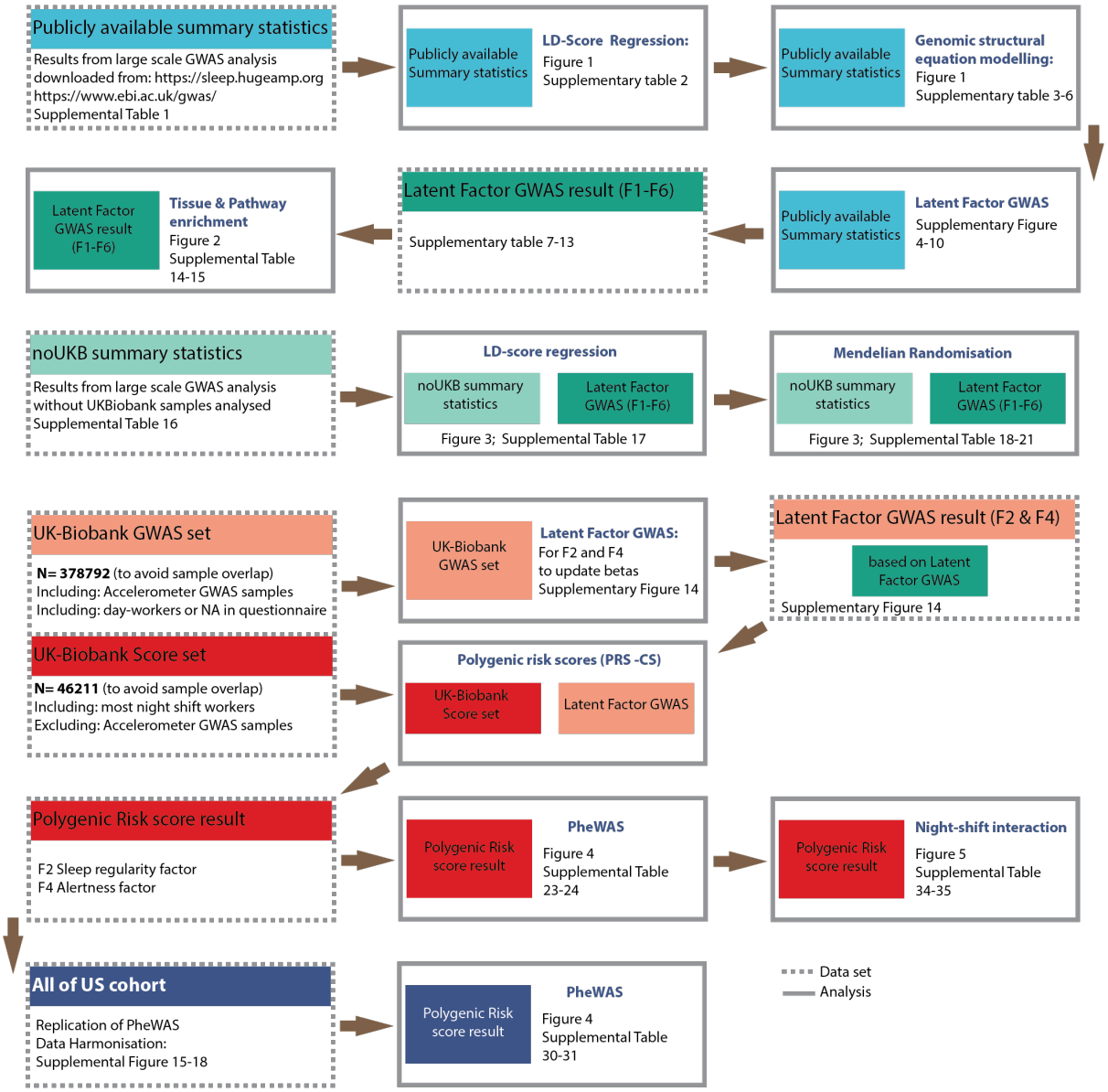
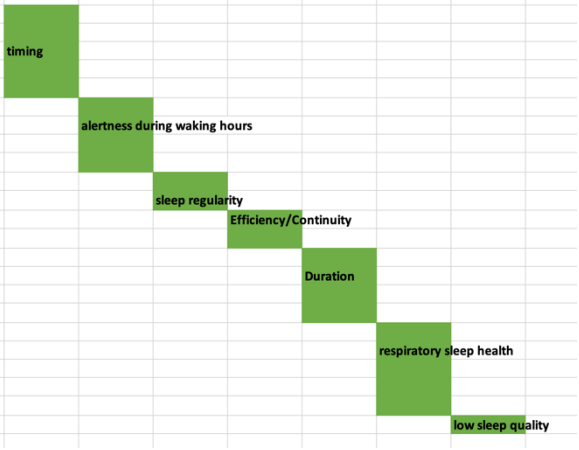


Supplemental Figure 1: Study flow and dataset overview. This diagram illustrates the analytical workflow, showing how each dataset was used within the specific analyses. It also maps each analysis to the corresponding result tables in the supplemental data and to figures in the main text or supplemental materials. Dotted outlines indicate datasets or key results generated in this study. Grey-framed boxes represent the analyses performed on each dataset.

5 factor model

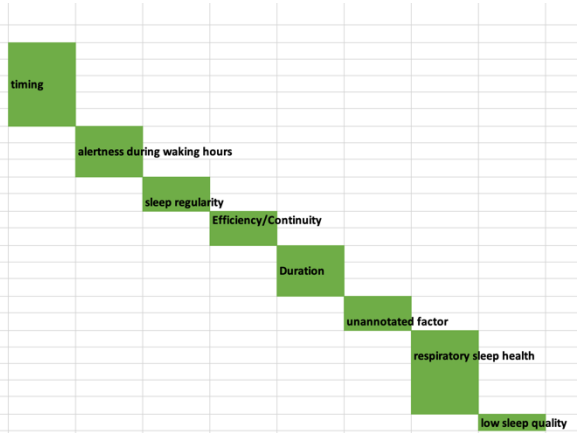
	GLS1	GLS4	GLS5	GLS3	GLS2
SR_chronotype	0.97	0.22	-0.36	-0.08	0.04
SR_morning_person	0.96	0.21	-0.37	-0.09	0.06
ACC_SLEEP_MIDP	0.88	0.18	-0.33	-0.06	0.05
ACC_L5_TIME	0.92	0.04	-0.22	-0.02	0.01
ACC_M10_TIME	0.9	0.12	-0.27	-0.21	0.06
SR_DaytimeNapping	-0.03	0.78	0.09	0.1	-0.07
SR_DaytimeSleepiness	-0.03	0.9	-0.02	-0.16	0
SR_DaytimeSleepiness_adjBMI	-0.03	0.87	-0.07	-0.15	0.02
ACC_DIURNAL_INACT	0.05	0.31	0.24	0.18	-0.02
ACC_SLEEP_DUR_SD	-0.06	-0.05	0.73	-0.09	0.16
relativeAmplitude	-0.04	-0.05	0.96	-0.24	0.03
ACC_SLEEP_EFF	0	0.06	0.61	-0.28	0.02
ACC_N_SLEEP_EPISODES	0.01	0.07	0.26	0.08	-0.03
SR_SleepDuration	-0.04	-0.01	0	1	0.05
SR_ShortSleep	-0.03	-0.16	-0.18	0.85	0.04
ACC_SLEEP_DUR	0.05	0.1	-0.34	0.42	0
SR_LongSleep	-0.02	0.23	0.14	0.56	0.05
SnoringBMIadj	0	0.12	-0.13	0.03	0.41
average_spo2	0.01	0.01	0.04	-0.01	0.72
minimum_spo2	-0.02	-0.1	0.16	0.05	0.96
sleep_apnea	-0.01	-0.11	0.05	0.05	1
Per90	0.04	-0.1	0.18	0.02	0.98
SR_Insomnia	0.03	0.28	0.18	-0.47	0.02



Supplemental Figure 2: Five-Factor Model in Exploratory Factor Analysis
The five-factor model closely aligns with the Ru-SATED framework, though we were unable to distinguish between sleep regularity and efficiency based on the data. The six- and seven-factor models are very similar, with the six-factor model introducing a new, unannotated factor. In the seven-factor model, sleep regularity and continuity are successfully separated into distinct factors, but the unannotated factor remains. The numbers represent standardized loadings, ranging from -1 to +1, on each factor.

6 factor model

	GLS1	GLS4	GLS6	GLS3	GLS2	GLS5
ACC_L5_TIME	0.93	0.06	-0.1	0.03	-0.09	0.01
ACC_M10_TIME	0.91	0.15	-0.12	-0.14	-0.17	0.06
SR_chronotype	0.96	0.22	-0.27	-0.07	-0.15	0.03
SR_morning_person	0.96	0.22	-0.27	-0.06	-0.18	0.05
ACC_SLEEP_MIDP	0.89	0.16	-0.3	-0.1	0.03	0.04
SR_DaytimeNapping	-0.01	0.71	0.12	0.01	0.35	-0.08
SR_DaytimeSleepiness	-0.01	0.87	0.14	-0.17	0.14	-0.01
SR_DaytimeSleepiness_adjBMI	-0.01	0.86	0.12	-0.14	0.09	0
relativeAmplitude	-0.06	-0.09	0.7	-0.33	0.28	0.05
ACC_SLEEP_DUR_SD	-0.08	-0.14	0.35	-0.29	0.41	0.18
ACC_SLEEP_EFF	0.02	0.15	0.84	-0.09	-0.17	0.02
ACC_N_SLEEP_EPISODES	0.02	0.11	0.39	0.18	0	-0.03
SR_LongSleep	-0.03	0.14	-0.1	0.37	0.61	0.04
SR_ShortSleep	-0.01	-0.08	0.05	1	0.04	0.03
SR_SleepDuration	-0.03	-0.02	0	0.96	0.42	0.05
ACC_SLEEP_DUR	0.03	-0.04	-0.78	0.11	0.56	0
ACC_DIURNAL_INACT	0.04	0.19	-0.08	-0.07	0.57	-0.02
SnoringBMIadj	0.01	0.17	0.02	0.11	-0.13	0.4
average_spo2	0.01	-0.03	-0.13	-0.11	0.13	0.73
minimum_spo2	-0.02	-0.06	0.13	0.06	-0.01	0.97
sleep_apnea	-0.01	-0.1	-0.06	0.01	0.01	1
Per90	0.04	-0.08	0.09	0	0.03	0.99
SR_Insomnia	0.02	0.2	-0.04	-0.63	0.15	0.02



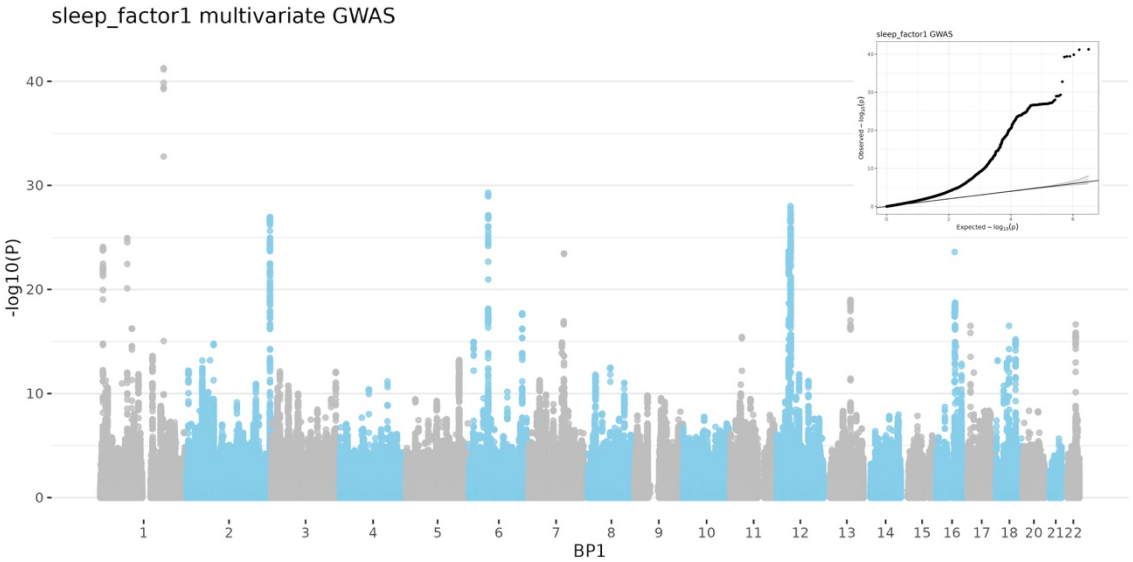
Supplemental Figure 3: Six-Factor Model in Exploratory Factor Analysis
The six-factor model does not introduce any new insights, except for the appearance of an unannotated factor that does not align well with the Ru-SATED model of sleep health.

7 factor model

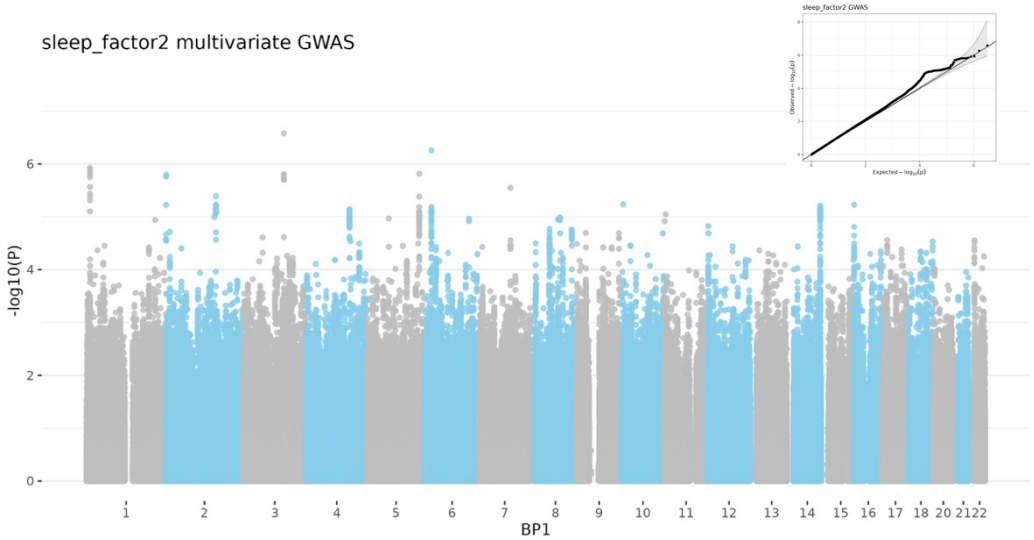
	GLS2	GLS4	GLS1	GLS7	GLS5	GLS6	GLS3
SR_chronotype	0.98	0.08	-0.38	0	-0.15	0.01	0.05
SR_morning_person	0.98	0.08	-0.4	0.01	-0.15	-0.01	0.07
ACC_L5_TIME	0.92	0.05	-0.2	-0.02	0.02	-0.05	0
ACC_M10_TIME	0.89	0.09	-0.28	0.02	-0.17	-0.08	0.06
ACC_SLEEP_MIDP	0.86	0.03	-0.37	0.01	-0.18	0.17	0.06
SR_DaytimeNapping	0	0.71	0.09	0.05	0.06	0.26	-0.09
SR_DaytimeSleepiness	0	1	0.05	-0.05	-0.08	0	-0.04
SR_DaytimeSleepiness_adjBMI	0	0.98	0.01	-0.06	-0.05	-0.04	-0.02
ACC_SLEEP_DUR_SD	-0.01	0.09	1	-0.29	-0.08	0.09	0.13
relativeAmplitude	-0.03	0	0.77	0.25	-0.21	0.07	0.04
ACC_N_SLEEP_EPISODES	0	-0.08	-0.22	0.69	0.07	0.18	0
ACC_SLEEP_EFF	0.02	0.06	0.15	0.83	-0.09	-0.16	0.03
SR_LongSleep	-0.03	0.1	0.09	0.05	0.34	0.6	0.05
SR_ShortSleep	0.01	-0.01	-0.14	0.03	0.86	0.02	0.01
SR_SleepDuration	-0.01	0.03	-0.01	0.08	0.92	0.35	0.03
ACC_SLEEP_DUR	0.01	-0.11	-0.13	-0.52	0.01	0.69	0.01
ACC_DIURNAL_INACT	0.02	0.06	0.08	0.14	-0.15	0.67	0
SnoringBMIadj	0.02	0.18	-0.09	-0.01	0.11	-0.13	0.4
average_spo2	-0.01	-0.08	0.01	-0.02	-0.15	0.17	0.76
minimum_spo2	-0.03	-0.09	0.07	0.12	0.03	0.01	0.97
sleep_apnea	-0.01	-0.08	0.1	-0.08	0.01	0	1
Per90	0.04	-0.07	0.16	0.03	0	0.01	0.98
SR_Insomnia	0	0.09	0.07	0.05	-0.63	0.2	0.05

timing
alertness during waking hours
sleep regularity
Efficiency/Continuity
Duration
unannotated factor
respiratory sleep health
low sleep quality

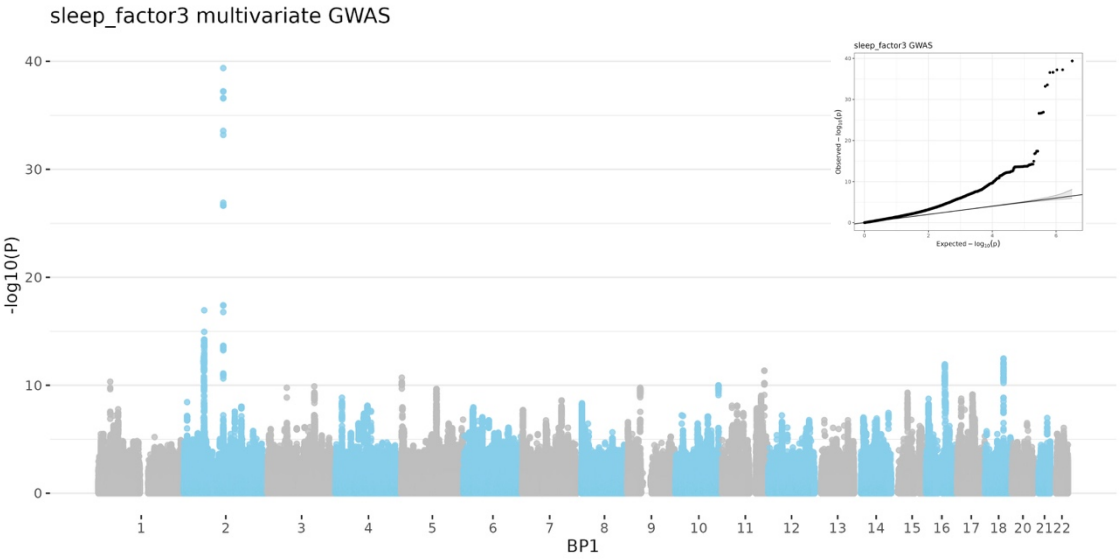
Supplemental Figure 4: Seven-Factor Model in Exploratory Factor Analysis
The seven-factor model successfully separates sleep regularity and efficiency but still includes an unannotated factor that lacks clear interpretation. Additionally, confirmatory factor analysis yielded worse results compared to the five-factor model.



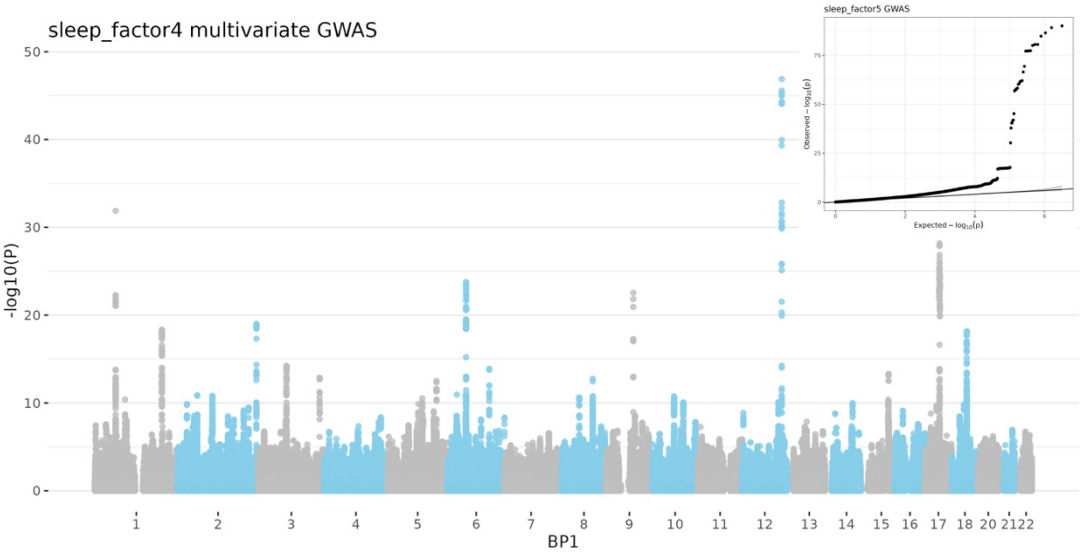
Supplemental Figure 5: GWAS -QC of Factor 1



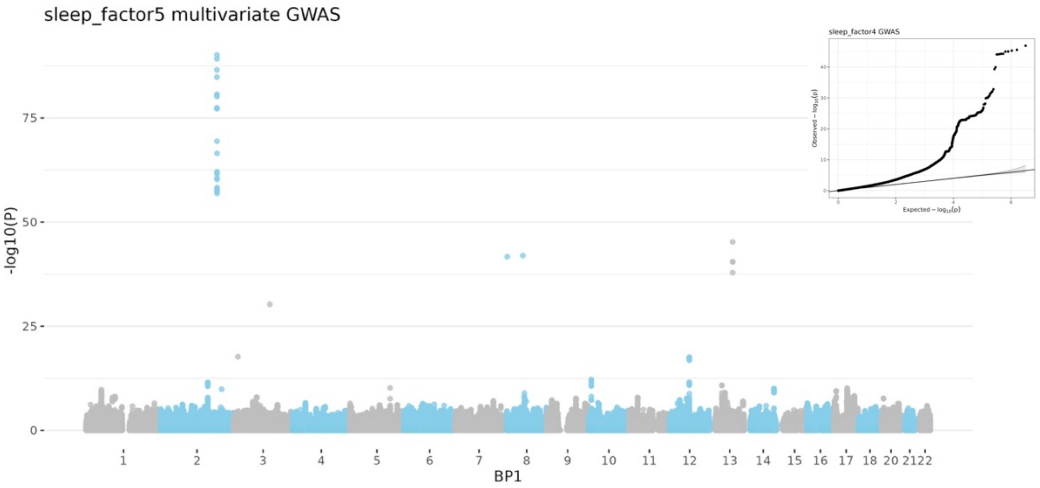
Supplemental Figure 6: GWAS -QC of Factor 2



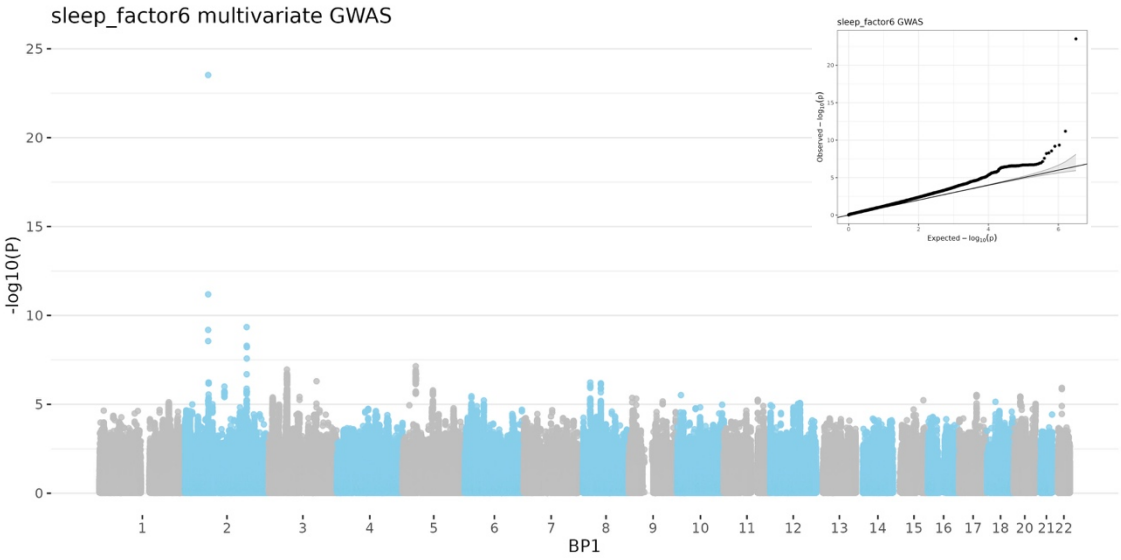
Supplemental Figure 7: GWAS -QC of Factor 3



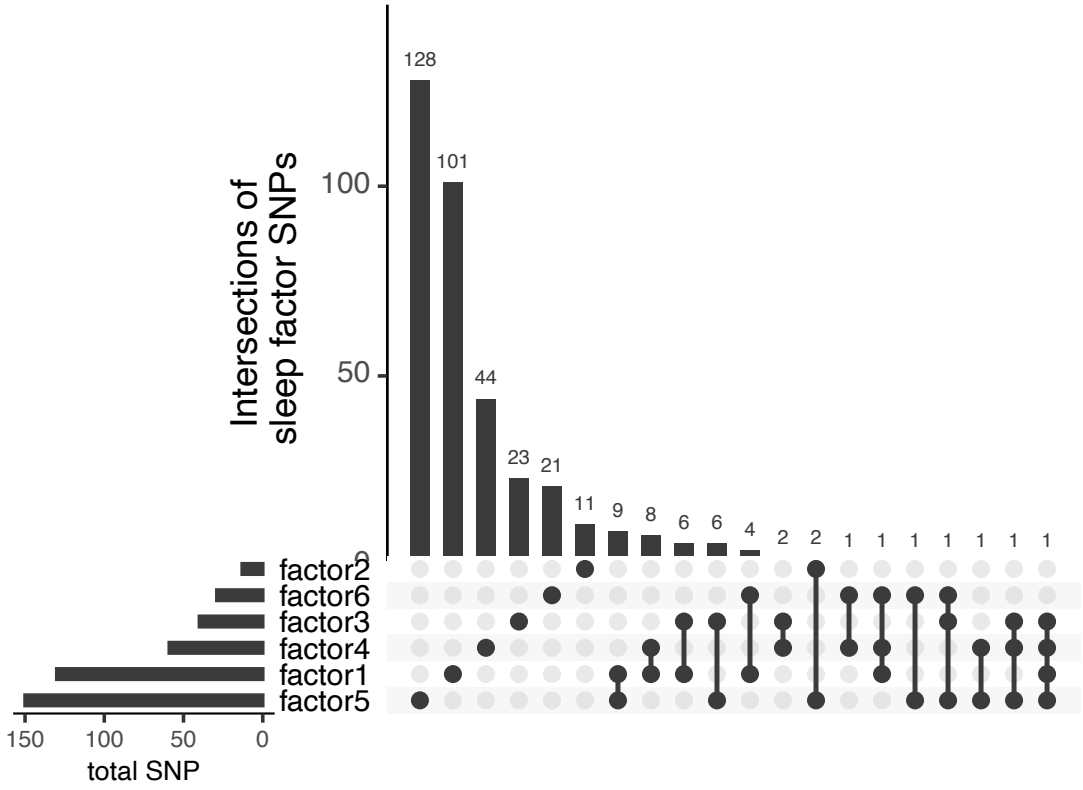
Supplemental Figure 8: GWAS -QC of Factor 4



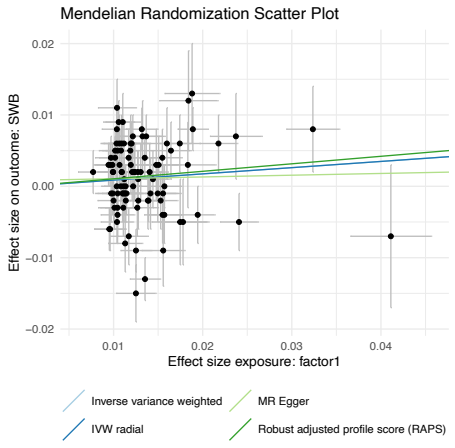
Supplemental Figure 9: GWAS -QC of Factor 5

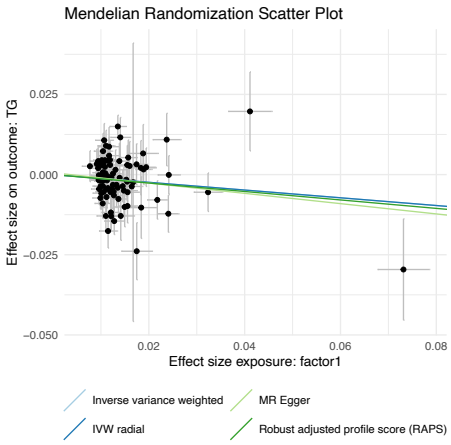


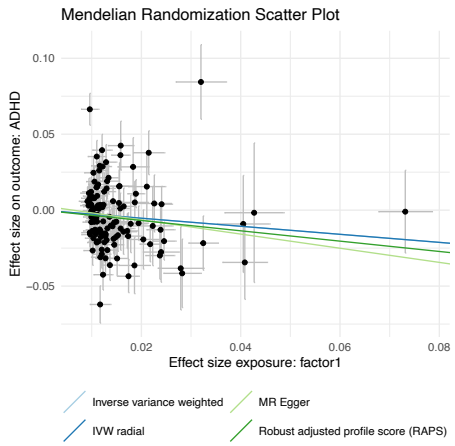
Supplemental Figure 10: GWAS -QC of Factor 6

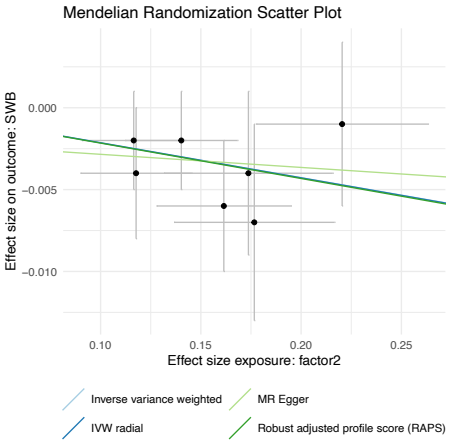


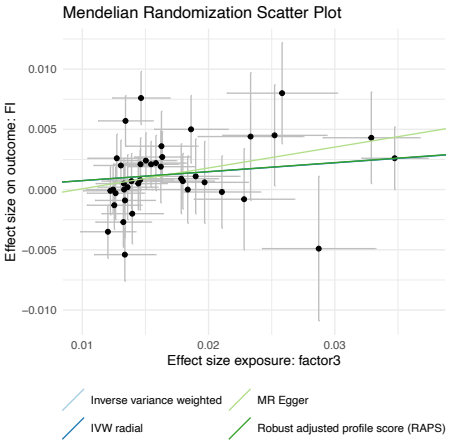
Supplemental Figure 11: overlap of genomic loci between 6 sleep factors

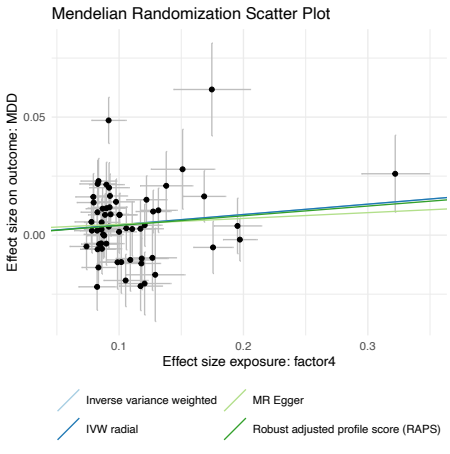

Mendelian Randomization Scatter Plot
Effect size on outcome: SWB
Effect size exposure: factor1
Inverse variance weighted
MR Egger
IVW radial
Robust adjusted profile score (RAPS)

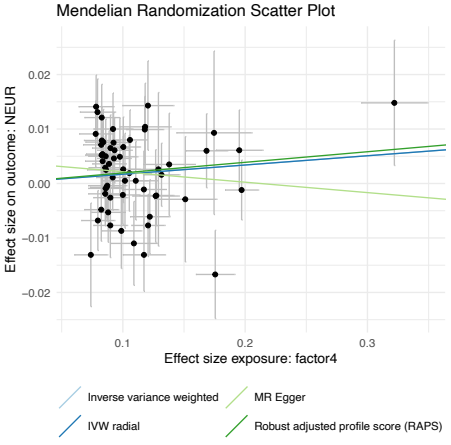

Mendelian Randomization Scatter Plot
Effect size on outcome: TG
Effect size exposure: factor1
Inverse variance weighted
MR Egger
IVW radial
Robust adjusted profile score (RAPS)

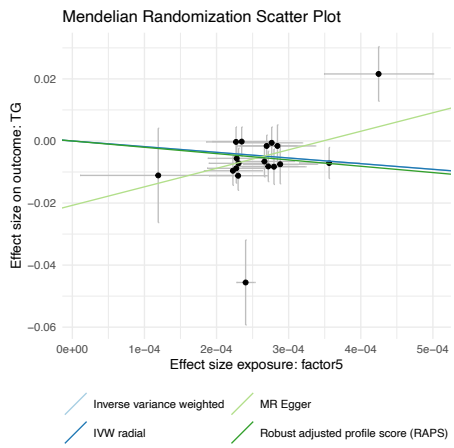

Mendelian Randomization Scatter Plot
Effect size on outcome: ADHD
Effect size exposure: factor1
Inverse variance weighted
MR Egger
IVW radial
Robust adjusted profile score (RAPS)

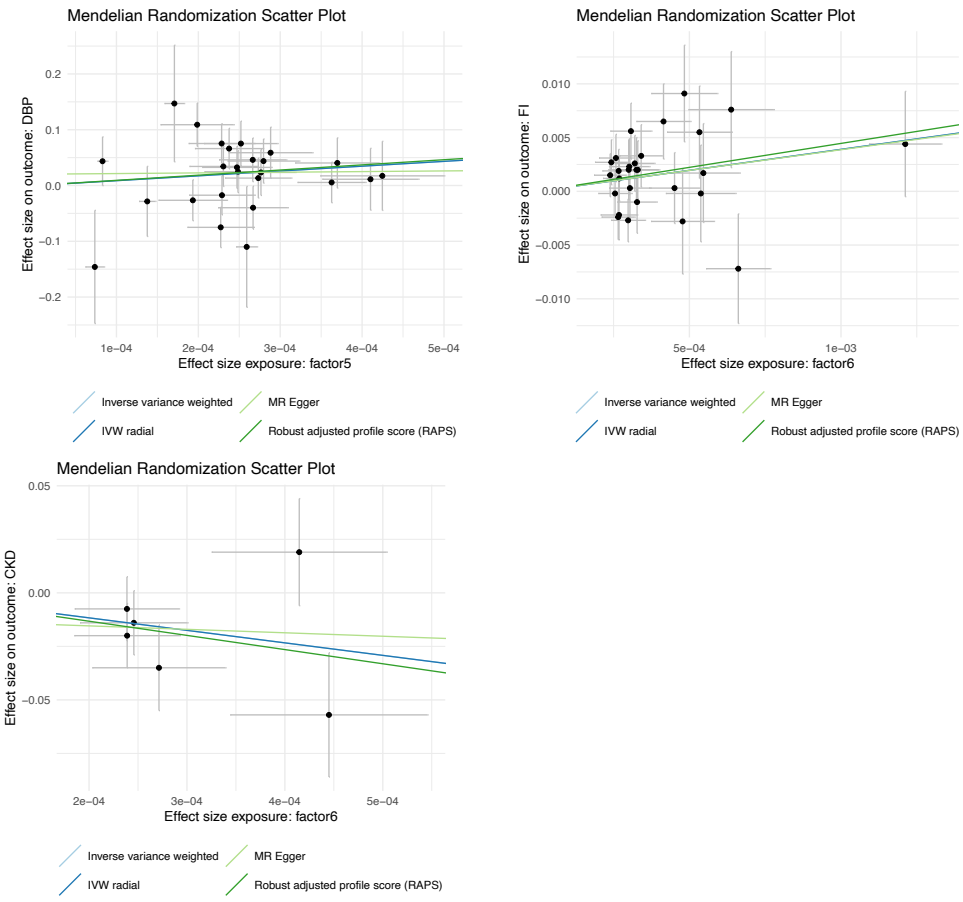

Mendelian Randomization Scatter Plot
Effect size on outcome: SWB
Effect size exposure: factor2
Inverse variance weighted
MR Egger
IVW radial
Robust adjusted profile score (RAPS)


Mendelian Randomization Scatter Plot
Effect size on outcome: FI
Effect size exposure: factor3
Inverse variance weighted
MR Egger
IVW radial
Robust adjusted profile score (RAPS)

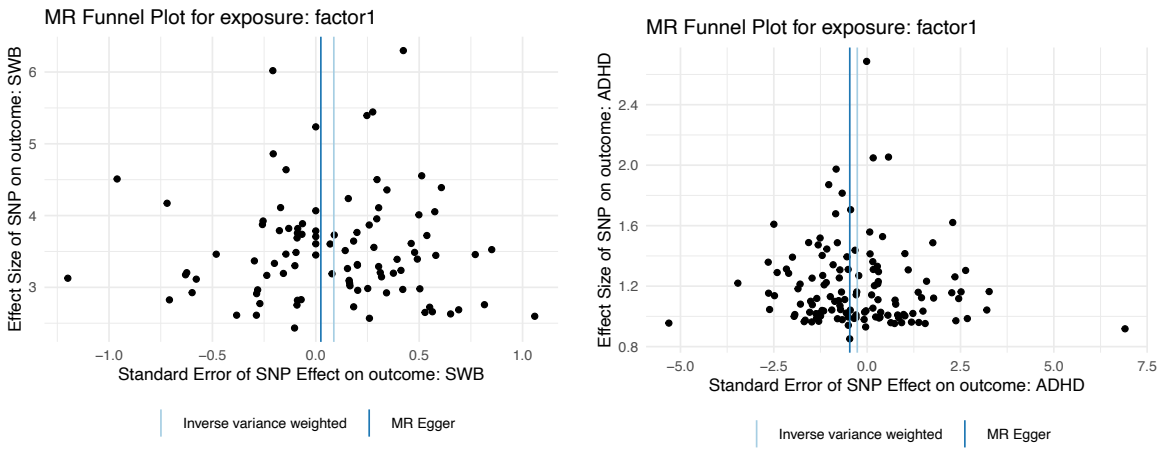

Mendelian Randomization Scatter Plot
Effect size on outcome: MDD
Effect size exposure: factor4
Inverse variance weighted
MR Egger
IVW radial
Robust adjusted profile score (RAPS)

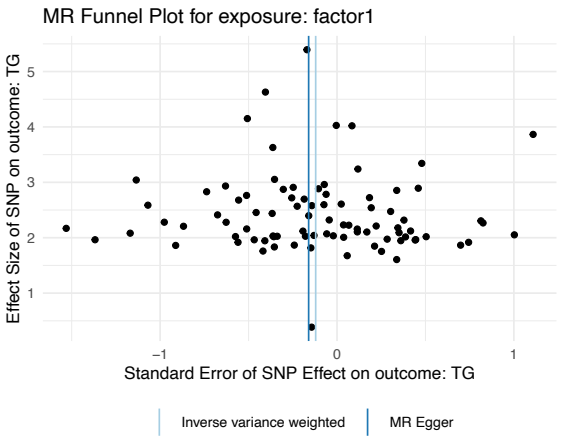

Mendelian Randomization Scatter Plot
Effect size on outcome: NEUR
Effect size exposure: factor4
Inverse variance weighted
MR Egger
IVW radial
Robust adjusted profile score (RAPS)

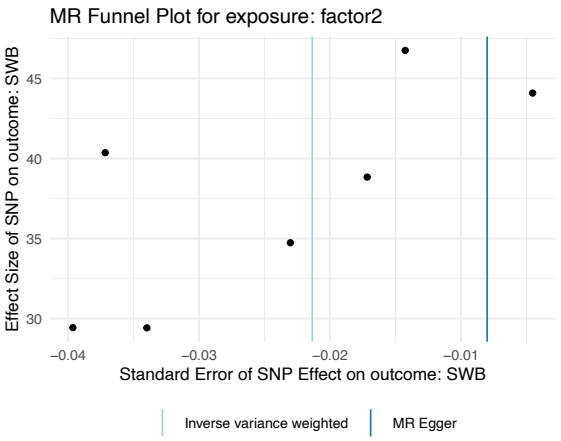

Mendelian Randomization Scatter Plot
Effect size on outcome: TG
Effect size exposure: factor5
Inverse variance weighted
MR Egger
IVW radial
Robust adjusted profile score (RAPS)

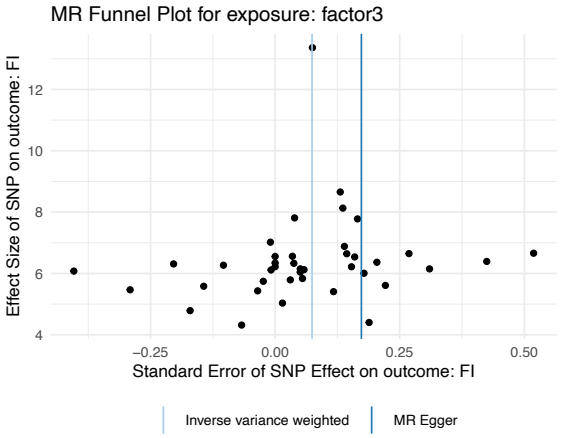


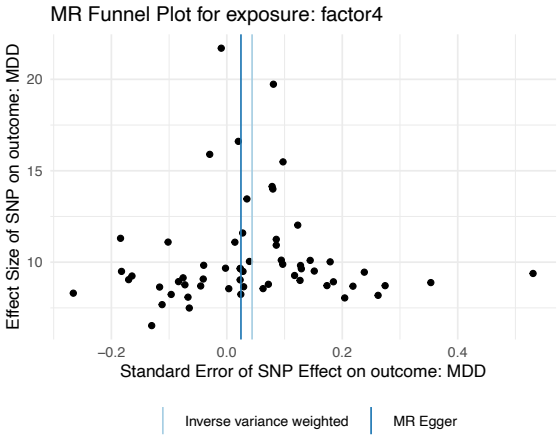
Supplemental Figure 12: Mendelian randomization plots illustrating the potential causal effects of sleep-related factors on cardiometabolic and mental health traits. The x-axis represents the coefficients of the sleep factors (exposures), while the y-axis displays the coefficients of the tested outcomes. Complete results from the MR analysis are detailed in Supplemental Tables 18-22. The plots shown highlight only those effects found to be significant in the MR analysis. These significant findings are also marked with red arrows in Figure 3.

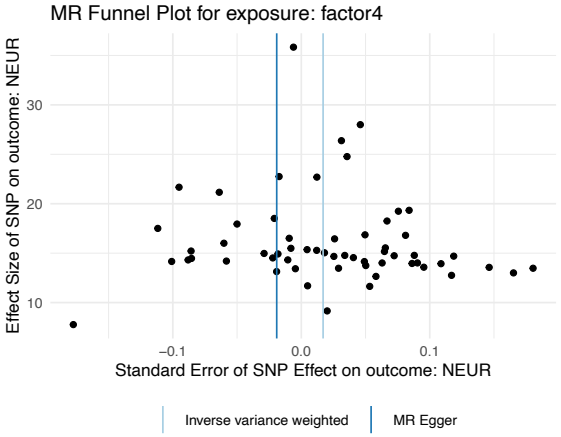


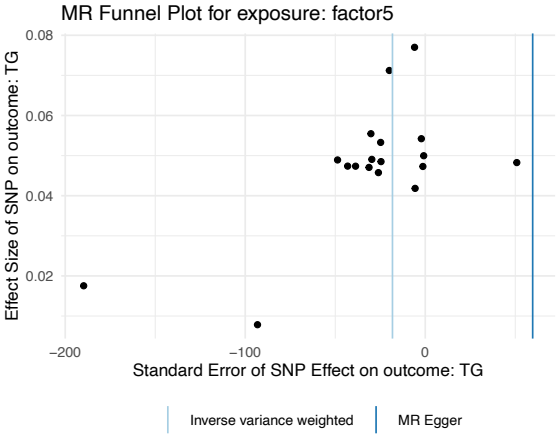

MR Funnel Plot for exposure: factor1
Effect Size of SNP on outcome: TG
Standard Error of SNP Effect on outcome: TG
Inverse variance weighted
MR Egger

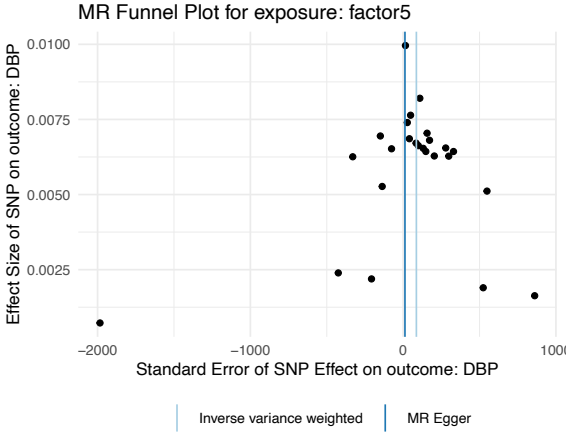

MR Funnel Plot for exposure: factor2
Effect Size of SNP on outcome: SWB
Standard Error of SNP Effect on outcome: SWB
Inverse variance weighted
MR Egger

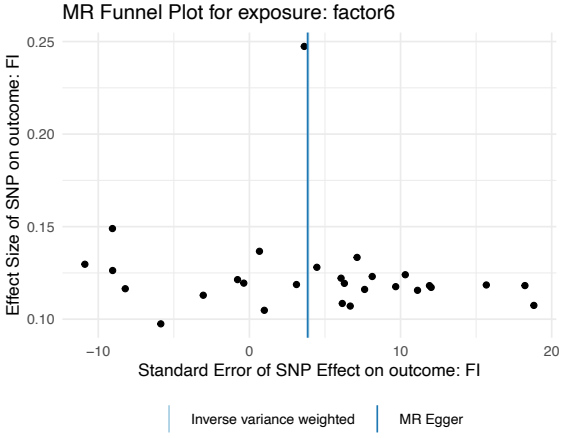

MR Funnel Plot for exposure: factor3
Effect Size of SNP on outcome: FI
Standard Error of SNP Effect on outcome: FI
Inverse variance weighted
MR Egger

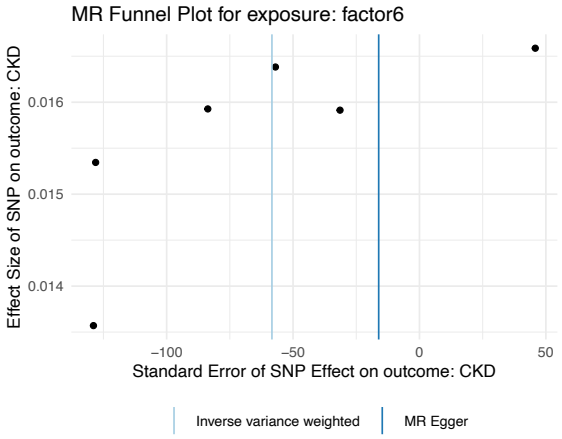

MR Funnel Plot for exposure: factor4
Effect Size of SNP on outcome: MDD
Standard Error of SNP Effect on outcome: MDD
Inverse variance weighted
MR Egger


MR Funnel Plot for exposure: factor4
Effect Size of SNP on outcome: NEUR
Standard Error of SNP Effect on outcome: NEUR
Inverse variance weighted
MR Egger

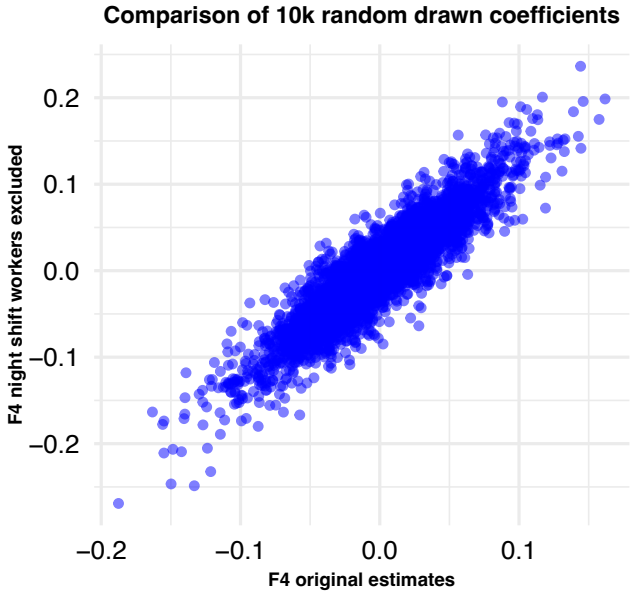

MR Funnel Plot for exposure: factor5
Effect Size of SNP on outcome: TG
Standard Error of SNP Effect on outcome: TG
Inverse variance weighted
MR Egger


MR Funnel Plot for exposure: factor5
Effect Size of SNP on outcome: DBP
Standard Error of SNP Effect on outcome: DBP
Inverse variance weighted
MR Egger

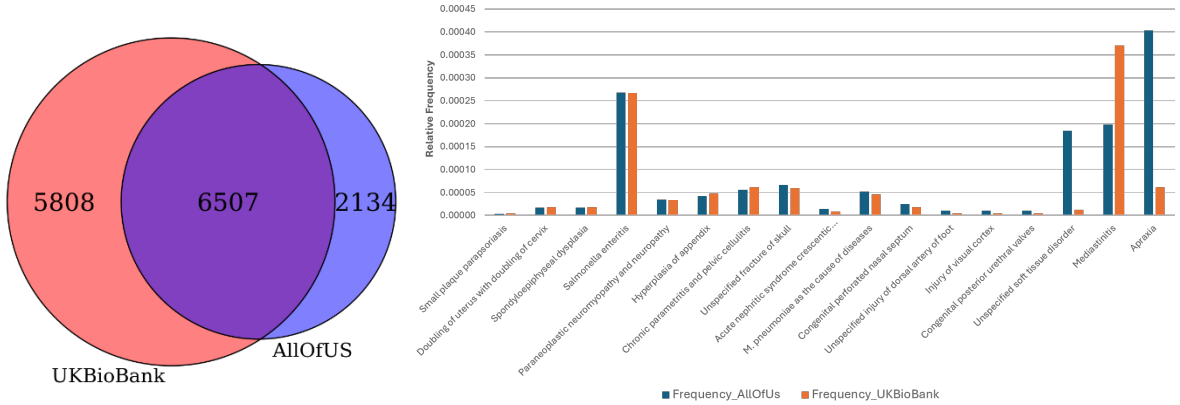

MR Funnel Plot for exposure: factor6
Effect Size of SNP on outcome: FI
Standard Error of SNP Effect on outcome: FI
Inverse variance weighted
MR Egger



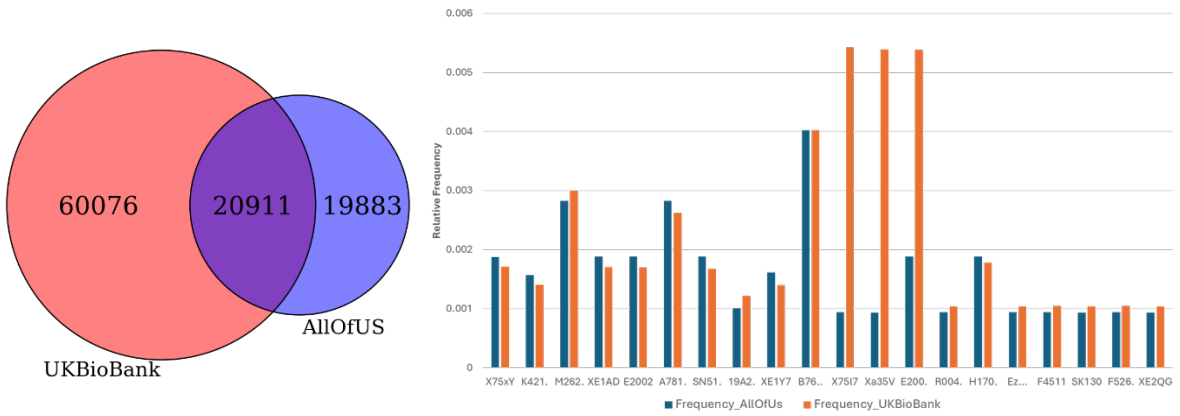
Supplemental Figure 13: Mendelian randomization funnel plots. These plots serve as a quality control (QC) tool. The effect sizes of the genetic instruments in the outcome dataset are plotted on the y-axis, and their standard errors are plotted on the x-axis. Ideally, the distribution of the points should form a symmetrical funnel shape (e.g., Factor 4 vs. MDD). If the points are skewed to one side, this may indicate the presence of directional pleiotropy. Additionally, outliers can be identified as individual points that fall outside the main distribution of the data. Results of all MR sensitivity analyses are provided in Supplemental Tables 18-22.



Supplemental Figure 14: Polygenic risk scores were calculated using the coefficients from genomicSEM, specifically for F2 and F4. To avoid introducing bias, we reran all GWAS for F4 after excluding the UK Biobank samples used in the PheWAS and PRS analyses. The plot compares effect sizes between the full sample and gSEM results from GWAS that excluded night shift workers including a subset of day shift workers.

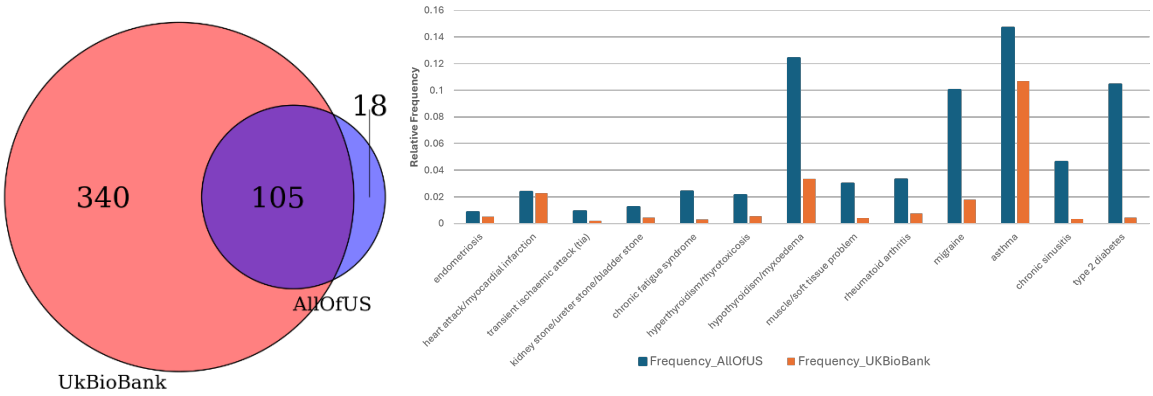


Supplemental Figure 15: ICD-10 code harmonization between the UKBiobank and AllOfUs databases. (A) A total of 6,507 ICD-10 codes are shared between the two datasets, representing 53% of the UKBiobank set and 75% of the AllOfUs set. Due to differences in ICD-10 code formatting, harmonization was performed by adapting AllOfUs codes to match the UKBiobank format. Specifically, AllOfUs uses the standard ICD-10 format (e.g., T50.A91S), whereas UKBiobank encodes only the first four characters without punctuation (e.g., T50A). This simplification results in a loss of specificity, which explains the 2,134 ICD-10 codes found exclusively in AllOfUs. For example, the code T50.A91S in AllOfUs corresponds to the less specific T50A in UKBiobank. Cancer-related ICD-10 codes were excluded from the harmonization process. (B) Barplot of the relative frequencies of selected conditions in the UK Biobank and AllOfUs databases. Most conditions display comparable relative frequencies between the two datasets. However, notable discrepancies are observed: conditions such as *soft tissue disorder* and *apraxia* appear more frequently in AllOfUs, while others, such as *mediastinitis*, show higher frequencies in the UK Biobank.

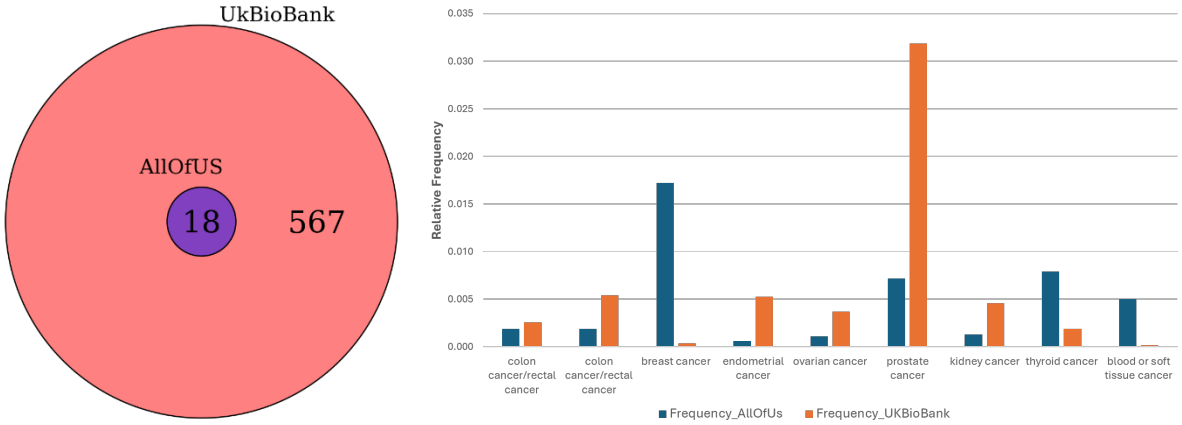


Supplemental Figure 16: CTV3 term harmonization between the UKBiobank and AllOfUs databases. (A) A total of 20,911 CTV3 codes are shared between the two datasets, corresponding to 26% of the UKBiobank set and 51% of the AllOfUs set. The CTV3 (Read v3) coding system is used exclusively in the UK and is considered obsolete in the US, where SNOMED CT has become the standard. Consequently, the harmonization was performed using a mapping table provided by the UK NHS to convert SNOMED CT terms (used in AllOfUs) to their CTV3 equivalents. The CTV3 system is complex, involving a combination of letters,

numbers, and punctuation marks, which complicates interpretation. The 19,883 terms found only in AllOfUs may be due to the inherent limitations and incompleteness of the mapping process, as the US dataset does not natively employ the CTV3 coding system. (B) Barplot of the relative frequencies of some CTV3 terms in the UK Biobank and AllOfUs databases. While many terms exhibit similar relative frequencies across the two datasets, notable discrepancies are observed, particularly in the UK Biobank, where several terms appear with higher frequency. This may be attributed to the native use and broader adoption of the CTV3 coding system within the UK Biobank, as opposed to its indirect mapping in AllOfUs.

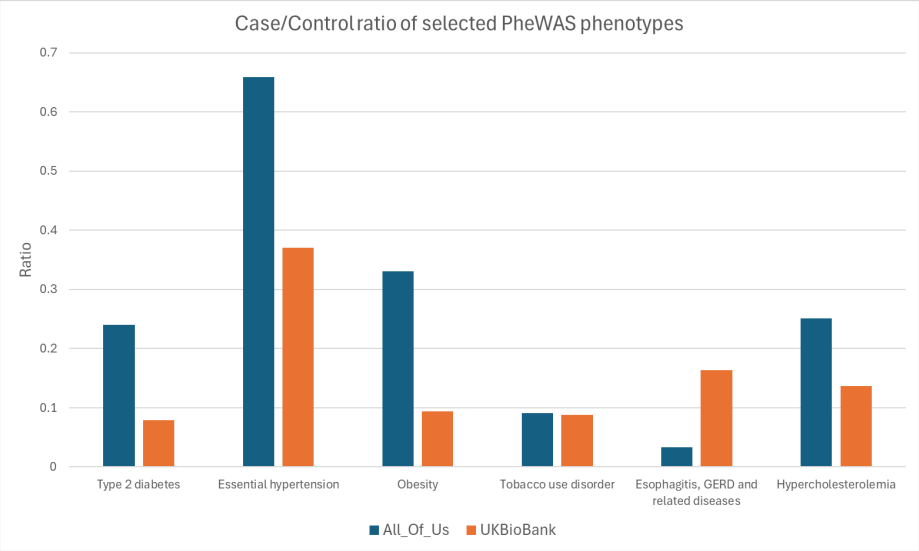


Supplemental Figure 17: Harmonization of self-reported conditions between the UKBioBank and AllOfUs databases. Self-reported conditions in All of Us tend to be less detailed than those in UK Biobank, resulting in a smaller total number of reported conditions. Many specific terms present in UK Biobank are either absent or aggregated in All of Us. Harmonization was performed by mapping AllOfUs conditions to their corresponding Data-Coding 6 codes. A mapping table was derived to align the terms of AllOfUs to the ones of the UKBioBank, ensuring compatibility. The 18 terms private to AllOfUs are the cancer conditions which cannot be encoded by the Data-Coding 6 and which are conseqeuntly excluded. (B) Barplot of the relative frequencies of some self-reported conditions in the UK Biobank and AllOfUs databases. Overall, the conditions always display a higher frequencies in the AllOfUs database.

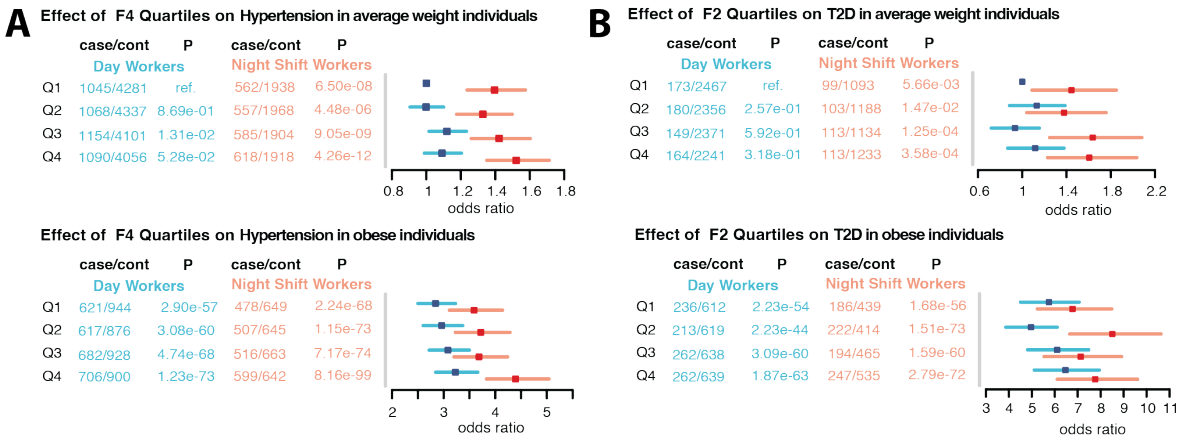


Supplemental Figure 18: Harmonization of cancer-related ICD10 codes between UKBioBank and AllOfUs databases. As the UKBioBank do not includer self-reported cancer condition, harmonization was performed by aligning the self-reported cancer conditions from the

AllOfUs (converted into ICD10 codes) with the full list of cancer-related codes available in the UKBioBank. (B) Barplot of the relative frequencies of some self-reported cancer conditions in the UK Biobank and AllOfUs databases. The two databases never show similar frequencies: generally, the UKBioBank shows higher values, but in cases of *breast cancer*, *thyroid cancer* or *blood cancer*, the AllOfUs shows higher values. These cancer-related conditions in the AllOfUs were isolated from other self-reported conditions (which could be mapped to UKBioBank's Data-Coding 6). Due to the self-reported nature of the cancer conditions, the descriptions are extremly superficial and lack specificity, resulting indeed in a limited number of cancer ICD-10 codes in the dataset.



Supplemental Figure 19: Comparison of selected case–control ratios obtained using the DeepPheWAS package on UK Biobank and All of Us data. Ratios are based on 46,211 UK Biobank participants and 131,729 All of Us participants. Full counts of cases, controls, and missing values are given in Supplemental Tables 23 and 29.



Supplemental Figure 20: Forest plot shows differences in PRS associations across shift work status, obesity and genetic risk strata. Participants were stratified into quartiles based on their scaled PRS for F4 and F2 (Q1–Q4) and categorized as either day or night shift workers. A composite categorical variable (QuartilePRS × ShiftWork x obese) was created with eight levels (e.g., "1_day_non_obese", "4_ever_obese"). Obese was defined as BMI > 30. The

reference group was set to Q1 day workers in normal weight participants. Forest plots display representing the model-estimated association for each stratum and its improvement over the reference group across PRS quartiles,shift work categories and obese and normal weight UKBiobank participants.