Supplementary Appendix

Real-world use of once-weekly semaglutide in patients with type 2 diabetes: pooled analysis of data from four SURE studies by baseline characteristic subgroups

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Supplemental Table 1: Baseline characteristics by baseline BMI

	<25 kg/m ²	≥25-<30 kg/m²	≥30-<35 kg/m²	≥35 kg/m²
N	39	232	406	518
Age, years	64.0 (9.2)	62.0 (10.4)	60.5 (10.7)	58.6 (11.2)
Female, n (%)	15 (38.5)	83 (35.8)	132 (32.5)	239 (46.1)
Race, n (%)				
White	29 (74.4)	199 (85.8)	374 (92.1)	484 (93.4)
Asian	9 (23.1)	18 (7.8)	19 (4.7)	15 (2.9)
Black or African	9 (23.1)	6 (2.6)	3 (0.7)	13 (2.5)
American	1 (2.6)	9 (3.9)	10 (2.5)	6 (1.2)
Other	1 (2.0)	9 (3.9)	10 (2.3)	0 (1.2)
Mean baseline HbA _{1c} , % (SD)	7.9 (1.2)	8.2 (1.3)	8.2 (1.5)	8.1 (1.5)
Baseline $HbA_{1c} < 7.0\%$, n (%)	7 (17.9)	32 (13.8)	64 (15.8)	123 (23.7)
Fasting plasma glucose, mmol/L* (SD)	9.4 (4.0)	8.9 (3.3)	9.1 (2.6)	9.4 (3.5)
Body weight, kg (SD)	68.7 (11.0)	82.5 (10.5)	96.1 (11.2)	116.6 (19.1)
BMI, kg/m ² (SD)	23.5 (1.4)	28.0 (1.4)	32.6 (1.4)	40.7 (5.4)
Diabetes duration, years (SD) [†]	13.6 (6.5)	13.4 (7.8)	12.7 (7.4)	11.2 (8.0)
eGFR, mL/min/1.73 m ^{2,‡}	85.3 (17.8)	83.7 (19.5)	83.6 (21.7)	85.4 (22.5)
Diabetic complications, n				
(%)	4 (10.3)	50 (21.6)	71 (17.5)	83 (16.0)
Diabetic retinopathy §	5 (12.8)	43 (18.5)	66 (16.3)	84 (16.2)
Diabetic neuropathy ^{II}	4 (10.3)	37 (15.9)	66 (16.3)	77 (14.9)
Diabetic nephropathy	4 (10.5)	37 (13.9)	00 (10.5)	// (14.9)
Comorbidities, n (%)				
Dyslipidemia	22 (56.4)	145 (62.5)	273 (67.2)	303 (58.5)
Hypertension	21 (53.8)	145 (62.5)	299 (73.6)	372 (71.8)
Coronary heart disease	6 (15.4)	45 (19.4)	78 (19.2)	66 (12.7)
Stroke	2 (5.1)	7 (3.0)	16 (3.9)	10 (1.9)
Heart failure	0	5 (2.2)	14 (3.4)	16 (3.1)
Peripheral vascular	0	8 (3.4)	6 (1.5)	12 (2.3)
disease		3 (31.1)	3 (2.5)	11 (1.0)
Prescribed starting dose				
of semaglutide, n (%)	•			2 (2 4)
<0.25 mg	0	0	0	2 (0.4)
0.25 mg	30 (76.9)	177 (76.3)	304 (74.9)	413 (79.7)
0.5 mg	7 (17.9)	41 (17.7)	66 (16.3)	74 (14.3)
1.0 mg	2 (5.1)	14 (6.0)	36 (8.9)	29 (5.6)

Reasons to initiate semaglutide , n (%)				
Improve glycemic	33 (84.6)	200 (86.2)	347 (85.5)	427 (82.4)
control				
Weight reduction	12 (30.8)	125 (53.9)	317 (78.1)	452 (87.3)
Issues with	2 (5.1)	17 (7.3)	20 (4.9)	18 (3.5)
hypoglycemia				
Address CV risk	12 (30.8)	49 (21.1)	111 (27.3)	123 (23.7)
Simplify regimen	12 (30.8)	87 (37.5)	119 (29.3)	115 (22.2)
Convenience	8 (20.5)	48 (20.7)	83 (20.4)	93 (18.0)
Other	2 (5.1)	7 (3.0)	11 (2.7)	23 (4.4)
Missing	0	0	0	1 (0.2)

N=39, 232, 406 and 518 for <25, \geq 25-<30, \geq 30-<35 and \geq 35, respectively, unless otherwise indicated; *n=16, n=116, n=185, n=253; † n=39, n=231, n=406, n=517; † n=25, n=175, n=304, n=397; § n=39, n=232, n=406, n=517; $^{\'}$ n=39, n=232, n=405, n=518. § More than one reason could be selected for initiating semaglutide. Data, which are based on the full analysis set, are mean (SD) or number (proportion) of patients. BMI, body mass index; CV, cardiovascular; eGFR, estimated glomerular filtration rate; SD, standard deviation.

Supplemental Table 2: Baseline characteristics by age

	<65 years	≥65 years
N	785	427
Age, years	54.0 (8.1)	71.3 (4.8)
Female, n (%)	323 (41.1)	150 (35.1)
Race, n (%)		
White	693 (88.3)	410 (96.0)
Asian	50 (6.4)	11 (2.6)
Black or African American	21 (2.7)	1 (0.2)
Other	21 (2.7)	5 (1.2)
Baseline HbA _{1c} , %	8.3 (1.6)	7.9 (1.3)
Baseline HbA _{1c} <7.0%, n (%)	142 (18.1)	89 (20.8)
Fasting plasma glucose, mmol/L*	9.3 (3.4)	9.0 (2.8)
Body weight, kg [†]	103.6 (21.7)	97.6 (19.0)
BMI, kg/m ^{2‡}	35.5 (6.9)	33.8 (5.9)
Diabetes duration, years §	10.9 (7.2)	14.7 (8.2)
eGFR, mL/min/1.73 m ^{2,}	92.2 (18.9)	70.2 (18.9)
Diabetic complications, n (%)	, , ,	
Diabetic retinopathy	124 (15.8)	86 (20.2)
Diabetic neuropathy	113 (14.4)	87 (20.4)
Diabetic nephropathy	92 (11.7)	92 (21.5)
Comorbidities, n (%)		
Dyslipidemia	456 (58.1)	298 (69.8)
Hypertension	505 (64.3)	341 (79.9)
Coronary heart disease	96 (12.2)	101 (23.7)
Stroke	17 (2.2)	19 (4.4)
Heart failure	17 (2.2)	18 (4.2)
Peripheral vascular disease	15 (1.9)	11 (2.6)
Prescribed starting dose of semaglutide,		
n (%)	2 (0.3)	0
<0.25 mg	602 (76.7)	335 (78.5)
0.25 mg	123 (15.7)	68 (15.9)
0.5 mg	58 (7.4)	24 (5.6)
1.0 mg	30 (7.4)	24 (3.0)
Reasons to initiate semaglutide		

treatment, n (%)		
Improve glycemic control	674 (85.9)	346 (81.0)
Weight reduction	616 (78.5)	300 (70.3)
Issues with hypoglycemia on current treatment	31 (3.9)	26 (6.1)
Address CV risk factors	187 (23.8)	113 (26.5)
Simplify current treatment regimen	207 (26.4)	130 (30.4)
Convenience	162 (20.6)	73 (17.1)
Other	30 (3.8)	14 (3.3)
Missing	0	1 (0.2)

N=785 and 427 for <65 and \geq 65, respectively, unless otherwise indicated; *n=375, n=199; †n=779, n=422; †n=775, n=420; $^{\$}$ n=590, n=323; $^{\$}$ n=784, n=426; $^{\$}$ n=783, n=427 $^{\$}$ More than one reason could be selected for initiating semaglutide. Data, which are based here for the full analysis set, are mean (SD) or number (proportion) of patients. CV, cardiovascular; eGFR, estimated glomerular filtration rate; SD, standard deviation.

Supplemental Table 3: Baseline characteristics by baseline HbA_{1c}

	<7%	≥7-≤8%	>8%-≤9%	>9%
N	231	414	305	262
Age, years	60.7 (11.2)	61.0 (11.0)	60.5 (10.0)	57.5 (11.3)
Female, n (%)	95 (41.1)	165 (39.9)	116 (38.0)	97 (37.0)
Race, n (%) White Asian Black or African American Other	216 (93.5) 8 (3.5) 3 (1.3) 4 (1.7)	375 (90.6) 24 (5.8) 8 (1.9) 7 (1.7)	281 (92.1) 10 (3.3) 4 (1.3) 10 (3.3)	231 (88.2) 19 (7.3) 7 (2.7) 5 (1.9)
Baseline HbA _{1c} , %	6.4 (0.5)	7.5 (0.3)	8.4 (0.3)	10.3 (1.2)
Baseline HbA_{1c} <7.0%, n (%)	231 (100.0)	0	0	0
Fasting plasma glucose, mmol/L*	7.1 (1.7)	8.4 (2.0)	9.6 (2.4)	13.0 (4.2)
Body weight, kg [†]	104.4 (21.8)	100.3 (19.8)	98.8 (19.7)	103.9 (22.9)
BMI, kg/m ^{2‡}	36.3 (6.9)	34.5 (6.4)	33.9 (5.9)	35.4 (7.2)
Diabetes duration, years§	11.0 (8.3)	12.7 (8.1)	13.1 (7.4)	11.6 (7.0)
eGFR, mL/min/1.73 m ²	82.0 (20.0)	83.5 (22.2)	86.2 (20.3)	85.9 (23.3)
Diabetic complications, n (%) Diabetic retinopathy Diabetic neuropathy Diabetic neuropathy	24 (10.5) 36 (15.7) 33 (14.3)	67 (16.2) 73 (17.6) 69 (16.7)	60 (19.7) 48 (15.7) 44 (14.4)	59 (22.5) 43 (16.5) 38 (14.5)
Comorbidities, n (%) Dyslipidemia Hypertension	135 (58.4) 167 (72.3) 45 (19.5)	269 (65.0) 300 (72.5) 61 (14.7)	200 (65.6) 210 (68.9) 48 (15.7)	150 (57.3) 169 (64.5) 43 (16.4)

Coronary heart disease	2 (0.9) 5 (2.2)	11 (2.7) 11 (2.7)	12 (3.9) 10 (3.3)	11 (4.2) 9 (3.4)
Stroke	6 (2.6)	7 (1.7)	5 (1.6)	8 (3.1)
Heart failure				
Peripheral				
vascular disease				
Prescribed starting dose of				
semaglutide, n (%)				
<0.25 mg	1 (0.4)	0	1 (0.3)	0
0.25 mg	160 (69.3)	309 (74.6)	241 (79.0)	227 (86.6)
0.5 mg	48 (20.8) 22 (9.5)	74 (17.9)	45 (14.8)	24 (9.2)
1.0 mg	22 (9.3)	31 (7.5)	18 (5.9)	11 (4.2)
Reasons to initiate				
semaglutide				
treatment, n (%)				
Improve glycemic control	107 (46.3)	368 (88.9)	292 (95.7)	253 (96.6)
Weight reduction	100 (01 1)	0.4.5 (7.6.4)	225 (72.2)	100 (71 0)
Issues with	188 (81.4)	315 (76.1)	225 (73.8)	188 (71.8)
hypoglycemia	6 (2.6)	28 (6.8)	11 (3.6)	12 (4.6)
Address CV risk	52 (22.5)	96 (23.2)	75 (24.6)	77 (29.4)
factors	- ()	(==:=)	(=,	(,
Simplify current regimen	77 (33.3)	130 (31.4)	73 (23.9)	57 (21.8)
Convenience	45 (40 5)	0.4 (0.0.0)	50 (47.0)	F ((2.2.5)
Other	45 (19.5)	84 (20.3)	52 (17.0)	54 (20.6)
Missing	12 (5.2)	13 (3.1) 0	6 (2.0) 0	13 (5.0) 1 (0.4)
	J	J	<u> </u>	± (0.7)

N=231, 414, 305 and 262 for <7%, \geq 7%- \leq -8%, >8%- \leq -9%, >9%, respectively, unless otherwise indicated; *n=124, n=206, n=146, n=98; †n=228, n=409, n=304, n=260; †n=226, n=407, n=303, n=259; \$n=231, n=412, n=305, n=262; "n=174, n=308, n=227, n=204; n=229, n=414, n=305, n=262 for diabetic retinopathy and n=230, n=414, n=305, n=261 for diabetic neuropathy. More than one

reason could be selected for initiating semaglutide. Data, which are based on the full analysis set, are mean (SD) or number (proportion) of patients. BMI, body mass index; eGFR, estimated glomerular filtration rate; SD, standard deviation.

Supplemental Table 4: Baseline characteristics by baseline diabetes duration

	<5 years	≥5-<10 years	≥10 years
N (FAS)	235	304	671
Age, years	53.6 (12.4)	59.5 (9.8)	62.6 (9.9)
Female, n (%)	84 (35.7)	121 (39.8)	267 (39.8)
Race, n (%)	,	` '	, ,
White	213 (90.6)	281 (92.4)	607 (90.5)
Asian	15 (6.4)	10 (3.3)	36 (5.4)
Black or African American	5 (2.1)	5 (1.6)	12 (1.8)
Other	2 (0.9)	8 (2.6)	16 (2.4)
Baseline HbA _{1c} , %	7.9 (1.6)	8.2 (1.5)	8.2 (1.4)
Baseline HbA_{1c} <7.0%, n (%)	69 (29.4)	49 (16.1)	113 (16.8)
Fasting plasma glucose, mmol/L*	9.0 (3.2)	9.2 (3.0)	9.3 (3.3)
Body weight, kg [†]	110.6 (23.4)	101.7 (21.7)	98.2 (18.7)
BMI, kg/m ^{2‡}	37.1 (7.4)	34.8 (6.8)	34.2 (6.0)
Diabetes duration, years	2.8 (1.4)	7.6 (1.5)	17.6 (6.1)
eGFR, mL/min/1.73 m ^{2§}	93.0 (20.8)	85.8 (19.6)	80.8 (21.9)
Diabetic complications, n (%) ^{II}			
Diabetic retinopathy	13 (5.5)	36 (11.8)	161 (24.1)
Diabetic neuropathy	18 (7.7)	34 (11.2)	147 (22.0)
Diabetic nephropathy	18 (7.7)	29 (9.5)	137 (20.4)
Comorbidities, n (%)			
Dyslipidemia	118 (50.2)	178 (58.6)	457 (68.1)
Hypertension	145 (61.7)	204 (67.1)	495 (73.8)
Coronary heart disease	25 (10.6)	44 (14.5)	128 (19.1)
Stroke	5 (2.1)	8 (2.6)	23 (3.4)
Heart failure	7 (3.0)	6 (2.0)	22 (3.3)
Peripheral vascular disease	3 (1.3)	3 (1.0)	20 (3.0)
Prescribed starting dose of semaglutide,			
n (%)			
<0.25 mg	0	1 (0.3)	1 (0.1)
0.25 mg	197 (83.8)	239 (78.6)	501 (74.7)
0.5 mg	27 (11.5)	47 (15.5)	117 (17.4)
1.0 mg	11 (4.7)	17 (5.6)	52 (7.7)
December initiate consolution	` '	` '	, ,
Reasons to initiate semaglutide			
treatment, n (%)¶	100 (00 0)	250 (04.0)	
Improve glycemic control Weight reduction	188 (80.0)	258 (84.9)	573 (85.4)
	196 (83.4)	223 (73.4)	497 (74.1)
Issues with hypoglycemia on current treatment	5 (2.1)	15 (4.9)	37 (5.5)
Address CV risk factors	56 (23.8)	70 (23.0)	
Simplify current treatment regimen	46 (19.6)	79 (26.0)	174 (25.9)
Convenience	32 (13.6)	59 (19.4)	211 (31.4)
Other	11 (4.7)	9 (3.0)	144 (21.5)
Missing	0	1 (0.3)	24 (3.6)
maanig		1 (0.3)	0

N=235, 304, and 671 and 262 for <5, \geq 5-<10 and \geq 10 years, respectively, unless otherwise indicated; *n=130, n=140, n=304; †n=232, n=302, n=665; †n=231, n=300, n=662; § n=180, n=227, n=505; "n=235, n=304, n=669. ¶More than one reason could be selected for initiating semaglutide. Data, which are based on the full analysis set, are mean (SD) or number (proportion) of patients. BMI, body mass index; eGFR, estimated glomerular filtration rate; FAS, full analysis set; SD, standard deviation.

Supplemental Table 5: Anti-hyperglycemic medication at baseline by baseline BMI

N (%)	<25 kg/m²	≥25-<30 kg/m²	≥30-<35 kg/m²	≥35 kg/m²
N	39	232	406	518
Metformin	32 (82.1)	177 (76.3)	317 (78.1)	405 (78.2)
Sulfonylureas	4 (10.3)	45 (19.4)	83 (20.4)	94 (18.1)
Alpha-glucosidase inhibitors	0	0	2 (0.5)	3 (0.6)
Thiazolidinediones	0	5 (2.2)	16 (3.9)	18 (3.5)
DPP-4 inhibitors	5 (12.8)	55 (23.7)	78 (19.2)	62 (12.0)
SGLT-2 inhibitors	18 (46.2)	106 (45.7)	186 (45.8)	182 (35.1)
Other anti-hyperglycemic drugs excluding insulin	0	7 (3.0)	7 (1.7)	2 (0.4)
Other GLP-1RA	3 (7.7)	40 (17.2)	99 (24.4)	108 (20.8)
Basal insulin	13 (33.3)	88 (37.9)	139 (34.2)	178 (34.4)
Premixed insulin	1 (2.6)	10 (4.3)	9 (2.2)	34 (6.6)
Fast-acting insulin	3 (7.7)	31 (13.4)	44 (10.8)	90 (17.4)
No medication	0	2 (0.9)	9 (2.2)	12 (2.3)
Oral anti-hyperglycemic drug only	23 (59.0)	112 (48.3)	198 (48.8)	235 (45.4)

Supplemental Table 6: Anti-hyperglycemic medication at baseline by age at baseline

N (%)	<65 years	≥65 years
N	785	427
Metformin	614 (78.2)	327 (76.6)
Sulfonylureas	136 (17.3)	92 (21.5)
Alpha-glucosidase inhibitors	3 (0.4)	2 (0.5)
Thiazolidinediones	30 (3.8)	9 (2.1)
DPP-4 inhibitors	119 (15.2)	82 (19.2)
SGLT-2 inhibitors	347 (44.2)	152 (35.6)
Other anti-hyperglycemic drugs excluding insulin	10 (1.3)	6 (1.4)
Other GLP-1RA	168 (21.4)	84 (19.7)
Basal insulin	268 (34.1)	153 (35.8)
Premixed insulin	29 (3.7)	26 (6.1)
Fast-acting insulin	109 (13.9)	61 (14.3)
No medication	16 (2.0)	10 (2.3)
Oral anti-hyperglycemic drug only	377 (48.0)	199 (46.6)
GLP-1RA switch	168 (21.4)	84 (19.7)

Supplemental Table 7: Anti-hyperglycemic medication at baseline by HbA_{1c} at baseline

N (%)	<7%	≥7% to ≤8%	>8%-≤9%	>9%
N	231	414	305	262
Metformin	182 (78.8)	319 (77.1)	242 (79.3)	198 (75.6)
Sulfonylureas	28 (12.1)	73 (17.6)	69 (22.6)	58 (22.1)
Alpha-glucosidase inhibitors	1 (0.4)	2 (0.5)	1 (0.3)	1 (0.4)
Thiazolidinediones	6 (2.6)	11 (2.7)	15 (4.9)	7 (2.7)
DPP-4 inhibitors	17 (7.4)	74 (17.9)	58 (19.0)	52 (19.8)
SGLT-2 inhibitors	71 (30.7)	189 (45.7)	135 (44.3)	104 (39.7)
Other anti-hyperglycemic drugs excluding insulin	1 (0.4)	7 (1.7)	6 (2.0)	2 (0.8)
Other GLP-1RA	59 (25.5)	97 (23.4)	61 (20.0)	35 (13.4)
Basal insulin	72 (31.2)	140 (33.8)	127 (41.6)	82 (31.3)
Premixed insulin	6 (2.6)	14 (3.4)	13 (4.3)	22 (8.4)
Fast-acting insulin	19 (8.2)	60 (14.5)	47 (15.4)	44 (16.8)
No medication	12 (5.2)	6 (1.4)	5 (1.6)	3 (1.1)
Oral anti-hyperglycemic drug only	107 (46.3)	204 (49.3)	134 (43.9)	131 (50.0)

Supplemental Table 8: Anti-hyperglycemic medication at baseline by diabetes duration at baseline

N (%)	<5 years	≥5-<10 years	≥10 years
N	235	304	671
Metformin	181 (77.0)	238 (78.3)	520 (77.5)
Sulfonylureas	23 (9.8)	56 (18.4)	148 (22.1)
Alpha-glucosidase inhibitors	0	1 (0.3)	4 (0.6)
Thiazolidinediones	2 (0.9)	10 (3.3)	27 (4.0)
DPP-4 inhibitors	26 (11.1)	59 (19.4)	116 (17.3)
SGLT-2 inhibitors	63 (26.8)	129 (42.4)	306 (45.6)
Other anti-hyperglycemic drugs excluding insulin	1 (0.4)	4 (1.3)	11 (1.6)
Other GLP-1RA	32 (13.6)	60 (19.7)	159 (23.7)
Basal insulin	36 (15.3)	70 (23.0)	315 (46.9)
Premixed insulin	6 (2.6)	15 (4.9)	34 (5.1)
Fast-acting insulin	10 (4.3)	20 (6.6)	140 (20.9)
No medication	14 (6.0)	2 (0.7)	10 (1.5)
Oral anti-hyperglycemic drug only	154 (65.5)	181 (59.5)	240 (35.8)

SUSTAIN trials (11-19)	SURE studies
Age 18 years (or at least 20 years	Age ≥18 years at the time of signing
for trials conducted in Japan)	the informed consent
 Diagnosed with type 2 diabetes with	Diagnosed with type 2 diabetes at
a baseline HbA _{1c} ≥7.0 or ≥7.5% with	least 12 weeks prior to inclusion
an upper limit of 10.0, 10.5 or 11.0%	 No upper or lower limit for HbA_{1c} or body mass index

Supplemental Table 10: Overview of systematically collected safety information in patients receiving semaglutide

Total N=1,212 (FAS)	Number of patients, n (%)	Events
Serious ADRs	11 (0.9)	18
Fatal events	3 (0.2)	3
Pregnancies	0	0
AEs in fetus/newborns	0	0
Severe or documented hypoglycemic episodes	57 (4.70)	198

Data are based on the full analysis set. Fatal events were due to 1) sepsis; 2) pancreatic carcinoma; and 3) sudden death in a patient with pre-existing hypertension, atrial fibrillation and myocardial infarction. In all three cases, the events were judged as unlikely to be related to semaglutide treatment by the treating physician. %, percentage of subjects experiencing at least one event; ADR, adverse drug reaction; AE, adverse event; EAS, effectiveness analysis set; FAS, full analysis set; n, number of subjects experiencing at least one event.

Supplemental Table 11: Overview of voluntarily reported adverse events in patients receiving semaglutide

Total N=1,212 (FAS)	Number of patients, n (%)	Events
All AEs	170 (14.0)	297
Severity of AEs		
Mild	109 (9.0)	175
Moderate	65 (5.4)	94
Severe	21 (1.7)	28
AEs leading to premature treatment	44 (3.6)	74
discontinuation		
Gastrointestinal AEs	108 (8.9)	166

Data are based on the full analysis set. %, percentage of subjects experiencing at least one event; AE, adverse event; FAS, full analysis set; n, number of subjects experiencing at least one event.