This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: https://orca.cardiff.ac.uk/id/eprint/128980/

This is the author’s version of a work that was submitted to / accepted for publication.

Citation for final published version:

Davis, Katrina, Coleman, Jonathan, Adams, Mark, Allen, Naomi, Breen, Gerome, Cullen, Breda, Dickens, Chris, Fox, Elaine, Graham, Nick, Holliday, Jo, Howard, Lousise, John, Ann, Williams, Lee, Mccable, Rose, McIntosh, Andrew, Pearsall, Roberts, Smith, Daniel, Sudlow, Cathie, Ward, Joey, Zammit, Stan ORCID: https://orcid.org/0000-0002-2647-9211 and Hotopf, Matthew 2020. Mental Health in UK Biobank – development, implementation and results from an online questionnaire completed by 157,366 participants: a reanalysis(a). BJPsych Open 6 (2), e18. 10.1192/bjo.2019.100 file

Publishers page: https://doi.org/10.1192/bjo.2019.100
<https://doi.org/10.1192/bjo.2019.100>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher’s version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See
http://orca.cf.ac.uk/policies.html for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.
Background

UK Biobank is a well-characterised cohort of over 500,000 participants including genetics, environmental data and imaging. An online mental health questionnaire was designed for UK Biobank participants to expand its potential.

Aims

Describe the development, implementation and results of this questionnaire.

Method

An expert working group designed the questionnaire, using established measures where possible, and consulting a patient group. Operational criteria were agreed for defining likely disorder and risk states, including lifetime depression, mania/hypomania, generalised anxiety disorder, unusual experiences and self-harm, and current post-traumatic stress and hazardous/harmful alcohol use.

Results

A total of 157,366 completed online questionnaires were available by August 2017. Participants were aged 45–82 (53% were ≥65 years) and 57% women. Comparison of self-reported diagnosed mental disorder with a contemporary study shows a similar prevalence, despite respondents being of higher average socioeconomic status. Lifetime depression was a common finding, with 24% (37,434) of participants meeting criteria and current hazardous/harmful alcohol use criteria were met by 21% (32,602), whereas other criteria were met by less than 8% of the participants. There was extensive comorbidity among the syndromes. Mental disorders were associated with a high neuroticism score, adverse life events and long-term illness; addiction and bipolar affective disorder in particular were associated with measures of deprivation.

Conclusions

The UK Biobank questionnaire represents a very large mental health survey in itself, and the results presented here show high face validity, although caution is needed because of selection bias. Built into UK Biobank, these data intersect with other health data to offer unparalleled potential for crosscutting biomedical research involving mental health.

Declaration of interest

G.B. reports grants from the National Institute for Health Research during the conduct of the study; support from Illumina Ltd and the European Commission outside the submitted work. B.C. reports grants from the Scottish Executive Chief Scientist Office during the conduct of the study. C.S. reports grants from the Medical Research Council and Wellcome Trust, during the conduct of the study; and is the former Chief Scientist for UK Biobank. M.H. reports grants for IMI RADAR-CNS and personal fees as an expert witness outside the submitted work. N.A. is Chief Scientist for UK Biobank. Other authors have nothing to declare.

Keywords

Mental health; UK Biobank; cohort study; depressive disorders; alcohol disorders.

Copyright and usage

© The Author(s) 2020. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted re-use, distribution, and reproduction in any medium, provided the original work is properly cited.

UK Biobank

UK Biobank is a very large, population-based cohort study established to identify the determinants of common life-threatening and disabling conditions. Most of these conditions, such as heart disease, stroke and mental disorders, are multifactorial, involving multiple genes of small effect, and complex relationships with environmental exposures. This means large samples are required to study associations between these exposures and disease, and to identify targets for treatment and prevention. The utility of traditional epidemiological study designs are often limited by their focus on single disorders or exposures and relatively modest sample sizes. UK Biobank is an open-access resource providing detailed characterisation of over half a million people aged 40–69 years at recruitment, with proposed long-term follow-up. Recruitment was completed in 2010, along with consent for future contact and linkage to routinely collected health-related data, such as those produced by the National Health Service (NHS). Baseline measures were extensive, from family history to sensory acuity (a searchable breakdown is available at www.ukbiobank.ac.uk), and the resource continues to grow. In 2017 genotyping of the whole cohort was complete, a range of blood biomarkers were released in 2019, and multimodal imaging is underway for 100,000 participants. Locality environmental factors, such as air pollution, are also available. The design of UK Biobank offers the opportunity to examine a wide range of
risk factors and outcomes in a sample that has the size to provide the power to detect small effects, making UK Biobank a highly efficient resource for observational epidemiology.

The impact of mental disorders on disability and quality of life is considerable, accounting for the equivalent of over 1.2 million person-years lost to disability from mental and substance-use disorders in England alone in 2013. The detrimental impact of mental disorders both on physical disease onset and outcomes is particularly notable for this project. The UK Biobank baseline data collection of mental health, consisted of several questions about mood and a neuroticism scale, expanded for the last 172 729 recruited participants with questions to allow provisional categorisation of mood disorders; however, there was considerable scope for further characterisation of mental disorders among participants. The availability of mental health phenotypes in conjunction with the wealth of other data in the UK Biobank offers considerable opportunities to study aetiological and prognostic factors, particularly the interplay between factors that have usually been in separate research domains.

Outcome ascertainment

Characterising mental disorders in a cohort such as UK Biobank poses challenges. First, most mental disorders manifest before age 30 years and have fluctuating courses, so a ‘snapshot’ of disorder status at one point in time, as identified by most screening tools, is likely to be less useful than a ‘lifetime’ history – although ‘lifetime’ instruments suffer more from measurement error such as recall bias. Second, traditional diagnostic approaches to mental disorders, relying upon clinician assessment at interview, would be prohibitively expensive in a cohort of this size. Third, using self-report of diagnosis or data from record linkages relies upon recognition of illness and reflects healthcare usage patterns, whereas many people with mental disorders never seek or receive treatment. In response to these challenges, we developed a dual approach: secondary care record linkage for identification of more severe illnesses such as schizophrenia and self-report of symptoms of common mental disorder, which might not have come to clinical attention. As part of our mental health phenotyping programme we therefore developed an online mental health questionnaire (MHQ) for participants to complete regarding lifetime symptoms of mental disorders. The MHQ aimed to exploit the efficiency of ‘e-surveys’ and provide the detail needed to identify mental health disorders without the need for a clinical assessment.

Aims

The present paper aims to describe the development, implementation and results of the MHQ. We provide descriptive data on the numbers of UK Biobank participants meeting diagnostic criteria for specific disorders and on the frequency of exposure to risk factors. We also evaluate the likely representativeness of respondents by comparing respondent sociodemographic characteristics to that of the UK population using census data and comparing self-reported mental disorder diagnosis with the Health Survey for England (HSE) data. This will assist researchers considering or undertaking epidemiological research to evaluate the potential strengths and weaknesses of using UK Biobank data to look at mental health.

Method

Questionnaire development

A mental health research reference group formed of approximately 50 individuals (see supplementary Appendix 1 available at https://doi.org/10.1192/bjo.2019.100) participated in discussions about a strategy for mental health phenotyping in UK Biobank, including a workshop in January 2015. From this, a smaller steering group was established and led the development of the MHQ. The group recommended that the MHQ should concentrate on depression, as it was likely to represent the greatest burden in the cohort, with some questions about other common disorders, including anxiety, alcohol misuse and addiction, plus risk factors for mental disorders not captured at participants’ baseline assessment.

The intention was to create a composite questionnaire out of previously existing and validated measures, taking into account participant acceptability (time, ease of use and ensuring questions were unlikely to offend), scope for collaborations with international studies (for example the Psychiatric Genomics Consortium) through making results comparable, and the need to balance depth and breadth of phenotyping. The base of the questionnaire was the measurement of lifetime depressive disorder using the Composite International Diagnostic Interview Short Form (CIDI-SF), modified to provide lifetime history, as used to identify cases and controls for some existing studies in the Psychiatric Genomics Consortium. The CIDI-SF uses a branching structure with screening questions and skip rules to limit detailed questions to the relevant areas for each participant. Other measures were then added to this, as summarised in supplementary Table SM1. Where the group were unable to find existing measures that fulfilled these criteria, questions were written or adapted, as indicated in supplementary Table SM1. These sections have not been externally validated, but the questions along with the full questionnaire can be seen on the UK Biobank website (http://biobank.ctsu.ox.ac.uk/crystal/refert.cgi?id=22), for researchers to evaluate.

Testing and ethical approval

The use of branching questions in the MHQ means that those with established and multiple mental disorders have a longer, more detailed, questionnaire. To improve acceptability in this group, we worked with a patient advisory group at the National Institute of Health Research (NIHR) Biomedical Research Centre at the South London and Maudsley NHS Foundation Trust in designing the questionnaire and invitation. We then piloted the questionnaire for functionality (for example ease of completion) among an online cohort of 14 836 volunteers aged over 50 and living in the UK, who completed the questionnaire as part of signing up to take part in the Platform for Research Online to investigate Genetics and Cognition in Ageing (PROTECT). Of those who started the questionnaire 98.8% completed it, taking a median time of 15 min. Some PROTECT participants commented that they wanted the opportunity to explain why they felt they had experienced symptoms of depression. In response to this, we added a question to the depression section on loss or bereavement, and a free-text box – neither were designed to change diagnostic algorithms, but may add to future analyses.

The questionnaire was approved as a substantial amendment to UK Biobank approval from the North West - Haydock Research Ethics Committee, 11/NW/0382. Participation in the UK Biobank is voluntary, and participants are free to withdraw at any time. Informed written consent was obtained by participants at baseline. Online questionnaires such as the MHQ are voluntary.

Administration to UK Biobank participants

We incorporated the final MHQ into the UK Biobank web-questionnaire platform and presented it to participants as an online questionnaire entitled ‘thoughts and feelings’. To participants who had agreed to email contact (339 092/503 328 participants, 67%) we sent a hyperlink to their personalised questionnaire.
Defining outcomes from the MHQ

Some suggested case definitions for the evaluation of the responses on the MHQ are detailed in supplementary Appendix 2. They arose either from the instruments used in the MHQ or by consensus criteria agreed by the working committee who wrote the MHQ. Diagnostic criteria were evaluated for depression (major depressive disorder), hypomania or mania, generalised anxiety disorder (GAD), hazardous/harmful alcohol use (alcohol use disorder) and post-traumatic stress disorder (PTSD). Addiction to substances and/or behaviour was defined based on self-report alone. Unusual experiences (describing potential symptoms of psychosis) and self-harm were also defined as phenomena that are important for phenotyping, but are not specific to any disorder. We combined outcomes to divide the cohort into five mood disorder groups, as shown in supplementary Fig. MD1.

Fulfilling the diagnostic criteria based on a self-report questionnaire does not allow us to rule out other psychiatric disorders, psychological or situational factors that might better explain the symptoms, which may have been elicited had there been a clinical evaluation. Therefore, we would regard any case classification arising from the MHQ as ‘likely’, rather than a confirmed psychiatric disorder. The issue becomes particularly problematic for disorders that are less common in the population, such as bipolar affective disorder, where literature shows that using questionnaires to screen the population may overestimate prevalence.22 Therefore, although we report the presence of hypomania/mania symptoms for the whole population, we only make the likely diagnosis of bipolar affective disorder in people with a history of depression, a subpopulation where the prevalence of bipolar affective disorder is higher, and therefore screening questionnaires have better positive predictive values.21

Analysis and data sharing

Data were supplied by UK Biobank on 8 August 2017 under application number 16577. This data is open-access subject to the usual access procedures (www.ukbiobank.ac.uk).

Formal operational criteria (supplementary Appendix 2) were written by K.A.S.D. based on consensus within the consortium (see Defining cases from the MHQ, above), with checks by J.R.I.C., G.B. and M.H. (whole) and C.D., N.G., W.L. and D.J.S. (mood disorders section). R code for analysis was developed by J.R.I.C., with the code posted for comments during development, trialled on pilot data and checked by K.A.S.D. and G.B. Portions of the data were analysed independently in parallel by other groups and subsequently compared (for example for mood disorders, by N.G./B.C.). The R code is freely available from Mendeley Data for the purpose of reproducing these analyses or developing further analyses (https://data.mendeley.com/datasets/kv677c2th4/3). We used R version 3.4.0–3.5.1 and MS Excel for analyses. We report numbers and proportions within the sample and do not attempt to give population prevalence estimates. Because of this, and the large sample size (the 95% CIs on all proportions have width of less than absolute 1%), CIs were thought not to add meaning, and so are not shown. A STrengthening the Reporting of OBServational studies in Epidemiology checklist is included in supplementary Appendix 3.

Comparison data

In order to describe the differences in the sample of participants in UK Biobank to the general population of the UK, Fry et al.24 compare UK Biobank data with census data, which we have replicated and extended. For health-related data, we have used the Health Survey for England (HSE), which is a face-to-face household survey carried out every year,25 that in 2014 involved around 8000 adult participants designed to be representative of the England adult population (with weighting in cases where sampling could not achieve this). Some topics are ‘core’ and are surveyed every year, whereas others are ‘supplementary’. Mental health appeared in the 2014 survey as a supplementary topic.17

Results

The setting, recruitment and methods of selection of participants in UK Biobank have been published elsewhere.1,4 For the MHQ study, 339 092 participants were sent an email invitation, and 157 366 (46% of those emailed) fully completed the questionnaire by July 2017 (available in August 2017) – which means that the MHQ had 31% coverage of the UK Biobank cohort. The coverage continues to grow as the questionnaire is still open for participants. Figure 1 shows the flow chart of UK Biobank participants who completed the MHQ. The median time for completion was 14 min, and 82% of respondents completed the questionnaire in under 25 min.

Supplementary Table SM2 shows participant characteristics for all UK Biobank participants and those who completed the MHQ compared with population-level data for UK residents in the same age range. The MHQ participants were aged 45–82 years, with 53% aged 65 or over, and 57% were female. They were different from the whole UK Biobank cohort and the general population by being better educated (for example 45% hold a degree v. 32% of all UK Biobank participants v. 23% in the census), of higher socio-economic status according to job type, and healthier (28% report long-standing illness or disability v. 32% all UK Biobank participants v. 37% census), with lower rates of current smoking.

Table 1 shows that 34% of respondents reported they had received at least one psychiatric diagnosis from a professional at some time, and 12% had received two or more. The most commonly reported diagnosis was depression, followed by ‘anxiety or nerves’. Data are compared with the population prevalence estimates from HSE for this age group.17 The comparison shows that the pattern and prevalence of diagnosis are similar; for example, a depression diagnosis was self-reported by 21% of individuals in both samples, eating disorder by around 1% and bipolar-related disorders by around 0.5%. The definition in the MHQ differed from that in the HSE for anxiety (the MHQ definition was broader) and addiction (MHQ did not require professional diagnosis), and the higher overall prevalence in the UK Biobank MHQ compared with the HSE (34.3% v. 28.0%) may be a result of those wider definitions.

Table 2 shows that 45% of participants met criteria for one or more operationally defined syndromes. Of the lifetime disorders, depression was most common (24% respondents participants),
then GAD (7%) and hypomania/mania (2%); current hazardous/harmful alcohol use was met by 21% and current PTSD by 6%. Lifetime unusual experiences were reported by 5% of respondents and self-harm by 4%. Supplementary Table SM3 shows that women and men were approximately equally likely to have a history of one or more of the defined syndromes (women 44% v. men 46%), but differed as to which criteria were met: women were more likely to have a history of depression or anxiety disorder, whereas men were more likely to meet criteria for a current hazardous/harmful alcohol use (women 14% v. men 30%). Table 2 also shows the substantial comorbidity of defined syndromes. Notably, around three-quarters of participants who met criteria for lifetime anxiety disorder also met criteria for lifetime depression. Also, although individuals meeting criteria for PTSD had more than a twofold risk of all of the lifetime syndromes compared with average, those identified with hazardous/harmful alcohol use had little extra risk of lifetime syndromes.

In Table 3, people meeting criteria for the lifetime occurrence of at least one of mood disorder, bipolar disorder, GAD, unusual experiences or self-reported addiction are seen to be more likely than those without to come from a younger age group, report adverse life events and have met criteria for loneliness or social isolation. They are more likely to have smoked cigarettes and/or used cannabis, and to have had a ‘longstanding illness’ at baseline (although the presence of a mental disorder may have been the illness to which the participants refer in some cases), but all groups were equally likely to be achieving recommended levels of physical activity. Markers of deprivation (area-level deprivation and rented housing) are raised in groups with a history of mental disorders, especially bipolar affective disorder and addictions.

The supplementary material includes a section on mood disorder, showing the results of analyses of MHQ participants by likely disorder categories (supplementary Fig. MD1). Supplementary Table MD1 shows the features of these groups. The characteristics of people who meet diagnostic criteria for depression appear to be shared by those with subthreshold depressive symptoms. Supplementary Table MD2 shows comorbidity, and demonstrates a gradient effect in the presence of a non-depression syndrome rising from 23% in no depression (mainly hazardous/harmful alcohol use) to 50% in recurrent depression. Supplementary Table MD3 shows that people with a history of depression or bipolar affective disorder tend to have worse scores for current mental health.

Discussion

Main findings relating to data-collection methods

This paper has described the development, implementation and principal descriptive findings from the UK Biobank MHQ. The implementation of this questionnaire demonstrates that a web-based questionnaire is an acceptable means of collecting mental health information at low cost and large scale. Although the data-collection methods might force more limited data acquisition than conventional interview methods, with associated uncertainties in true diagnostic categorisation, we suggest that the survey achieved an acceptable trade-off between depth of phenotypic information and scale of sample size. This means that the UK Biobank MHQ sample can usefully fill a gap between clinical samples with detailed mental health disorder information but poor generalisability (for example, Clinical Records Interactive Search) and larger
cohorts with superficial identification of mental disorder (such as the baseline UK Biobank cohort or 23andMe\textsuperscript{c}).

The MHQ achieved a participation rate of 31\% of the original UK Biobank participants and 46\% of those emailed. This response rate is substantially higher than previous UK Biobank questionnaires, largely owing to the attention paid to ensure the acceptability of the invitation and questionnaire and the efficient use of reminders.

**Main findings from the questionnaire**

Those who completed the MHQ appear to be better educated and have higher socioeconomic status (job title, household income, home ownership and area-level deprivation) than those recruited into UK Biobank overall, and the UK population. Despite this, we found that rates of self-report diagnoses were similar to population

---

**Table 1** Respondent reports of mental health diagnoses by a professional (self-reported without physician diagnosis for addiction) compared with diagnoses reported in the Health Survey for England (HSE) 2014\textsuperscript{b}

| UK Biobank MHQ responses, age 45–82 years (n = 157,366) | HSE, age 45–84 years (n = 3,272) |
|--------------------------------------------------------|----------------------------------|
| n | % in sample | n | Prevalence (95\% CI) |
|---|------------|---|---------------------|
| All psychiatric disorders | 723 | 0.5 | 11 | 0.3 (0.2–0.6) |
| Schizophrenia | 157 | 0.1 | NR | – |
| Any other type of psychosis or psychotic illness | 604 | 0.4 | NR | – |
| Depression | 33,424 | 21.2 | 679 | 20.8 (19.4–22.2) |
| Mania, hypomania, bipolar or manic-depression | 837 | 0.5 | 13 | 0.4 (0.2–0.7) |
| Anxiety, nerves or generalised anxiety disorder\textsuperscript{b} | 22,036 | 14.0 | 170 | 5.2 (4.5–6.0) |
| Panic attacks | 8,704 | 5.5 | 262 | 8.0 (7.1–9.0) |
| Agoraphobia | 599 | 0.4 | NR | – |
| Social anxiety or social phobia | 1,962 | 1.2 | NR | – |
| Any other phobia (for example disabling fear of heights or spiders) | 2,153 | 1.4 | 27 | 0.8 (0.6–1.2) |
| Obsessive–compulsive disorder | 982 | 0.6 | 11 | 0.3 (0.2–0.6) |
| A personality disorder | 385 | 0.2 | 13 | 0.4 (0.2–0.7) |
| All eating disorders | 1,851 | 1.2 | 26 | 0.8 (0.5–1.2) |
| Anorexia nervosa | 891 | 0.6 | NR | – |
| Bulimia nervosa | 503 | 0.3 | NR | – |
| Psychological overeating or binge-eating | 707 | 0.4 | NR | – |
| Autism, Asperger’s or autistic spectrum disorder | 223 | 0.1 | NR | – |
| Attention-deficit or attention-deficit hyperactivity disorder | 133 | 0.1 | 4 | 0.1 (0.0–0.3) |
| Any addiction or dependence | 9,386 | 6.0 | NR | – |
| Alcohol or drug addiction\textsuperscript{c} | 5,002 | 3.2 | 30 | 0.9 (0.6–1.3) |
| Physical alcohol dependence | 946 | 0.6 | NA | – |
| Summary | | | | |
| None of above | 103,346 | 65.7 | 2356 | 72.0 (70.4–73.5) |
| ≥1 of above | 54,020 | 34.3 | 916 | 28.0 (26.5–29.6) |
| ≥2 of above | 19,400 | 12.3 | NR | – |

MHQ, mental health questionnaire; NR, not reported.

a. UK Biobank participants were asked: ‘Have you been diagnosed with one or more of the following mental health problems by a professional, even if you don’t have it currently? Check all that apply: by professional we mean: any doctor, nurse or person with specialist training such as a psychologist or therapist. Please include disorders even if you did not need treatment for them or if you did not agree with the diagnosis’. HSE participants were asked to identify all the mental health conditions they had experienced, then asked whether they had been told by a doctor, psychologist or professional that they had it.

b. HSE participants were asked about generalised anxiety disorder, and not about anxiety and nerves more generically.

c. UK Biobank participants were asked: ‘Have you been addicted to or dependent on one or more things, including substances (not cigarettes/coffee) or behaviours (such as gambling)?’ HSE definition of addiction includes physician diagnosis.

---

**Table 2** Comorbidity between operationally defined syndromes\textsuperscript{a}

| Overall | Depression\textsuperscript{b} | Hypomania/mania\textsuperscript{d} | Anxiety disorder\textsuperscript{d} | Unusual experiences\textsuperscript{e} | Self-harm\textsuperscript{f} | Haz/harm alcohol use\textsuperscript{g} | PTSD\textsuperscript{h} |
|---------|-------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------|-------------------------------|------------------|
| Prevalence, n (%) | (n = 157,366) | (n = 157,366) | (n = 157,366) | (n = 157,366) | (n = 157,366) | (n = 157,366) | (n = 157,366) |
| Depression\textsuperscript{b} | 37,434 (24) | – | 15,500 (4) | 8,444 (23) | 3,649 (10) | 4,240 (11) | 8,156 (22) |
| Hypomania/mania\textsuperscript{d} | 2,396 (2) | 15,500 (65) | – | 7,788 (32) | 598 (25) | 4,533 (19) | 6,600 (28) |
| Anxiety disorder\textsuperscript{d} | 11,111 (7) | 8,444 (76) | 7,788 (7) | – | 1,511 (14) | 1,704 (15) | 2,634 (24) |
| Unusual experiences\textsuperscript{e} | 7,803 (5) | 3,649 (47) | 598 (8) | 1,511 (20) | – | 1,225 (16) | 1,784 (23) |
| Self-harm\textsuperscript{f} | 6,672 (4) | 4,240 (62) | 453 (7) | 1,704 (25) | 1,225 (18) | – | 1,890 (28) |
| Current | Hazardous/harmful alcohol use\textsuperscript{g} | 32,602 (21) | 8,156 (25) | 660 (2) | 2,634 (8) | 1,784 (5) | 1,890 (6) |
| PTSD\textsuperscript{h} | 10,064 (6) | 6,373 (63) | 657 (7) | 3,274 (33) | 1,594 (16) | 1,719 (17) | 2,572 (26) |

PTSD, post-traumatic stress disorder.

a. Percentages refer to the proportion of participants with the row syndrome who also have column syndrome. See footnotes b–h, and supplementary Appendix 2 for ‘case’ definitions.

b. Criteria met for major depressive disorder on Composite International Diagnostic Interview Short Form (CIDC-SF) lifetime.

c. Criteria met for hypomania/mania lasting for at least 1 week.

d. Criteria met for generalised anxiety disorder on CIDC-SF lifetime.

e. Reported potential hallucination or delusion at any point in their life.

f. Reported self-harm at some point in their life, asked to report self-harm ‘whether or not you meant to end your life’.

g. Score above cut-off for alcohol use disorder (PAS) on Alcohol Use Disorder Identification Tool during the past year.

h. Criteria met for post-traumatic stress disorder (PTSD) on PTSD Checklist - Short version (PCL-S) in the past month.
estimates from the HSE. The patterns of association between disorders and demographics were also broadly as predicted by previous research, which adds to the face validity of the questionnaire. For example, depression and anxiety were more common in women, whereas addiction and alcohol misuse were more common in men, and all disorders were less common in respondents older than 65 years. The decrease in prevalence of lifetime disorder with increasing age has been previously noted in cross-sectional estimates from the HSE. The patterns of association between disorders and demographics were also broadly as predicted by previous research, which adds to the face validity of the questionnaire. For example, depression and anxiety were more common in women, whereas addiction and alcohol misuse were more common in men, and all disorders were less common in respondents older than 65 years. The decrease in prevalence of lifetime disorder with increasing age has been previously noted in cross-sectional studies, although the causes and implications are not clearly understood. 28 29 The high level of hazardous/harmful alcohol (using the Alcohol Use Disorder Identification Tool) is consistent with the Adult Psychiatric Morbidity Survey 2014, where they comment on increased numbers in older age groups since 2007. 30

‘Healthy volunteer’ selection bias

The ‘healthy volunteer’ selection bias within the UK Biobank has been previously explored, 28 29 and further variables influencing participation in the MHQ can be predicted and have been found, such as an interest in mental health and good cognition. 30 The impact of selection biases on disease prevalence are likely to be particularly strong for mental health disorders, where disorder status or symptoms may influence participation in research, 12 32 33 and many risk factors for these disorders, including genetic risk, can be associated with non-participation. 30 Therefore, the results of the MHQ should not be used to provide prevalence estimates.

However, the pattern of the measured risk factors among the participants with mental disorders in the MHQ, including neuroticism, trauma, loneliness and housing tenure, was in accordance with established literature, supporting the use of the data to study the relationships between exposures and outcomes. Previous work on health surveys with selection bias because of non-participation, including UK Biobank, have indicated that they can be used to give estimates of association, 14 32 35 although biased results may occur in some cases. 16 37 For example, the relative under-participation of unskilled workers in the MHQ (around one-fifth of the proportion in the population) could mask an association with a variable that was related to unskilled work.

**Strengths and limitations**

We developed a questionnaire through a consensus approach with clear aims of capturing enough data to characterise participants as having a lifetime history of depression and other phenotypes. Validated instruments were used where possible. The consortium working on the questionnaire included mental health researchers and members of the UK Biobank team working in collaboration to develop the optimum approach. The derived variables of likely categorical diagnoses will be added to the UK Biobank resource, facilitating those less familiar with mental health to use the results

---

**Table 3** Selected personal characteristics, socioeconomic factors, risk factors and health behaviours by status for likely lifetime occurrence of operationally defined syndromes (people may be included in more than one category)

| Characteristics | No ‘lifetime’ criteria met<sup>a</sup> (n = 108 752) | Depression<sup>b</sup> (n = 37 434) | Bipolar type<sup>c</sup> (n = 931) | Anxiety disorder (GAD)<sup>d</sup> (n = 11 11) | Unusual experiences<sup>e</sup> (n = 7 803) | Addiction<sup>f</sup> (n = 9 936) |
|-----------------|-----------------------------------------|---------------------------------|----------------------------------|---------------------------------------------|-----------------------------------|----------------------------------|
| **Personal characteristics** | | | | | | |
| Age, n (%) | 45–54 | 14 364 (13) | 7145 (19) | 228 (24) | 2348 (21) | 1485 (19) | 2013 (21) |
| | 55–64 | 33 307 (31) | 14 829 (40) | 417 (45) | 4470 (40) | 2904 (37) | 3428 (37) |
| | 65–74 | 51 706 (48) | 13 739 (37) | 261 (28) | 3892 (35) | 2960 (38) | 3466 (37) |
| ≥75 (oldest is 82) | | | | | | | |
| Gender, n (%) | Female | 93 76 (9) | 1741 (5) | 25 (3) | 401 (4) | 454 (6) | 479 (5) |
| | White | 105 072 (97) | 36 297 (97) | 892 (96) | 10 749 (97) | 7503 (96) | 9307 (96) |
| **Known risk factors** | | | | | | |
| Neuroticism score, mean (s.d.) | 3.2 (2.8) | 5.6 (3.3) | 3.8 (3.1) | 7.1 (3.3) | 5.2 (3.5) | 5.4 (3.5) |
| **Social isolation** | | | | | | |
| **Illness** | | | | | | |
| Smoking status, n (%) | 2976 (3) | 2367 (6) | 94 (10) | 971 (9) | 570 (7) | 669 (7) |
| | Current | 6235 (6) | 3638 (10) | 155 (17) | 1026 (9) | 854 (11) | 1109 (12) |
| | Daily | 888 (1) | 912 (4) | 63 (7) | 346 (3) | 258 (3) | 867 (9) |
| Physical activity, n (%) | 26 341 (24) | 13 363 (36) | 503 (54) | 4581 (41) | 3242 (42) | 3588 (38) |
| Moderate activity ≥ three times a week | 39 677 (36) | 13 988 (37) | 345 (37) | 4174 (38) | 2846 (36) | 3602 (38) |

---

**Notes:**

- a. Criteria not met for depression, generalised anxiety disorder (GAD), unusual experiences or addiction.
- b. Criteria met for disorder on Composite International Diagnostic Interview Short Form (CIDI-SF) lifetime.
- c. Criteria met for both lifetime depression and lifetime mania.
- d. Reported potential hallucination or delusion at any point in their life.
- e. Positively endorsed: “have you been addicted to or dependent on one or more things, including substances (not cigarettes/coffee) or behaviours (such as gambling)?”
- f. Age where mental health questionnaire completed, derived from date of birth.
- g. Townsend Deprivation Score, most deprived (TDS ≥2).
- h. Includes rent social and rent private, excludes other categories of housing tenure.
- i. From baseline assessment 2006–2010
- j. Criteria met for possible abuse or neglect on Childhood Trauma Screener.
- k. Criteria met for adverse situations as an adult: lack of confiding relationship, abusive relationships and money problems.
- l. Reports one or more of six situations that are known to be triggers for trauma-related disorders.
- m. There is some overlap between the adult screen and loneliness screen, which both ask about confiding relationships: adult screen includes lack of confiding relationship over the adult lifetime; loneliness includes lack of confiding relationship at the time of baseline assessment.
efficiently. The UK Biobank data, including that from the MHQ, is available to researchers and we have made the code used to derive the results in this paper freely available, allowing other researchers both to query our findings and build upon them for their own work.

The ‘healthy volunteer’ effect may limit applications of the data. The questionnaire was also heavily reliant on participant report, which may be affected by the stigma of reporting psychiatric symptoms, and tends to underestimate lifetime prevalence through forgetting or re-evaluating distant events. [41, 42] This caveat on ‘life-time’ disorder is another reason this data is more suitable for association studies than prevalence estimates. Researchers considering the use of UK Biobank data will need to assess the likely impact of selection bias and recall bias on a case-by-case basis, as this will affect whether UK Biobank is suitable and the choice of mental health data within UK Biobank. [39]

As a result of restrictions of time and space, the questionnaire was limited in the topics it could cover. The focus of the questionnaire was on categorical diagnoses rather than dimensional traits, which will tend to confirm conventional ICD/DSM nosology of psychiatric disorder and may not suit some research. [40] In particular, tools were chosen that are based on DSM-IV disorders, which reflects current practise (for example National Institute for Health and Care Excellence guidelines on depression and anxiety use DSM-IV rather than ICD). The proportion of participants with mental disorders and new users of UK Biobank. As a result of restrictions of time and space, the questionnaire was limited in the topics it could cover. The focus of the questionnaire was on categorical diagnoses rather than dimensional traits, which will tend to confirm conventional ICD/DSM nosology of psychiatric disorder and may not suit some research. In particular, tools were chosen that are based on DSM-IV disorders, which reflects current practise (for example National Institute for Health and Care Excellence guidelines on depression and anxiety use DSM-IV rather than ICD). The proportion of participants with mental disorders and new users of UK Biobank. In conclusion, UK Biobank offers a unique opportunity to research common disorders in a well-characterised longitudinal cohort of UK adults. A detailed MHQ has now been completed by 157 366 participants, including self-report, operationally defined lifetime disorder status and detailed phenotype information on mood disorder. The proportion of participants with mental disorders and the patterns of participants experiencing symptoms and disorders was as expected despite a ‘healthy volunteer’ selection bias. Further work on mental health phenotyping for UK Biobank includes validation of Hospital Episode Statistics for mental health diagnoses, incorporation of general practice records, trianguulation of health record and questionnaire data, and investigation of further putative phenotypes. Existing projects utilising UK Biobank mental health data can be seen in a searchable database of approved research (http://www.ukbiobank.ac.uk/approved-research/).

This study also demonstrates the substantial burden of mental health disorders, including potentially dangerous patterns of alcohol consumption. Given the known impact of mental health on physical health, mental health data and its associations should interest researchers from every biomedical specialty. This study suggests that UK Biobank could be a powerful tool for such studies, and as it is open to all bona fide health researchers for work in the public good, we hope this study will inspire both existing and new users of UK Biobank.

Implications

In conclusion, UK Biobank offers a unique opportunity to research common disorders in a well-characterised longitudinal cohort of UK adults. A detailed MHQ has now been completed by 157 366 participants, including self-report, operationally defined lifetime disorder status and detailed phenotype information on mood disorder. The proportion of participants with mental disorders and the patterns of participants experiencing symptoms and disorders was as expected despite a ‘healthy volunteer’ selection bias. Further work on mental health phenotyping for UK Biobank includes validation of Hospital Episode Statistics for mental health diagnoses, incorporation of general practice records, trianguulation of health record and questionnaire data, and investigation of further putative phenotypes. Existing projects utilising UK Biobank mental health data can be seen in a searchable database of approved research (http://www.ukbiobank.ac.uk/approved-research/).

This study also demonstrates the substantial burden of mental health disorders, including potentially dangerous patterns of alcohol consumption. Given the known impact of mental health on physical health, mental health data and its associations should interest researchers from every biomedical specialty. This study suggests that UK Biobank could be a powerful tool for such studies, and as it is open to all bona fide health researchers for work in the public good, we hope this study will inspire both existing and new users of UK Biobank.

London, and South London and Maudsley NHS Foundation Trust, South London and Maudsley NHS Foundation Trust, King’s College London; and South London and Maudsley NHS Foundation Trust, NIHR Biomedical Research Centre, UK, Jonathan R.J. Coleman, PhD, Lecturer in Statistical Genetics, Institute of Psychiatry, Psychology and Neuroscience, King’s College London; and South London and Maudsley NHS Foundation Trust, NIHR Biomedical Research Centre, UK, Breda Cullen, PhD, Senior Lecturer, Institute of Health and Wellbeing, University of Glasgow, UK, Chris Dickens, PhD, Professor of Mathematical Medicine, Institute of Health Research, University of Exeter Medical School, University of Exeter, UK, Elaine Fox, FRPS, Professor of Psychology and Affective Neuroscience, Department of Experimental Psychology, University of Oxford, UK, Nick Graham, MRCPsych, Clinical Lecturer in General Psychiatry, Institute of Health and Wellbeing, University of Glasgow, UK, Jo Holliday, PhD, Senior Research Facilitator, University of Oxford, and UK Biobank; UK Biobank, Nuffield Department of Population Health, University of Oxford Big Data Institute, UK, Louise M. Howard, PhD, NIHR Research Professor in Women’s Mental Health and NIHR Senior Investigator, Section of Women’s Mental Health, Institute of Psychiatry, Psychology and Neuroscience, King’s College London, UK; Ann Johnson, MD, Professor of Public Health and Psychiatry and Consultant Public Health Medicine, Population Data Science, Farr Institute of Health Informatics Research, Swansea University Medical School, Swansea University, and Public Health Wales NHS Trust, UK, William Lee, PhD, Consultant Liaison Psychiatrist and Honorary Clinical Senior Lecturer, Devon Partnership NHS Trust, and University of Exeter Medical School, University of Exeter, UK, Rose McCabe, PhD, Professor of Clinical Communication, School of Health Sciences, City, University of London, UK, Andrew Mcintosh, MRCPsych, Professor of Biological Psychiatry, Division of Psychiatry, University of Edinburgh, UK, Robert Pearseall, MRCPsych, Consultant Psychiatrist and Honorary Clinical Senior Lecturer in Psychiatry, Institute of Health and Wellbeing, University of Glasgow, UK, Daniel J. Smith, MRCPsych, Lecturer in Psychiatry, Institute of Health and Wellbeing, University of Glasgow, UK, Cathie Sodlow, FRCPsych, Director of the British Heart Foundation Data Science Centre, BHF Data Science Centre, Former Chief Scientist, UK Biobank, and Chair of Neurology and Clinical Epidemiology, Centre for Medical Informatics, Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, UK, Jooy Ward, MSC, Researcher, Institute of Health and Wellbeing, University of Glasgow, UK, Stan Zammit, MBMB, Lecturer in General Psychiatry, Centre for Academic Mental Health, University of Bristol; and Institute of Psychological Medicine and Clinical Neurosciences, University of Cardiff, Cardiff University School of Medicine, UK, Matthew Hotopf, FRCPsych, Director, National Institute for Health Research Biomedical Research Centre at the Maudsley, Institute of Psychiatry, Psychology and Neuroscience, King’s College London; and South London and Maudsley NHS Foundation Trust, NIHR Biomedical Research Centre, UK.

Correspondence: Matthew Hotopf. Email: matthew.hotopf@kcl.ac.uk

First received 28 Jun 2019, final revision 19 Nov 2019, accepted 17 Dec 2019

Funding

This paper represents independent research funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King’s College London. High performance computing facilities were funded with capital equipment grants from the GTI Charity (TR130050) and Maudsley Charity (£980), and individual authors acknowledge the following additional funding: M.A. is supported by a Wellcome Trust Strategic Award (Reference 10436/Z/14/Z). B.C. is funded by the Scottish Executive Chief Scientist Office (DTP/74/2003) and by The Dr Mortimer and Theresa Sackler Foundation (CA-04). W.L. is supported by the National Institute for Health Research (NIHR) Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, Department of Health, ERC, Scottish Government, UK Biobank or other funders or institutions.

The questionnaire was developed and administered with UK Biobank funding. Individual authors were funded by their institutions and research grants. No funding body influenced the study design or the writing of this article. M.A. had access to all data through a standard data-sharing agreement (material transfer agreement) with UK Biobank and retains final responsibility for the decision to submit the article for publication.

Acknowledgements

We thank the staff and participants of UK Biobank, the PROTECT study and the South London and Maudsley NHS Foundation Trust Service Users Group for their participation. High performance computing facilities were funded with capital equipment grants from the Guy’s and St Thomas’s Charity (TR130050) and Maudsley Charity (£980).

Data availability

Available from UK Biobank subject to standard procedures (www.ukbiobank.ac.uk). Code for replication available from Mendley Data (http://dx.doi.org/10.17632/ktz/w73zrhv.3).

Authors contribution

All authors’ contribution met the ICME criteria for authorship. K.A.S.D., G.B., E.F., L.M.H., A.J., R.M., AM, J.D.S., CS., S.Z. and M.H. designed the study. N.A. and J.H. co-ordinated the delivery.
1 Sudlow C, Gallagher J, Allen N, Beral V, Burton P, Danesh J, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. PLoS Med 2015; 12: e1001779.

2 Weissman MM, Brown AS, Talati A. Translational epidemiology in psychiatry: linking population to clinical and basic sciences. Arch Gen Psychiatry 2012; 68: 600–8.

3 Bell V. Open science in mental health research. Lancet Psychiatry 2017; 4: 525–6.

4 Conroy M, Sellers J, Effingham M, Littlejohns TJ, Boutilworth C, Gilleons L, et al. The advantages of UK Biobank’s open-access strategy for health research. J Intern Med 2012; 272: 389–97.

5 Prince M, Patel V, Saxena S, Maj M, Maselko J, Phillips MR, et al. No health without mental health. Lancet 2007; 370: 859–77.

6 Newton JN, Briggs ADM, Murray CI, Dicker D, Foreman KJ, Wang H, et al. Changes in health in England, with analysis by English regions and areas of deprivation, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015; 386: 2257–74.

7 Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet 2012; 380: 37–43.

8 Cohen BE, Edmondson D, Kronish IM. State of the art review: depression, stress, anxiety, and cardiovascular disease. Am J Hypertens 2015; 28: 1295–302.

9 Chang CK, Hayes RD, Broadbent MTM, Hotopf M, Davies E, Moller H, et al. A cohort study on mental disorders, stage of cancer at diagnosis and subsequent survival. BMJ Open 2014; 4: e004295.

10 Smith DJ, Nicholl Bl, Cullen B, Martin D, U-Haqqi E, 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: e76362.

11 Kessler RC, Andrews G, Colpe LJ, EMS,托H, et al. The prevalence and disability of mental disorders in the United States: Results from the National Comorbidity Survey Replication. Arch Gen Psychiatry 2003; 60: 572–80.

12 Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. Lifetime and 12-month prevalence of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005; 62: 617–30.

13 Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. Lifetime and 12-month prevalence of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005; 62: 617–30.

14 Newson RS, Karlsson H, Termeier H. Epidemiological fallacies of modern psychiatric research. Nord J Psychiatry 2011; 65: 226–37.

15 Davis KAS, Bashford O, Jewell A, Shetty H, Stewart RJ, Sudlow CLM, et al. Using UK biobank data to identify people with mental illness and other long-term conditions. BMJ Open 2016; 6: e011219.

16 Pitman A, Osborn DPJ, King MB. The use of internet-mediated cross-sectional studies in mental health research. BIPsych Adv 2015; 21: 175–84.

17 Bridges S. Health survey for England 2014: mental health problems. In HSE 2014 (ed Health and Social Care Information Centre), Office of National Statistics, 2015.

18 Kessler RC, Andrews G, Mroczek D, Ustun B, Wittenchen HU. The World Health Organization composite international diagnostic interview short-form (CIDI-SF). Int J Methods Psychiatr Res 1998; 7: 171–85.

19 Levinson D, Potash J, Mostafavi S, Battle A, Zhu X, Weissman M. Brief assessment of major depression for genetic studies: validation of CIDI-SF screening with SCID interviews. Eur Neuropsychopharmacol 2017; 27: S448.

20 Robotham D, Wykes T, Rose D, Doughty L, Strange S, Neale J, et al. Service user and carer priorities in a Biomedical Research Centre for mental health. J Ment Health 2016; 25: 185–9.

21 Weneses KA, Brooker H, Ballard C, McCambridge J, Stenton R, Corbett A. Utility, reliability, sensitivity and validity of an online test system designed to monitor changes in cognitive function in clinical trials. Int J Geriatr Psychiatry 2017; e63–e92.