Supplementary Appendix & Figures

Search Strategies:

PubMED:

((("diabetes mellitus, type 2"[MeSH Terms] OR "diabetes mellitus, type 2/drug therapy"[MeSH Terms] OR "diabetes mellitus, typ2 [MeSH Terms] 2/therapy"[MeSH Terms] OR "diabetes mellitus, type 2/prevention and control"[MeSH Terms] OR "type 2 diabetes"[Title/Abstract] OR "non-insulin-dependent diabetes mellitus"[Title/Abstract] OR "NIDDM"[Title/Abstract]) AND ("pharmacology, clinical"[MeSH Terms] OR "pharmacology"[Title/Abstract] OR "drug*"[Title/Abstract] OR "medication*"[Title/Abstract] OR "therap*"[Title/Abstract] OR "Nateglinide"[tiab] OR "Repaglinide"[tiab] OR "Glipizide"[tiab] OR "Glimepiride"[tiab] OR "Glyburide"[tiab] OR "Saxagliptin"[tiab] OR "Sitagliptin"[tiab] OR "Linagliptin"[tiab] OR "Alogliptin"[tiab] OR "Metformin"[tiab] OR "Rosiglitazone"[tiab] OR "Pioglitazone"[tiab] OR "Canagliflozin"[tiab] OR "Dapagliflozin"[tiab] OR "Empagliflozin"[tiab] OR "Colesevelam"[tiab] OR "Pramlintide"[tiab] OR "Albiglutide"[tiab] OR "Dulaglutide"[tiab] OR "Exenatide"[tiab] OR "Liraglutide"[tiab] OR "Lixisenatide"[tiab] OR "Semaglutide"[tiab] OR "Gliclazide"[tiab] OR "Glibenclamide"[tiab] OR "Vildagliptin"[tiab] OR "Teneligliptin"[tiab] OR "Ertugliflozin" [tiab] OR "Tirzepatide"[tiab] OR "Mounjaro"[tiab]) AND ("Child"[MeSH Terms] OR "Adolescent"[MeSH Terms] OR "Pediatrics"[MeSH Terms:noexp] OR "child*"[Title/Abstract] OR "children*"[Title/Abstract] OR "adolescen*"[Title/Abstract] OR "juvenil*"[Title/Abstract] OR "youth*"[Title/Abstract] OR "teen*"[Title/Abstract] OR "pubescen*"[Title/Abstract] OR "pediatric*"[Title/Abstract]) AND ("Randomized Controlled Trial"[Publication Type] OR "random allocation"[MeSH Terms] OR "double-blind method"[MeSH Terms] OR "single-blind method"[MeSH Terms] OR "random*"[Title/Abstract] OR "Placebos"[MeSH Terms] OR "placebo"[Title/Abstract] OR (("singl*"[Text Word] OR "doubl*"[Text Word] OR "trebl*"[Text Word] OR "tripl*"[Text Word]) AND ("mask*"[Text Word] OR "blind*"[Text Word] OR "dumm*"[Text Word])))) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms]))

EMBASE:

('non insulin dependent diabetes mellitus'/exp OR 'type 2 diabetes':ab,ti OR ('non insulin dependent diabetes mellitus' NEAR/5 child) OR ('non insulin dependent diabetes mellitus' NEAR/5 adolesence) OR ('non insulin dependent diabetes mellitus' NEAR/5 youth) OR ('non insulin dependent diabetes mellitus' NEAR/5

pediatric)) AND ('pharmacology':ab,ti OR 'drug':ab,ti OR 'medication':ab,ti OR 'therap':ab,ti OR 'Nateglinide':ab,ti OR 'Repaglinide':ab,ti OR 'Glipizide':ab,ti OR 'Glimepiride':ab,ti OR 'Glyburide':ab,ti OR 'Saxagliptin':ab,ti OR 'Sitagliptin':ab,ti OR 'Linagliptin':ab,ti OR 'Alogliptin':ab,ti OR 'Metformin':ab,ti OR 'Rosiglitazone':ab,ti OR 'Pioglitazone':ab,ti OR 'Canagliflozin':ab,ti OR 'Dapagliflozin':ab,ti OR 'Empagliflozin':ab,ti OR 'Colesevelam':ab,ti OR 'Pramlintide':ab,ti OR 'Albiglutide':ab,ti OR 'Dulaglutide':ab,ti OR 'Exenatide':ab,ti OR 'Liraglutide':ab,ti OR 'Lixisenatide':ab,ti OR 'Semaglutide':ab,ti OR 'Gliclazide':ab,ti OR 'Glibenclamide':ab,ti OR 'Vildagliptin':ab,ti OR 'Teneligliptin':ab,ti OR 'Ertugliflozin':ab,ti OR 'Tirzepatide':ab,ti OR 'Mounjaro':ab,ti) AND ('Child'/exp OR 'adolescence'/exp OR 'child*':ab,ti OR 'children*':ab,ti OR 'adolescen*':ab,ti OR 'juvenil*':ab,ti OR 'youth*':ab,ti OR 'teen*':ab,ti OR 'pubescen*':ab,ti OR 'pediatric*':ab,ti) AND (random*:ab,ti OR placebo*:de,ab,ti OR (double NEXT/1 blind*)):ab,ti

SCOPUS:

(Type 2 diabetes mellitus) AND (Pharmacology Or Therapy OR Management) AND (children OR adolescents OR Pediatrics) AND (Randomized Control Trial)

ClinicalTrials.gov

The applied filters Studies With Results | Interventional Studies | Type 2 Diabetes | 18 years, Child |

Phase 3, 4

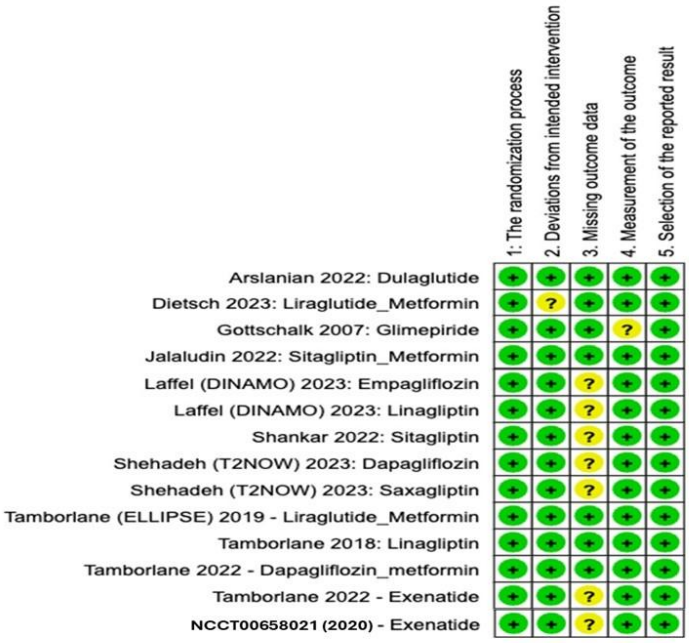

Figure S1: Risk of Bias of Included Studies

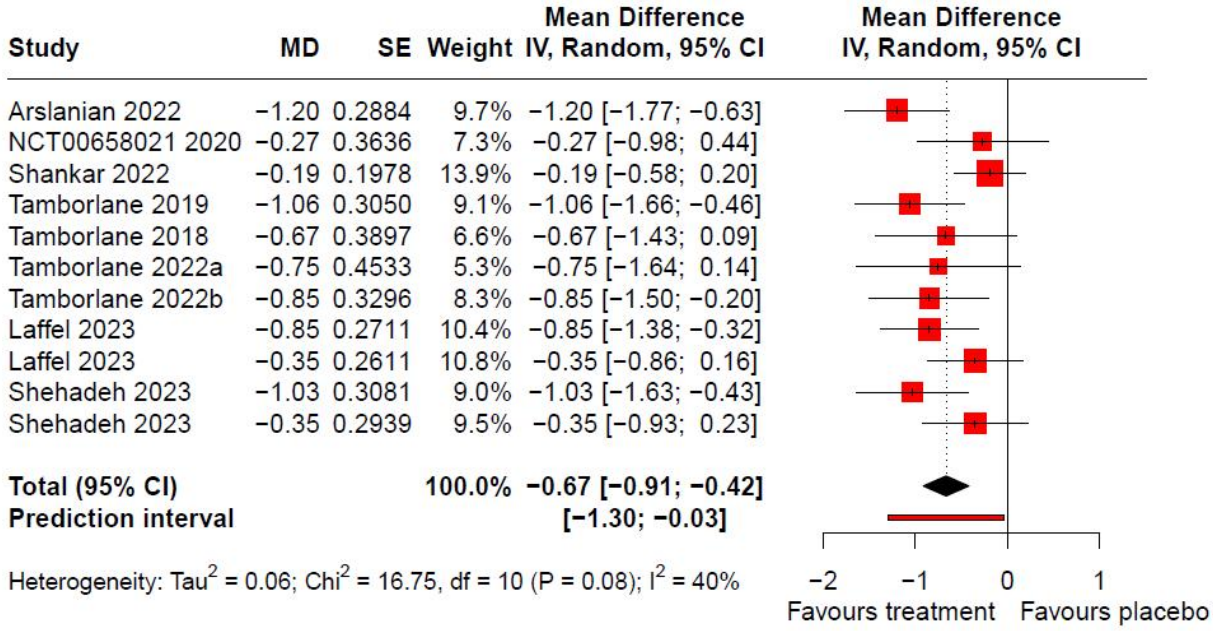

Figure S2: Pairwise meta-analysis (HbA1c)

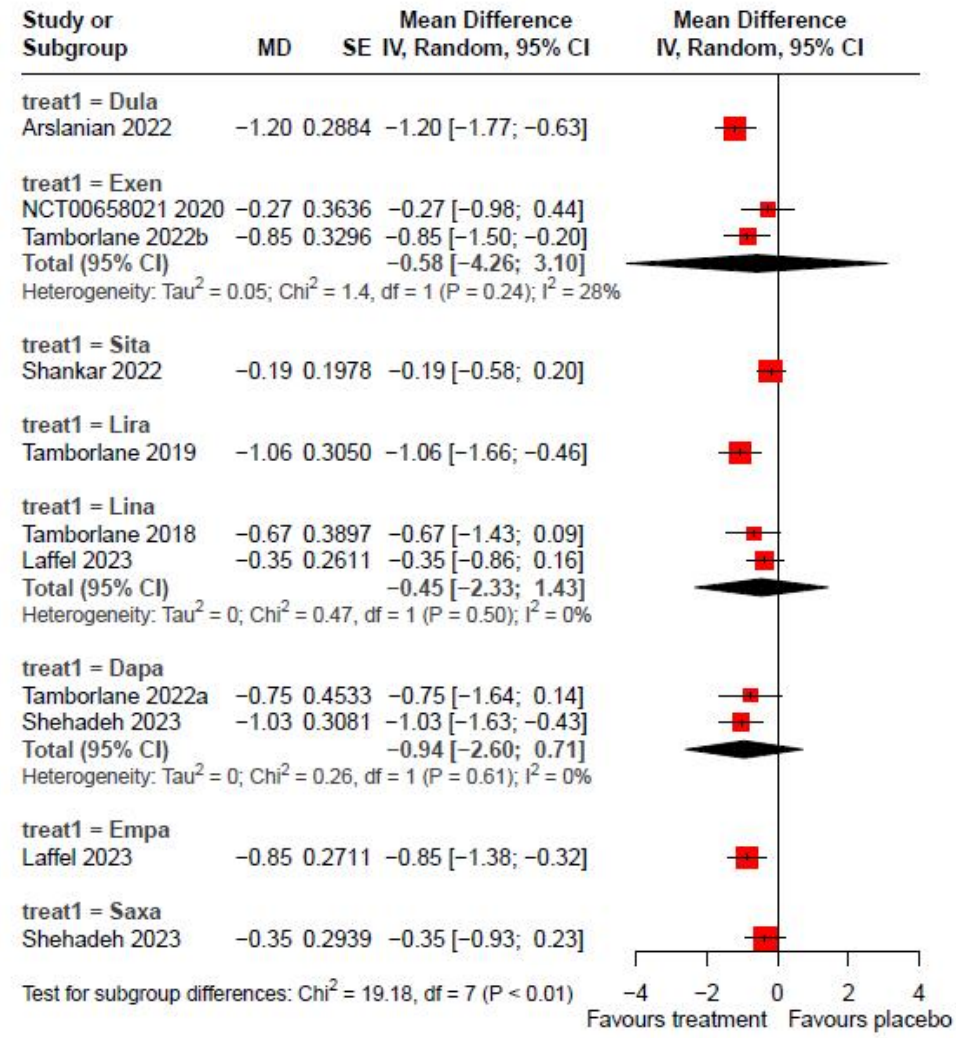

Figure S3. Pairwise meta-analysis (HbA1c) drug classes.

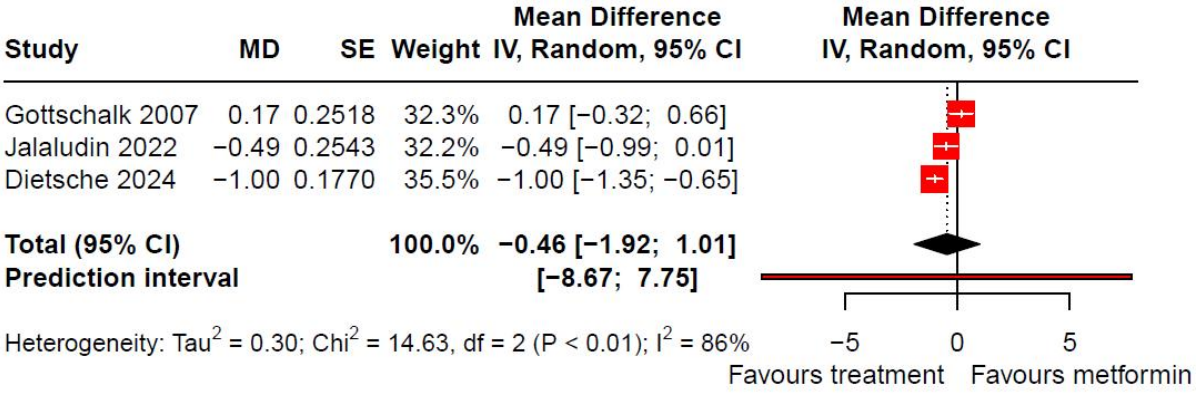

Figure S4. Pairwise meta-analysis (HbA1c) drug vs metformin.

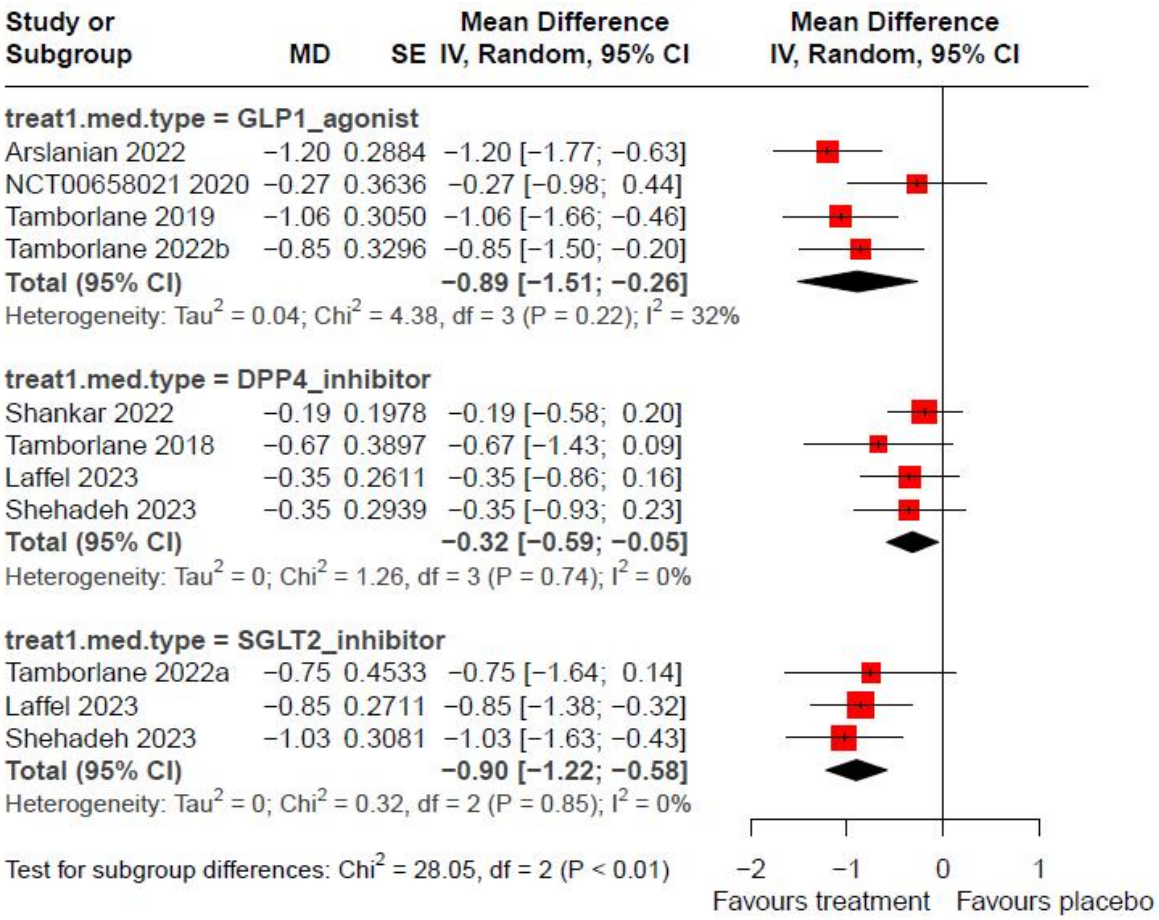

Figure S5: Drug classes and HbA1c

	Dapa	Dula	Empa	Exen	Glim	Lina	Lira	Metf	Plac	Saxa	Sita
Dapa	0.00	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Dula	-0.26	0.00	NA	NA	NA	NA	NA	NA	NA	NA	NA
Empa	0.07	0.33	0.00	NA	NA	NA	NA	NA	NA	NA	NA
Exen	0.35	0.61	0.28	0.00	NA	NA	NA	NA	NA	NA	NA
Glim	1.25	1.51	1.18	0.89	0.00	NA	NA	NA	NA	NA	NA
Lina	0.49	0.75	0.42	0.14	-0.76	0.00	NA	NA	NA	NA	NA
Lira	0.03	0.29	-0.04	-0.32	-1.22	-0.46	0.00	NA	NA	NA	NA
Metf	1.08	1.34	1.01	0.72	-0.17	0.59	1.05	0.00	NA	NA	NA
Plac	0.94	1.20	0.87	0.59	-0.31	0.45	0.91	-0.14	0.00	NA	NA
Saxa	0.64	0.89	0.56	0.28	-0.61	0.14	0.61	-0.44	-0.31	0.00	NA
Sita	0.69	0.95	0.62	0.34	-0.56	0.20	0.66	-0.39	-0.25	0.05	0

Figure S6. Network league table for HbA1c

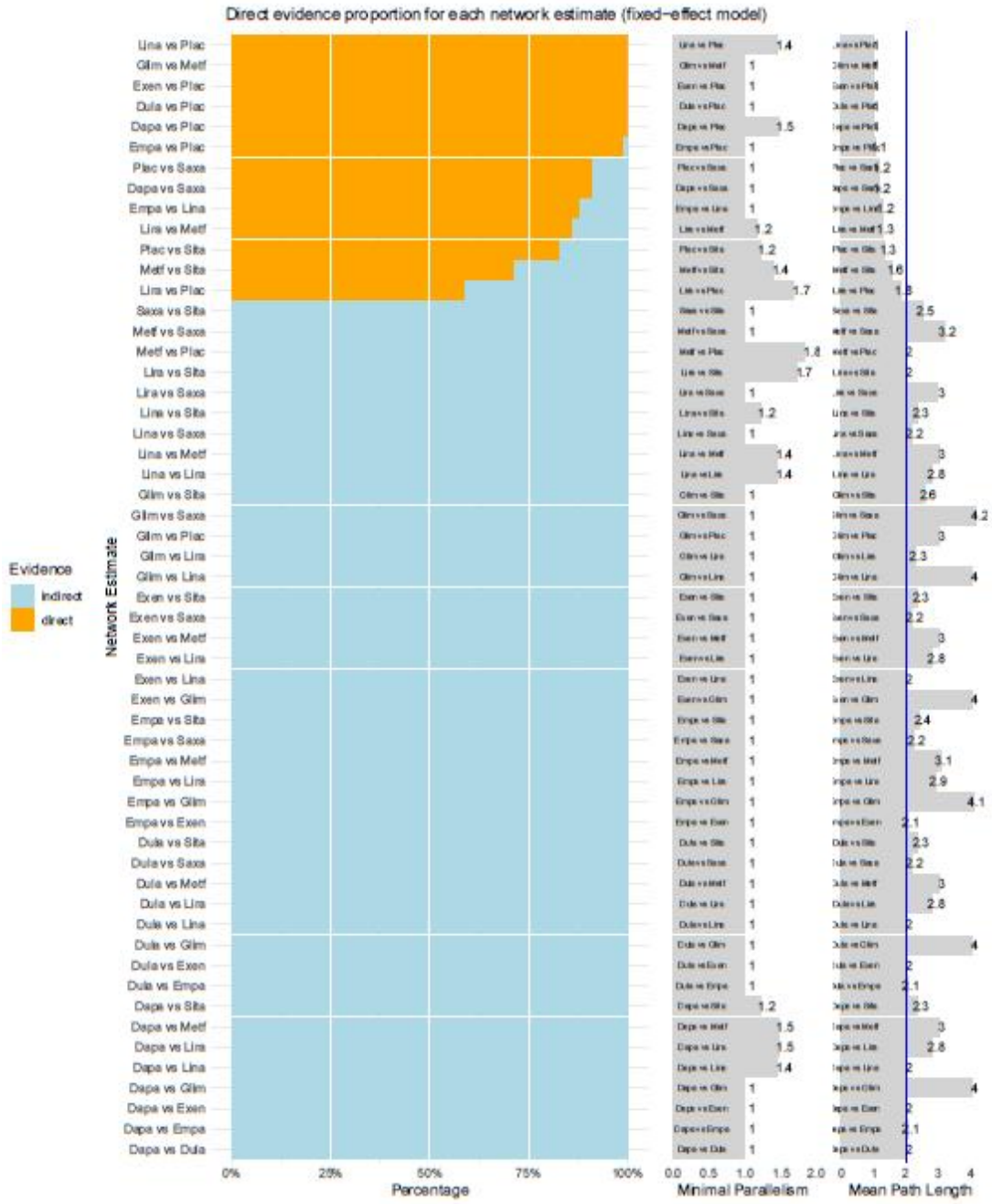

Figure S7. Direct evidence plot for HbA1c.

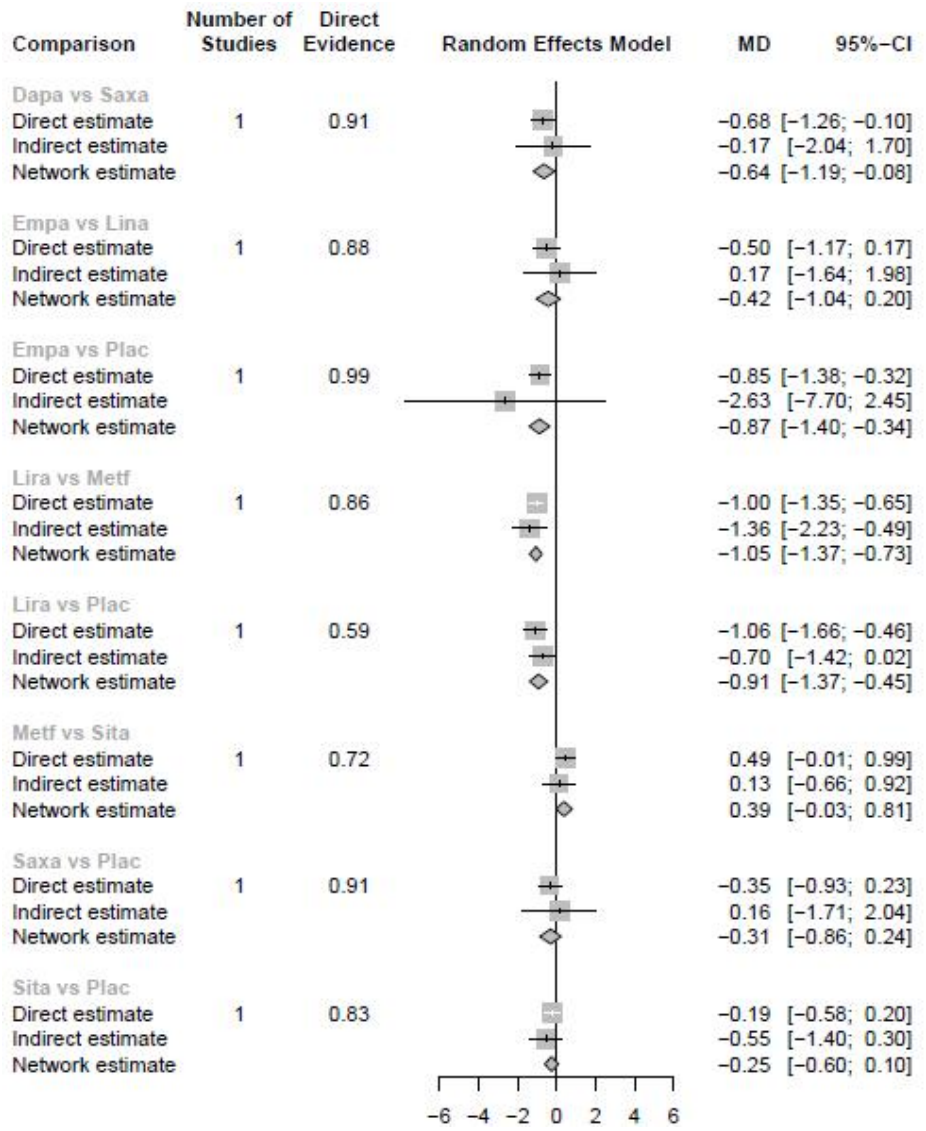

Figure S8. Forest plot for separate direct and indirect evidence for HbA1c.

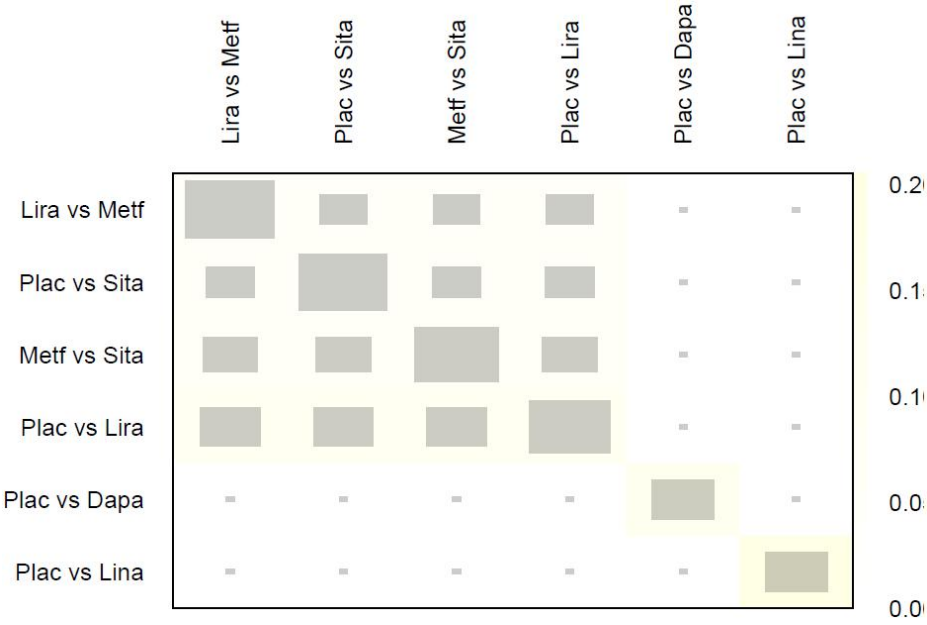

Figure S9. Network heat plot to evaluate the inconsistency of the network model.

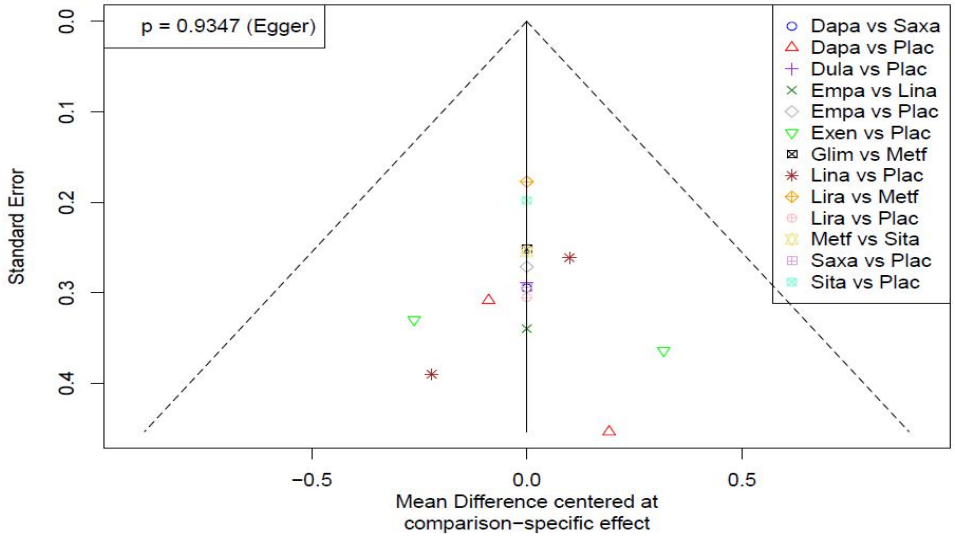

Figure S10. Funnel plot analysis for HbA1c analysis.

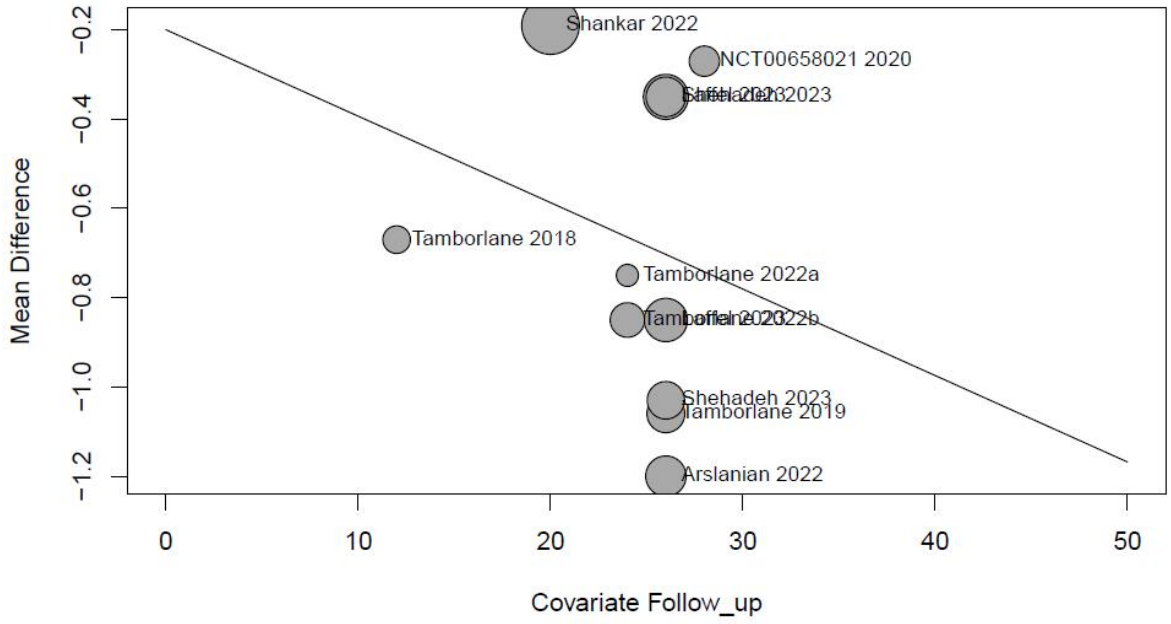

Figure S11. Subgroup analysis (HbA1c) of follow up.

```
##       P-score
## Dula  0.9240
## Dapa  0.8103
## Lira  0.7943
## Empa  0.7652
## Exen  0.5865
## Lina  0.4920
## Saxa  0.3942
## Sita  0.3695
## Plac  0.1775
## Metf  0.1239
## Glim  0.0625
```

Figure S12. The p score ranking for drugs for lowering HbA1c.

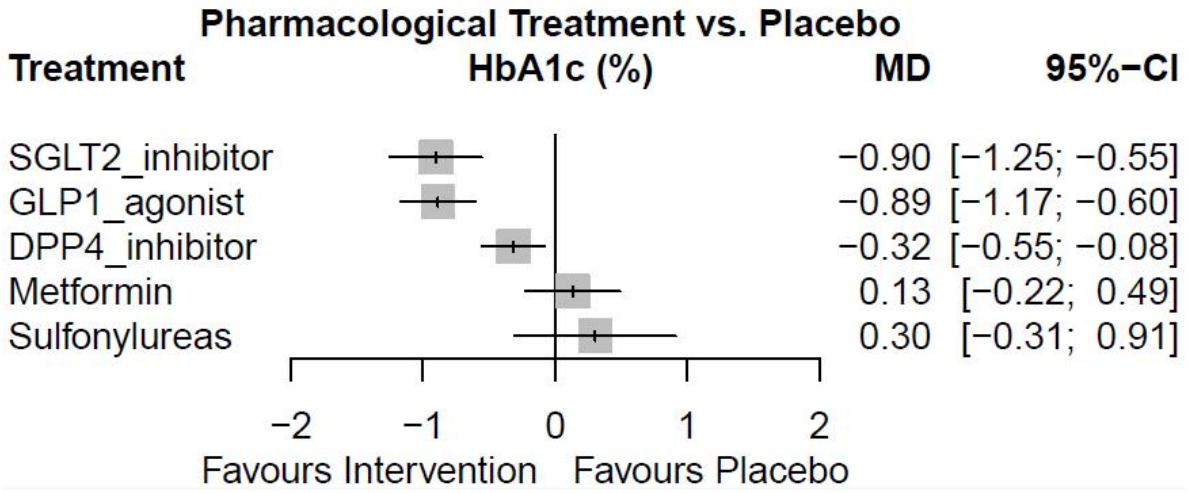

Figure S13. Network meta-analysis for HbA1c according to drug class.

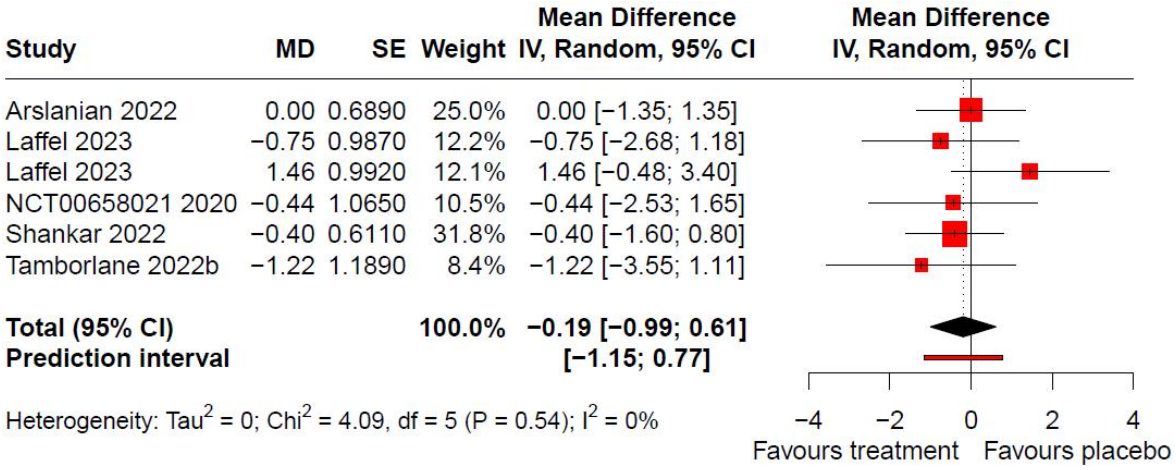

Figure S14. Pairwise meta-analysis body weight changes.

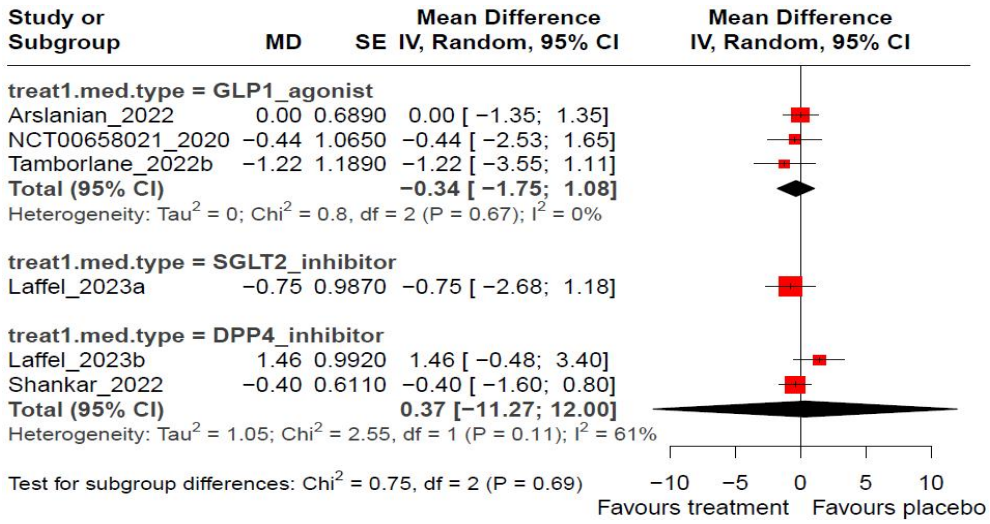

Figure S15. Pairwise meta-analysis for body weight drug classes.

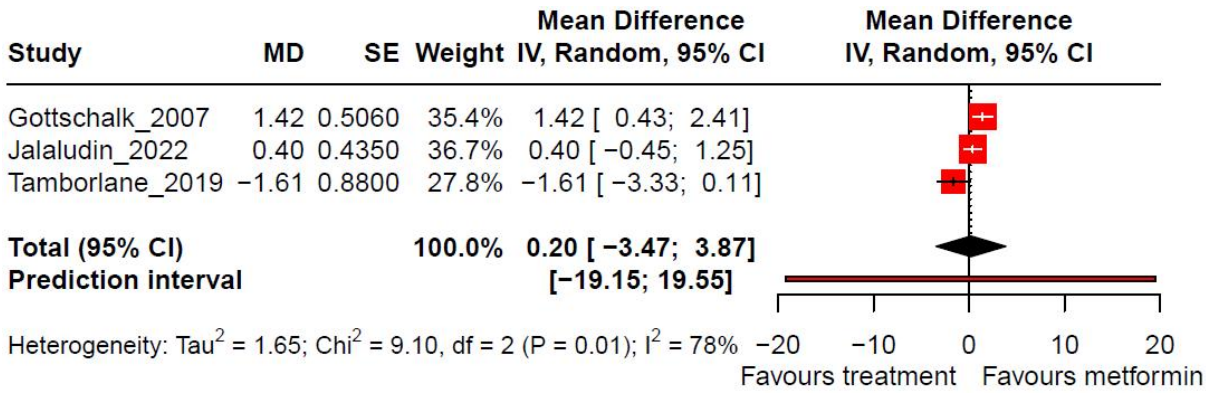

Figure S16. Pairwise meta-analysis drug vs metformin on body weight change.

```
##       P-score
## Lira   0.9529
## Metf   0.6849
## Exen   0.6543
## Empa   0.6339
## Sita   0.5279
## Dula   0.3965
## Plac   0.3731
## Glim   0.2019
## Lina   0.0746
```

Figure S17. Treatment ranking p values for body weight changes.

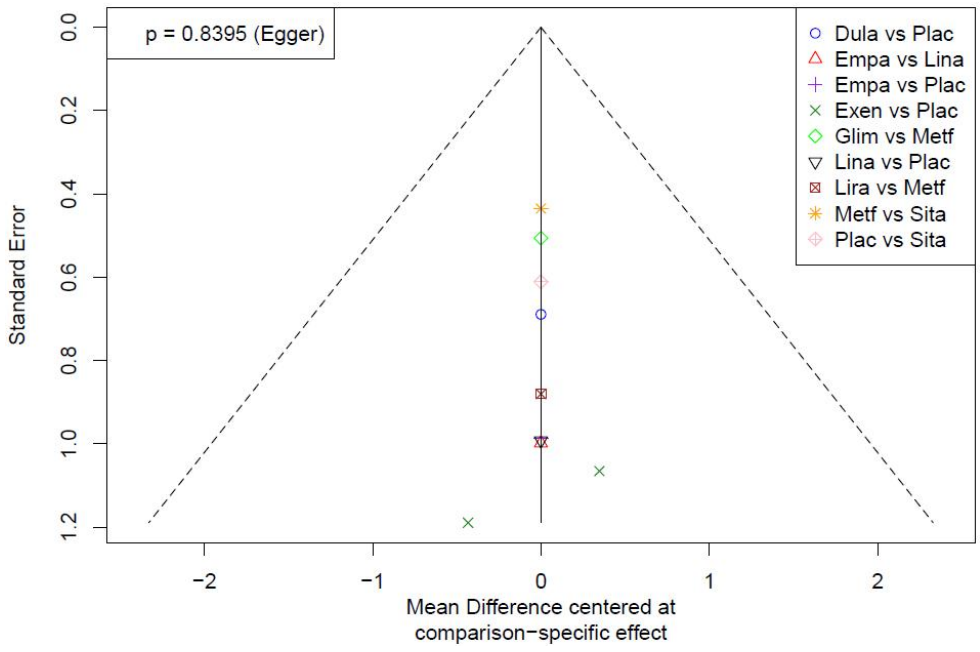

Figure S18. Funnel plot for body weight meta-analysis.

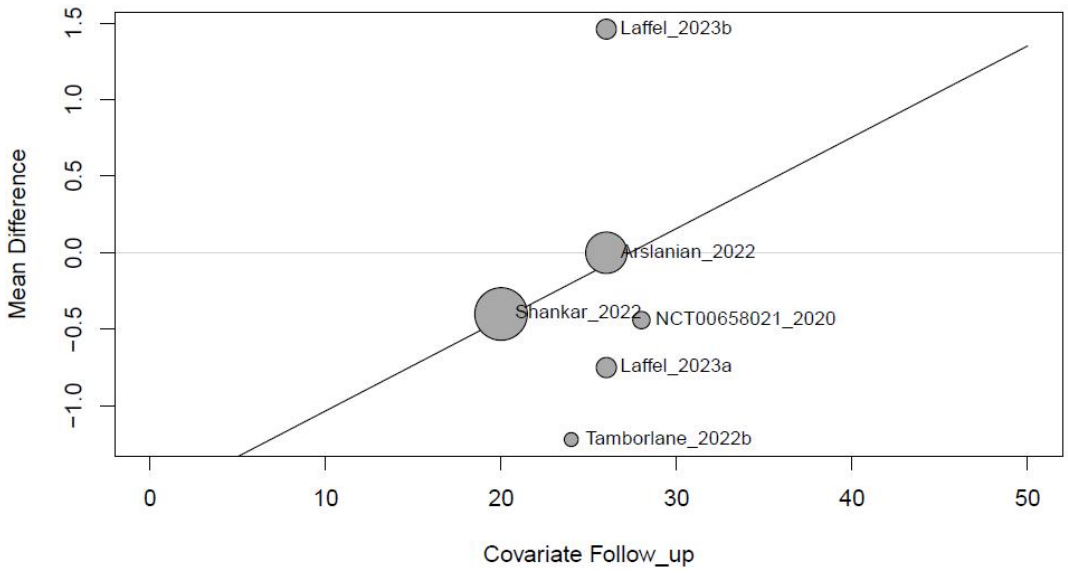

Figure S19. Subgroup follow up duration analysis on body weight.

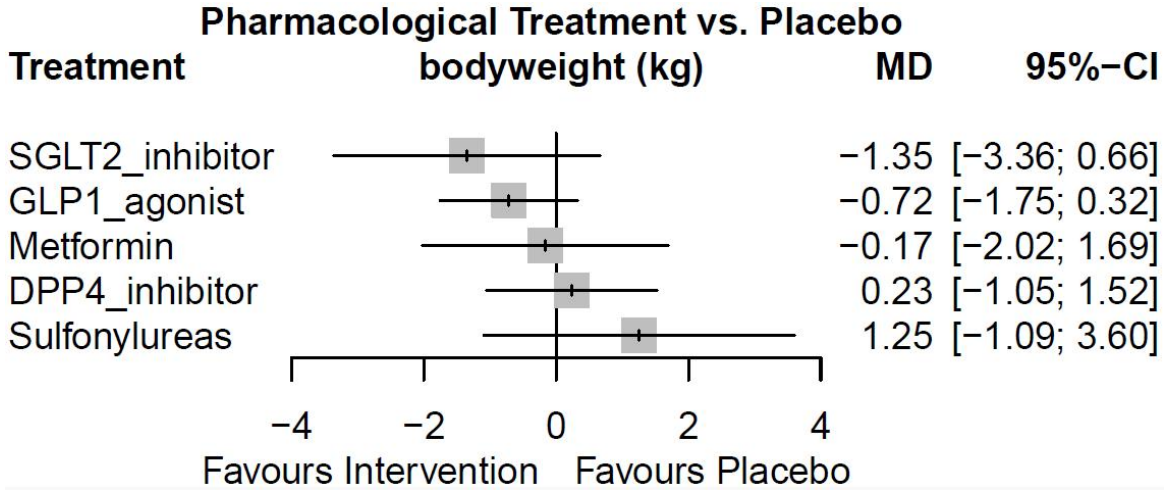

Figure S20. Network meta-analysis for body weight changes according to drug classes.

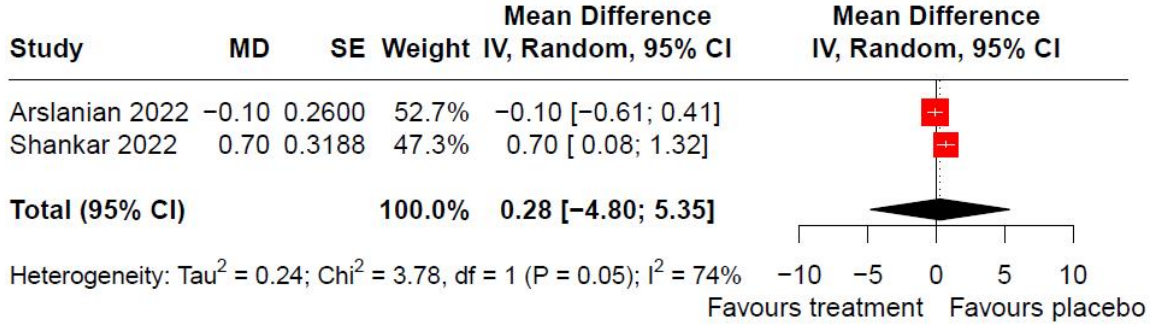

Figure S21. Pairwise meta-analysis for BMI changes.

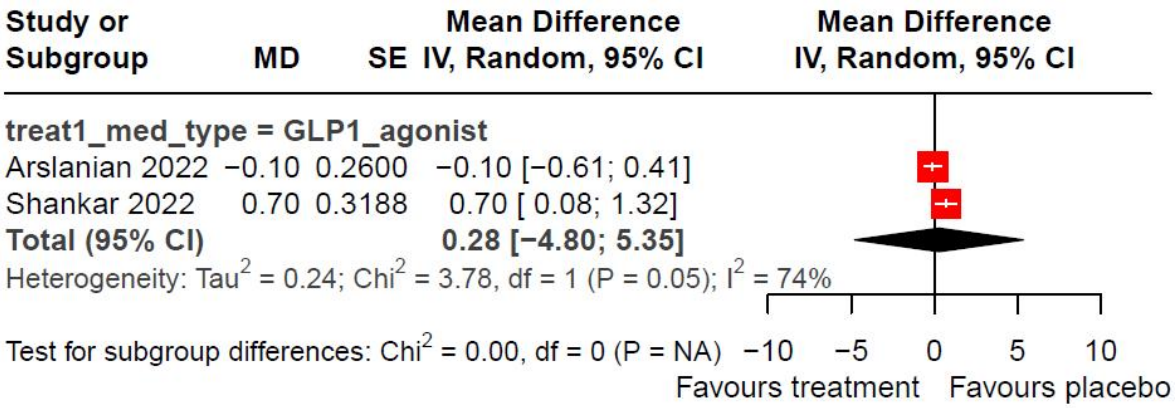

Figure S22. Pairwise meta-analysis for BMI changes.

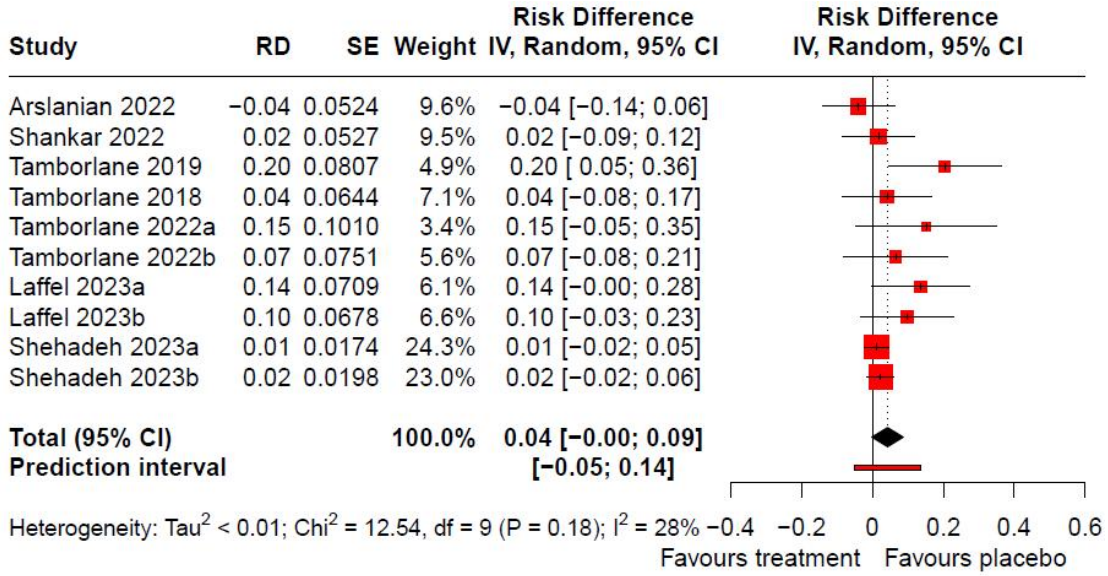

Figure S23. Pairwise meta-analysis for level 1 hypoglycemia events.

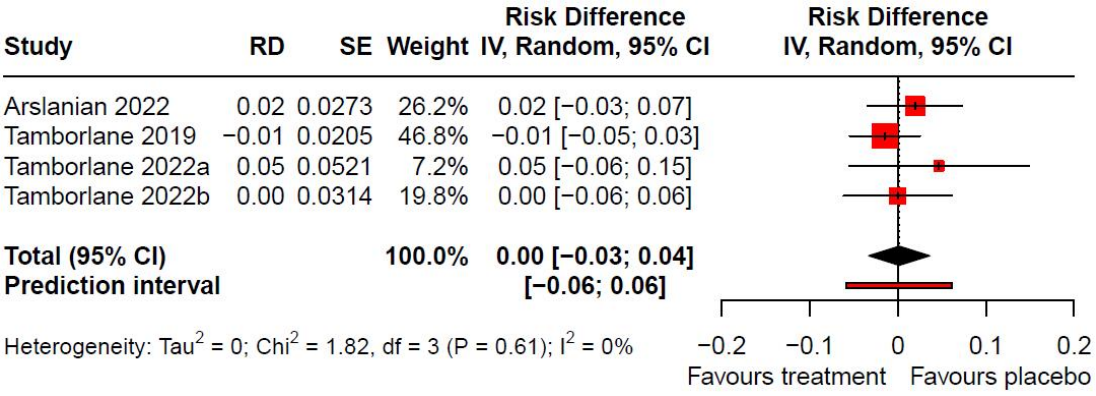

Figure S24. Pairwise meta-analysis for level 2 hypoglycemia events.

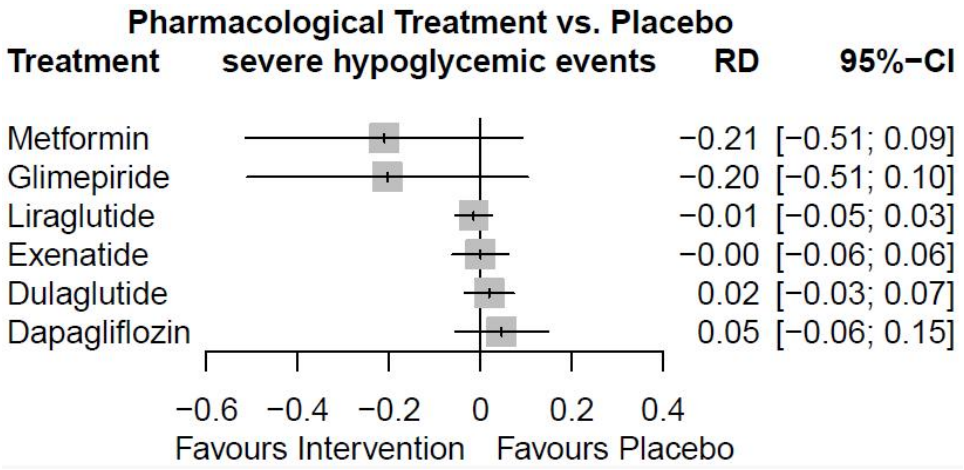

Figure S25. Network meta-analysis forest plot for level 2 hypoglycemia events.

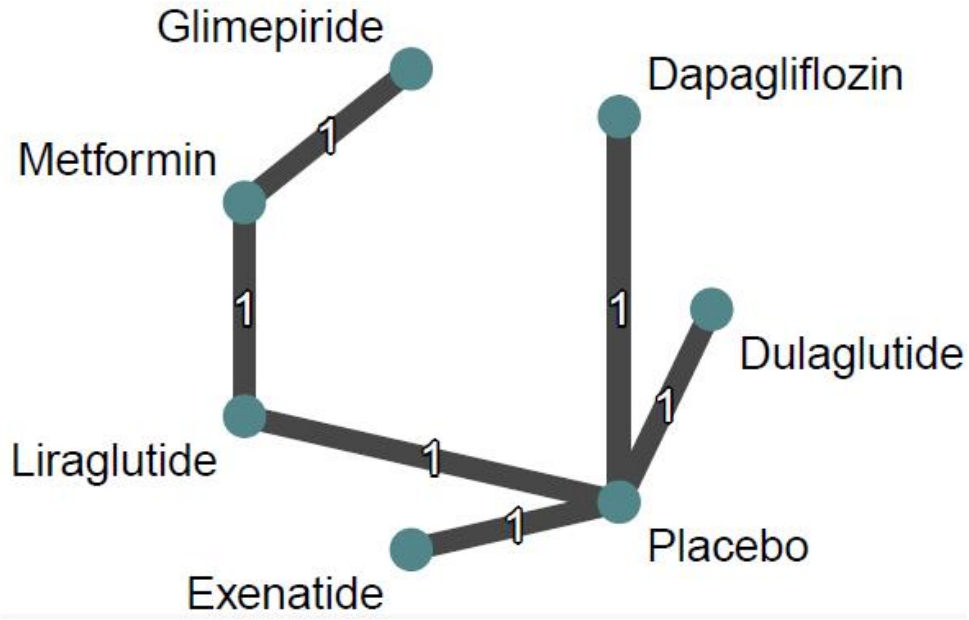

Figure S26. Network meta-analysis graph for level 2 hypoglycemia events.

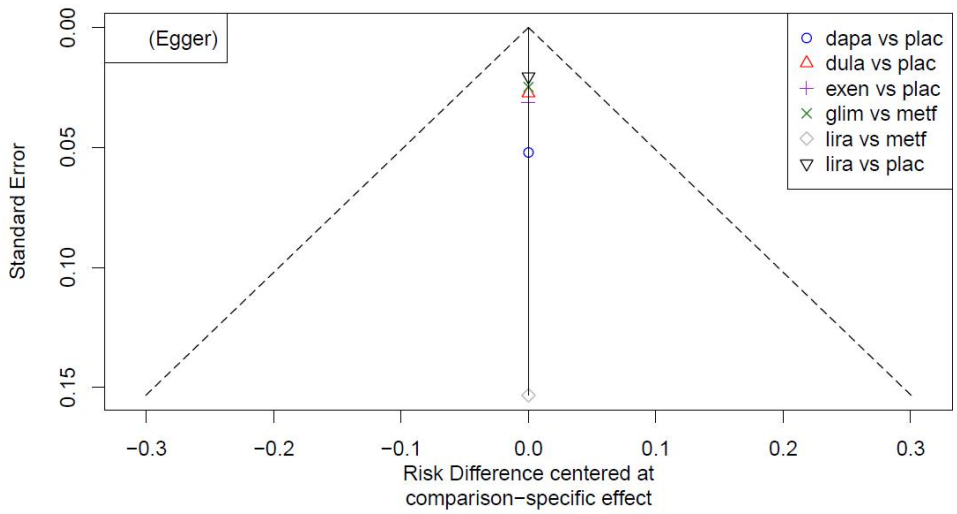

Figure S27. Funnel plot for studies showing level 2 hypoglycemia events.

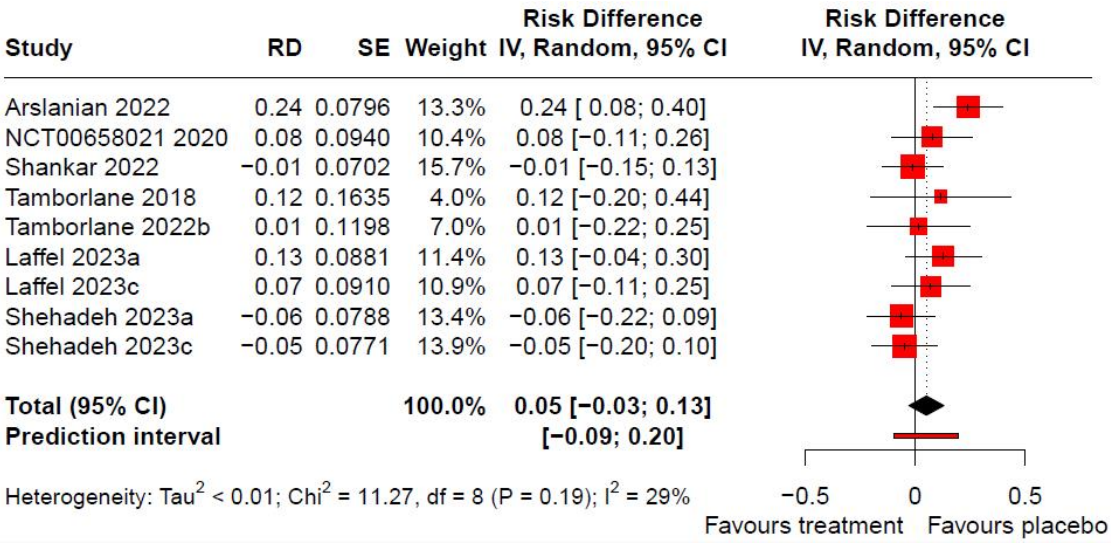

Figure S28. Pairwise meta-analysis for minor adverse events based on studies.

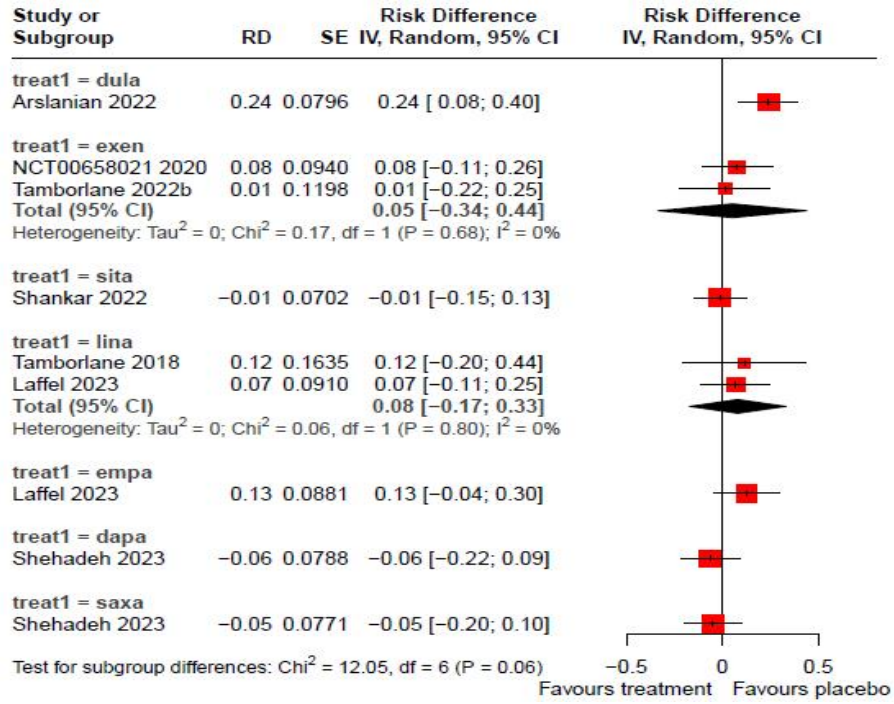

Figure S29. Pairwise meta-analysis for minor adverse events by drugs.

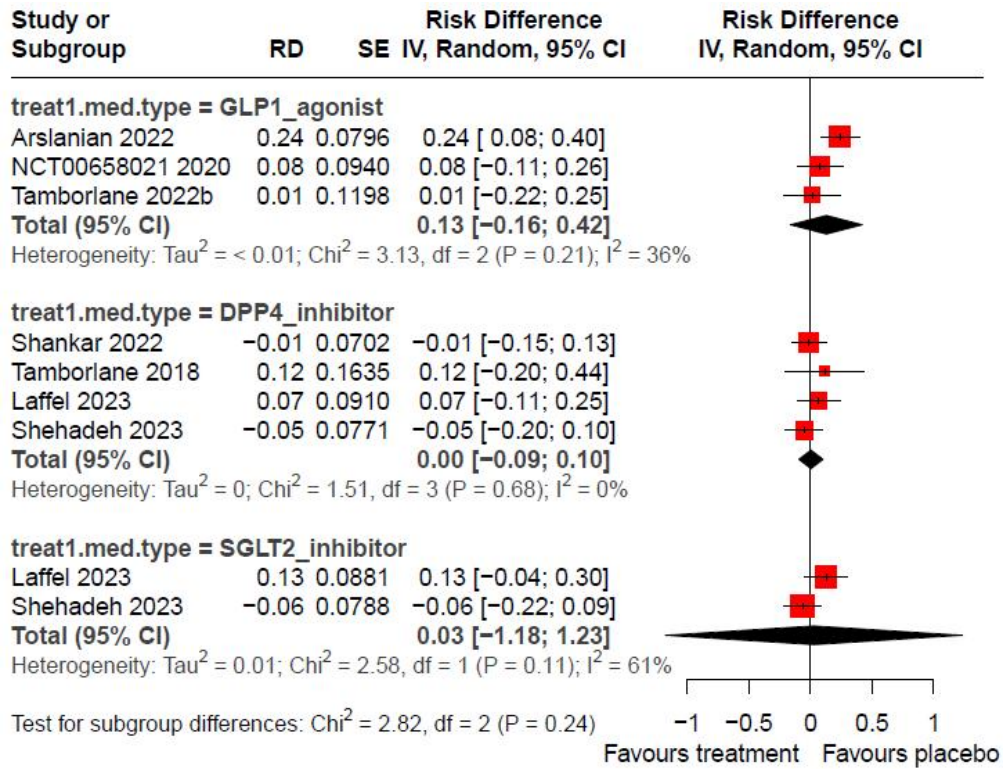

Figure S30. Pairwise meta-analysis for minor adverse events by drug classes.

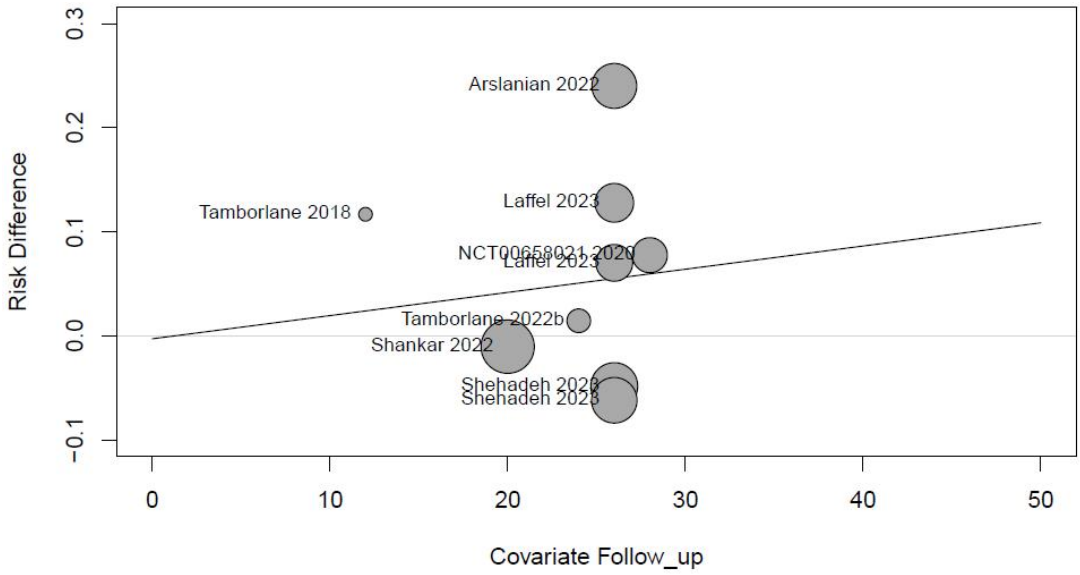

Figure S31. Mixed effects model meta-analysis for minor adverse events.

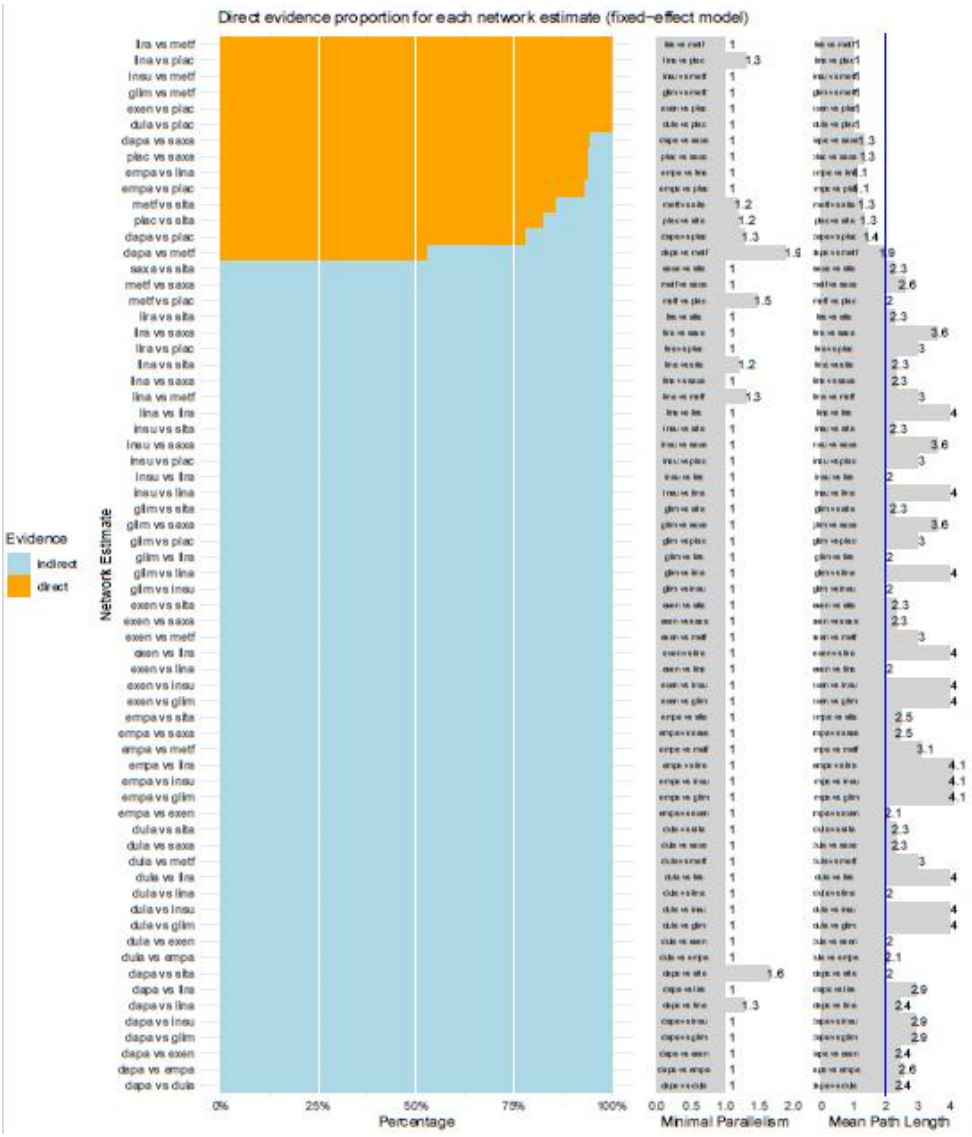

Figure S32. Direct evidence plot for minor adverse events.

```
##       P-score
## dapa   0.6993
## lira   0.6859
## saxa   0.6831
## metf   0.6732
## sita   0.6569
## glim   0.6052
## plac   0.5558
## insu   0.5123
## exen   0.3850
## lina   0.3165
## empa   0.1883
## dula   0.0385
```

Figure S33. Treatment ranking p-score for minor adverse events.

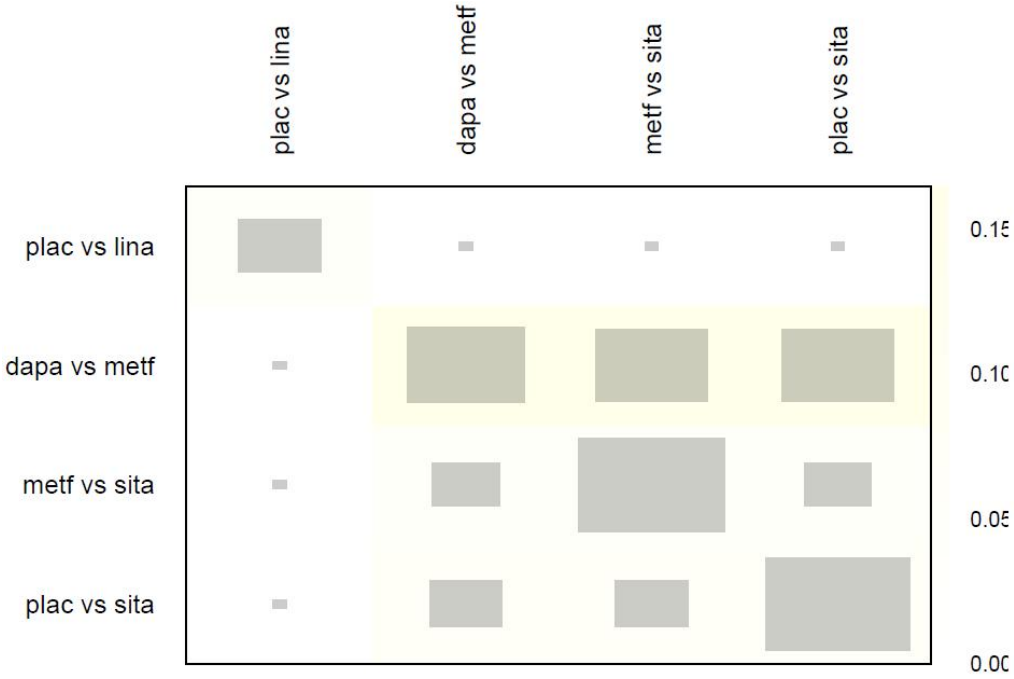

Figure S34. Network heat map for minor adverse events.

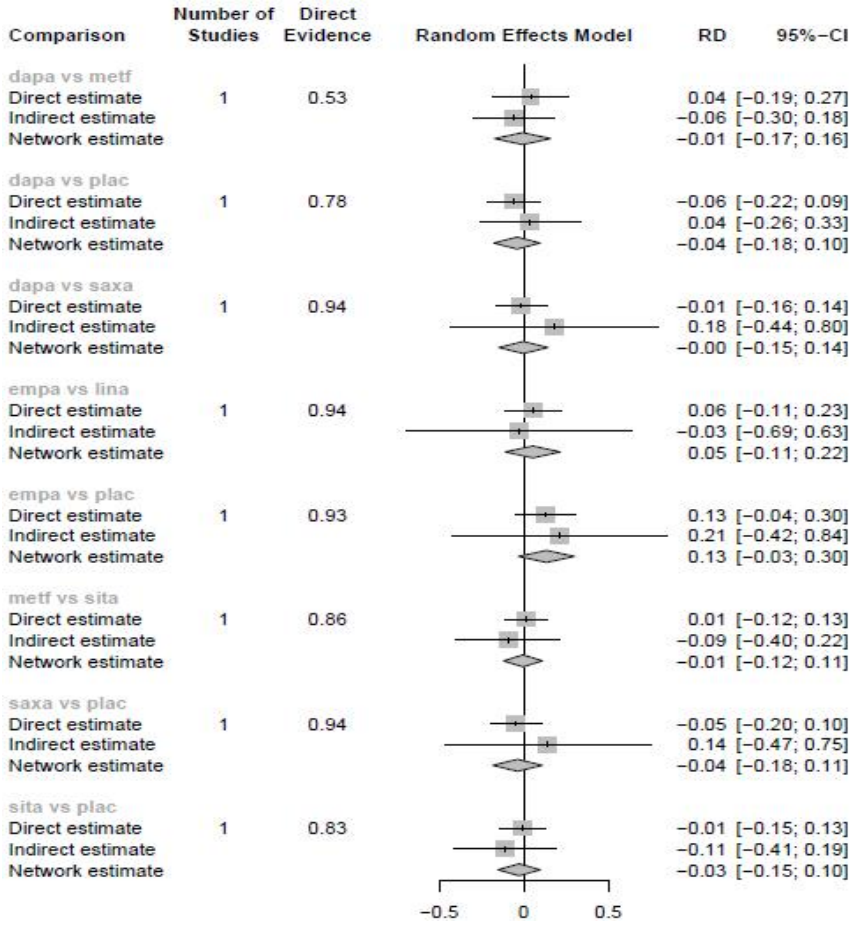

Figure S35. Forest plot to separate direct from indirect evidence for major adverse events.

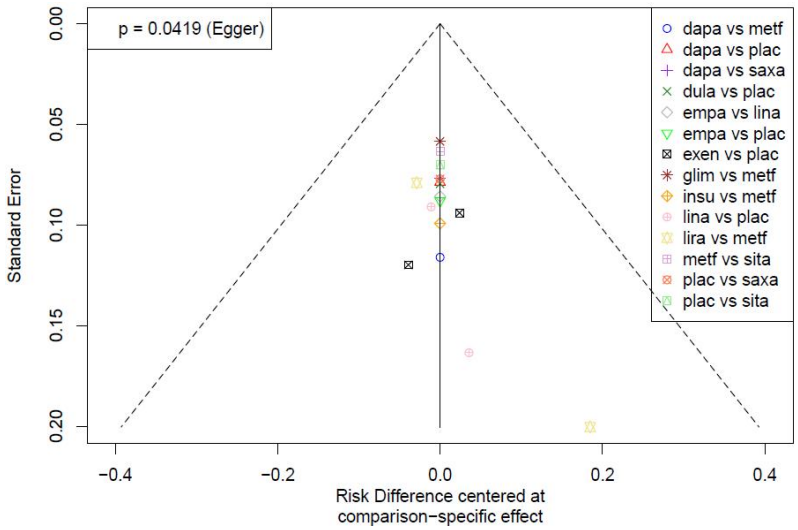

Figure S36. Funnel plot for network meta-analysis - minor adverse events.