Case and control definitions for the UK Biobank Mental Health questionnaire (MHQ1)

Tables refer to the tables in results section and supplementary material of Davis et al. *Mental Health in UK Biobank – development, implementation and results from an online questionnaire completed by 157,366 participants.*

Control definitions are fairly stringent, for applications where higher certainty that control groups do not contain cases is required. For the above paper, non-caseness was used rather than the control definitions below, and this may be preferred for many purposes.

Tables	**Disorder / Exposure**	**Rule in English**	**Fields and codes**	**Notes and references**
Mood disorder				
All	Depression	**Case: Depression ever.** At least one core symptom of depression, most or all of the day on most or all days for a two week period, with at least five depressive symptoms that represent a change from usual occurring over the same time-scale, with some or a lot of impairment.	Persistent sadness (20446) = Yes OR Loss of interest (20441) = Yes AND How much of day (20436) = Most of day or All day long AND Did you feel this way (20439) = Almost every day or Every day AND Impairment (20440) = Somewhat or A lot AND Total number of symptoms endorsed (core and others) >= 5 • Persistent sadness (core) 20446; Loss of interest (core) 20441; Tired or low energy 20449; Gain or loss of weight 20536 = Gain, Loss or Gain and loss; Sleep change 20532; Trouble concentrating 20435; Feeling worthless 20450; Thinking about death 20437	CIDI-SF (Composite International Diagnostic Interview – Short Form), depression module, lifetime version. Scored based on DSM definition of major depressive disorder *Kessler RC, Andrews G, Mroczek D, Ustun B, Wittchen HU. The World Health Organization composite international diagnostic interview short-form (CIDI-SF). Int J Methods Psychiatr Res. 1998;7(4):171-85.*
MD1, MD2, MD3	Depression	**Case: Subthreshold depressive symptoms ever.** Does not meet diagnostic criteria for depression on the CIDI, but has at least one of: (i) endorses persistent depression or anhedonia on CIDI; (ii) PHQ-9 (current depressive symptoms) is over threshold for mild depression; (iii) reports clinician diagnosis of depression	NOT Case {depression ever} AND ((reported diagnosis of depression 20544 or 20002) OR Core symptoms from above OR PHQ score >5)	Case plus control plus subthreshold should include all participants with valid responses Subthreshold symptoms may have clinical significance *National Institute for Health and Clinical Excellence. Depression in adults: recognition and management. NICE Clinical Guideline CG90 (available at https://www.nice.org.uk/guidance/cg90) 2009 (updated 2016).*
nil	Depression	**Control: Depression ever.** Not endorsing depression or screening positive on PHQ or CIDI	NOT (reported diagnosis of depression 20544 or 20002) AND NOT Core symptoms from above AND PHQ score ≤5	Case plus control plus subthreshold should include all participants with valid responses. By excluding subthreshold symptoms, we can be confident that this group has not experienced a classical depressive episode
MD1, MD2, MD3	Depression	**Case: Depression single episode.**	Case {depression ever} AND Number of episodes (20442)=1 AND NOT case {bipolar type I}	Single episode, recurrent depression and bipolar type I should include all depression cases with valid responses

			Excluded if number of episodes missing or bipolar state missing	
MD1, MD2, MD3	Depression	**Case: Recurrent depression.**	{depression ever} AND Number of episodes (20442) >1 or -999 (too many to count) AND NOT case {bipolar type I} Excluded if number of episodes missing or bipolar state missing	Single episode, recurrent depression and bipolar type I should include all depression cases with valid responses
nil	Depression	***Variant: Depression single episode triggered by loss***	{depression single episode} AND worst depression start within two months of traumatic event (20447) = yes	Cases of single episode triggered by loss could be selectively excluded for some analyses, although likely to exclude some true cases of major depressive episode
MD3	Depression	**Score: PHQ-9.** score items 0-4 and sum (Little interest or pleasure in doing things 20514, Feeling down, depressed, or hopeless 20510, Trouble sleeping 20517, Feeling tired 20519, Poor appetite or overeating 20511, Feeling bad about yourself 20507, Trouble concentrating 20508, Moving or speaking slowly or fidgety or restless 20518, Thoughts that you would be better off dead 20513)	("20514, 20510, 20517, 20519, 20511, 20507, 20508, 20518, 20513") (subtract 9 if items scored 1-5) If value missing, count as "0" when scoring 0-4	*Kroenke K, Spitzer RL, Williams JB, Löwe B. The patient health questionnaire somatic, anxiety, and depressive symptom scales: a systematic review. Gen Hosp Psychiatry. 2010;32(4):345-59.*
nil	Depression	**Case: Current depression.** PHQ +ve and CIDI+ve Reports symptoms in the last two weeks that have bothered them. Current depression is indicated by five or more items marked to bother at or above a certain intensity: "more than half of days" for first eight items, "some days" for last item.	{depression ever} AND Little interest or pleasure in doing things 20514 more than half days OR Feeling down, depressed, or hopeless 20510 more than half days AND Total symptoms endorsed as occurring more than half days (or some or more days for last item) ≥ 5 • Little interest or pleasure in doing things 20514, Feeling down, depressed, or hopeless 20510, Trouble sleeping 20517, Feeling tired 20519, Poor appetite or overeating 20511, Feeling bad about yourself 20507, Trouble concentrating 20508, Moving or speaking slowly or fidgety or restless 20518, Thoughts that you would be better off dead 20513	For identifying likely depression, can use "diagnostic algorithm" based on DSM criteria, alternatively total score. This is using "diagnostic algorithm" *Manea L, Gilbody S, McMillan D. Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): a meta-analysis. CMAJ. 2012;184(3):E191-E6*
nil	Depression	**Control: Current depression.** PHQ score ≤5	PHQ score ≤5	A score of above 5 on PHQ can be used as a cut-off for mild depression. Therefore this control group excludes people with possible mild depression, as well as those who meet full criteria in the diagnostic algorithm. *Manea L, Gilbody S, McMillan D. Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): a meta-analysis. CMAJ. 2012;184(3):E191-E6*

nil	Depression	***Variant: Current severe depression*** *As current depression (above) with PHQ score > 15*	{depression current} AND PHQ score >15	*Manea L, Gilbody S, McMillan D. Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): a meta-analysis. CMAJ. 2012;184(3):E191-E6*
2, MD2	Mania	**Symptoms: Hypomania / Mania.** Endorses features of hypomania / mania lasting for a week or more, whether or not they were disruptive, and whether or not a depression ever case. Requires "High-hyper" plus three other symptoms or "Irritable" plus four other symptoms	High/Hyper 20501 = 01 OR Irritable 20502 = 01 AND Four features from: • High/Hyper 20501; Active 20548(01); Talkative 20548(02); Less sleep 20548(03); Creative/ideas 20548(04); Restless 20548(5); Confident 20548(6); Thoughts racing 20548(7); Easily distracted 20548(8) AND Duration 20492 = A week or more	Based on DSM-IV definition of hypo/mania. This includes likely cases of bipolar affective disorder type I, possible bipolar type II (where symptoms last a week), recurrent mania without clear depression, and antidepressant-induced symptoms of hypomania / mania. *Smith DJ, Nicholl BI, Cullen B, Martin D, Ul-Haq Z, Evans J, et al. Prevalence and characteristics of probable major depression and bipolar disorder within UK biobank: cross-sectional study of 172,751 participants. PLoS One. 2013;8(11):e75362*
3, MD1, MD2, MD3	Mania	**Case: Bipolar affective disorder type I.** Ever manic/hyper or irritable, plus at least three other features (four if never manic/hyper), plus duration a week or more, plus symptoms caused significant problems. Requires also to be case for depression ever.	Case {depression ever} AND High/Hyper 20501 = 01 OR Irritable 20502 = 01 AND Four features from: • High/Hyper 20501; Active 20548(01); Talkative 20548(02); Less sleep 20548(03); Creative/ideas 20548(04); Restless 20548(5); Confident 20548(6); Thoughts racing 20548(7); Easily distracted 20548(8) AND Duration 20492 = A week or more AND Symptoms caused problem 20493 = yes	Case for depression is not required in DSM-IV diagnostic criteria but is added here to improve the positive predictive value of the test (see text and references). This definition does not exclude antidepressant-induced mania. *Cerimele et al. The prevalence of bipolar disorder in primary care samples: a systematic review, General Hospital Psychiatry 36 (2014) 19-25* *Carvalho, A. F., Y. Takwoingi, et al. (2015). "Screening for bipolar spectrum disorders: a comprehensive meta-analysis of accuracy studies." Journal of affective disorders **172:** 337-346*
nil	Mania	***Variant: Case bipolar type II*** *As above, without disruption from symptoms*	*Case {depression ever}* *AND* *High/Hyper 20501 = 01 OR* *Irritable 20502 = 01* *AND* *Four features as above* *AND* *Duration 20492 = A week or more*	There is less agreement over the definition of bipolar affective disorder type II. DSM-IV criteria require symptoms for four days or more. Here is one week, so could be predicted to miss some cases.
nil	Mania	**Control: Hypomania / Mania** Not included in hypomania / mania symptoms, nor categorised as bipolar on last UKB classification, nor self-reported bipolar	NOT {hypomania/mania} AND NOT {categorised bipolar on last UKB categorisation 20126 = 1 or 2} AND NOT {self-reported bipolar 20544=10}	
Anxiety				
2,3, MD2	GAD	**Case: GAD Ever.** Excessive worrying about a number of issues, occurring most days for six months and difficult to control, with three or more somatic symptoms and functional impairment.	Worried tense of anxious (20421) = Yes AND Duration (20420) >= 6 months or All my life AND	CIDI-SF (Composite International Diagnostic Interview – Short Form), GAD module, lifetime version. Scored based on DSM definition of GAD

			Most days (20538) = Yes AND Excessive: More than most (20425) OR Stronger than most (20542) AND Number of issues: More than one thing (20543) OR Different worries (20540) AND Difficult to control: Difficult to stop worrying (20541) OR Couldn't put it out of mind (20539) OR Difficult to control (20537) AND Functional impairment: Role interference (20418) = Some or A lot AND 3 somatic symptoms out of: • Restless. 20426; Keyed up or on edge. 20423; Easily tired. 20429; Having difficulty keeping your mind on what you were doing. 20419; More irritable than usual. 20422; Having tense, sore, or aching muscles. 20417; Often having trouble falling or staying asleep. 20427	*Kessler RC, Andrews G, Mroczek D, Ustun B, Wittchen HU. The World Health Organization composite international diagnostic interview short-form (CIDI-SF). Int J Methods Psychiatr Res. 1998;7(4):171-85.* *National Institute for Health and Clinical Excellence. Generalised anxiety disorder and panic disorder in adults: management. NICE Clinical Guideline CG113 (available at https://www.nice.org.uk/guidance/cg113) 2011*
nil	GAD	**Control: GAD ever.** Not meeting criteria for GAD ever nor scoring over low cut-off for GAD-7	NOT case {GAD ever} AND GAD-7 score < 5	Excluding those that screen positive for mild anxiety means that there is greater confidence that this group have not had anxiety disorder
MD3	GAD	**Score: GAD-7** Score 0-3 and sum a) Feeling nervous, anxious or on edge 20506 b) Not being able to stop or control worrying 20509 c) Worrying too much about different things 20520 d) Trouble relaxing 20515 e) Being so restless that it is hard to sit still 20516 f) Becoming easily annoyed or irritable 20505 g) Feeling afraid as if something awful might happen 20512	Sum {Feeling nervous, anxious or on edge 20506, Not being able to stop or control worrying 20509, Worrying too much about different things 20520, Trouble relaxing 20515, Being so restless that it is hard to sit still 20516, Becoming easily annoyed or irritable 20505, Feeling afraid as if something awful might happen 20512} 0,1,2,3 (nb in biobank coded 1-4, subtract 7 to adjust) If item missing, score 0 when scoring 0-3	*Kroenke K, Spitzer RL, Williams JB, Löwe B. The patient health questionnaire somatic, anxiety, and depressive symptom scales: a systematic review. Gen Hosp Psychiatry. 2010;32(4):345-59*
nil	GAD	**Case: Current anxiety.** GAD-7 score ≥10 and case GAD ever	Case {GAD ever} AND GAD-7 score ≥10 Where each item scored 0-3	Can be scored with cut-offs for mild, moderate and severe, with cut-offs at 5, 10 and 15. 10 chosen to represent moderate. *Kroenke K, Spitzer RL, Williams JB, Löwe B. The patient health questionnaire somatic, anxiety, and depressive symptom scales: a systematic review. Gen Hosp Psychiatry. 2010;32(4):345-59*
nil	PTSD	**Score: PCL-6** Sum of scores on questions representing the core symptoms of PTSD Score 1-5 and sum	Sum {20497Repeated disturbing thoughts of stressful experience in past month, 20498Felt very upset when reminded of stressful experience in past month, 20495Avoided activities or	Using PHQ item for concentration, scores out of 29 (conventionally scores out of 30), and will make it slightly harder to reach conventional threshold.

		20497Repeated disturbing thoughts of stressful experience in past month 20498Felt very upset when reminded of stressful experience in past month 20495Avoided activities or situations because of previous stressful experience in past month 20496Felt distant from other people in past month 20494Felt irritable or had angry outbursts in past month 20508 Trouble concentrating (scored 1-4)	situations because of previous stressful experience in past month, 20496Felt distant from other people in past month, 20494Felt irritable or had angry outbursts in past month} 1,2,3,4,5 + {20508 Trouble concentrating} 1,2,3,4 (nb biobank coded 0-4, subtract 5 to adjust)	*Lang AJ, Stein MB. An abbreviated PTSD checklist for use as a screening instrument in primary care. Behaviour research and therapy. 2005;43(5):585-94*
2, MD2	PTSD	**Case: PTSD.** PCL-6 sum of scores 14 or greater is positive screen	(20497Repeated disturbing thoughts + 20498Felt very upset when reminded + 20495Avoided activities or situations + 20496Felt distant + 20494Felt irritable or had angry outbursts + 20508 Trouble concentrating)>13	Does not currently require catastrophic trauma, but refers to "stressful event" in the text of the questions as this is not an exhaustive list of possible trauma.
nil	PTSD	**Control: PTSD.** PCL-6 sum of scores 13 or less is positive screen. Include those who do not complete PCL-6 due to stop rule.	Answered (20497Repeated disturbing thoughts + 20498Felt very upset when reminded + 20495Avoided activities or situations) AND NOT {Case: PTSD}	
Other symptoms				
2,3, MD2	Unusual experiences	**Symptom: Unusual experience.** Endorsed possible hallucination or delusion	Heard unreal voice 20463 = yes OR Saw unreal vision 20471 = yes OR Believed unreal conspiracy 20468 = yes OR Believed unreal communication or signs 20474 = yes	Adapted by group from CIDI questions *Nuevo R, Chatterji S, Verdes E, Naidoo N, Arango C, Ayuso-Mateos JL. The Continuum of Psychotic Symptoms in the General Population: A Cross-national Study. Schizophrenia Bulletin. 2012;38(3):475-85*
nil	Unusual experiences	**Symptom: Recent unusual experience.** Reports hallucination or delusion in the last year	Frequency in last year 20467>0	
nil	Unusual experiences	**Control: Unusual experience.** Not endorsing psychotic illness or reporting symptoms	NOT Endorsed diagnosis 20544 of schizophrenia [2] or other psychotic illness [3] AND NOT {ever hallucination} OR {ever delusion}	
nil	Self-harm	**Case: Life not worth living.** Ever felt life not worth living	20479 life NWL = yes (1 or 2)	
2, MD2	Self-harm	**Case: Self harm.** Ever harmed self, whether or not meant to die	20480 Self harmed = Yes	Self harm is further divided by whether have ever self-harmed with intent to die (question 20483)
nil	Self-harm	**Case: Non-suicidal self-harm** Self-harm without intention to end life	20480 Self harmed = Yes 20483 Attempted suicide = No	
nil	Self-harm	**Case: Suicide attempt** Ever harmed self with intent to end life	20483 Attempted suicide = Yes	Does not rule out that on different occasion engaged in NSSI behaviour.
Alcohol and addiction				
MD3	Alcohol	**Score: AUDIT**		

		Asks about "in the last year" apart from last two questions. (Note coding on UKB is from 1-5, so requires adjustment) Sum individual scores	PART 1 Hazard: Frequency (scored 0-4) 20414, typical drinks (score 0-4) 20403, six or more drinks (scored 0-4) 20416 PART 2 Dependence: Unable to stop (scored 0-4) 20413, failed to do what expected due to drinking (scored 0-4) 20407, needed to drink first thing (scored 0-4) 20412 PART 3 Harm: Guilt due to drinking (scored 0-4) 20409, unable to remember due to drink (scored 0-4) 20408, injury due to drinking ever (scored 0,2,4) 20411, advice to cut down ever (scored 0,2,4) 20405	Can be scored using algorithm or cut-offs, with more literature on the latter approach. Using cut-off of 8 is to indicate likelihood of moderate severity, 16 indicates severe, and lower cut-offs have been used to identify hazardous drinking (as opposed to drinking already causing harm). *Reinert, D. F. and J. P. Allen (2007). "The alcohol use disorders identification test: an update of research findings." Alcoholism: Clinical and Experimental Research 31(2): 185-199*
2, MD2	Alcohol	**Case: Hazardous / Harmful Alcohol Use.** Alcohol use disorder of moderate severity (also called hazardous/harmful drinking) is predicted by score of 8 or more.	{AUDIT score} >=8	*Babor, T. F., J. C. Higgins-Biddle, et al. (2001). "AUDIT: The alcohol use disorders identification test: Guidelines for use in primary health care."* *Drummond, C., O. McBride, N. Fear and E. Fuller (2016). Alcohol dependence. Mental health and wellbeing in England: Adult Psychiatric Morbidity Survey. S. McManus, P. Bebbington, R. Jenkins and T. Brugha. Leeds, NHS Digital.*
nil	Alcohol	**Control: Hazardous / Harmful Alcohol Use.** Uses inverse of the algorithmic diagnosis of hazardous drinking from AUDIT, excluding those who reported alcohol addiction in this questionnaire or reported at baseline they had stopped drinking due to illness, on drs advice or as a health precaution	AUDIT –ve ((Drinks alcohol 30414 = 0) OR **(**Typical drinks 20403 = "1 or 2" AND Six or more 20416 = "Never")) AND NOT {ever alcohol dependence} AND NOT reason for reducing amount of alcohol drunk 2664 = "ill health", "doctor's advice"or "health precaution" [1,2or3]	This is particularly strict control group to avoid including participants recovering from alcohol harm/dependence in the definition.
3	Addiction	**Case: Addiction ever.** Endorses "Ever addicted to any substance or behaviour"	"Ever addicted to any substance or behaviour" 20401=1	
1	Addiction	**Case: Substance addiction.** Endorses ever addicted to alcohol or drugs or medication.	Alcohol 20406 = Yes (1) OR Illicit/recreational drugs = Yes (1) OR Medication = Yes (1)	
nil	Addiction	**Case: Current addiction:** Endorses "addiction or dependence ongoing"	20457=1 or 20504=1 or 20415=1 or 20432=1	
1	Addiction	**Case Alcohol dependence ever.** Endorses "physically dependent on alcohol"	20404=1	
nil	Addiction	**Control: Addiction ever.** Not endorsing addiction, or other indicators of misuse: screening AUDIT in severe alcohol use disorder range or daily use of cannabis	NOT {ever addiction} AND NOT {AUDIT score >16} AND {daily cannabis} defined below	
Exposures				
S1, MD1	Trauma	**Exposure: Childhood adverse events.** Based on answers to the five questions of Childhood Trauma Screen (CTS), all scored 1-5. A score over the threshold on any question is screen positive.	20489Felt loved as a child ≤3 OR 20488Physically abused by family as a child ≥2 OR 20487Felt hated by family member as a child ≥2	CTS takes one question from each domain of the Childhood Trauma Questionnaire. Thresholds taken from thresholds for represented domain.

			OR 20490Sexually molested as a child ≥2 OR 20491Someone to take to doctor when needed as a child ≤4	*Walker, E. A., et al. (1999). "Adult health status of women with histories of childhood abuse and neglect." The American Journal of Medicine **107**(4): 332-339*
S1, MD1	Trauma	**Exposure: Adult adverse events.** Based on answers to the five questions of Adult Trauma Screen (written for this questionnaire), all scored 1-5. A score over the threshold on any question is screen positive.	20522Been in a confiding relationship as an adult ≤3 20523Physical violence by partner or ex-partner as an adult ≥2 20521Belittlement by partner or ex-partner as an adult ≥2 20524Sexual interference by partner or ex-partner without consent as an adult ≥2 20525Able to pay rent/mortgage ≤4	Scoring algorithm based on Childhood Trauma Screen and consensus. Note some overlap with baseline questions included in loneliness score.
S1, MD1	Trauma	**Exposure: Catastrophic trauma.** Endorsed one or more events from checklist	20531Victim of sexual assault = Yes, within last 12 months {2} OR Yes, but not in the last 12 months {1} 20529Victim of physically violent crime = Yes, within last 12 months {2} OR Yes, but not in the last 12 months {1} 20526Been in serious accident believed to be life-threatening = Yes, within last 12 months {2} OR Yes, but not in the last 12 months {1} 20530Witnessed sudden violent death = Yes, within last 12 months {2} OR Yes, but not in the last 12 months {1} 20528Diagnosed with life-threatening illness = Yes, within last 12 months {2} OR Yes, but not in the last 12 months {1} 20527Been involved in combat or exposed to war-zone = Yes, within last 12 months {2} OR Yes, but not in the last 12 months {1}	
nil	Cannabis	**Exposure: Cannabis ever.** Endorsed taking cannabis at least once in life.	20453 Ever taken cannabis >0	
S1, MD1	Cannabis	**Exposure: Cannabis daily.** Maximum frequency of taking cannabis when using is every day	20454 frequency = every day {4}	
nil	Cannabis	**Control: Cannabis ever.** Reported no cannabis use	20453 Ever taken cannabis = No {0}	
Other				
MD3	Wellbeing	**Score: Wellbeing.** Sum last three questions	General happiness 20458{scored 1-6} + Happiness with health 20459{scored 1-6} + Life meaningful 20460 {scored 1-5)	
nil	Any	**Case: Any distress.** Endorsing functional impairment or help-seeking due to mental distress, reports diagnosis or screens positive for specific condition	(Ever help for mental distress 20499 = yes) OR (Ever impairing mental distress = yes) OR (Mental health problem diagnosed 20544 = {1-18}) OR Case {Depression ever, GAD ever, Addiction ever, Bipolar ever,	

			Psychotic experiences, PTSD, Self harm ever}	
nil	Any	**Control: Any distress.** Not endorsing mental distress or conditions, and screens negative	Ever help for mental distress 20499 = no AND Ever impairing mental distress = yes AND NOT (Mental health problem diagnosed 20544 = {1-18 or -818 or -819}) AND NOT Case {Depression ever, GAD ever, Addiction ever, Bipolar ever, Psychotic experiences, PTSD Self harm ever}	Inverse of case. Case plus control will contain all participants that had valid results in all sections
Non-MHQ				
S1, MD1	Other	**Exposure: Social isolation** **Score > 1, where one mark each for:** -"Including yourself, how many people are living together in your household? Include those who usually live in the house such as students living away from home during term time, partners in the armed forces or professions such as pilots"=0 -"How often do you visit friends or family or have them visit you?" = less than once a month - "Which of the following [leisure/social activities] do you engage in once a week or more often?" =none		*Elovainio, M., C. Hakulinen, et al. "Contribution of risk factors to excess mortality in isolated and lonely individuals: an analysis of data from the UK Biobank cohort study." The Lancet Public Health **2**(6): e260-e266*
S1, MD1	Other	**Exposure: Loneliness** **Score > 1, where one mark each for:** "Do you often feel lonely?" = yes "How often are you able to confide in someone close to you?" = never or almost never		*Elovainio, M., C. Hakulinen, et al. "Contribution of risk factors to excess mortality in isolated and lonely individuals: an analysis of data from the UK Biobank cohort study." The Lancet Public Health **2**(6): e260-e266*