

SUPPLEMENTARY FIGURES

SGLT2-i plus MET compared to MET monotherapy for T2DM						
Patient or population: patients with T2DM						
Settings:						
Intervention: SGLT2-i plus MET						
Comparison: MET monotherapy						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk MET monotherapy	Corresponding risk SGLT2-i plus MET				
HbA1c (sensitivity analysis) HbA1c Follow-up: 12-26 weeks		The mean hba1c (sensitivity analysis) in the intervention groups was 0.47 lower (0.54 to 0.41 lower)		2709 (10 studies)	⊕⊕⊕⊕ moderate ¹	
HbA1c (sensitivity analysis) - Asian subjects HbA1c Follow-up: 18-24 weeks		The mean hba1c (sensitivity analysis) - asian subjects in the intervention groups was 0.61 lower (0.71 to 0.5 lower)		1025 (4 studies)	⊕⊕⊕⊕ moderate ¹	
HbA1c (sensitivity analysis) - non-Asian subjects HbA1c Follow-up: 12-26 weeks		The mean hba1c (sensitivity analysis) - non-asian subjects in the intervention groups was 0.4 lower (0.48 to 0.31 lower)		1684 (6 studies)	⊕⊕⊕⊕ moderate ¹	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval;
GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

¹ Funnel diagrams of HbA1c

Supplementary Figure 1. GRADE approach to assess the overall confidence for HbA1c.

SGLT2-i plus MET compared to MET monotherapy for T2DM						
Patient or population: patients with T2DM						
Settings:						
Intervention: SGLT2-i plus MET						
Comparison: MET monotherapy						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk MET monotherapy	Corresponding risk SGLT2-i plus MET				
FPG FPG Follow-up: 12-26 weeks		The mean fpg in the intervention groups was 1.2 lower (1.34 to 1.07 lower)		2464 (10 studies)	⊕⊕⊕⊕ high	
FPG - Asian subjects FPG Follow-up: 18-24 weeks		The mean fpg - asian subjects in the intervention groups was 1.51 lower (1.75 to 1.28 lower)		767 (4 studies)	⊕⊕⊕⊕ high	
FPG - non-Asian subjects FPG Follow-up: 12-26 weeks		The mean fpg - non-asian subjects in the intervention groups was 1.04 lower (1.21 to 0.88 lower)		1697 (6 studies)	⊕⊕⊕⊕ high	

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Supplementary Figure 2. GRADE approach to assess the overall confidence for FPG.

SGLT2-i plus MET compared to MET monotherapy for T2DM

Patient or population: patients with T2DM

Settings:

Intervention: SGLT2-i plus MET

Comparison: MET monotherapy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	MET monotherapy	SGLT2-i plus MET				
Body Weight Body Weight Follow-up: 12-26 weeks		The mean body weight in the intervention groups was 1.69 lower (1.89 to 1.48 lower)		2310 (9 studies)	⊕⊕⊕⊕ high	
Body Weight - Asian subjects Body Weight Follow-up: 18-24 weeks		The mean body weight - asian subjects in the intervention groups was 1.69 lower (1.98 to 1.41 lower)		767 (4 studies)	⊕⊕⊕⊕ high	
Body Weight - non-Asian subjects Body Weight Follow-up: 12-26 weeks		The mean body weight - non-asian subjects in the intervention groups was 1.68 lower (1.97 to 1.39 lower)		1543 (5 studies)	⊕⊕⊕⊕ high	

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Very low quality: We are very uncertain about the estimate.

Supplementary Figure 3. GRADE approach to assess the overall confidence for Body Weight.

SGLT2-i plus MET compared to MET monotherapy for T2DM

Patient or population: patients with T2DM

Settings:

Intervention: SGLT2-i plus MET

Comparison: MET monotherapy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	MET monotherapy	SGLT2-i plus MET				
SBP SBP Follow-up: 12-26 weeks		The mean sbp in the intervention groups was 3.16 lower (4.21 to 2.1 lower)		1675 (7 studies)	⊕⊕⊕⊕ high	
SBP - Asian subjects SBP Follow-up: 18-24 weeks		The mean sbp - asian subjects in the intervention groups was 3.5 lower (5.3 to 1.7 lower)		749 (4 studies)	⊕⊕⊕⊕ high	
SBP - non-Asian subjects SBP Follow-up: 12-26 weeks		The mean sbp - non-asian subjects in the intervention groups was 2.98 lower (4.28 to 1.68 lower)		926 (3 studies)	⊕⊕⊕⊕ high	

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CI: Confidence interval;

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Supplementary Figure 4. GRADE approach to assess the overall confidence for SBP.

SGLT2-i plus MET compared to MET monotherapy for T2DM

Patient or population: patients with T2DM

Settings:

Intervention: SGLT2-i plus MET

Comparison: MET monotherapy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk MET monotherapy	Corresponding risk SGLT2-i plus MET				
Serious Adverse events SAEs Follow-up: 12-26 weeks	Study population		OR 0.93 (0.59 to 1.48)	2581 (9 studies)	⊕⊕⊕⊕ high	
	29 per 1000	27 per 1000 (17 to 42)				
	Moderate					
	30 per 1000	28 per 1000 (18 to 44)				
Serious Adverse events - Asian subjects SAEs Follow-up: 18-24 weeks	Study population		OR 0.89 (0.43 to 1.84)	888 (3 studies)	⊕⊕⊕⊕ high	
	36 per 1000	33 per 1000 (16 to 65)				
	Moderate					
	41 per 1000	37 per 1000 (18 to 73)				
Serious Adverse events - non-Asian subjects SAEs Follow-up: 12-26 weeks	Study population		OR 0.96 (0.52 to 1.76)	1693 (6 studies)	⊕⊕⊕⊕ high	
	25 per 1000	24 per 1000 (13 to 43)				
	Moderate					
	24 per 1000	23 per 1000 (13 to 41)				

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CI: Confidence interval; OR: Odds ratio;

GRADE Working Group grades of evidence

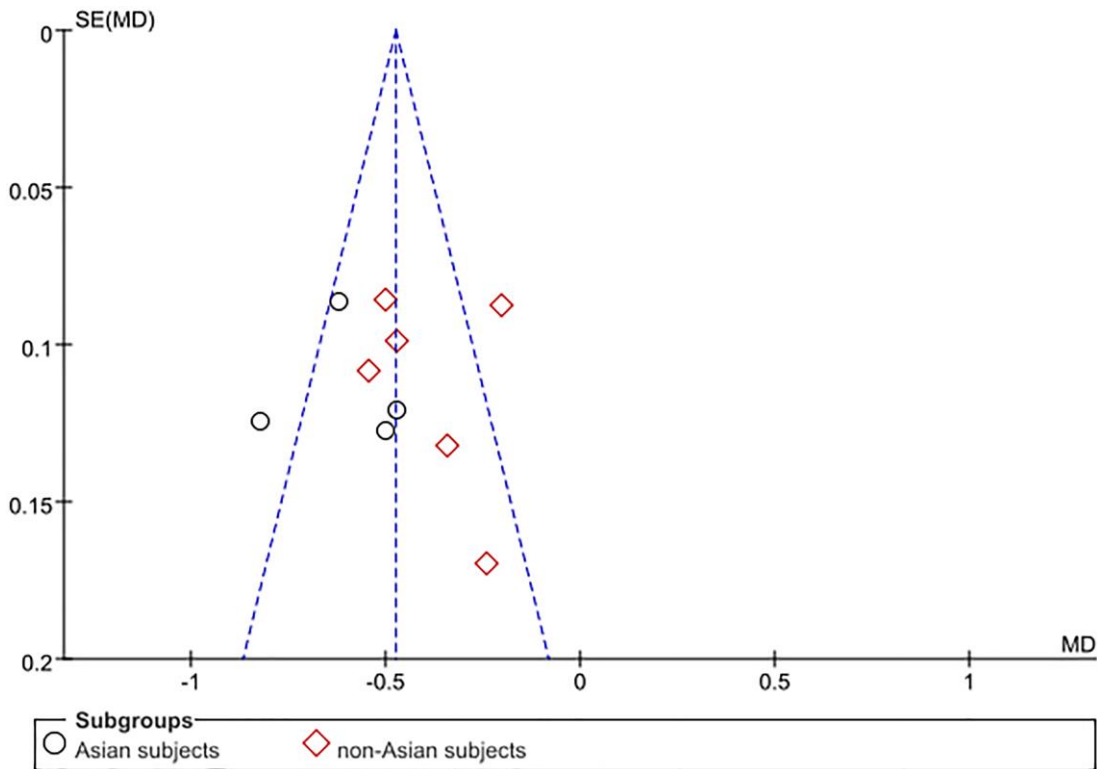
High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

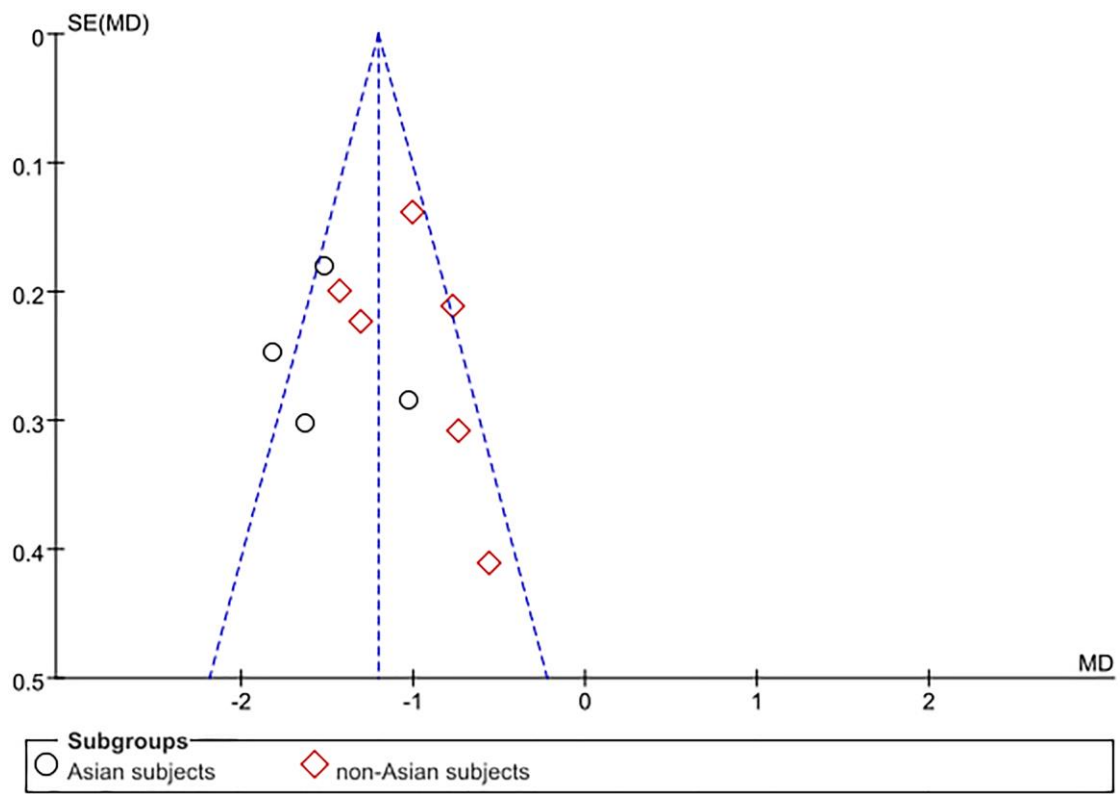
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

Supplementary Figure 5. GRADE approach to assess the overall confidence for SAEs.



Supplementary Figure 6. Funnel diagrams of HbA1c.



Supplementary Figure 7. Funnel diagrams of FPG.