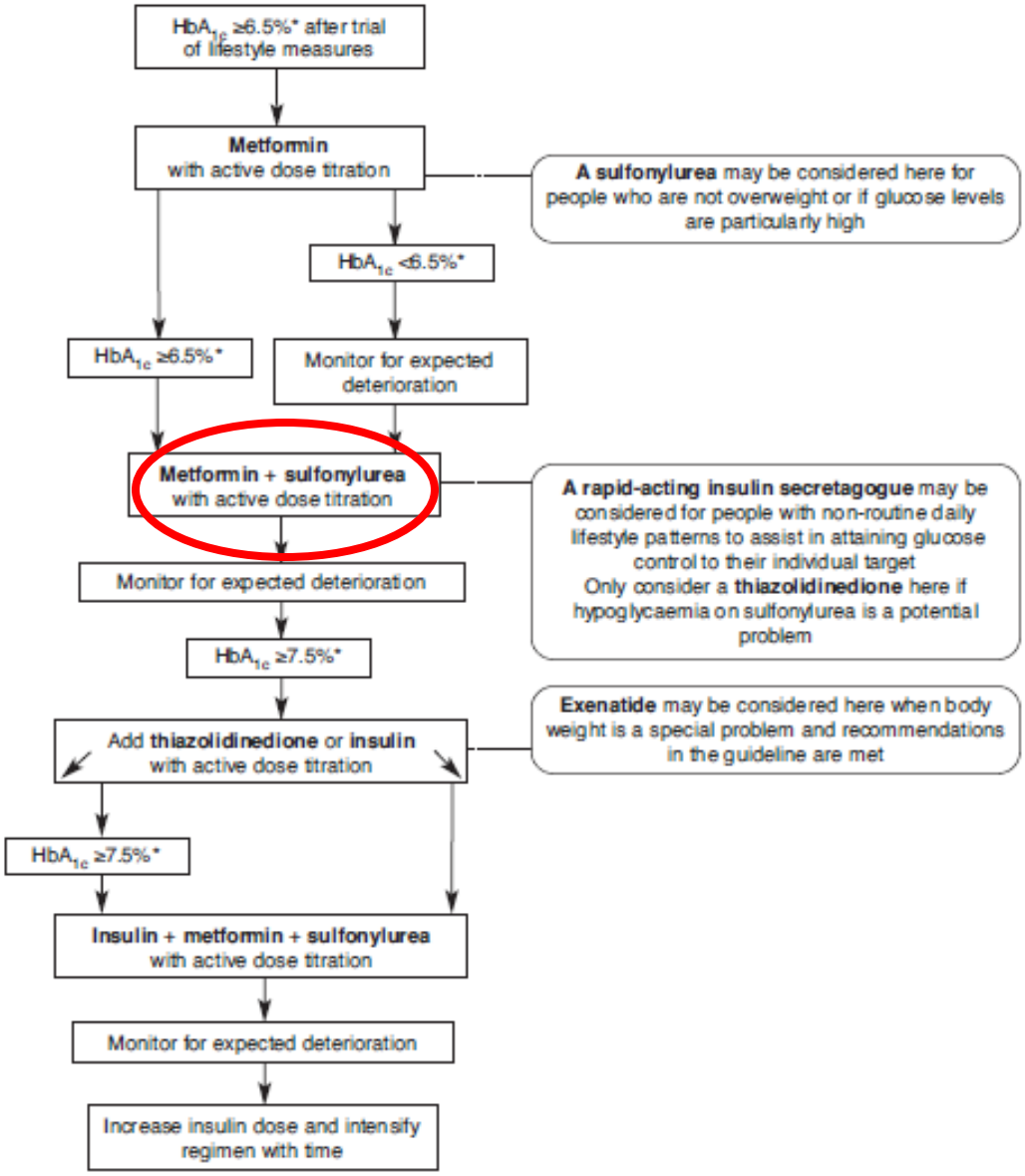

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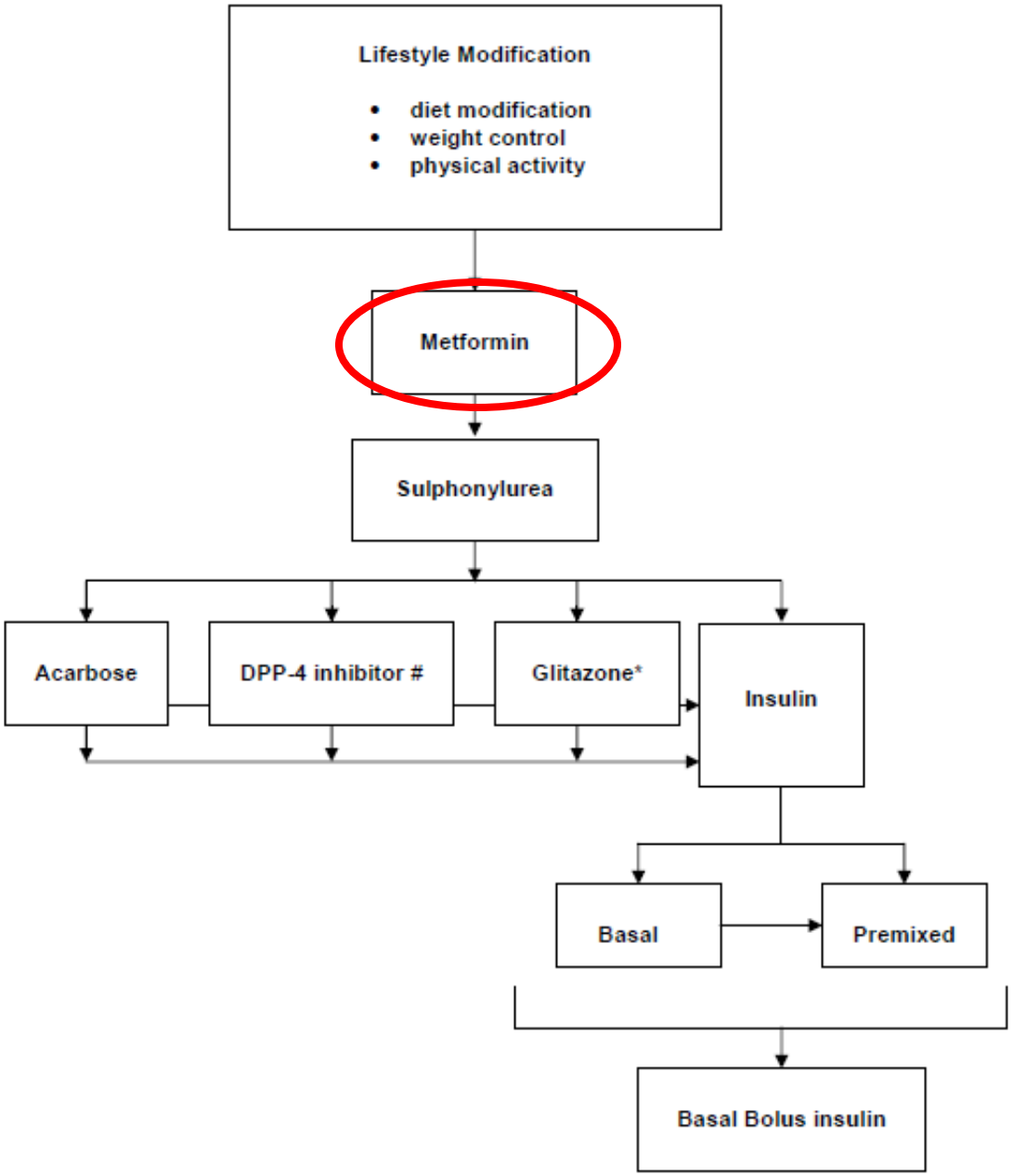

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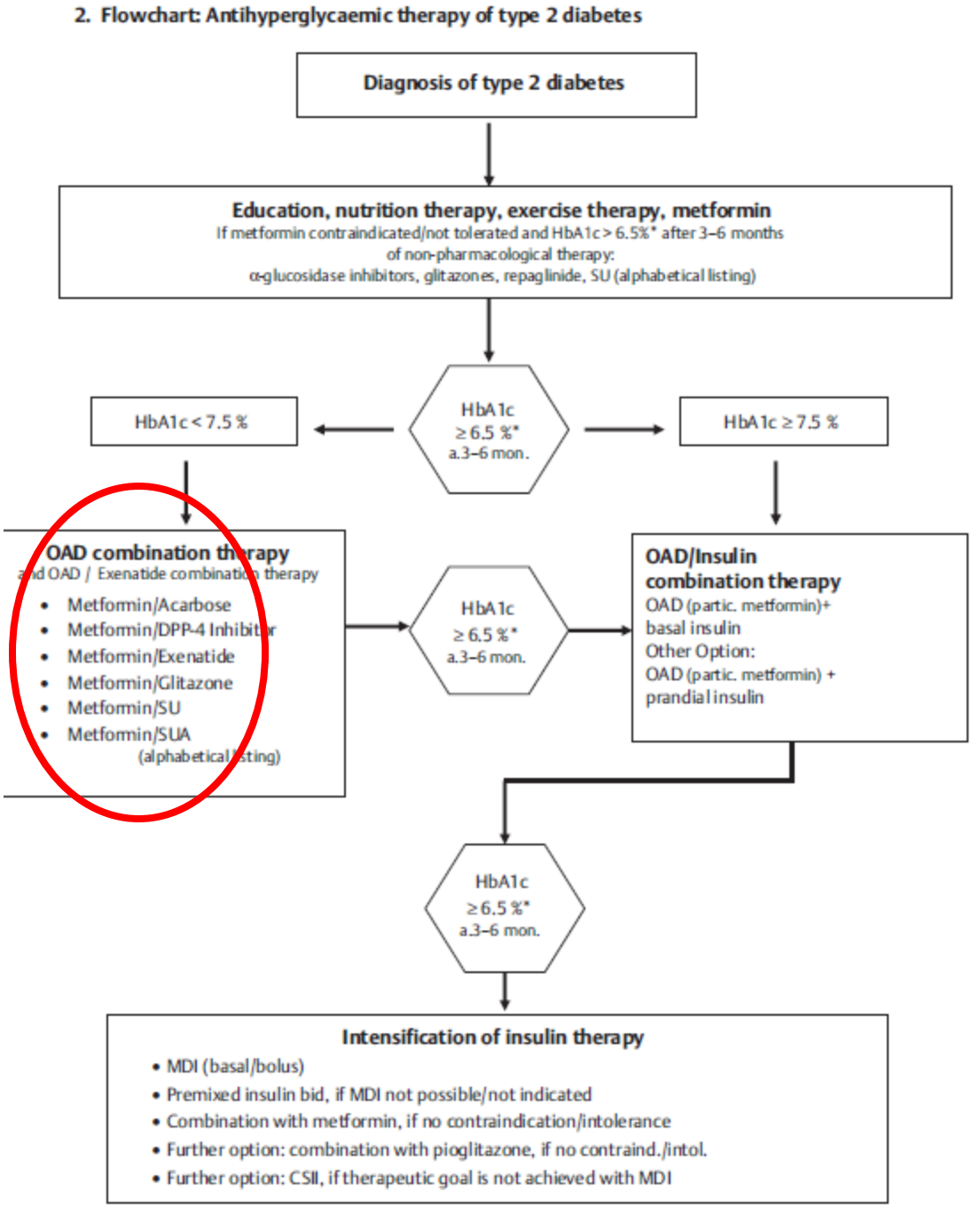
2. Flowchart: Antihyperglycaemic therapy of type 2 diabetes
Diagnosis of type 2 diabetes
Education, nutrition therapy, exercise therapy, metformin
If metformin contraindicated/not tolerated and HbA1c > 6.5%* after 3–6 months of non-pharmacological therapy:
α-glucosidase inhibitors, glitazones, repaglinide, SU (alphabetical listing)
HbA1c ≥ 6.5 %* a.3–6 mon.
HbA1c < 7.5 %
HbA1c ≥ 7.5 %
OAD combination therapy
add OAD / Exenatide combination therapy
Metformin/Acarbose
Metformin/DPP-4 Inhibitor
Metformin/Exenatide
Metformin/Glitazone
Metformin/SU
Metformin/SUA
(alphabetical listing)
HbA1c ≥ 6.5 %* a.3–6 mon.
OAD/Insulin combination therapy
OAD (partic. metformin)+ basal insulin
Other Option:
OAD (partic. metformin) + prandial insulin
HbA1c ≥ 6.5 %* a.3–6 mon.
Intensification of insulin therapy
MDI (basal/bolus)
Premixed insulin bid, if MDI not possible/not indicated
Combination with metformin, if no contraindication/intolerance
Further option: combination with pioglitazone, if no contraind./intol.
Further option: CSII, if therapeutic goal is not achieved with MDI

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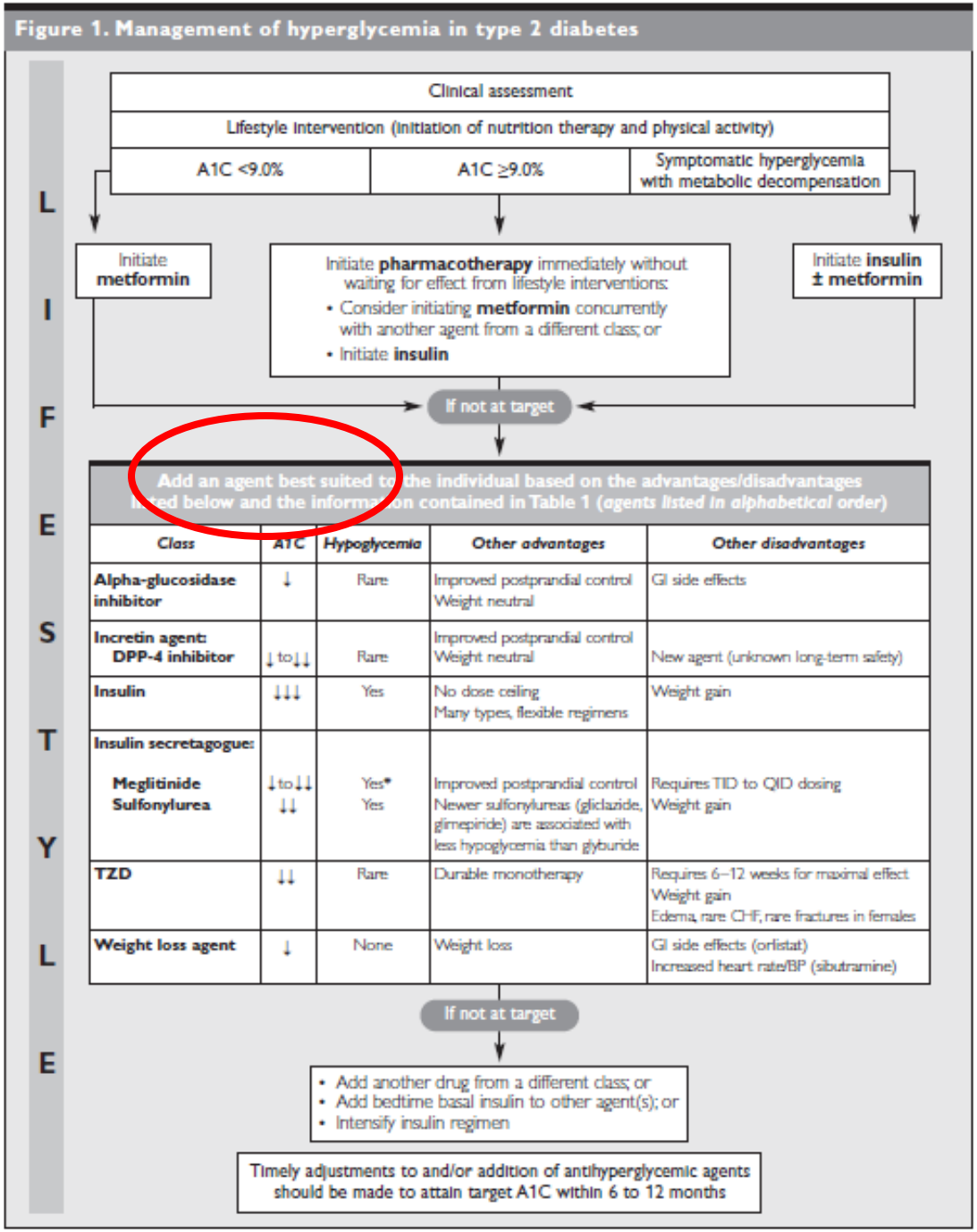
Figure 1. Management of hyperglycemia in type 2 diabetes



LIFESTYLE

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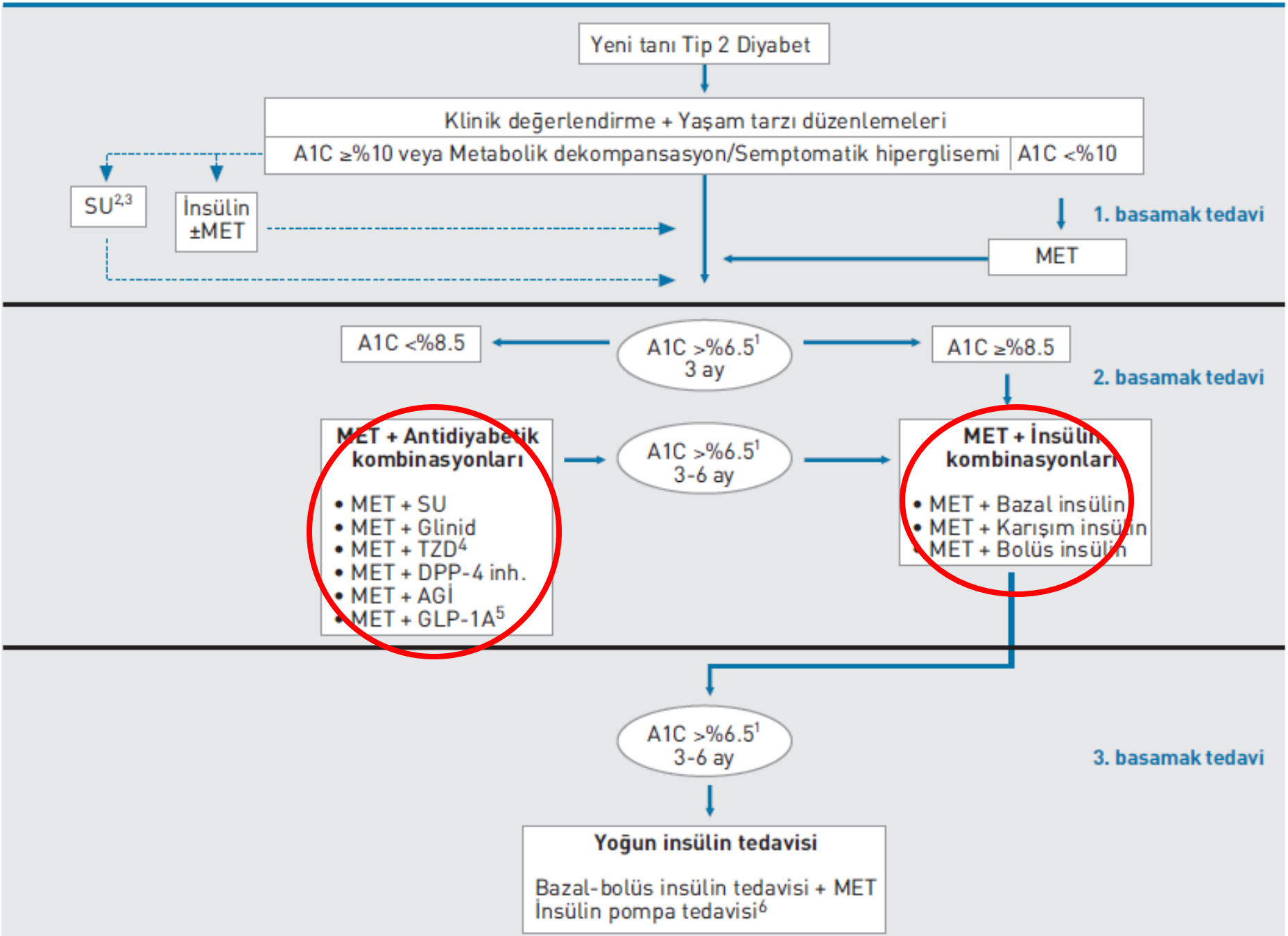

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  - HbA1c seviyesine göre kombine olarak tedaviye başlanmasını öneren algoritmler vardır
- İkinci basamakta tüm kombinasyonlarda bulunur
  - Metformin kesilerek başka ilaçla monoterapi önerilmez
  - Diğer ajan hastanın özelliğine göre seçilir metformine eklenir

Glisemi kontrolünde farmakolojik tedavi

- Biguanidler
- Thiazolidinedonlar (Glitazonlar)
- Sulfonilüreler
- Glinidler
- Alfaglikozidaz enzim inhibitörleri
- DPP4 inhibitörleri
- İnkretin analogları
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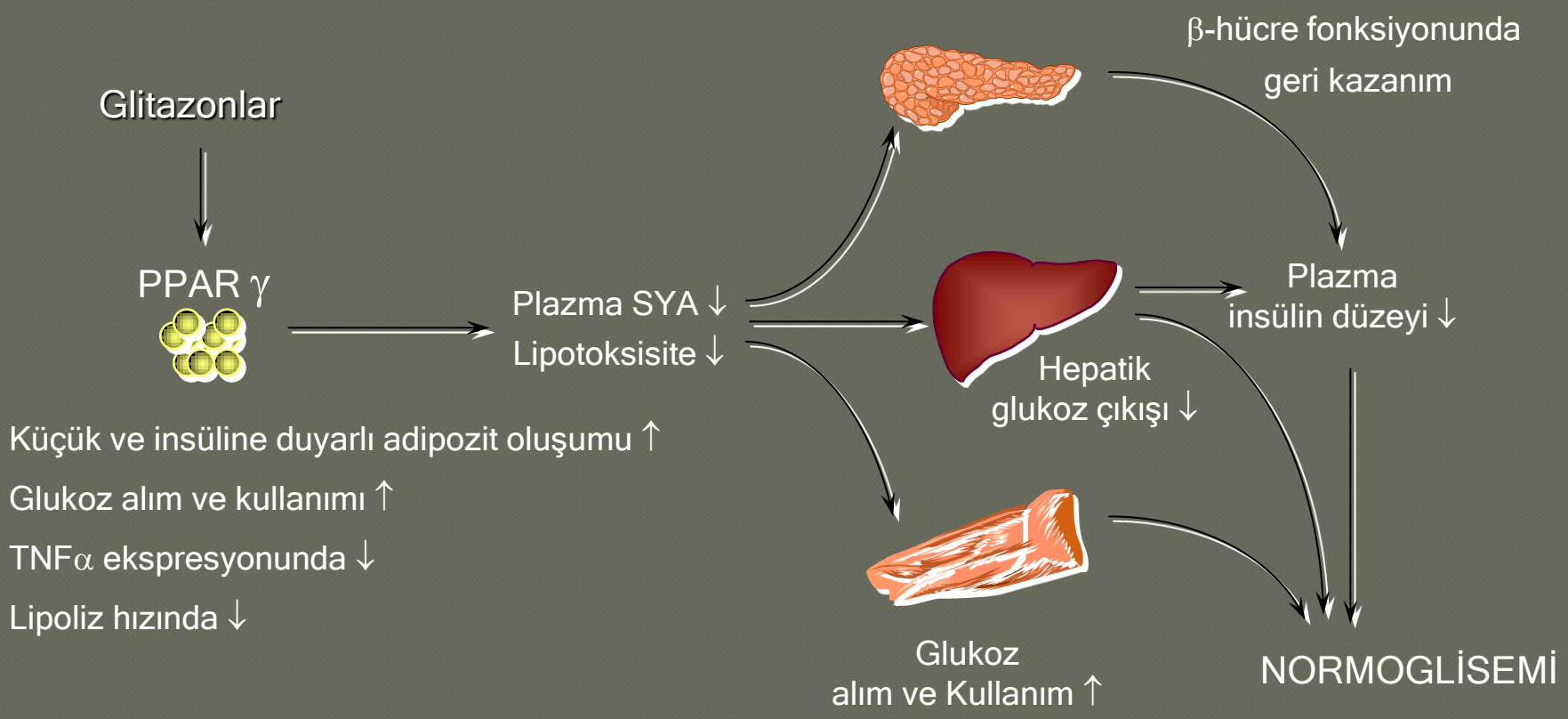
- İnsülinler

Glitazonların, PPAR$_\gamma$ aktivasyonu yoluyla hedef dokularda insülin direncine azaltıcı etkisi



TZD lerin olası etki mekanizmaları

- Plazma serbest yağ asitleri düzeyini azaltarak
- Adipoz dokunun endokrin fonksiyonunu değiştirerek
- Yağ konfigürasyonu değişiklikleri oluşturarak

TZD - Avantajları

- KŞ düşürmede etkin ilaçlardır
- Hipoglisemi riski yoktur
- Renal yetmezlikte doz ayarlaması gerekmez
- İleri yaşlarda kullanılabilir
- Kontrendikasyonları azdır
- Toleransı yüksektir
- Tüm OAD lerle kombine edilebilirler
- Plazma insülin seviyesini artırmazlar
- Beta hücre fonksiyonunu koruyucu etkisi olabilir ?
- Diyabetten koruyucu etki mümkün ?
- Mikroalbuminüriyi azaltma etkisi ?

Tiazolidinedionların yan etkileri

• Ödem	R: 3.75	P: 2.42
• Kalp yetmezliği	R: 2.09	P: 1.60
• Kilo artışı	R: 2.2 kg	P: 3.6
• Hipoglisemi	Nadir	
• Anemi	0.9 g/dl	
• Kemik kırığı	R: 2.38	P: 2.59
• LDL artışı	R: 16.6 mg/dl	P: 2.7 mg/dl
• KC enzim yüksekliği		
• Miyokard infarktüsü		

Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes

Table 4. Rates of Myocardial Infarction and Death from Cardiovascular Causes.

Study	Rosiglitazone Group	Control Group	Odds Ratio (95% CI)	P Value
	no. of events/total no. (%)			
Myocardial infarction				
Small trials combined	44/10,285 (0.43)	22/6106 (0.36)	1.45 (0.88–2.39)	0.15
DREAM	15/2,635 (0.57)	9/2634 (0.34)	1.65 (0.74–3.68)	0.22
ADOPT	27/1,456 (1.85)	41/2895 (1.42)	1.33 (0.80–2.21)	0.27
Overall			1.43 (1.03–1.98)	0.03
Death from cardiovascular causes				
Small trials combined	25/6,845 (0.36)	7/3980 (0.18)	2.40 (1.17–4.91)	0.02
DREAM	12/2,635 (0.46)	10/2634 (0.38)	1.20 (0.52–2.78)	0.67
ADOPT	2/1,456 (0.14)	5/2895 (0.17)	0.80 (0.17–3.86)	0.78
Overall			1.64 (0.98–2.74)	0.06

Nissen SE. N Engl J Med 2007;356:2457-2471

Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2 diabetes (RECORD): a multicentre, randomised, open-label trial

	Rosiglitazone (N=2220)	Active control (N=2227)	HR	Rate difference per 1000 person-years	p
CV death or CV hospitalisation	321	323	0·99 (0·85 to 1·16)	−0·2 (−4·5 to 4·1)	0·93
All-cause death	136	157	0·86 (0·68 to 1·08)	−1·7 (−4·3 to 0·9)	0·19
CV death	60	71	0·84 (0·59 to 1·18)	−0·9 (−2·7 to 0·9)	0·32
Myocardial infarction*	64	56	1·14 (0·80 to 1·63)	0·6 (−1·1 to 2·4)	0·47
Stroke*	46	63	0·72 (0·49 to 1·06)	−1·4 (−3·1 to 0·2)	0·10
CV death, MI, or stroke	154	165	0·93 (0·74 to 1·15)	−1·0 (−3·9 to 1·9)	0·50
Heart failure*	61	29	2·10 (1·35 to 3·27)	2·6 (1·1 to 4·1)	0·0010

Data are numbers, HR (95% CI), or rate differences (95% CI). CV=cardiovascular. MI=myocardial infarction. *Fatal and non-fatal.

Table 4: **Deaths and hospitalisations from cardiovascular causes**

Home PD. Lancet 2009;373:2125-2135

Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlled trial

	First events			Total events	
	Pioglitazone (n=2605)	Placebo (n=2633)	HR (95% CI)	Pioglitazone	Placebo
Death	177	186	0·96 (0·78–1·18)	177	186
Non-fatal MI (including silent MI)	119	144	0·83 (0·65–1·06)	131	157
Stroke	86	107	0·81 (0·61–1·07)	92	119
Major leg amputation	26	26	1·01 (0·58–1·73)	28	28
Acute coronary syndrome	56	72	0·78 (0·55–1·11)	65	78
Coronary revascularisation	169	193	0·88 (0·72–1·08)	195	240
Leg revascularisation	80	65	1·25 (0·90–1·73)	115	92
Total	..	..	..	803	900

Data refer to first event of that particular type. MI=myocardial infarction.

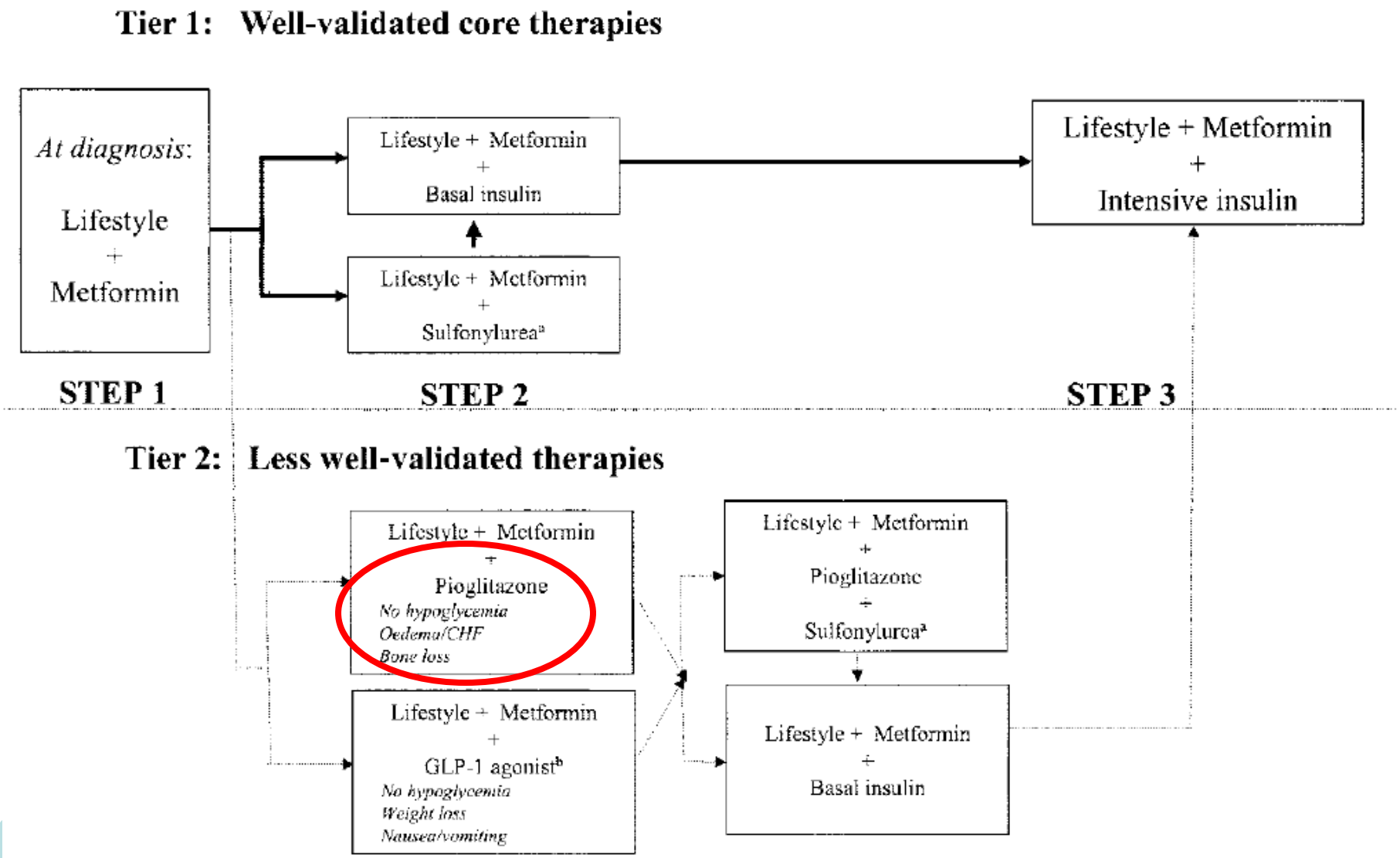
Table 4: **Effect of pioglitazone and placebo on each component of the primary endpoint**

Dormandy JA. Lancet 2005;373:1279-1289

TZD - dezavantajları

- Etkinliği uzun sürede ortaya çıkar
- Etkinliği doz bağımlı ve değişken
- Kilo artışına neden olur
- Su retansiyonu- ödem yapabilir
- Konjestif kalp yetmezliğinde kontrendike
- Lipid profiline etki
- Uzun süreli klinik deneyim (?)
- Kırık riski
- Karaciğer toksisitesi
- Pahalı

T2DM tedavisinde ADA-EASD konsensus algoritmi



UK

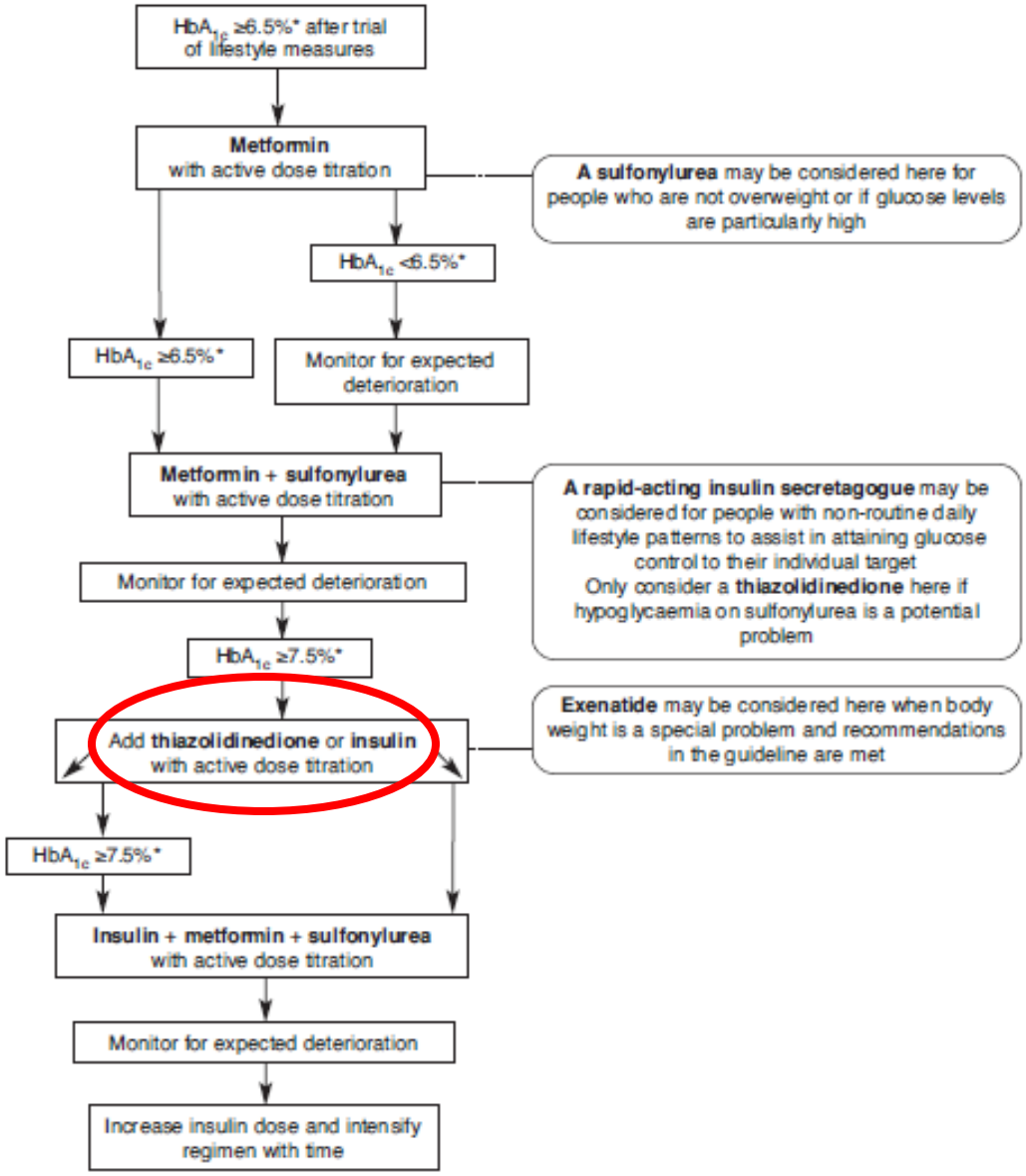
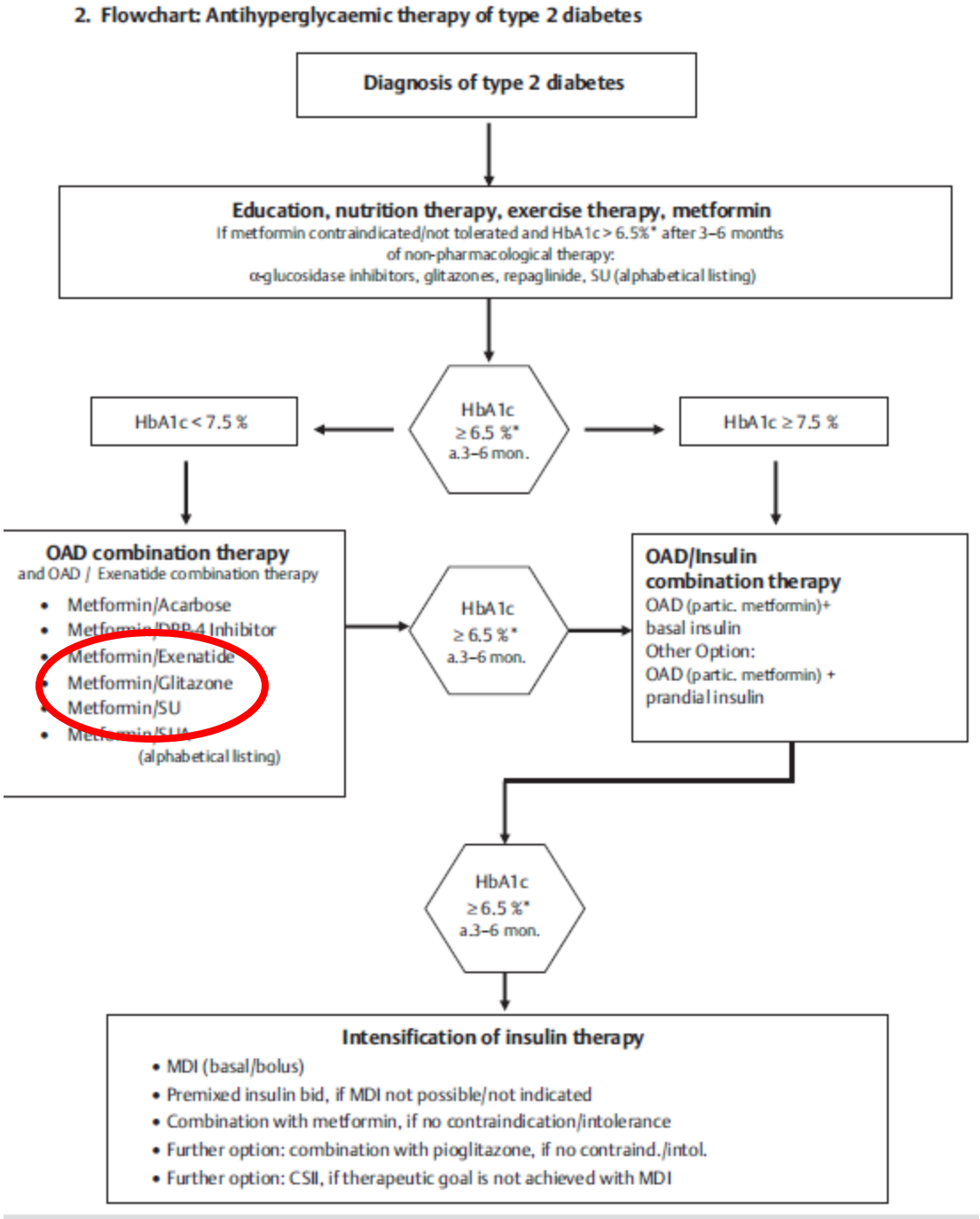


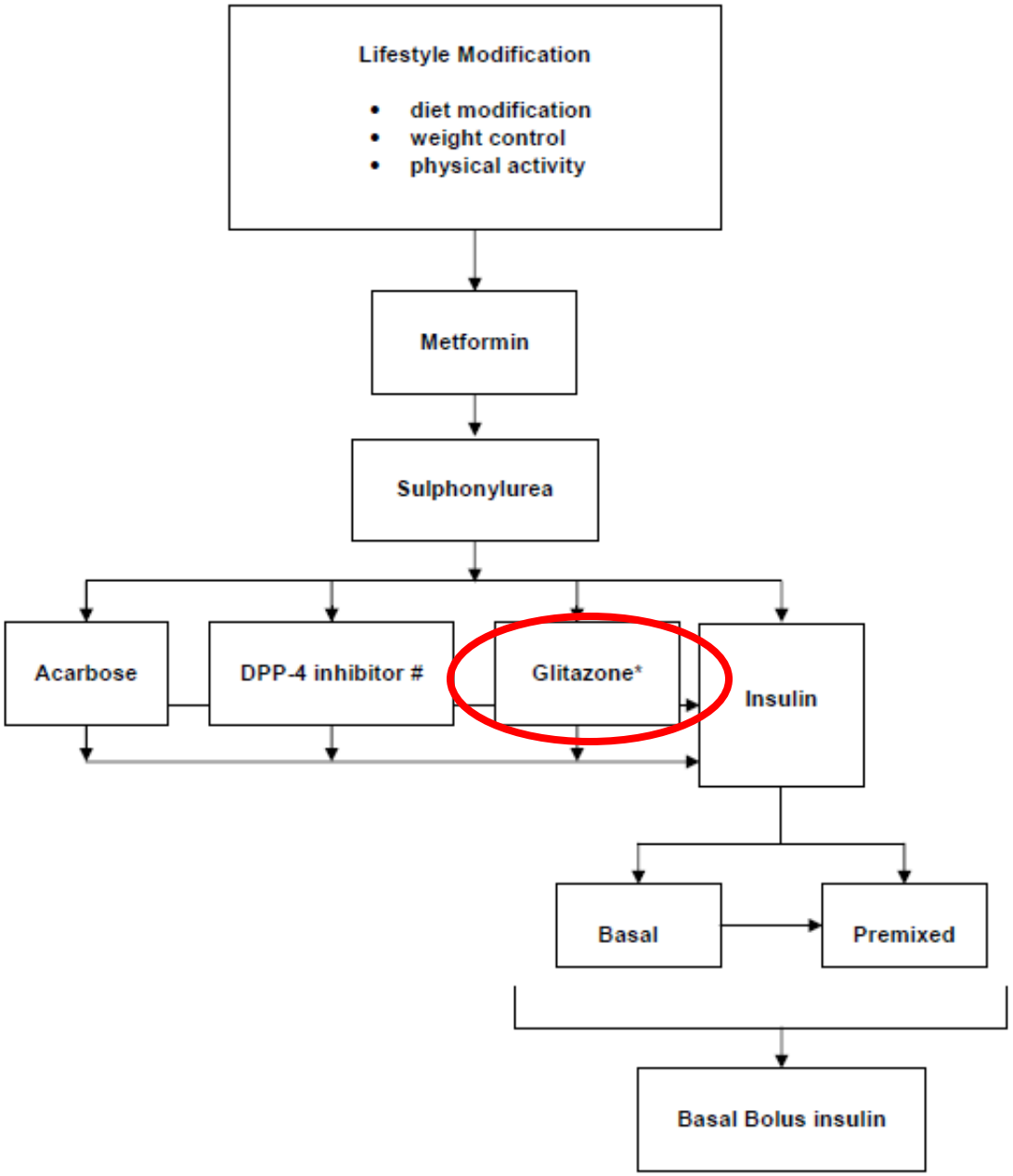
Figure 3.1 Scheme for the pharmacotherapy of glucose lowering in people with Type 2 diabetes
For details see recommendations on glucose lowering targets, clinical monitoring, use of oral agents, and use of insulin
* or as individually agreed

GER


2. Flowchart: Antihyperglycaemic therapy of type 2 diabetes
Diagnosis of type 2 diabetes
Education, nutrition therapy, exercise therapy, metformin
If metformin contraindicated/not tolerated and HbA1c > 6.5%* after 3–6 months of non-pharmacological therapy:
α-glucosidase inhibitors, glitazones, repaglinide, SU (alphabetical listing)
HbA1c ≥ 6.5 %* a.3–6 mon.
HbA1c < 7.5 %
HbA1c ≥ 7.5 %
OAD combination therapy
and OAD / Exenatide combination therapy
Metformin/Acarbose
Metformin/DPP-4 Inhibitor
Metformin/Exenatide
Metformin/Glitazone
Metformin/SU
(alphabetical listing)
HbA1c ≥ 6.5 %* a.3–6 mon.
OAD/Insulin combination therapy
OAD (partic. metformin)+ basal insulin
Other Option:
OAD (partic. metformin) + prandial insulin
HbA1c ≥ 6.5 %* a.3–6 mon.
Intensification of insulin therapy
MDI (basal/bolus)
Premixed insulin bid, if MDI not possible/not indicated
Combination with metformin, if no contraindication/intolerance
Further option: combination with pioglitazone, if no contraind./intol.
Further option: CSII, if therapeutic goal is not achieved with MDI

AUS

Management algorithm for blood glucose control in type 2 diabetes



Kanada

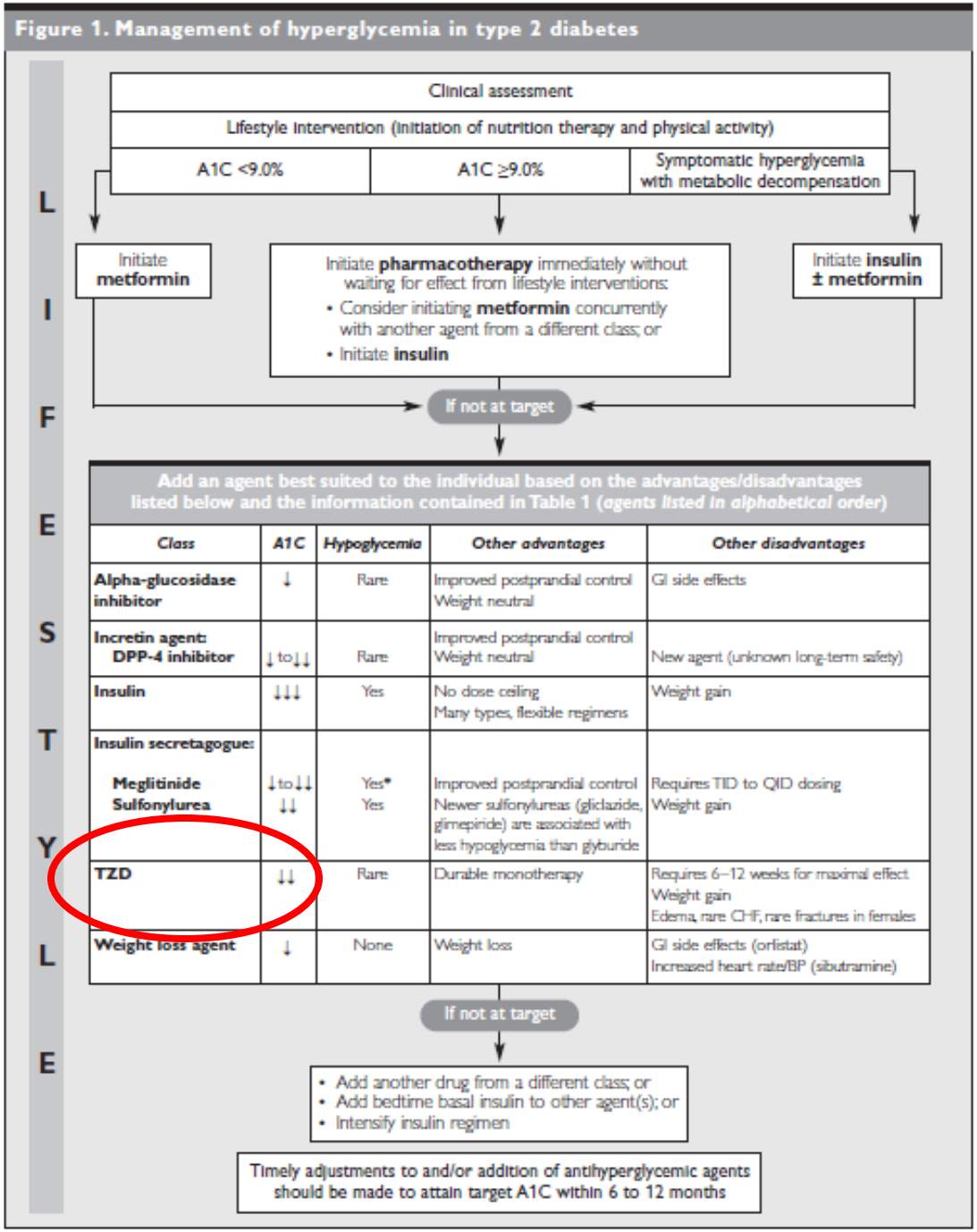


Figure 1. Management of hyperglycemia in type 2 diabetes
Clinical assessment
Lifestyle intervention (initiation of nutrition therapy and physical activity)
A1C <9.0%
A1C ≥9.0%
Symptomatic hyperglycemia with metabolic decompensation
Initiate metformin
Initiate pharmacotherapy immediately without waiting for effect from lifestyle interventions:
• Consider initiating metformin concurrently with another agent from a different class; or
• Initiate insulin
Initiate insulin ± metformin
If not at target
Add an agent best suited to the individual based on the advantages/disadvantages listed below and the information contained in Table 1 (agents listed in alphabetical order)
Class | A1C | Hypoglycemia | Other advantages | Other disadvantages
Alpha-glucosidase inhibitor | ↓ | Rare | Improved postprandial control, Weight neutral | GI side effects
Incretin agent: DPP-4 inhibitor | ↓ to ↓↓ | Rare | Improved postprandial control, Weight neutral | New agent (unknown long-term safety)
Insulin | ↓↓↓ | Yes | No dose ceiling, Many types, flexible regimens | Weight gain
Insulin secretagogue:
Meglitinide | ↓ to ↓↓ | Yes* | Improved postprandial control | Requires TID to QID dosing
Sulfonylurea | ↓↓ | Yes | Newer sulfonylureas (gliclazide, glimepiride) are associated with less hypoglycemia than glyburide | Weight gain
TZD | ↓↓ | Rare | Durable monotherapy | Requires 6–12 weeks for maximal effect, Weight gain, Edema, rare CHF, rare fractures in females
Weight loss agent | ↓ | None | Weight loss | GI side effects (orlistat), Increased heart rate/BP (sibutramine)
If not at target
• Add another drug from a different class; or
• Add bedtime basal insulin to other agent(s); or
• Intensify insulin regimen
Timely adjustments to and/or addition of antihyperglycemic agents should be made to attain target A1C within 6 to 12 months
LIFESTYLE

AACE/ACE Diabetes Algorithm *For Glycemic Control*

A1C Goal ≤ 6.5%*

LIFESTYLE MODIFICATION

A1C 6.5 – 7.5%**

Monotherapy

MET	TZD [2]	DPP4 [1]	AGI [3]

2 - 3 Mos.***

Dual Therapy

MET	+	GLP-1 or DPP4 [1]
		TZD [2]
		Glinide or SU [5]
TZD	+	GLP-1 or DPP4 [1]
MET	+	Colesevelam
		AGI [3]

2 - 3 Mos.***

Triple Therapy

MET + GLP-1 or DPP4 [1]	+	TZD [2]
		Glinide or SU [4,7]

2 - 3 Mos.***

INSULIN ± Other Agent(s) [6]

A1C 7.6 – 9.0%

Dual Therapy [8]

MET	+	GLP-1 or DPP4 [1,10]
		or TZD [2]
		SU or Glinide [4,5]

2 - 3 Mos.***

Triple Therapy [9]

MET	+	GLP-1 or DPP4 [1]	+ TZD [2]
		GLP-1 or DPP4 [1]	+ SU [7]
		TZD [2]	

2 - 3 Mos.***

INSULIN ± Other Agent(s) [6]

A1C > 9.0%

Drug Naive / *Under Treatment*

Symptoms / *No Symptoms*

INSULIN ± Other Agent(s) [6]

MET	+	GLP-1 or DPP4 [1]	+ SU [7]
		TZD [2]	
		GLP-1 or DPP4 [1]	+ TZD [2]

INSULIN ± Other Agent(s) [6]

AACE/ACE Algorithm for Glycemic Control Subcommittee

Cochairpersons:
Helena W. Rodbard, MD, FACP, MACE
Paul S. Jellinger, MD, MACE

Zachary T. Bloomgarden, MD, FACE
Jaime A. Davidson, MD, FACP, MACE
Daniel Einhorn, MD, FACP, FACE
Alan J. Garber, MD, PhD, FACE
James R. Gavin III, MD, PhD
George Grunberger, ND, FACP, FACE
Yehuda Handelsman, MD, FACP, FACE
Edward S. Horton, MD, FACE
Harold Lebovitz, MD, FACE
Philip Levy, MD, MACE
Etie S. Moghissi, MD, FACP, FACE
Stanley S. Schwartz, MD, FACE

* May not be appropriate for all patients

** For patients with diabetes and A1C ≤ 6.5%, pharmacologic Rx may be considered

*** If A1C goal not achieved safely

[1] DPP4 if ↑ PPG and ↑ FPG or GLP-1 if ↑↑ PPG

[2] TZD if metabolic syndrome and/or nonalcoholic fatty liver disease (NAFLD)

[3] AGI if ↑ PPG

[4] Glinide if ↑ PPG or SU if ↑ FPG

[5] Low-dose secretagogue recommended

[6] a) Discontinue insulin secretagogue with sulfonylurea insulin
b) Can use pramlintide with prandial insulin

[7] Decrease secretagogue by 50% when added to GLP-1 or DPP-4

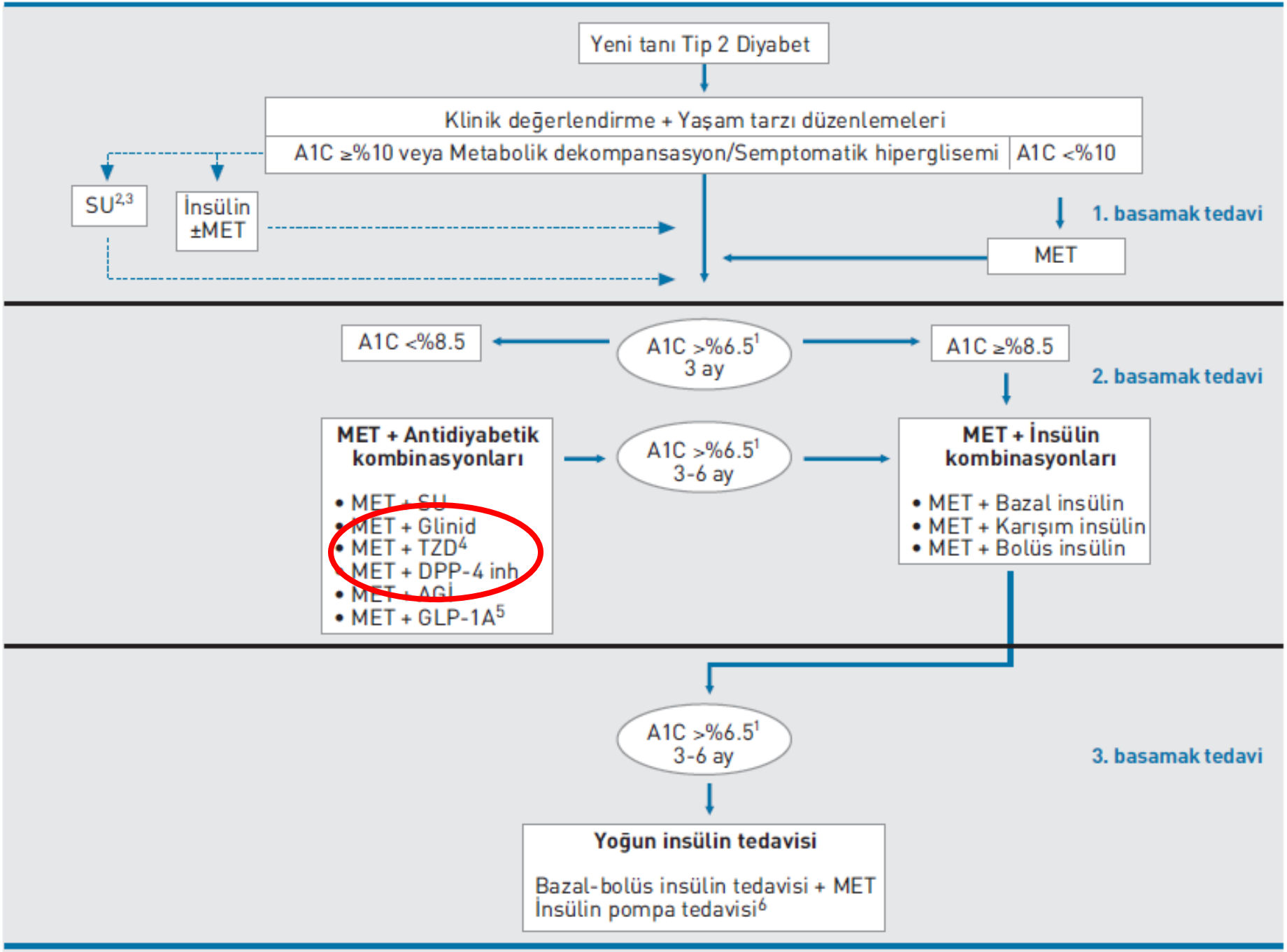
[8] If A1C <8.5%, combination Rx with agents that cause hypoglycemia should be used with caution

[9] If A1C > 9.5%, in patients on Dual Therapy, insulin should be considered

[10] GLP-1 not approved for initial combination Rx

Available at www.aace.com/pub

ŞEKİL 9.1 | **Tip 2 diyabetli hastalarda tedavi algoritması**



TZD lerin algoritmlerdeki yeri

- Monoterapide kullanılmazlar, kombinasyon tedavisinde kullanılırlar
- Kombinasyon tedavisinde insülin ile kombine edilmezler
- Etkinlik için en az 6 hafta beklenmelidir
- Kalp yetmezliği olanlarda kullanılmamalıdır
- Koroner arter hastalığı olanlarda roziglitazon kullanılmamalıdır
- NASH li hastalarda tercih edilebilir

DM tedavisinde kullanılabilecek ajanlar

- İnsülinler
- İnsülin analogları
- Alternatif insülin uygulama yöntemleri
- Endojen insülin salgılatıcıları
- Beta hücre rejenerasyonuna etkili ajanlar
- İnsülin mimetikler
- Karbohidrat sindirimini baskılayanlar
- Glukoz absorbsiyonunu baskılayanlar
- İnkretin hormon düzenleyiciler

- Sistemik insülin duyarlılaştırıcılar
- Hepatik insülin duyarlılaştırıcılar
- Global insülin duyarlılaştırıcılar
- GLP-1 agonistleri
- DPPIV inhibitörleri
- Amylin analogları
- Kontrinsüliner hormon baskılayıcıları
- Antilipolitik ajanlar
- Yağ asidi oksidasyonu inhibitörleri
- Glukoneogenez inhibitörleri
- VLDL sentez inhibitörleri
- Glikojenoliz inhibitörleri
- Obezite ilaçları