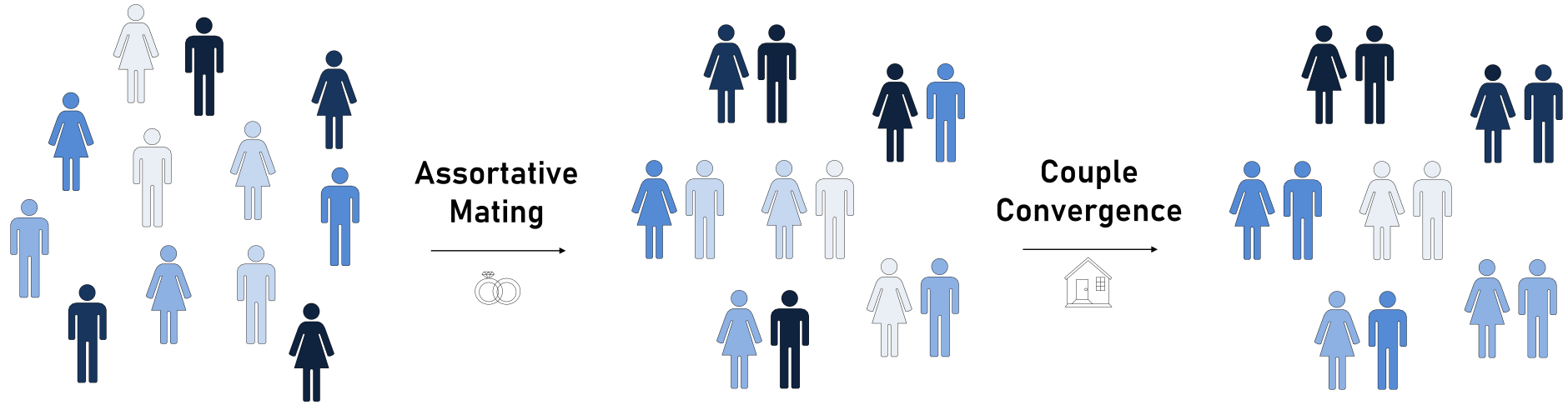
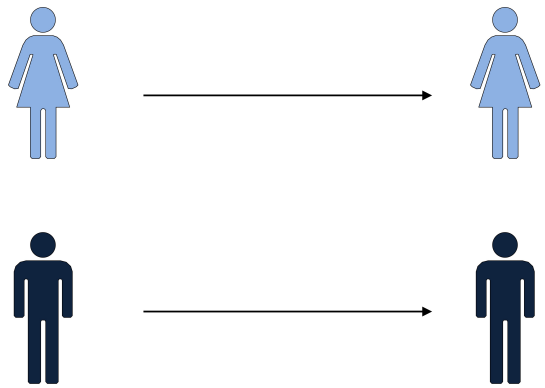
Causal effects due to social networks

Background

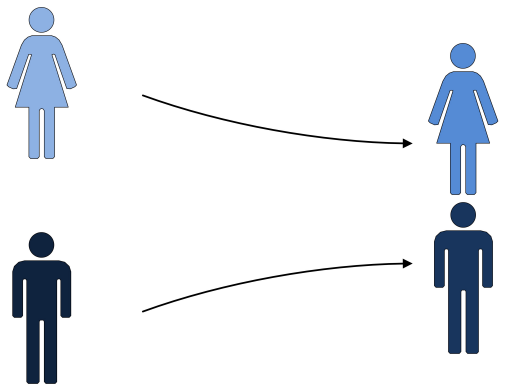
- **Assortative mating**: observation of increased phenotypic similarity between couples compared to random pairs.
- People tend to choose partners more similar to themselves.
- Unknown to what extent couples converge and influence each other over time.



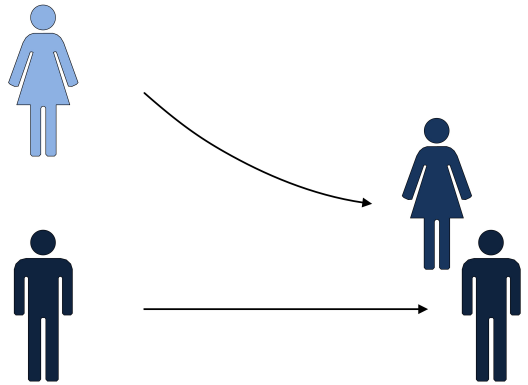
Possible convergence paths



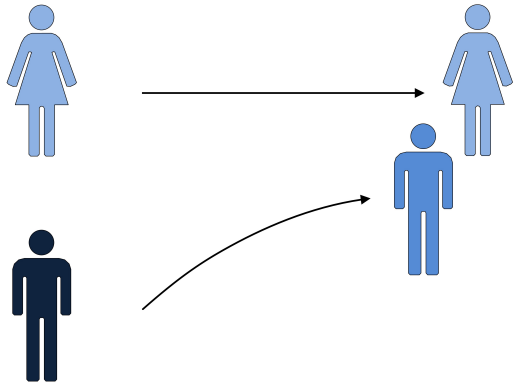
Non Convergence



Convergence

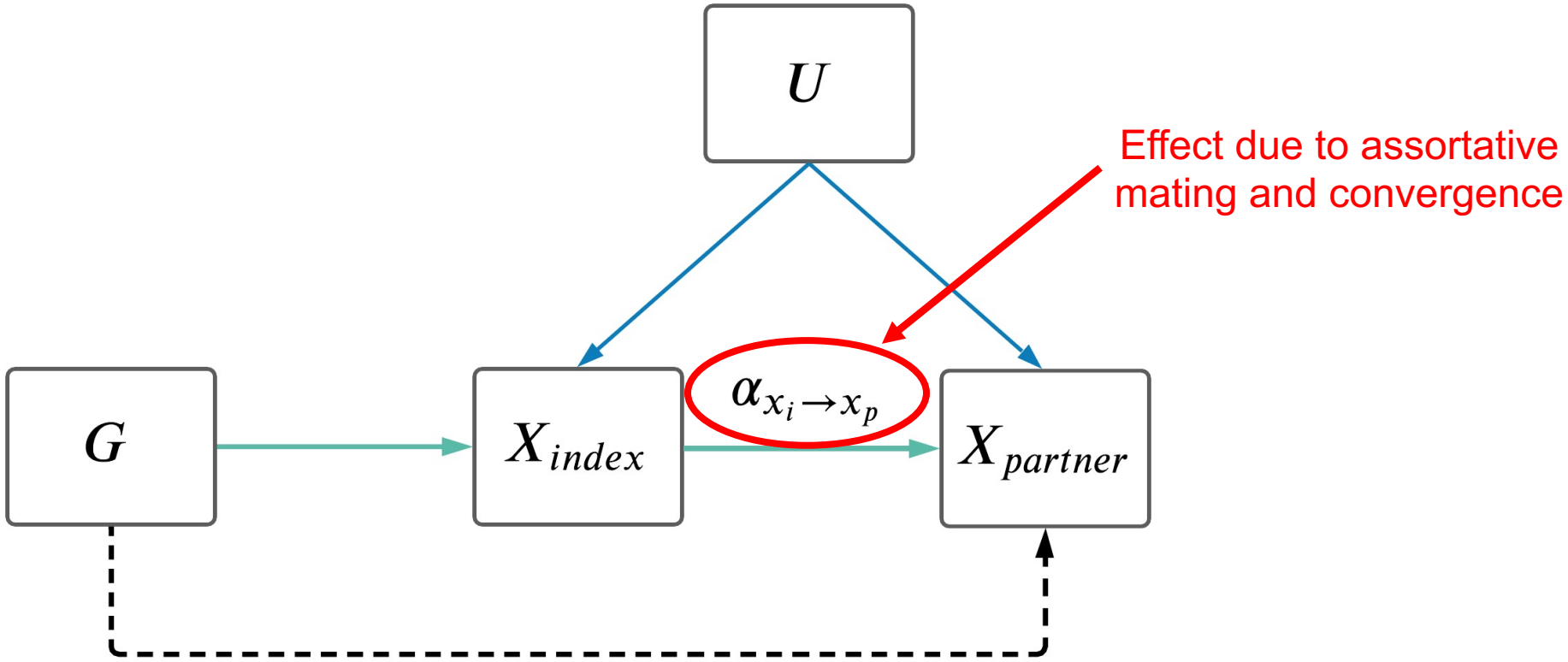


Male Influence

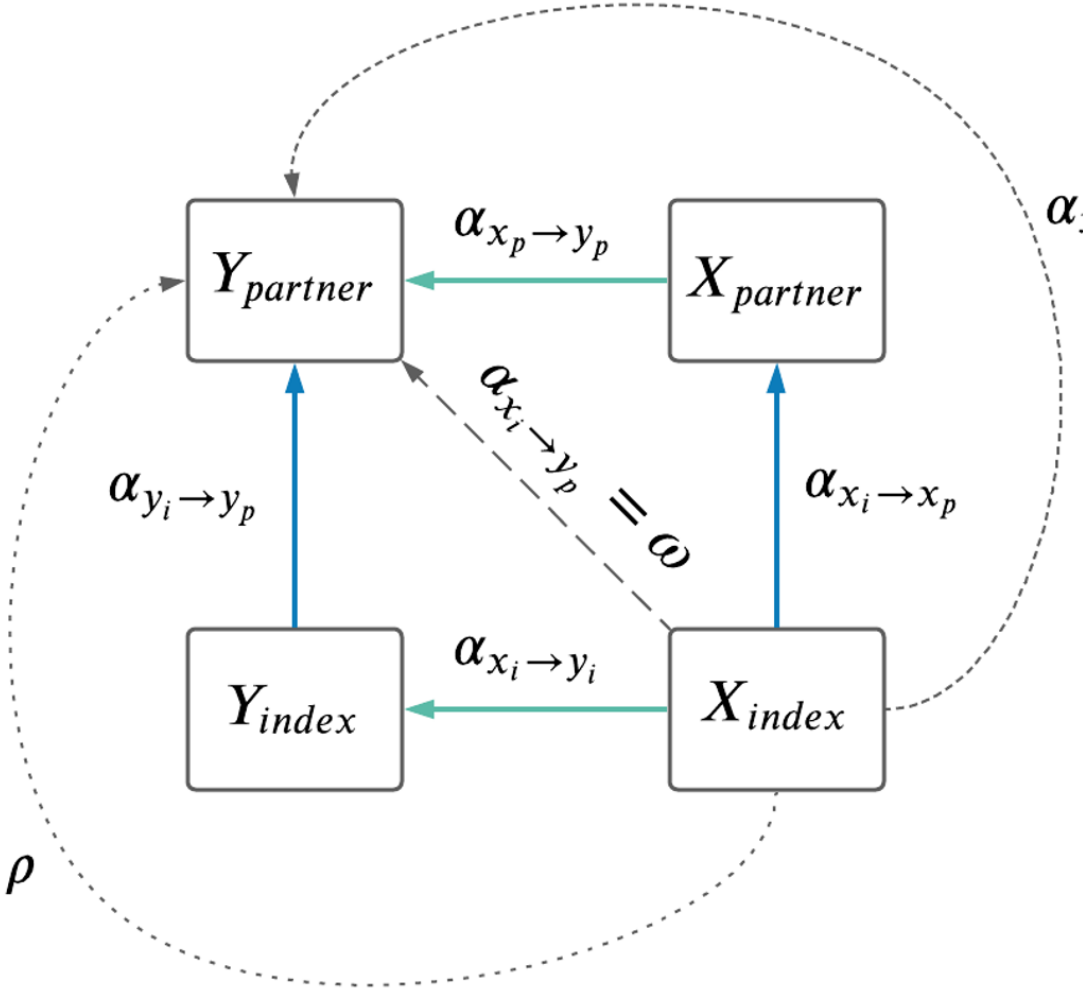


Female Influence

Theory: causal effects in mating pairs

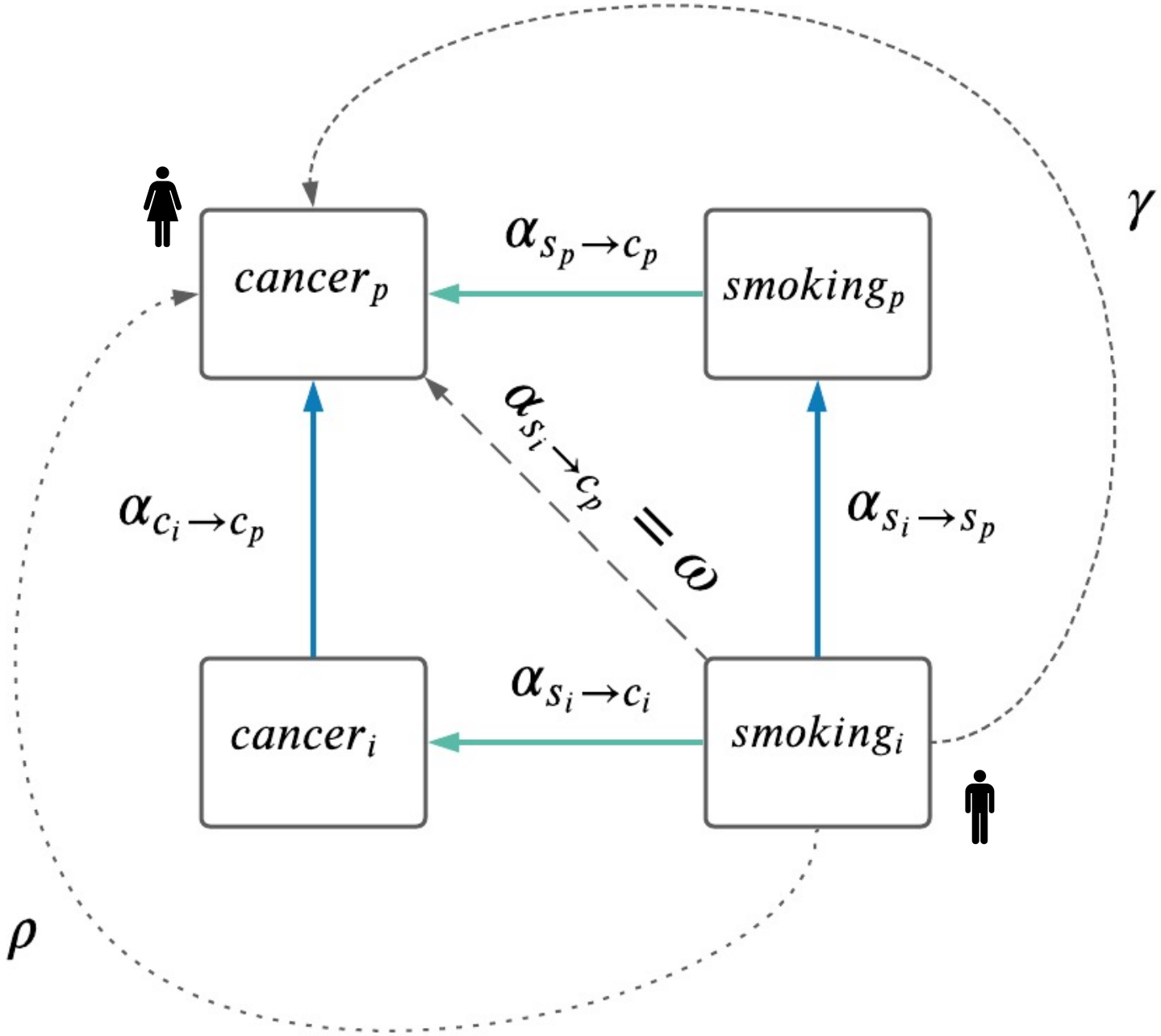


Two trait MR model

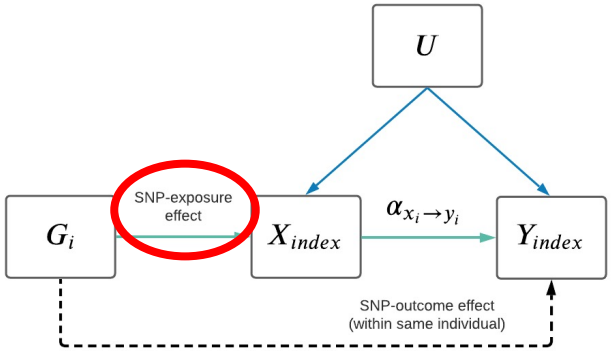


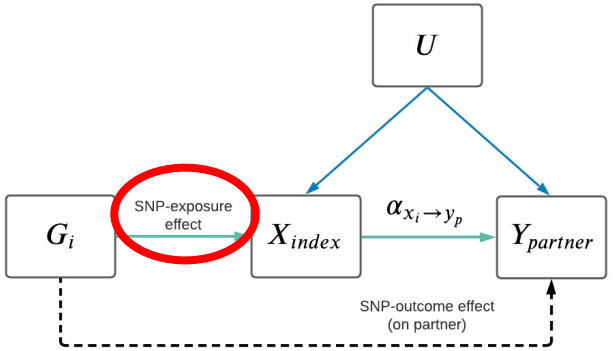
$$\alpha_{x_i \to x_p} \times \alpha_{x_p \to y_p} = \gamma$$

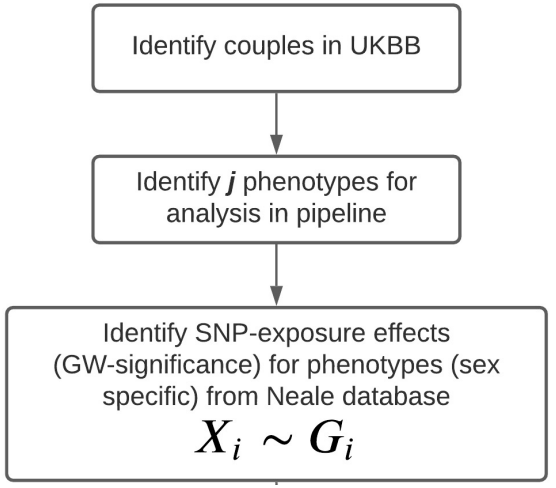
$$\alpha_{x_i \to y_i} \times \alpha_{y_i \to y_p} = \rho$$


$cancer_p$
$smoking_p$
$cancer_i$
$smoking_i$
$\alpha_{s_p \to c_p}$
$\alpha_{s_i \to c_p} = \omega$
$\alpha_{c_i \to c_p}$
$\alpha_{s_i \to s_p}$
$\alpha_{s_i \to c_i}$
γ
ρ

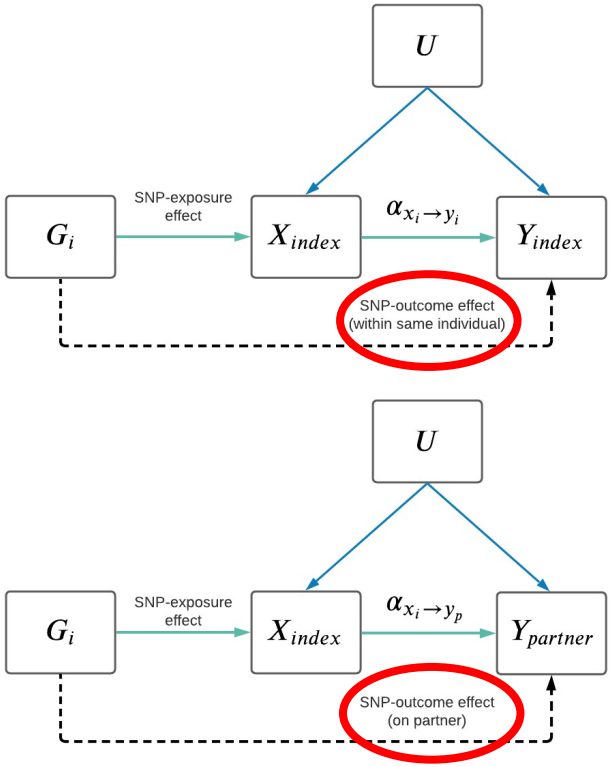
Pipeline overview

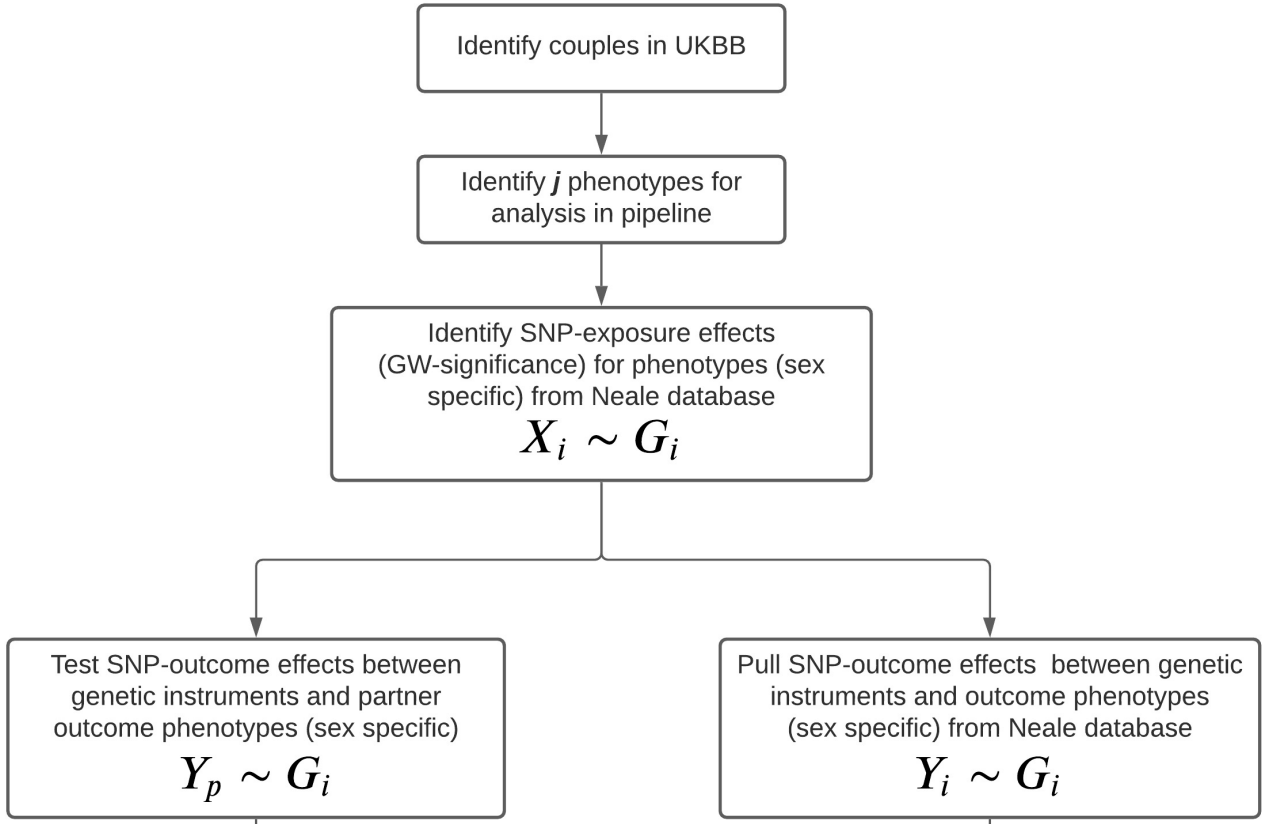




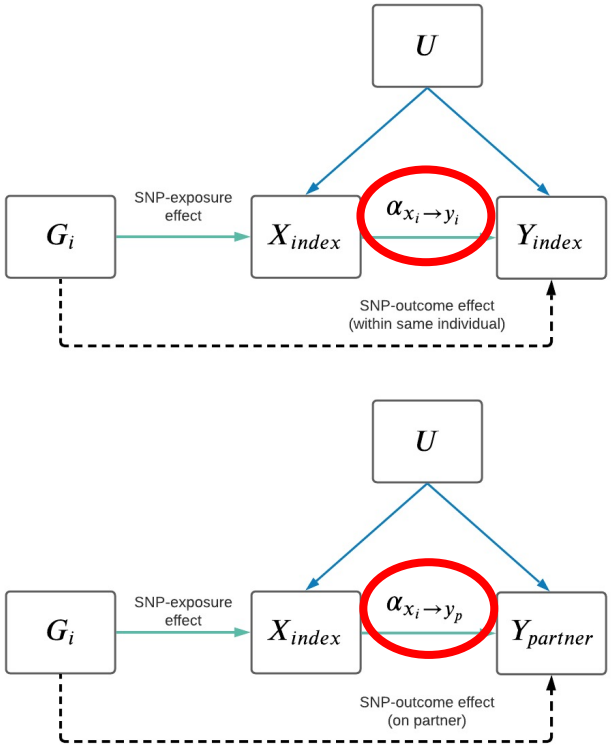


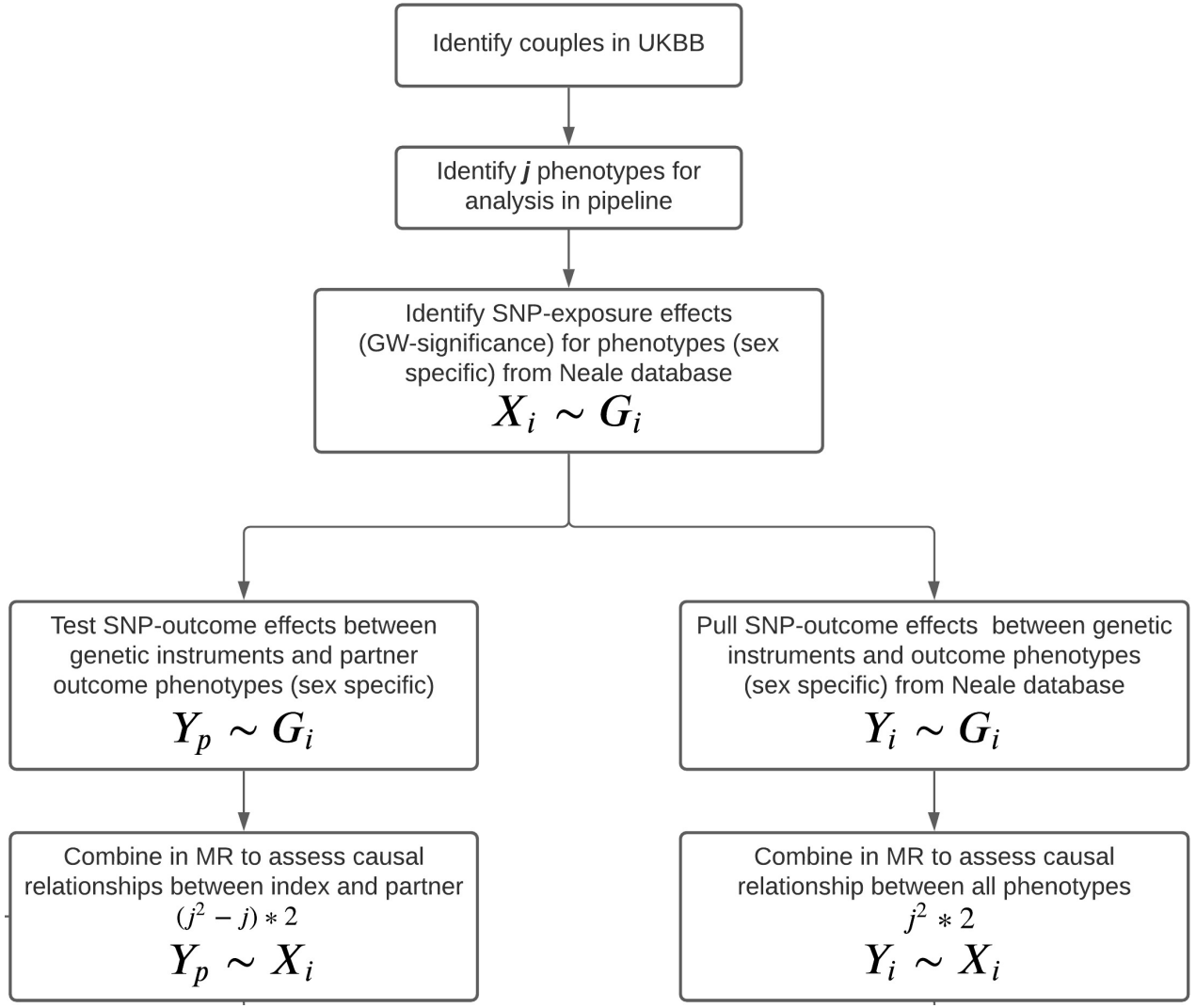
Pipeline overview



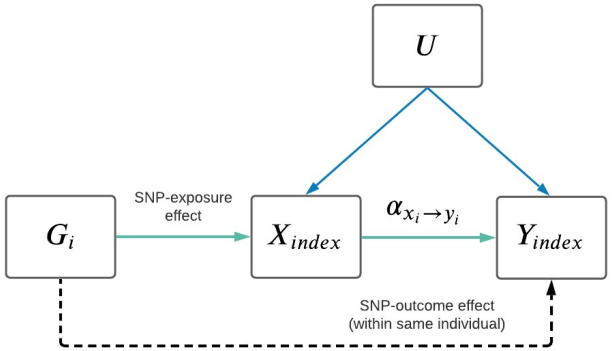


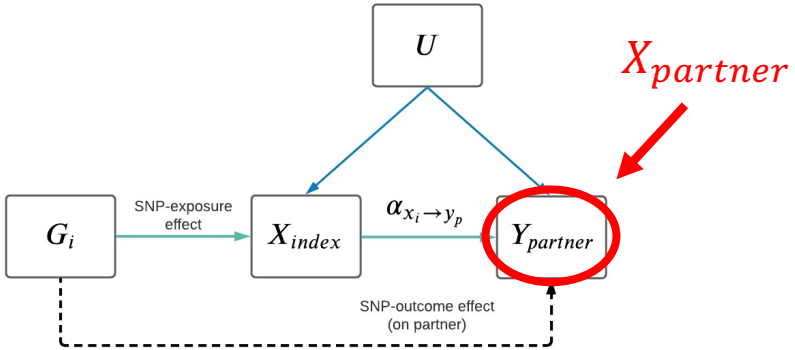
Pipeline overview





Pipeline overview





Identify couples in UKBB

Identify ***j*** phenotypes for analysis in pipeline

Identify SNP-exposure effects (GW-significance) for phenotypes (sex specific) from Neale database

$$X_i \sim G_i$$

Test SNP-outcome effects between genetic instruments and partner outcome phenotypes (sex specific)

$$Y_p \sim G_i$$

Pull SNP-outcome effects between genetic instruments and outcome phenotypes (sex specific) from Neale database

$$Y_i \sim G_i$$

Combine in MR to assess causal relationships between index and partner

$(j^2 - j) * 2$

$$Y_p \sim X_i$$

Combine in MR to assess causal relationship between all phenotypes

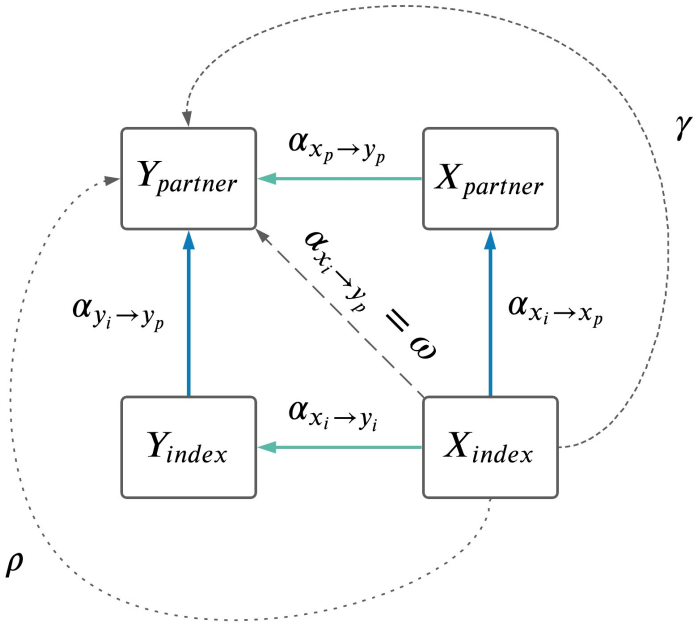
$j^2 * 2$

$$Y_i \sim X_i$$

Restrict to only MRs where exposure is the same as outcome for downstream analyses

$$X_p \sim X_i$$

Pipeline overview



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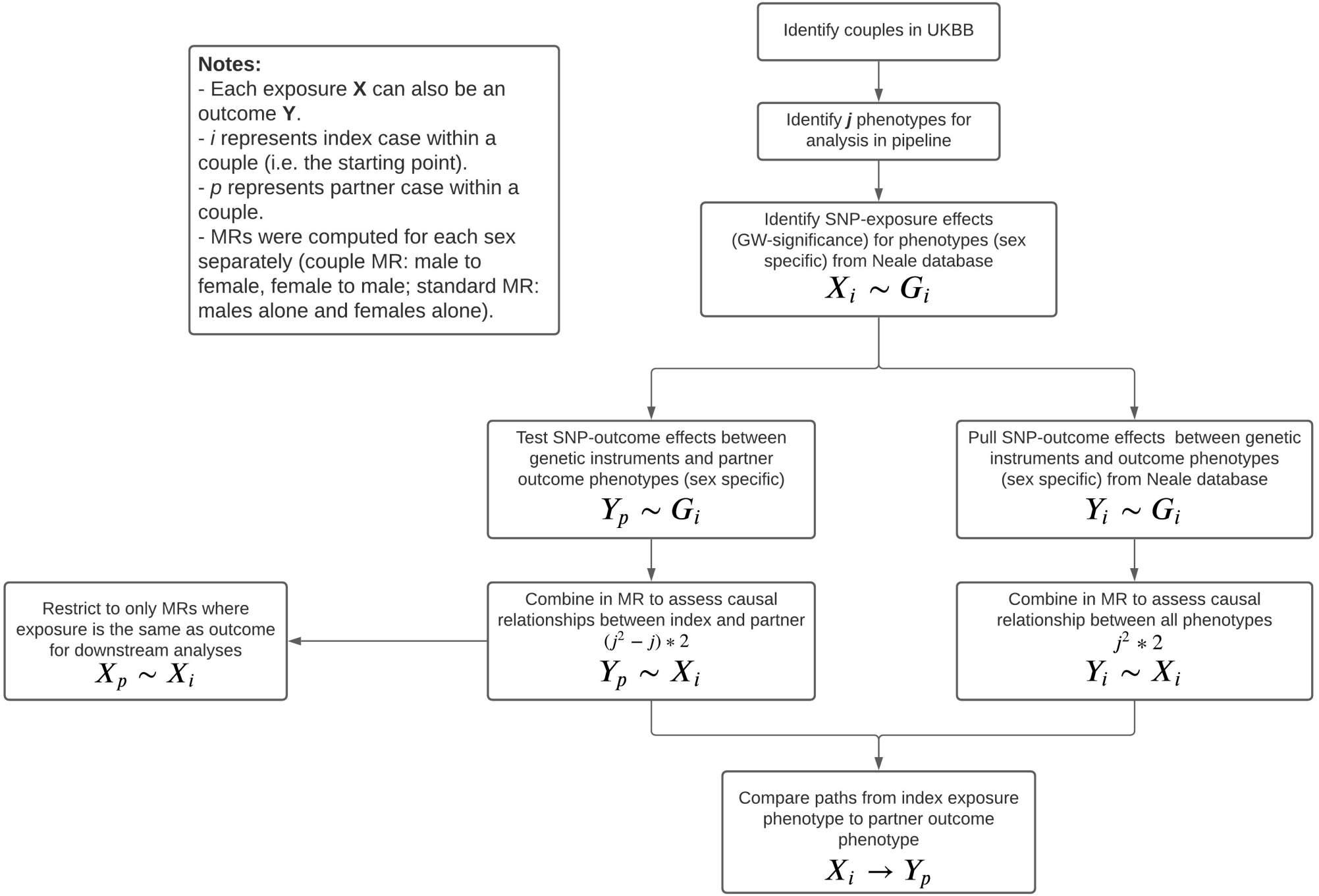
Compare paths from index exposure phenotype to partner outcome phenotype

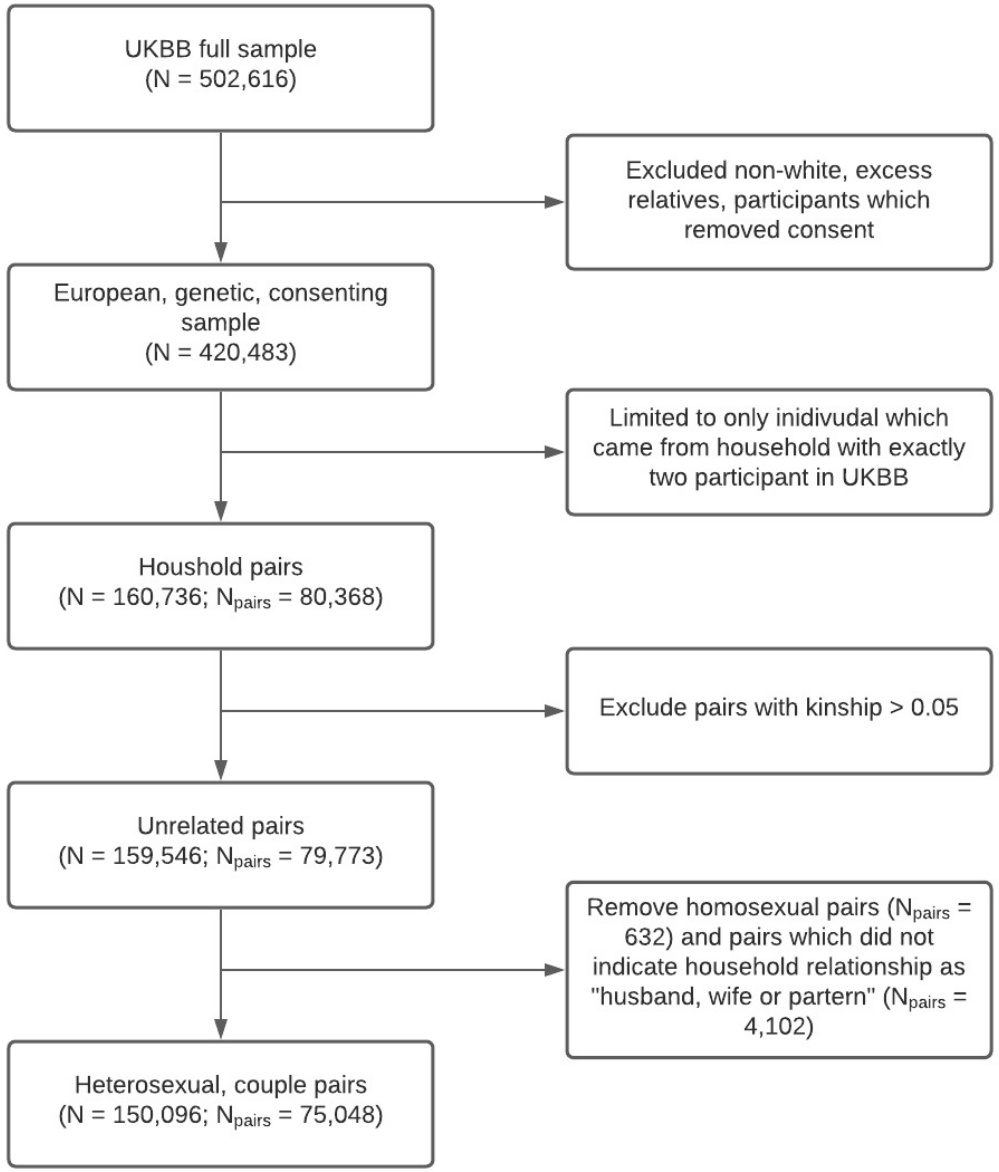
$$X_i \to Y_p$$

Pipeline overview

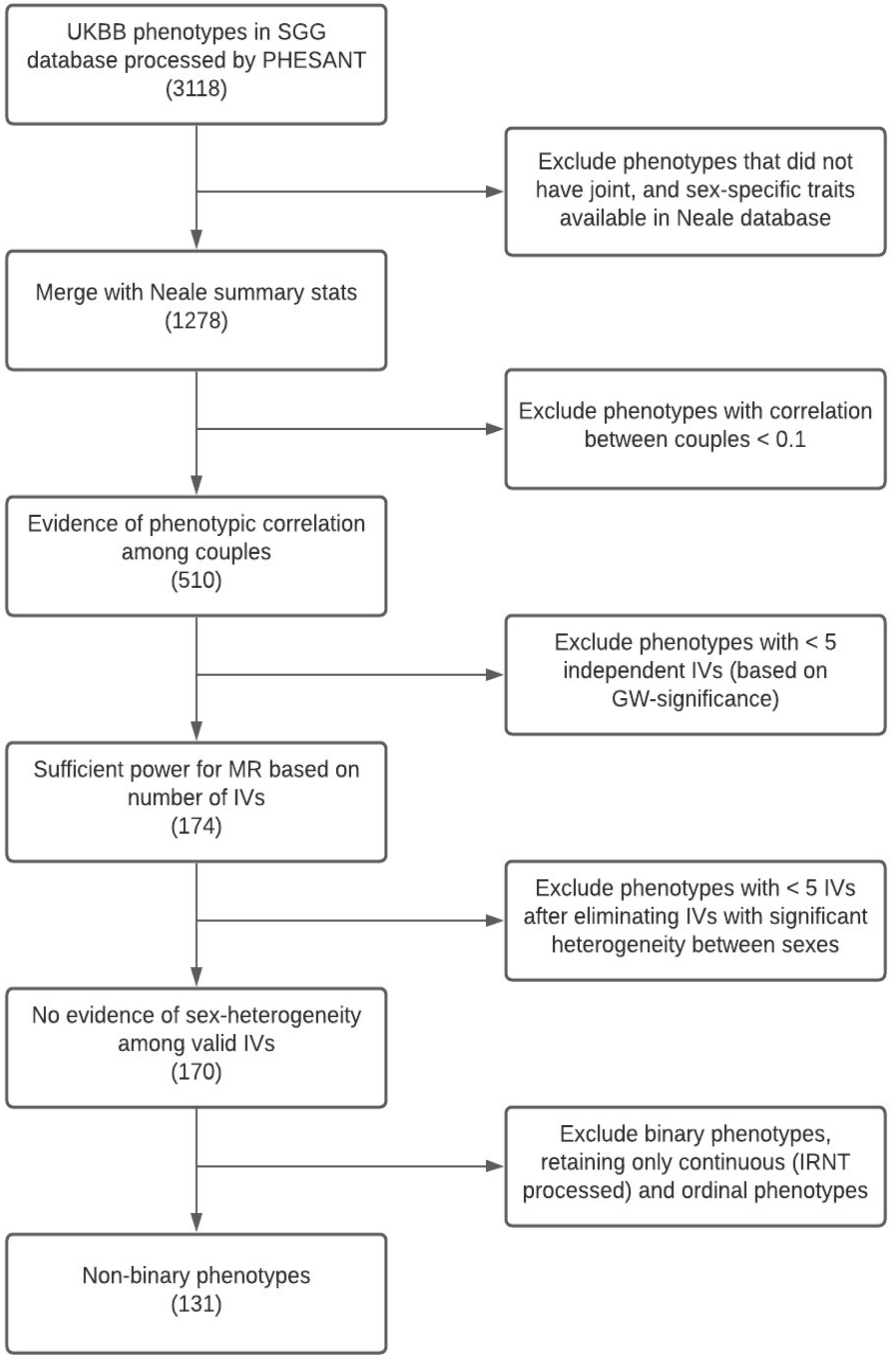
Notes:
- Each exposure **X** can also be an outcome **Y**.
- *i* represents index case within a couple (i.e. the starting point).
- *p* represents partner case within a couple.
- MRs were computed for each sex separately (couple MR: male to female, female to male; standard MR: males alone and females alone).



Couple identification in the UKBB

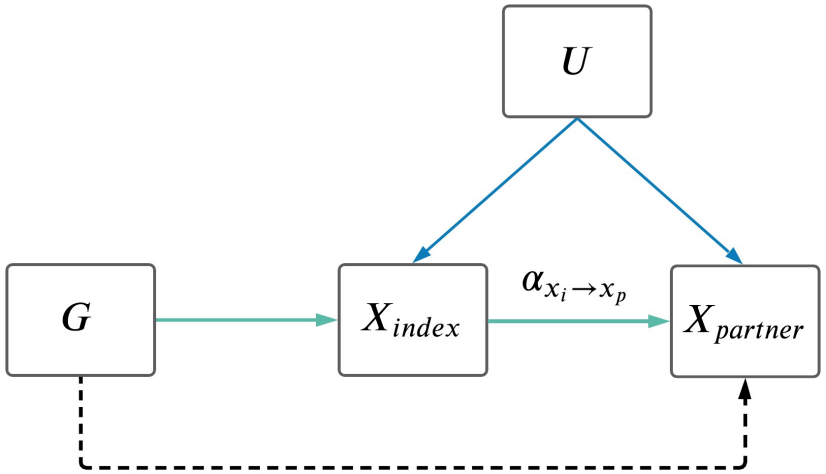


Phenotype selection in UKBB



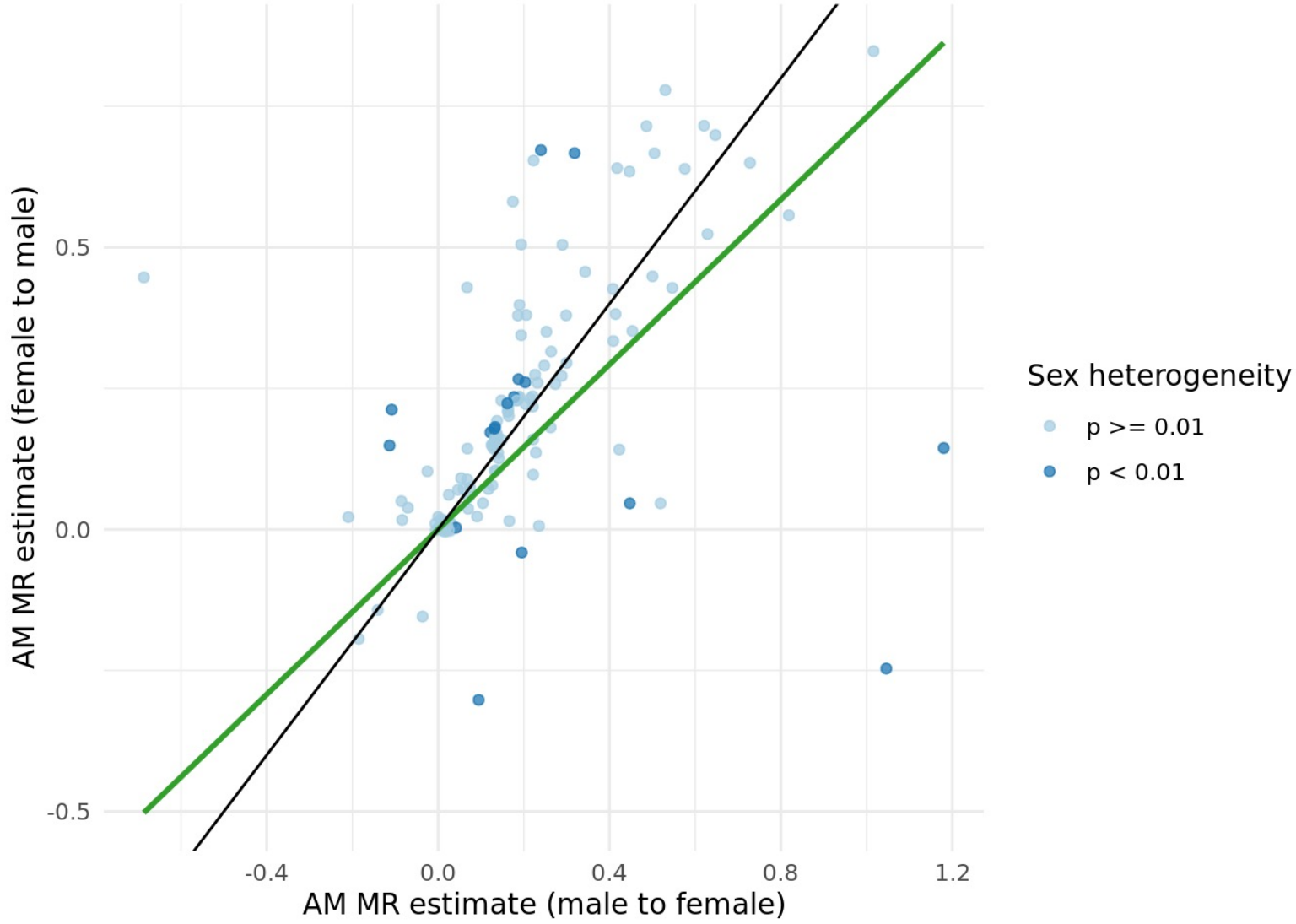
AM mendelian randomization results

- **131** phenotypes tested.
- **80** significant after adjusting for multiple hypothesis testing (using PC adjustment).
- Of these 80:
  - **1** showed significant difference between sexes.
  - **2** showed significant pattern across time spent together.

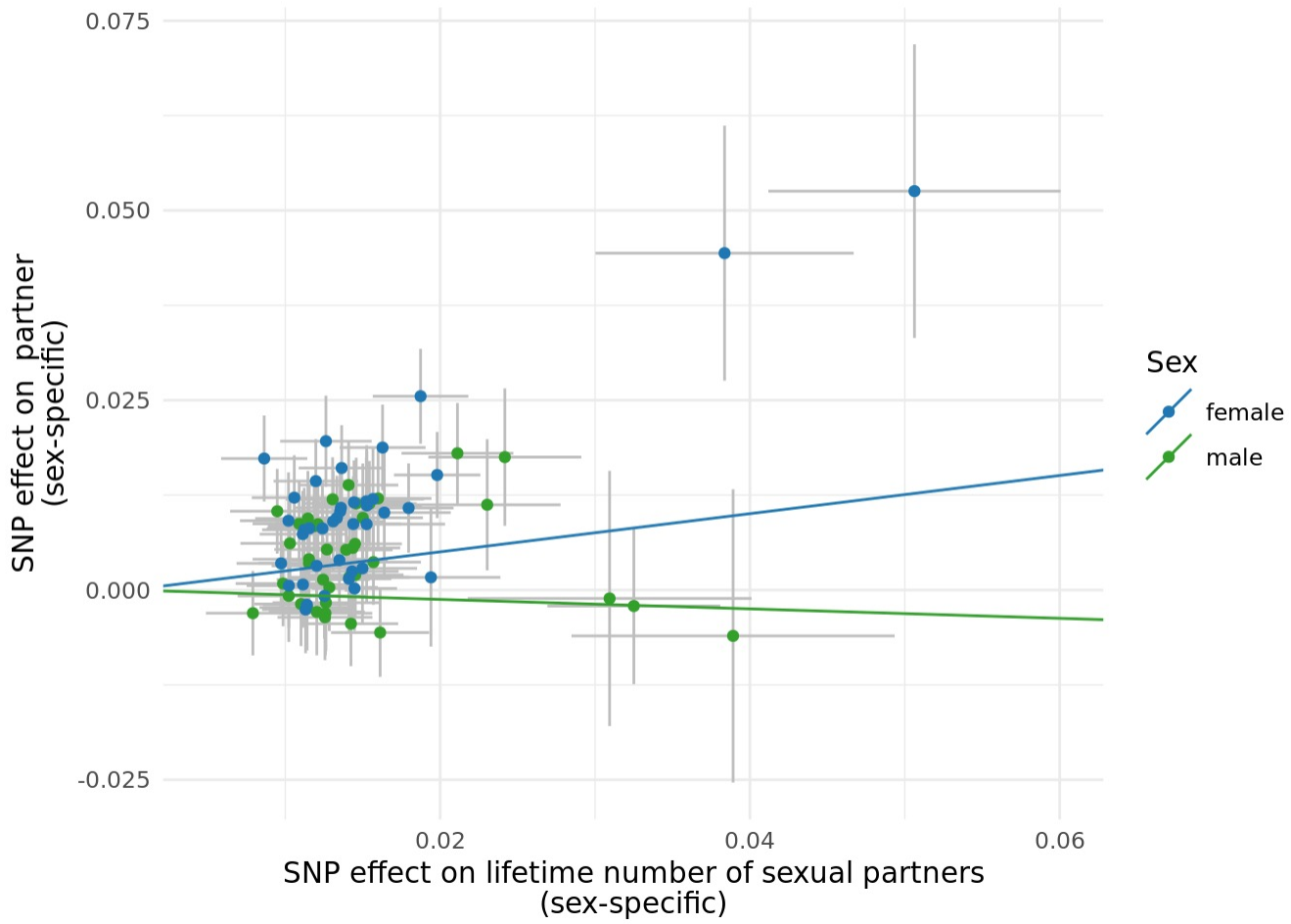


description	IVW_meta_beta	IVW_meta_pval
Standing height	0.22	0.0e+00
Comparative height size at age 10	0.30	3.9e-121
Average total household income before tax	0.67	5.2e-112
Sitting height	0.15	1.6e-96
Trunk fat-free mass	0.15	9.5e-78
Body mass index (BMI)	0.21	2.6e-75
Trunk predicted mass	0.15	5.3e-75
Leg fat percentage (right)	0.25	2.6e-74
Leg fat mass (left)	0.23	4.6e-74
Whole body fat-free mass	0.15	3.9e-73
Leg fat percentage (left)	0.25	6.3e-73
Whole body water mass	0.15	3.0e-72
Leg fat mass (right)	0.23	1.2e-69
Body mass index (BMI)	0.21	5.8e-67
Whole body fat mass	0.21	6.6e-66
Basal metabolic rate	0.15	5.5e-64
Forced expiratory volume in 1-second (FEV1), predicted	0.20	1.3e-61
Arm fat-free mass (right)	0.15	4.6e-60
Arm predicted mass (right)	0.15	1.9e-57
Trunk fat mass	0.19	1.9e-56
Body fat percentage	0.21	5.9e-56
Time spent watching television (TV)	0.60	6.9e-56
Arm predicted mass (left)	0.15	3.8e-53
Arm fat mass (left)	0.19	8.0e-52
Leg fat-free mass (left)	0.14	4.1e-51
Arm fat-free mass (left)	0.14	6.7e-51
Leg fat-free mass (right)	0.14	1.8e-50
Arm fat mass (right)	0.19	4.9e-50

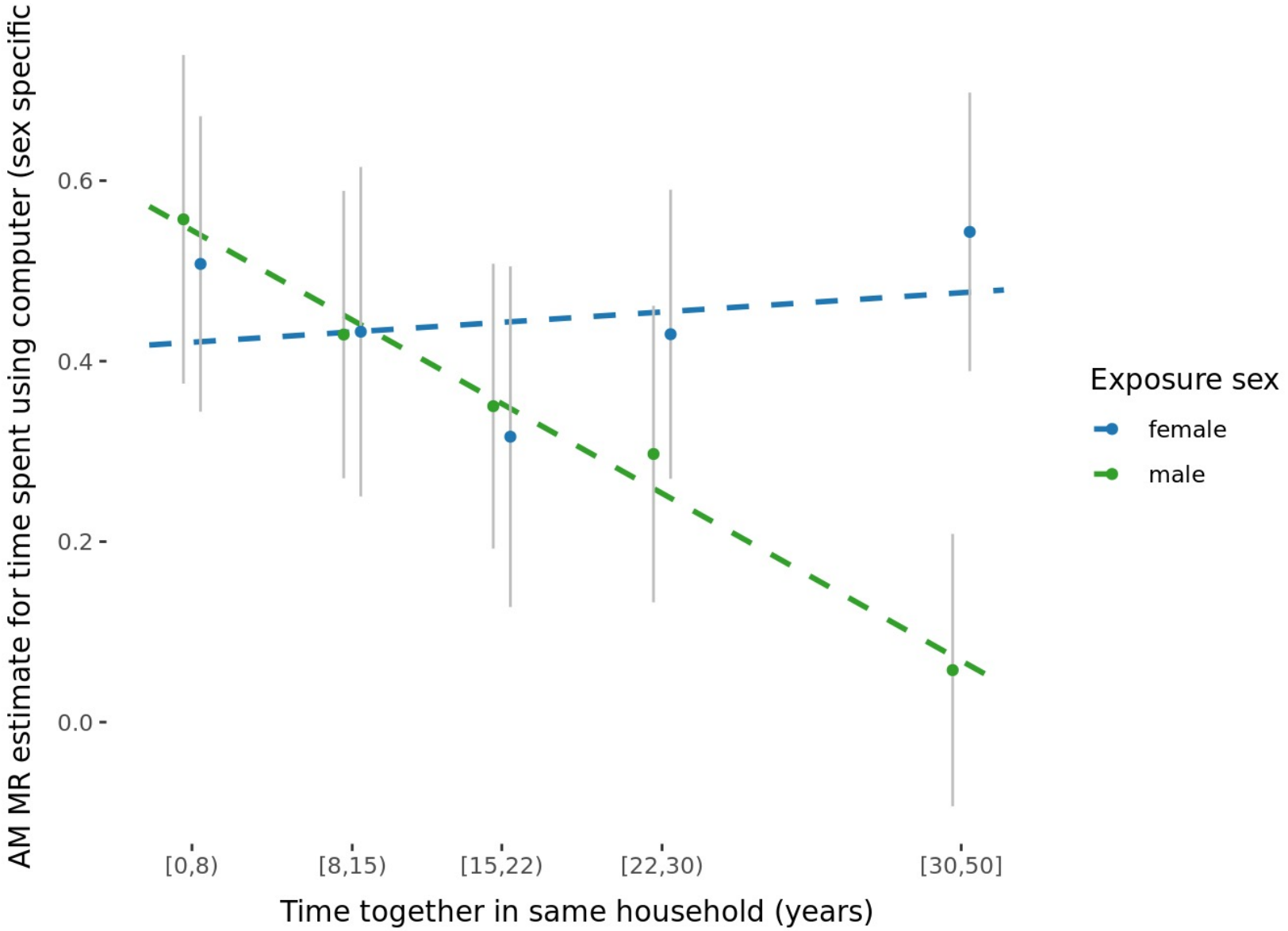
Assortative mating MR ($X_i \rightarrow X_p$), sex-differences



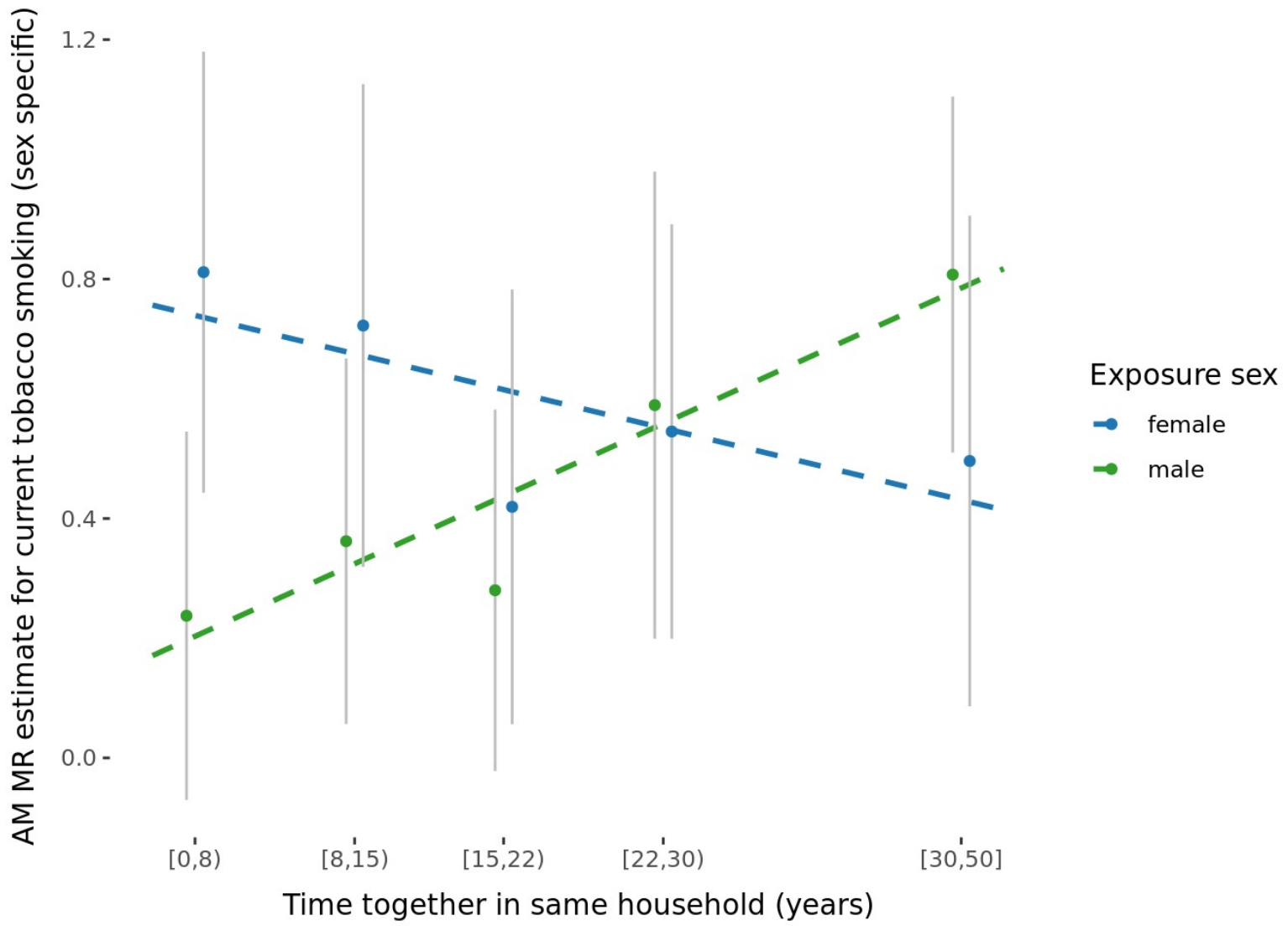
Assortative mating MR ($X_i \rightarrow X_p$), sex-differences



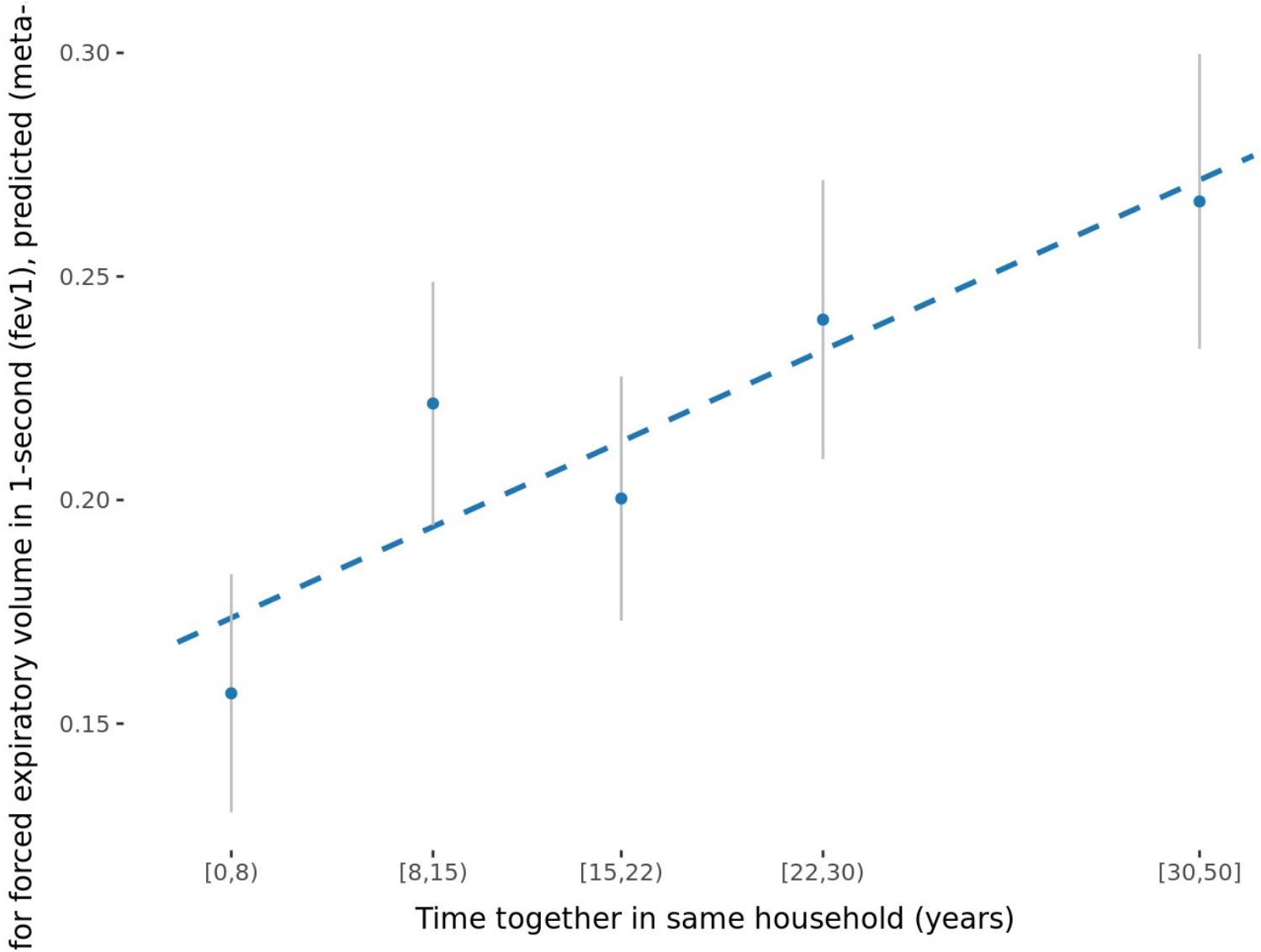
Assortative mating MR ($X_i \rightarrow X_p$), impact of time-together

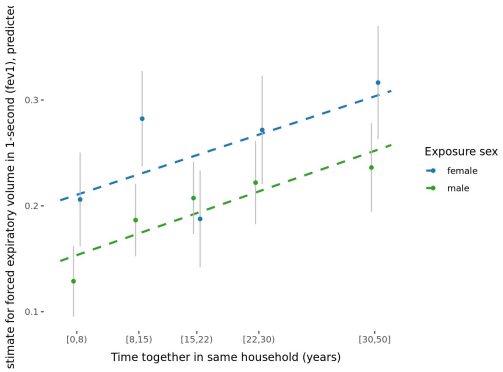


Assortative mating MR ($X_i \rightarrow X_p$), impact of time-together

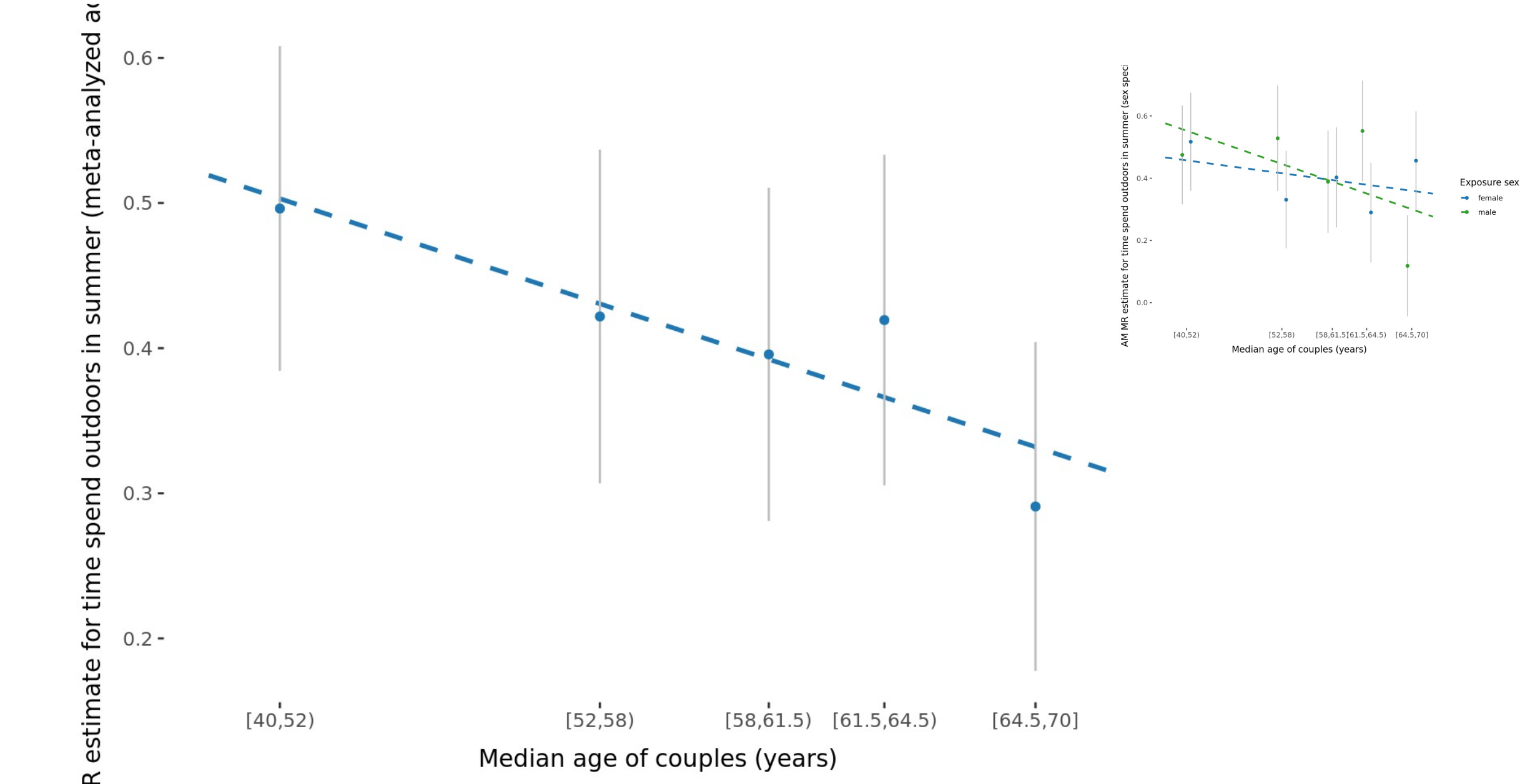


Assortative mating MR ($X_i \rightarrow X_p$), impact of time-together



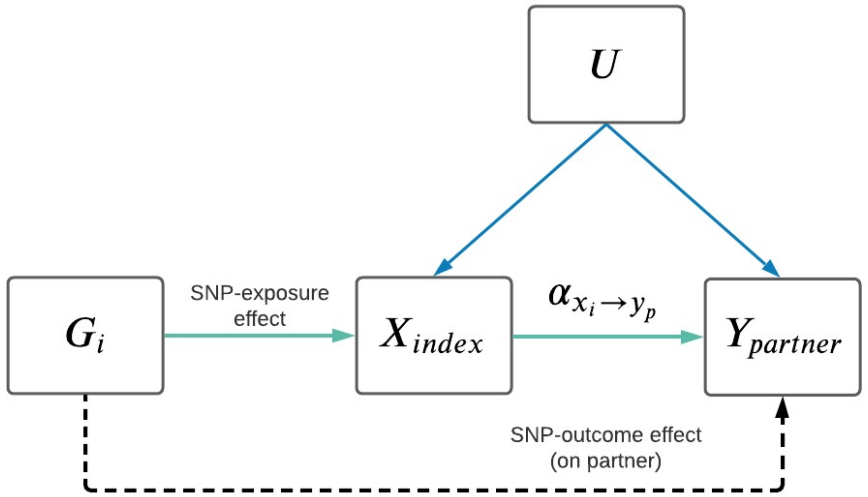


Assortative mating MR ($X_i \rightarrow X_p$), impact of age



Two-trait mendelian randomization results

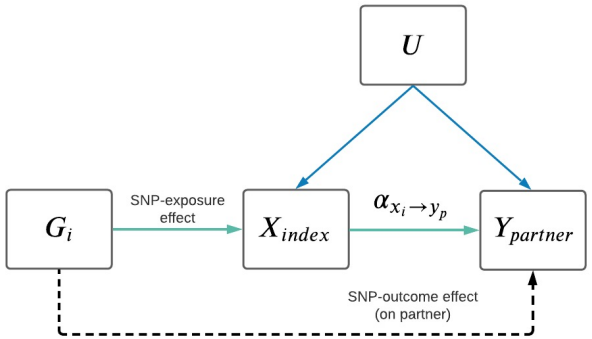
- **131** phenotypes tested.
- **131²** MRs (x 2, one for each direction: M ➡️ F and F ➡️ M).
- After meta-analyzing across sexes, **1965** significant after adjusting for multiple hypothesis testing ($p < 0.05/131^2$)

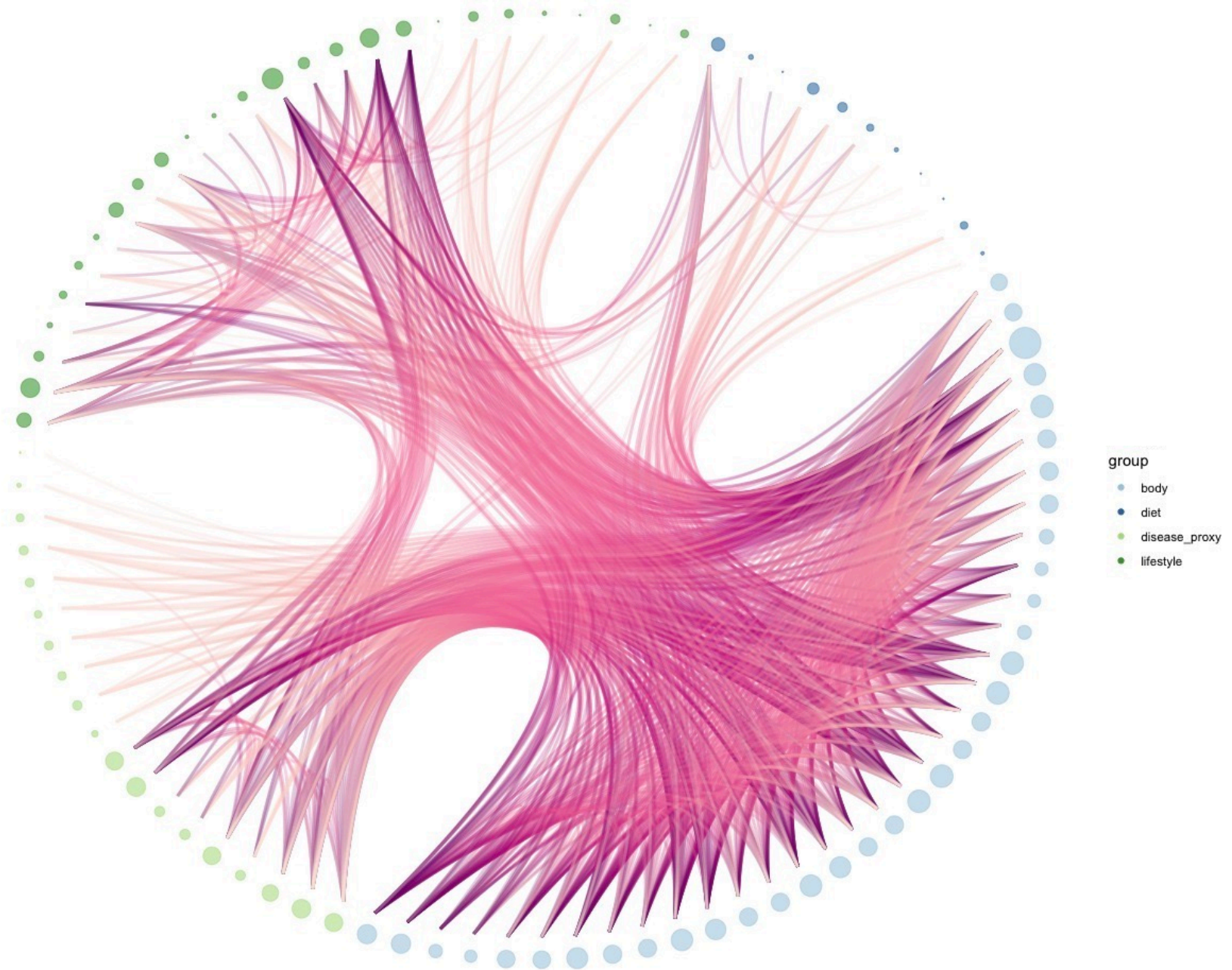


exposure_description	outcome_description	same_trait	IVW_meta_beta	IVW_meta_pval
Standing height	Standing height	TRUE	0.22	0.0e+00
Comparative height size at age 10	Standing height	FALSE	0.39	2.8e-204
Forced expiratory volume in 1-second (FEV1), predicted	Standing height	FALSE	0.31	2.3e-189
Sitting height	Standing height	FALSE	0.21	5.2e-175
Standing height	Sitting height	FALSE	0.16	1.2e-170
Standing height	Comparative height size at age 10	FALSE	0.16	8.6e-158
Trunk predicted mass	Standing height	FALSE	0.22	2.6e-133
Trunk fat-free mass	Standing height	FALSE	0.22	3.6e-133
Comparative height size at age 10	Comparative height size at age 10	TRUE	0.30	3.9e-121
Whole body fat-free mass	Standing height	FALSE	0.22	4.2e-117
Whole body water mass	Standing height	FALSE	0.22	8.0e-117
Comparative height size at age 10	Sitting height	FALSE	0.28	3.2e-113
Average total household income before tax	Average total household income before tax	TRUE	0.67	5.2e-112
Forced expiratory volume in 1-second (FEV1), predicted	Sitting height	FALSE	0.22	3.9e-108
Standing height	Trunk fat-free mass	FALSE	0.12	8.4e-104
Standing height	Trunk predicted mass	FALSE	0.12	3.6e-103
Basal metabolic rate	Standing height	FALSE	0.20	9.7e-101
Arm fat-free mass (right)	Standing height	FALSE	0.21	1.0e-99
Forced expiratory volume in 1-second (FEV1), predicted	Comparative height size at age 10	FALSE	0.22	1.0e-98
Standing height	Forced expiratory volume in 1-second (FEV1), predicted	FALSE	0.14	7.9e-98
Sitting height	Sitting height	TRUE	0.15	1.6e-96
Sitting height	Comparative height size at age 10	FALSE	0.15	2.8e-94
Arm predicted mass (right)	Standing height	FALSE	0.21	4.0e-92
Standing height	Whole body fat-free mass	FALSE	0.12	2.4e-91
Standing height	Whole body water mass	FALSE	0.12	2.2e-90
Forced vital capacity (FVC), Best measure	Standing height	FALSE	0.26	2.3e-90

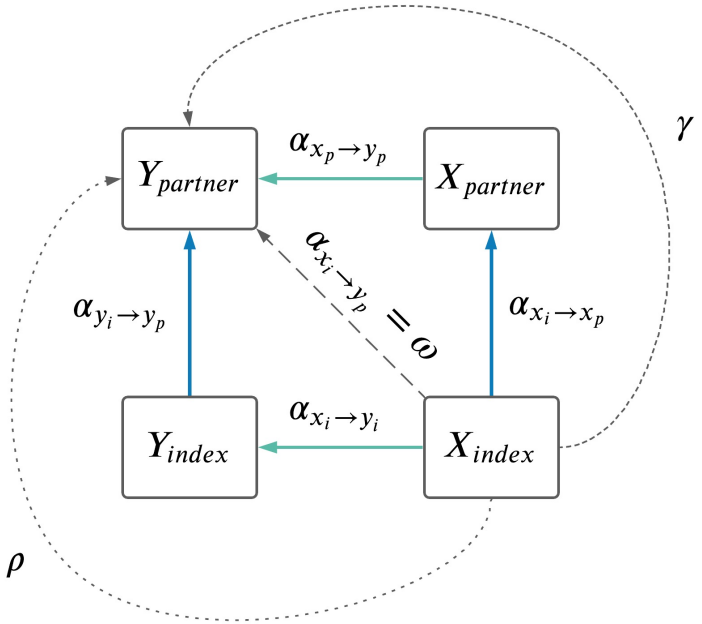
exposure_description	outcome_description	same_trait	IVW_meta_beta	IVW_meta_pval
Age completed full time education	Average total household income before tax	FALSE	0.57	4.4e-39
Age completed full time education	Age completed full time education	TRUE	0.57	2.7e-31
Average total household income before tax	Age completed full time education	FALSE	0.36	6.3e-28
Time spent watching television (TV)	Age completed full time education	FALSE	-0.46	2.8e-25
Leg fat percentage (left)	Age completed full time education	FALSE	-0.17	2.9e-25
Body mass index (BMI)	Age completed full time education	FALSE	-0.14	4.5e-24
Age completed full time education	Time spent watching television (TV)	FALSE	-0.47	8.4e-24
Leg fat percentage (right)	Age completed full time education	FALSE	-0.16	4.8e-23
Standing height	Age completed full time education	FALSE	0.068	5.5e-23
Body mass index (BMI)	Age completed full time education	FALSE	-0.13	1.9e-21
Sitting height	Age completed full time education	FALSE	0.073	1.2e-17
Leg fat mass (right)	Age completed full time education	FALSE	-0.12	1.3e-16
Leg fat mass (left)	Age completed full time education	FALSE	-0.12	2.2e-16
Body fat percentage	Age completed full time education	FALSE	-0.13	9.2e-16
Time spend outdoors in summer	Age completed full time education	FALSE	-0.43	4.7e-15
Arm fat percentage (right)	Age completed full time education	FALSE	-0.12	7.7e-15
Age completed full time education	Leg fat percentage (left)	FALSE	-0.38	1.0e-14
Arm fat percentage (left)	Age completed full time education	FALSE	-0.12	1.1e-14
Age completed full time education	Job involves heavy manual or physical work	FALSE	-0.45	7.4e-14
Age completed full time education	Leg fat percentage (right)	FALSE	-0.37	7.5e-14
Age completed full time education	Average weekly red wine intake	FALSE	0.39	3.4e-13
Whole body fat mass	Age completed full time education	FALSE	-0.10	3.4e-13
Age completed full time education	Body mass index (BMI)	FALSE	-0.35	4.5e-13
Age completed full time education	Home location - north co-ordinate (rounded)	FALSE	-0.24	1.3e-12
Age completed full time education	Body mass index (BMI)	FALSE	-0.35	2.0e-12
Arm fat mass (right)	Age completed full time education	FALSE	-0.098	2.9e-12
Age completed full time education	Overall health rating	FALSE	-0.30	1.3e-11

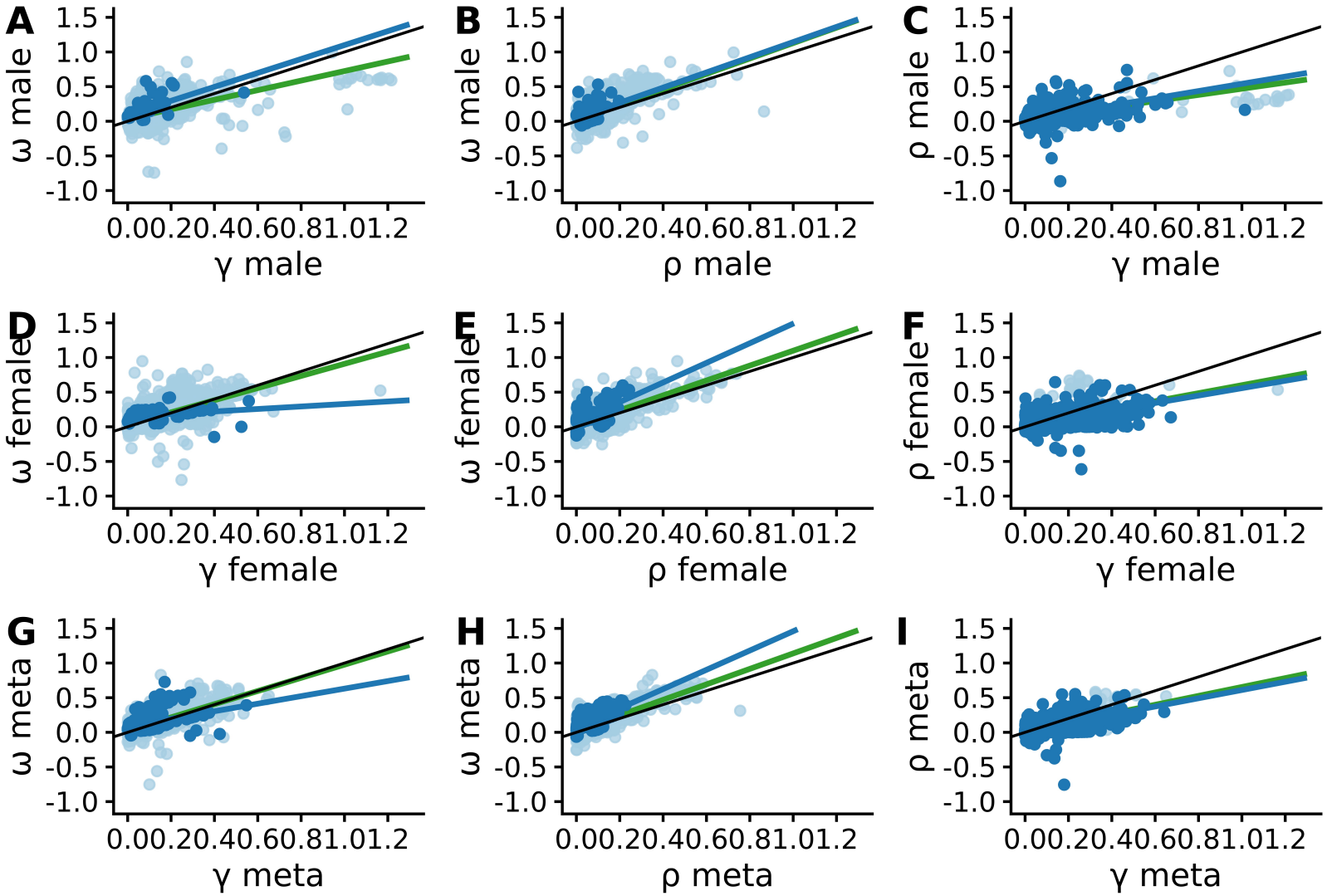
exposure_description	outcome_description	same_trait	IVW_meta_beta	IVW_meta_pval
Alcohol intake frequency.	Alcohol intake frequency.	TRUE	0.26	4.4e-32
Body mass index (BMI)	Alcohol intake frequency.	FALSE	0.11	3.1e-22
Body mass index (BMI)	Alcohol intake frequency.	FALSE	0.11	1.4e-20
Time spent watching television (TV)	Alcohol intake frequency.	FALSE	0.37	2.1e-20
Average total household income before tax	Alcohol intake frequency.	FALSE	-0.29	3.1e-20
Leg fat percentage (left)	Alcohol intake frequency.	FALSE	0.13	5.3e-20
Leg fat percentage (right)	Alcohol intake frequency.	FALSE	0.12	8.2e-18
Arm fat percentage (right)	Alcohol intake frequency.	FALSE	0.11	1.3e-17
Arm fat mass (left)	Alcohol intake frequency.	FALSE	0.10	1.2e-16
Leg fat mass (right)	Alcohol intake frequency.	FALSE	0.10	1.3e-16
Leg fat mass (left)	Alcohol intake frequency.	FALSE	0.10	4.5e-16
Arm fat mass (right)	Alcohol intake frequency.	FALSE	0.099	1.7e-15
Arm fat percentage (left)	Alcohol intake frequency.	FALSE	0.10	5.2e-15
Body fat percentage	Alcohol intake frequency.	FALSE	0.10	3.4e-14
Whole body fat mass	Alcohol intake frequency.	FALSE	0.090	9.8e-13
Usual walking pace	Alcohol intake frequency.	FALSE	-0.47	2.8e-12
Average weekly red wine intake	Alcohol intake frequency.	FALSE	-0.48	3.4e-12
Trunk fat mass	Alcohol intake frequency.	FALSE	0.087	3.8e-12
Job involves heavy manual or physical work	Alcohol intake frequency.	FALSE	0.35	1.3e-10
Alcohol intake frequency.	Leg fat percentage (right)	FALSE	0.15	8.4e-10
Fluid intelligence score	Alcohol intake frequency.	FALSE	-0.15	1.4e-09
Alcohol intake frequency.	Average weekly red wine intake	FALSE	-0.18	1.7e-09
Age completed full time education	Alcohol intake frequency.	FALSE	-0.27	4.3e-09
Alcohol intake frequency.	Leg fat percentage (left)	FALSE	0.15	4.5e-09
Alcohol intake frequency.	Fluid intelligence score	FALSE	-0.22	9.2e-09
Alcohol intake frequency.	Leg fat mass (right)	FALSE	0.14	5.1e-08
Alcohol intake frequency.	Body fat percentage	FALSE	0.13	6.8e-08
Alcohol intake frequency.	Leg fat mass (left)	FALSE	0.14	1.3e-07
Alcohol intake frequency.	Job involves heavy manual or physical	FALSE	0.16	5.2e-07


U
G_i
SNP-exposure effect
X_{index}
$\alpha_{x_i \to y_p}$
$Y_{partner}$
SNP-outcome effect (on partner)


group
body
diet
disease_proxy
lifestyle

Comparison of paths from index to partner $(X_i \rightarrow Y_p)$

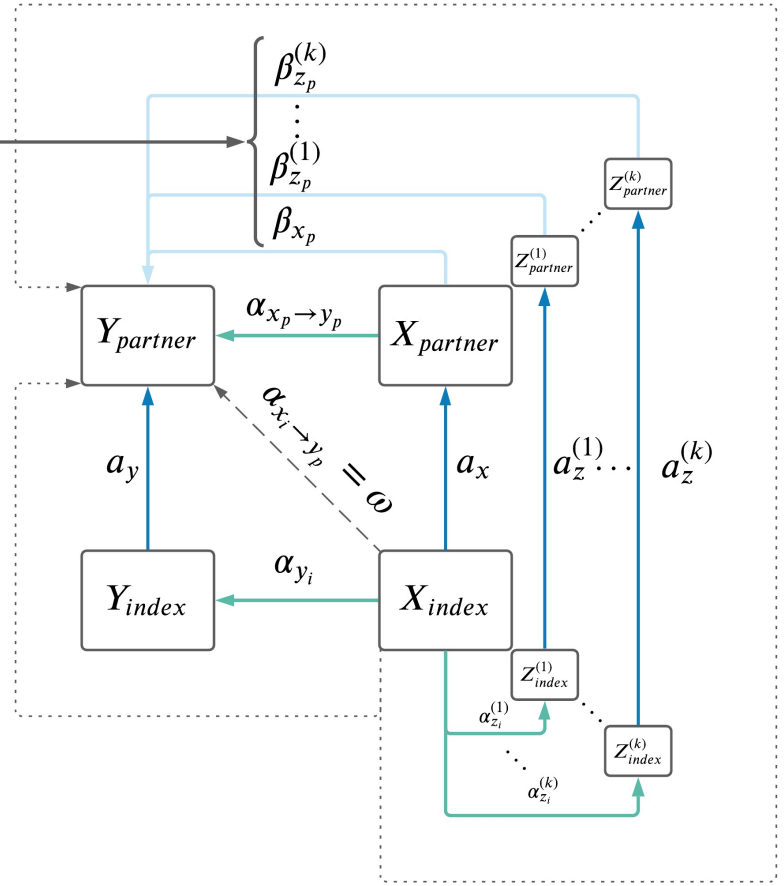




Expanded model allowing for indirect effects

$$Y_p = \beta_{x_p} X_p + \beta_{z_p}^{(1)} Z_p^{(1)} + \ldots + \beta_{z_p}^{(k)} Z_p^{(k)} + \varepsilon$$

$$a_x \beta_{x_p} + \sum_{j=1}^{k} \alpha_{z_i}^{(j)} a_z^{(j)} \beta_{z_p}^{(j)} = \gamma$$



$$\alpha_{y_i} a_y = \rho$$

Next steps

- Expand to MV model to allow for indirect effects.
- Include dietary summary variables?
- Examine impact of geography (specifically with genetic PCs).
- Include binary traits (i.e. diseases)?