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**ESM Table 1** Meta-analysis results for tirzepatide versus placebo, GLP-1 RAs, and basal insulin for achievement of different HbA<sub>1c</sub> targets

Intervention	Comparator	Participants with outcome/analysed, n		Odds ratio (95% CI)	I <sup>2</sup> , %
		Tirzepatide arm	Comparator arm		
<b>HbA<sub>1c</sub> &lt; 53 mmol/mol (&lt; 7%)</b>					
Tirzepatide 5 mg	Placebo	236/292	62/284	16.25 (8.98 to 29.41)	53
	GLP-1 RAs	432/516	402/515	1.47 (1.07 to 2.02)	0
	Basal insulin	555/681	711/1331	3.51 (2.49 to 4.94)	55
Tirzepatide 10 mg	Placebo	250/286	62/284	30.70 (10.14 to 92.98)	83
	GLP-1 RAs	454/509	402/515	4.08 (0.74 to 22.41)	87
	Basal insulin	597/666	711/1331	6.92 (5.25 to 9.12)	0
Tirzepatide 15 mg	Placebo	279/338	64/304	20.87 (10.20 to 42.74)	67
	GLP-1 RAs	469/517	402/515	2.84 (1.96 to 4.11)	0
	Basal insulin	630/686	711/1331	9.02 (6.70 to 12.14)	0
<b>HbA<sub>1c</sub> ≤ 48 mmol/mol (≤ 6.5%)</b>					
Tirzepatide 5 mg	Placebo	214/292	29/284	28.72 (10.71 to 77.00)	69
	GLP-1 RAs	376/516	326/515	1.80 (1.00 to 3.24)	56
	Basal insulin	467/681	466/1331	3.63 (2.71 to 4.87)	52
Tirzepatide 10 mg	Placebo	232/286	29/284	44.95 (14.89 to 135.67)	55
	GLP-1 RAs	418/509	326/515	3.77 (1.28 to 11.08)	81
	Basal insulin	525/666	466/1331	6.26 (5.02 to 7.81)	0
Tirzepatide 15 mg	Placebo	223/289	29/284	35.66 (16.43 to 77.39)	56
	GLP-1 RAs	435/517	326/515	3.19 (2.29 to 4.43)	5
	Basal insulin	572/686	466/1331	8.47 (6.70 to 10.70)	0
<b>HbA<sub>1c</sub> &lt; 39 mmol/mol (&lt; 5.7%)</b>					
Tirzepatide 5 mg	Placebo	69/292	5/284	11.70 (1.93 to 70.75)	56
	GLP-1 RAs	137/516	92/515	1.69 (1.25 to 2.28)	0
	Basal insulin	166/681	52/1331	7.43 (5.33 to 10.36)	0
Tirzepatide 10 mg	Placebo	93/286	5/284	25.48 (10.09 to 64.37)	0

	GLP-1 RAs	214/509	92/515	3.95 (1.64 to 9.50)	27
	Basal insulin	240/666	52/1331	12.80 (9.26 to 17.69)	0
Tirzepatide 15 mg	Placebo	138/289	5/284	45.76 (18.21 to 114.99)	0
	GLP-1 RAs	252/517	92/515	7.13 (1.53 to 33.17)	61
	Basal insulin	315/686	52/1331	19.53 (14.20 to 26.86)	0
CI, confidence interval; GLP-1 RAs, Glucagon-like peptide-1 receptor agonists					

**ESM Table 2** Meta-analysis results for tirzepatide versus placebo, GLP-1 RAs, and basal insulin for achievement of body weight loss of at least 5%, 10%, and 15%

Intervention	Comparator	Participants with outcome/analysed, n		Odds ratio (95% CI)	I <sup>2</sup> , %
		Tirzepatide arm	Comparator arm		
<b>Weight loss ≥ 5%</b>					
Tirzepatide 5 mg	Placebo	161/292	22/284	14.49 (8.63 to 24.33)	0
	GLP-1 RAs	342/516	282/515	1.96 (1.01 to 3.80)	61
	Basal insulin	438/679	100/1337	23.16 (15.47 to 34.67)	50
Tirzepatide 10 mg	Placebo	193/288	22/284	28.58 (10.22 to 79.94)	24
	GLP-1 RAs	414/510	282/515	4.79 (1.95 to 11.73)	74
	Basal insulin	552/670	100/1337	60.01 (36.63 to 98.29)	60
Tirzepatide 15 mg	Placebo	207/289	22/284	33.62 (14.02 to 80.60)	45
	GLP-1 RAs	433/517	282/515	4.57 (3.38 to 6.18)	0
	Basal insulin	595/686	100/1337	84.02 (50.65 to 139.40)	58
<b>Weight loss ≥ 10%</b>					
Tirzepatide 5 mg	Placebo	69/292	2/284	34.31 (9.54 to 123.40)	0
	GLP-1 RAs	174/516	122/515	1.65 (1.26 to 2.18)	0
	Basal insulin	249/679	25/1337	28.24 (16.62 to 47.99)	34
Tirzepatide 10 mg	Placebo	114/288	2/284	74.04 (20.85 to 262.92)	0
	GLP-1 RAs	263/510	122/515	3.68 (2.30 to 5.88)	23
	Basal insulin	365/670	25/1337	58.52 (36.31 to 94.32)	20
Tirzepatide 15 mg	Placebo	126/289	2/284	87.42 (24.58 to 311.00)	0
	GLP-1 RAs	321/517	122/515	5.46 (4.15 to 7.18)	0
	Basal insulin	464/686	25/1337	102.68 (66.91 to 157.56)	0
<b>Weight loss ≥ 15%</b>					
Tirzepatide 5 mg	Placebo	26/292	0/284	16.72 (3.10 to 90.09)	0
	GLP-1 RAs	73/516	41/515	1.91 (1.28 to 2.87)	0
	Basal insulin	89/679	5/1337	35.16 (14.51 to 85.18)	0
Tirzepatide 10 mg	Placebo	58/288	0/284	46.81 (9.10 to 240.91)	0

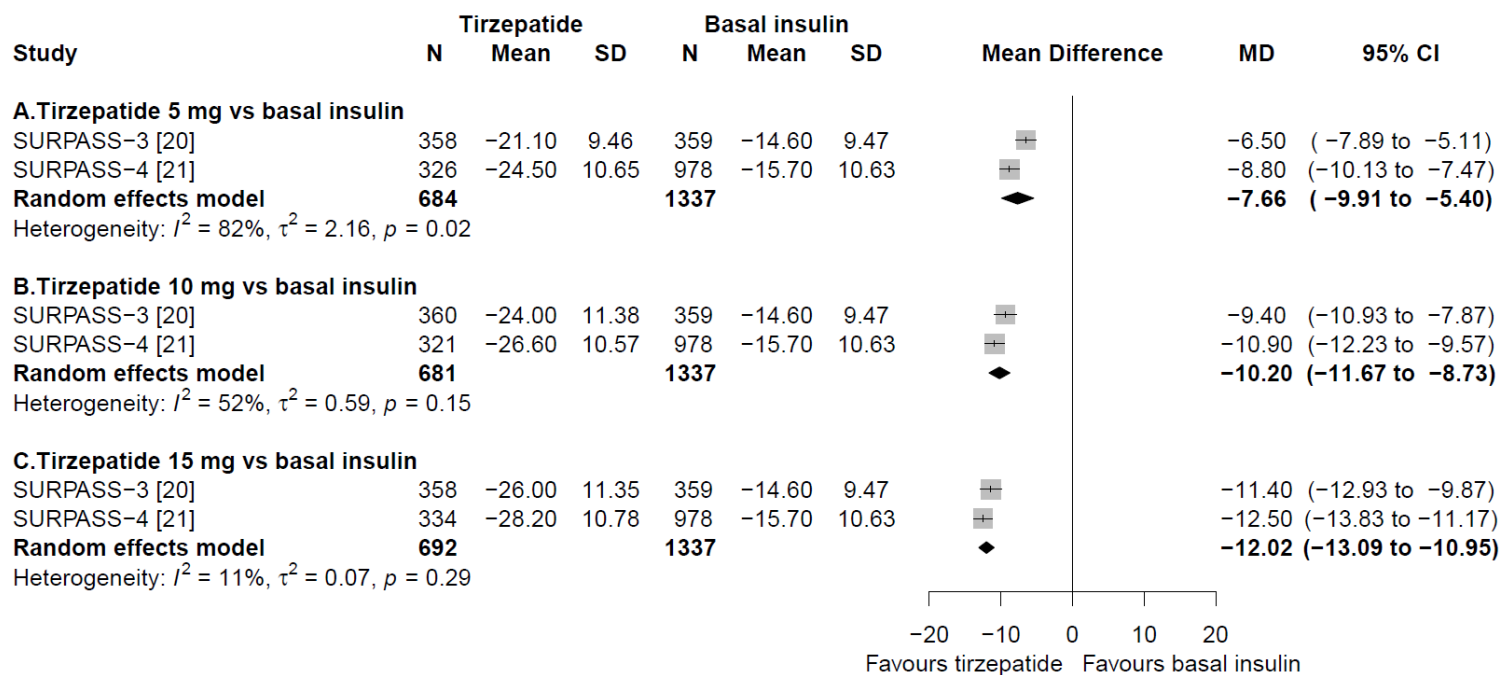
	GLP-1 RAs	138/510	41/515	5.00 (1.95 to 12.86)	29
	Basal insulin	176/670	5/1337	73.53 (28.05 to 192.76)	5
Tirzepatide 15 mg	Placebo	76/289	0/284	64.61 (12.56 to 332.32)	0
	GLP-1 RAs	198/517	41/515	7.18 (4.97 to 10.37)	0
	Basal insulin	272/686	5/1337	137.20 (49.17 to 382.79)	8
CI, confidence interval; GLP-1 RAs, Glucagon-like peptide-1 receptor agonists					

**ESM Table 3** Meta-analysis results for tirzepatide versus placebo, GLP-1 RAs, and basal insulin for discontinuation due to adverse events and for incidence of serious adverse events

Intervention	Comparator	Participants with outcome/analysed, n		Odds ratio (95% CI)	I <sup>2</sup> , %
		Tirzepatide arm	Comparator arm		
<b>Discontinuation due to adverse events</b>					
Tirzepatide 5 mg	Placebo	16/292	8/286	1.99 (0.83 to 4.77)	0
	GLP-1 RAs	33/525	25/523	1.34 (0.78 to 2.29)	0
	Basal insulin	62/687	59/1360	3.08 (1.34 to 7.06)	61
Tirzepatide 10 mg	Placebo	19/291	8/286	2.39 (1.02 to 5.59)	0
	GLP-1 RAs	43/520	25/523	1.23 (0.30 to 5.09)	72
	Basal insulin	65/688	59/1360	3.45 (0.72 to 16.58)	89
Tirzepatide 15 mg	Placebo	35/350	9/312	3.64 (1.51 to 8.78)	13
	GLP-1 RAs	53/523	25/523	2.29 (1.39 to 3.75)	0
	Basal insulin	75/697	59/1360	3.99 (1.00 to 15.98)	86
<b>Serious adverse events</b>					
Tirzepatide 5 mg	Placebo	15/292	15/286	1.00 (0.47 to 2.12)	0
	GLP-1 RAs	34/525	16/523	1.23 (0.17 to 9.12)	67
	Basal insulin	77/687	215/1360	0.94 (0.51 to 1.75)	71
Tirzepatide 10 mg	Placebo	18/291	15/286	1.22 (0.59 to 2.50)	0
	GLP-1 RAs	28/520	16/523	1.80 (0.96 to 3.39)	0
	Basal insulin	74/688	215/1360	0.84 (0.63 to 1.13)	0
Tirzepatide 15 mg	Placebo	12/350	15/312	0.80 (0.37 to 1.75)	0
	GLP-1 RAs	29/523	16/523	1.65 (0.64 to 4.26)	27
	Basal insulin	67/697	215/1360	0.80 (0.39 to 1.63)	77
CI, confidence interval; GLP-1 RAs, Glucagon-like peptide-1 receptor agonists					

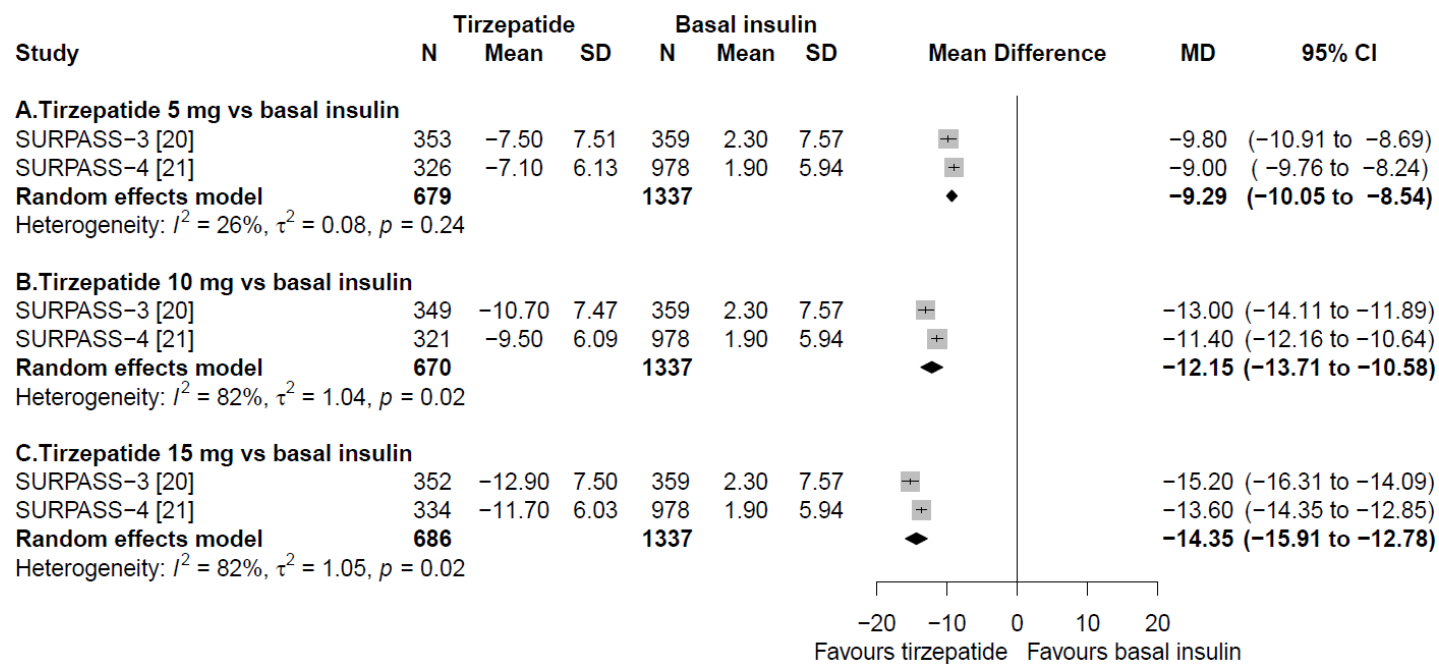
**ESM Fig. 1** Meta-analysis results for tirzepatide versus basal insulin for change in HbA<sub>1c</sub> (mmol/mol).

MD, mean difference



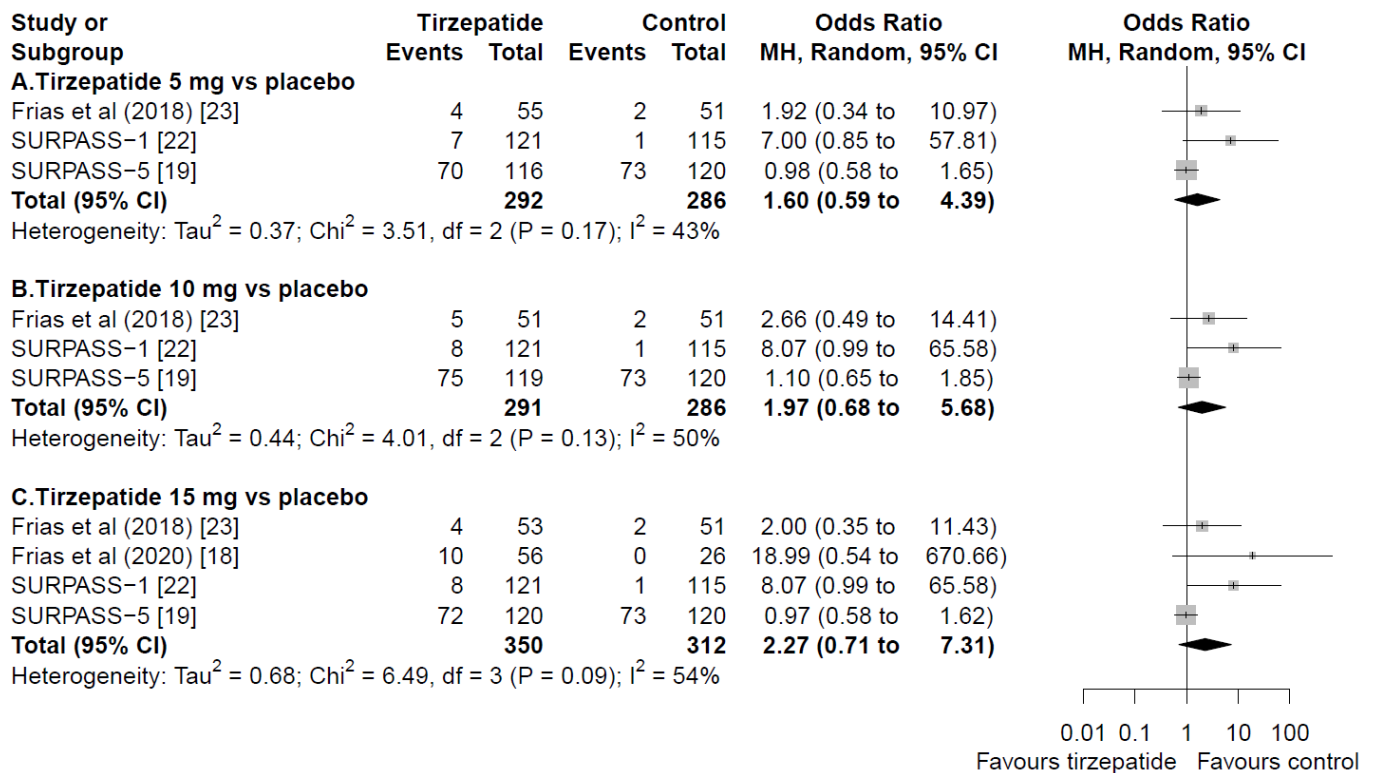
**ESM Fig. 2** Meta-analysis results for tirzepatide versus basal insulin for change in body weight (kg).

MD, mean difference





**ESM Fig. 3** Meta-analysis results for tirzepatide versus placebo for incidence of hypoglycaemia



**ESM Fig. 4** Meta-analysis results for tirzepatide versus basal insulin for incidence of hypoglycaemia

