Fig S1 The forest plot of MR estimates from gut microbiota on adrenal medulla identified with IVW.

Exposure	Outcome	beta	lower 95%CI	upper 95%CI	pvalue
Allisonella	Adrenomedullin levels	−0.077	−0.141	−0.012	0.020
Anaerofilum	Adrenomedullin levels	0.070	0.001	0.139	0.048
Bilophila	Adrenomedullin levels	−0.115	−0.220	−0.010	0.032
RuminococcaceaeUCG005	Adrenomedullin levels	0.154	0.042	0.266	0.007
Ruminococcus2	Adrenomedullin levels	−0.108	−0.208	−0.008	0.034

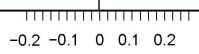


Fig S2 Forest plot of the significance estimates for the relationship between gut microbiota and the zona glomerulosa of the adrenal cortex, determined through the IVW method.

Exposure	Outcome	beta	lower 95%CI	upper 95%CI	pvalue
Intestinimonas	Hyperaldosteronism	0.617	0.403	0.944	0.026
Prevotella9	Hyperaldosteronism	1.538	1.052	2.251	0.026
Veillonella	Hyperaldosteronism	2.002	1.004	3.992	0.049
Parasutterella	Hyperaldosteronism	1.510	1.005	2.268	0.047

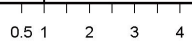


Fig S3 The forest plot of MR estimates for the relationship between gut microbiota and the zona fasciculata of the adrenal cortex, determined through the IVW method.

Exposure	Outcome	beta	lower 95%CI	upper 95%CI	pvalue
Barnesiella	Cortisol(plasma)	−0.201	−0.352	−0.051	0.009
FamilyXIIIUCG001	Cortisol(plasma)	0.222	0.041	0.402	0.016
Fusicatenibacter	Cortisol(plasma)	0.185	0.037	0.333	0.014
RuminococcaceaeNK4A214group	Cortisol(plasma)	−0.184	−0.359	−0.008	0.040
RuminococcaceaeUCG010	Cortisol(plasma)	−0.247	−0.456	−0.038	0.020
Sutterella	Cortisol(plasma)	0.181	0.021	0.340	0.027
Eubacteriumventriosumgroup	Cortisol(urine)	−0.300	−0.595	−0.005	0.046
Anaerofilum	Cortisol(urine)	0.218	0.014	0.423	0.036
Barnesiella	Cortisol(urine)	−0.420	−0.730	−0.110	0.008
Eggerthella	Cortisol(urine)	−0.356	−0.566	−0.145	0.001
Parasutterella	Cortisol(urine)	0.251	0.004	0.497	0.047

Fig S4 The forest plot of MR estimates for the relationship between gut microbiota and the zona reticularis of the adrenal cortex, determined through the IVW method.

Exposure	Outcome	beta	lower 95%CI	upper 95%CI	pvalue
Eubacteriumrectalegroup	Estradiol	0.019	0.008	0.031	0.001
Sellimonas	Estradiol	0.008	0.002	0.013	0.006
Subdoligranulum	Estradiol	−0.011	−0.020	−0.001	0.026
Sutterella	Estradiol	−0.009	−0.018	−0.001	0.025
Eubacteriumcoprostanoligenesgroup	androgen	0.041	0.004	0.077	0.028
Ruminococcustorquesgroup	androgen	−0.041	−0.082	0.000	0.048
Parabacteroides	androgen	−0.075	−0.150	0.000	0.050

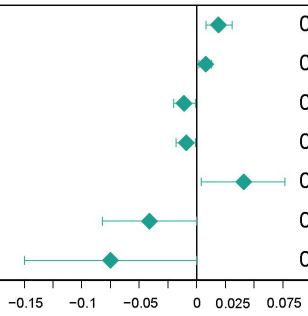


Fig S5 Scatter plots of MR estimates from genetically predicted portions of gut microbiota on adrenal medulla function. a, Alisonella and adrenal medulla function; b**,** Anaerofilum and adrenal medulla function; c, Bilophila and adrenal medulla function; d, RuminococcaceaeUCG005 and adrenal medulla function； e, Ruminococcus2 and adrenal medulla function.

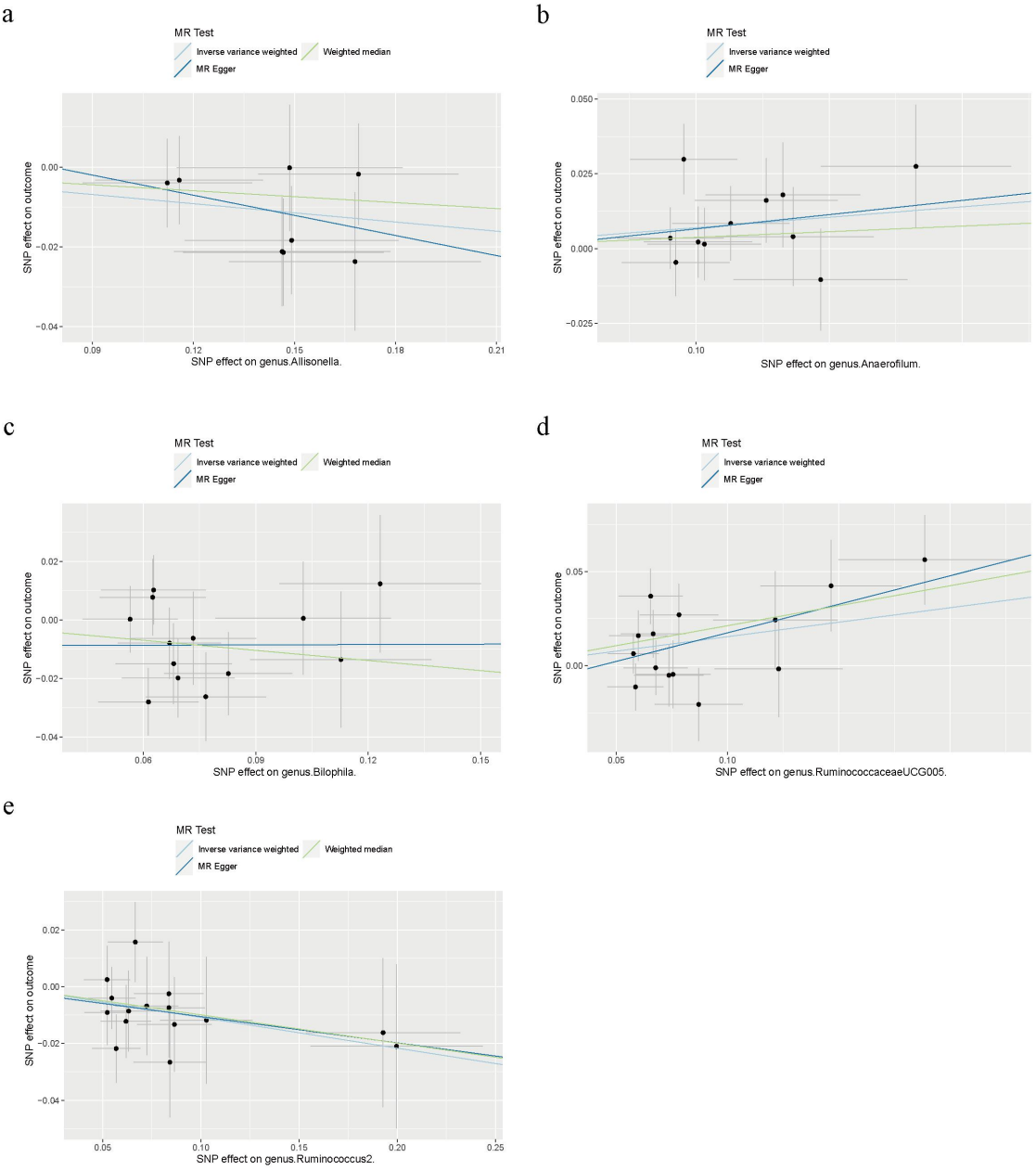


Fig S6 Scatter plots of MR estimates from genetically predicted gut microbiota on adrenal cortex zona glomerulosa function. a, Intestinimonas and adrenal cortex zona glomerulosa function; b, Parasutterella and cortex zona glomerulosa function; c, Prevotella9 and adrenal cortex zona glomerulosa function; d, Veillonella and adrenal cortex zona glomerulosa function.

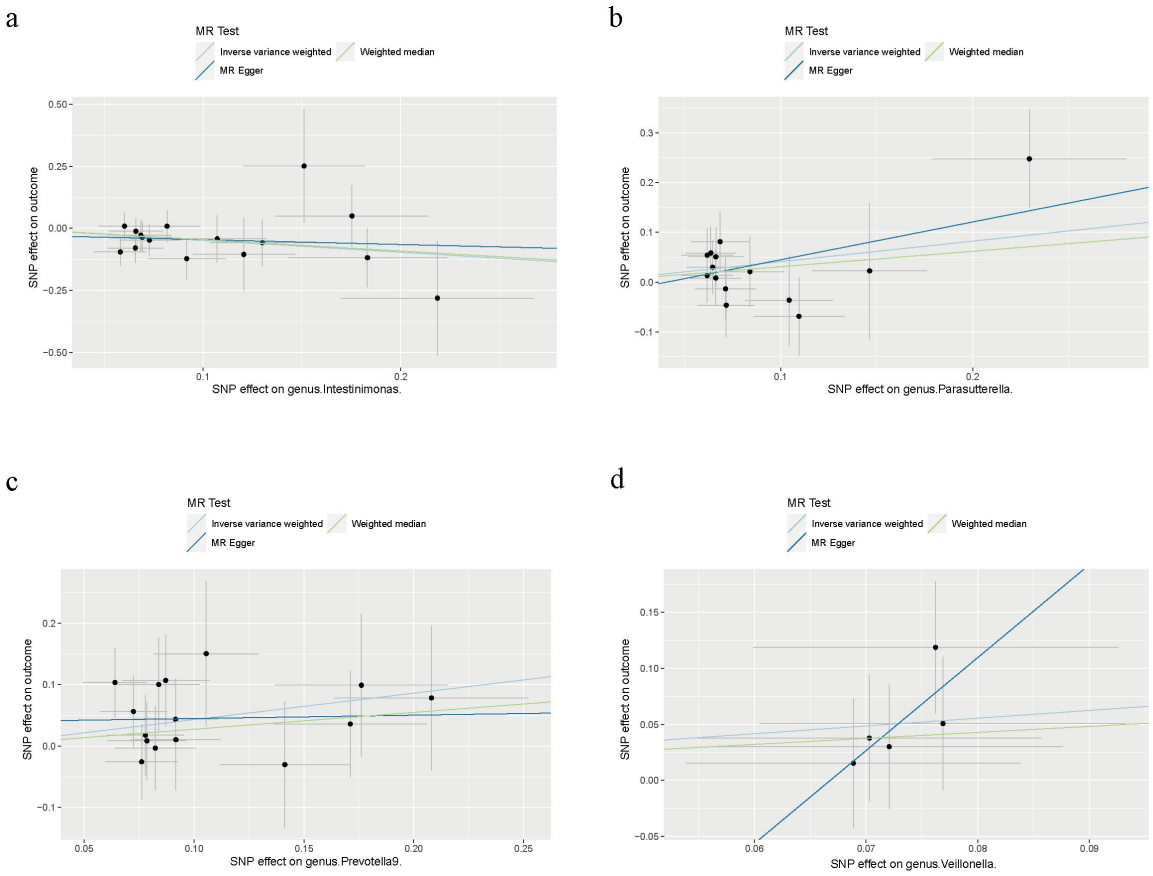


Fig S7 Scatter plots of MR estimates from genetically predicted gut microbiota on adrenal cortex zona fasciculata function (plasma cortisol). a, Barnesiella and adrenal cortex zona fasciculata function; b, FamilyXIIIUCG001 and adrenal cortex zona fasciculata function; c, Fusicatenibacterid and adrenal cortex zona fasciculata function; d, RuminococcaceaeNK4A214group and adrenal cortex zona fasciculata function; e, RuminococcaceaeUCG010 and adrenal cortex zona fasciculata function; f, Sutterella and adrenal cortex zona fasciculata function.

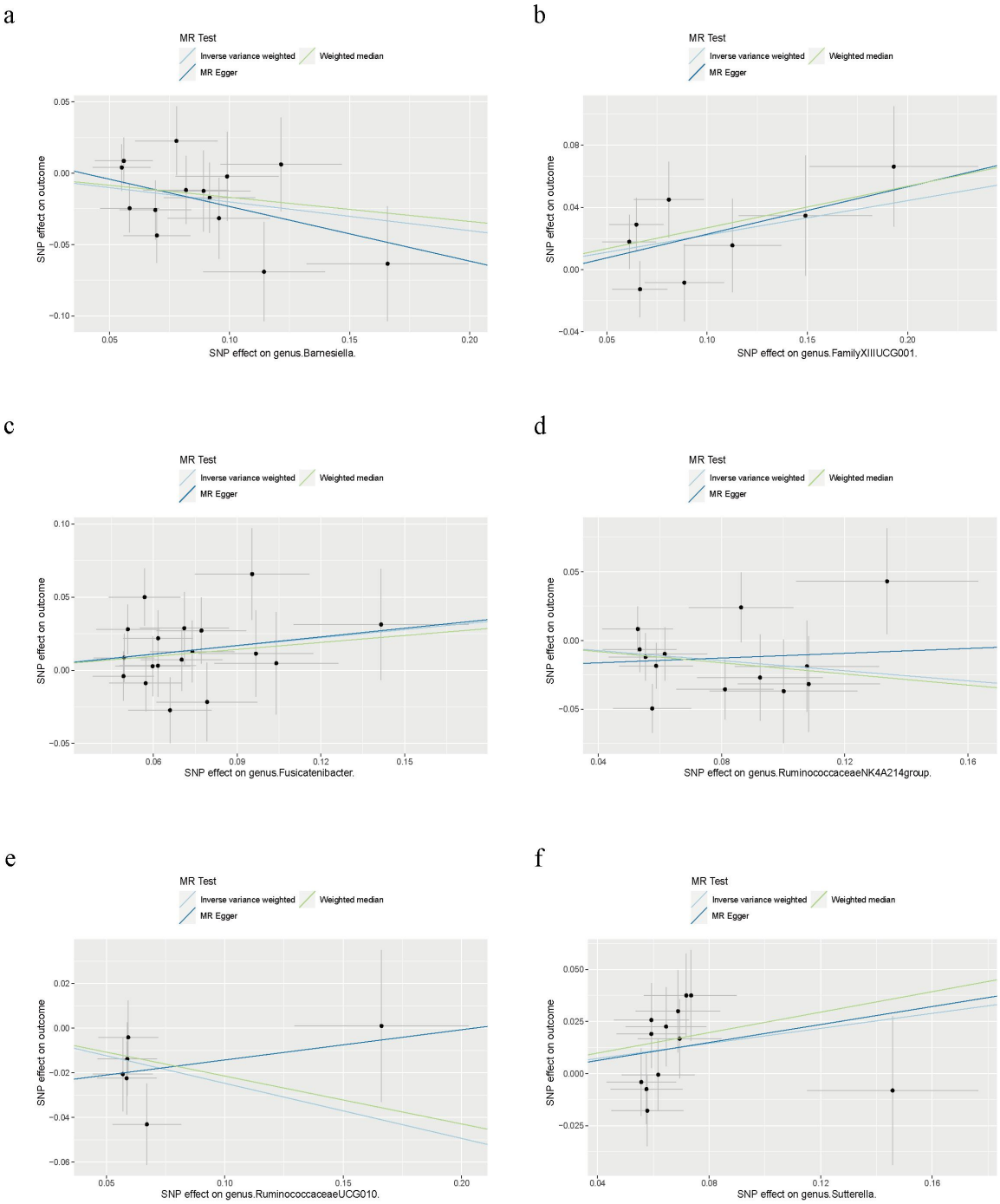
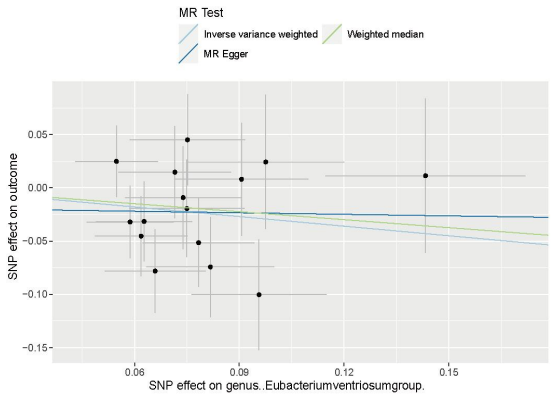


Fig S8 Scatter plots of MR estimates from genetically predicted gut microbiota on adrenal cortex zona fasciculata function (urine cortisol). a, Eubacteriumventriosumgroup and adrenal cortex zona fasciculata function; b, Anaerofilum and adrenal cortex zona fasciculata function; c,Barnesiella and adrenal cortex zona fasciculata function; d, Eggerthella and adrenal cortex zona fasciculata function; e, Parasutterella and adrenal cortex zona fasciculata function.

a



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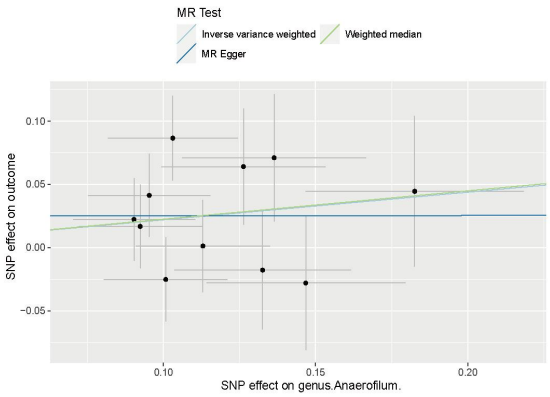

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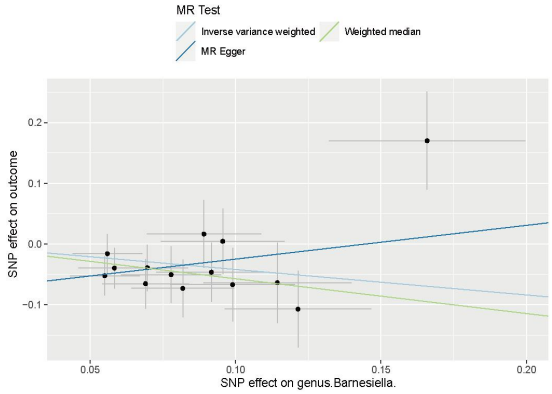

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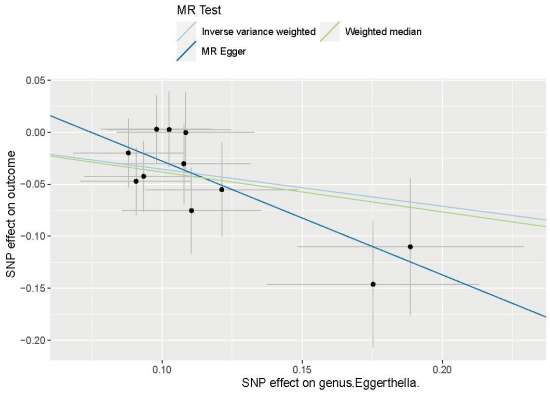

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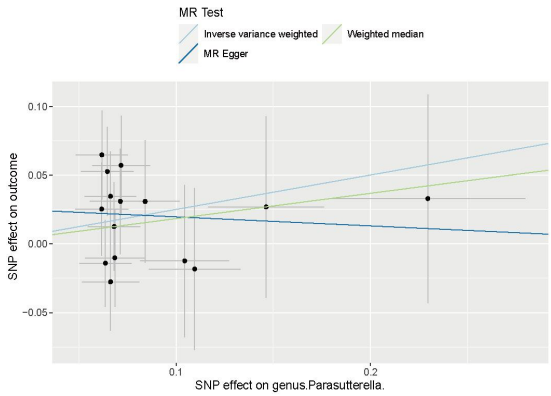


Fig S9 Scatter plots of MR estimates from genetically predicted gut microbiota on adrenal cortex zona reticularis function (estradiol). a, Eubacteriumrectalegroup and adrenal cortex zona reticularis function; b, Selimonas and adrenal cortex zona reticularis function; c, Subdoligranulum and adrenal cortex zona reticularis function; d, Sutterella and adrenal cortex zona reticularis function.

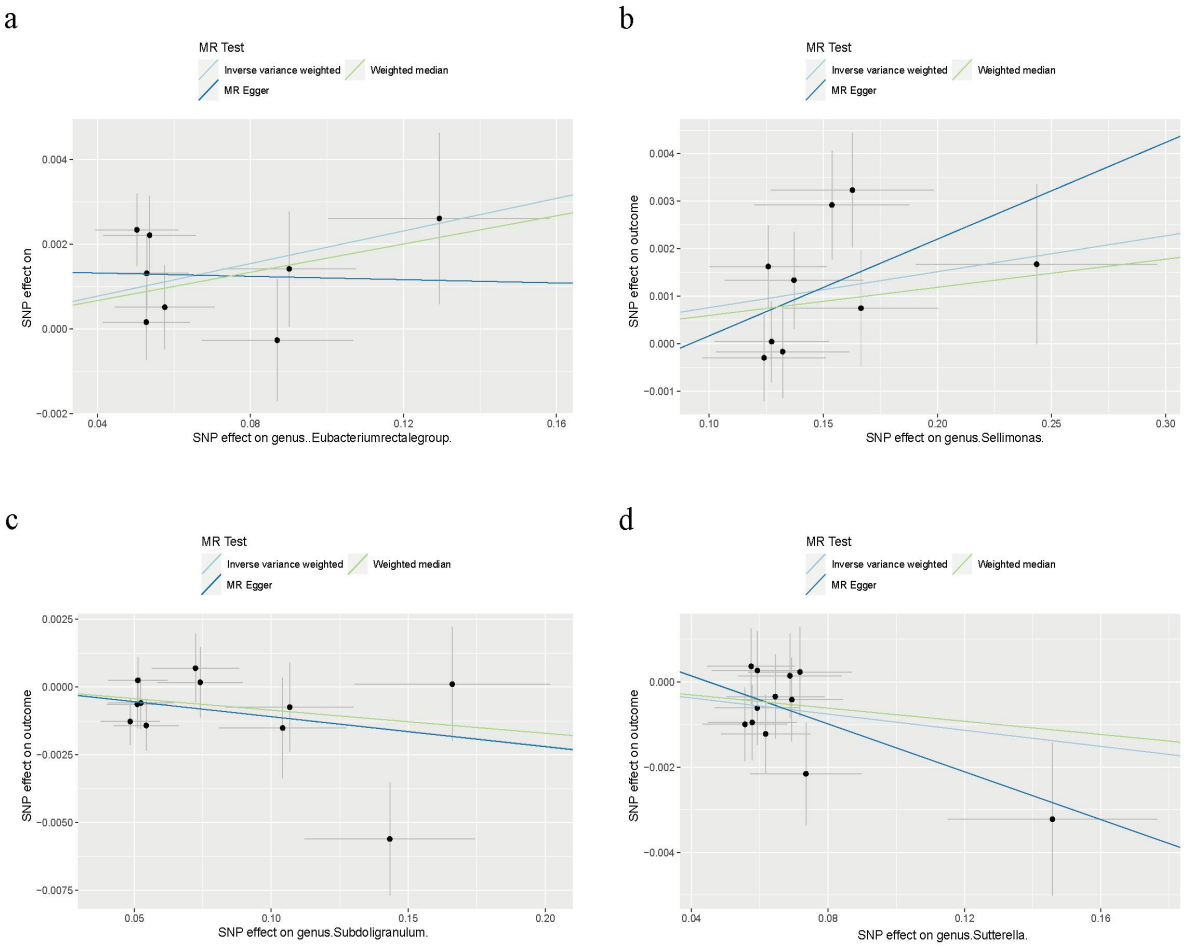
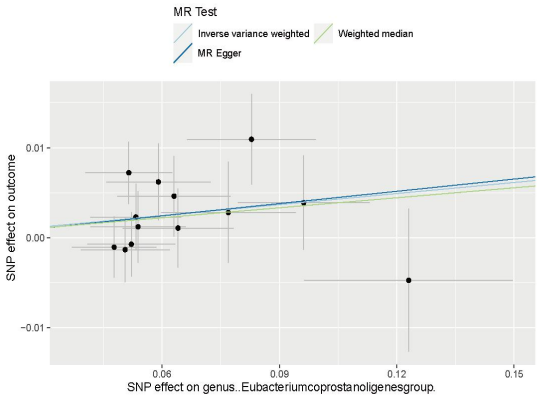


Fig S10 Scatter plots of MR estimates from genetically predicted gut microbiota on adrenal cortex zona reticularis function (androgen). a, Eubacteriumcoprostanoligenesgroup and adrenal cortex zona reticularis function; b, Ruminococcustorquesgroupid and adrenal cortex zona reticularis function; c, Parabacteroides and adrenal cortex zona reticularis function.

a



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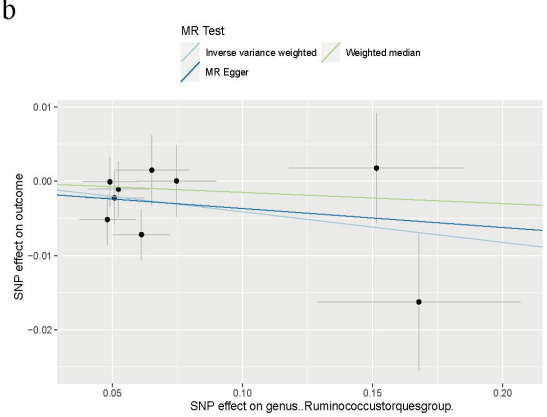

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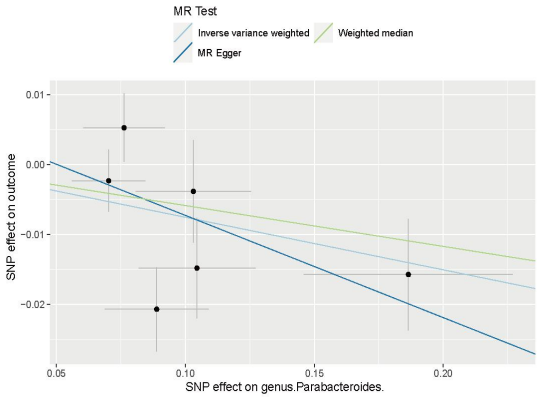


Fig S11 Funnel plots and Leave-one-out plots of MR estimates from genetically predicted portions of gut microbiota on adrenal medulla function. a,f, Alisonella and adrenal medulla function; b,g, Anaerofilum and adrenal medulla function; c,h, Bilophila adrenal medulla function; d,i, RuminococcaceaeUCG005 and adrenal medulla function; e,j, Ruminococcus2 and adrenal medulla function.

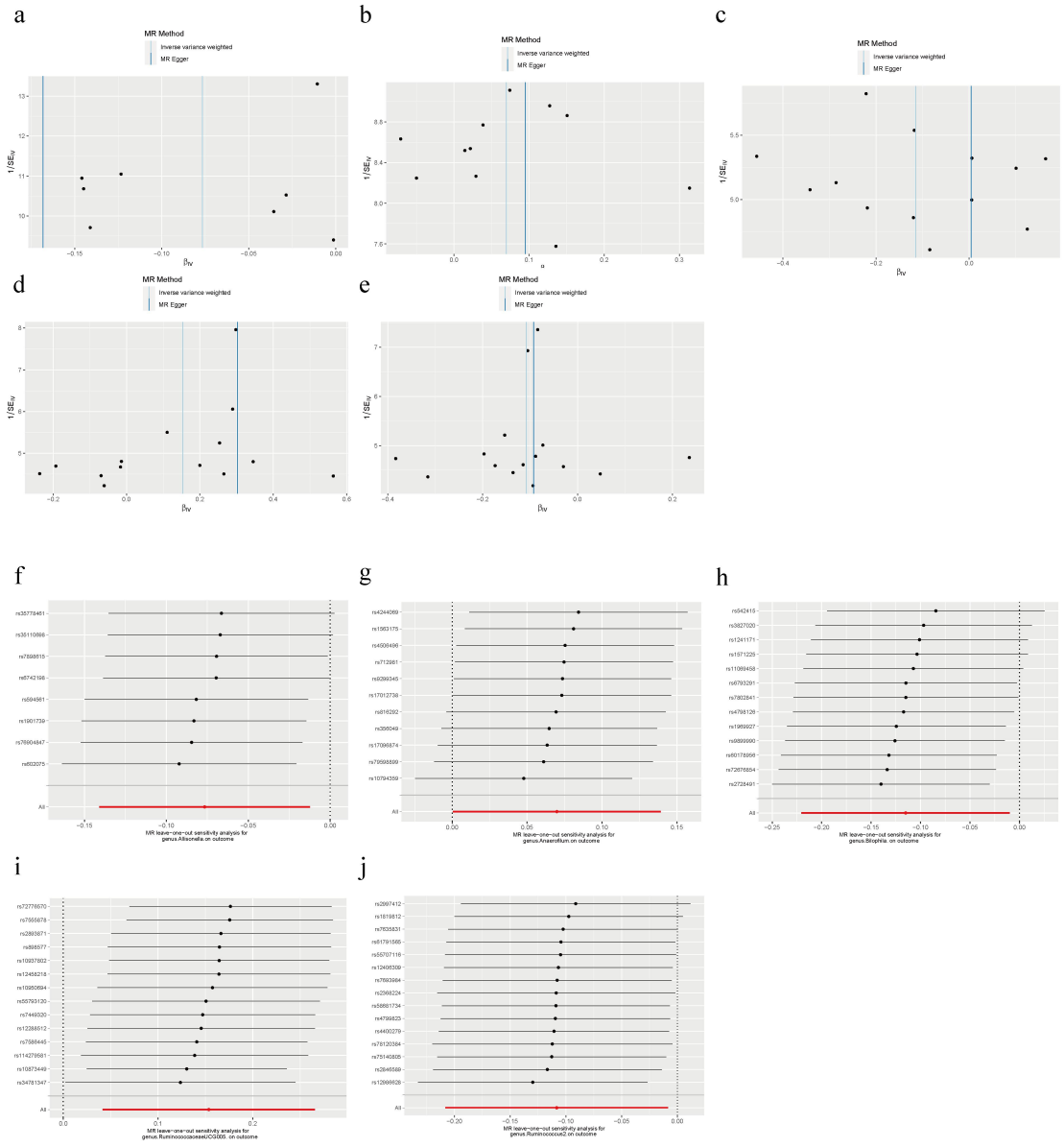


Fig S12 Funnel plots and Leave-one-out plots of MR estimates from genetically predicted portions of gut microbiota on adrenal cortex zona glomerulosa function. a,e, Intestinimonas and adrenal cortex zona glomerulosa function; b,f, Parasutterella and cortex zona glomerulosa function; c,g, Prevotella9 and adrenal cortex zona glomerulosa function; d,h, Veillonella and adrenal cortex zona glomerulosa function.

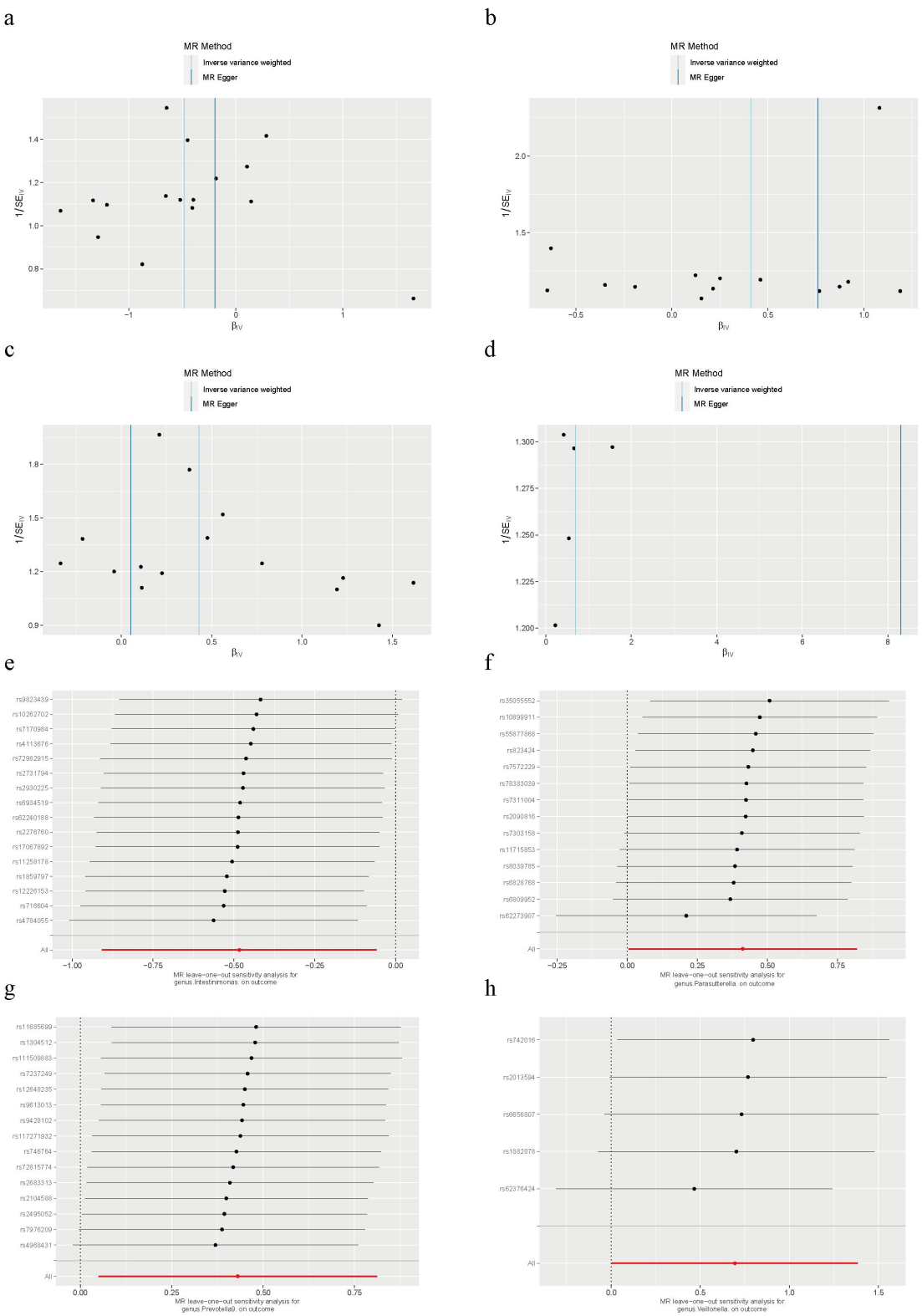


Fig S13 Funnel plots and Leave-one-out plots of MR estimates from genetically predicted portions of gut microbiota on adrenal cortex zona fasciculata function (plasma cortisol). a,g, Barnesiella and adrenal cortex zona fasciculata function; b,h, FamilyXIIIUCG001 and adrenal cortex zona fasciculata function; c,i, Fusicatenibacterid and adrenal cortex zona fasciculata function; d,j, RuminococcaceaeNK4A214group and adrenal cortex zona fasciculata function; e,k, RuminococcaceaeUCG010 and adrenal cortex zona fasciculata function; f,l, Sutterella and adrenal cortex zona fasciculata function.

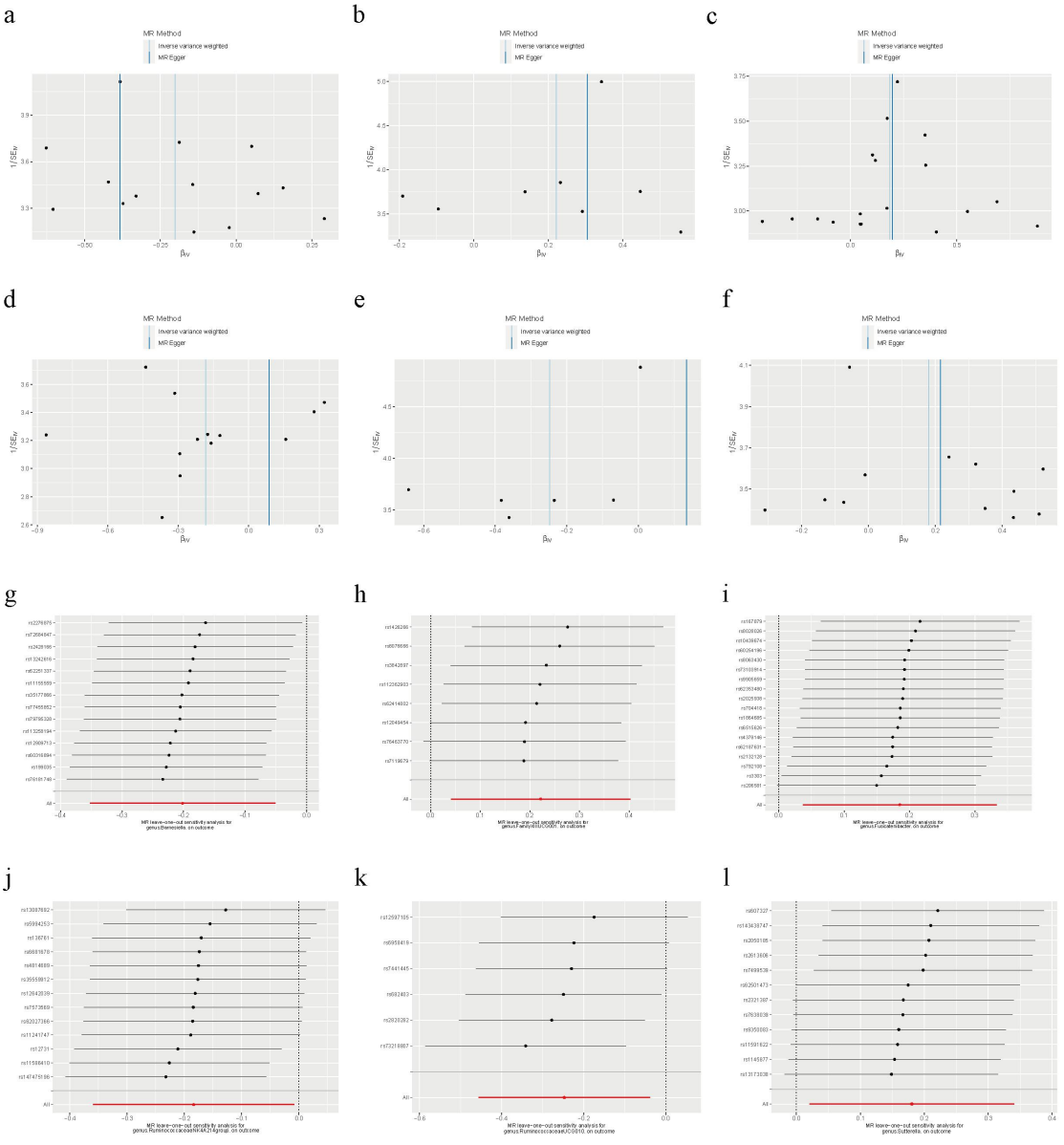


Fig S14 Funnel plots and Leave-one-out plots of MR estimates from genetically predicted portions of gut microbiota on adrenal cortex zona fasciculata function (urine cortisol). a,f, Eubacteriumventriosumgroup and adrenal cortex zona fasciculata function; b,g, Anaerofilum and adrenal cortex zona fasciculata function; c,h, Barnesiella and adrenal cortex zona fasciculata function;d,i, Eggerthella and adrenal cortex zona fasciculata function; e,j, Parasutterella and adrenal cortex zona fasciculata function.

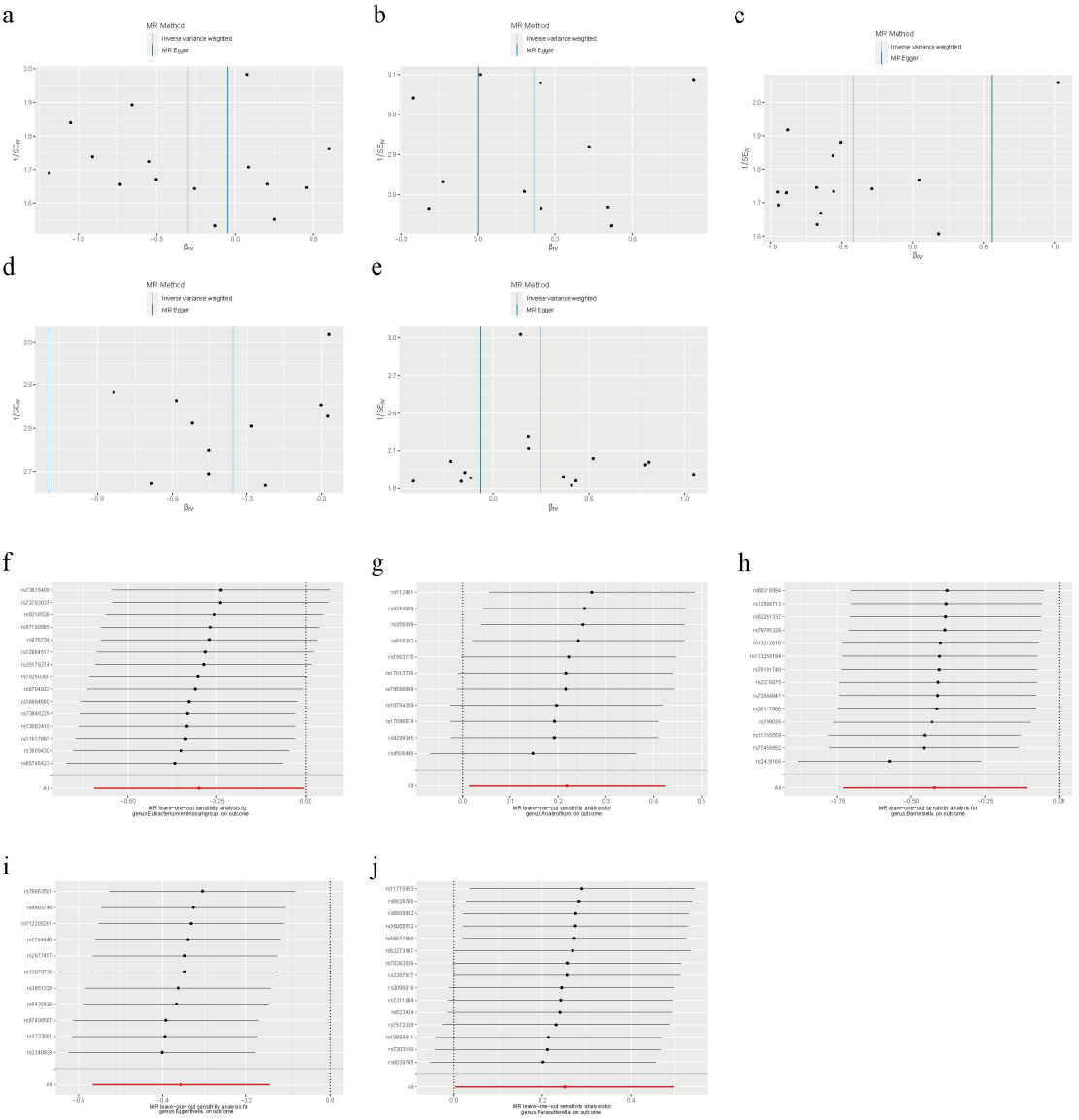


Fig S15 Funnel plots and Leave-one-out plots of MR estimates from genetically predicted portions of gut microbiota on adrenal cortex zona reticularis function (estradiol). a,e, Eubacteriumrectalegroup and adrenal cortex zona reticularis function; b,f, Selimonas and adrenal cortex zona reticularis function; c,g, Subdoligranulum and adrenal cortex zona reticularis function; d,h, Sutterella and adrenal cortex zona reticularis function.

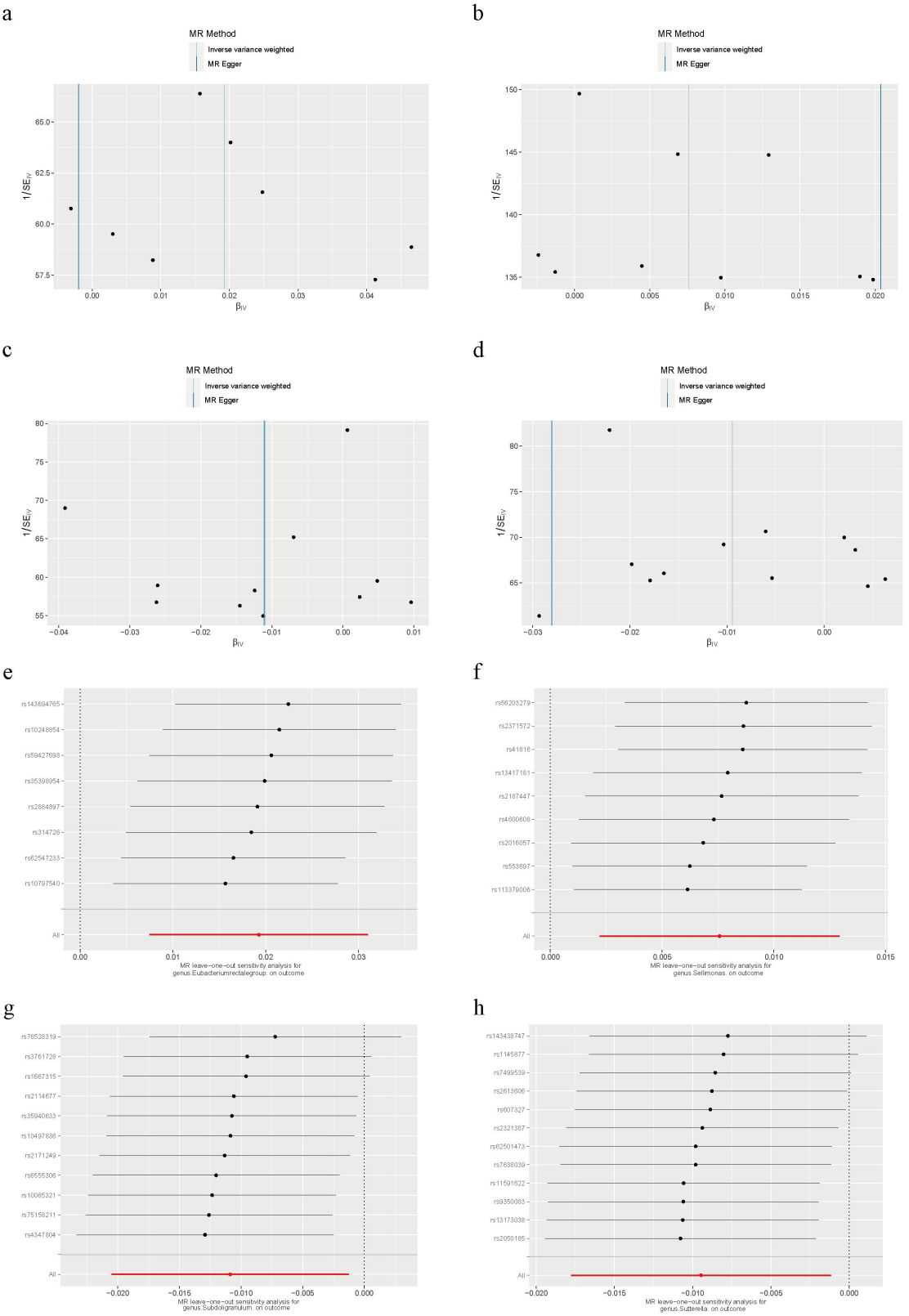
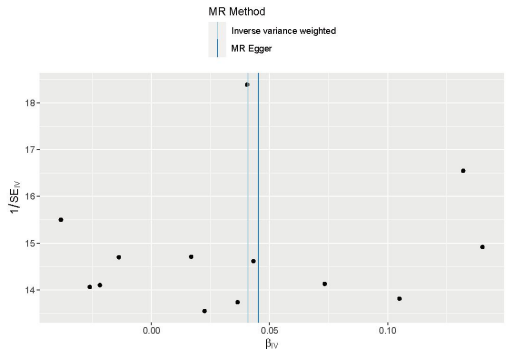


Fig S16 Funnel plots and Leave-one-out plots of MR estimates from genetically predicted portions of gut microbiota on adrenal cortex zona reticularis function (androgen). a,d, Eubacteriumcoprostanoligenesgroup and adrenal cortex zona reticularis function; b,e, Ruminococcustorquesgroupid and adrenal cortex zona reticularis function; c,f, Parabacteroides and adrenal cortex zona reticularis function.

a



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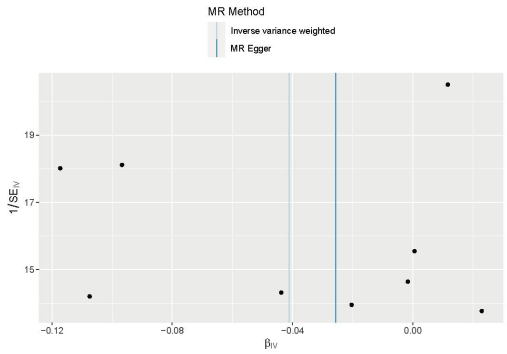

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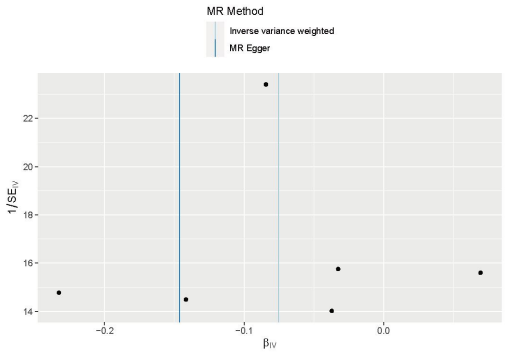

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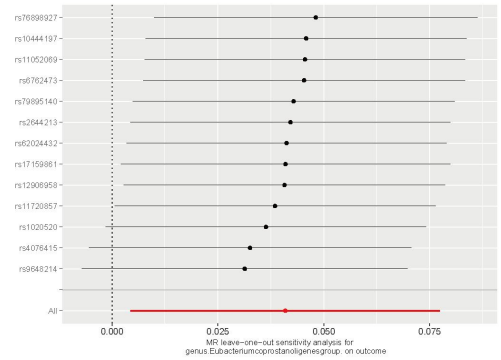

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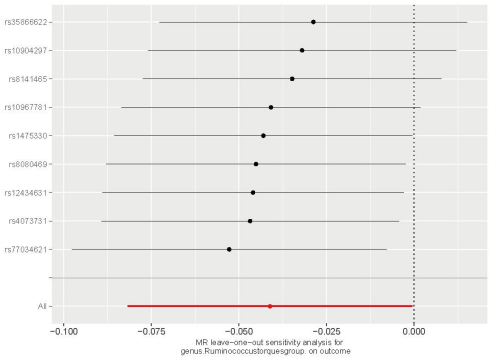

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