



UNMET NEED

GUIDELINES

MACE

STROKE

ADDITIONAL
CVOT RESULTS

EFFICACY

SAFETY AND
TOLERABILITY

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SUMMARY

For adult patients with T2D¹

The Ozempic[®] Zone delivers 3 proven benefits

**PROVEN CV RISK REDUCTION^{1,2*}****POWERFUL GLYCAEMIC CONTROL^{1,3,4†}****COMPELLING WEIGHT LOSS^{1‡}****Ozempic[®] is #1 in GLP-1 RA^{5§}**
3.4 million patients worldwide on Ozempic^{®5§}

The image shown is a model and not a real patient.

*Results apply to Ozempic[®] 0.5 mg and 1 mg plus SOC vs placebo plus SOC in adults with T2D who have high CV risk, established ASCVD or both.²

†Results apply to Ozempic[®] across SUSTAIN trials, which included placebo, sitagliptin, dulaglutide, exenatide ER, insulin glargine, canagliflozin and liraglutide.^{1,3,4} **SUSTAIN 4:** Mean change in HbA_{1c} at Week 30 (+ MET ± SU), baseline 8.2% (N=1089): -1.2% Ozempic[®] 0.5 mg (n=362), (*P*<0.0001) and -1.6% Ozempic[®] 1 mg (n=360), (*P*<0.0001) vs -0.8% study-titrated insulin glargine (n=360).^{1,6} **SUSTAIN 7:** Mean change in HbA_{1c} at Week 40 (+ MET), baseline 8.2% (N=1201): -1.5% Ozempic[®] 0.5 mg (n=301) vs -1.1% dulaglutide 0.75 mg (n=299), (*P*<0.0001); -1.8% Ozempic[®] 1 mg (n=300) vs -1.4% dulaglutide 1.5 mg (n=299), (*P*<0.0001).^{1,7}

‡Ozempic[®] is not indicated for weight loss.¹

§Based on volume sales data: IQVIA-MIDAS database R3M 05.2022.⁵

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; CV=cardiovascular; GLP-1 RA=glucagon-like peptide-1 receptor agonist; SOC=standard of care; ASCVD=atherosclerotic cardiovascular disease; ER=extended-release; MET=metformin; SU=sulphonylurea.



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ONCE-WEEKLY
OZEMPIC[®]
semaglutide injection



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Many of your patients may have both CVD and T2D

Previous MI

Family history
of strokeWorried about MI
and stroke risk

Very high CV risk*

High CV risk*

The images shown are models and not real patients.

*CV risk based on 2019 ESC/EASD guidelines.⁸ Complete patient risk factors are shown for each patient in the Patient Profiles section.

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; CVD=cardiovascular disease; T2D=type 2 diabetes; MI=myocardial infarction; CV=cardiovascular; ESC=European Society of Cardiology; EASD=European Association for the Study of Diabetes.



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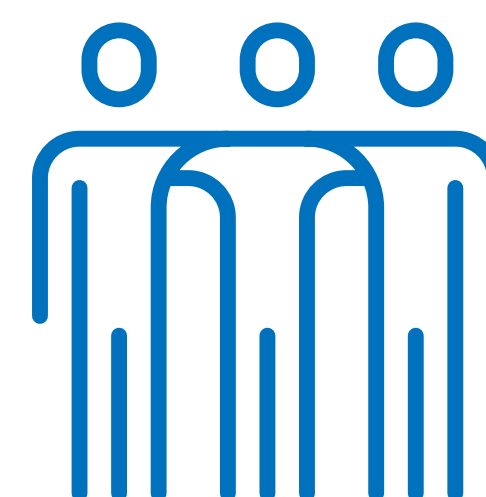
Why is it important to address MI and stroke risk for patients with T2D?

**↓ 19 YEARS**

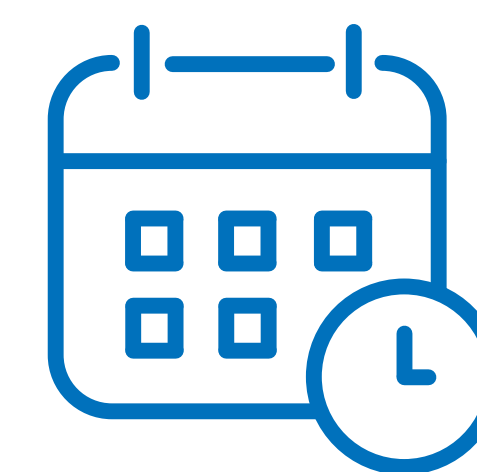
LIFE EXPECTANCY WAS
REDUCED BY UP TO
19 YEARS IN ADULTS
WITH DIABETES,
STROKE AND MI^{9*}

**MI AND
STROKE**

RISK OF STROKE OR
MI 2–3 TIMES HIGHER
IN PEOPLE WITH T2D
VS THOSE WITHOUT¹⁰

**ASCVD**

THE MOST PREVALENT
CV COMPLICATION
AMONG PATIENTS
WITH T2D IS ASCVD¹¹

**14.6 YEARS**

ASCVD OCCURS
14.6 YEARS EARLIER
AND WITH A GREATER
MORTALITY RISK IN
PEOPLE WITH DIABETES
VS THOSE WITHOUT^{12,13}

ASCVD is the principal cause of death and disability in T2D, making CV-risk management vital¹²

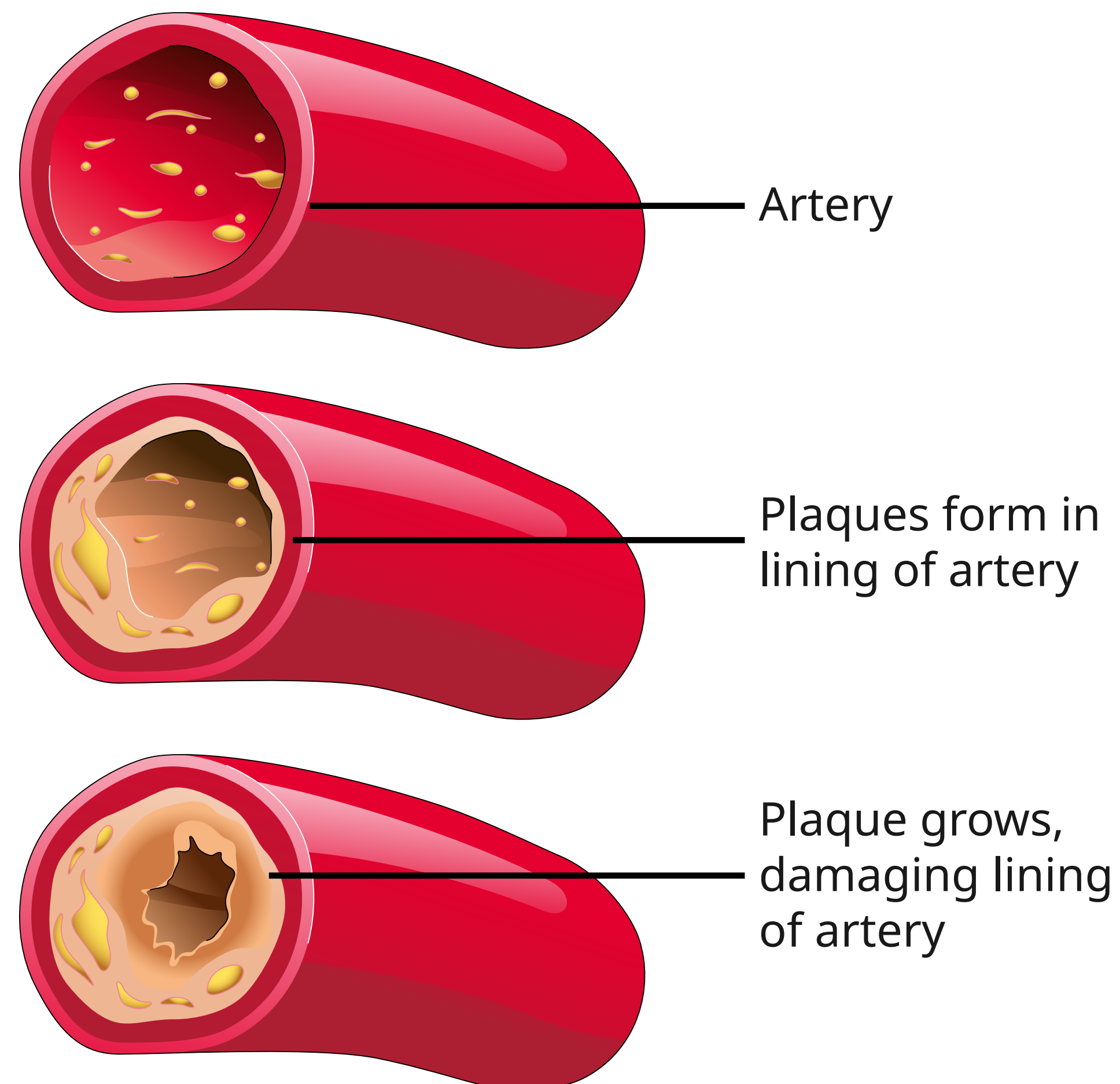
[ASCVD: a closer look](#)[Prevalence of CVD in T2D](#)

*Survival estimates for adults aged 50–54 years.⁹

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; MI=myocardial infarction; T2D=type 2 diabetes; ASCVD=atherosclerotic cardiovascular disease; CV=cardiovascular; CVD=cardiovascular disease.



ASCVD: a closer look



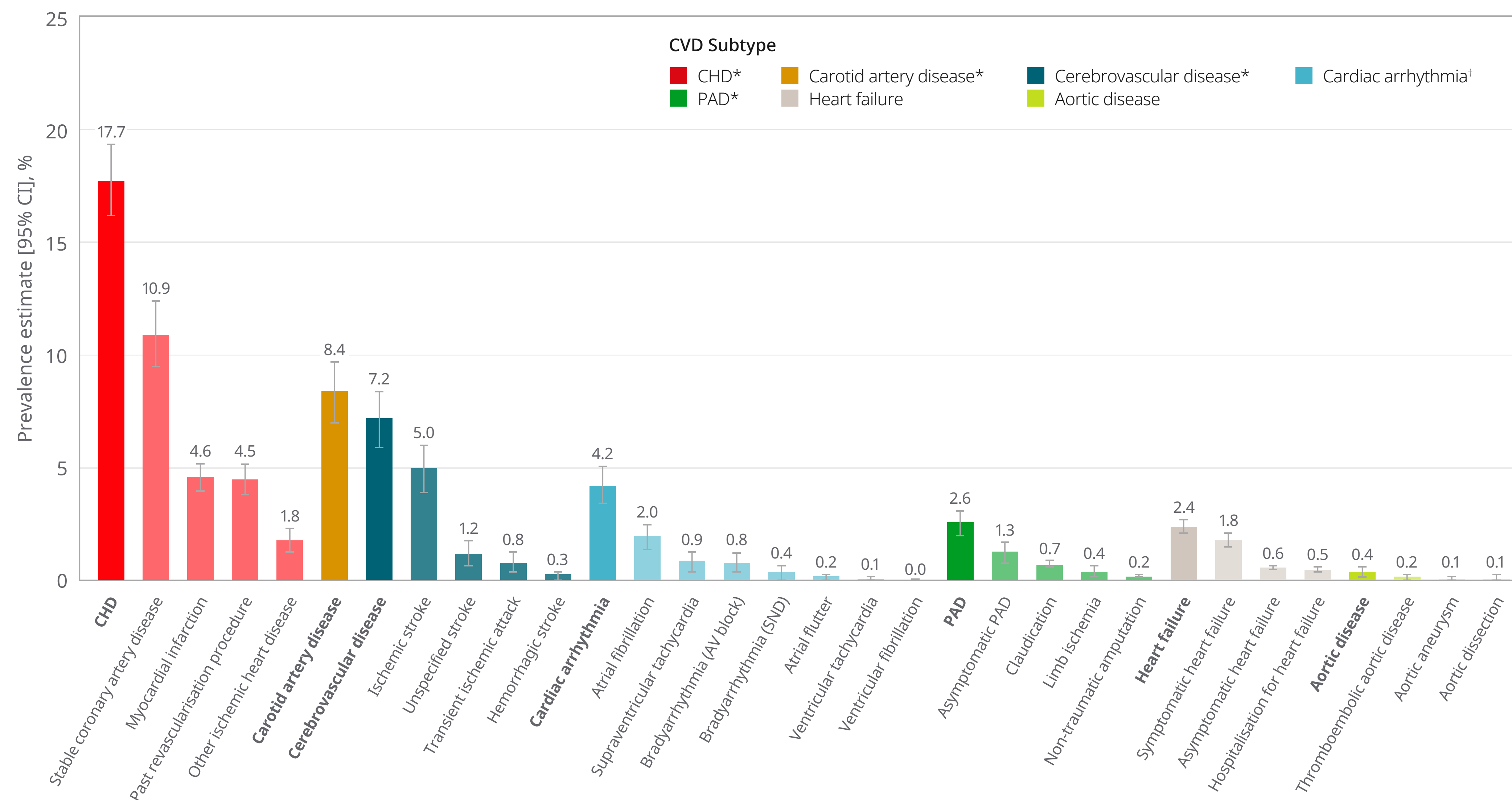
- ASCVD may occur when plaques form in the lining of major conduit arteries, provoking chronic inflammation. Over time, these plaques can build up and ultimately rupture, causing a blood clot^{14,15}
- The extent of ASCVD progression depends on the risk factors and arterial susceptibility¹⁴

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; ASCVD=atherosclerotic cardiovascular disease.



Approximately 9/10 patients with established CVD and T2D have ASCVD¹¹

Overall weighted CVD prevalence in people with T2D by CVD subtype and diagnosis¹¹



Data are overall prevalence estimates (95% CI), which were calculated as weighted estimates to account for the size of the diabetes population of each country and the sampling of participants by healthcare setting, if it was different from as planned. CVD subtypes are in bold font, contributing diagnoses are in plain font. Diagnoses are not mutually exclusive; one participant may have multiple diagnoses.¹¹

*Categorised as ASCVD.¹¹

†Included conduction abnormalities.¹¹

MACE=major adverse cardiovascular outcomes; CVOT=cardiovascular outcomes trial; CVD=cardiovascular disease; T2D=type 2 diabetes; ASCVD=atherosclerotic cardiovascular disease; CI=confidence interval; CHD=coronary heart disease; AV=atrioventricular; SND=sinus node dysfunction; PAD=peripheral artery disease.



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Patients with CVD and T2D may face complications

Consider the following:



~**1 IN 4**

patients with CVD also have T2D^{16*}



The recent CAPTURE study found

~**9 OUT OF 10**

patients with established CVD and T2D have ASCVD¹¹



CAPTURE also found that only ~2 IN 10

patients with T2D are prescribed a glucose-lowering treatment with a proven CV benefit^{17†}

Patients with CVD and T2D not receiving a therapy with proven CV benefit continue to be at higher risk of a CV event

[More about CAPTURE](#)

*CVD is defined as heart failure, cerebrovascular accident, coronary heart disease, and/or peripheral arterial disease.¹⁶

†Glucose-lowering treatments with proven CVD benefit include certain GLP-1 RAs and SGLT-2is.¹⁷

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; CVD=cardiovascular disease; T2D=type 2 diabetes; ASCVD=atherosclerotic cardiovascular disease; CV= cardiovascular; GLP-1 RA=glucagon-like peptide-1 receptor agonist; SGLT-2i=sodium-glucose co-transporter 2 inhibitor.



More about CAPTURE

Primary and secondary analyses within CAPTURE explored the following in patients with T2D:^{11,17}

- The prevalence of different types of CVD
- The clinical management of CVD

CAPTURE studied nearly 10,000 people with T2D in 13 countries across 5 continents:¹¹



Who was the typical CAPTURE patient?¹¹

- Median HbA_{1c}: 7.3%
- Median years living with T2D: 10.7
- Median age: 64 years

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; CVD=cardiovascular disease.



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Multiple international organisations address the connection between CVD and T2D

For adults with T2D and established ASCVD, a GLP-1 RA with proven CV benefit should be considered early in the treatment of T2D^{8,12,18–21}

ESC/EASD 2019

GLP-1 RAs

WITH PROVEN CVD BENEFIT

are recommended for a risk reduction of CV events in patients on metformin with atherosclerosis or very high/high CV risk, irrespective of HbA_{1c}.^{8*}

ASA/AHA 2021

A GLP-1 RA THERAPY

SHOULD BE ADDED TO METFORMIN

independently of baseline HbA_{1c} for the prevention of future vascular events, in patients with established ASCVD, including ischaemic stroke.¹⁸

ACC 2020

A GLP-1 RA THERAPY

WITH PROVEN CV BENEFIT

is recommended for patients with established or who are at very high risk of ASCVD.¹⁹

AACE/ACE 2020

A GLP-1 RA

WITH PROVEN CVD BENEFIT

should be considered independently of glycaemic control, in patients with established or high risk for ASCVD.^{20*}

AACE 2022

A GLP-1 RA

WITH PROVEN BENEFIT

for reduction in the risk of stroke should be used in patients with T2D and established/high risk of ASCVD.^{21†}

*SGLT-2is are also recommended.^{8,20}

†In persons with insulin resistance, prediabetes, or T2D and a prior transient ischaemic attack or stroke, pioglitazone should be considered to reduce the risk of recurrent stroke.²¹

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; CVD=cardiovascular disease; T2D=type 2 diabetes; ASCVD=atherosclerotic cardiovascular disease; GLP-1 RA=glucagon-like peptide-1 receptor agonist; CV=cardiovascular; ESC=European Society of Cardiology; EASD=European Association for the Study of Diabetes; ASA=American Stroke Association; AHA=American Heart Association; ACC=American College of Cardiology; AACE = American Association of Clinical Endocrinologists; ACE=American College of Endocrinology; SGLT-2i=sodium-glucose co-transporter 2 inhibitor.



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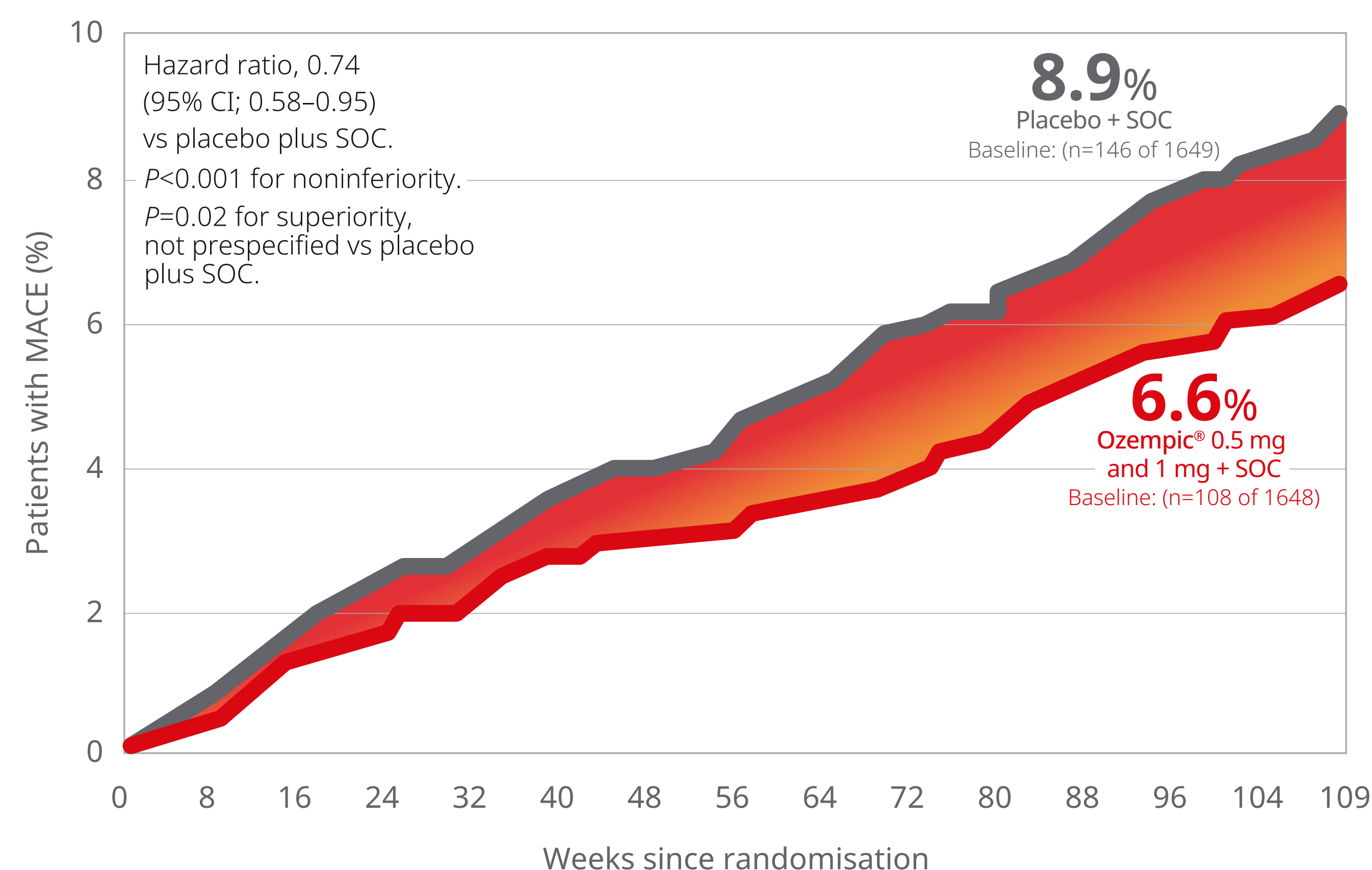


Composite
primary endpoint
26%
RRR OF MACE
when added to
SOC^{1,2*}
(2.3% ARR at 109 weeks)²

In adult patients with T2D who have high CV risk, established ASCVD or both^{2*}

**After 2 years, Ozempic® significantly reduced
the risk of MACE²**

Time to first confirmed MACE²



NNT
45
Number needed
to treat to prevent
1 MACE (2 Years)^{2,22}



Composite MACE endpoint: CV death, nonfatal MI, or nonfatal stroke.¹

[SUSTAIN 6 Study Design](#)[Patient Characteristics](#)

*When added to SOC. SOC included, but was not limited to, oral antidiabetic treatment, insulin, antihypertensives, diuretics and lipid-lowering therapies.²³

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; CV=cardiovascular; ASCVD=atherosclerotic cardiovascular disease; RRR=relative risk reduction; SOC=standard of care; ARR=absolute risk reduction; CI=confidence interval; NNT=number needed to treat; MI=myocardial infarction.



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SUSTAIN 6 – A 2-year CVOT for Ozempic®¹ ✱

3297
patients²

Inclusion criteria:
T2D, HbA_{1c} ≥7%
Age ≥60 years with at least
1 CV risk factor[†]

(17% of patients)

OR

Age ≥50 years with established
CV disease* **(83% of patients)**
• Ischaemic heart disease: **60.5%**
• MI: **32.5%**
• Ischaemic stroke: **11.6%**

1:1:1:1
*double-blinded
randomisation*²

Ozempic® 1 mg
Ozempic® 0.5 mg

Placebo 1 mg
Placebo 0.5 mg



**Diabetes and CV
standards of care**²

Treatment duration 2 years^{2†}

Primary composite outcome¹

Time from randomisation to
first occurrence of MACE



CV death



Nonfatal MI



Nonfatal stroke

*Established CV disease (previous CV, cerebrovascular or peripheral vascular disease) or chronic heart failure (New York Heart Association class II or III) or chronic kidney disease stage 3 or higher.²

[†]Defined as persistent microalbuminuria (30–299 mg/g) or proteinuria, hypertension and LV hypertrophy by electrocardiogram or imaging, LV systolic or diastolic dysfunction by imaging or ankle/brachial index <0.9 of those in the trial.²³

[‡]Trial consisted of 104 weeks of treatment (including 4–8 weeks of dose-escalation period), with a subsequent 5-week follow-up period.²

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; CV=cardiovascular; MI=myocardial infarction; LV=left ventricular.



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SUSTAIN 6 – Patient characteristics at baseline^{2,23}

Patients with established CVD*	Gender	Mean age	Mean weight/BMI	Mean HbA _{1c}	Mean diabetes duration
83%	61% male	65 years	92.1 kg/ 32.8 kg/m²	8.7%	13.9 years

Most commonly used CV SOC agents²³

Statins	73%
Acetylsalicylic acid	64%
Beta blockers	57%
ACE inhibitors	50%
Loop diuretics	17%

CV risk factors at baseline^{2,23}

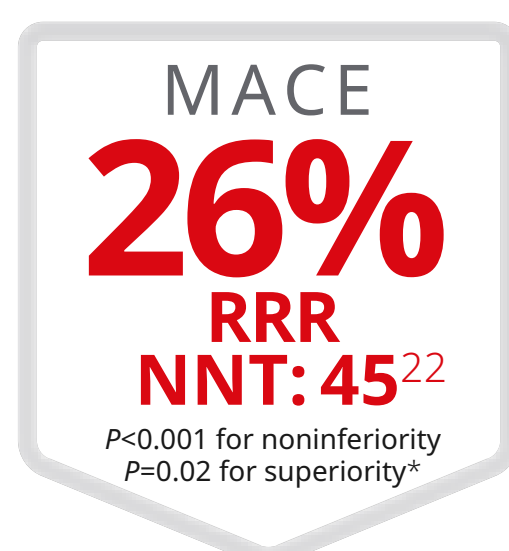
Mean systolic blood pressure:	135.6 mm Hg
Mean diastolic blood pressure:	77.0 mm Hg
Low-density lipoprotein cholesterol:	82.3 mg/dL
Never smoked:	45%

*Age ≥50 years with established CVD (previous CV, cerebrovascular or peripheral vascular disease), chronic heart failure (New York Heart Association class II or class III), or chronic kidney disease of stage 3 or higher.²
MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; CVD=cardiovascular disease; BMI=body mass index; CV=cardiovascular; SOC=standard of care; ACE=angiotensin-converting enzyme.

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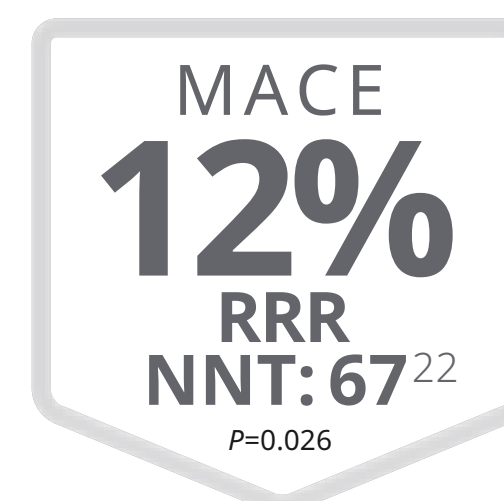
CVOTs in T2D: A closer look

SUSTAIN 6² (semaglutide vs placebo)



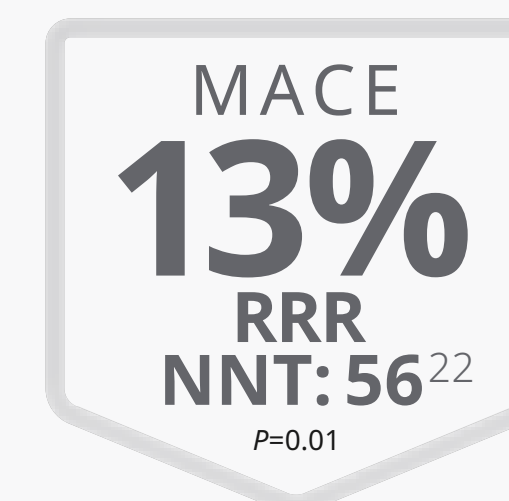
- ♥ CV death=-2%
[HR=0.98 (95% CI, 0.65–1.48; P=0.92)]
- ♥ Nonfatal stroke=-39%
[HR=0.61 (95% CI, 0.38–0.99; P=0.04)]
- ♥ Nonfatal MI=-26%
[HR=0.74 (95% CI, 0.51–1.08; P=0.12)]

REWIND²⁴ (dulaglutide vs placebo)



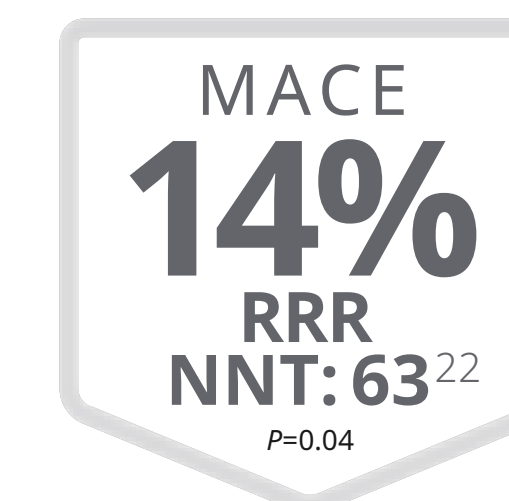
- ♥ CV death[†]=-9%
[HR=0.91 (95% CI, 0.78–1.06; P=0.21)]
- ♥ Nonfatal stroke=-24%
[HR=0.76 (95% CI, 0.61–0.95; P=0.017)]
- ♥ Nonfatal MI=-4%
[HR=0.96 (95% CI, 0.79–1.16; P=0.65)]

LEADER²⁵ (liraglutide vs placebo)



- ♥ CV death=-22%
[HR=0.78 (95% CI, 0.66–0.93; P=0.007)]
- ♥ Nonfatal stroke=-11%
[HR=0.89 (95% CI, 0.72–1.11; P=0.30)]
- ♥ Nonfatal MI=-12%
[HR=0.88 (95% CI, 0.75–1.03; P=0.11)]

EMPA-REG²⁶ (empagliflozin vs placebo)



- ♥ CV death=-38%
[HR=0.62 (95% CI, 0.49–0.77; P<0.001)]
- ♥ Nonfatal stroke=24%
[HR=1.24 (95% CI, 0.92–1.67; P=0.16)]
- ♥ Nonfatal MI=-13%
[HR=0.87 (95% CI, 0.70–1.09; P=0.22)]

Please note that CVOTs differ by trial design.
Therefore, the results cannot be used as a head-to-head comparison.

CVOT Patient Characteristics

The image shown is a model and not a real patient.

*Testing for superiority for primary outcome was not prespecified.²

[†]Includes deaths of unknown cause.²⁴

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; RRR=relative risk reduction; NNT=number needed to treat; CV=cardiovascular; HR=hazard ratio; CI=confidence interval; MI=myocardial infarction.

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Who were the patients in these CVOTs?

	SUSTAIN 6^{2,23} (semaglutide vs placebo)	REWIND^{24,27} (dulaglutide vs placebo)	LEADER^{25,28} (liraglutide vs placebo)	EMPA-REG^{26,29} (empagliflozin vs placebo)
CV RISK	83% established CVD	31% established CVD	81% established CVD	>99% established CVD
CV HISTORY				
PRIOR MI	32%	16.2%	31%	47%
HEART FAILURE	24%	8.6%	18%	10%
MEAN DIABETES DURATION	14 years	10 years	13 years	>10 years
MEAN HbA _{1c}	8.7%	7.3%	8.7%	8.1%
INSULIN USE	58%	24%	44.6%	48%
TRIAL DURATION	2 years	5.4 years	3.5–5 years	3.1 years*

**Please note that CVOTs differ by trial design.
Therefore, the results cannot be used as a head-to-head comparison.**

*Median observation time.²⁹

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; CV=cardiovascular; CVD=cardiovascular disease; MI=myocardial infarction.



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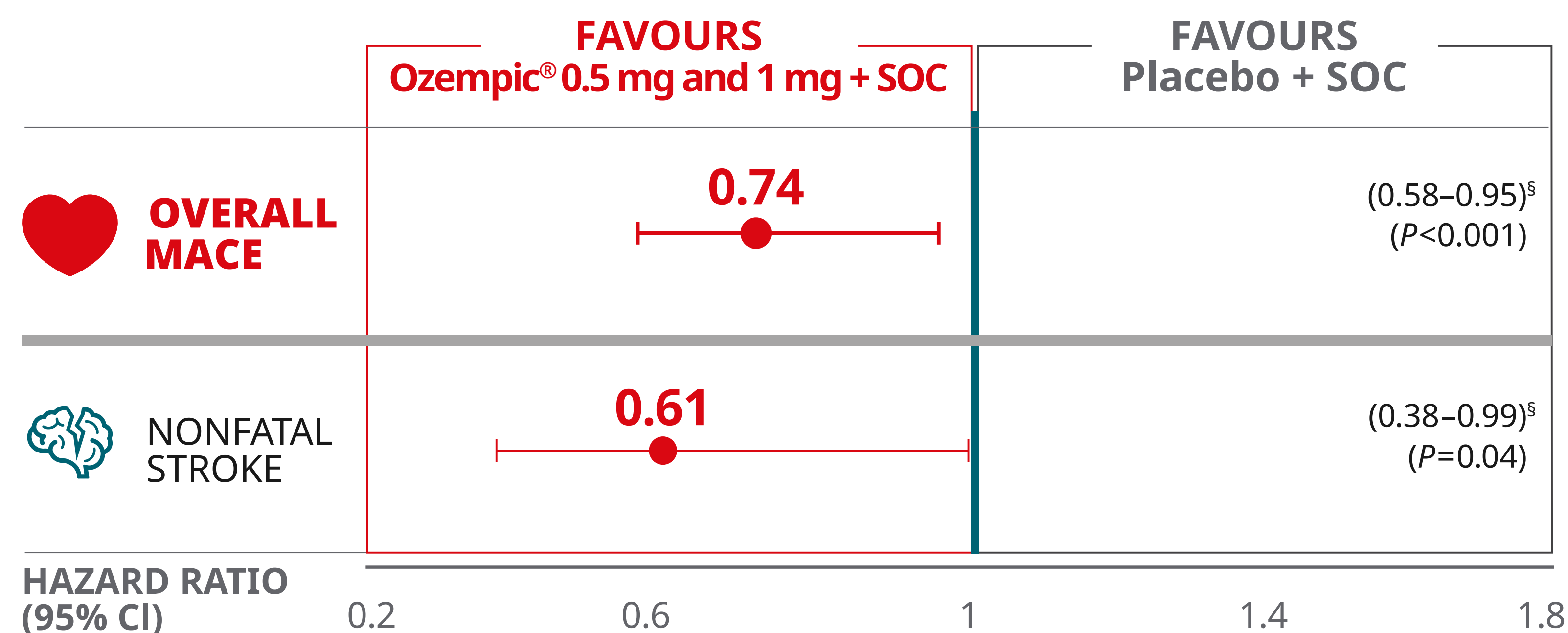


39%
SIGNIFICANT
REDUCTION
IN RATE OF
NONFATAL
STROKE DROVE
THE MACE
REDUCTION^{2‡§}

In adult patients with T2D who have high CV risk, established ASCVD or both^{2*}

**Ozempic® significantly reduced the risk of MACE,
driven by nonfatal stroke^{1,2}**

Composite primary endpoint: 26% RRR of MACE (2.3% ARR at 109 weeks)^{1,2†}



Additional CV-related outcomes

*When added to SOC. SOC included, but was not limited to, oral antidiabetic treatment, insulin, antihypertensives, diuretics and lipid-lowering therapies.²³

[†]Absolute rates for nonfatal stroke: 2.7% (n=44 of 1649) with placebo vs 1.6% (n=27 of 1648) with Ozempic® (0.5 mg and 1 mg). There was no significant change in the rate of nonfatal MI or CV death.²

[‡]The primary endpoint in the SUSTAIN 6 CVOT was time to first occurrence of a 3-part composite outcome that included CV death, nonfatal MI or nonfatal stroke.^{1,2}

[§]Hazard ratio vs placebo (95% CI). Mean study observation time of 2.1 years. Cox proportional-hazards model with treatment as factor and stratified according to all combinations of stratification factors used in the randomisation.²

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; CV=cardiovascular; ASCVD=atherosclerotic cardiovascular disease; RRR=relative risk reduction; ARR=absolute risk reduction; SOC=standard of care; CI=confidence interval; MI=myocardial infarction.



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In adult patients with T2D who have high CV risk, established ASCVD or both^{2*}

Ozempic[®] did more than reduce the risk of MACE²³

Additional CV-related outcomes from the CVOT for Ozempic[®]:²³



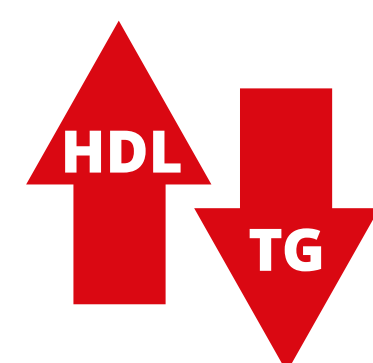
Lower rate of systolic blood pressure

2.6 mm Hg lower with the 1 mg dose vs placebo ($P<0.001$)



Statistically significant change in LDL cholesterol ratio vs placebo

ETR vs placebo for the 0.5 mg dose was 0.96 mg/dL ($P<0.05$)



Statistically significant change in HDL cholesterol and triglycerides ratio vs placebo

HDL: ETR vs placebo for the 1 mg dose was 1.04 mg/dL ($P<0.0001$)

Triglycerides: ETR vs placebo for the 1 mg dose was 0.93 mg/dL ($P<0.001$)

*When added to SOC. SOC included, but was not limited to, oral antidiabetic treatment, insulin, antihypertensives, diuretics and lipid-lowering therapies.²³

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; CV=cardiovascular; ASCVD=atherosclerotic cardiovascular disease; LDL=low-density lipoprotein; ETR=estimated treatment ratio; HDL=high-density lipoprotein; TG=triglycerides; SOC=standard of care.



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In stroke patients, diabetes is an independent risk factor for stroke recurrence³⁰



RISK OF STROKE
RECURRENCE WAS



IN STROKE PATIENTS
WITH DIABETES VS
THOSE WITHOUT³⁰

DIABETES HAS BEEN
ASSOCIATED WITH



FOLLOWING A STROKE VS THE
GENERAL POPULATION^{31,32}

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial.



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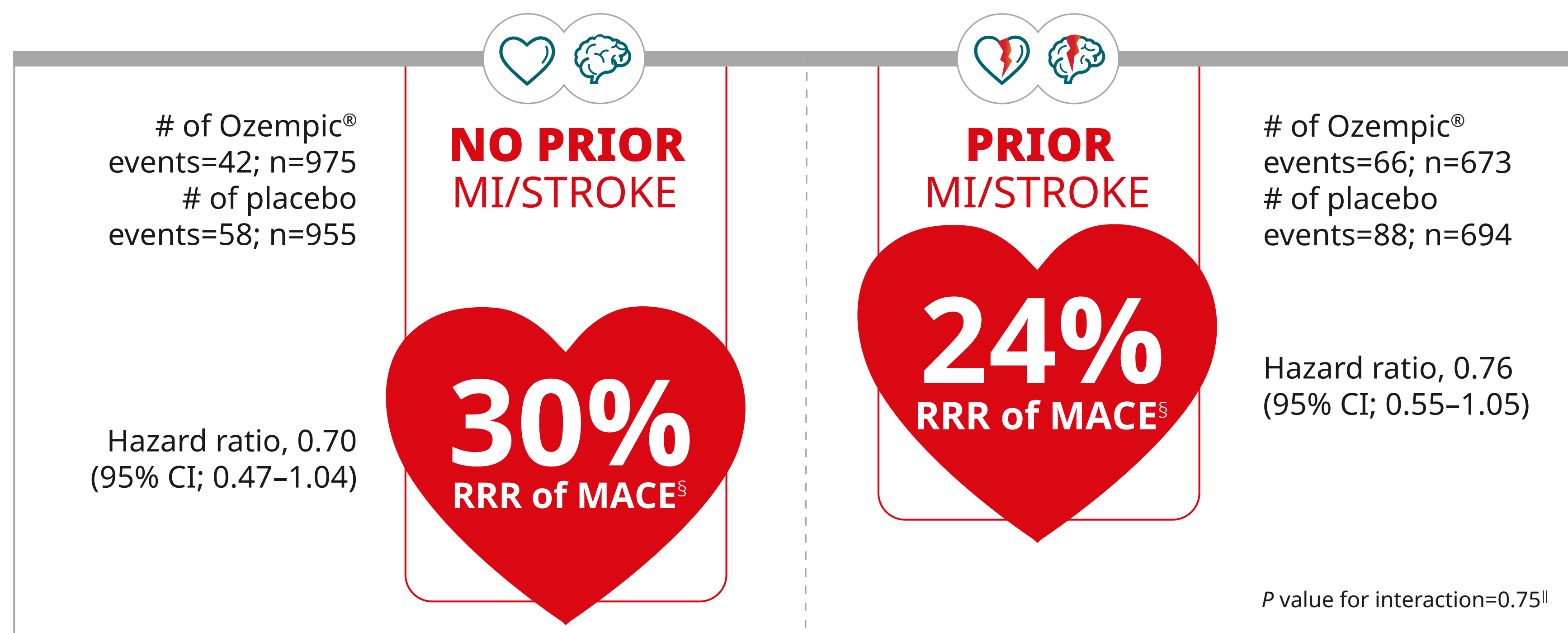
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In adult patients with T2D who have high CV risk, established ASCVD or both^{2*}

Ozempic® delivered consistent effects across patients with and without history of MI/stroke²³

Post-hoc subgroup analysis of the composite primary endpoint^{23†‡}



*When added to SOC. SOC included, but was not limited to, oral antidiabetic treatment, insulin, antihypertensives, diuretics and lipid-lowering therapies.²³

[†]# of MACE: Ozempic® (n=108 of 1648) and placebo (n=146 of 1649). Hazard ratio, 0.74 (95% CI; 0.58–0.95). $P < 0.001$ for noninferiority vs placebo plus SOC; $P = 0.02$ for superiority, not prespecified.²

[‡]The consistency in the treatment effect for the primary outcome was explored in multiple subgroup analyses based on baseline information (eg. age, sex, baseline HbA_{1c}, insulin use, history of renal impairment, and CVD status, including prior history of MI or stroke). Included patients who met the inclusion criteria predefined in the study.²³

[§]Composite MACE endpoint included: CV death, nonfatal MI, or nonfatal stroke.¹

^{||}P value was estimated using Cox proportional-hazards models for the test of the interaction effect with no adjustments for multiplicity.²³

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; CV=cardiovascular; ASCVD=atherosclerotic cardiovascular disease; MI=myocardial infarction; CI=confidence interval; RRR=relative risk reduction; SOC=standard of care; CVD=cardiovascular disease.



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ONCE-WEEKLY
OZEMPIC[®]
semaglutide injection



UNMET NEED

GUIDELINES

MACE

STROKE

ADDITIONAL
CVOT RESULTS

EFFICACY

SAFETY AND
TOLERABILITY

DOSING

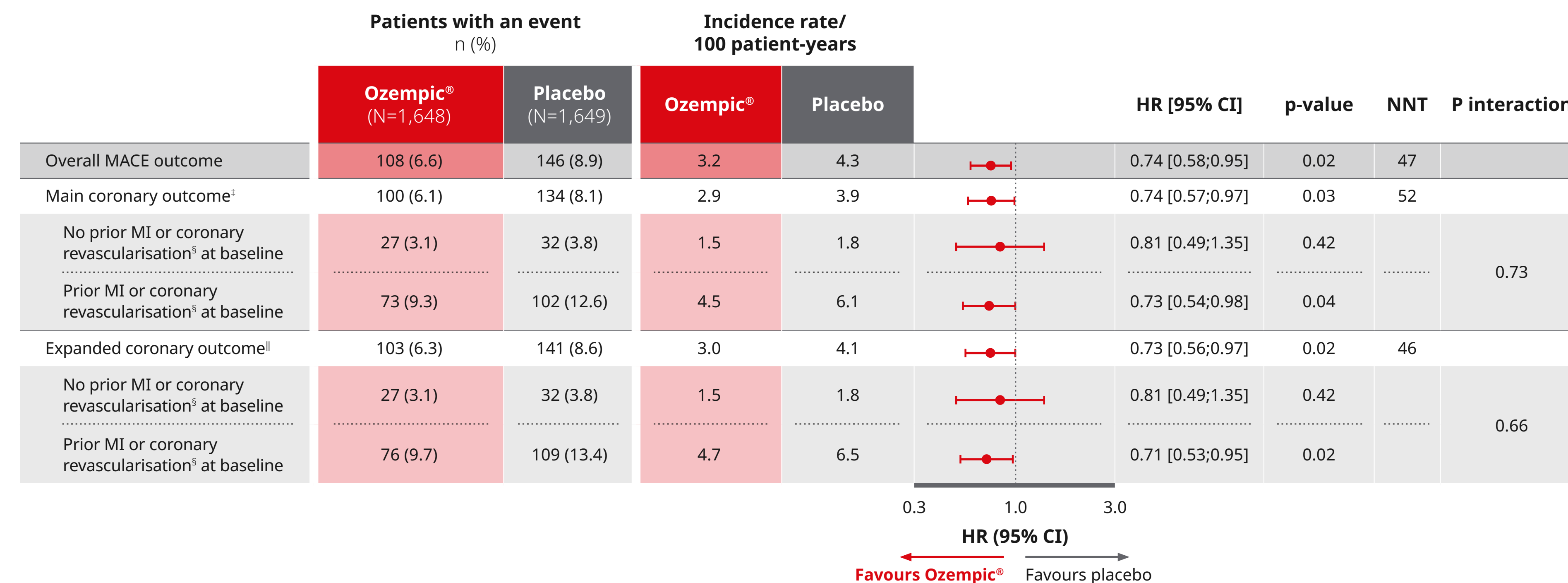
PATIENT
PROFILES

SUMMARY

**REDUCED
RISK**
OF CORONARY
OUTCOMES IN
BOTH PRIMARY
AND SECONDARY
PREVENTION^{33*†}

In adult patients with T2D with or at high risk for CVD

Ozempic® reduced the risk of composite coronary outcomes vs placebo, irrespective of prior MI or revascularisation status^{33*†}



Results are from an exploratory post-hoc analysis.³³

*Results are from post-hoc analyses of the SUSTAIN-6 CVOT. Post-hoc analyses assessed the effects of once-weekly Ozempic® (0.5 mg and 1 mg doses pooled) plus SOC on composite coronary outcomes in the SUSTAIN-6 trial population (N=3297) vs placebo plus SOC. The median follow-up duration was 2.1 years.³³

†When added to SOC. SOC included, but was not limited to, oral antidiabetic treatment, insulin, antihypertensives, diuretics and lipid-lowering therapies.²³

‡The main coronary outcome was a composite of MI (both fatal and nonfatal) or coronary revascularisation (defined as coronary artery bypass graft surgery or percutaneous coronary intervention).³³

§Defined as coronary artery bypass graft surgery or percutaneous coronary intervention.³³

||The expanded coronary outcome was a composite of MI, coronary revascularisation, or unstable angina.³³

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; CVD=cardiovascular disease; MI=myocardial infarction; HR=hazard ratio; CI=confidence interval; NNT=number needed to treat; SOC=standard of care.



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semaglutide injection



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DOSING

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SUMMARY

SEMAGLUTIDE
REDUCED
THE RISK OF
MACE ACROSS
A RANGE OF
CV RISK^{34,35}

Semaglutide's CV effects in patients with T2D may span across the CV risk continuum^{34,35}

- In a pooled post-hoc analysis of semaglutide CVOTs where patients with T2D and high CV risk were re-categorised into CV risk subgroups using the REWIND CVD criteria, semaglutide **reduced the risk of MACE** (primary endpoint) relative to placebo in both the **established CVD subgroup** (HR=0.74 [95% CI, 0.59–0.92]) **and the CV risk factor subgroup** (HR=0.84 [95% CI, 0.55–1.28; *P*=0.60))^{34*}
- In a pooled post-hoc meta-analysis of 18 semaglutide phase 3a trials including a broad T2D population, semaglutide **reduced the risk of MACE** (primary endpoint) vs several comparators (HR=0.77 [95% CI, 0.64–0.93]) **across the continuum of baseline CV risk**^{35†}

Results are from post-hoc analyses.^{34,35}

*Results are from an exploratory post-hoc analysis that assessed the impact of semaglutide plus SOC vs placebo plus SOC on CV outcomes in a pooled population of SUSTAIN 6 (semaglutide s.c. 0.5 mg and 1 mg) and PIONEER 6 (semaglutide oral target dose 14 mg) patients who were re-categorised into CV risk subgroups according to REWIND CVD criteria (N=6480).^{2,34,36} The key criteria differences between the trials were patients with CKD, CHF, prior TIA, or prior haemorrhagic stroke were categorised with established CVD in SUSTAIN 6 and PIONEER 6, but as having CV risk factors only in REWIND. The primary endpoint was a composite of MACE (CV death, nonfatal MI, or nonfatal stroke).³⁴

†Results are from a post-hoc meta-analysis of data from 18 phase 3a SUSTAIN and PIONEER trials, with patients distributed across the continuum of baseline CV risk using a CV risk prediction model (N=17645). Data were pooled according to the randomised treatment; semaglutide (0.5 and 1 mg s.c. and 3, 7 and 14 mg oral) or comparator (placebo, sitagliptin, exenatide ER, insulin glargine, dulaglutide, liraglutide and empagliflozin). Primary endpoint was time to first MACE (CV death, nonfatal MI, or nonfatal stroke).³⁵

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; CV=cardiovascular; T2D=type 2 diabetes; CVD=cardiovascular disease; HR=hazard ratio; CI=confidence interval; SOC=standard of care; s.c.=subcutaneous; CKD=chronic kidney disease; CHF=chronic heart failure; TIA=transient ischaemic attack; MI = myocardial infarction; ER=extended-release.



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semaglutide injection



UNMET NEED

GUIDELINES

MACE

STROKE

ADDITIONAL
CVOT RESULTS

EFFICACY

SAFETY AND
TOLERABILITY

DOSING

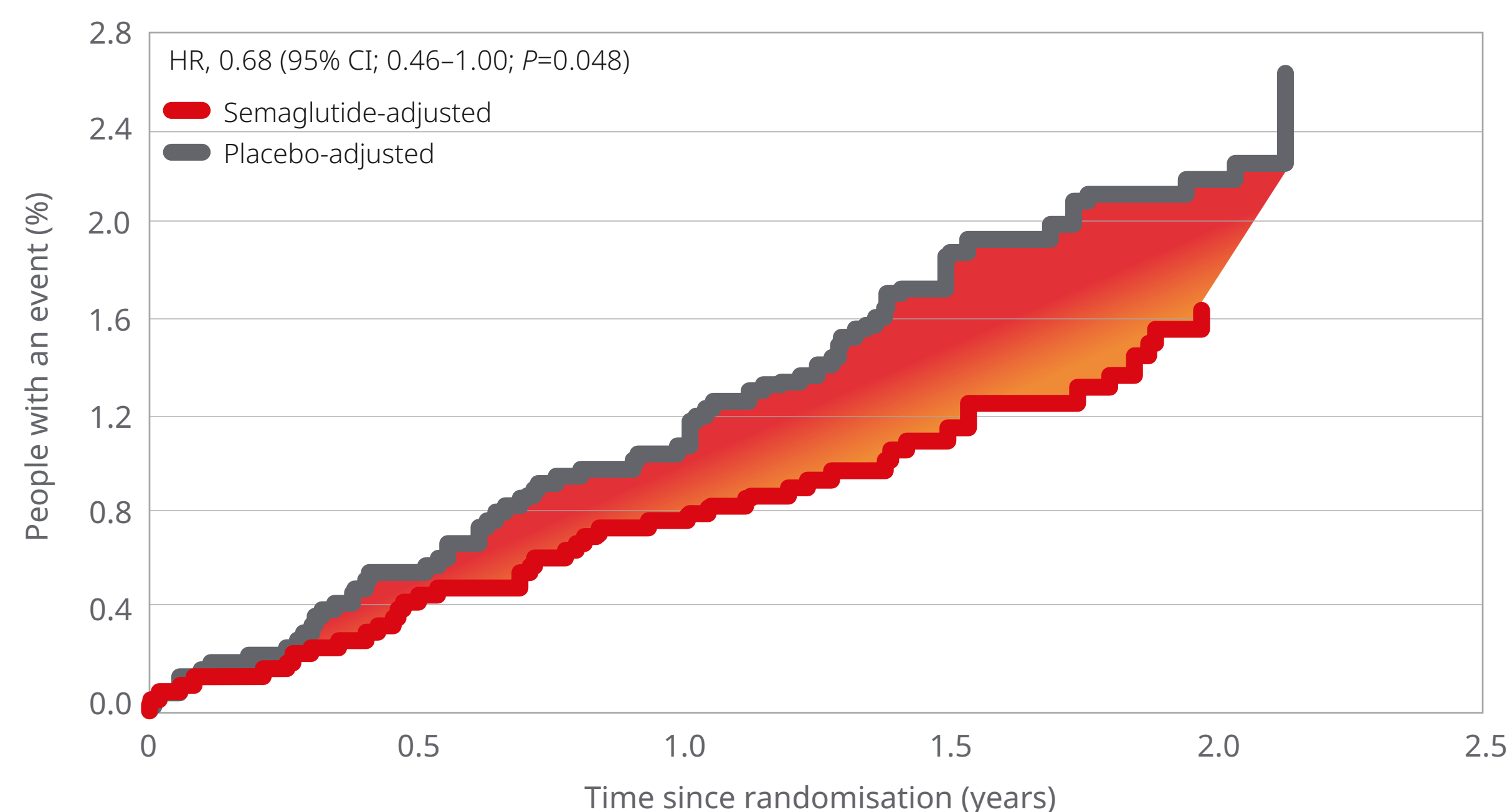
PATIENT
PROFILES

SUMMARY

OZEMPIC®
– HIGHEST
PROBABILITY
TO RANK
1ST
OF THE GLP-1
RAs IN STROKE
AND MI
REDUCTION³⁸

Reduction in the risk of stroke in primary and secondary prevention with semaglutide³⁷

- In a pooled exploratory post-hoc analysis of semaglutide CVOTs, semaglutide reduced the risk of any first stroke compared with placebo in patients with T2D at high CV risk (HR=0.68 [95% CI, 0.46–1.00; $P=0.048$])^{37*}
 - Also, the risk of stroke was reduced with semaglutide vs placebo irrespective of prior stroke at baseline^{37*}



- A network meta-analysis indirectly comparing GLP-1 RAs showed that Ozempic® had the highest probability to rank first in reducing stroke and MI^{38†}

Results are from an exploratory post-hoc analysis and network meta-analysis, respectively.^{37,38}

*Results are from an exploratory post-hoc analysis that assessed the effects of semaglutide plus SOC vs placebo plus SOC on stroke and its subtypes in a pooled population of SUSTAIN 6 (semaglutide s.c. 0.5 mg and 1 mg) and PIONEER 6 (semaglutide oral target dose 14 mg) (N=6480).^{2,36,37} Time to first occurrence of any type of stroke (fatal and nonfatal; transient ischaemic attacks were not included) and stroke subtypes, including ischaemic and haemorrhagic strokes, as well as unknown subtypes, were investigated.³⁷

†Results are from a network meta-analysis that indirectly compared the CV safety and mortality effects among different GLP-1 RAs in patients with T2D. A total of 7 GLP-1 RA CVOTs were included where each compared the CV safety of a GLP-1 RA (lixisenatide, liraglutide, semaglutide s.c., exenatide, albiglutide, dulaglutide and semaglutide oral) to placebo, both as an added on therapy to the SOC (N=56004).³⁸

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; CV=cardiovascular; HR=hazard ratio; CI=confidence interval; GLP-1 RA=glucagon-like peptide-1 receptor agonist; MI=myocardial infarction; SOC=standard of care; s.c.=subcutaneous.



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UNMET NEED

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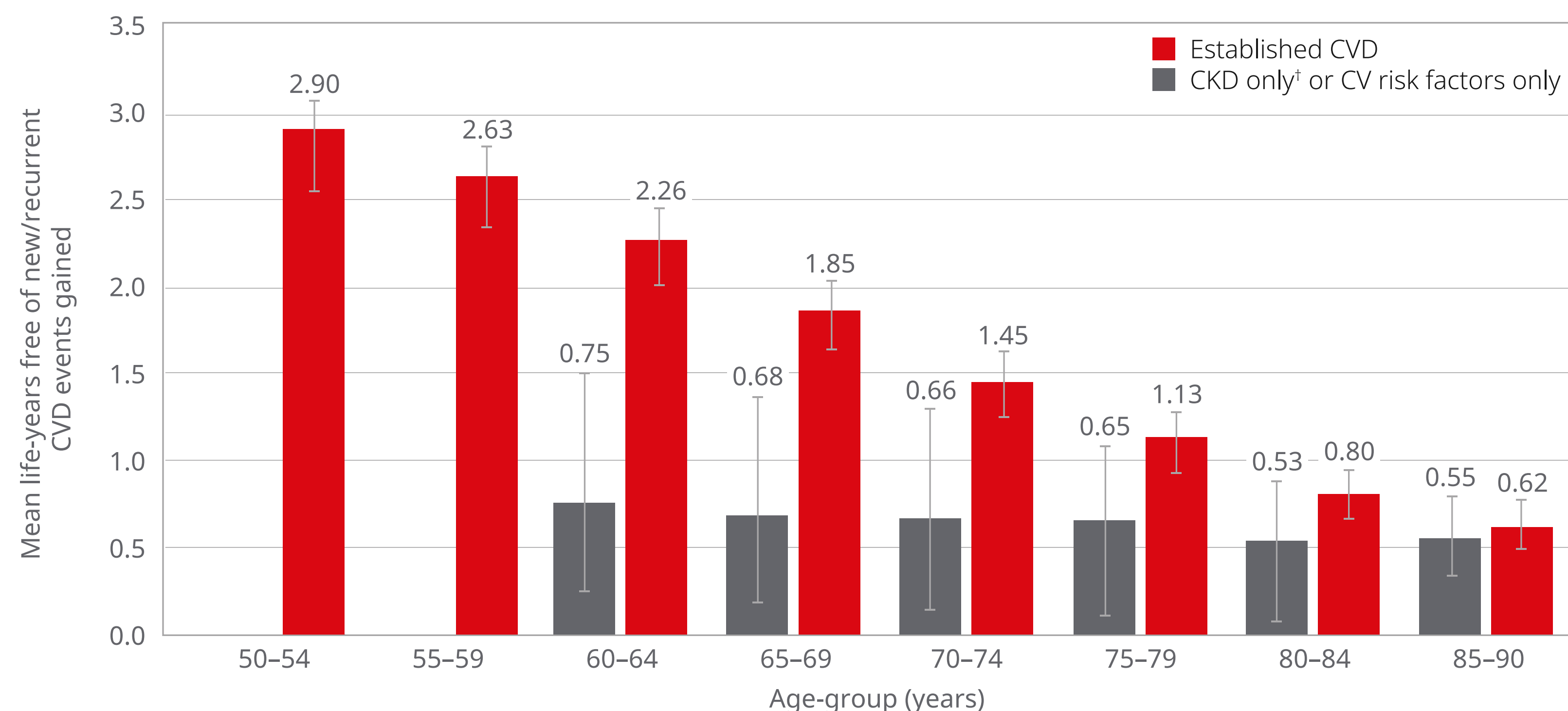
PATIENT
PROFILES

SUMMARY

MEAN
**INCREASE
OF 1.7
LIFE-YEARS**
FREE OF NEW/
RECURRENT CVD
EVENTS WITH
SEMAGLUTIDE³⁹

In adult patients with T2D and high risk of CVD

**Semaglutide was associated with a gain in life-years
free of new/recurrent CVD events³⁹***



**The greatest absolute benefit was seen in patients with higher
baseline risk and who were younger at treatment initiation³⁹**

*Results are from a study that used the DIAL model to estimate the effect of adding semaglutide to SOC on life-years free of new/recurrent CVD events in people with T2D and high risk of CVD, using pooled data from SUSTAIN 6 (semaglutide s.c. 0.5 mg and 1 mg) and PIONEER 6 (semaglutide oral target dose 14 mg) (N=6480). The DIAL model is an externally validated, competing risk-adjusted model that is currently the only lifetime risk prediction tool for people with T2D and has been recommended for use by the European Society of Cardiology. Key outcomes were absolute gain in life-years free of new/recurrent CVD events, defined as life-years free of new or current MACE (CV death, nonfatal MI, or nonfatal stroke) and 10-year CVD risk, defined as 10-year risk of new or recurrent MACE.³⁹

†eGFR <60 mL/min/1.73 m² (estimated using the CKD-EPI creatinine equation) and no established CVD.³⁹

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; CVD=cardiovascular disease; CKD=chronic kidney disease; CV=cardiovascular; DIAL= Diabetes Lifetime-perspective prediction; SOC=standard of care; s.c.=subcutaneous; MI=myocardial infarction; eGFR=estimated glomerular filtration rate; CKD-EPI=Chronic Kidney Disease Epidemiology Collaboration.



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ONCE-WEEKLY
OZEMPIC[®]
semaglutide injection

[UNMET NEED](#)[GUIDELINES](#)[MACE](#)[STROKE](#)[ADDITIONAL
CVOT RESULTS](#)[EFFICACY](#)[SAFETY AND
TOLERABILITY](#)[DOSING](#)[PATIENT
PROFILES](#)[SUMMARY](#)

**Ozempic[®] can get the majority of patients
to the ADA goal of HbA_{1c} <7%^{1,3,4,40}**

UP TO

80%



ACHIEVED ADA TARGET OF HbA_{1c}

<7%

vs OTHER DIABETES TREATMENTS^{1,3,4,40*}

The image shown is a model and not a real patient.

*In head-to-head studies vs dulaglutide, insulin glargine, sitagliptin, liraglutide and canagliflozin.^{1,3,4}

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; ADA=American Diabetes Association.

[R](#)[SmPC](#)[Study Designs](#)

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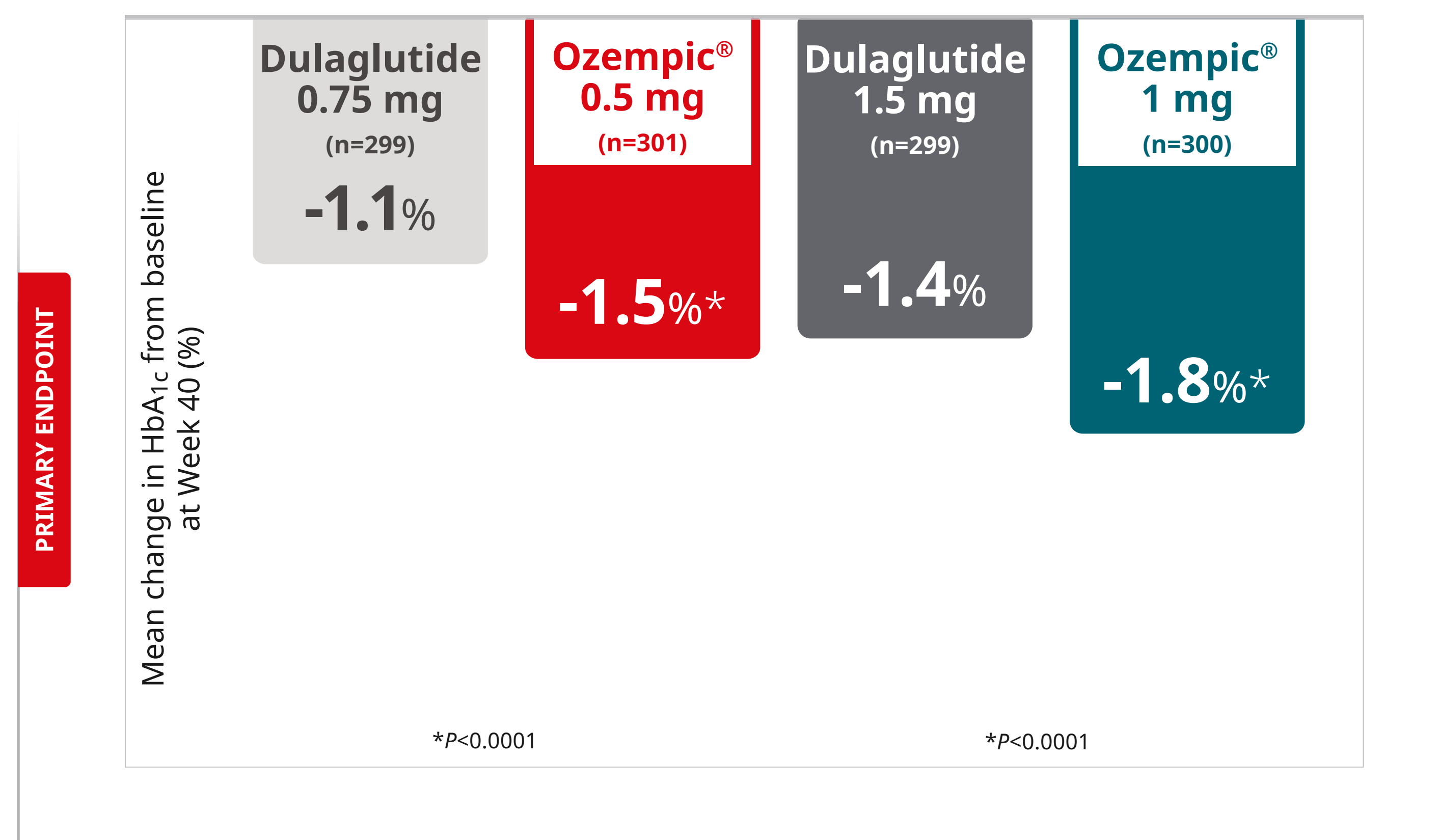
SUMMARY

In adult patients with T2D

Ozempic® demonstrated superior glycaemic control vs dulaglutide^{1,7}

In patients on metformin

Superior glycaemic control vs dulaglutide^{1,7}

SUSTAIN 7: Mean baseline HbA_{1c} 8.2%

SIGNIFICANT
DROP IN MEAN
HbA_{1c}
VS DULAGLUTIDE
1.5 mg BY UP TO
1.8%
WITH
OZEMPIC® 1 mg
(P<0.0001)^{1,7}

SUSTAIN 7: Results are from a 40-week, randomised, open-label, active-controlled trial in 1201 adult patients with T2D comparing Ozempic® 0.5 mg with dulaglutide 0.75 mg and Ozempic® 1 mg with dulaglutide 1.5 mg.⁷ MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes.



UNMET NEED

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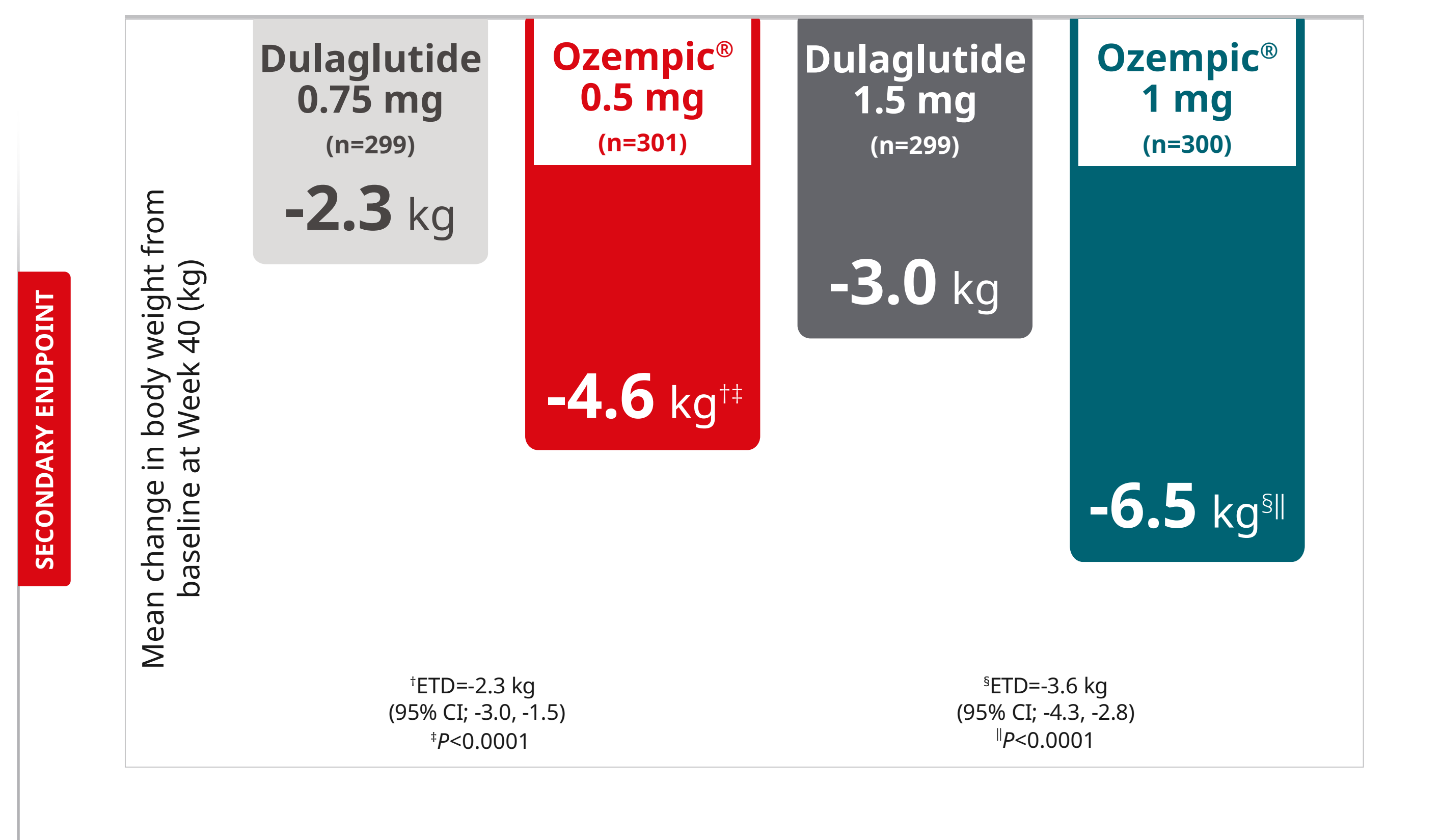
PATIENT
PROFILES

SUMMARY

Compelling weight loss vs dulaglutide^{1,7*}

In patients on metformin

Superior weight reduction vs dulaglutide across the dose range^{1,7}



SUSTAIN 7: Mean baseline weight 95.2 kg

Ozempic[®] delivered >2X the weight loss of dulaglutide^{1,7*}

**SIGNIFICANT
LOSS IN
MEAN WEIGHT
BY UP TO
6.5 KG**
WITH OZEMPIC[®] 1 mg
VS DULAGLUTIDE 1.5 mg
($P < 0.0001$)^{1,7*}

SUSTAIN 7: Results are from a 40-week, randomised, open-label, active-controlled trial in 1201 adult patients with T2D comparing Ozempic[®] 0.5 mg with dulaglutide 0.75 mg and Ozempic[®] 1 mg with dulaglutide 1.5 mg.⁷

*Ozempic[®] is not indicated for weight loss.¹

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; ETD=estimated treatment difference; CI=confidence interval; T2D=type 2 diabetes.



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semaglutide injection



The safety of Ozempic® was evaluated across multiple clinical trials and across all dose levels¹

No dose adjustments required with Ozempic® in the following special populations¹

PATIENTS WITH RENAL IMPAIRMENT

- Patients reporting severe adverse gastrointestinal reactions when initiating or escalating doses of Ozempic® should be monitored for renal function
- Ozempic® is not recommended for patients with end-stage renal disease
- Experience with the use of Ozempic® in patients with severe renal impairment is limited

PATIENTS WITH HEPATIC IMPAIRMENT

- Use caution in patients with severe hepatic impairment
- Limited clinical trial experience in patients with severe hepatic impairment

PATIENTS ≥65 YEARS

- No overall differences in safety or efficacy were detected between these patients and younger patients, but therapeutic experience in patients ≥75 years is limited

Patients taking oral contraceptives¹

- When co-administered, Ozempic® did not change the overall exposure of oral contraceptive 0.03 mg ethinyl estradiol/0.15 mg levonorgestrel, so is not expected to decrease the clinical effectiveness of oral contraceptives
- No treatment break for oral contraceptives is required when initiating or escalating doses of Ozempic®

Overall low incidence of severe hypoglycaemia^{1,3,4,41*}

- Incidence of severe hypoglycaemia was ≤1.5% when Ozempic® was used with insulin¹

GI events^{4,7,42}

- GI tolerability comparable with other GLP-1 RAs

Pancreatitis^{1,4,7,42}

- Low frequency of acute pancreatitis in clinical studies

Diabetic retinopathy complications¹

- Caution should be exercised when using Ozempic® in patients with diabetic retinopathy treated with insulin
 - These patients should be monitored and treated according to clinical guidelines

*Data comprises patients in SUSTAIN studies 1–5 and 7–10 but excludes patients on concomitant sulphonylurea, insulin or both.^{1,3,4,41}

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; GI=gastrointestinal; GLP-1 RA= glucagon-like peptide-1 receptor agonist.



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HbA_{1c} control within your control: Ozempic® once-weekly dose options for a range of patients¹

Gradual dose escalation designed to help patients adjust to therapy¹



Administer Ozempic® once weekly on the same day each week, at any time of the day, with or without meals¹



The image shown is a model and not a real patient.

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial.



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***Do you have T2D patients
who would benefit from
once-weekly Ozempic[®],
a GLP-1 RA with
proven CV benefit?^{1,8}***

**Learn more about how you can help
your patients manage CVD and T2D**

Assess CV risk

The images shown are models and not real patients.

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; GLP-1 RA= glucagon-like peptide-1 receptor agonist; CV=cardiovascular; CVD=cardiovascular disease.



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Estimation of CV risk is a key component of the 2019 ESC/EASD Guidelines⁸

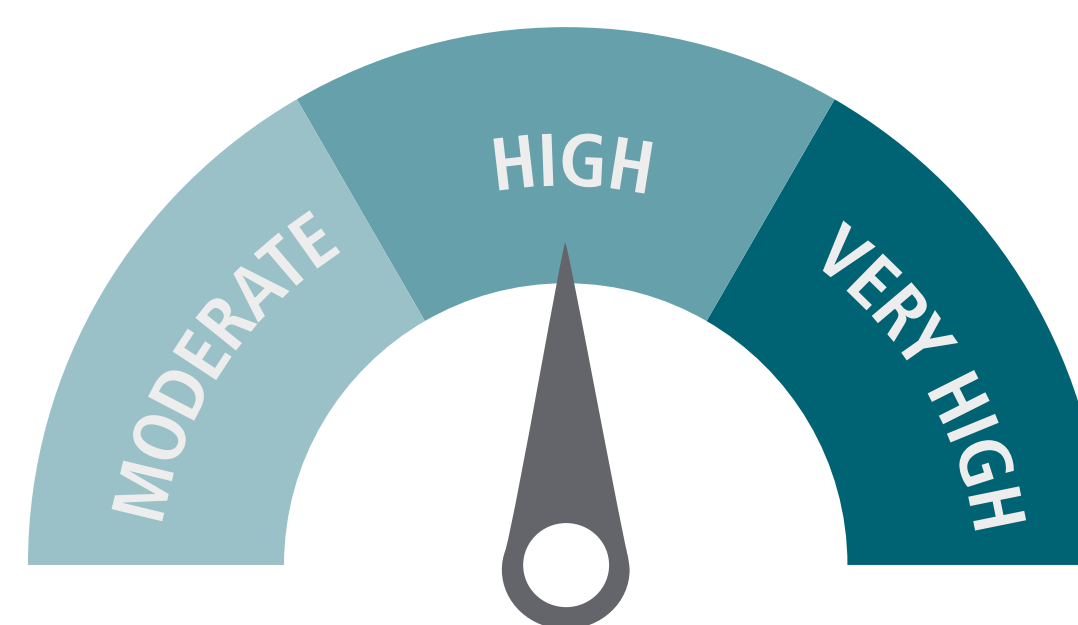
How to identify patients who can benefit most from treatment of CV risk factors



Very High Risk⁸

Patients with diabetes and established CVD, or any of the following:

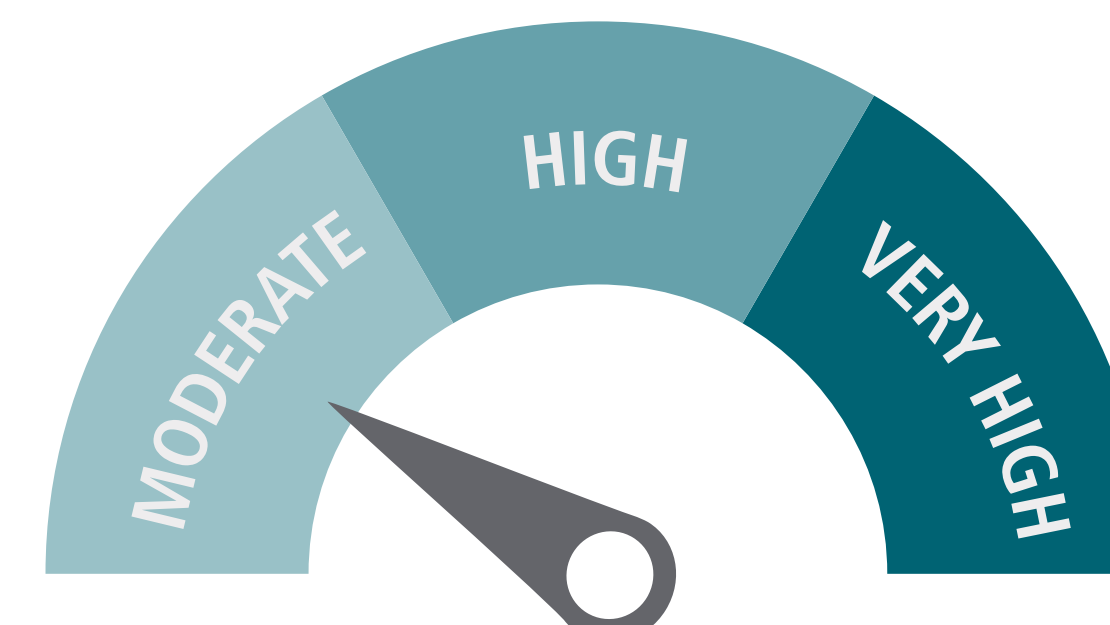
- ✓ Other target organ damage*
- ✓ ≥3 major risk factors (eg, age, hypertension, dyslipidaemia, smoking or obesity)
- ✓ Early onset T1D of long duration (>20 years)



High Risk⁸

Patients with a diabetes duration of ≥10 years

- ✓ Without target organ damage
- ✓ Any additional risk factor (patient may have hypertension, dyslipidaemia, be obese or be a smoker)



Moderate Risk⁸

Young patients (T1D aged <35 years or T2D aged <50 years)

- ✓ With a diabetes duration of <10 years without other risk factors



The 2019 ESC/EASD Guidelines recommend the use of a GLP-1 RA or SGLT-2i with a proven CV benefit for patients with CVD and T2D, or who are at very high or high CV risk, to reduce the risk of CV events⁸

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*Proteinuria, renal impairment defined as eGFR <30 mL/min/1.73 m², left ventricular hypertrophy or retinopathy.⁸

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; CV=cardiovascular; ESC=European Society of Cardiology; EASD=European Association for the Study of Diabetes; CVD=cardiovascular disease; T1D=type 1 diabetes; T2D=type 2 diabetes; GLP-1 RA=glucagon-like peptide-1 receptor agonist; SGLT-2i=sodium-glucose co-transporter 2 inhibitor; eGFR=estimated glomerular filtration rate.



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Meet Rebecca*

A long-time patient with T2D and established ASCVD



Very High CV Risk

Patient history

Rebecca is a 62-year-old woman presenting with chest pain after years of dealing with T2D and trying to balance her cholesterol levels and blood pressure. She takes multiple medications, but she is still not meeting her treatment goals – she is obese, her cholesterol and HbA_{1c} levels are too high, and she's exhausted all the time. Around 10 years ago, Rebecca suffered a heart attack, and she is increasingly concerned she may have another CV event.



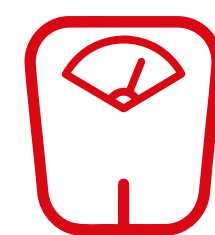
Had an MI; stents inserted 10 years ago



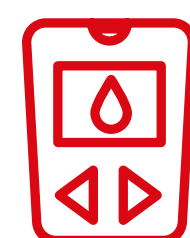
History of hypertension and dyslipidaemia



Chronic fatigue



Obese



Diagnosed with T2D 12 years ago; HbA_{1c} not controlled; currently experiencing mild background diabetic neuropathy

Lab results and medical history



Do you have patients like Rebecca who may benefit from additional CV risk management?

The image shown is a model and not a real patient.

*The character and accompanying description are for representation purposes only and do not reflect a real patient.

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; ASCVD=atherosclerotic cardiovascular disease; CV=cardiovascular; MI=myocardial infarction.



 Lab results*		
Blood pressure	134/85 mm Hg	↑ HIGH ⁴³
Total cholesterol	290 mg/dL	↑ HIGH ⁴⁴
– LDL-C	182 mg/dL	↑ HIGH ⁴⁴
– HDL-C	35 mg/dL	↓ LOW ⁴⁴
Triglycerides	400 mg/dL	↑ HIGH ⁴⁴
eGFR	76 mL/min/1.73 m ²	✓ NORMAL ⁴⁵
BMI	31 kg/m ²	↑ Obese ⁴⁶
HbA _{1c}	7.6%	↑ HIGH ⁴⁷

 Current medication:*			
Atorvastatin	80 mg/day	Pioglitazone	30 mg/day
Enalapril	10 mg/day	Sitagliptin	100 mg/day
Metformin	1000 mg 2x/day	Pregabalin	150 mg/day

*The lab results and prescriptions are based on a patient example and not a real patient.
MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; LDL-C=low-density lipoprotein cholesterol; HDL-C=high-density lipoprotein cholesterol; eGFR=estimated glomerular filtration rate; BMI=body mass index.



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Meet Peter*

A patient with high CVD risk, uncontrolled T2D and obesity



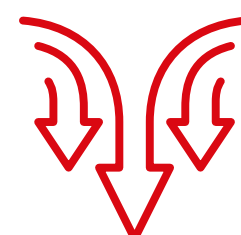
High CV Risk

Patient history

Peter is a 52-year-old man recently referred to you by his GP for ongoing chest pain. Peter has anxiety and is concerned about his heart health due to a history of CVD in his family – he lost his father to stroke. While he has been working hard to manage his T2D, Peter has also had difficulty adhering to his recommended diet and exercise regimens during the COVID-19 lockdown and has gained substantial weight. He has been taking oral medication for his T2D but remains worried about life-changing CV events like stroke and MI. Recently, Peter has been experiencing erectile dysfunction.[†] He is unsure if this is a physical symptom or stress related. Peter worries he won't be able to lose the weight, regain his health and gain back his confidence.



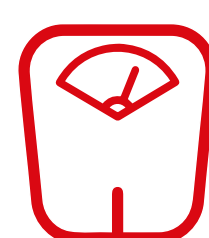
Family history of CVD



Recent history of
erectile dysfunction



Diagnosed with T2D
10 years ago



Obese: gained 10 kg over
the course of 1 year during
the COVID-19 lockdown

Lab results and medical history



**Do you have patients like Peter who may
benefit from additional CV risk management?**

The image shown is a model and not a real patient.

*The character and accompanying description are for representation purposes only and do not reflect a real patient.

[†]ED can influence CVD risk, and CVD risk assessment may be needed in men presenting with ED.⁴⁸

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; CVD=cardiovascular disease; T2D=type 2 diabetes; CV=cardiovascular; GP=general practitioner; MI=myocardial infarction; ED=erectile dysfunction.



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ONCE-WEEKLY
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 Lab results*		
Blood pressure	130/85 mm Hg	↑ HIGH ⁴³
Total cholesterol	150 mg/dL	✓ NORMAL ⁴⁴
– LDL-C	93 mg/dL	✓ NORMAL ⁴⁴
– HDL-C	45 mg/dL	✓ NORMAL ⁴⁴
Triglycerides	600 mg/dL	↑ HIGH ⁴⁴
eGFR	78 mL/min/1.73 m ²	✓ NORMAL ⁴⁵
BMI	31 kg/m ²	↑ Obese ⁴⁶
HbA _{1c}	8.2%	↑ HIGH ⁴⁷

 Current medication:*			
Metformin	1000 mg 2x/day	Glipizide	5 mg 2x/day

*The lab results and prescriptions are based on a patient example and not a real patient.
MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; LDL-C=low-density lipoprotein cholesterol; HDL-C=high-density lipoprotein cholesterol; eGFR=estimated glomerular filtration rate; BMI=body mass index.



UNMET NEED

GUIDELINES

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Meet Anna*

A middle-aged patient with a recent T2D diagnosis and a history of obesity



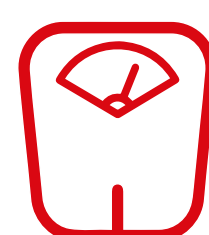
High CV Risk

Patient history

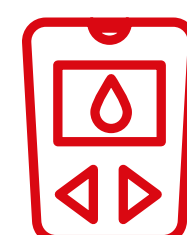
Anna is a 48-year-old receptionist referred to you for a heart check-up before she starts an exercise program. Anna is also obese and has trouble getting her weight under control due to her sedentary lifestyle and difficulties managing her T2D. She was recently diagnosed with sleep apnoea and is even more concerned about her health now. Anna has been taking medications for her T2D but remains worried about CV events like MI and stroke. She is aware of her CV risk and is motivated to make a change to improve her health and quality of life.



Family history of CVD



Long history of obesity and lack of exercise since her 20s



Diagnosed with T2D
5 years ago

Lab results and medical history



Do you have patients like Anna who may benefit from additional CV risk management?

The image shown is a model and not a real patient.

*The character and accompanying description are for representation purposes only and do not reflect a real patient.

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; CV=cardiovascular; MI=myocardial infarction; CVD=cardiovascular disease.



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Study Designs

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ONCE-WEEKLY
OZEMPIC[®]
semaglutide injection



Lab results*

Blood pressure	132/86 mm Hg	↑ HIGH ⁴³
Total cholesterol	221 mg/dL	↑ HIGH ⁴⁴
– LDL-C	130 mg/dL	↑ HIGH ⁴⁴
– HDL-C	35 mg/dL	↓ LOW ⁴⁴
Triglycerides	256 mg/dL	↑ HIGH ⁴⁴
eGFR	68 mL/min/1.73 m ²	✓ NORMAL ⁴⁵
BMI	35 kg/m ²	↑ Obese ⁴⁶
HbA _{1c}	7.8%	↑ HIGH ⁴⁷

Current medication:*

Metformin	1000 mg 2x/day
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*The lab results and prescriptions are based on a patient example and not a real patient.
MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; LDL-C=low-density lipoprotein cholesterol; HDL-C=high-density lipoprotein cholesterol; eGFR=estimated glomerular filtration rate; BMI=body mass index.



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SUMMARY



In adult patients with T2D

Choose Ozempic® as your first injectable

Get adult patients with T2D into the Ozempic® Zone¹

PROVEN CV RISK REDUCTION^{1,2★}

26% RRR of MACE vs placebo (2.3% ARR at 109 weeks) in patients with T2D and high CV risk

POWERFUL GLYCAEMIC CONTROL^{1,3,4†}

Up to 80% achieved ADA target of HbA_{1c} <7% vs other diabetes treatments^{1,3,4,40‡}

COMPELLING WEIGHT LOSS^{1,7§}

Greater weight reduction (vs dulaglutide) was seen as dosage increased, with a mean weight loss of up to -6.5 kg with Ozempic® 1 mg

The image shown is a model and not a real patient.

*Results apply to Ozempic® 0.5 mg and 1 mg plus SOC vs placebo plus SOC in adults with T2D who have high CV risk, established ASCVD or both.²

†Results apply to Ozempic® across SUSTAIN trials, which included placebo, sitagliptin, dulaglutide, exenatide ER, insulin glargine, canagliflozin and liraglutide.^{1,3,4} **SUSTAIN 4:** Mean change in HbA_{1c} at Week 30 (+ MET ± SU), baseline 8.2% (N=1089): -1.2% Ozempic® 0.5 mg (n=362), (*P*<0.0001) and -1.6% Ozempic® 1 mg (n=360), (*P*<0.0001) vs -0.8% study-titrated insulin glargine (n=360).^{1,6} **SUSTAIN 7:** Mean change in HbA_{1c} at Week 40 (+ MET), baseline 8.2% (N=1201): -1.5% Ozempic® 0.5 mg (n=301) vs -1.1% dulaglutide 0.75 mg (n=299), (*P*<0.0001); -1.8% Ozempic® 1 mg (n=300) vs -1.4% dulaglutide 1.5 mg (n=299), (*P*<0.0001).^{1,7}

‡In head-to-head studies vs dulaglutide, insulin glargine, sitagliptin, liraglutide and canagliflozin.^{1,3,4}

§Ozempic® is not indicated for weight loss.¹ **SUSTAIN 4:** Mean change in body weight at Week 30 (+ MET ± SU), baseline 93.5 kg (N=1089): -3.5 kg Ozempic® 0.5 mg (n=362), (*P*<0.0001) and -5.2 kg Ozempic® 1 mg (n=360), (*P*<0.0001) vs +1.15 kg study-titrated insulin glargine (n=360).^{1,6} **SUSTAIN 7:** Mean change in body weight at Week 40 (+ MET), baseline 95.2 kg (N=1201): -4.6 kg Ozempic® 0.5 mg (n=301) vs -2.3 kg dulaglutide 0.75 mg (n=299), (*P*<0.0001); -6.5 kg Ozempic® 1 mg (n=300) vs -3.0 kg dulaglutide 1.5 mg (n=299), (*P*<0.0001).^{1,7}

MACE=major adverse cardiovascular events; CVOT=cardiovascular outcomes trial; T2D=type 2 diabetes; CV=cardiovascular; RRR=relative risk reduction; ARR=absolute risk reduction; ADA=American Diabetes Association; SOC=standard of care; ASCVD=atherosclerotic cardiovascular disease; ER=extended-release; MET=metformin; SU=sulphonylurea.



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ONCE-WEEKLY
OZEMPIC[®]
semaglutide injection



ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS



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STUDY DESIGNS

SUSTAIN 1: Monotherapy vs placebo⁴⁹

A 30-week, randomised, double-blind, placebo-controlled, parallel-group, multicentre trial to evaluate the efficacy and safety of Ozempic® vs placebo. A total of 388 patients with type 2 diabetes inadequately controlled with diet and exercise were randomised to receive once-weekly Ozempic® 0.5 mg (n=128), Ozempic® 1 mg (n=130) or placebo (n=129). The primary endpoint was change in mean HbA_{1C} at week 30, and the confirmatory secondary endpoint was change in mean body weight at Week 30.

SUSTAIN 2: Head-to-head vs sitagliptin^{1,50}

A 56-week, randomised, double-blind, double-dummy, active-controlled, parallel-group, multicentre trial to compare the efficacy and safety of Ozempic® vs sitagliptin. A total of 1231 patients with type 2 diabetes inadequately controlled on metformin and/or thiazolidinediones were randomised to receive once-weekly Ozempic® 0.5 mg (n=409), once-weekly Ozempic® 1 mg (n=409) or once-daily sitagliptin 100 mg (n=407). The primary endpoint was change in HbA_{1C} at Week 56, and the confirmatory secondary endpoint was change in body weight at Week 56.

SUSTAIN 3: Head-to-head vs exenatide ER^{1,42}

A 56-week, randomised, open-label, active-controlled, parallel-group, multicentre trial to compare the efficacy and safety of Ozempic® vs exenatide ER. A total of 813 patients with type 2 diabetes inadequately controlled on oral antidiabetic drugs (metformin, and/or thiazolidinediones, and/or sulphonylureas) were randomised to receive once-weekly Ozempic® 1 mg (n=404) or once-weekly exenatide ER 2 mg (n=405). The primary endpoint was change in HbA_{1C} at Week 56, and the confirmatory secondary endpoint was change in body weight at Week 56.

SUSTAIN 4: Head-to-head vs insulin glargine^{1,6}

A 30-week, randomised, open-label, parallel-group, multicentre trial to compare the efficacy and safety of Ozempic® vs insulin glargine. A total of 1089 insulin-naïve patients with type 2 diabetes inadequately controlled on metformin alone or in combination with sulphonylurea were randomised to receive once-weekly Ozempic® 0.5 mg (n=362), once-weekly Ozempic® 1 mg (n=360) or once-daily insulin glargine with a starting dose of 10 IU (n=360). The primary endpoint was change in mean HbA_{1C} at Week 30, and the confirmatory secondary endpoint was change in mean body weight at Week 30.

SUSTAIN 5: As add-on to basal insulin vs placebo^{1,51}

A 30-week, randomised, double-blind, placebo-controlled, parallel-group, multicentre trial to demonstrate the superiority of Ozempic® in combination with basal insulin vs placebo. A total of 397 patients inadequately controlled on basal insulin with or without metformin were randomised to once-weekly Ozempic® 0.5 mg (n=132), Ozempic® 1 mg (n=131) or placebo (n=133). Randomisation was stratified according to HbA_{1C} at screening and use of metformin. Patients with HbA_{1C} ≤8% at screening reduced the insulin dose by 20% at start of trial to reduce the risk of hypoglycaemia. The primary endpoint was change in HbA_{1C} at Week 30, and the confirmatory secondary endpoint was change in body weight at Week 30.

SUSTAIN 6: CV outcomes^{1,2,23}

A 104-week, randomised, double-blind, placebo-controlled, parallel-group trial to evaluate CV safety of Ozempic®. A total of 3297 patients with type 2 diabetes and high risk of CV events were randomised based on evidence of CV disease, insulin treatment and renal impairment to once-weekly Ozempic® 0.5 mg (n=826), Ozempic® 1 mg (n=822) or placebo (n=1649) in addition to standard of care treatments such as oral antidiabetic treatments, insulin, antihypertensives, diuretics and lipid-lowering therapies at investigator discretion. The primary endpoint was time from randomisation to first occurrence of a major adverse cardiovascular event: cardiovascular death, nonfatal myocardial infarction or nonfatal stroke.



SUSTAIN 6: CV outcomes^{1,2,23}

A 104-week, randomised, double-blind, placebo-controlled, parallel-group trial to evaluate CV safety of Ozempic®. A total of 3297 patients with type 2 diabetes and high risk of CV events were randomised based on evidence of CV disease, insulin treatment and renal impairment to once-weekly Ozempic® 0.5 mg (n=826), Ozempic® 1 mg (n=822) or placebo (n=1649) in addition to standard of care treatments such as oral antidiabetic treatments, insulin, antihypertensives, diuretics and lipid-lowering therapies at investigator discretion. The primary endpoint was time from randomisation to first occurrence of a major adverse cardiovascular event: cardiovascular death, nonfatal myocardial infarction or nonfatal stroke.

Inclusion criteria were HbA_{1c} ≥7%; previously on 0–2 oral antidiabetic drugs (OADs), basal or pre-mix insulin +/- 0–2 OADs; ≥50 years with established CV disease (≥1 coexisting condition); ≥60 years with at least 1 CV risk factor as determined by the investigator. Exclusion criteria were treatment with a dipeptidyl peptidase-4 inhibitor within 30 days before screening or with a GLP-1 receptor agonist or insulin other than basal or pre-mixed within 90 days before screening; a history of an acute coronary or cerebrovascular event within 90 days before randomisation; planned revascularisation of a coronary, carotid or peripheral artery; or long-term dialysis.

SUSTAIN 7: Head-to-head vs dulaglutide⁷

A 40-week, randomised, open-label, active-controlled, parallel-group, multicentre, multinational, 4-armed trial to compare the efficacy and safety of Ozempic® vs dulaglutide. A total of 1201 patients with type 2 diabetes inadequately controlled on metformin were randomised to receive Ozempic® 0.5 mg (n=301), Ozempic® 1 mg (n=300), dulaglutide 0.75 mg (n=299) or dulaglutide 1.5 mg (n=299) once weekly. The primary endpoint was change in HbA_{1c} at Week 40, and the confirmatory secondary endpoint was change in body weight at Week 40.

SUSTAIN 8: Head-to-head vs canagliflozin³

A 52-week, confirmatory, randomised (1:1), double-blind, double-dummy, active-comparator, parallel-group trial to compare the efficacy and safety of once-weekly Ozempic® 1 mg vs once-daily oral canagliflozin 300 mg, both in combination with metformin. 788 adults with type 2 diabetes inadequately controlled with metformin were randomised. The primary endpoint was change in HbA_{1c} at Week 52, and the confirmatory secondary endpoint was change in body weight at Week 52.

SUSTAIN 9: As add-on to SGLT-2i vs placebo⁴¹

A randomised, double-blind, parallel-group trial to compare the efficacy and safety of Ozempic® as add-on to SGLT-2i monotherapy or in combination with either metformin or sulphonylurea vs placebo. 302 patients with type 2 diabetes and inadequate glycaemic control, despite >90 days of treatment with an SGLT-2i, were randomly assigned (1:1) to receive Ozempic® 1 mg or volume-matched placebo once weekly for 30 weeks. Existing antidiabetic medications, including SGLT-2i treatment, were continued during the trial. The primary outcome was change in HbA_{1c} from baseline at Week 30, with confirmatory secondary outcome of change in body weight over the same period.

SUSTAIN 10: Head-to-head vs liraglutide⁴

An open-label, parallel-group, multicentre trial conducted in 11 European countries to compare the efficacy and safety of Ozempic® vs liraglutide in 577 adults with type 2 diabetes, on 1 to 3 oral antidiabetic drugs. Patients were randomised 1:1 to Ozempic® 1 mg once weekly or liraglutide 1.2 mg once daily. Randomisation was stratified by background medication of sulphonylureas +/- metformin, SGLT-2i +/- metformin, SU and SGLT-2i +/- metformin or metformin monotherapy. Primary endpoint was change in HbA_{1c} from baseline to Week 30 and the confirmatory secondary endpoint was change in body weight from baseline to Week 30.

SUSTAIN FORTE: Ozempic® 1 mg vs 2 mg⁵²

Study design: 40-week, randomised, active-controlled, parallel-group, double-blind, phase 3B efficacy and safety trial of Ozempic® 2 mg vs Ozempic® 1 mg in patients with type 2 diabetes in need of treatment intensification. Patients: A total of 961 adult patients with inadequately controlled type 2 diabetes (HbA_{1c} 8.0%–10.0%) on metformin with or without a sulphonylurea were randomised 1:1 to 2 mg (n=480) or 1 mg (n=481) of once-weekly Ozempic®. Primary endpoint: Change in HbA_{1c} from baseline at Week 40. Confirmatory secondary endpoint: Change in body weight from baseline at Week 40.