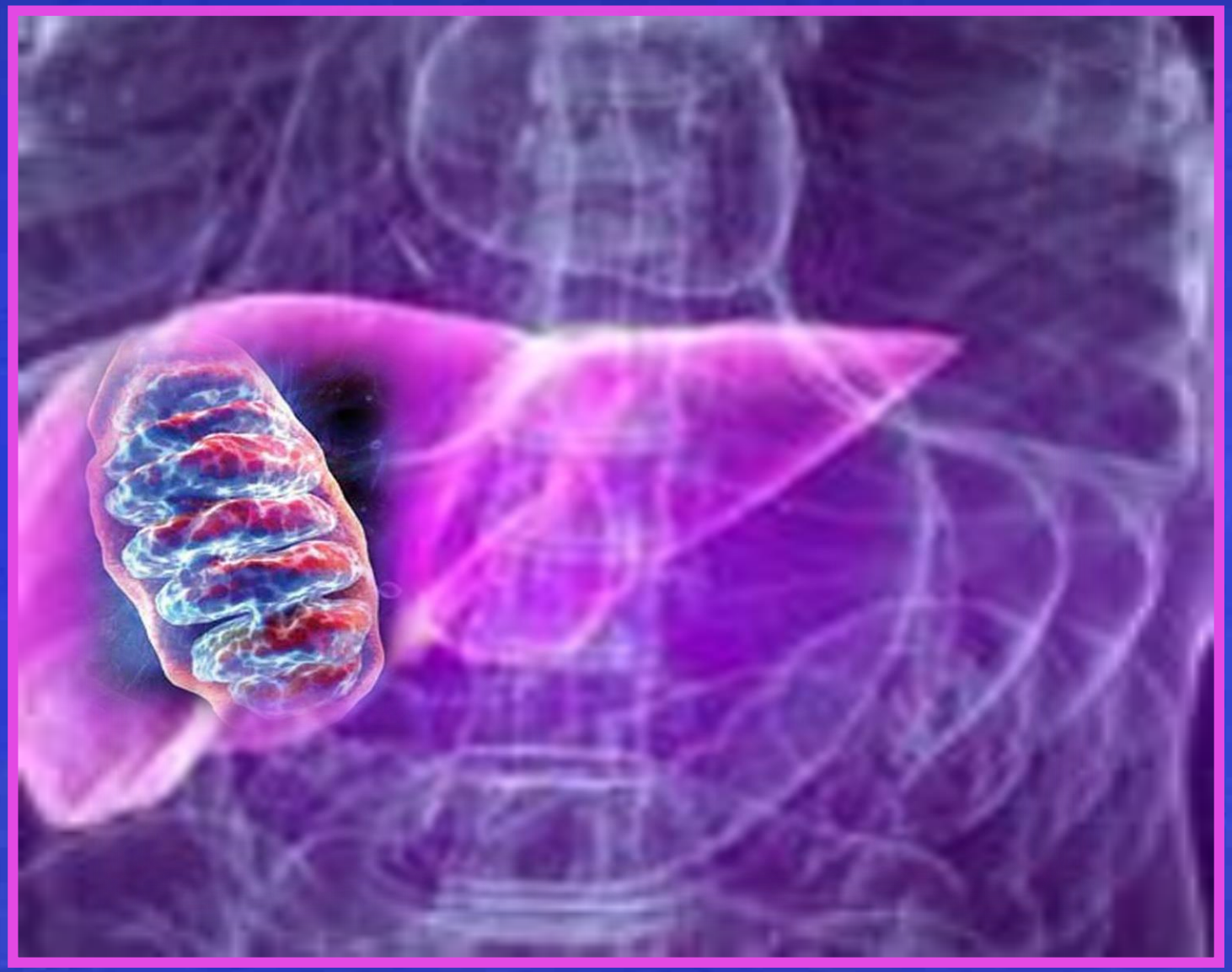
Φαρμακευτική αγωγή ασθενών με Σακχαρώδη Διαβήτη. Ο ρόλος της μετφορμίνης

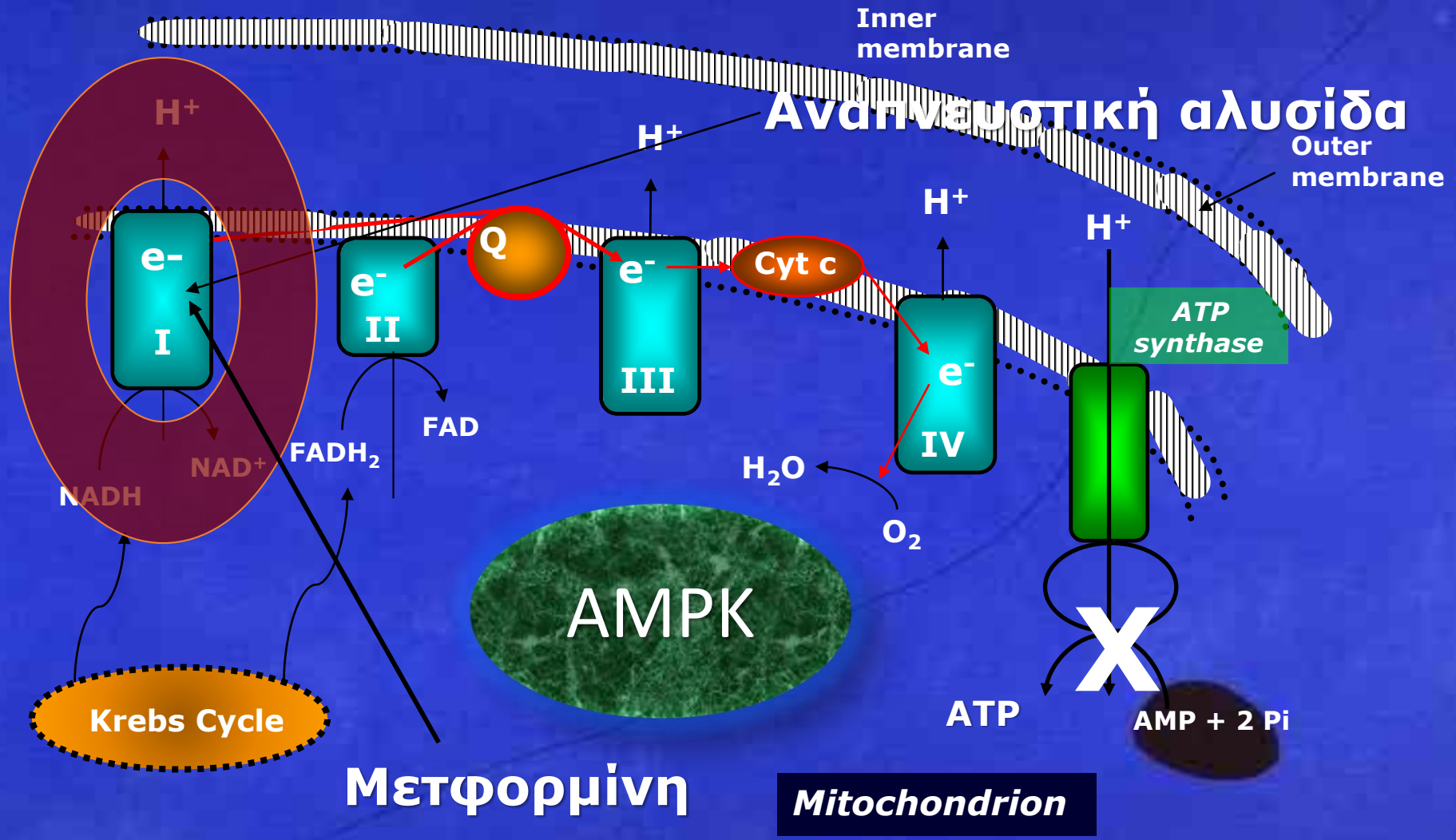
Ιωάννα Ζωγράφου
Διαβητολογικό Κέντρο
Β΄ Προπαιδευτική Παθολογική Κλινική Γ.Ν.Θ. Ιπποκράτειο


Μετφορμίνη

Η μετφορμίνη δρα στα μιτοχόνδρια των ηπατοκυττάρων



Η αναστολή της αναπνευστικής αλυσίδας ενεργοποιεί την AMPK...



Biochem. J. (2000) 348, 607±614

AMPK

- Ενεργοποιείται κάθε φορά που ελαττώνονται τα ενδοκυττάρια επίπεδα του ATP

- Επάγει καταβολικές αντιδράσεις και αναστέλλει αναβολικές αντιδράσεις ώστε τα επίπεδα του ATP να επανέλθουν στο φυσιολογικό

Zhou G et al , J Clin Invest. 2001;108(8):1167

Ο κεντρικός κυτταρικός αισθητήρας και ρυθμιστής του ενεργειακού μεταβολισμού

Clinical Science 2012; 122: 253–270

Luengo et al. BMC Biology 2014, 12:82

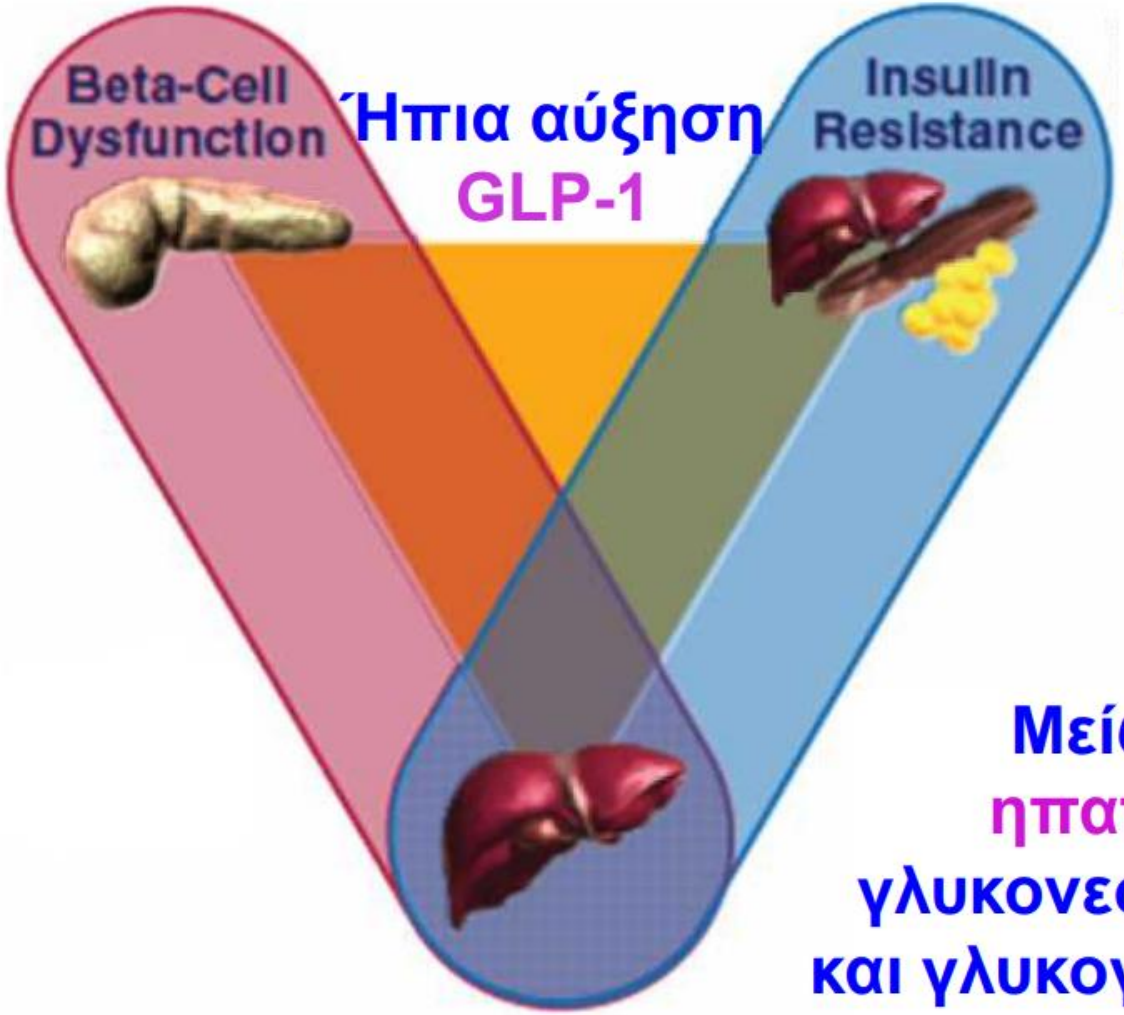
Ενεργοποίηση
AMPK

Αντιγήρανση

Μακροζωία

Cell Reports, 2014; DOI: 10.1016/j.celrep.2014.08.006
Luengo et al. BMC Biology 2014, 12:82

Μηχανισμοί δράσης της μεταφορμίνης



Ήπια αύξηση GLP-1

Αύξηση ινσουλινοευαισθησίας β-κυττάρων παγκρέατος, μυών, λιπώδους ιστού

Μείωση ηπατικής γλυκονεογένεσης και γλυκογονόλυσης

Diabetology & Metabolic Syndrome 2013;5:6

Η μετφορμίνη έχει συγκεκριμένα πλεονεκτήματα

αποτελεσματική

↓υπογλυκαιμίες

δεν αυξάνει το σωματικό βάρος

φθηνή

2017

th Monotherapy unless:

eater than or equal to 9%, **consider Dual Therapy.**

C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 8.2).

Monotherapy — Metformin — Lifestyle Management

EFFICACY*	high
HYPO RISK	low risk
WEIGHT	neutral/loss
SIDE EFFECTS	GI/lactic acidosis
COSTS*	low

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Dual Therapy — Metformin + — Lifestyle Management

	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
EFFICACY*	high	high	intermediate	intermediate	high	highest
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk
WEIGHT	gain	gain	neutral	loss	loss	gain
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
COSTS*	low	low	high	high	high	high

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Triple Therapy — Metformin + — Lifestyle Management

Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +
TZD	SU	SU	SU	SU	TZD
or DPP-4-i	or DPP-4-i	or TZD	or TZD	or TZD	or DPP-4-i
or SGLT2-i	or SGLT2-i	or SGLT2-i	or DPP-4-i	or SGLT2-i	or SGLT2-i
or GLP-1-RA	or GLP-1-RA	or Insulin†	or GLP-1-RA	or Insulin†	or GLP-1-RA
or Insulin†	or Insulin†		or Insulin†		

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

Combination Injectable Therapy (See Figure 8.2)

METFORMIN

OLD OR GOLD ?

2021

depends on comorbidities, patient-centered treatment factors, including cost and access considerations, and gement needs and generally includes metformin and comprehensive lifestyle modification^

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

ICATORS OF HIGH RISK, HF, CKD†

NONE

RECOMMEND INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE‡

+ASCVD/INDICATORS OF HIGH RISK*

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

IF A1C ABOVE TARGET

- For patients on a GLP-1 RA, consider incorporating SGLT2i with proven CVD benefit and vice versa[1]
- TZD[2]

+HF*

SGLT2i with proven benefit in this population[1]

+CKD**

CKD and albuminuria (e.g., ≥200 mg/g creatinine)

CKD without albuminuria (e.g., eGFR <60 mL/min/1.73 m²)

PREFERABLY

SGLT2i with primary evidence of reducing CKD progression

OR

SGLT2i with evidence of reducing CKD progression in CVOTs

OR

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

For patients with CKD (e.g., eGFR <60 mL/min/1.73 m²) without albuminuria, recommend the following to decrease cardiovascular risk

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

If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA and vice versa

If A1C remains above target, consider treatment intensification based on comorbidities, patient-centered treatment factors, and management needs

Incorporate agents that provide adequate EFFICACY to achieve and maintain glycemic goals

Higher glycemic efficacy therapy: GLP-1 RA; insulin; combination approaches (Table 9.2)

- **Consider additional comorbidities, patient-centered treatment factors, and management needs in choice of therapy, as below:**

MINIMIZE HYPOGLYCEMIA

No/low inherent risk of hypoglycemia: DPP-4i, GLP-1 RA, SGLT2i, TZD

For SU or basal insulin, consider agents with lower risk of hypoglycemia[3,4]

IF A1C ABOVE TARGET

Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

MINIMIZE WEIGHT GAIN/ PROMOTE WEIGHT LOSS

PREFERABLY

GLP-1 RA with good efficacy for weight loss

OR

SGLT2i

IF A1C ABOVE TARGET

For patients on a GLP-1 RA, consider incorporating SGLT2i and vice versa

- If GLP-1 RA not tolerated or indicated, consider DPP-4i (weight neutral)

Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

CONSIDER COST AND ACCESS

Available in generic form at lower cost:

- Certain insulins: consider insulin available at the lowest acquisition cost
- SU
- TZD

IF A1C ABOVE TARGET

Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

1. Proven benefit refers to label indication (see Table 9.2)
2. Low dose may be better tolerated though less well studied for CVD effects
3. Choose later generation SU to lower risk of hypoglycemia
4. Risk of hypoglycemia: degludec / glargine U-300 < glargine U-100 / detemir < NPH insulin
5. Consider country- and region-specific cost of drugs

^For adults with overweight or obesity, lifestyle modification to achieve and maintain ≥5% weight loss and ≥150 min/week of moderate- to vigorous-intensity physical activity is recommended (See Section 5: Facilitating Behavior Change and Well-being to Improve Health Outcomes).
†Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.
‡Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.
*Refer to Section 10: Cardiovascular Disease and Risk Management.
**Refer to Section 11: Chronic Kidney Disease and Risk Management and specific medication label for eGFR criteria.

FIRST-LINE THERAPY depends on comorbidities, patient-centered treatment factors, including cost and access considerations, and management needs and generally includes metformin and comprehensive lifestyle modification^

RECOMMEND INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE‡

+ASCVD/INDICATORS OF HIGH RISK*

EITHER/OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1]

IF A1C ABOVE TARGET

- For patients on a GLP-1 RA, consider incorporating SGLT2i with proven CVD benefit and vice versa[1]
- TZD[2]

+HF*

SGLT2i with proven benefit in this population[1]

+CKD**

- CKD and albuminuria (e.g., ≥200 mg/g creatinine)
- CKD without albuminuria (e.g., eGFR <60 mL/min/1.73 m²)

PREFERABLY

SGLT2i with primary evidence of reducing CKD progression

OR

SGLT2i with evidence of reducing CKD progression in CVOTs

OR

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

For patients with CKD (e.g., eGFR <60 mL/min/1.73 m²) without albuminuria, recommend the following to decrease cardiovascular risk

EITHER/OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1]

If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA and vice versa

If A1C remains above target, consider treatment intensification based on comorbidities, patient-centered treatment factors, and management needs

Incorporate agents that provide adequate EFFICACY to achieve and maintain glycemic goals

Higher glycemic efficacy therapy: GLP-1 RA; insulin; combination approaches (Table 9.2)

- **Consider additional comorbidities, patient-centered treatment factors, and management needs in choice of therapy, as below:**

MINIMIZE HYPOGLYCEMIA

No/low inherent risk of hypoglycemia: DPP-4i, GLP-1 RA, SGLT2i, TZD

For SU or basal insulin, consider agents with lower risk of hypoglycemia[3,4]

IF A1C ABOVE TARGET

Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

MINIMIZE WEIGHT GAIN/ PROMOTE WEIGHT LOSS

PREFERABLY

GLP-1 RA with good efficacy for weight loss

OR

SGLT2i

IF A1C ABOVE TARGET

For patients on a GLP-1 RA, consider incorporating SGLT2i and vice versa

- If GLP-1 RA not tolerated or indicated, consider DPP-4i (weight neutral)

Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

CONSIDER COST AND ACCESS

Available in generic form at lower cost:

- Certain insulins: consider insulin available at the lowest acquisition cost
- SU
- TZD

IF A1C ABOVE TARGET

Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

1. Proven benefit refers to label indication (see Table 9.2)
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†Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.
‡Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.
*Refer to Section 10: Cardiovascular Disease and Risk Management.
**Refer to Section 11: Chronic Kidney Disease and Risk Management and specific medication label for eGFR criteria.

2022

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.

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

2022

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GLP-1 RA# with proven CVD benefit **EITHER/OR** SGLT2i§ with proven CVD benefit

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Current or prior symptoms of HF with documented HFrEF or HFpEF

+HF

SGLT2i§ with proven HF benefit in this population

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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

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Neutral:
DPP-4i, Metformin

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Neutral:
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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.

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

HEALTHY LIFESTYLE B… -MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)

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

+HF
Current or prior symptoms of HF with documented HFrEF or HFpEF

Goal: Cardiorenal Risk Reduction in High-Risk Patients wit… …prehensive 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 ris…
While definitions vary, mos… comprise ≥ 55 years of ag… with two or more additiona… risk factors (including obes… hypertension, smoking dyslipidaemia or albuminur…

+CKD
eGFR < 60 mL/min per 1.73 m² OR albuminuria (ACR ≥ 3.0 mg/mmol (30mg/g)). These measurements may vary over time; thus, a repeat …easure is required to document CKD.

+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
SGLT2i[§] with proven HF benefit in this population

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

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 additional cardiorenal risk reduction or glycaemic lowering needed

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

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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

+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 symptoms of HF documented HFrEF or

SGLT2i[§] with proven HF benefit in this population

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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.

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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

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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:

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

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

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

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eGFR < 60 ml/min per 1.73 m² OR albuminuria (ACR ≥ 3.0 mg/mmol (30mg/g)). These measurements may vary over time; thus, a repeat measure is required to document CKD.

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

+ASCV

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Very High:
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Neutral:
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If additional cardiorenal risk reduction or glycaemic lowering needed

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Identify barriers to goals:

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

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

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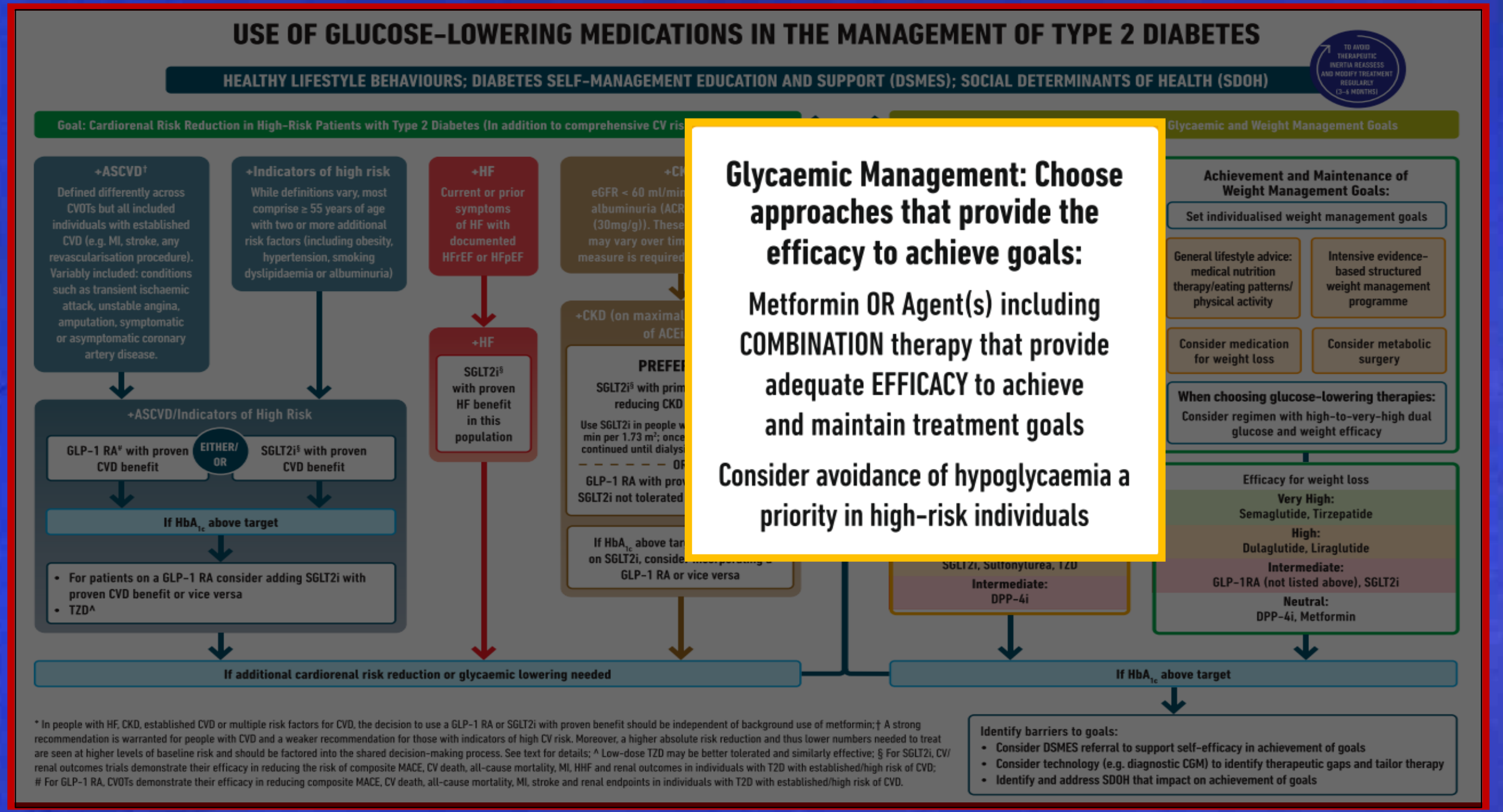

Glycaemic Management: Choose approaches that provide the efficacy to achieve goals:

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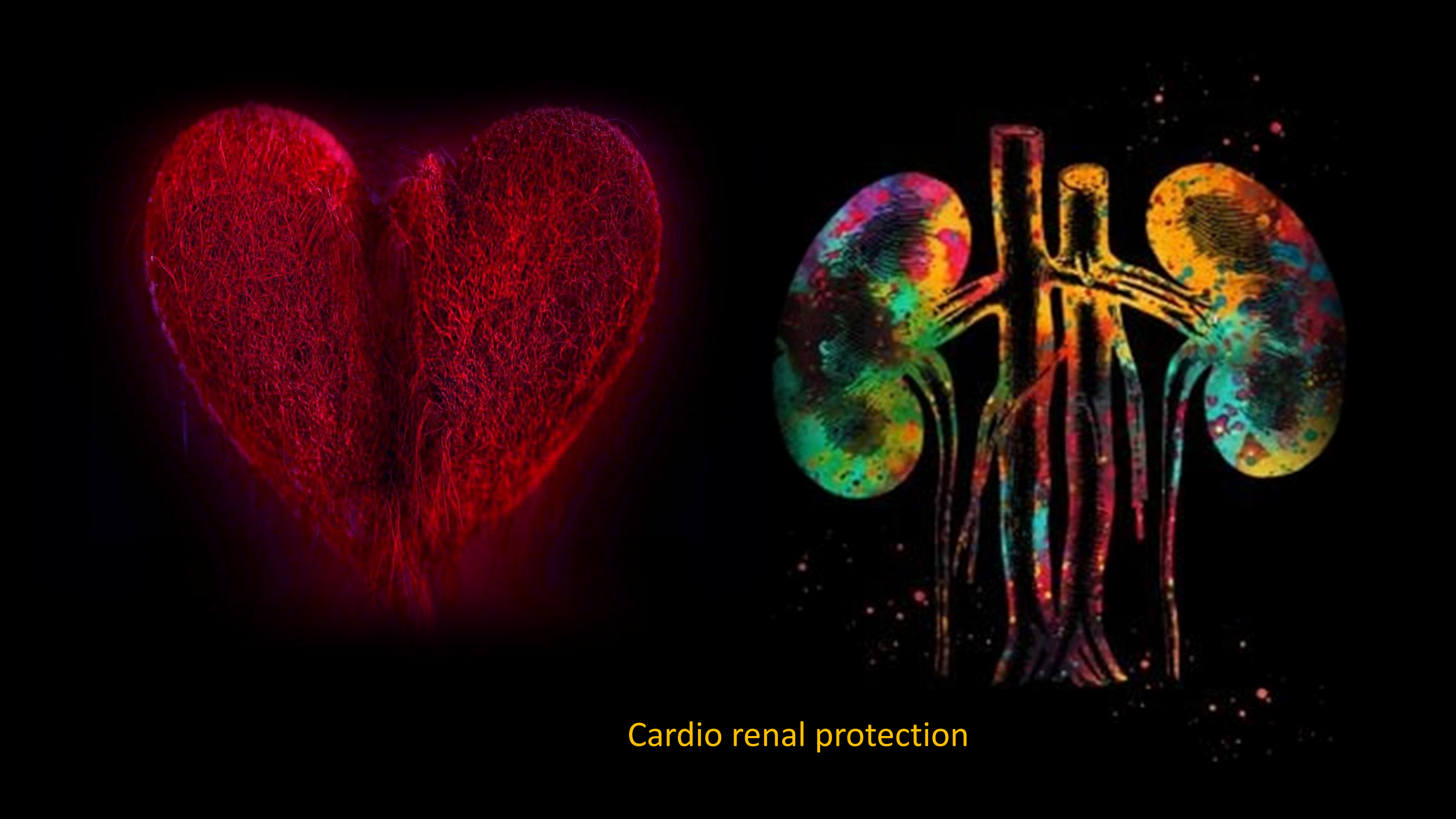
Consider avoidance of hypoglycaemia a priority in high-risk individuals

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

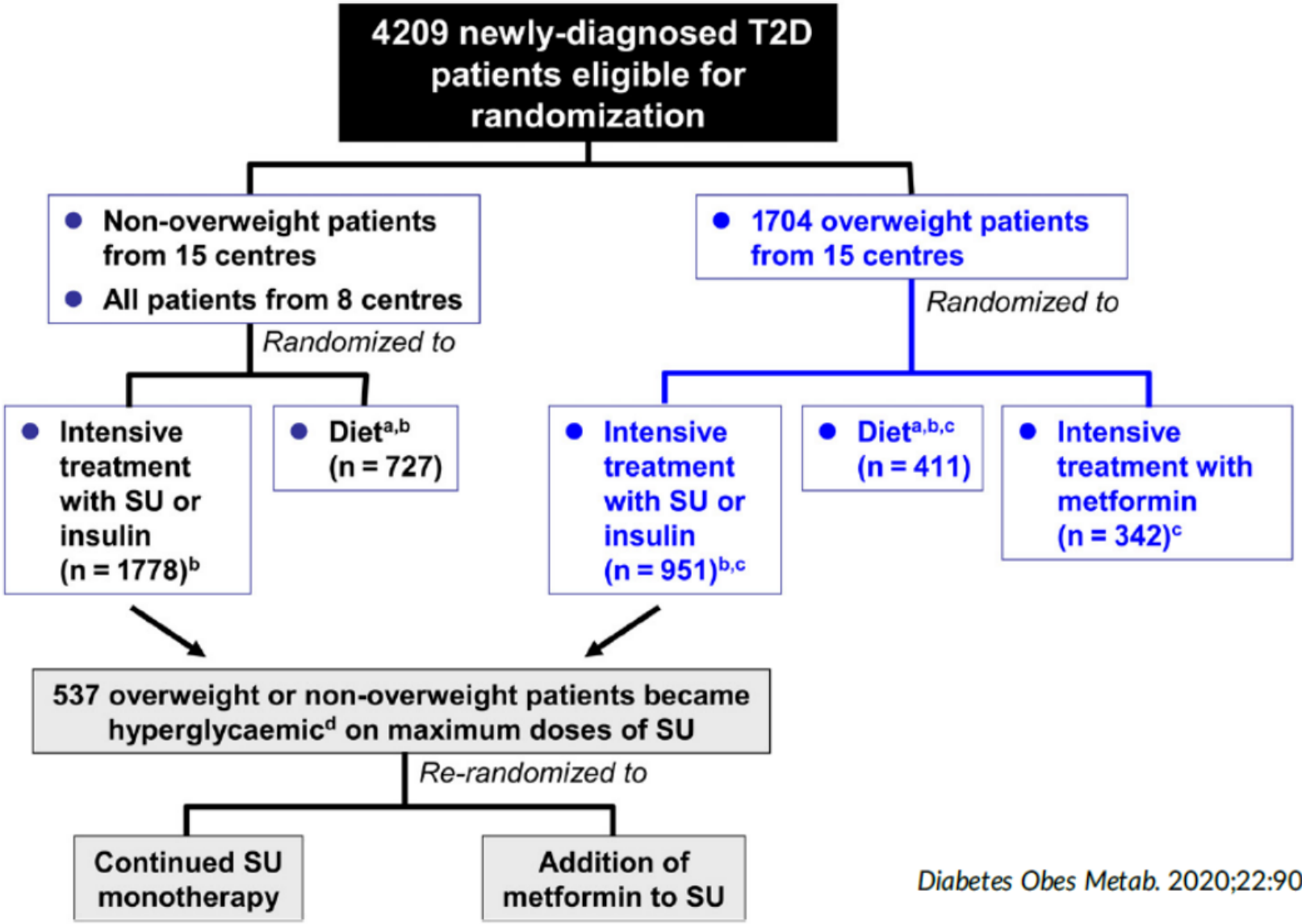


Cardio renal protection


Η μετφορμίνη τι έχει να μας προσφέρει;

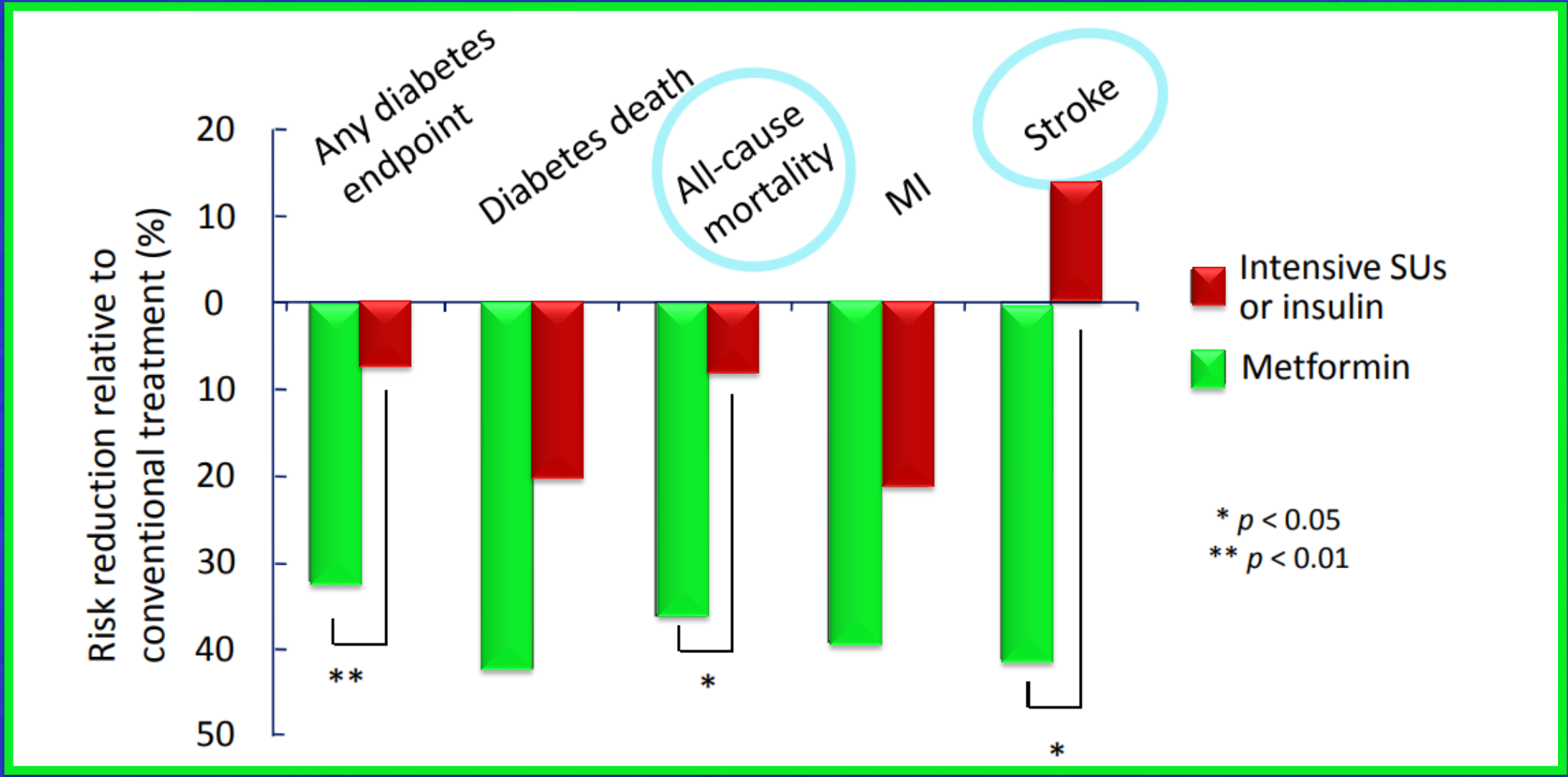
Με τη UKPDS, η μετφορμίνη αναδείχθηκε στην Ευρώπη ως άριστη και ασφαλής αντιδιαβητική αγωγή

UK Prospective Diabetes Study



Diabetes Obes Metab. 2020;22:904–915

UKPDS 34: ΣΥΓΚΡΙΣΗ ΤΩΝ ΟΜΑΔΩΝ SU/ΙΝΣΟΥΛΙΝΗΣ ΚΑΙ ΜΕΤΦΟΡΜΙΝΗΣ



UKPDS 34: Lancet 1998;352:854–65

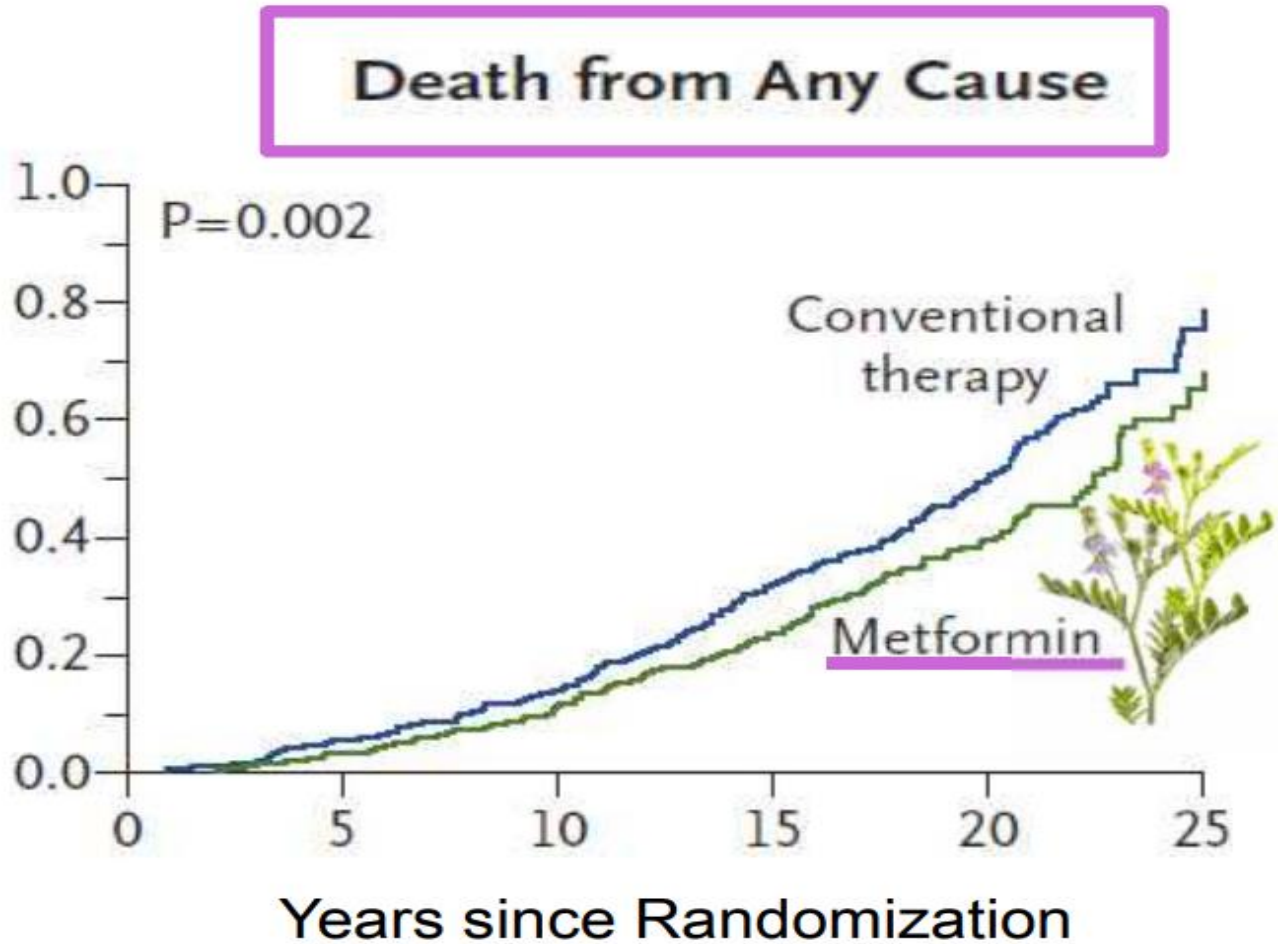
Legacy effect 10 years after metformin

Aggregate Endpoint		1997	2007
Any diabetes related endpoint	*RRR:*	32%	**21%**
	P:	0.0023	**0.013**
Microvascular disease	*RRR:*	29%	**16%**
	P:	0.19	**0.31**
Myocardial infarction	*RRR:*	39%	**33%**
	P:	0.010	**0.005**
All-cause mortality	*RRR:*	36%	**27%**
	P:	0.011	**0.002**

RRR – Relative Risk Reduction, P – Log Rank

UKPDS 80.N Eng J Med 2008;359:1577-1589

UKPDS open: λιγότεροι συνολικοί θάνατοι στην ομάδα της μετφορμίνης έως και 25 χρόνια μετά



Hollman RR et al, N Engl J Med. 2008; 359(15):1577

HOME trial

ORIGINAL INVESTIGATION

Long-term Effects of Metformin on Metabolism and Microvascular and Macrovascular Disease in Patients With Type 2 Diabetes Mellitus

Adriaan Kooy, MD, PhD; Jolien de Jager, MD; Philippe Lehert, PhD; Daniël Bets, MSc; Michiel G. Wulffelé, MD, PhD; Ab J. M. Donker, MD, PhD; Coen D. A. Stehouwer, MD, PhD

Arch Intern Med. 2009;169(6):616-625.
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HOME trial

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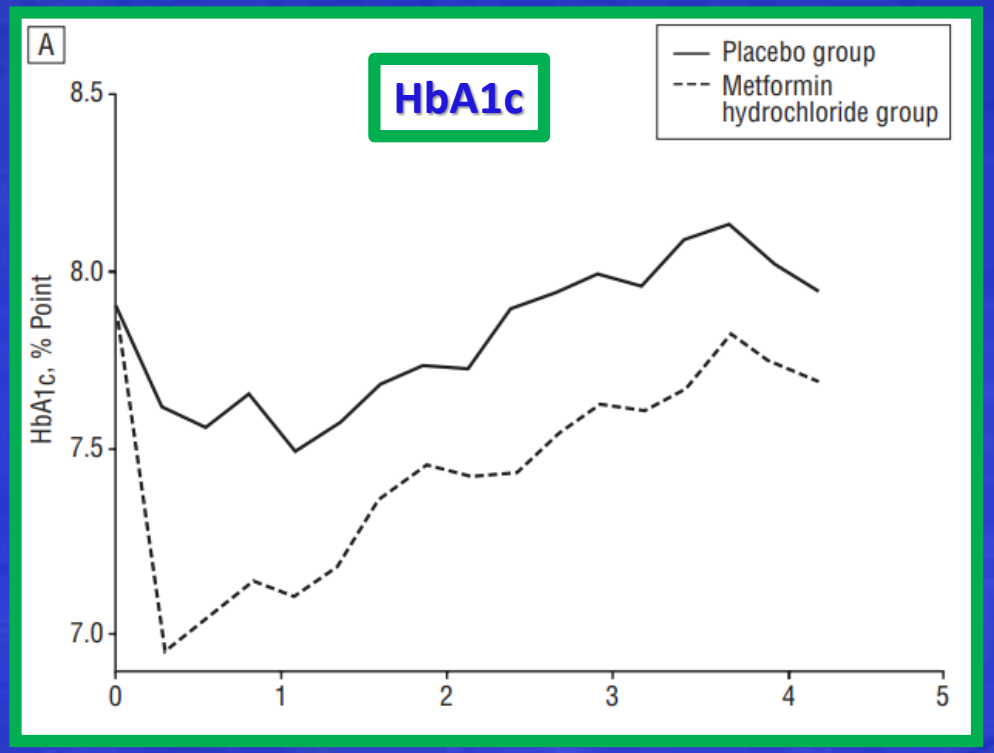
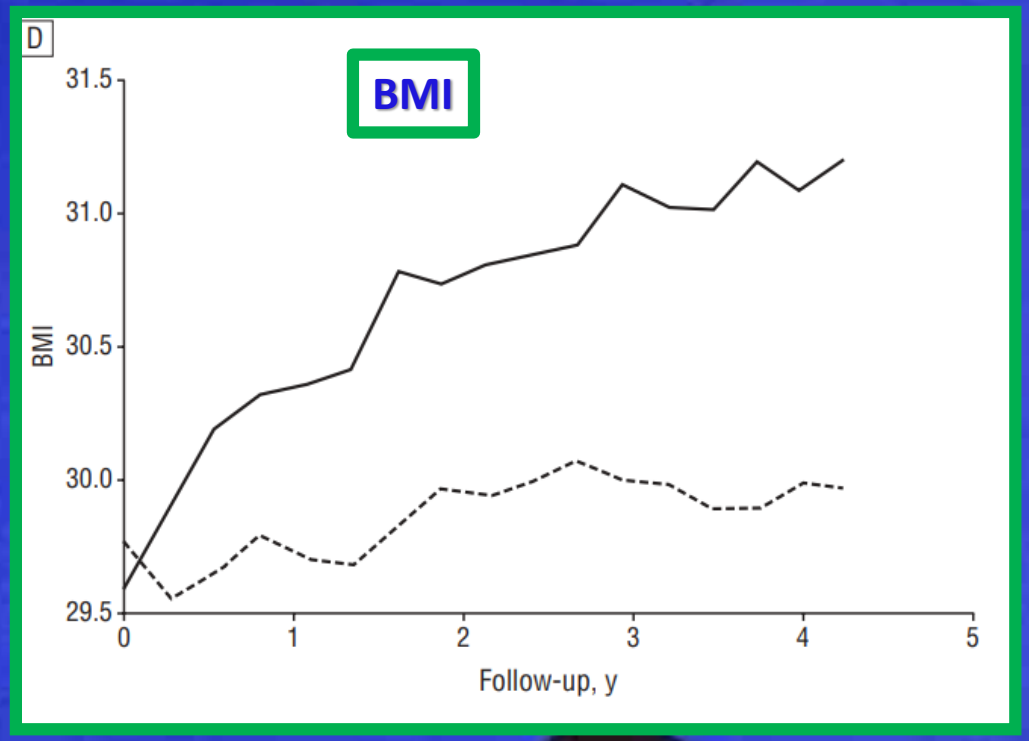
Double-blind RCT metformin vs placebo added to patients treated with insulin
n= 390
Primary end point: an aggregate of microvascular and macrovascular morbidity and mortality
The secondary end points: microvascular and macrovascular morbidity and mortality, as separate aggregate scores.

Arch Intern Med. 2009;169(6):616-625.
doi:10.1001/archinternmed.2009.20

HOME trial

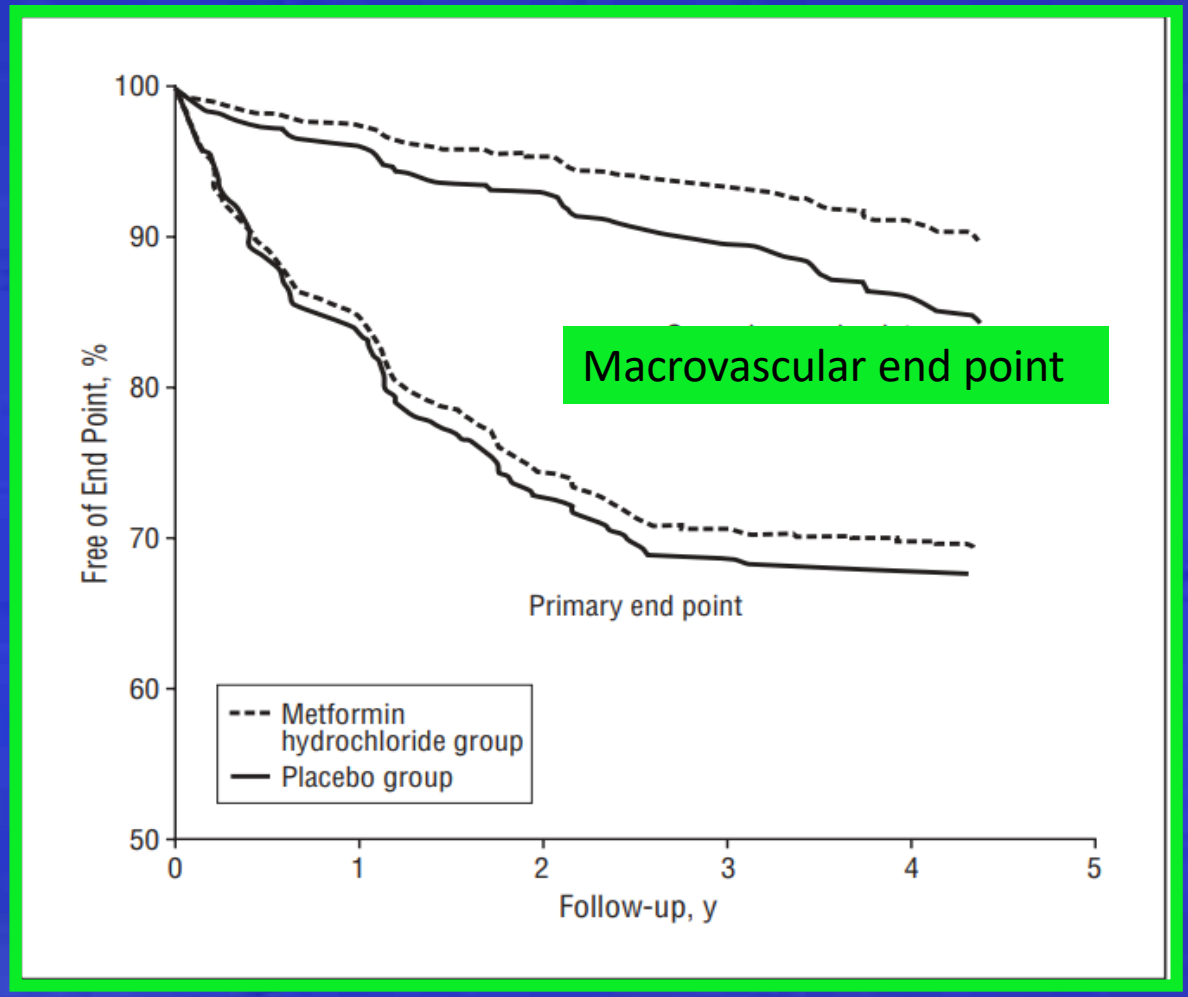




Arch Intern Med. 2009;169(6):616-625.
doi:10.1001/archinternmed.2009.20

HOME trial

Metformin treatment was not associated with an improvement in the primary end point



The number needed to treat to prevent 1 macrovascular end point was 16 (95% confidence interval, 9-67)

Arch Intern Med. 2009;169(6):616-625.
doi:10.1001/archinternmed.2009.20

SPREAD-DIMCAD

Cardiovascular and Metabolic Risk
ORIGINAL ARTICLE

Effects of Metformin Versus Glipizide on Cardiovascular Outcomes in Patients With Type 2 Diabetes and Coronary Artery Disease

DIABETES CARE, VOLUME 36, MAY 2013

SPREAD-DIMCAD

Treatment with metformin for 3 years substantially reduced major cardiovascular events in a median follow-up of 5.0 years compared with glipizide.

DIABETES CARE, VOLUME 36, MAY 2013

ORIGINAL INVESTIGATION Open Access

Effect of metformin on all-cause and cardiovascular mortality in patients with coronary artery diseases: a systematic review and an updated meta-analysis

Yechen Han[1,2], Hongzhi Xie[1,2], Yongtai Liu[1,2], Peng Gao[1,2], Xufei Yang[1,2] and Zhujun Shen[1,2*]

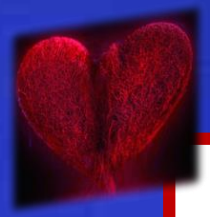
Σκοπός της συστηματικής ανασκόπησης και μετα-ανάλυσης είναι η εκτίμηση των επιδράσεων της μετφορμίνης στη θνητότητα και την καρδιακή λειτουργία σε ασθενείς με στεφανιαία νόσο (CAD)

Han et al. Cardiovasc Diabetol (2019) 18:96

40 μελέτες με 1.066.408 ασθενείς

Metformin reduces cardiovascular mortality, all-cause mortality and CV events in CAD patients.

Han et al. Cardiovasc Diabetol (2019) 18:96



Metformin Use Is Associated With a Lower Risk of Hospitalization for Heart Failure in Patients With Type 2 Diabetes Mellitus: a Retrospective Cohort Analysis

Chin-Hsiao Tseng, MD, PhD

American Heart Association.

Η χρήση μετφορμίνης σε ασθενείς με ΣΔτ2 σχετίζεται με χαμηλότερο κίνδυνο νοσηλείας για καρδιακή ανεπάρκεια

Journal of the American Heart Association. 2019;8:e011640

ORIGINAL INVESTIGATION

Open Access

Metformin treatment in heart failure with preserved ejection fraction: a systematic review and meta-regression analysis

Amera Halabi[1,2], Jonathan Sen[1,4], Quan Huynh[1,2] and Thomas H. Marwick[1,2,3*]

Halabi et al. Cardiovasc Diabetol (2020) 19:124
https://doi.org/10.1186/s12933-020-01100-w

Table 1 Characteristics of included studies for incident heart failure outcomes in patients with a reported ejection fraction ≥ 50%

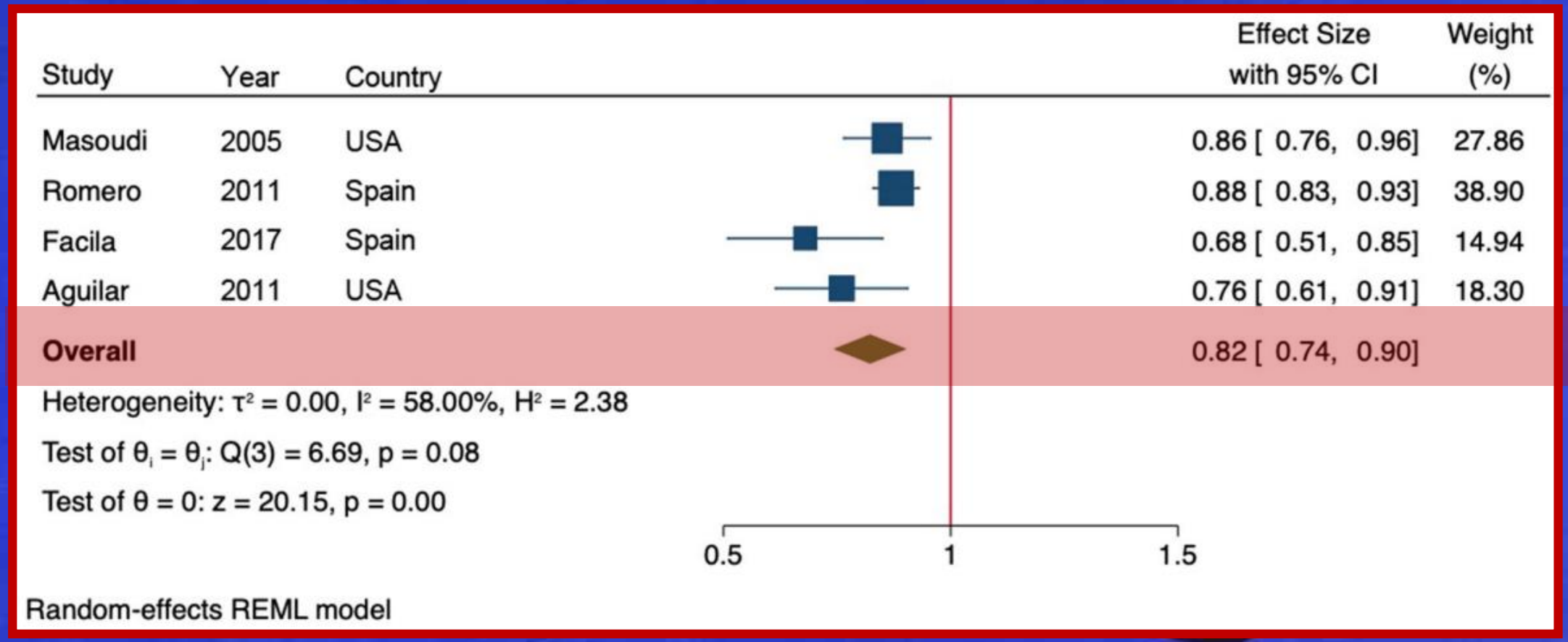
Study	Year	Country	Design	Population	Sample Size	Mean age (years)	Sex (% females)	% of patients with LVEF ≥ 50%	Follow-up (years)
Masoudi et al. [20]	2005	USA	Observational, retrospective cohort	T2DM, age ≥ 65 years, hospitalisation with HF	13,930	76	58	23	1.0
Romero et al. [21]	2011	Spain	Observational, prospective cohort	New-onset T2DM, HF	1519	72	54	51	4.7
Facila et al. [19]	2017	Spain	Observational, retrospective cohort	T2DM, discharged with diagnosis of acute decompensated HF	835	72	49	49	2.4
Aguilar et al. [18]	2011	USA	Observational, retrospective cohort	T2DM, prior diagnosis of HF	6185	68	7	45[a]	2

T2DM type 2 diabetes mellitus, *HF* heart failure, *USA* United States of America, *LVEF* left ventricular ejection fraction

[a] Study reported percentage of patients with LVEF≥ 40%

Halabi et al. Cardiovasc Diabetol (2020) 19:124
https://doi.org/10.1186/s12933-020-01100-w

Meta-analysis of effect estimates for mortality in heart failure patients treated with metformin therapy



Halabi et al. Cardiovasc Diabetol (2020) 19:124
https://doi.org/10.1186/s12933-020-01100-w

ΜΕΤΦΟΡΜΙΝΗ:ΥΠΟΧΩΡΗΣΗ ΚΑΡΔΙΑΚΗΣ ΙΝΩΣΗΣ

Cardiovascular Research (2010) 87, 504–513

Effect of metformin on cardiovascular outcomes in randomized trials

Study (Reference)	Participants	Comparator	Endpoint	RR/HR/OR (95% CI)
Individual Trial				
UKPDS 1998 [61]	Newly diagnosed T2DM, $n = 753$	Diet	All-cause mortality	0.64 (0.45–0.91)
			Any diabetes related endpoint	0.68 (0.53–0.87)
UKPDS 2008 [3]	Newly diagnosed T2DM, $n = 753$	Diet	All-cause mortality	0.73 (0.59–0.89)
			Any diabetes related endpoint	0.79 (0.66–0.95)
HOME 2009 [62]	Insulin using T2DM, $n = 390$	Placebo	Macrovascular aggregate score	0.61 (0.40–0.94)
SPREAD-DIMCAD 2013 [63]	T2DM with coronary artery disease, $n = 304$	Sulfonylurea	Macrovascular aggregate score	0.54 (0.30–0.90)
Meta analysis	**Trials**			
Lamanna 2011 [57]	10	No therapy, placebo, active comparators	All-cause mortality	1.10 (0.80–1.51)
	12		Cardiovascular events	0.94 (0.82–1.07)
Boussageon 2012 [58]	11	Diet, placebo, no treatment, metformin add-on, metformin withdrawal	All-cause mortality	0.99 (0.75–1.31)
	10		Myocardial infarction	0.90 (0.74–1.09)
Griffin 2017 [59]	13	Diet, lifestyle, placebo	All-cause mortality	0.96 (0.84–1.09)
	7		Myocardial infarction	0.89 (0.75–1.06)
Monami 2021 [64]	13	Placebo/no therapy, active comparators	All-cause mortality	0.80 (0.60–1.07)
	2		MACE	0.52 (0.37–0.73)

Pharmaceuticals 2022, 15, 312. https://doi.org/10.3390/ph15030312

Effect of metformin on cardiovascular outcomes in randomized trials

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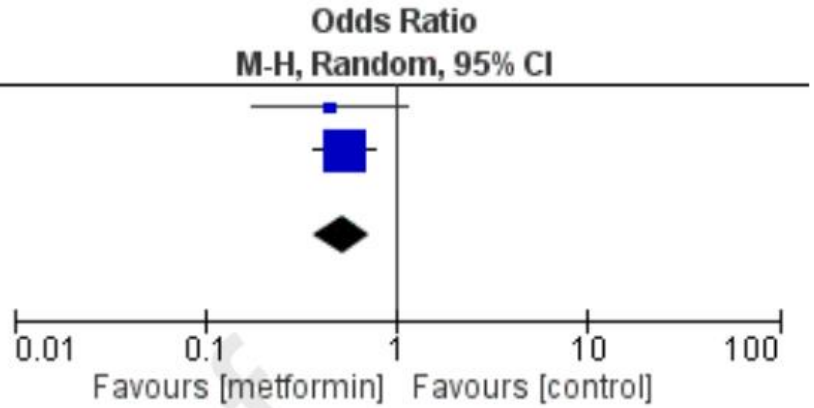
Pharmaceuticals 2022, 15, 312. https://doi.org/10.3390/ph15030312

Metfomin is significantly associated with lower risk of MACEs

Study or Subgroup	Metformin Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Hong 2013	7	156	14	148	13.0%	0.45 [0.18, 1.15]
UKPDS 34	55	342	109	411	87.0%	0.53 [0.37, 0.76]
Total (95% CI)		**498**		**559**	**100.0%**	**0.52 [0.37, 0.73]**
Total events	62		123			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.11$, $df = 1$ ($P = 0.75$); $I^2 = 0\%$

Test for overall effect: $Z = 3.80$ ($P = 0.0001$)



Monami, 2021

ORIGINAL ARTICLE

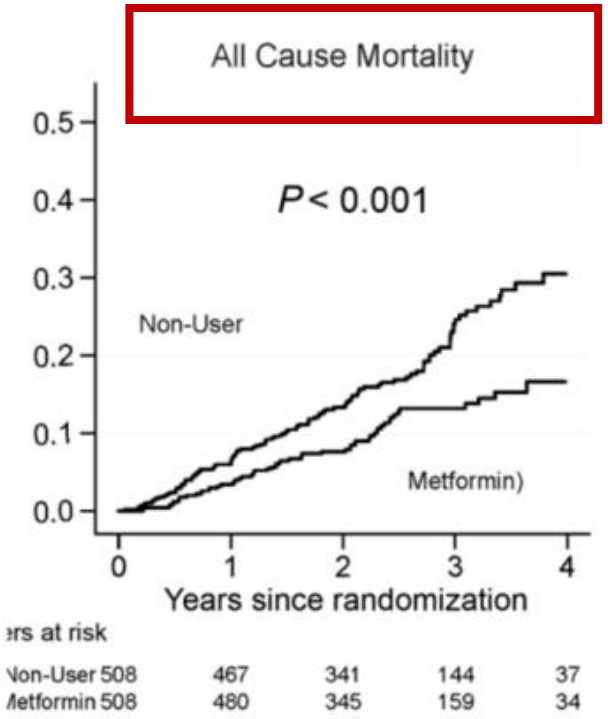
Metformin use and cardiovascular events in patients with type 2 diabetes and chronic kidney disease

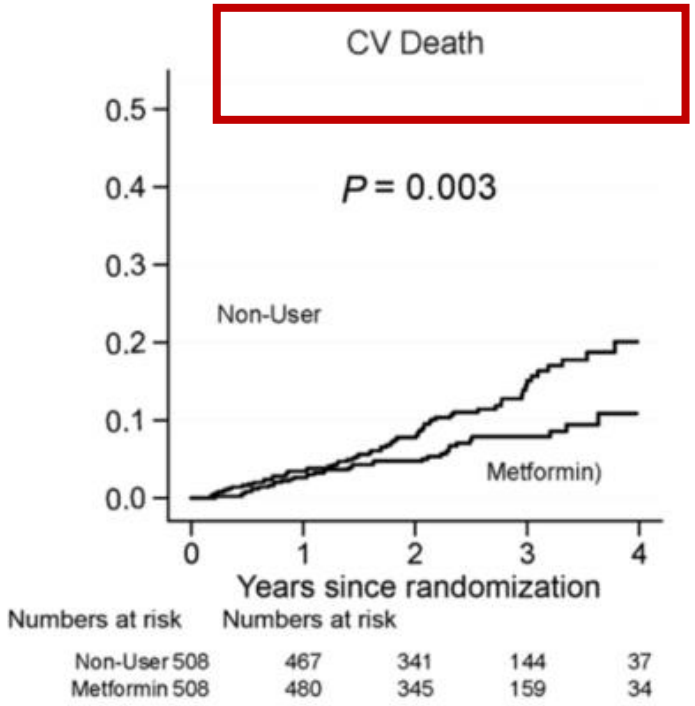
Μελέτη με **4038** ασθενείς με **ΣΔτ2, ΧΝΝ** και **αναιμία**

Diabetes Obes Metab. 2019;21:1199–1208

Μείωση της θνησιμότητας από όλες τις αιτίες και την καρδιαγγειακή θνησιμότητα

Metformin use and cardiovascular events in patients with type 2 diabetes and chronic kidney disease





Diabetes Obes Metab. 2019;21:1199–1208.

Diabetes Obes Metab. 2019;21:1199–1208

The Long-term Effects of Metformin on Patients With Type 2 Diabetic Kidney Disease

Soie Kwon,[1,2] Yong Chul Kim,[1] Jae Yoon Park,[3] Jeonghwan Lee,[2] Jung Nam An,[4] Clara Tammy Kim,[5] Sohee Oh,[6] Seokwoo Park,[7,8] Dong Ki Kim,[1,8] Yun Kyu Oh,[2,8] Yon Su Kim,[1] Chun Soo Lim,[2,8] and Jung Pyo Lee[2,8]

Diabetes Care 2020;43:948–955 | https://doi.org/10.2337/dc19-0936

Η πρώτη μελέτη που δείχνει τις ευεργετικές επιδράσεις της μετφορμίνης σε έναν μεγάλο πληθυσμό ασθενών με ΣΔτ2 και Νεφρική νόσο και για μεγάλη περίοδο παρακολούθησης.
(Έτη παρακολούθησης για την μετφορμίνη 8.2 +/- 4.5)

The Long-term Effects of Metformin on Patients With Type 2 Diabetic Kidney Disease

Στόχος μελέτης :

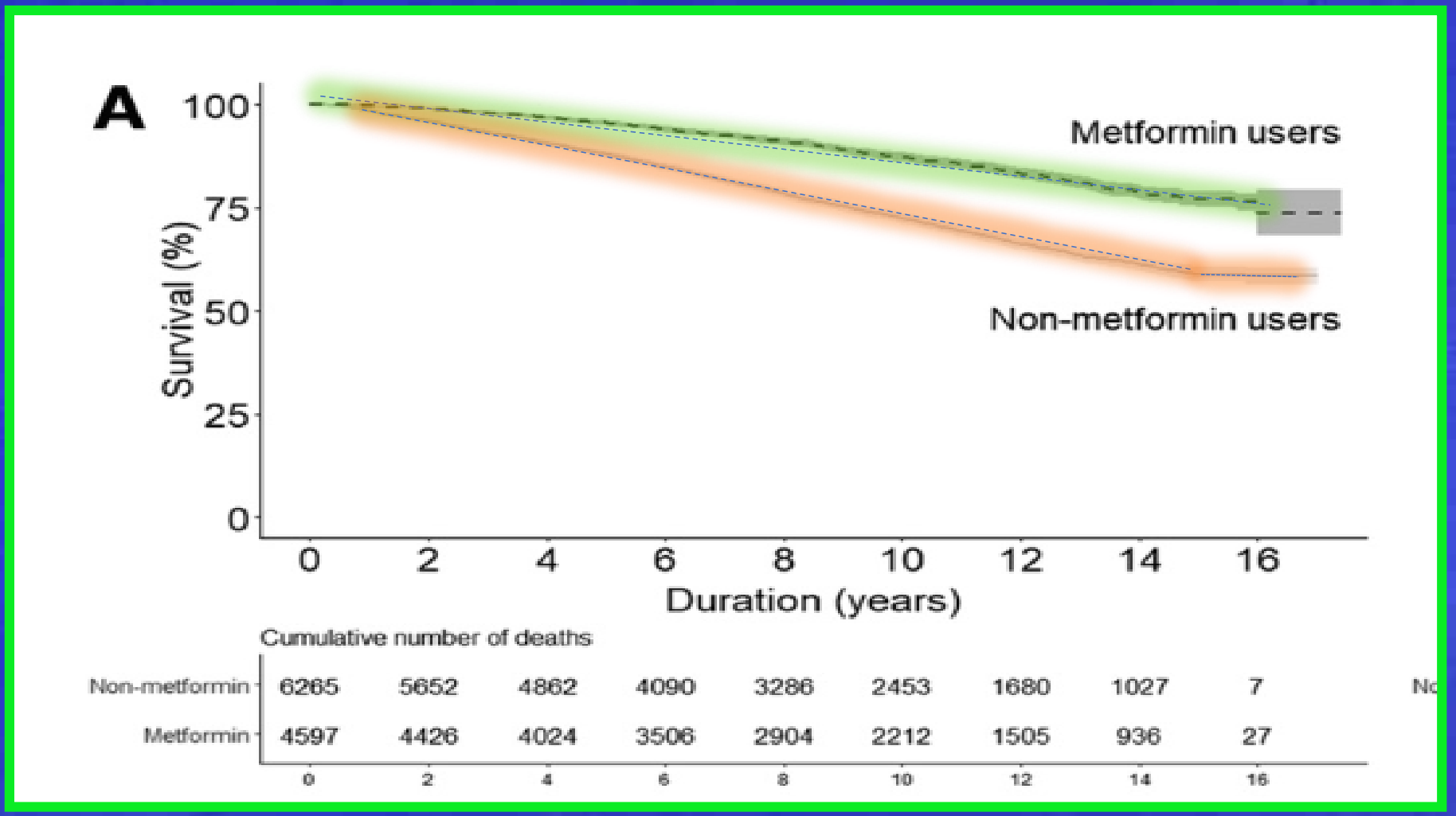
Έλεγχος αποτελεσματικότητας και ασφάλειας μετφορμίνης σε ΣΔ και ΧΝΝ

- Αναδρομική μελέτη παρατήρησης
- Ν. Κορέα, 2001-2016
- Πρωτογενή καταληκτικά σημεία : **ολική θνητότητα** από κάθε αίτιο
  εξέλιξη σε ΧΝΝ τελικού σταδίου

- 10.426 ασθενών με ΣΔτ2 και Νεφρική νόσο
- 4597 ασθενείς λάμβαναν μετφορμίνη και 6265 δεν έλαβαν ποτέ

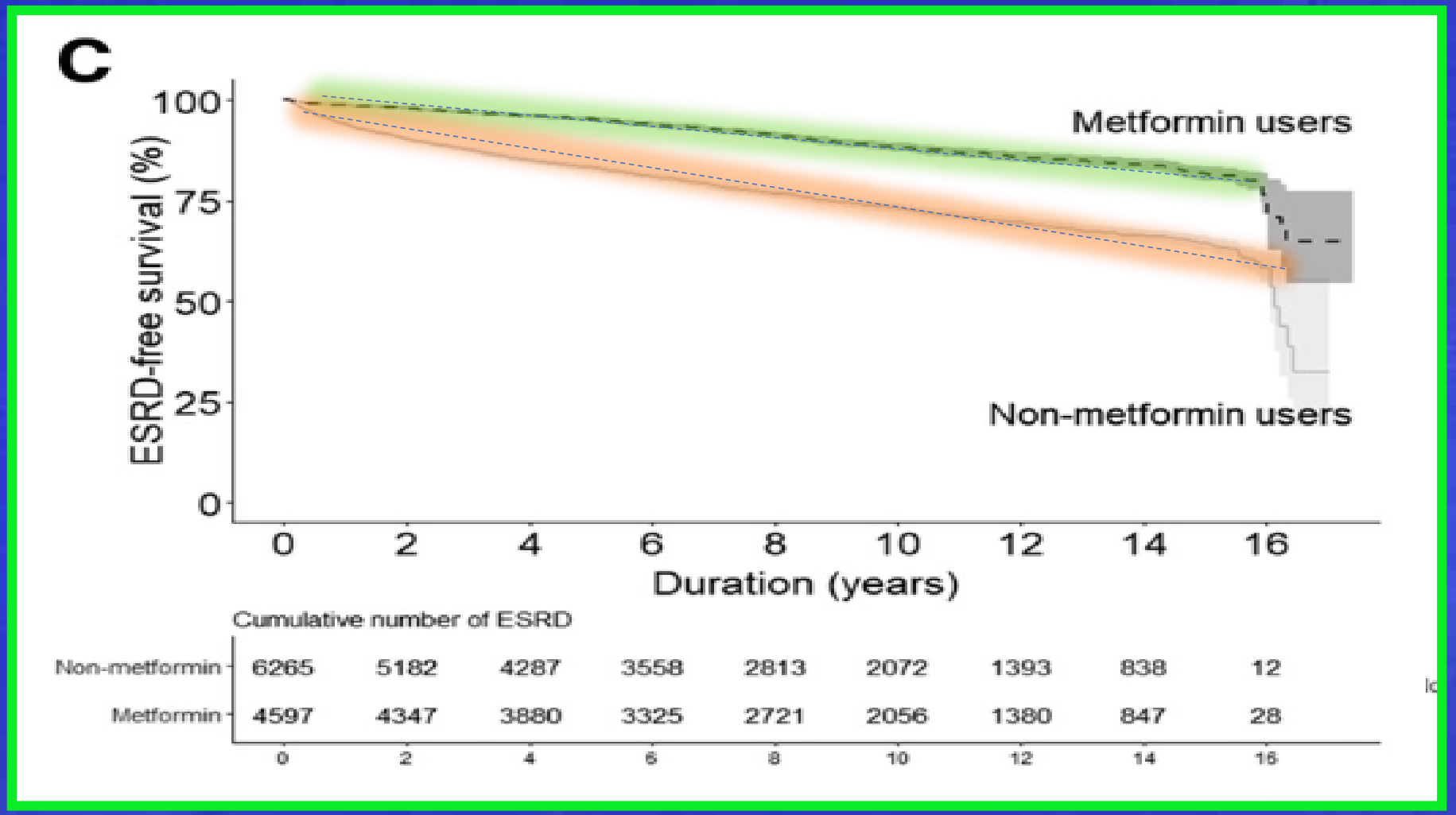
Diabetes Care 2020;43:948–955

The Long-term Effects of Metformin on Patients With Type 2 Diabetic Kidney Disease -All cause Mortality



Diabetes Care 2020;43:948–955

The Long-term Effects of Metformin on Patients With Type 2 Diabetic Kidney Disease –ESRD progression



Diabetes Care 2020;43:948–955

The Long-term Effects of Metformin on Patients With Type 2 Diabetic Kidney Disease

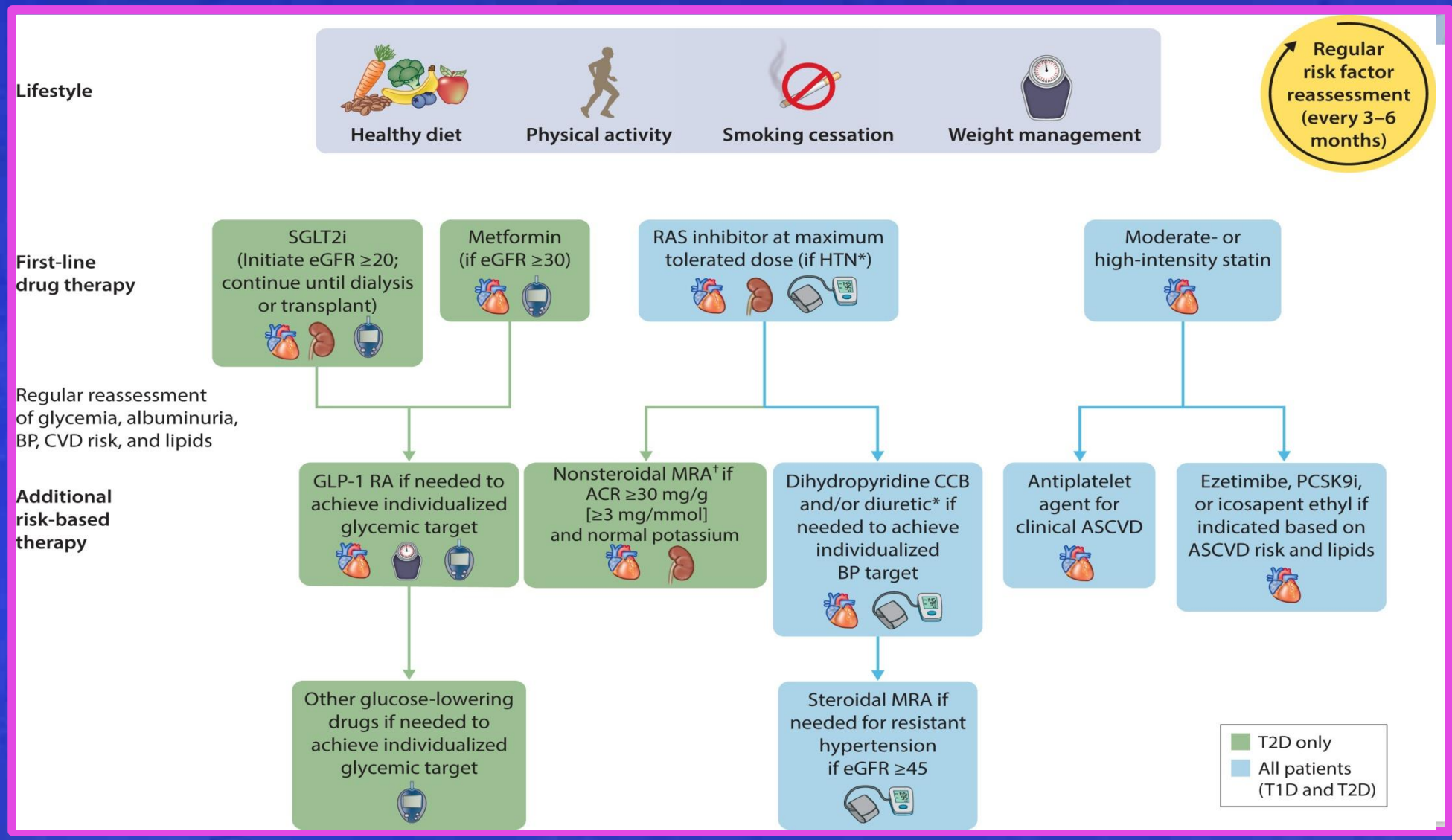
Αποτελέσματα

- Η χρήση Μετφορμίνης σε ασθενείς με χρόνια νεφρική νόσο , προχωρημένου σταδίου, 3b, είχε ως αποτέλεσμα τη **μείωση κινδύνου**
  α) θανάτου από κάθε αίτιο 35%
  β) εξέλιξης της νόσου σε ESRD 33% (νεφρική νόσο τελικού σταδίου) χωρίς να παρατηρηθεί αύξηση κινδύνου γαλακτικής οξέωσης

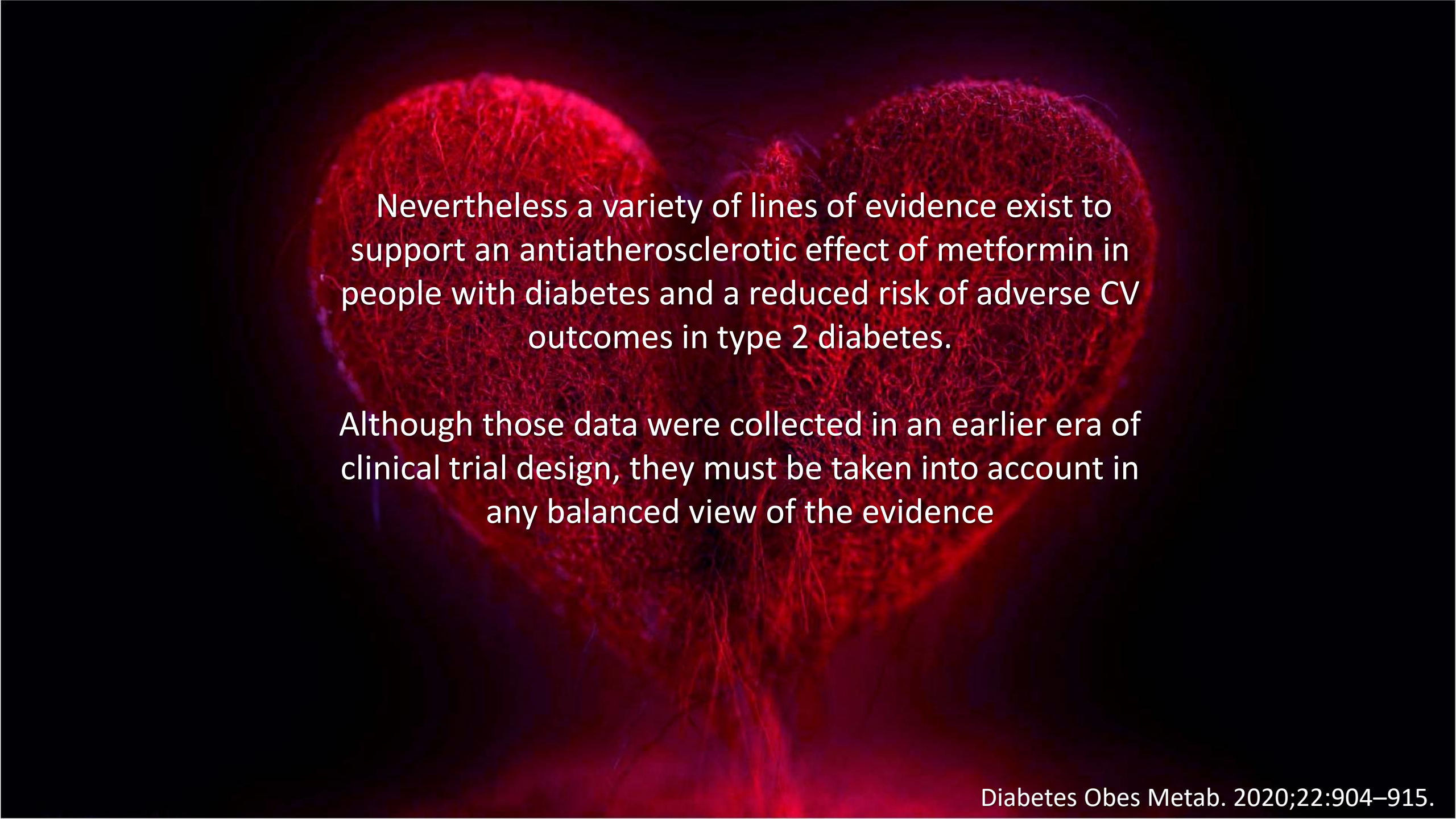
Diabetes Care 2020;43:948–955


MALA: Metformin Associated Lactic Acidosis

ΚΑΤΕΥΘΥΝΤΗΡΙΕΣ ΟΔΗΓΙΕΣ ΝΕΦΡΟΛΟΓΩΝ ΓΙΑ ΣΔτ2 ΚΑΙ ΧΝΝ KDIGO



https://kdigo.org/guidelines/diabetes-ckd/



Nevertheless a variety of lines of evidence exist to support an antiatherosclerotic effect of metformin in people with diabetes and a reduced risk of adverse CV outcomes in type 2 diabetes.

Although those data were collected in an earlier era of clinical trial design, they must be taken into account in any balanced view of the evidence

Diabetes Obes Metab. 2020;22:904–915.

REVIEW

Annals of Internal Medicine

Comparative Effectiveness of Glucose-Lowering Drugs for Type 2 Diabetes

A Systematic Review and Network Meta-analysis

Apostolos Tsapas, MD, MSc (Oxon), PhD*; Ioannis Avgerinos, MD, MSc*; Thomas Karagiannis, MD, MSc, PhD*; Konstantinos Malandris, MD, MSc; Apostolos Manolopoulos, MD, MSc; Panagiotis Andreadis, MD, MSc; Aris Liakos, MD, MSc, PhD; David R. Matthews, MD, DPhil; and Eleni Bekiari, MD, MSc, PhD

Comparative efficacy of glucose-lowering medications on body weight and blood pressure in patients with type 2 diabetes: A systematic review and network meta-analysis

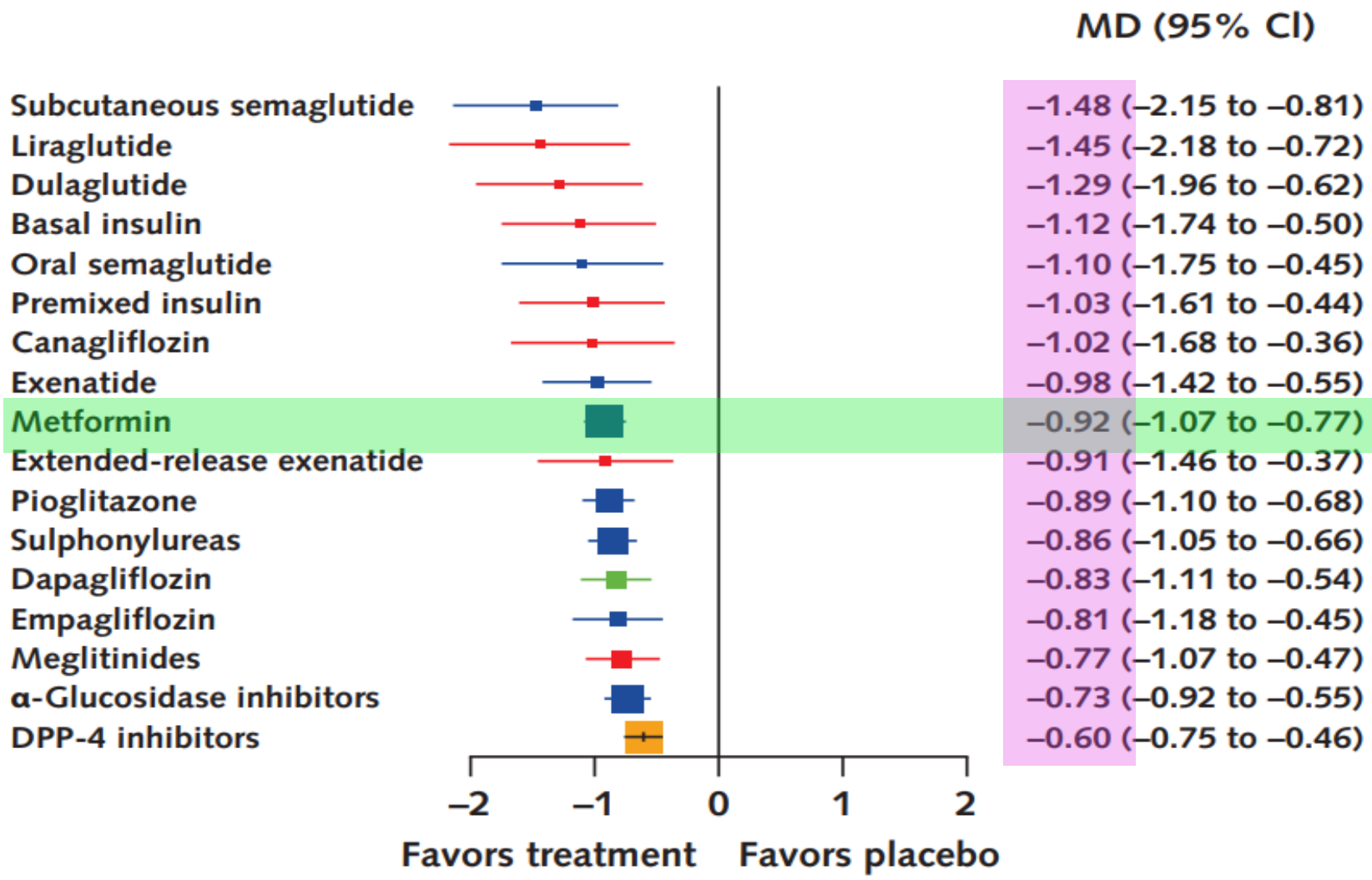
Apostolos Tsapas MD[1,2,3] | Thomas Karagiannis MD[1] | Panagiota Kakotrichi MD[1] | Ioannis Avgerinos MD[1] | Chrysanthi Mantsiou MD[1] | Georgios Tousinas MD[1] | Apostolos Manolopoulos MD[1] | Aris Liakos MD[1] | Konstantinos Malandris MD[1] | David R. Matthews MD[3,4] | Eleni Bekiari MD[1,2]

Change in Hemoglobin A1c Level in Drug-Naive Patients

GLP-1

Insulin

Μετφορμίνη

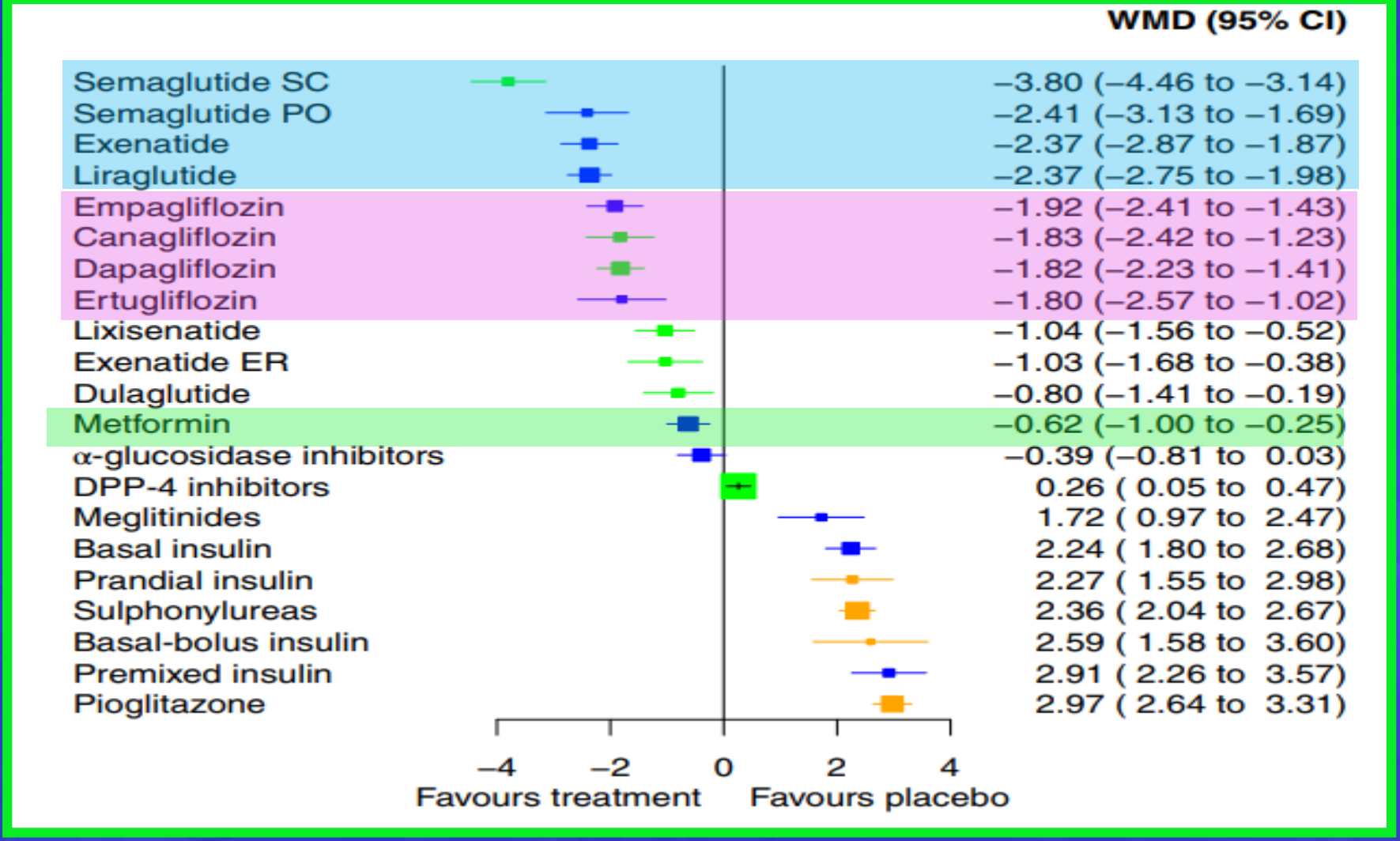


Network meta-analysis results for change in body weight (kg) compared with placebo

GLP-1

SGLT2

Μετφορμίνη

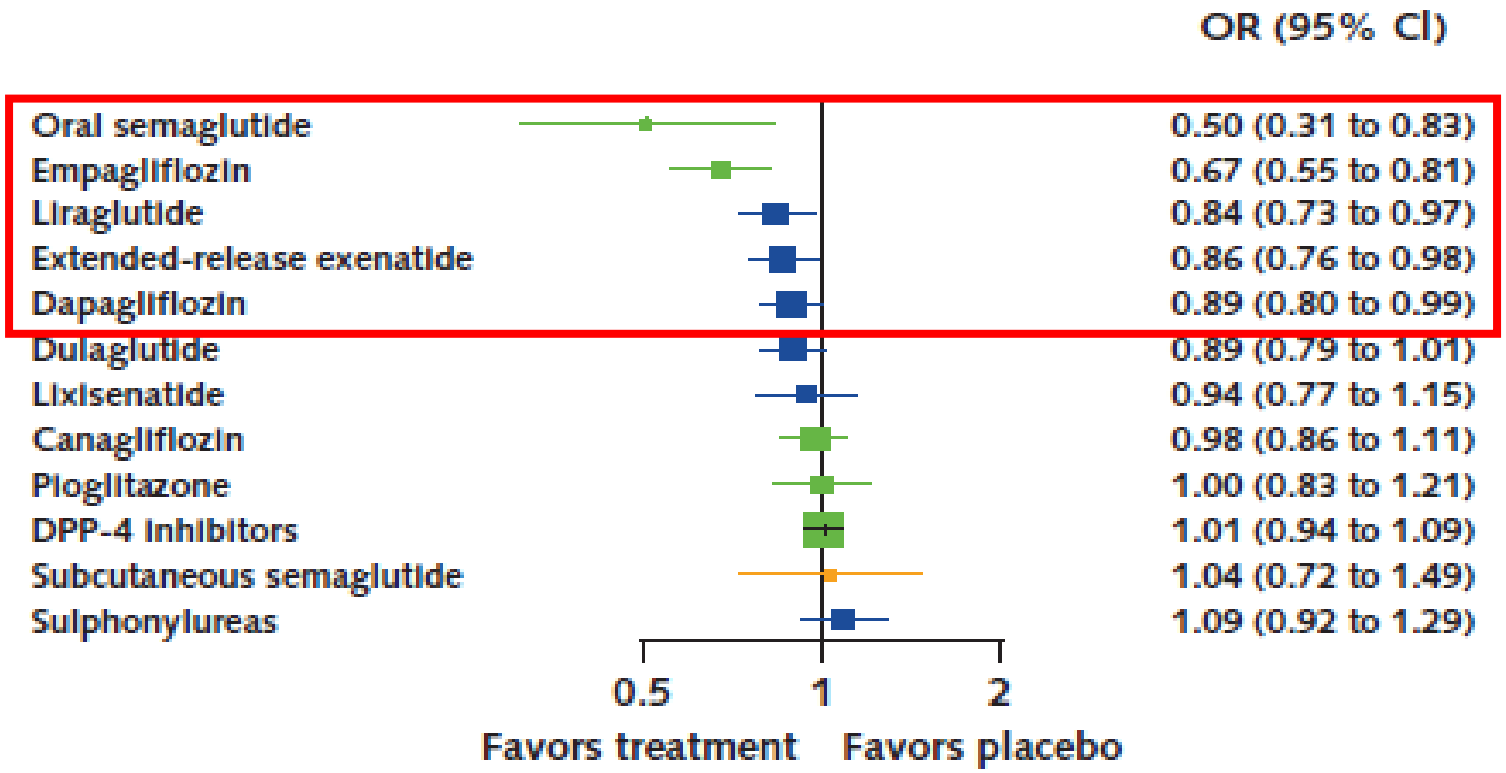


Diabetes ObesMetab.2021 Sep;23(9):2116-2124

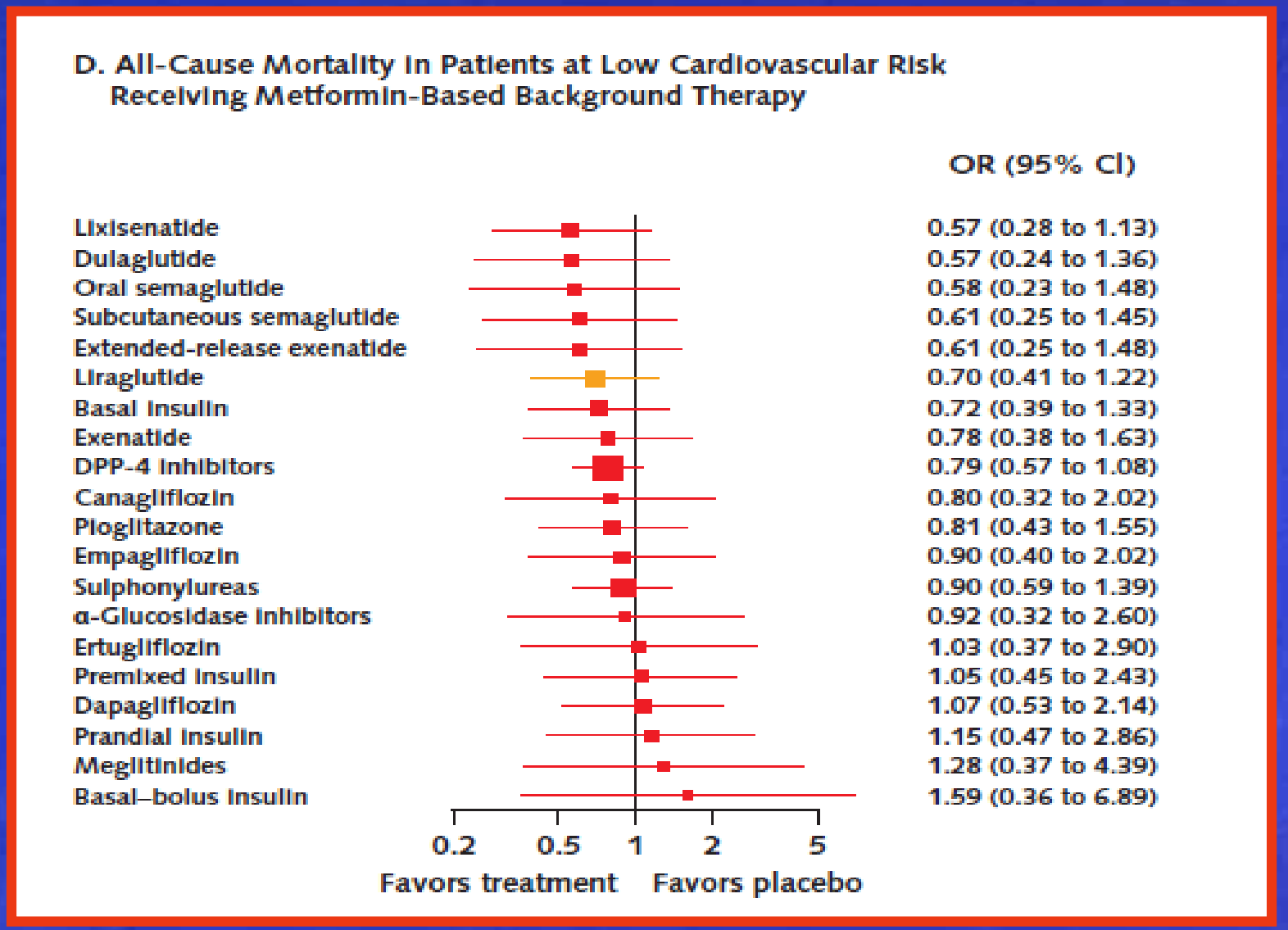
Mortality

All cause mortality in Patients **at increased Cardiovascular Risk**

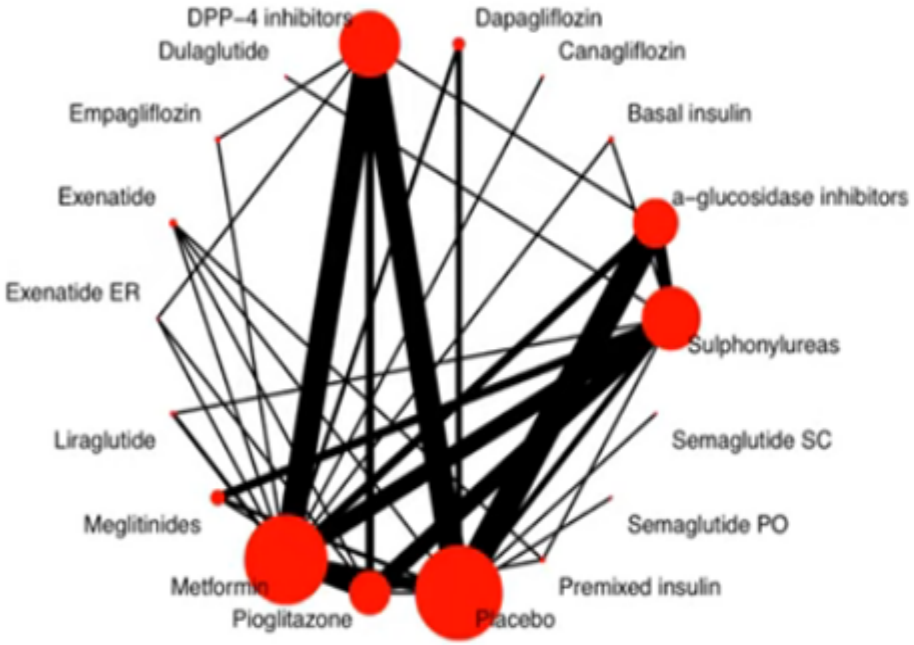
C. All-Cause Mortality in Patients at Increased Cardiovascular Risk Receiving Metformin-Based Background Therapy

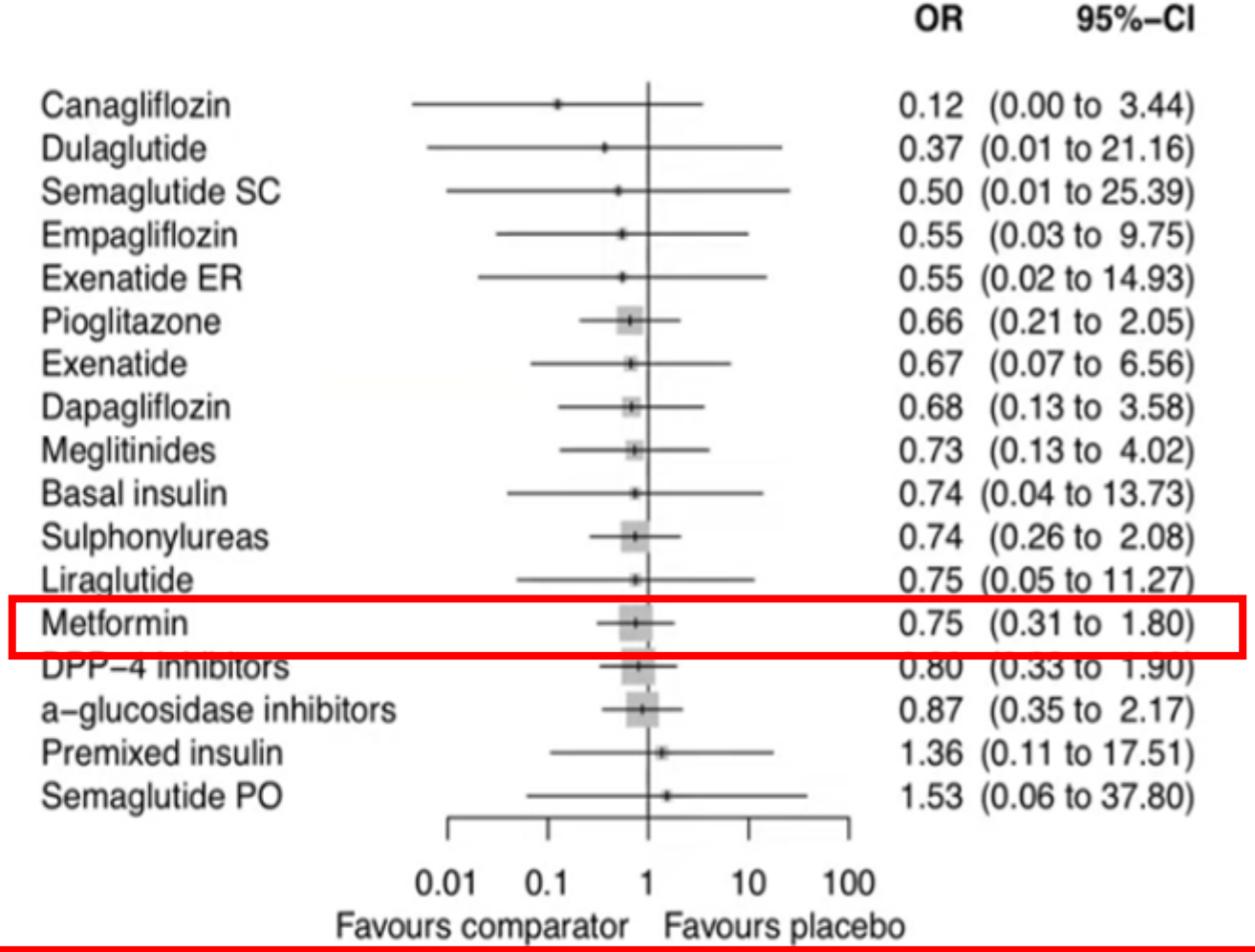


All cause mortality in Patients **at low Cardiovascular Risk**



Cardiovascular mortality in Patients **at low Cardiovascular Risk, without metformin at background**





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

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

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

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:

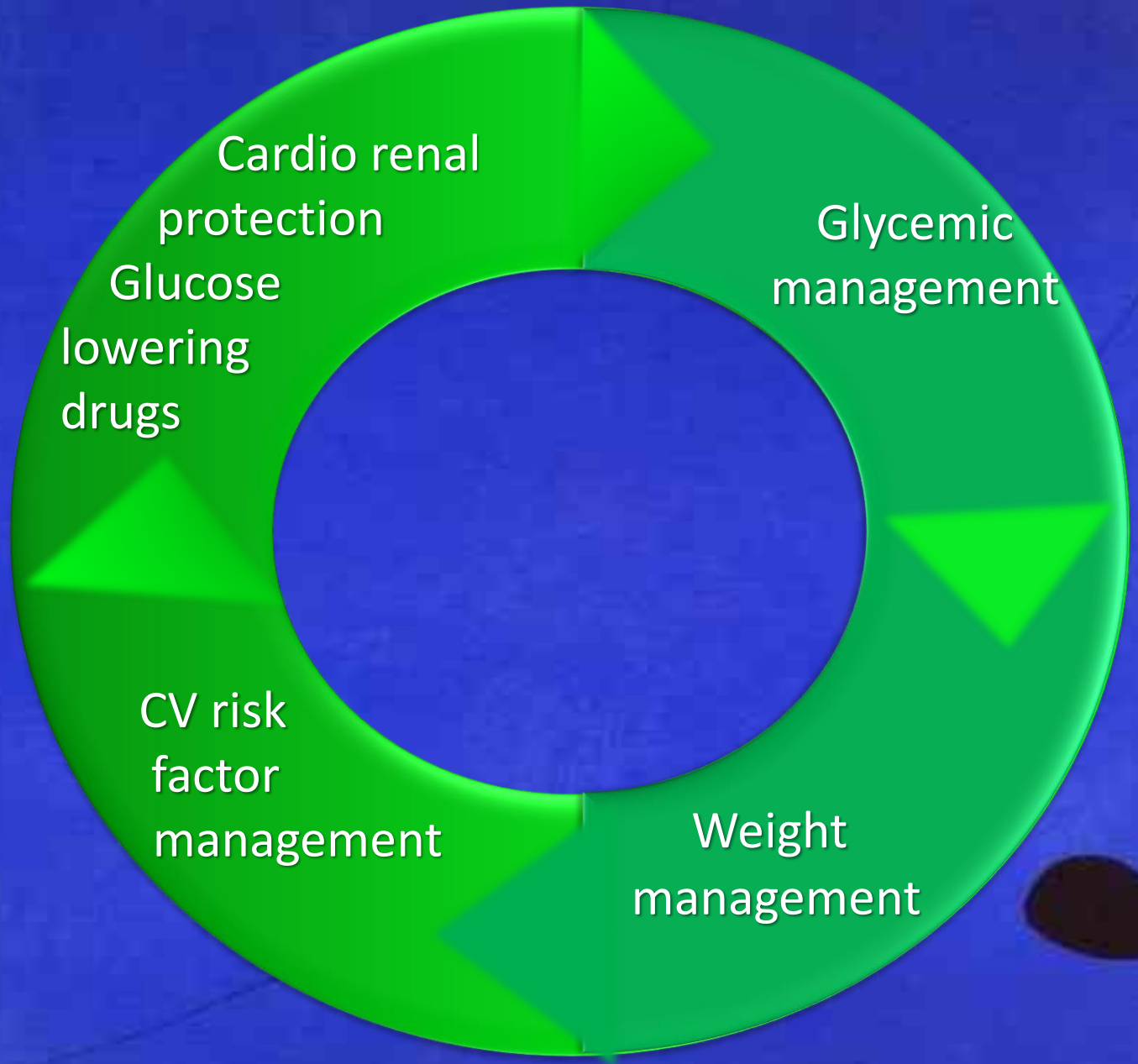
- Consider DSMES referral to support self-efficacy in achievement of goals
- Consider technology (e.g. diagnostic CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact on achievement of goals

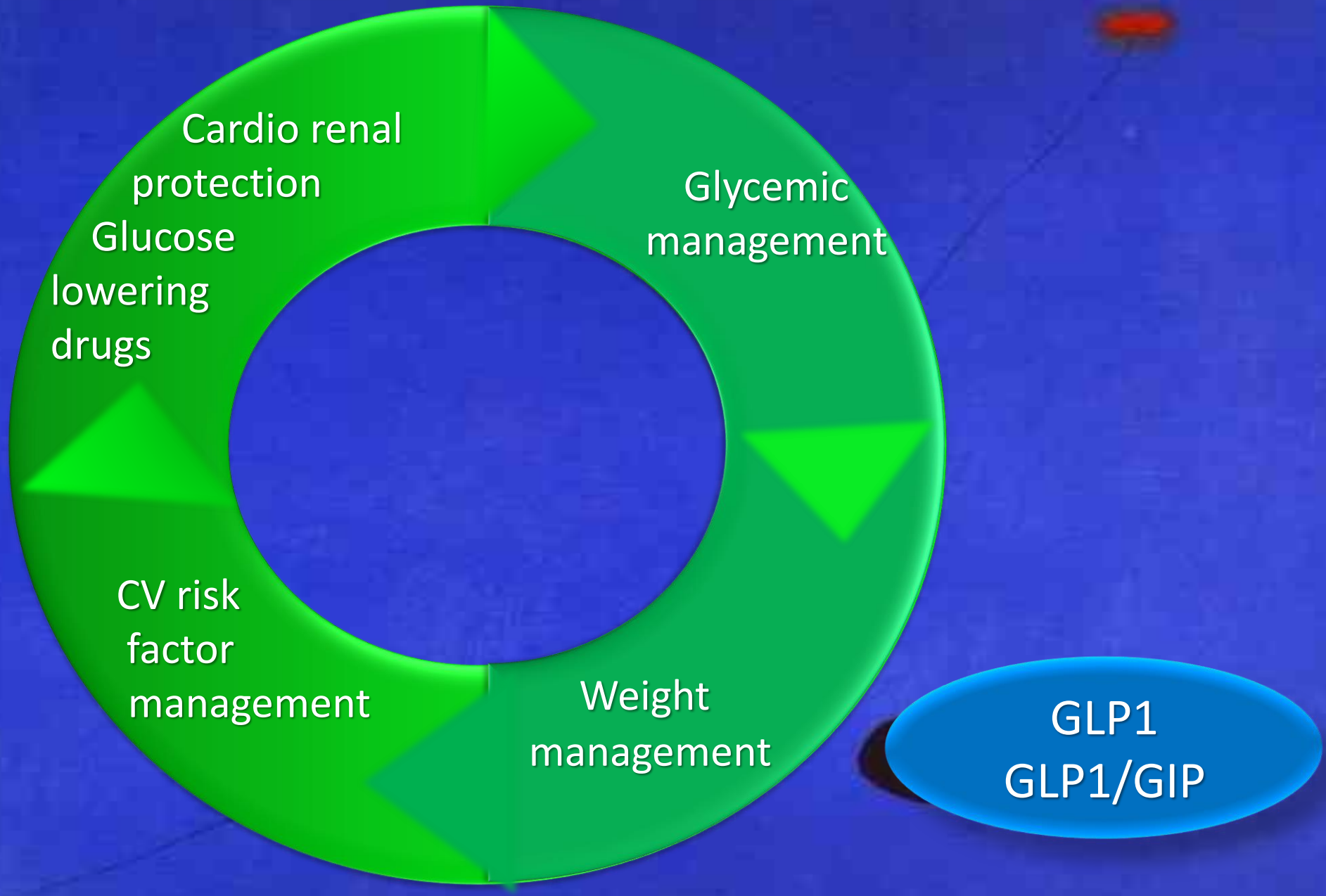
* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators 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.

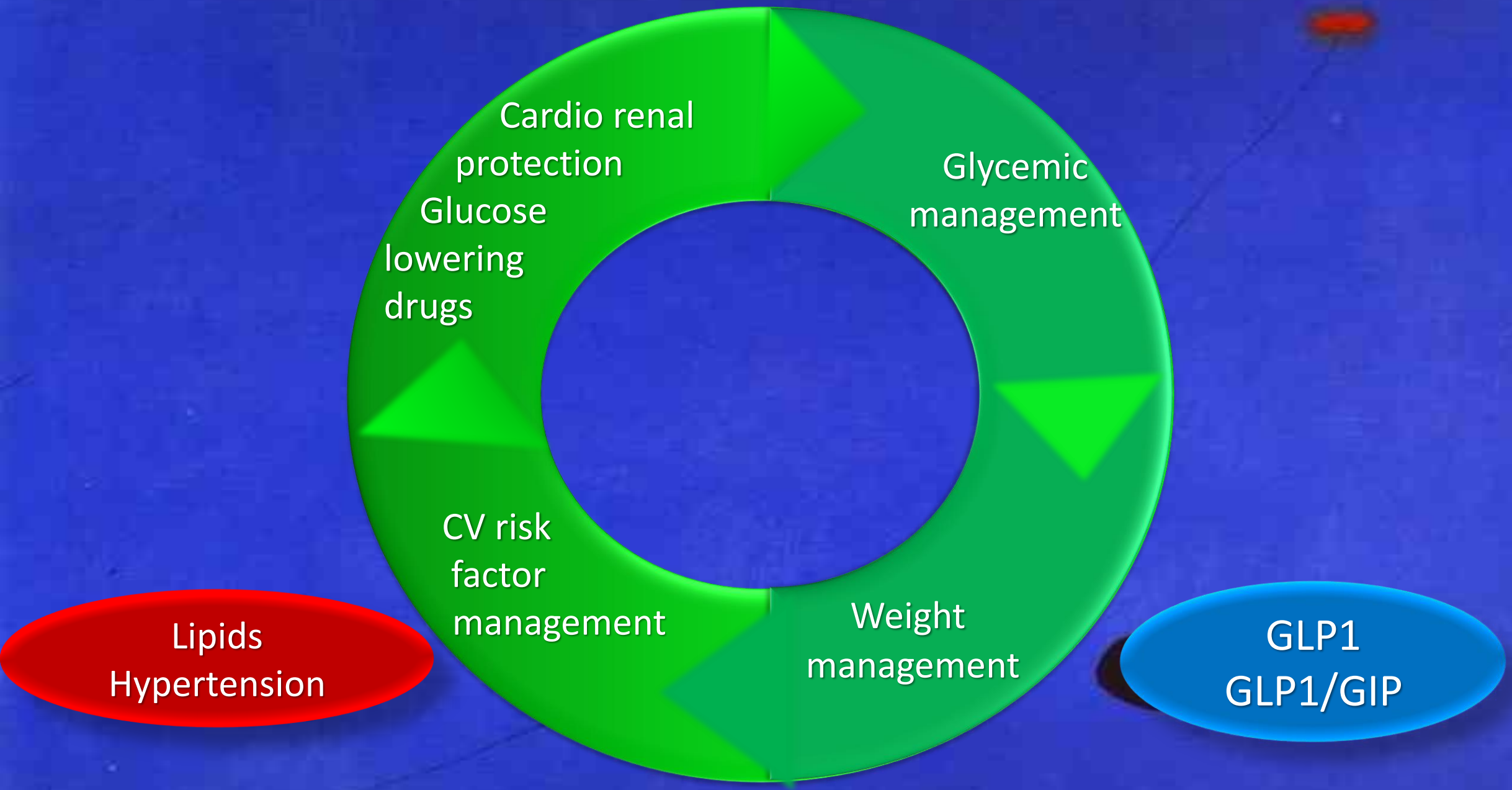
Diabetes Care 2022; https://doi.org/10.2337/dci22-0034. *Diabetologia* 2022; https://doi.org/10.1007/s00125-022-05787-2.

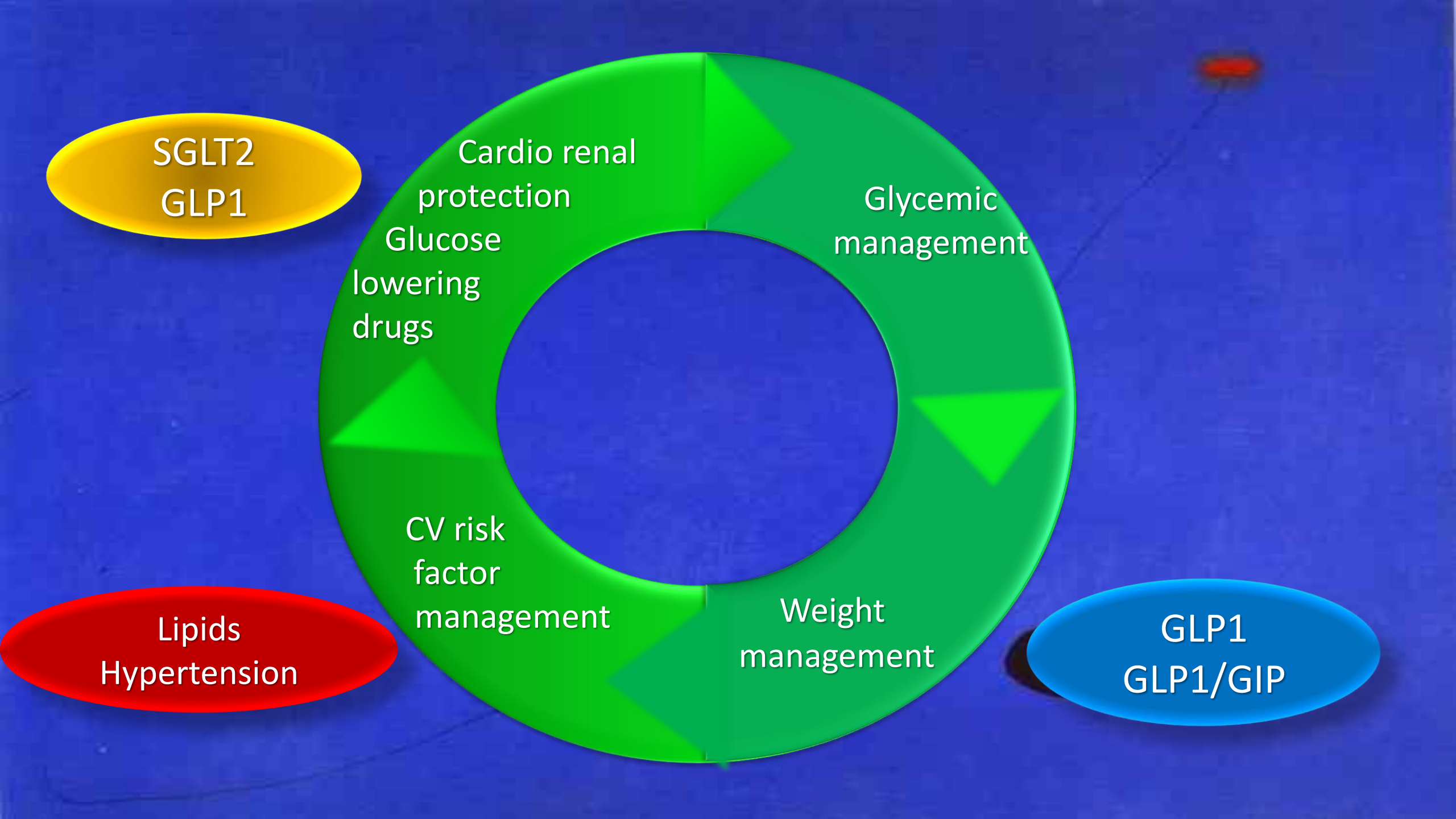
Ένας ξεχασμένος εχθρός

Η υπεργλυκαιμία


Cardio renal protection
Glucose lowering drugs
Glycemic management
CV risk factor management
Weight management


Cardio renal protection
Glucose lowering drugs
Glycemic management
CV risk factor management
Weight management
GLP1
GLP1/GIP


Cardio renal protection
Glucose lowering drugs
Glycemic management
CV risk factor management
Weight management
Lipids
Hypertension
GLP1
GLP1/GIP


SGLT2
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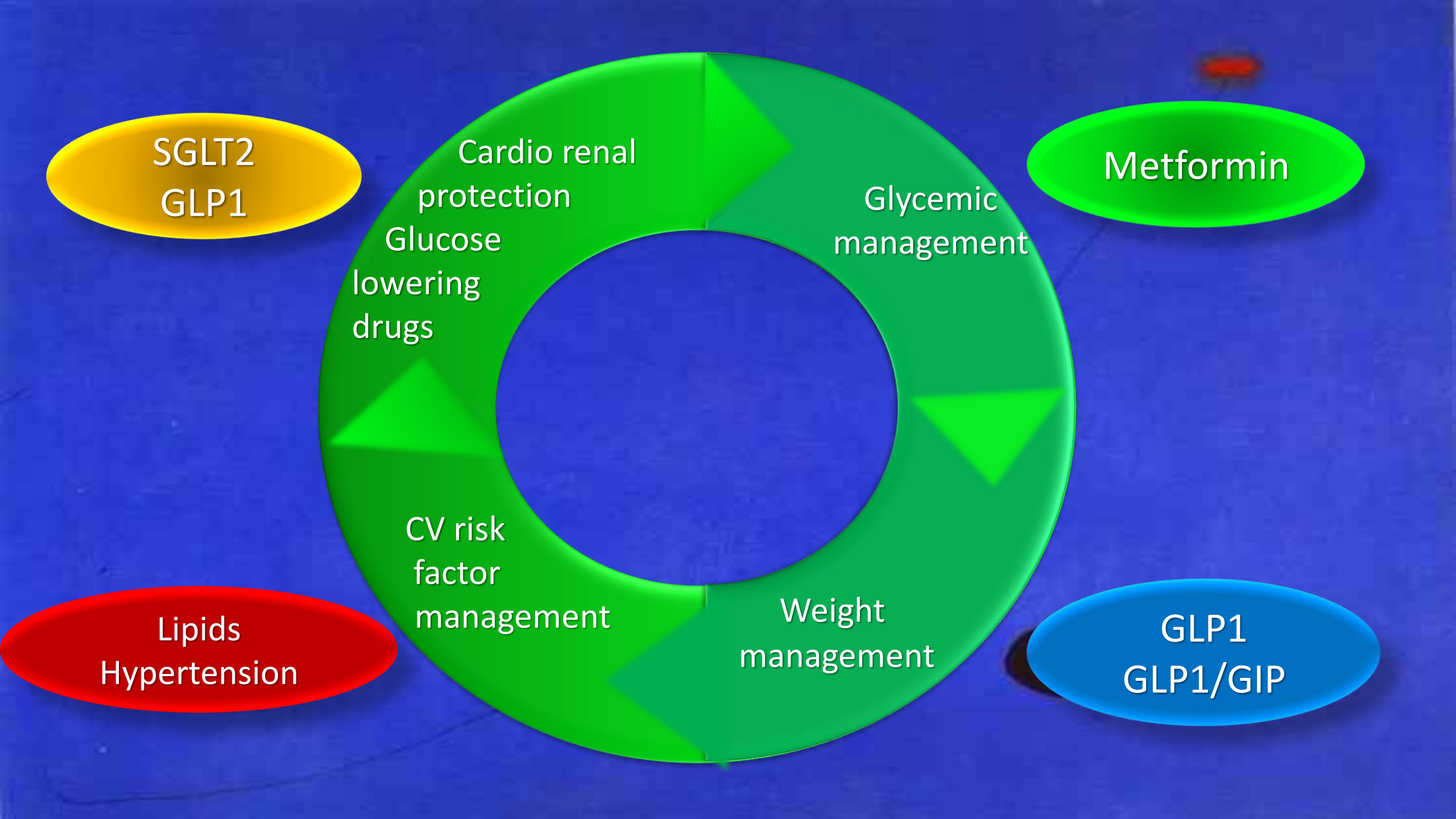
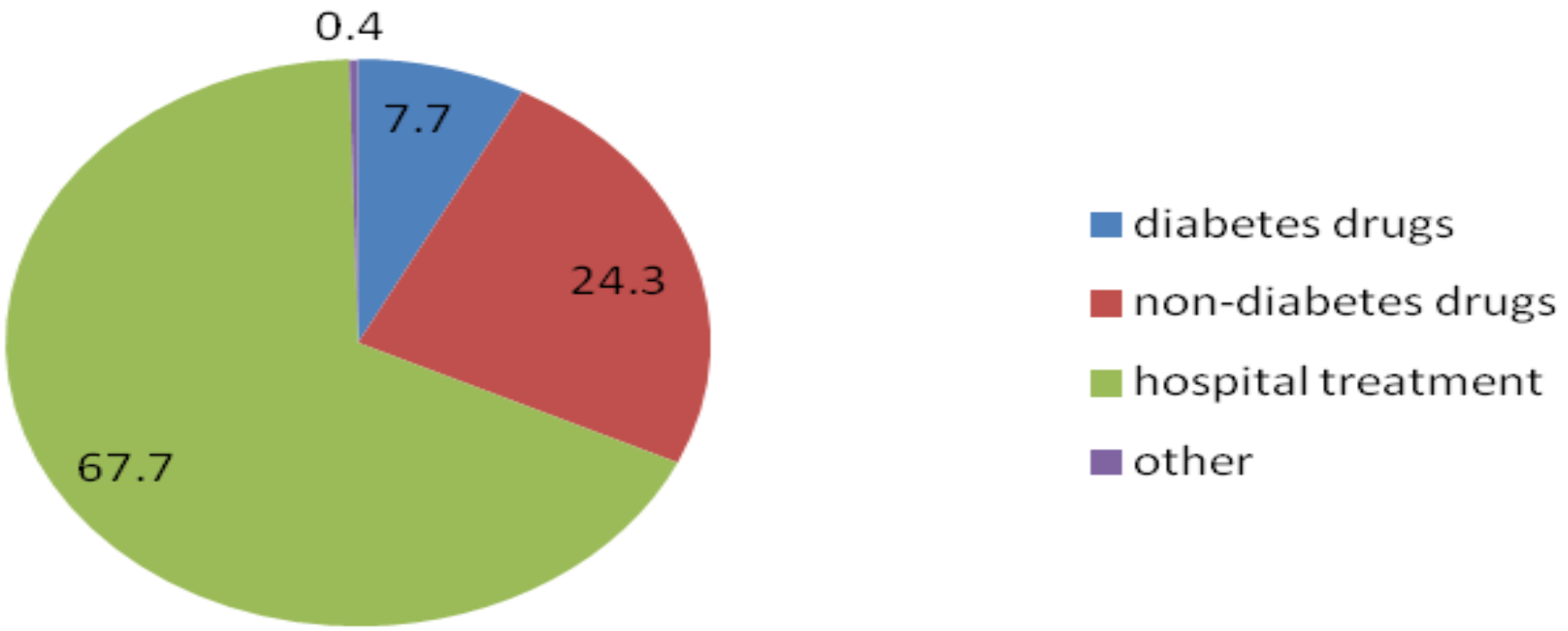
GLP1
GLP1/GIP


SGLT2
GLP1
Cardio renal protection
Glucose lowering drugs
Glycemic management
Metformin
CV risk factor management
Weight management
Lipids
Hypertension
GLP1
GLP1/GIP


TAMEION

Spending as % of total diabetes care costs, average of UK, France, Italy, Spain*



LSE Health, London School of Economics

Κόστος

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or

you can pay me later

Annals of Internal Medicine

ORIGINAL RESEARCH

First-Line Therapy for Type 2 Diabetes With Sodium–Glucose Cotransporter-2 Inhibitors and Glucagon-Like Peptide-1 Receptor Agonists

A Cost-Effectiveness Study

Jin G. Choi*; Aaron N. Winn, PhD*; M. Reza Skandari, PhD; Melissa I. Franco, MPH; Erin M. Staab, MPH; Jason Alexander, MD; Wen Wan, PhD; Mengqi Zhu, MS; Elbert S. Huang, MD, MPH; Louis Philipson, MD, PhD; and Neda Laiteerapong, MD, MS

Ann Intern Med. doi:10.7326/M21-2941, 4 October 2022.

Background: Guidelines recommend sodium–glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP1) receptor agonists as second-line therapy for patients with type 2 diabetes. Expanding their use as first-line therapy has been proposed but the clinical benefits may not outweigh their costs.

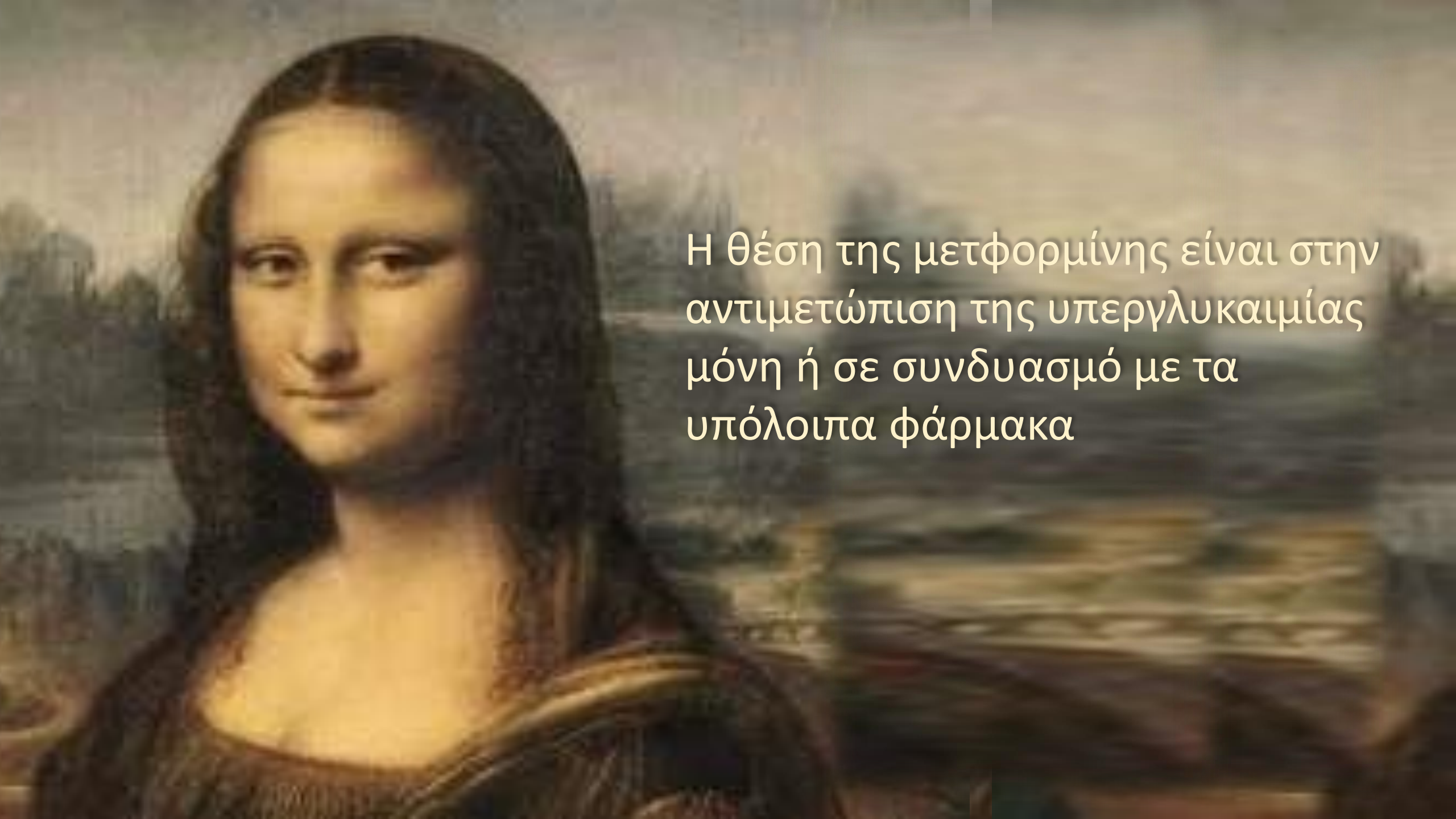
Objective: To evaluate the lifetime cost-effectiveness of a strategy of first-line SGLT2 inhibitors or GLP1 receptor agonists.

Conclusion: **As first-line agents, SGLT2 inhibitors and GLP1 receptor agonists would improve type 2 diabetes outcomes, but their costs would need to fall by at least 70% to be cost effective.**

Ann Intern Med. doi:10.7326/M21-2941, 4 October 2022.

OLD but GOLD


SGLT2
Metformin
GLP1


Η θέση της μετφορμίνης είναι στην αντιμετώπιση της υπεργλυκαιμίας μόνη ή σε συνδυασμό με τα υπόλοιπα φάρμακα


Metformin “all time classic”


Ευχαριστώ