

SUPPLEMENTARY DATA

Supplementary Table 1. Baseline Characteristics of Participants According to Cardiovascular and Severe Hypoglycemic Events

	SHE and CV event (N=116)	SHE and no CV event (N=350)
Age at Randomization (years)	65 (61, 71)	63 (56, 70)
Female sex	31 (26.7%)	150 (42.9%)
Race		
White	83 (71.6%)	227 (64.9%)
Black	11 (9.5%)	35 (10.0%)
Asian	10 (8.6%)	40 (11.4%)
Other	12 (10.3%)	48 (13.7%)
Duration of type 2 diabetes (years)	16 (11, 23)	14 (9, 21)
History of CV disease		
Coronary artery disease	91 (78.4%)	198 (56.6%)
Cerebrovascular disease	34 (29.3%)	56 (16.0%)
Peripheral artery disease	25 (21.6%)	63 (18.0%)
CV event		
Prior CV event	107 (92.2%)	254 (72.6%)
CV disease without prior event	0 (0%)	6 (1.7%)
Neither prior CV event nor disease	9 (7.8%)	90 (25.7%)
Heart failure	43 (37.1%)	55 (15.7%)
Charlson Comorbidity Index	8 (6, 9)	6 (4, 7)
Systolic blood pressure (mmHg)	132 (122, 145)	136 (125, 148)
Diastolic blood pressure (mmHg)	77 (68, 81)	78 (70, 83)
Heart rate (bpm)	73 (65, 82)	72 (65, 80)
Body mass index (kg/m ²)	32.9 (28.9, 37.5)	31.2 (27.4, 35.6)
HbA1c (%)	8.2 (7.5, 9.2)	8.1 (7.5, 8.8)
Total cholesterol (mg/dL)	151 (131, 183)	166 (139, 199)
LDL (mg/dL)	79 (61, 104)	90 (67, 120)
HDL (mg/dL)	38 (32, 47)	42 (35, 50)
Triglycerides (mg/dL)	167 (104, 230)	161 (106, 222)
eGFR (mL/min/1.73m ²)	62 (52, 84)	72 (58, 87)
eGFR (mL/min/1.73m ²)		
≥90	20 (17.2%)	76 (21.8%)
60-89	46 (39.7%)	173 (49.6%)
30-59	50 (43.1%)	100 (28.7%)
CV medications		
Aspirin	96 (82.8%)	229 (65.4%)
Thienopyridines	40 (34.5%)	58 (16.6%)

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	SHE and CV event (N=116)	SHE and no CV event (N=350)
Any anti-platelets	105 (90.5%)	258 (73.7%)
ACEI or ARB	90 (77.6%)	284 (81.1%)
Beta blockers	85 (73.3%)	193 (55.1%)
Calcium channel blockers	42 (36.2%)	118 (33.7%)
Any anti-hypertensive	114 (98.3%)	315 (90.0%)
Statin	100 (86.2%)	266 (76.0%)
Any lipid lowering medication	101 (87.1%)	277 (79.1%)
Diuretics	80 (69.0%)	155 (44.3%)
Diabetes medications		
Biguanide	68 (58.6%)	245 (70.0%)
Sulfonylurea	25 (21.6%)	123 (35.1%)
Insulin	92 (79.3%)	235 (67.1%)
Dose in units per kg body weight	0.82 (0.51, 1.15)	0.70 (0.40, 1.03)
DPP-4i	7 (6.0%)	48 (13.7%)
TZD	4 (3.4%)	10 (2.9%)
Other	3 (2.6%)	11 (3.1%)
Insulin, sulfonylurea, or NSS	111 (95.7%)	324 (92.6%)

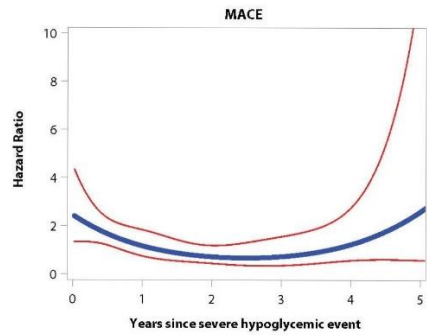
Data presented as number and percentage or median (25th, 75th percentile).

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CV, cardiovascular; DPP-4i, dipeptidyl peptidase-4 inhibitor; eGFR, estimated glomerular filtration rate; HbA_{1c}, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NSS, non-sulfonylurea secretagogues; SHE, severe hypoglycemic event; TZD, thiazolidinedione.

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Supplementary Figure 1. Time-Dependent Hazard Ratio Plots With 95% Confidence Intervals and Numbers at Risk for A) MACE and B) Cardiovascular Death

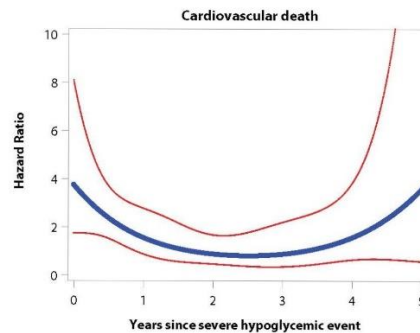
A.



P=0.0312

Year following SHE	Number at risk	Events in last 6 months
0.0	417	-
0.5	343	22
1.0	292	8
1.5	248	5
2.0	195	7
2.5	157	2
3.0	114	1
3.5	83	0
4.0	45	2
4.5	24	3
5.0	8	0
5.5	4	0

B.



P=0.0563

Year following SHE	Number at risk	Events in last 6 months
0.0	452	-
0.5	381	12
1.0	335	3
1.5	287	6
2.0	235	3
2.5	192	1
3.0	141	2
3.5	106	0
4.0	61	3
4.5	35	2
5.0	13	0
5.5	7	0