

Figure S1. Multivariable Mendelian Randomization (MVMR) strategy in this study.

This figure shows the MVMR design of drug-target MR analysis with HbA1c GWAS data adjusted for body mass index (BMI), systolic blood pressure, smoking status, and alcohol drinker status to explore the robustness of genetically predicted levels of HbA1c when targeting a specific gene by the corresponding drug on the risk of ovarian cancer (OC).

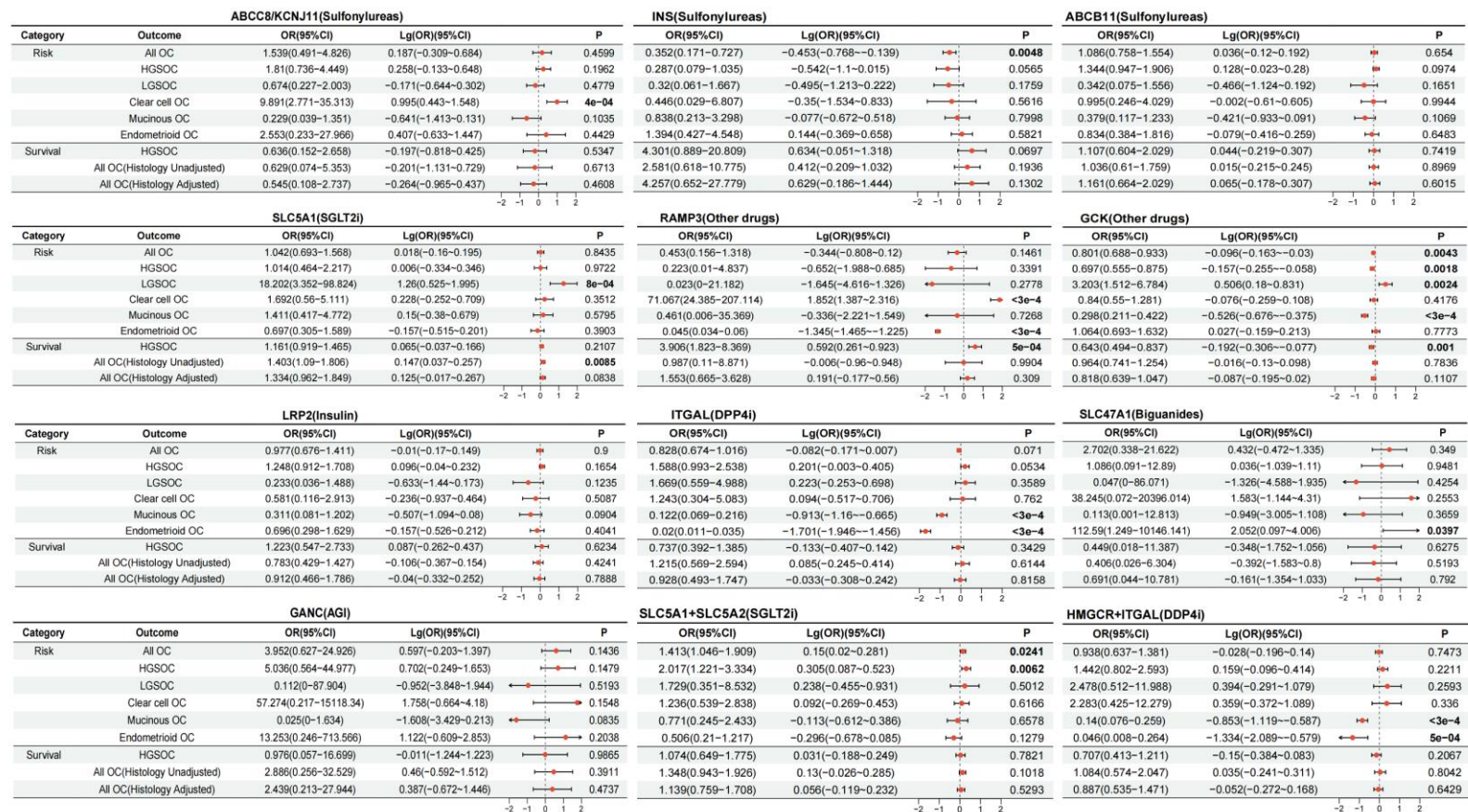


Figure S2. Forest plots of the effects of the antidiabetic drug targets on 9 OC phenotypes.

This Figure was an appendix of Figure 2. All results were derived from the principal MR analysis. The effects (ORs) were adjusted to reflect a per-SD decrease in genetically predicted levels of HbA1c when targeting the specific gene with the corresponding drug on the risk of OC.

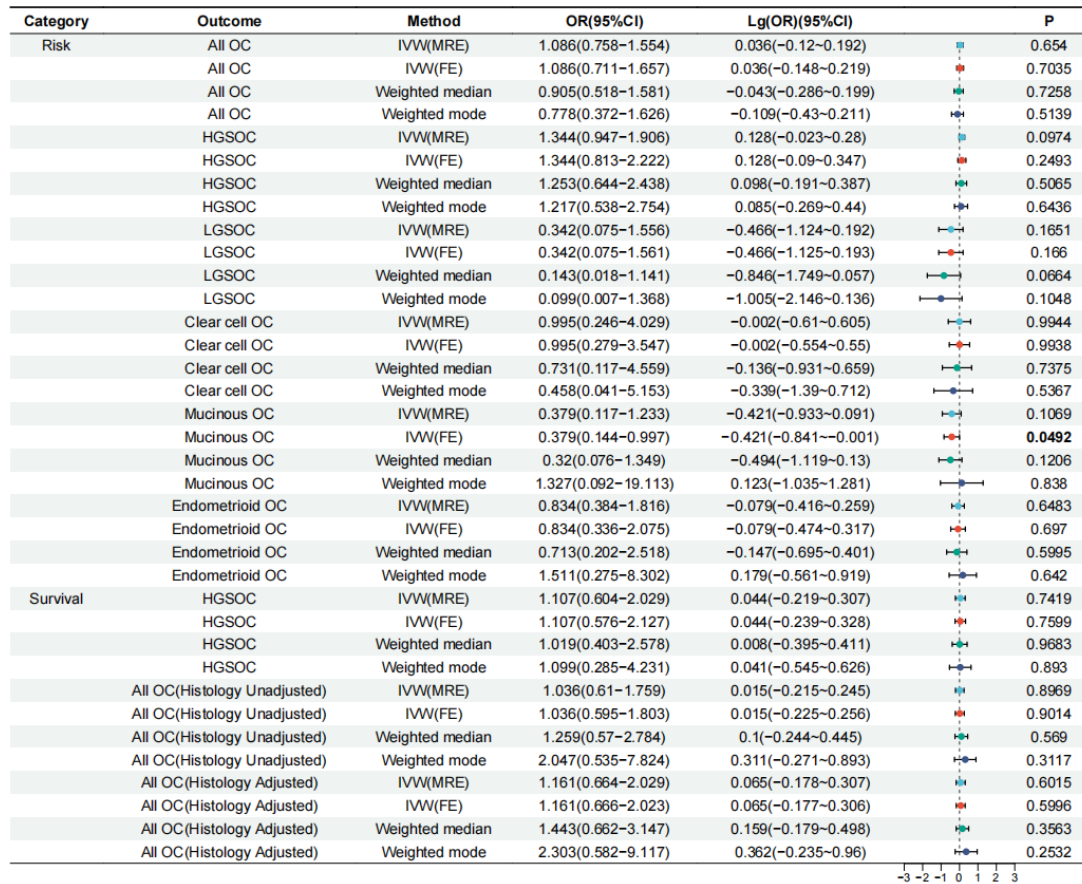


Figure S3. Forest plots of the effects of ABCB11 (Sulfonylureas) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects) weighted median, and weighted mode to assess the association between ABCB11 and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

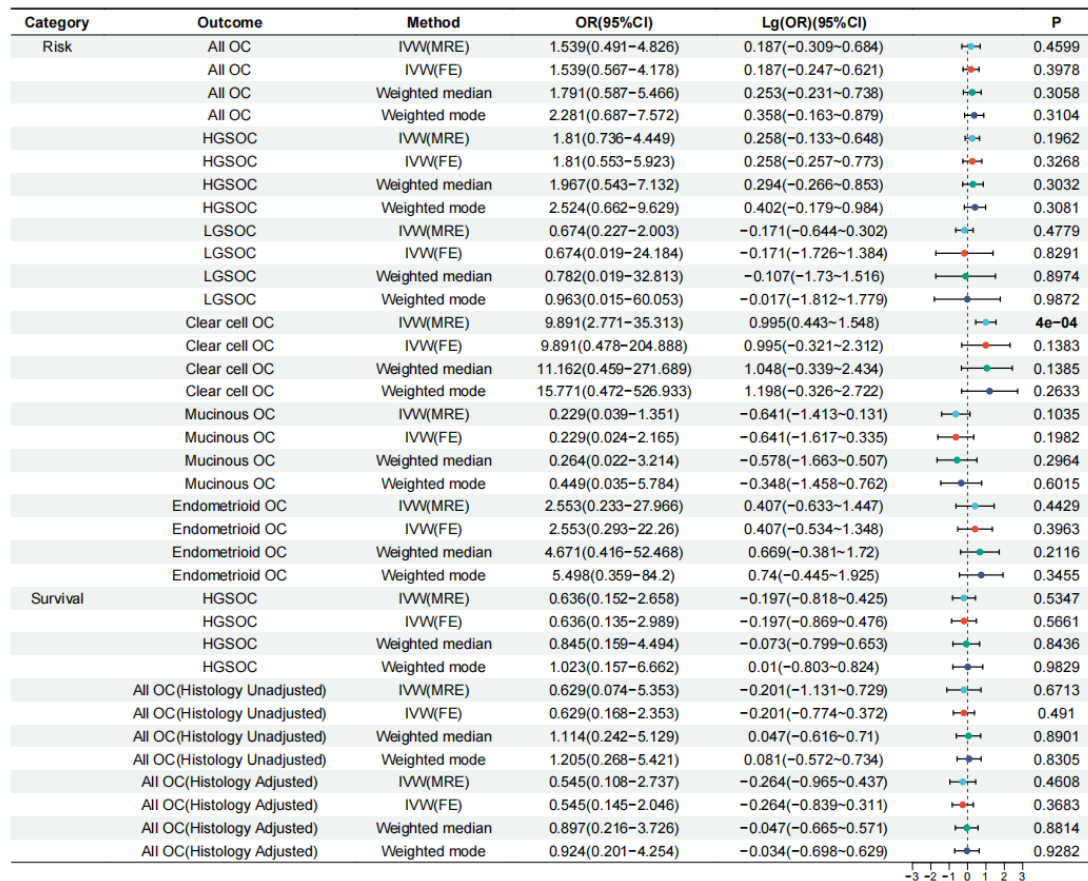


Figure S4. Forest plots of the effects of ABCC8/KCNJ11(Sulfonylureas) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between ABCC8/KCNJ11 and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

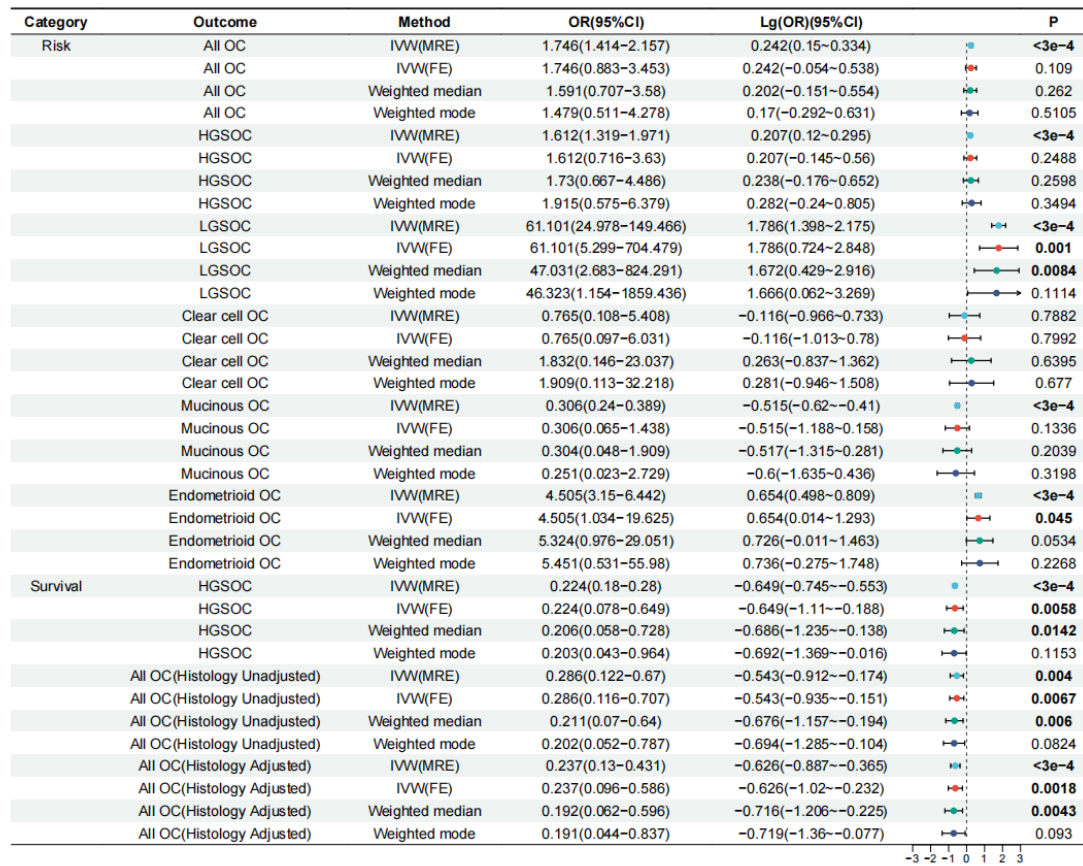


Figure S5. Forest plots of the effects of AKR1A1(Other drugs) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between AKR1A1 and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

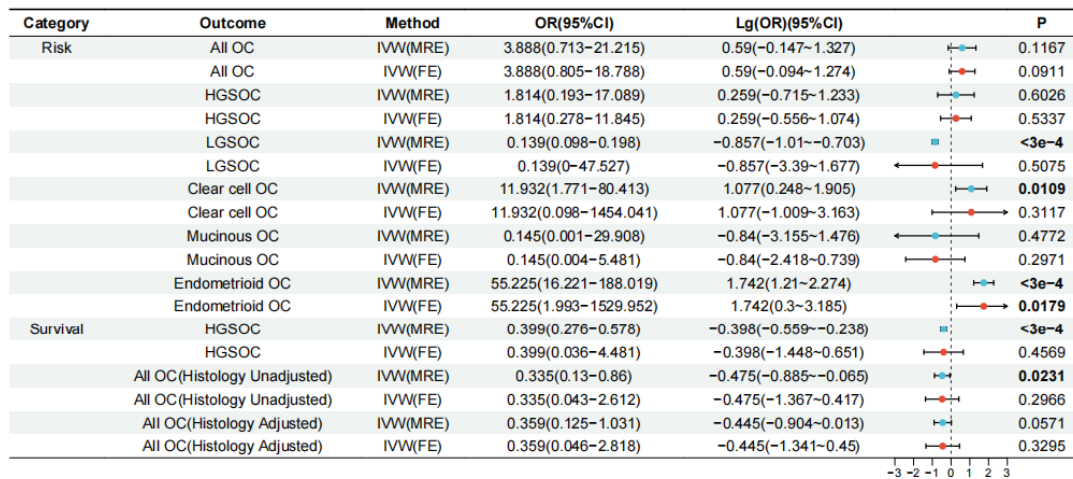


Figure S6. Forest plots of the effects of CPT1A(Sulfonylureas) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects) and IVW (fixed effects) to assess the association between CPT1A and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

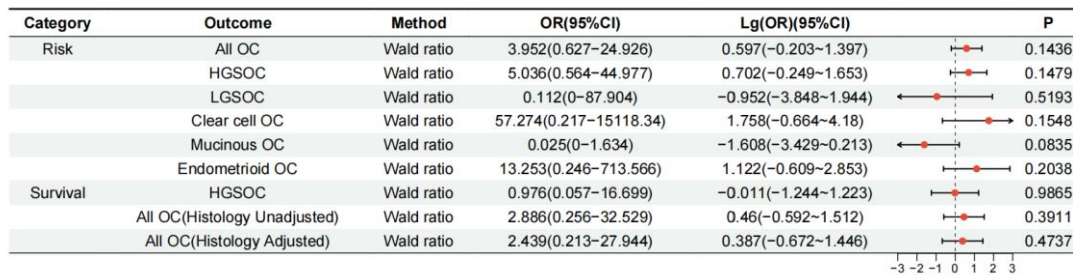


Figure S7. Forest plots of the effects of GANC(AGI) on 9 OC phenotypes with different MR methods.

The analysis employed the wald ratio method to assess the association between GANC and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

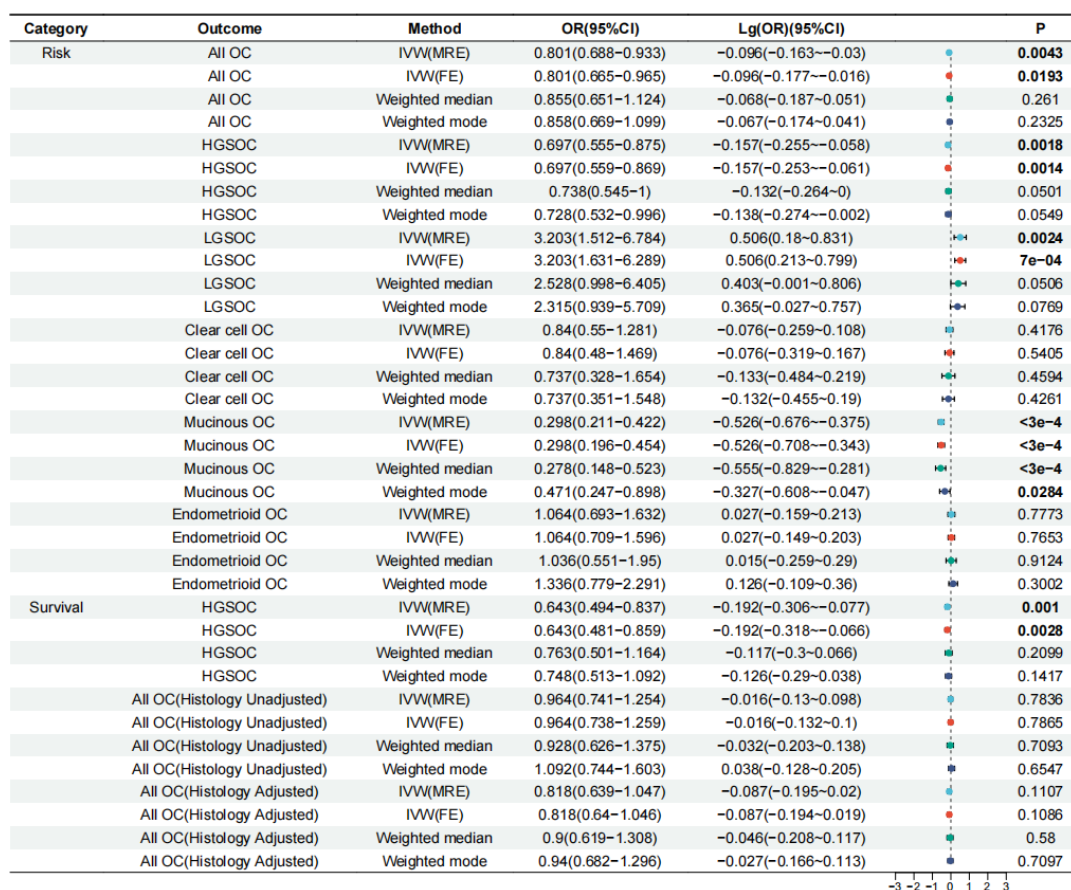


Figure S8. Forest plots of the effects of GCK(Other drugs) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between GCK and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

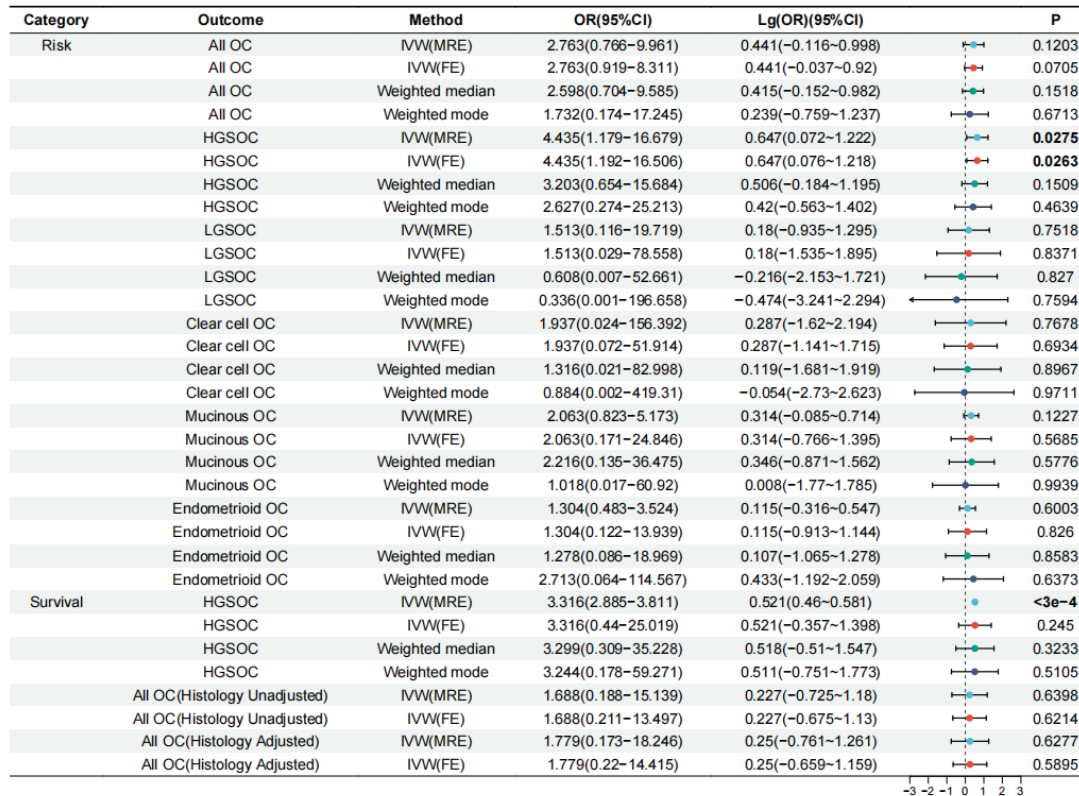


Figure S9. Forest plots of the effects of GLP1R(GLP–1RA) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between GLP1R and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

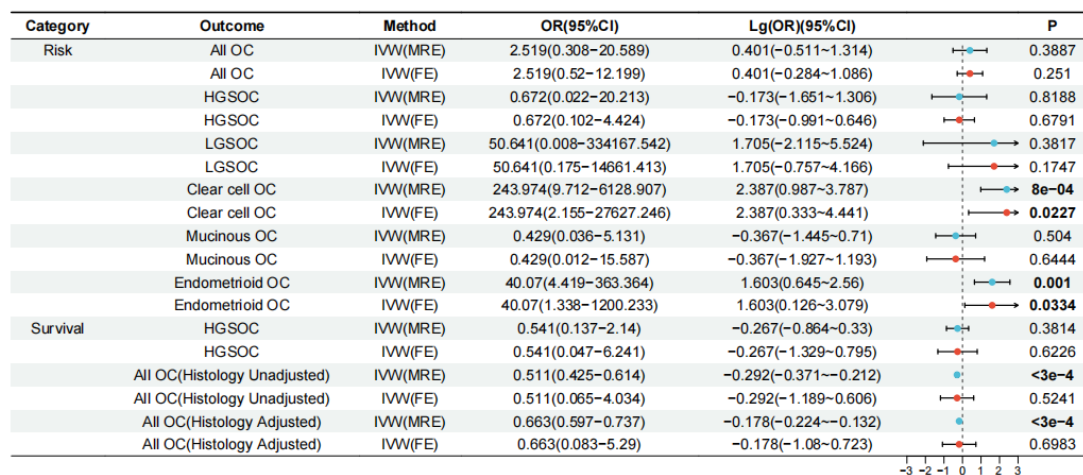


Figure S10. Forest plots of the effects of HMGCN(DPP4i) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects) and IVW (fixed effects) to assess the association between HMGCN and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

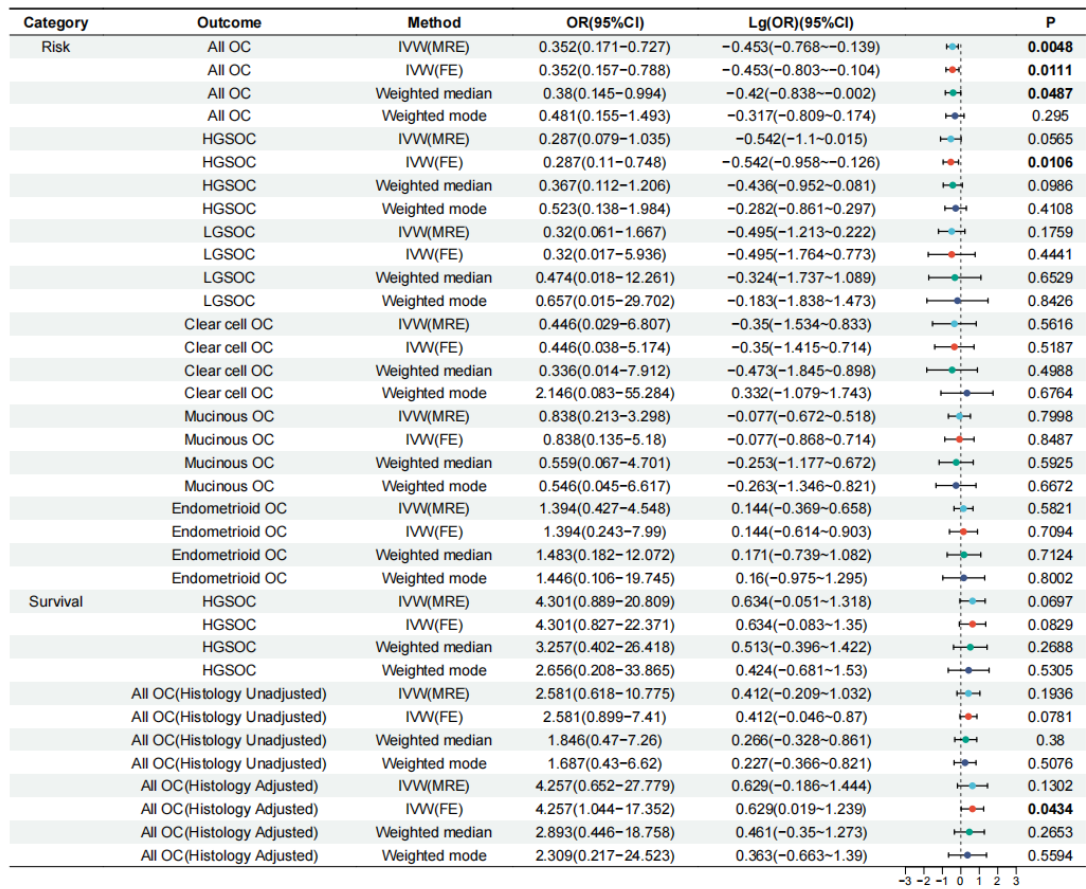


Figure S11. Forest plots of the effects of INS(Sulfonylureas) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between INS and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

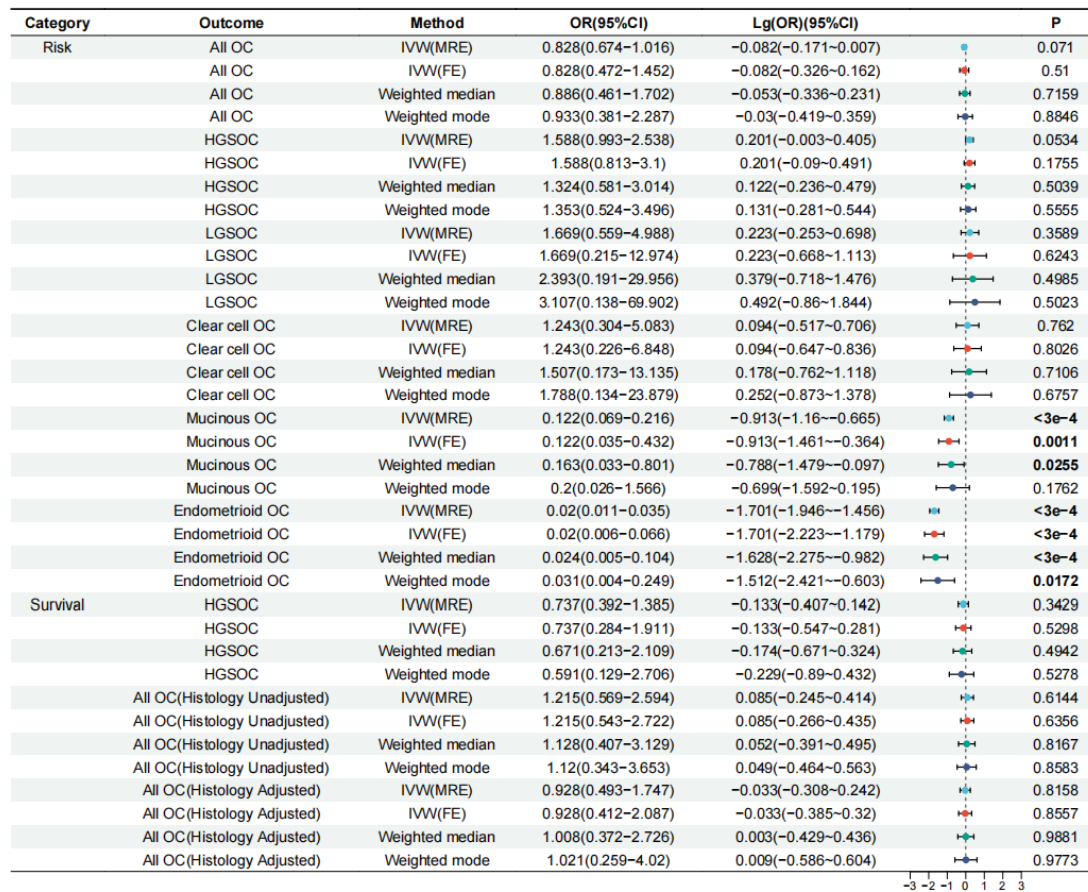


Figure S12. Forest plots of the effects of ITGAL(DPP4i) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between ITGAL and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

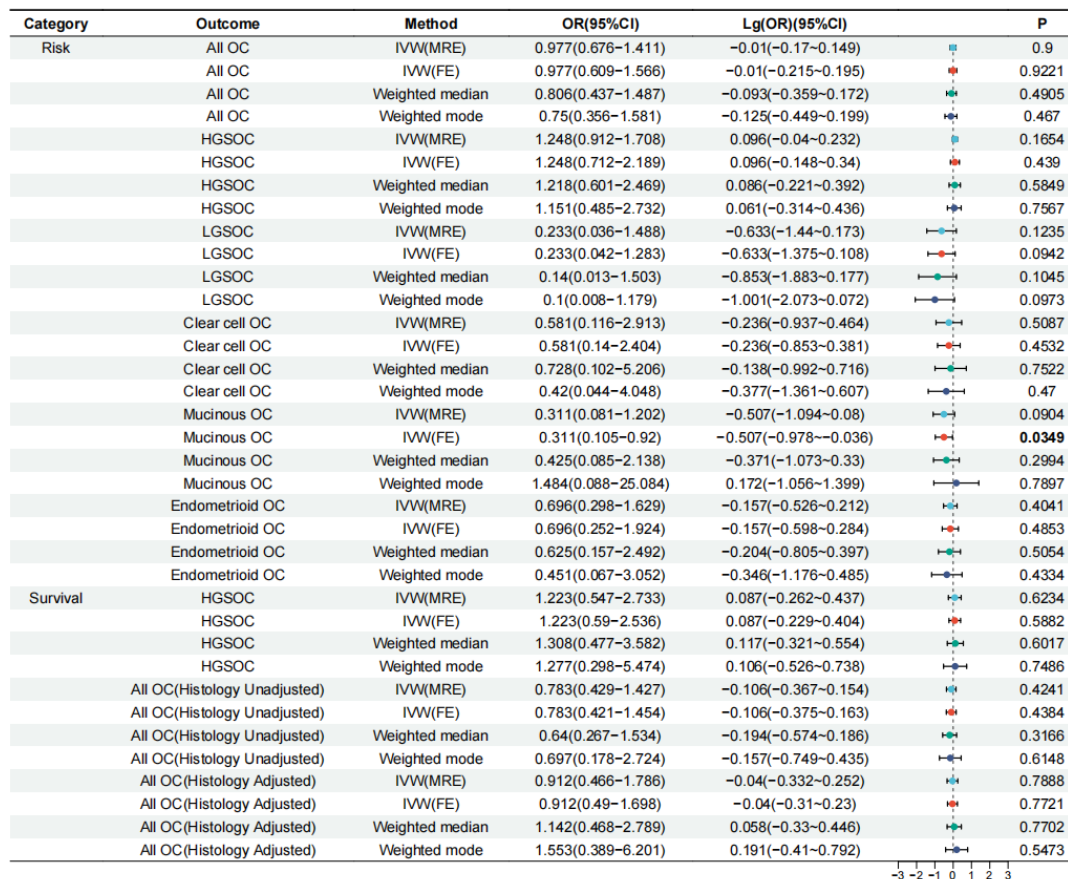


Figure S13. Forest plots of the effects of LRP2(Insulin) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between LRP2 and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

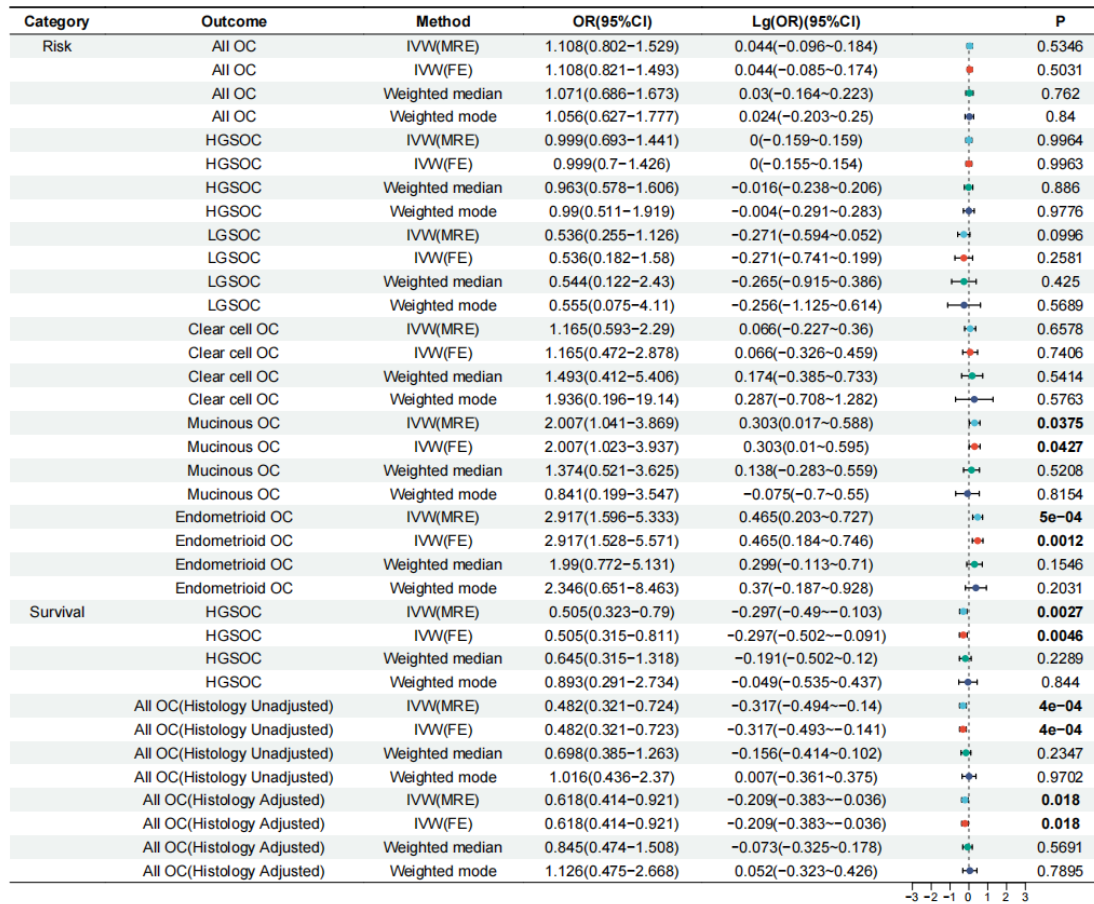


Figure S14. Forest plots of the effects of PPARG(Sulfonylureas/TZDs) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between PPARG and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

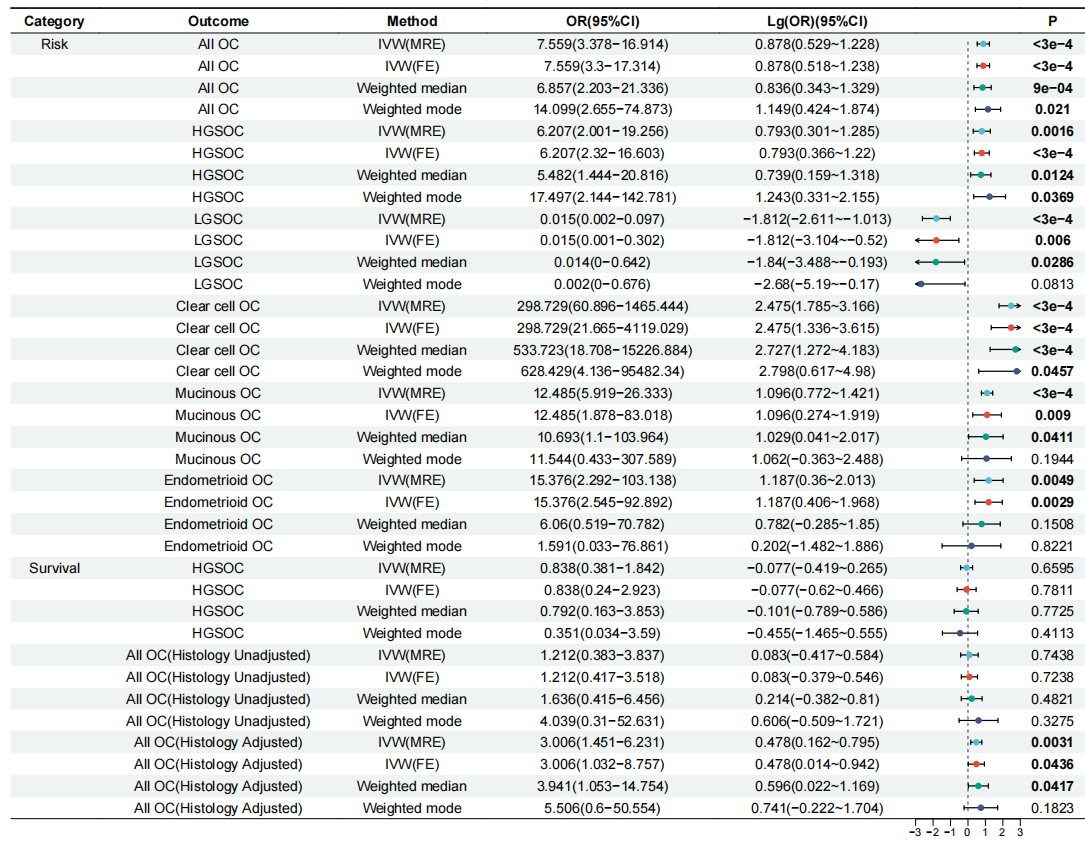


Figure S15. Forest plots of the effects of RAMP2(Other drugs) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between RAMP2 and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

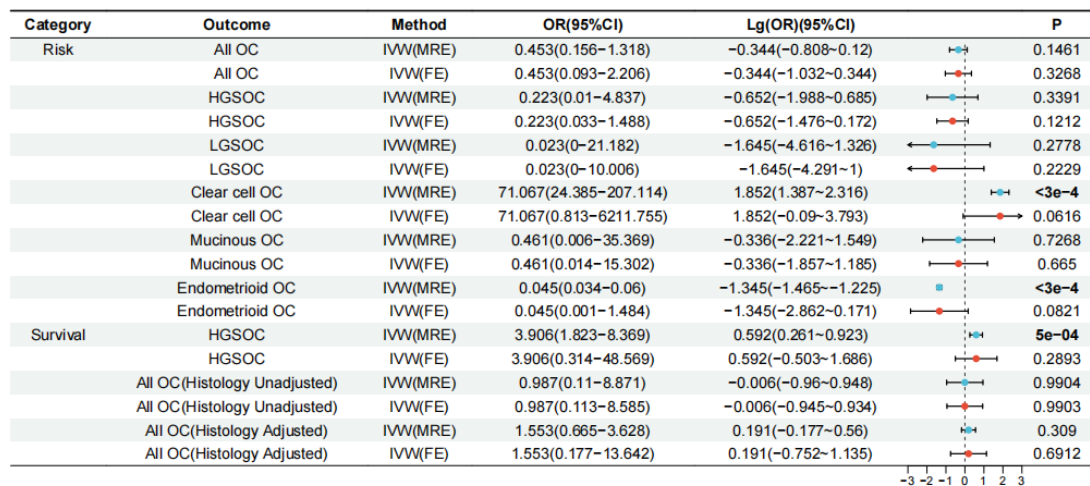


Figure S16. Forest plots of the effects of RAMP3(Other drugs) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects) and IVW (fixed effects) to assess the association between RAMP3 and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

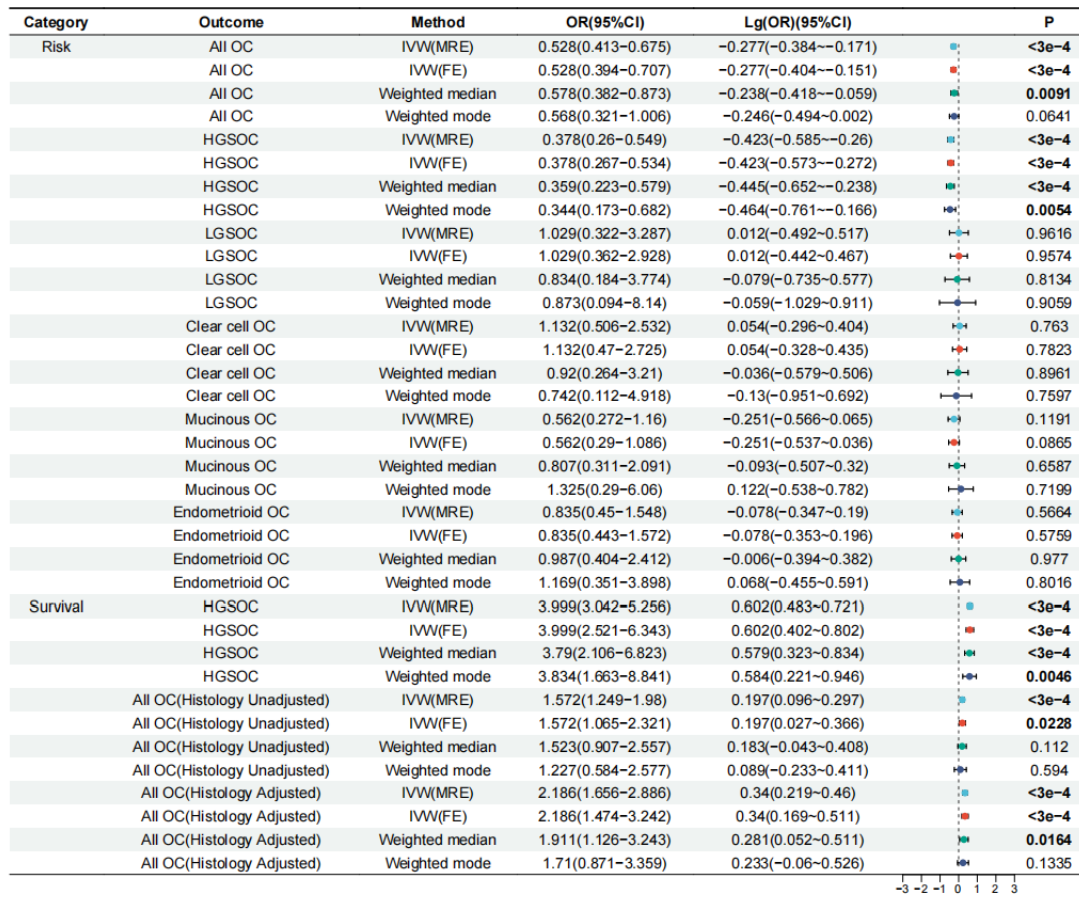


Figure S17. Forest plots of the effects of RXRB(TZDs) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between RXRB and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

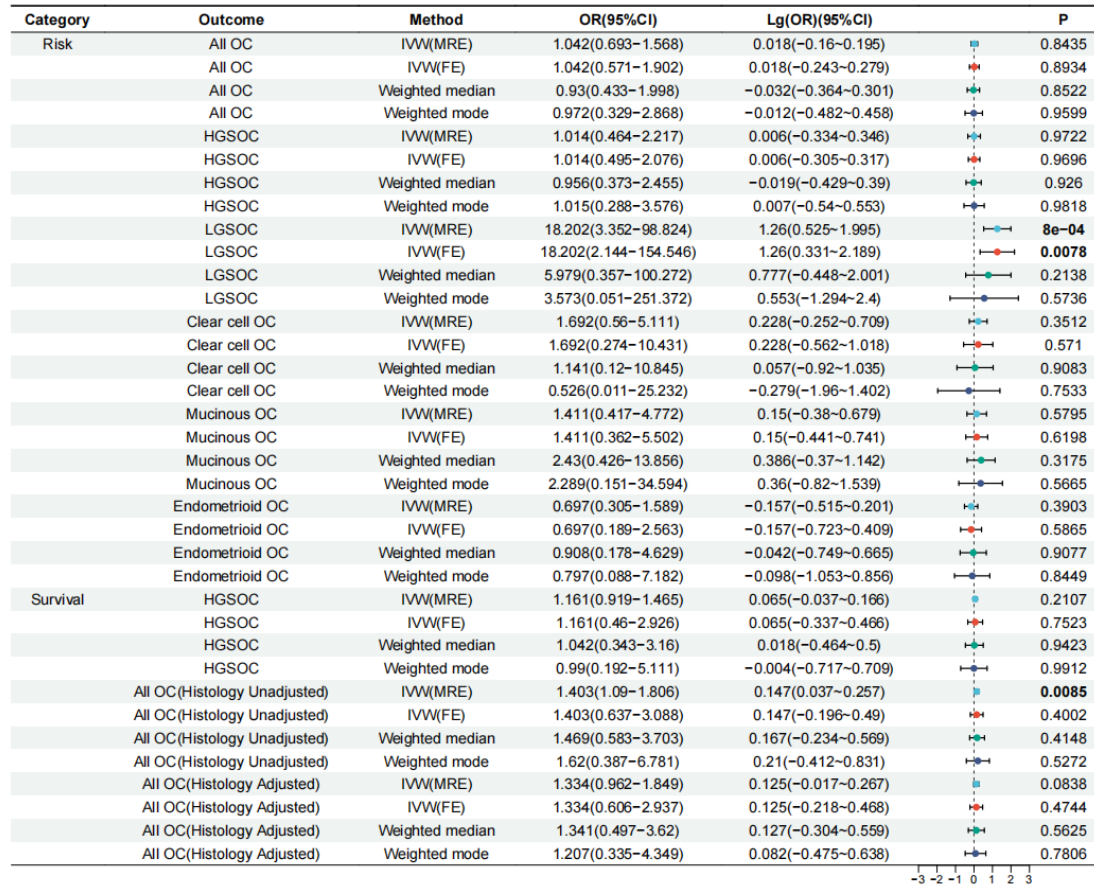


Figure S18. Forest plots of the effects of SLC5A1(SGLT2i) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between SLC5A1 and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

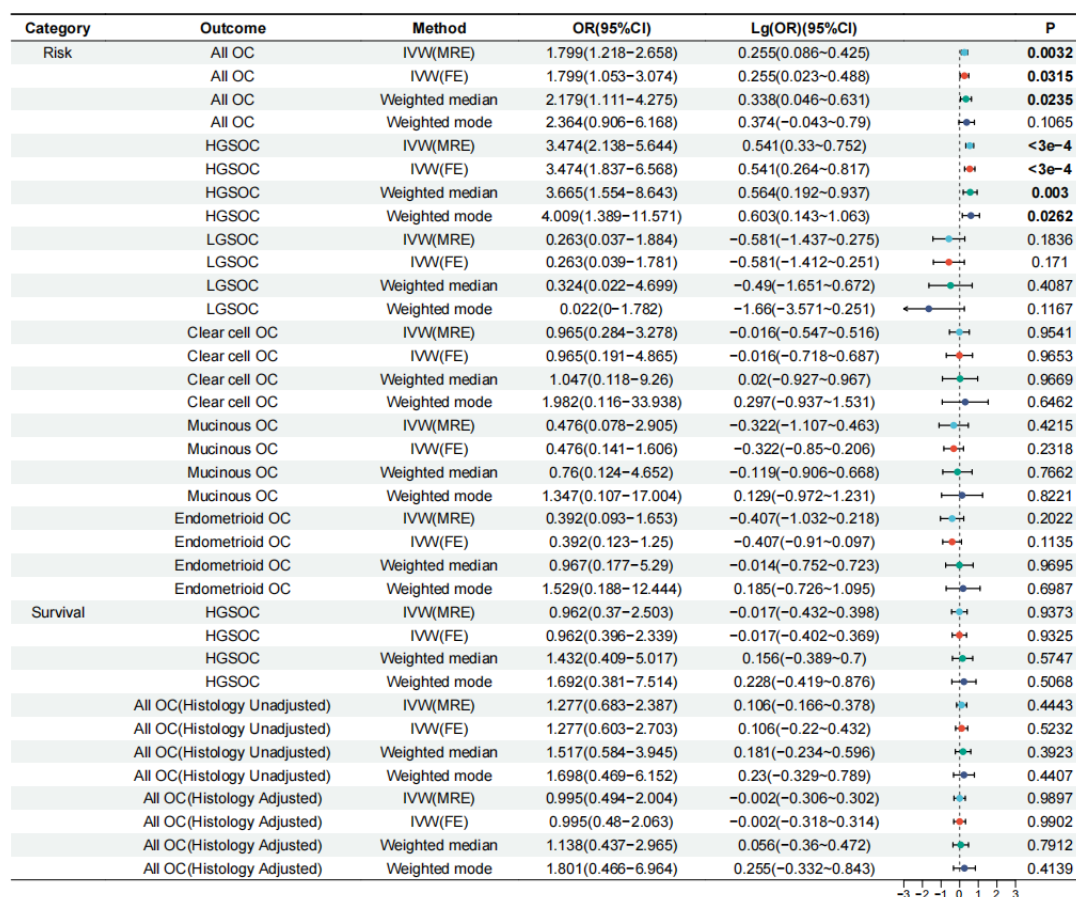


Figure S19. Forest plots of the effects of SLC5A2(SGLT2i) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between SLC5A2 and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

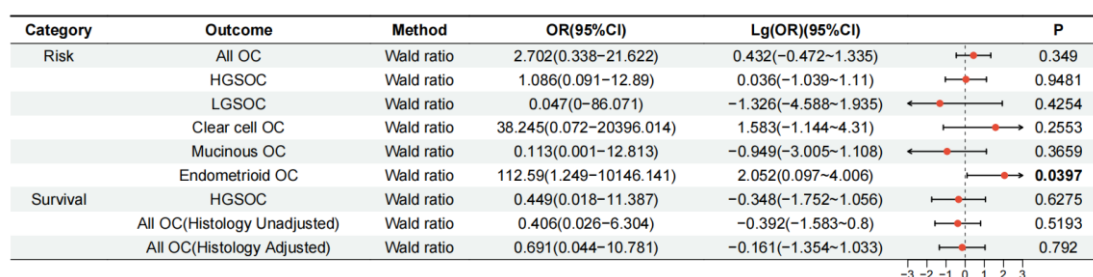


Figure S20. Forest plots of the effects of SLC47A1(Biguanides) on 9 OC phenotypes with different MR methods.

The analysis employed the wald ratio method to assess the association between SLC47A1 and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

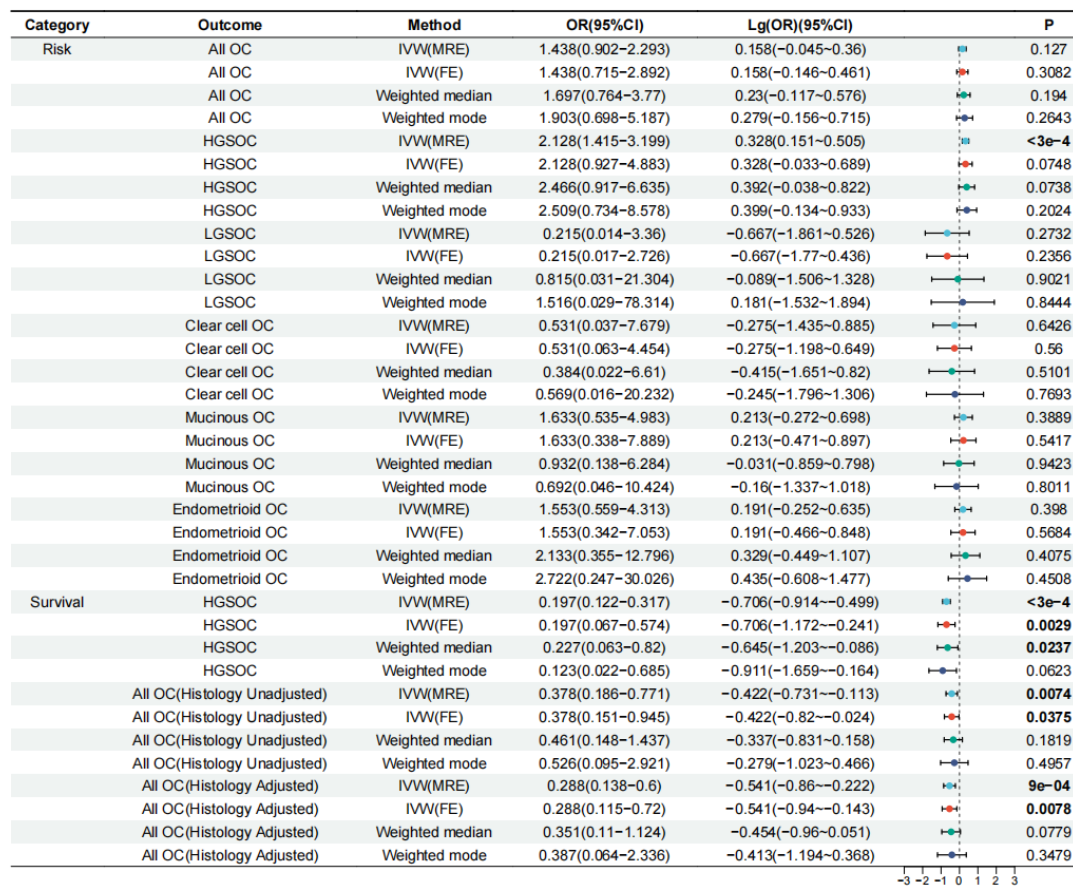


Figure S21. Forest plots of the effects of VEGFA/SLC29A1(Sulfonylureas/TZDs) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between VEGFA/SLC29A1 and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

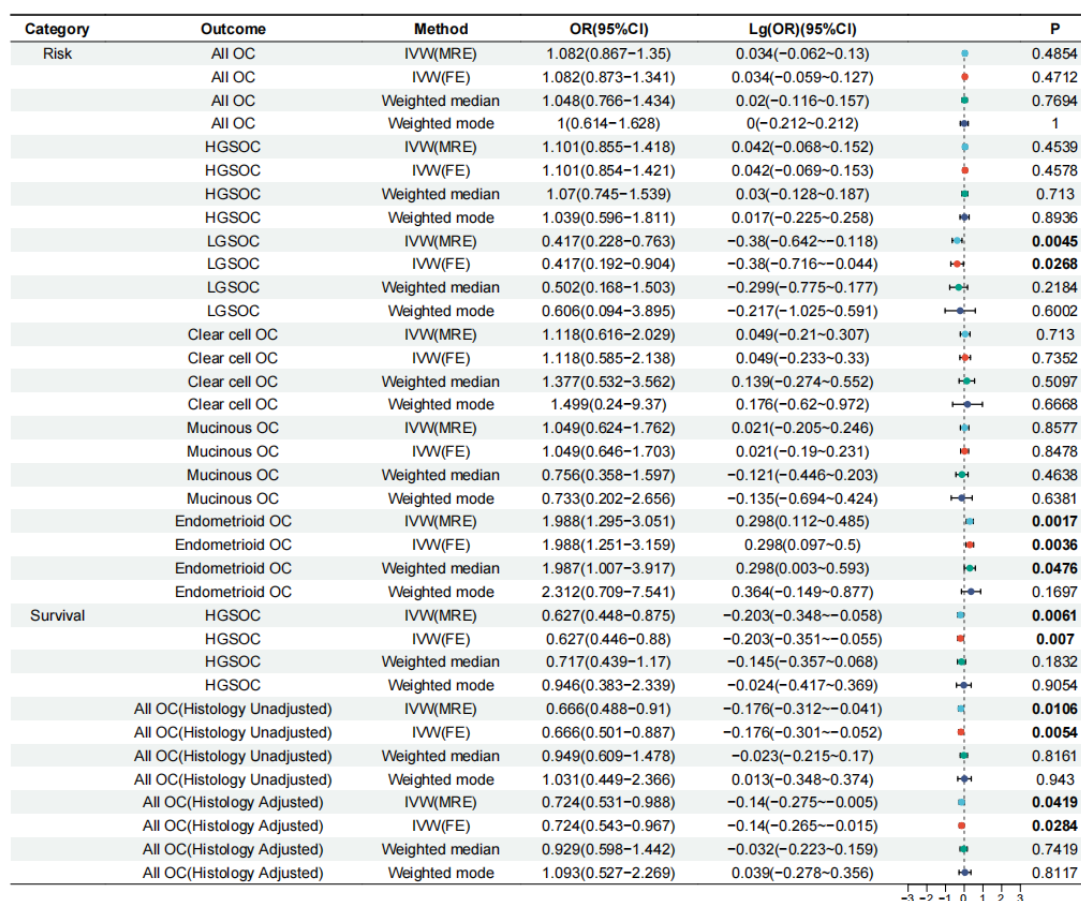


Figure S22. Forest plots of the effects of ABCC8/KCNJ11+ABCB11+CPT1A+INS+PPAR γ +VEGFA(Sulfonylureas) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between combined targets of (ABCC8/KCNJ11+ABCB11+CPT1A+INS+PPAR γ +VEGFA) and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

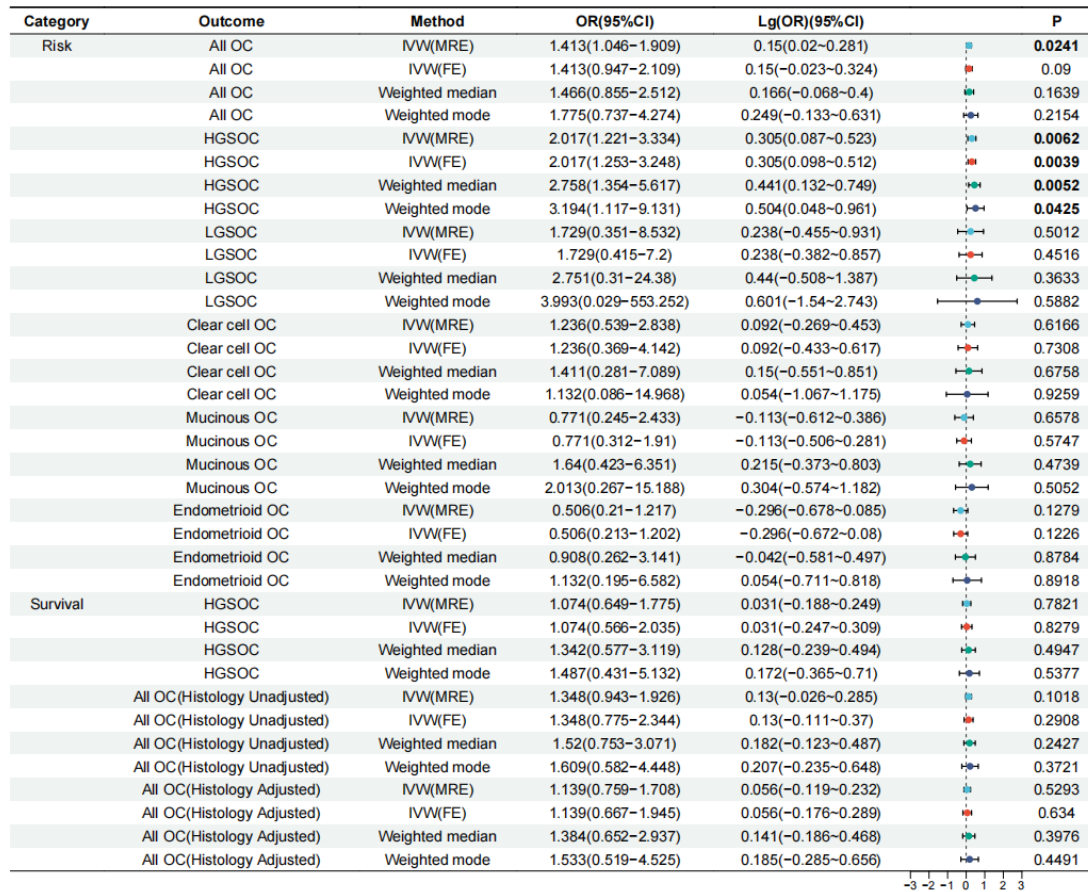


Figure S23. Forest plots of the effects of SLC5A1+SLC5A2(SGLT2i) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between combined targets of (SLC5A1+SLC5A2) and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

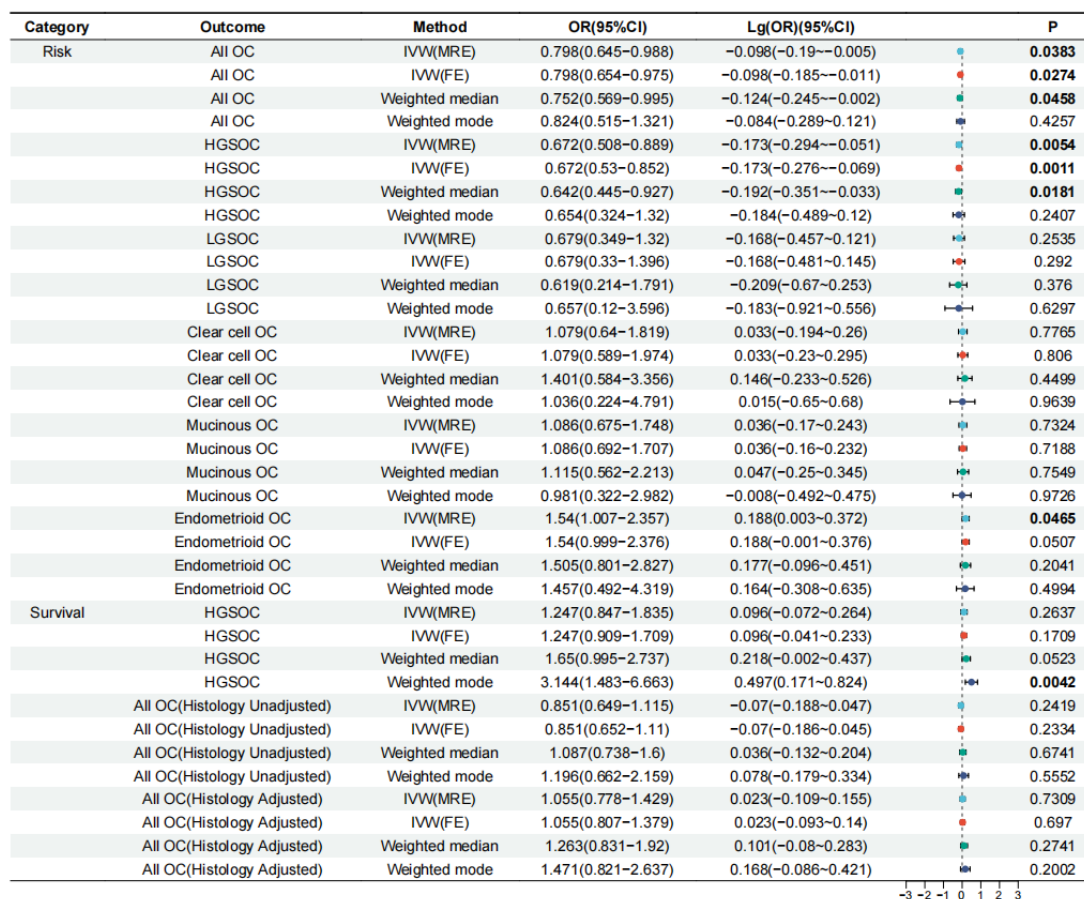


Figure S24. Forest plots of the effects of SLC29A1+RXRB+PPARG(TZDs) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between combined targets of (SLC29A1+RXRB+PPARG) and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

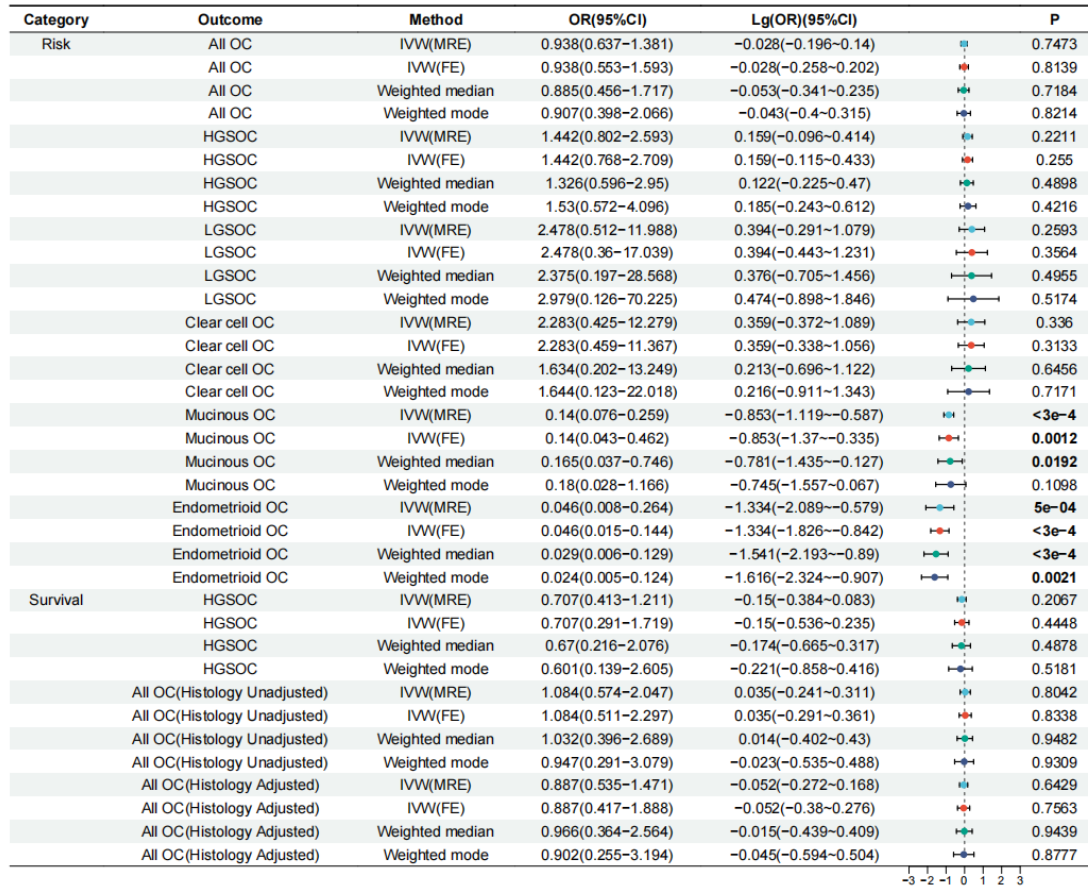


Figure S25. Forest plots of the effects of HMGCR+ITGAL(DDP4i) on 9 OC phenotypes with different MR methods.

The analysis employed the IVW (multiplicative random effects), IVW (fixed effects), weighted median, and weighted mode to assess the association between combined targets of (HMGCR+ITGAL) and OC outcomes. OR and their 95%CI were plotted on a logarithmic scale (Lg(OR)(95%CI)) to illustrate the strength and direction of the association; values greater than 0 indicate a risk factor, while values less than 0 suggest a protective factor.

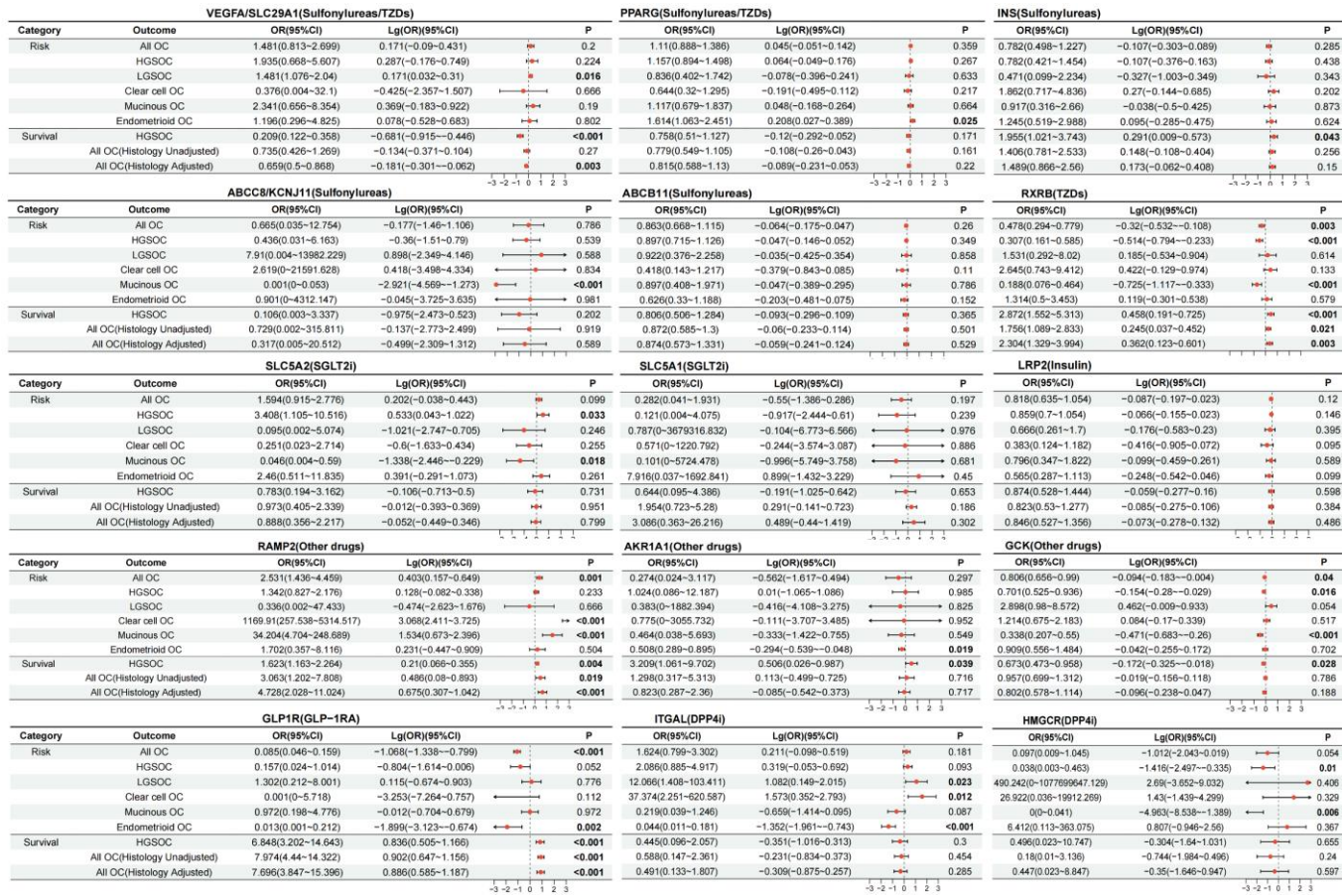


Figure S26. Forest plots of the effects of the antidiabetic drug gene targets on 9 OC phenotypes in the MVMR analysis.

These graphs evaluate the impact of specific genetic targets of antidiabetic drugs on nine different OC phenotypes. Utilizing a MVMR design of drug-target MR analysis with HbA1c GWAS data and adjusted for BMI, systolic blood pressure, smoking status, and alcohol consumption to explore the robustness of the effect of genetically predicted HbA1c levels with specific genes targeted by corresponding drugs, on OC.

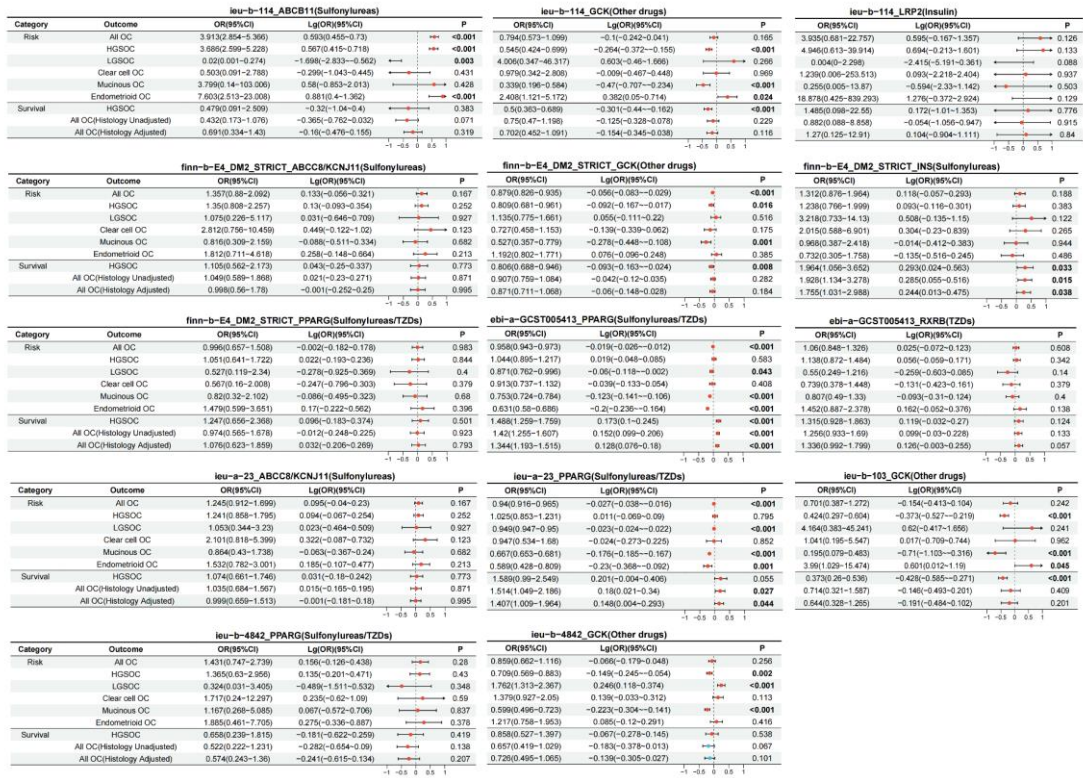


Figure S27. Forest plots of the effects of the antidiabetic drug gene targets on 9 OC phenotypes in replication analysis.

Each heading represents an IEU GWAS ID, including: HbA1c (Within family GWAS consortium, MAGIC), T2DM (DIAGRAM, FinnGen, Sílvia Bonàs-Guarch), and fasting glucose (MAGIC), along with the target gene (drug). All results are derived from the principal MR analysis. The OR reflects the impact of a per-SD reduction in genetically predicted HbA1c, T2DM or fasting glucose levels on OC phenotypes when targeting specific genes with corresponding drugs.

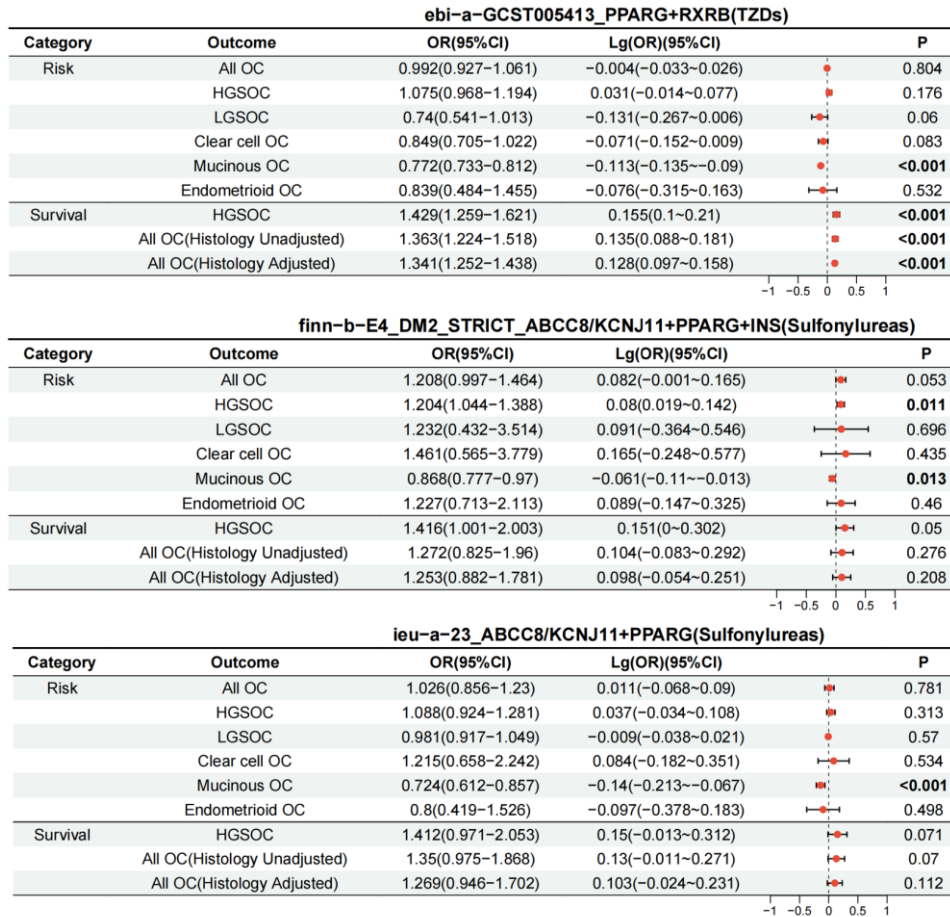


Figure S28. Forest plots of the effects of the combined targets on 9 OC phenotypes in replication analysis.

Each heading represents an IEU GWAS ID, including: HbA1c (Within family GWAS consortium, MAGIC), T2DM (DIAGRAM, FinnGen, Silvia Bonàs-Guarch), and fasting glucose (MAGIC), along with the combined targets (drug). All results are derived from the principal MR analysis. The OR reflects the impact of a per-SD reduction in genetically predicted HbA1c, T2DM or fasting glucose levels on OC phenotypes when targeting specific genes with corresponding drugs.

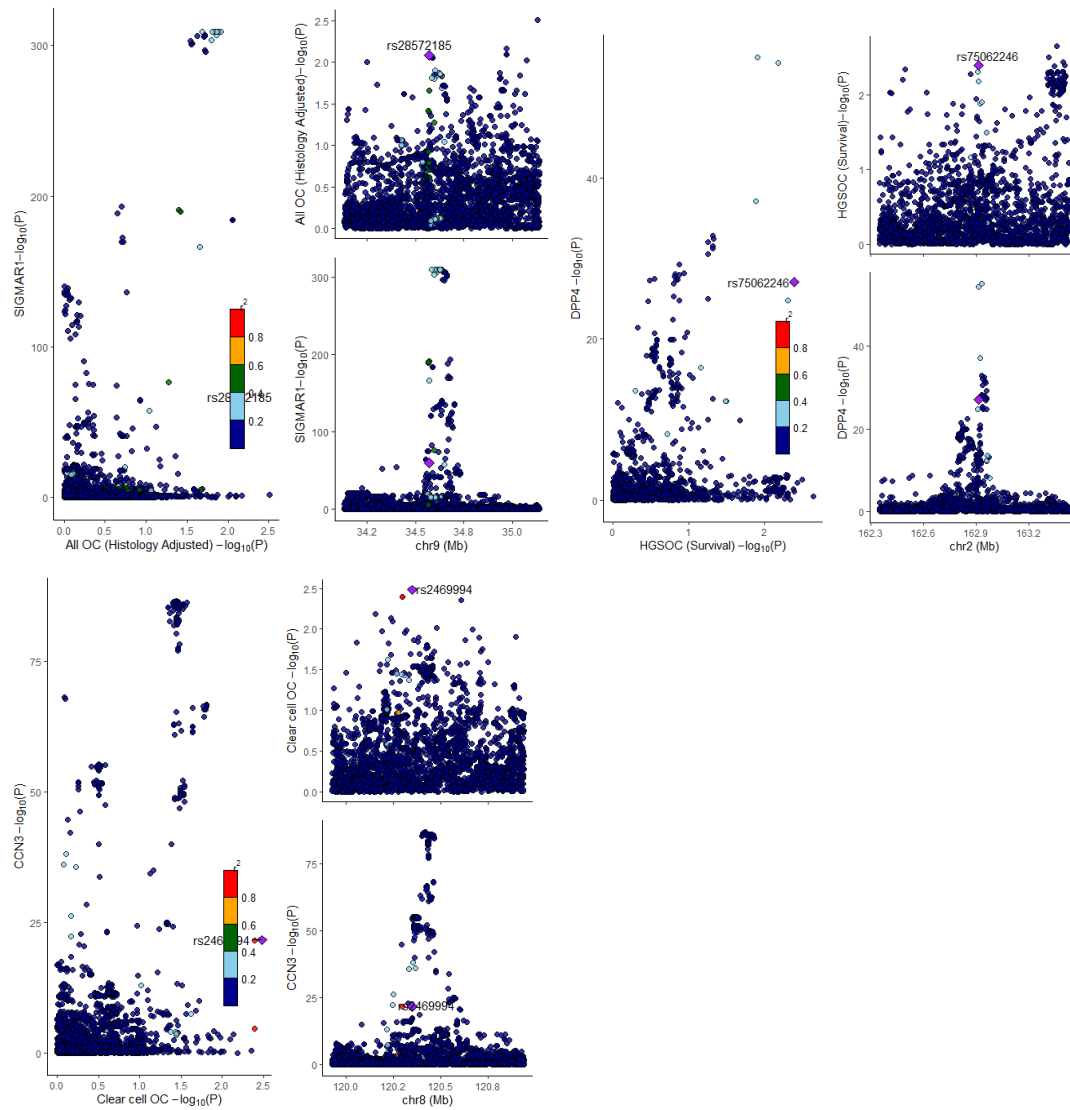


Figure S29. Regional colocalization plot of target genes with OC.

This Figure was an appendix of Figure 4B. Only results with high colocalization ($PPH4 > 0.75$) were shown.