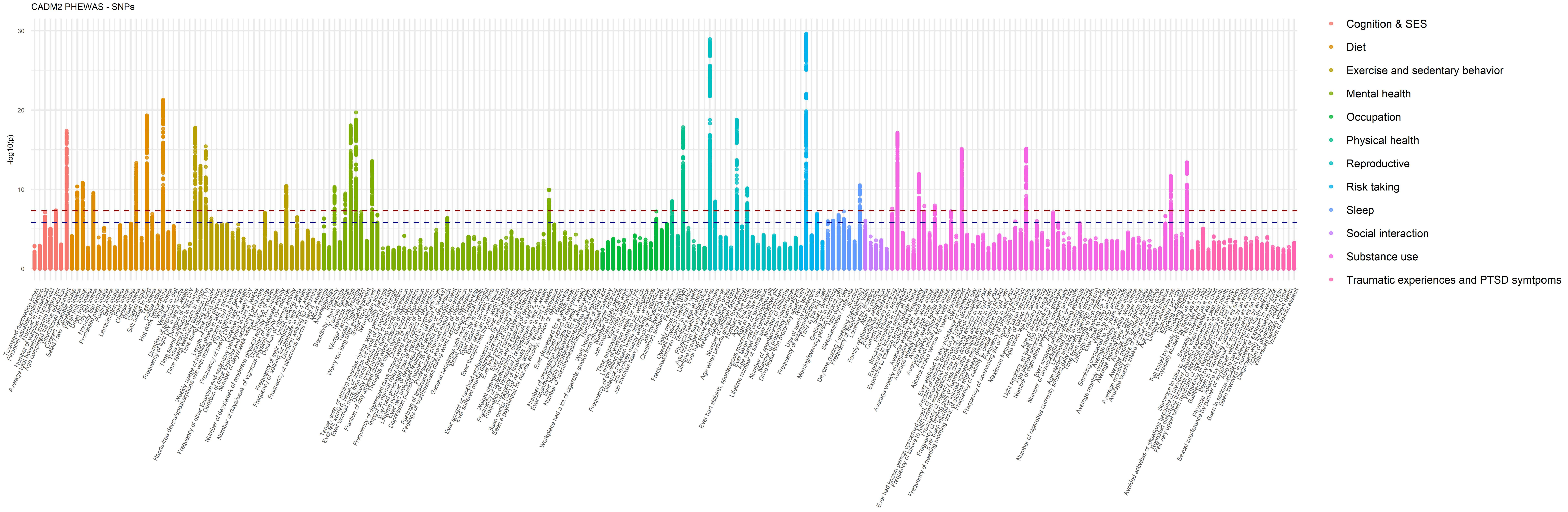
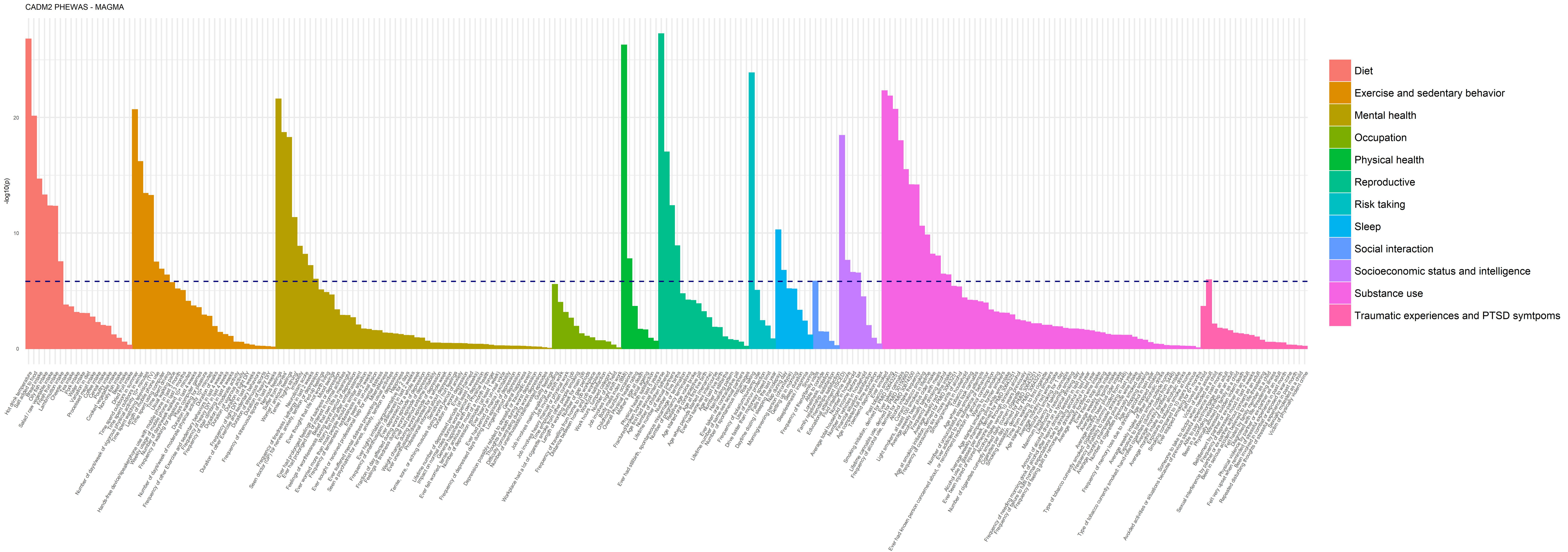
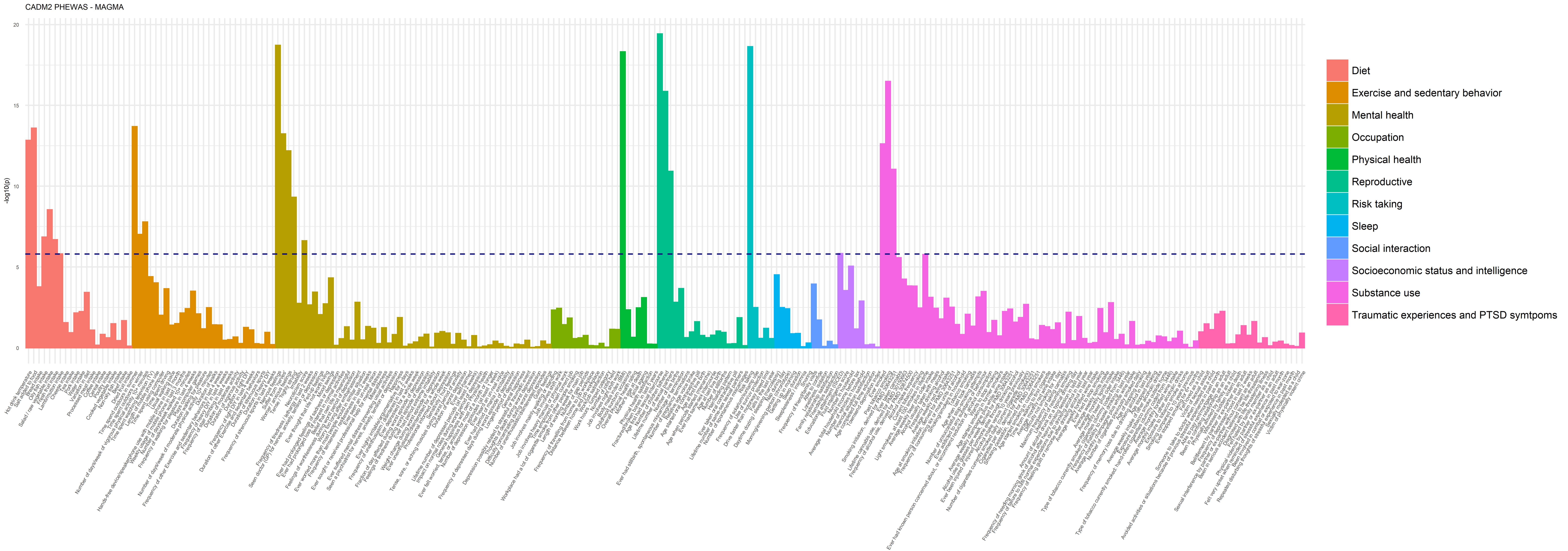
Supplementary Figures

Figure S1. PheWAS results. Panel **a)** shows the associations of the SNP-based test for all 242 traits. The x-axis shows the traits (colored by trait category) and the y-axis the p-values of the association. Each dot represents a SNP association. SNPs exceeding the red horizontal line have a p-value significant at a genome-wide threshold of p=5E-08. The blue horizontal line represents the suggestive threshold of p=1.55E-06. Full SNP-based results are given in Supplementary Figure 1. Panel **b)** shows the results of the MAGMA gene-based test (for all 242 traits), with p-values on the y-axis. The red dotted line represents a threshold of p=2.62E-06. Panel **c)** shows the results of the MAGMA gene-based test (for all 242 traits), after additional correction for MSOA regions (birthplace and current address). p-values on the y-axis. The red dotted line represents a threshold of p=2.62E-06.

Figure S2. Number of significant trait associations per comparison gene (with SNP associations at p<5E-08). On the right the CADM2 gene, the only one with more than 13 trait associations. See Tables S4 and S5 for the association results per comparison gene.


CADM2 PHEWAS - SNPs
-log10(p)
30
20
10
0
Cognition & SES
Diet
Exercise and sedentary behavior
Mental health
Occupation
Physical health
Reproductive
Risk taking
Sleep
Social interaction
Substance use
Traumatic experiences and PTSD symtpoms


CADM2 PHEWAS - MAGMA
-log10(p)
0
10
20
Diet
Exercise and sedentary behavior
Mental health
Occupation
Physical health
Reproductive
Risk taking
Sleep
Social interaction
Socioeconomic status and intelligence
Substance use
Traumatic experiences and PTSD symtpoms
Hot drink temperature
Salt added to food
Bread intake
Oily fish intake
Salad / raw vegetable intake
Fresh fruit intake
Lamb/mutton intake
Cheese intake
Tea intake
Pork intake
Water intake
Variation in diet
Processed meat intake
Coffee intake
Cereal intake
Poultry intake
Cooked vegetable intake
Non-oily fish intake
Beef intake
Dried fruit intake
Time spend outdoors in summer
Time spent outdoors in winter
Number of days/week of vigorous physical activity 10+ minutes
Time spent watching television (TV)
Length of mobile phone use
Time spent using computer
Time spent driving
Usual walking pace
Hands-free device/speakerphone use with mobile phone in last 3 month
Weekly usage of mobile phone in last 3 months
Number of days/week walked 10+ minutes
Frequency of walking for pleasure in last 4 weeks
Plays computer games
Duration walking for pleasure
Number of days/week of moderate physical activity 10+ minutes
Duration of walks
Frequency of other Exercise and sedentary behaviors in last 4 weeks
Frequency of heavy DIY in last 4 weeks
Frequency of stair climbing in last 4 weeks
Duration of moderate activity
Duration of vigorous activity
Duration of light DIY
Frequency of light DIY in last 4 weeks
Duration of other Exercise and sedentary behaviors
Duration of strenuous sports
Duration of heavy DIY
Frequency of strenuous sports in last 4 weeks
Nervous feelings
Suffer from 'nerves'
Worrier / anxious feelings
Tense / 'highly strung'
Irritability
Neuroticism score
Frequency of tiredness / lethargy in last 2 weeks
Seen doctor (GP) for nerves, anxiety, tension or depression
Fed-up feelings
Ever thought that life not worth living
Mood swings
Ever had prolonged feelings of sadness or depression
Ever had prolonged loss of interest in normal activities
Belief that own life is meaningful
Feelings of worthlessness during worst period of depression
Worry too long after embarrassment
Ever worried more than most people would in similar situation
Frequency of tenseness / restlessness in last 2 weeks
Ever seen an un-real vision
Ever sought or received professional help for mental distress
Miserableness
Ever suffered mental distress preventing usual activities
Seen a psychiatrist for nerves, anxiety, tension or depression
Happiness
Ever highly irritable/argumentative for 2 days
Frequency of unenthusiasm / disinterest in last 2 weeks
Ever depressed for a whole week
Fraction of day affected during worst episode of depression
Feelings of tiredness during worst episode of depression
Ever had period extreme irritability
Weight change during worst episode of depression
Ever unenthusiastic/disinterested for a whole week
Professional informed about depression
Sensitivity / hurt feelings
Tense, sore, or aching muscles during worst period of anxiety
Duration of worst depression
Ever self-harmed
Lifetime number of depressed periods (at least 2 weeks)
Impact on normal roles during worst period of depression
General happiness with own Physical health
Ever felt worried, tense, or anxious for most of a month or longer
Number of depression episodes (at least 1 week)
Ever heard an un-real voice
Ever had period of mania / excitability
Frequency of depressed days during worst episode of depression
Longest period of depression
General happiness
Depression possibly related to stressful or traumatic event
Thoughts of death during worst depression
Difficulty concentrating during worst depression
Number of unenthusiastic/disinterested episodes
Guilty feelings
Job involves mainly walking or standing
Job involves shift work
Job involves heavy manual or physical work
Time employed in main current job
Workplace had a lot of cigarette smoke from other people smoking
Length of working week for main job
Number of gap periods
Frequency of travelling from home to job workplace
Distance between home and job workplace
Work/job satisfaction
Work hours - lumped category
Number of jobs held
Job involves night shift work
Body mass index (BMI)
Childhood sunburn occasions
Overall Physical health rating
Mother's age at death
Facial ageing
Physical health satisfaction
Fractured/broken bones in last 5 years
Age first had sexual intercourse
Number of children fathered
Lifetime number of sexual partners
Number of live births
Ever had stillbirth, spontaneous miscarriage or termination
Number of pregnancy terminations
Relative age voice broke
Age started oral contraceptive pill
Age at first live birth
Age when periods started (menarche)
Ever had same-sex intercourse
Age at last live birth
Number of stillbirths
Hair/balding pattern
Ever taken oral contraceptive pill
Lifetime number of same-sex sexual partners
Number of spontaneous miscarriages
Risk taking
Frequency of solarium/sunlamp use
Use of sun/uv protection
Drive faster than motorway speed limit
Falls in the last year
Daytime dozing / sleeping (narcolepsy)
Nap during day
Morning/evening person (chronotype)
Getting up in morning
Sleep duration
Sleeplessness / insomnia
Snoring
Frequency of friend/family visits
Able to confide
Loneliness, isolation
Family relationship satisfaction
Friendships satisfaction
Educational attainment (ISCED)
Fluid intelligence score
Number in household
Average total household income before tax
Number of vehicles in household
Financial situation satisfaction
Age completed full time education
Townsend deprivation index
Ever smoked
Past tobacco smoking
Smoking initiation, derived for PMID 30643251
Ever taken cannabis
Lifetime cannabis use, derived for PMID 30150663
Frequency of alcohol use, derived for PMID 30874500
Alcohol intake frequency
Current tobacco smoking
Light smokers, at least 100 smokes in lifetime
Average weekly beer plus cider intake
Alcohol usually taken with meals
Frequency of drinking alcohol
Average weekly red wine intake
Age at smoking initiation, derived for PMID 30643251
Frequency of consuming six or more units of alcohol
Smoking/smokers in household
Tobacco smoking
Age when last took cannabis
Number of unsuccessful stop-smoking attempts
Ever addicted to any substance or behaviour
Ever had known person concerned about, or recommend reduction of, alcohol consumption
Wants to stop smoking
Age started smoking in former smokers
Average weekly champagne plus white wine intake
Alcohol use in glasses per week, derived for PMID 30643251
Ever been injured or injured someone else through drinking alcohol
Alcohol intake versus 10 years previously
Number of cigarettes currently smoked daily (current cigarette smokers)
Cigarettes per day, derived for PMID 30643251
Smoking cessation, derived for PMID 30643251
Time from waking to first cigarette
Age started smoking in current smokers
Average monthly red wine intake
Difficulty not smoking for 1 day
Maximum frequency of taking cannabis
Likelihood of resuming smoking
Amount of alcohol drunk on a typical drinking day
Frequency of needing morning drink of alcohol after heavy drinking session in last year
Frequency of failure to fulfil normal expectations due to drinking alcohol in last year
Frequency of feeling guilt or remorse after drinking alcohol in last year
Average weekly fortified wine intake
Ever tried to stop smoking
Average weekly spirits intake
Average monthly spirits intake
Average monthly beer plus cider intake
Type of tobacco currently smoked: cigarettes (dummy coded from 3446)
Frequency of inability to cease drinking in last year
Average monthly champagne plus white wine intake
Number of cigarettes previously smoked daily
Age of stopping smoking
Frequency of memory loss due to drinking alcohol in last year
Age stopped smoking
Average weekly intake of other alcoholic drinks
Exposure to tobacco smoke outside home
Type of tobacco currently smoked: hand-rolled cigarettes (dummy coded from 3446)
Average monthly fortified wine intake
Average monthly intake of other alcoholic drinks
Exposure to tobacco smoke at home
Smoking compared to 10 years previous
Ever stopped smoking for 6+ months
Someone to take to doctor when needed as a child
Felt loved as a child
Avoided activities or situations because of previous stressful experience in past month
Victim of sexual assault
Able to pay rent/mortgage as an adult
Been in a confiding relationship as an adult
Physically abused by family as a child
Witnessed sudden violent death
Belittlement by partner or ex-partner as an adult
Sexual interference by partner or ex-partner without consent as an adult
Frequency of depressed mood in last 2 weeks
Been in serious accident believed to be life-threatening
Felt hated by family member as a child
Diagnosed with life-threatening illness
Physical violence by partner or ex-partner as an adult
Felt very upset when reminded of stressful experience in past month
Been involved in combat or exposed to war-zone
Sexually molested as a child
Repeated disturbing thoughts of stressful experience in past month
Victim of physically violent crime


CADM2 PHEWAS - MAGMA
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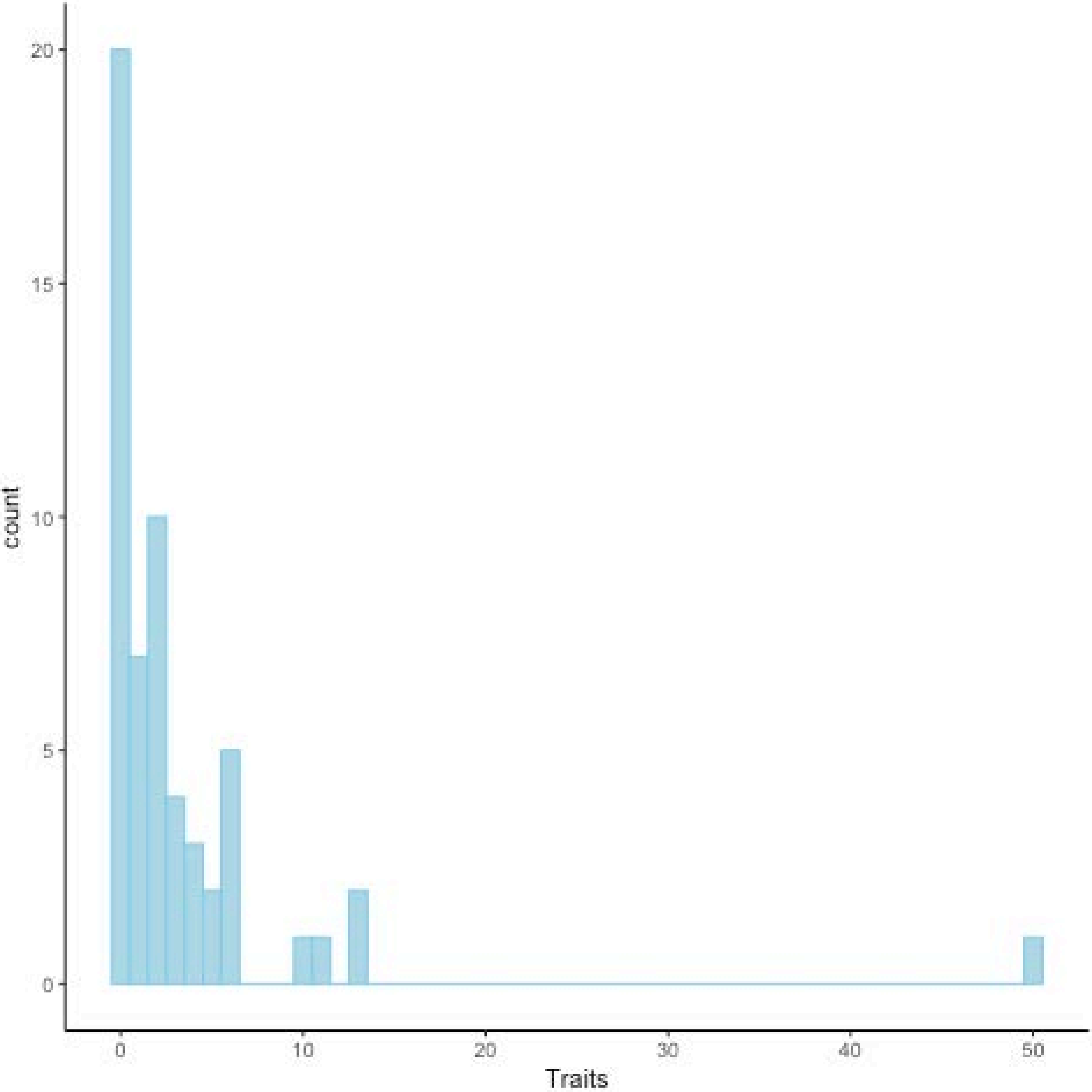
Traumatic experiences and PTSD symtpoms


count
20
15
10
5
0
0
10
20
30
40
50
Traits