7.2% (6.8, 7.6). At baseline, 82.5% and 5.8% of patients were taking statins and ezetimibe respectively. LDL-C was ≤55 mg/dL in 14.3%; 55.1 to 70 in 18.4%, 70.1 to 100 in 35% and >100 in 32.3%. Each 10 mg/dL of higher LDL-C was associated with increased risk of CV death (HR 1.06; 95% CI 1.04–1.09) and MACE (HR 1.05; 95% CI 1.03–1.07). The probability of MACE as a function of baseline LDL-C, along with 95% confidence limits, is depicted in the Figure.

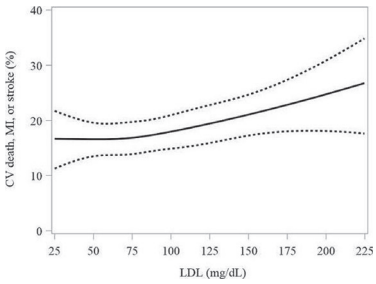

Figure 1

Conclusions: While the majority of DM patients with stable CV disease in real world practice were on LDL-C lowering therapy, only one third had an LDL-C at or below current target goals and only one in seven patients were below more stringent AACE-proposed LDL target. Every 10 mg higher LDL-C was independently associated with a 6% increased hazard for CV death and 5% for MACE.
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P1878
Reduction in systolic blood pressure with semaglutide treatment is not due to weight loss alone: data from SUSTAIN 1-5

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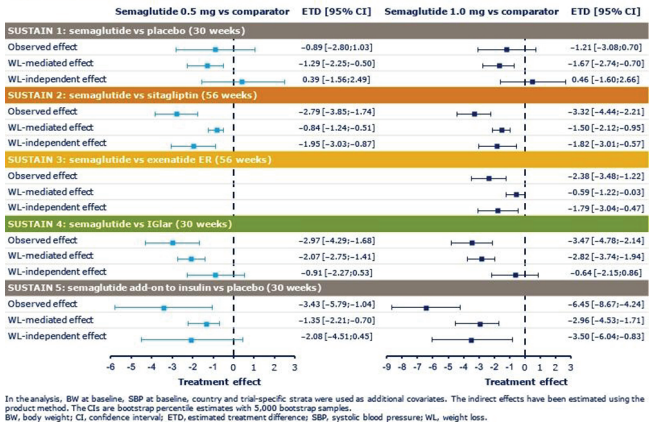
Background: Elevated blood pressure (BP) and excess body weight (BW) are common in type 2 diabetes (T2D). Weight loss (WL) is associated with a reduction in BP. Glucagon-like peptide-1 (GLP-1) receptor agonist class effects include reduction of blood glucose, BW and BP. Semaglutide, a GLP-1 analogue for the treatment of T2D, significantly reduced HbA1c, BW and systolic BP (SBP) vs comparators across the phase 3a SUSTAIN clinical trial programme.
Purpose: To investigate the contribution of WL to the reduction in SBP associated with semaglutide treatment across SUSTAIN 1–5.
Methods: SUSTAIN 1–5 included subjects with inadequately controlled T2D, randomised to once-weekly, subcutaneous semaglutide 0.5 or 1.0 mg (1.0 mg in SUSTAIN 3), or comparator for 30 or 56 weeks. Comparators were placebo (SUSTAIN 1 and 5), sitagliptin (SUSTAIN 2), exenatide extended release (SUSTAIN 3) and insulin glargine (SUSTAIN 4). Mediation analyses were performed post hoc to quantify the relative contribution of WL (mediator) to the treatment effect of semaglutide on SBP; WL was considered an indirect effect (WL-mediated), the effect not mediated by WL was considered a direct effect of semaglutide on SBP (WL-independent). Reduction in SBP was also evaluated across weight-change categories. Analyses were conducted on individual trials, due to differences in populations, comparators and background therapy.
Results: Across the SUSTAIN 1–5 trials (n=3,918), mean changes in SBP (baseline 128.8–134.8 mmHg) ranged from –2.6 to –5.1 mmHg and –2.7 to –7.3 mmHg, with semaglutide 0.5 and 1.0 mg, respectively, vs –1.0 to –2.3 mmHg with comparators (p<0.02 vs comparator for all trials except SUSTAIN 1 [both doses] and SUSTAIN 5 [lower dose]). Mean changes in BW (baseline 89.5–95.8 kg) ranged from –3.5 to –4.3 kg and –4.5 to –6.4 kg with semaglutide 0.5 and 1.0 mg, respectively, vs –1.9 to +1.2 kg with comparators (p<0.0001 vs comparator for all trials). WL-mediated and WL-independent effects of semaglutide on SBP reduction for each trial are shown in the Figure. There were greater reductions in SBP with semaglutide (vs comparators) across all weight-change categories evaluated. In the >4.0 kg WL category, mean change in SBP was –3.0 to –6.8 and –4.4 to –9.3 mmHg with semaglutide 0.5 and 1.0 mg, respectively, vs –4.0 to +1.1 mmHg with comparators. In the 0–4.0 kg WL category, mean change in SBP was –2.0 to –4.8 mmHg and –0.7 to –5.2 mmHg with semaglutide 0.5 and 1.0 mg, respectively, vs -2.1 to -4.2 mmHg with comparators. For subjects with no WL/BW gain, mean change in SBP was –1.5 to +1.5 mmHg and –5.4 to +1.0 mmHg with semaglutide 0.5 and 1.0 mg, respectively, vs –1.0 to +1.1 mmHg with comparators.
Conclusion: With semaglutide, greater WL was generally associated with greater reductions in SBP. However, the SBP reduction observed with semaglutide was driven by both WL-mediated and WL-independent mechanisms.
Funding Acknowledgements: Sponsored by Novo Nordisk A/S

Figure. Mediation analysis showing the observed effect of semaglutide (vs comparator) on SBP for each trial as well as the WL-mediated and WL-independent effects



In the analysis, BW at baseline, SBP at baseline, country and trial-specific strata were used as additional covariates. The indirect effects have been estimated using the product method. The CIs are bootstrap percentile estimates with 5,000 bootstrap samples.
BW, body weight; CI, confidence interval; ETD, estimated treatment difference; SBP, systolic blood pressure; WL, weight loss.

P1879
Empagliflozin reduces mortality and hospitalisation for heart failure irrespective of cardiovascular risk score at baseline

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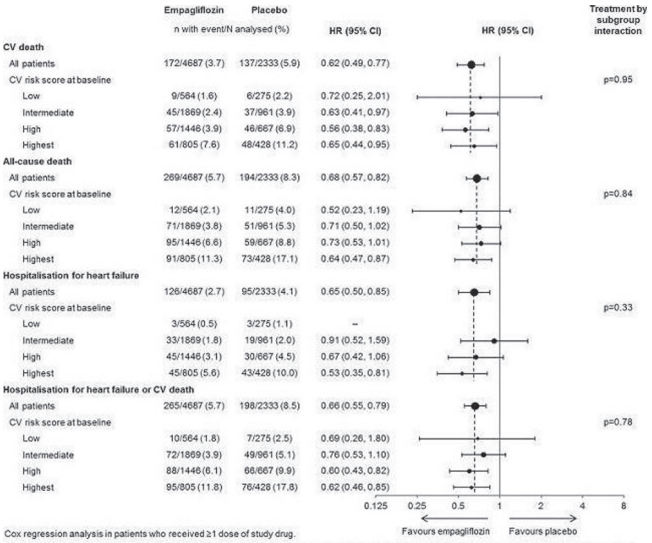
Background: In the EMPA-REG OUTCOME trial in patients with type 2 diabetes and established cardiovascular (CV) disease, empagliflozin added to standard of care reduced CV death vs placebo by 38% (HR 0.62 [95% CI 0.49, 0.77]), all-cause death by 32% (HR 0.68 [95% CI 0.57, 0.82]) and hospitalisation for heart failure (HHF) by 35% (HR 0.65 [95% CI 0.50, 0.85]). We investigated whether residual CV risk at baseline influenced the effect of empagliflozin on these outcomes.
Methods: We investigated CV death, all-cause death, HHF and the composite of HHF or CV death with empagliflozin vs placebo in subgroups by degree of CV risk at baseline based on the 10-point TIMI Risk Score for Secondary Prevention (TRS 2°P). P-values for treatment-by-subgroup interaction were obtained from tests of homogeneity of treatment group differences among subgroups with no adjustment for multiple testing.
Results: Based on the TRS 2°P risk score, of 7020 patients who received study drug in the EMPA-REG OUTCOME trial, 12%, 40%, 30% and 18% were at low, intermediate, high and highest residual CV risk, respectively, at baseline. In the placebo group, from low to highest predicted risk, the proportion of patients with CV death increased from 2.2% to 11.2% and the proportion of patients with HHF increased from 1.1% to 10.0%. Effects of empagliflozin on CV death, all-cause death, HHF and HHF or CV death were consistent across subgroups by baseline CV risk score (Figure).



Cox regression analysis in patients who received ≥1 dose of study drug.
The 10-point TRS 2°P included (1 point each): heart failure; hypertension; age ≥75 years; diabetes; prior stroke; prior coronary artery bypass graft surgery; peripheral artery disease; eGFR <60 ml/min/1.73m²; current smoking; prior myocardial infarction.
Residual CV risk: low = ≤2 points; intermediate = 3 points; high = 4 points; highest = ≥5 points.

Conclusion: The benefits of empagliflozin on key clinical outcomes in the EMPA-