Figure 1. Time to Dementia with GLP-1 Receptor Agonists versus Placebo in Pooled RCTs

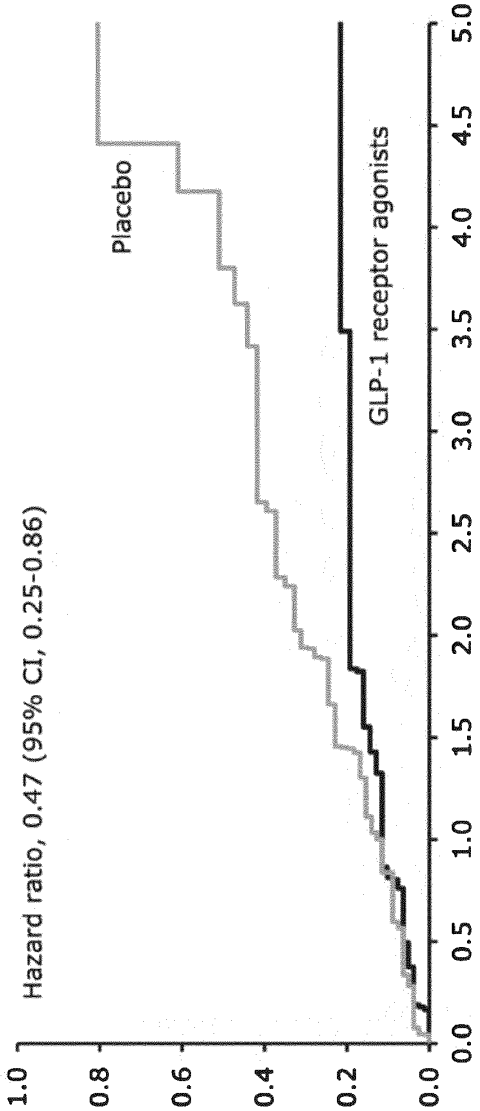


Fig. 1

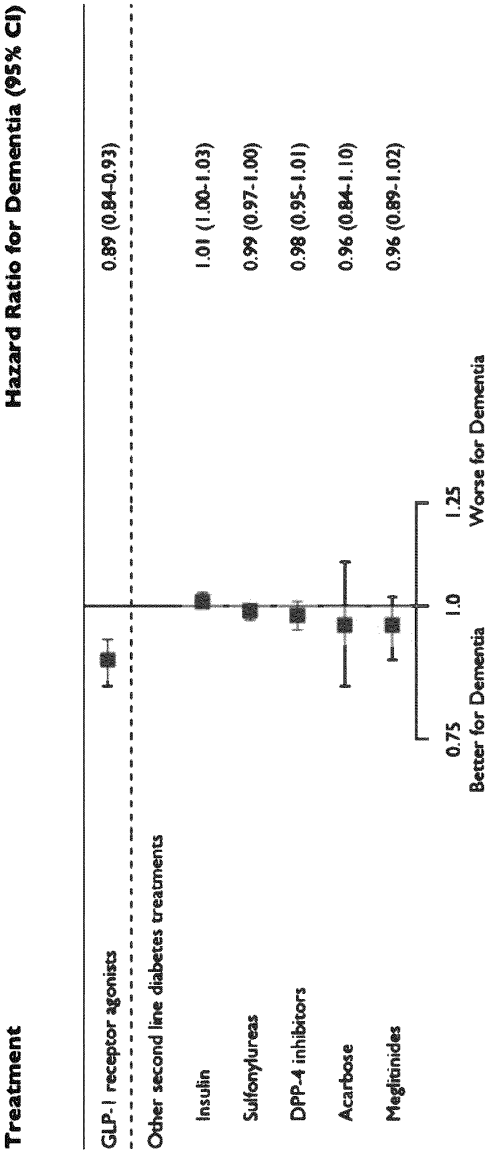

Treatment
Hazard Ratio for Dementia (95% CI)
GLP-1 receptor agonists
0.89 (0.84-0.93)
Other second line diabetes treatments
Insulin
1.01 (1.00-1.03)
Sulfonylureas
0.99 (0.97-1.00)
DPP-4 inhibitors
0.98 (0.95-1.01)
Acarbose
0.96 (0.84-1.10)
Meglitinides
0.96 (0.89-1.02)
0.75
1.0
1.25
Better for Dementia
Worse for Dementia

Fig. 2

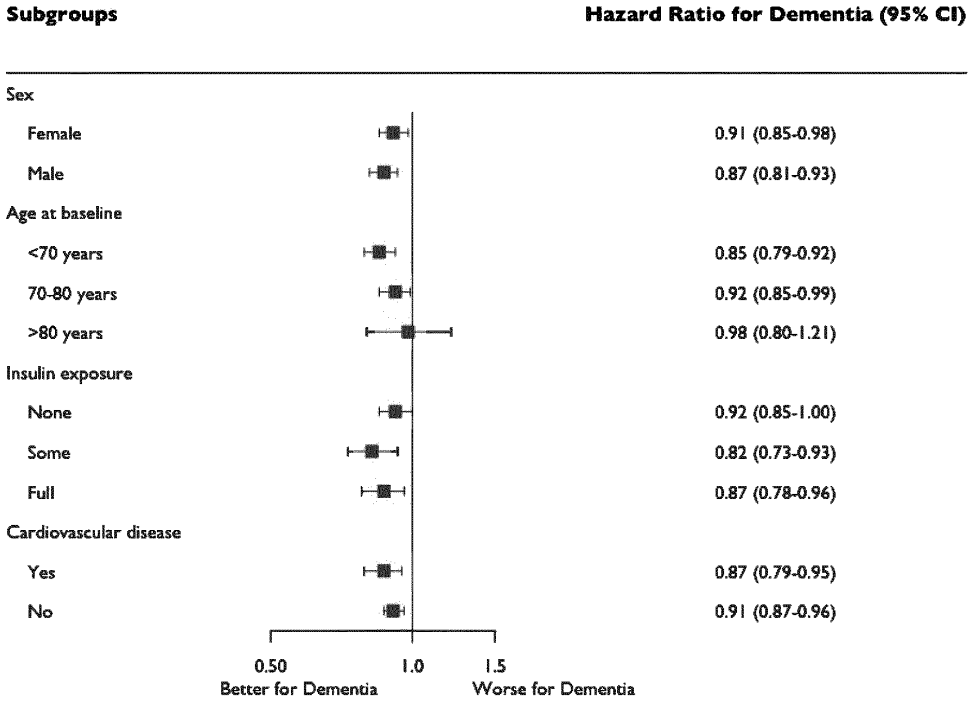

Subgroups
Hazard Ratio for Dementia (95% CI)
Sex
Female
0.91 (0.85-0.98)
Male
0.87 (0.81-0.93)
Age at baseline
<70 years
0.85 (0.79-0.92)
70-80 years
0.92 (0.85-0.99)
>80 years
0.98 (0.80-1.21)
Insulin exposure
None
0.92 (0.85-1.00)
Some
0.82 (0.73-0.93)
Full
0.87 (0.78-0.96)
Cardiovascular disease
Yes
0.87 (0.79-0.95)
No
0.91 (0.87-0.96)
0.50
1.0
1.5
Better for Dementia
Worse for Dementia

Fig. 3

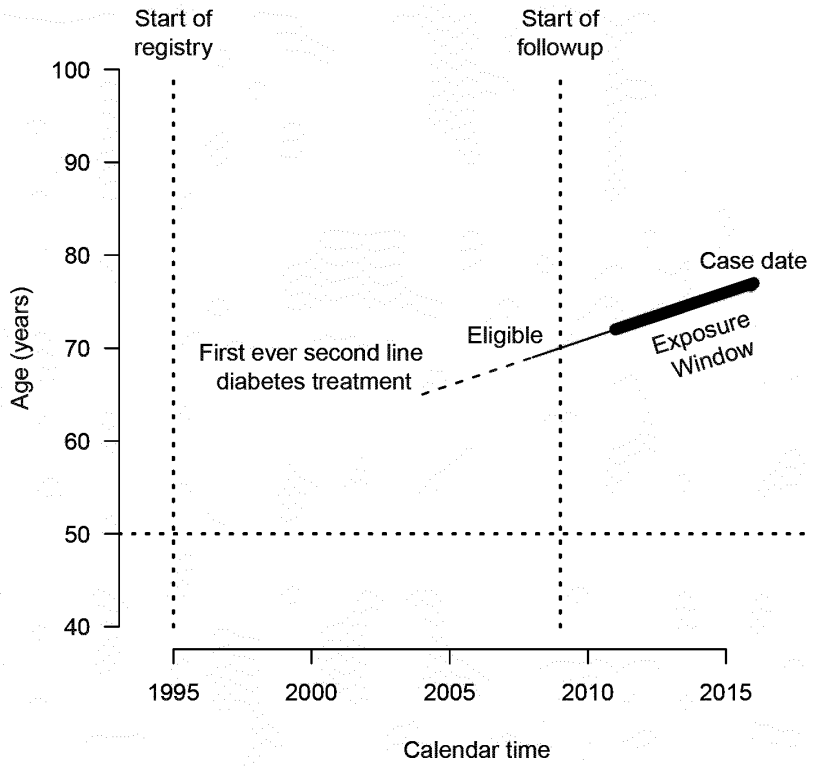

Start of registry
Start of followup
100
90
80
70
60
50
40
Age (years)
Case date
Eligible
Exposure Window
First ever second line diabetes treatment
1995
2000
2005
2010
2015
Calendar time

Fig. 4

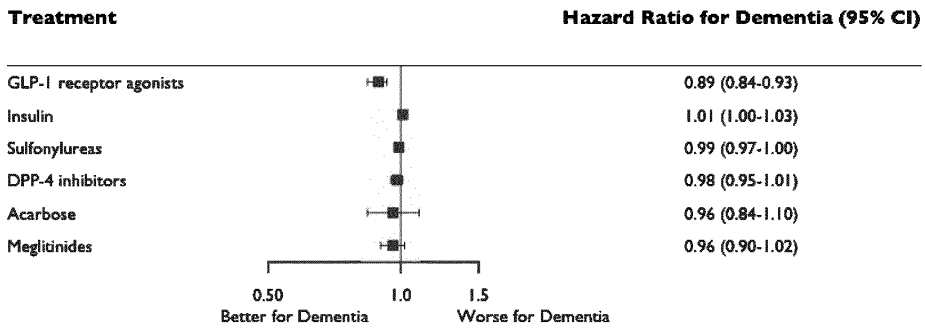

Treatment
Hazard Ratio for Dementia (95% CI)
GLP-1 receptor agonists
Insulin
Sulfonylureas
DPP-4 inhibitors
Acarbose
Meglitinides
0.89 (0.84-0.93)
1.01 (1.00-1.03)
0.99 (0.97-1.00)
0.98 (0.95-1.01)
0.96 (0.84-1.10)
0.96 (0.90-1.02)
0.50
1.0
1.5
Better for Dementia
Worse for Dementia

Fig. 5A

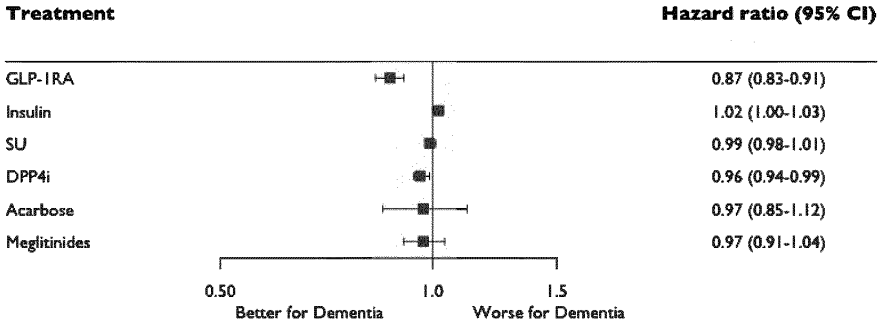

Treatment
Hazard ratio (95% CI)
GLP-1RA
Insulin
SU
DPP4i
Acarbose
Meglitinides
0.87 (0.83-0.91)
1.02 (1.00-1.03)
0.99 (0.98-1.01)
0.96 (0.94-0.99)
0.97 (0.85-1.12)
0.97 (0.91-1.04)
0.50
1.0
1.5
Better for Dementia
Worse for Dementia

Fig. 5B

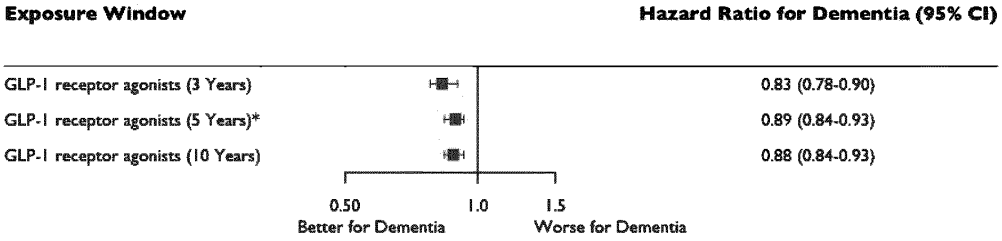


Fig. 6A

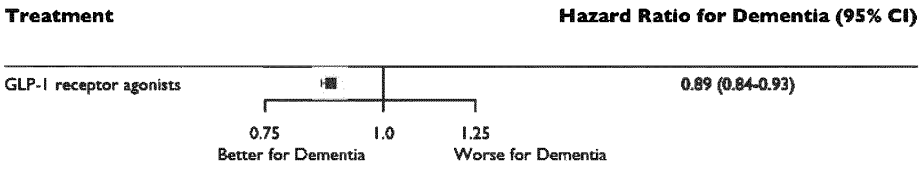


Fig. 6B

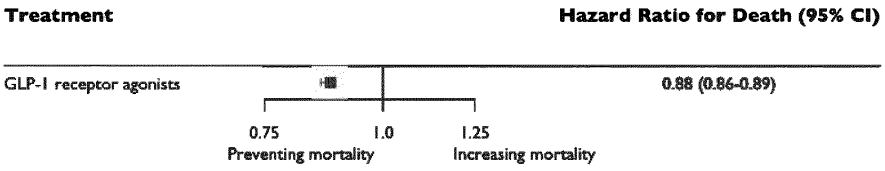


Fig. 6C

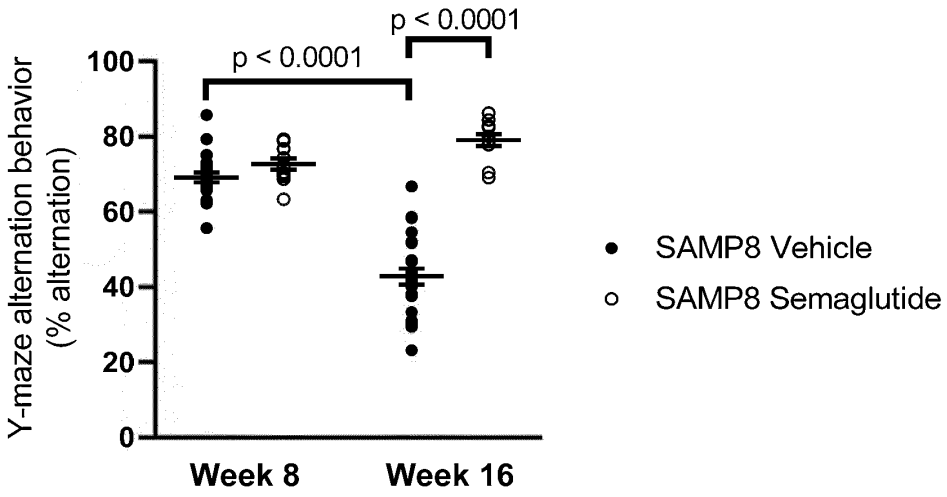

p < 0.0001
p < 0.0001
Y-maze alternation behavior
(% alternation)
100
80
60
40
20
0
Week 8
Week 16
SAMP8 Vehicle
SAMP8 Semaglutide

Fig. 7

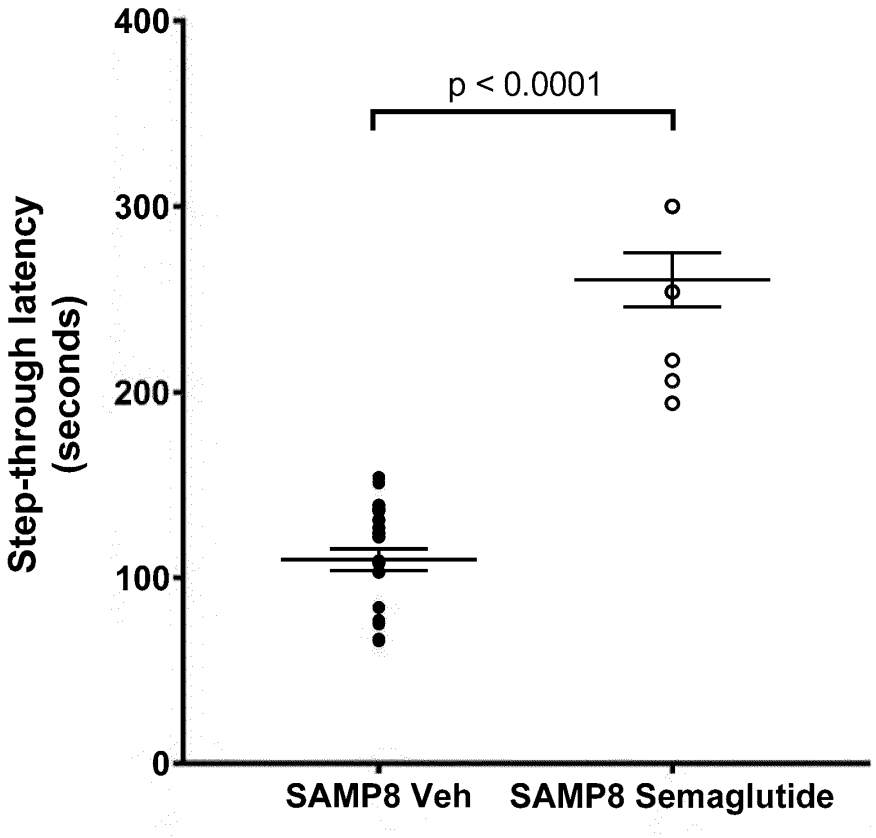

400
300
200
100
0
Step-through latency (seconds)
p < 0.0001
SAMP8 Veh
SAMP8 Semaglutide

Fig. 8

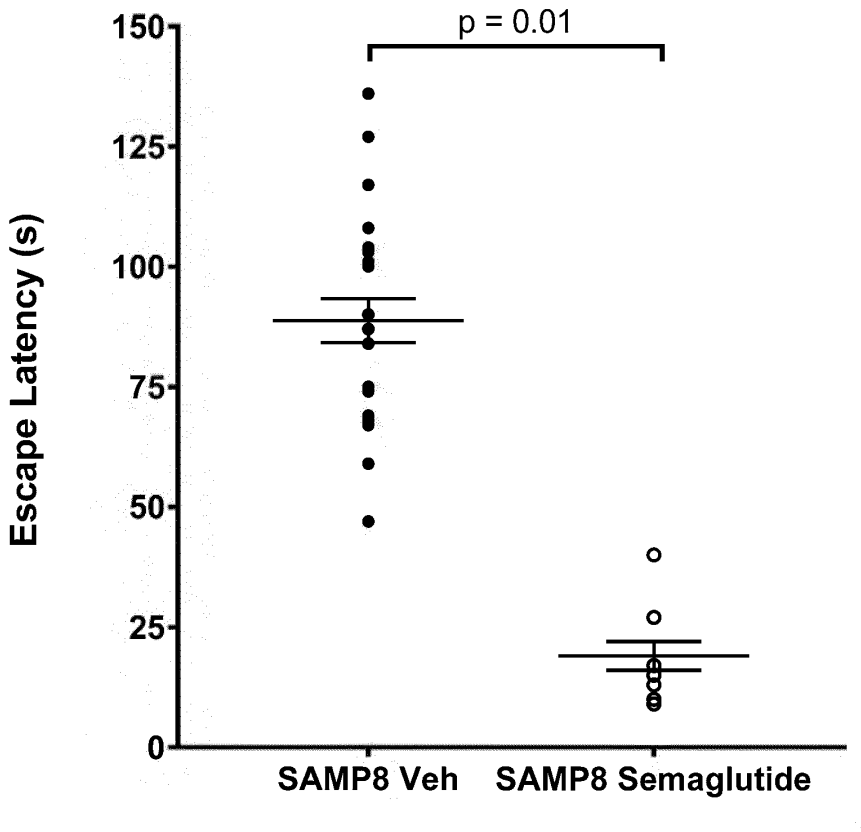

p = 0.01
150
125
100
75
50
25
0
Escape Latency (s)
SAMP8 Veh
SAMP8 Semaglutide

Fig. 9

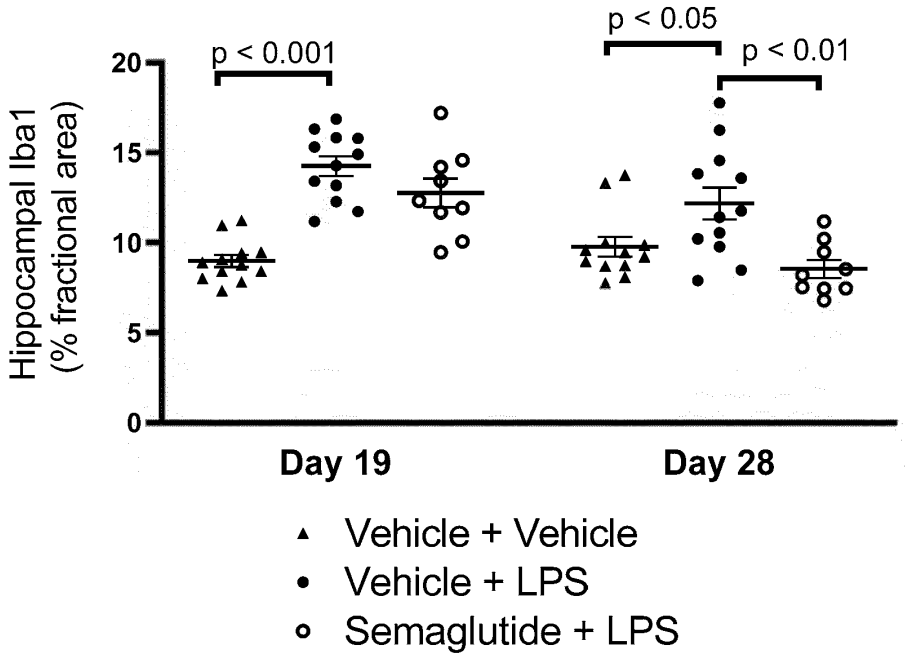

p < 0.001
p < 0.05
p < 0.01
Hippocampal Iba1
(% fractional area)
20
15
10
5
0
Day 19
Day 28
Vehicle + Vehicle
Vehicle + LPS
Semaglutide + LPS

Fig. 10