

Appendix 6 Risk of incretin-based therapies on digestive system cancers in the subgroup analysis

Characteristics (No.of studies)	Insulin	Met	SGLT-2	SU	TZD	AGIs
All trials (84)	1.00 (0.31,3.20)	2.69 (0.62,11.66)	0.16 (0.02,1.47)	0.68 (0.35,1.32)	2.04 (0.60,6.95)	0.29 (0.01,7.19)
Mean age						
≤60 years(69)	0.81 (0.24,2.79)	2.19 (0.48,10.04)	0.16 (0.02,1.40)	0.55 (0.24,1.27)	1.68 (0.47,6.07)	NA
>60 years (15)	NA	NA	NA	0.70 (0.15,3.29)	NA	0.30(0.01,7.61)
duration						
≤5 years (31)	NA	2.25 (0.29,17.39)	NA	NA	2.29 (0.30,17.71)	NA
5-10 years (69)	0.53 (0.11,2.55)	NA	0.13 (0.01,2.84)	0.52 (0.22,1.20)	1.36 (0.22,8.24)	NA
>10 years (19)	2.47 (0.42,14.38)	NA	NA	0.89 (0.10,7.58)	NA	NA
Unclear (22)	NA	3.28 (0.11,97.43)	0.21 (0.01,4.77)	2.13 (0.38,11.87)	NA	0.28 (0.01,7.76)
Mean HbA1c%						
≤7.5% (10)	NA	NA	NA	0.51 (0.10,2.54)	NA	0.30 (0.01,7.58)
7.5%-8.0% (37)	0.17 (0.01,3.65)	NA	0.16 (0.02,1.48)	0.62 (0.24,1.60)	2.58 (0.10,66.93)	NA
8.0%-8.5% (56)	1.11 (0.25,4.98)	1.22 (0.09,15.69)	NA	0.68 (0.18,2.53)	1.32 (0.21,8.32)	NA
>8.5% (30)	1.03 (0.06,16.88)	4.50 (0.45,44.69)	NA	NA	2.09 (0.21,20.73)	NA

Unclear (8)	NA	NA	NA	NA	NA	NA
Trial duration						
≤24 weeks (73)	0.87 (0.05,14.98)	5.42 (0.21,141.60)	0.22 (0.01,4.82)	NA	2.72 (0.10,71.51)	0.29 (0.01,7.71)
24-48 weeks (22)	0.24 (0.03,1.64)	1.07 (0.06,17.70)	0.10 (0.00,2.35)	0.14 (0.01,1.80)	1.29 (0.14,11.76)	NA
>48 weeks (46)	5.01 (0.54,46.14)	3.06 (0.31,30.62)	NA	0.74 (0.37,1.49)	0.95 (0.11,7.99)	NA
Sample size						
≤500 (127)	0.12 (0.01,2.71)	2.15 (0.45,10.29)	0.20 (0.01,4.40)	0.70 (0.18,2.78)	2.08 (0.51,8.49)	0.21 (0.01,5.35)
>500 (14)	1.40 (0.40,4.89)	NA	0.13 (0.01,2.83)	0.62 (0.29,1.34)	0.30 (0.01,7.60)	NA