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New-onset mental disorders increase among patients with metabolic diseases after the COVID-19 pandemic

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There is limited information on new-onset mental disorders in adults with metabolic diseases following the COVID-19 pandemic. Here, we aimed to examine the changes in mental health following the COVID-19 pandemic and identify factors associated with the development of new-onset mental disorders. Among 90,580 UK Biobank participants diagnosed with COVID-19 between Jan 31, 2020 and Oct 31, 2022, those who completed both baseline and follow-up mental health questionnaires in 2016–2017 and 2022–2023 were included in the analysis. New-onset depression, anxiety, and alcohol use disorder following the COVID-19 pandemic, as well as changes in mental health scores, were assessed. Furthermore, their association with sociodemographic, clinical, and self-perceived emotional state-related exposures was examined. Prevalent metabolic diseases were significantly associated with a higher risk of new-onset depression (hypertension: odds ratio [OR], 1.22; 95% CI 1.01–1.47; diabetes: OR 1.8; 95% CI 1.25–2.6; obesity: OR 1.66; 95% CI 1.43–1.95) and anxiety (hypertension: OR 1.32; 95% CI 1.06–1.63; diabetes: OR 1.66; 95% CI 1.06–2.62; obesity: OR 1.2; 95% CI 0.99–1.44) following COVID-19 pandemic. There was a significant increase of Patient Health Questionnaire-9 (PHQ-9; beta, 0.32; 95% CI 0.29–0.35) and Generalized Anxiety Disorder-7 (GAD-7; beta, 0.10; 95% CI 0.06–0.13) scores throughout the COVID-19 pandemic, while Alcohol Use Disorder Identification Test (AUDIT) score decreased over time (beta, − 0.24; 95% CI − 0.30 to − 0.18). Preexisting metabolic diseases were associated with the accelerated increase in the PHQ-9 and GAD-7 scores following the pandemic. Adults with metabolic diseases are associated with an increased risk of new-onset depression, anxiety, and alcohol use disorders following the COVID-19 pandemic.

Keywords COVID-19, Metabolic diseases, Mental health, Depression, Anxiety

Mental disorders are a global health issue that cause a substantial socioeconomic burden and is related to unfavorable health outcomes[1,2]. Mental health is profoundly affected by environmental factors, and the Coronavirus Disease 2019 (COVID-19) pandemic has threatened global mental health via a huge shift in public policy aimed at suppressing viral spread-outs by enforcing physical and societal restrictions (e.g., mask requirements, lockdowns, and physical distancing)[3,4]. In the context of COVID-19 itself, neuropsychiatric sequelae, such as fatigue, depression, anxiety, and cognitive dysfunctions, could manifest potentially in relation to neuroinflammation or central nervous system invasion[5,6].

Apparently, individuals with metabolic diseases, including diabetes, hypertension, and obesity, are at increased risk for mental disorders due to the complex interactions of physical, socioeconomical, and genetic factors, which is also linked to serious short- and long-term complications and adverse outcomes[7–10]. Identifying patterns of mental health change following the pandemic in patients with metabolic diseases and understanding

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their socioeconomic implications is therefore crucial to mitigate disease burden, prevent the worsening of mental health, and guide targeted intervention. A systematic review of mental health problems in the pandemic period revealed significant increases in anxiety, depression, sleep problems, and a substance use disorders; however, most studies were conducted in the general population, students, and health-care workers and focused on short-term prevalence after COVID-19 infection[4,11–15]. Large-scale, well-controlled longitudinal studies that examine the link between peri-pandemic mental distress in patients with metabolic diseases at the demographic, clinical, and societal levels remain scarce.

UK Biobank is a prospective study that involves comprehensive data on demographic, biochemical, and genetic information, including a recently released 6-year interval longitudinal follow-up mental well-being questionnaire[16]. Factors such as social interaction and self-perceived emotional state (e.g., loneliness or resilience), which are also available in the study, are worth investigating to demonstrate the nature of peri-COVID-19 mental health, given the significance of the social environment in the development of mental disorders and the circumstances surrounding the COVID-19 pandemic[17].

In this study, we examined longitudinal changes in mental health throughout the COVID-19 pandemic and explored a comprehensive set of factors associated with the development of new-onset mental disorders in ~ 60,000 UK Biobank participants. We hypothesized that individuals with prevalent metabolic diseases would be at an increased risk of new-onset mental disorders and worsening of mental health.

Methods

Study setting and participants

The UK Biobank is a prospective cohort study consisting of 502,536 participants aged 37–69 years when recruited in 2006–2010[16]. The baseline assessment included comprehensive phenotypic and genotypic information obtained from touch-screen questionnaire and interview (e.g., lifestyle, health, and socioeconomic status), physical and functional measures, biochemical assays, and genotyping. Health-related outcomes were obtained from self-reported data or linkage to electronic health records in national datasets.

Mental health web-questionnaire (MHQ) is a set of self-report questions to capture symptoms of possible mental disorders—mainly depression and anxiety—even in people who did not receive a formal diagnosis or have medical records in the linked national health datasets. Baseline MHQ including domains of current depression, anxiety disorder, and alcohol misuse, was completed by ~ 1/3 of participants during 2016–2017. Follow-up questionnaires were sent to approximately 330,000 participants during 2022–2023 to identify change in mental health-related experiences and psychiatric symptoms throughout time.

Among participants diagnosed with COVID-19 infection between Jan 1, 2020 (the date of the first diagnosed COVID-19 case in the UK) and Oct 31, 2022 (two weeks prior to the initiation of the follow-up MHQ survey) (Supplementary Fig. 1), a subset of participants who completed both baseline and follow-up MHQ were include in the study to assess the impact of the COVID-19 pandemic on mental health and to explore the factors involved in new-onset mental disorder. (Fig. 1).

Assessment of depression, anxiety, and alcohol use disorder

Assessments of depression, anxiety, and alcohol use disorder were conducted using MHQ at baseline and follow-up, which incorporates established screening and severity assessment tools to evaluate the mental health status of the participants. The Patient Health Questionnaire-9 (PHQ-9) is a widely used, 9-item questionnaire to evaluate the likely presence or absence and severity of current depression, and the Generalized Anxiety Disorder-7 (GAD-7) is a validated screening tool comprising 7-items for symptoms of generalized anxiety disorders[18–20]. The Alcohol Use Disorder Identification Test (AUDIT) is a 10-item screening tool to assess hazardous alcohol use by examining alcohol consumption patterns and the problematic consequences of drinking[21]. These scales were employed to identify the presence of relevant mental disorders and measure the degree of mental distress at the baseline and follow-up. Details of the items in each scale are available in Supplementary Data 1.

Ascertainment of exposures

Demographic, clinical, and occupational exposures included age, sex, smoking status (current, former, never), alcohol consumption frequency (less than once a week, 1–2, 3–4, 7 times/week), body mass index (BMI), waist circumference, systolic blood pressure (BP), biochemical assays, prevalent comorbidity, shift work (never, sometimes–always), and current employment status (employed, retired). Social interaction-related exposures included frequency of seeing friends and family in person and frequency of speaking to friends and family on a voice call. Factors related to loneliness and resilience were taken from 3-item UCLA loneliness scale[22,23] and Brief Resilience Scales[24]. Details of collected variables are described in Supplementary Data 2.

Statistical analyses

Baseline characteristics were presented as percentages for categorical variables, means with SDs, or medians with interquartile ranges.

In the cohort of participants who completed both baseline and follow-up questionnaires, participants with baseline PHQ-9, GAD-7, or AUDIT scores < 10—indicative of a lower likelihood of preexisting mental health issues before the COVID-19 pandemic—were included in the analysis to identify the factors related to the new-onset mental disorders and worsening of mental health post-pandemic. New-onset depression, anxiety disorder, and alcohol use disorders were defined as follow-up scores ≥ 10 on each assessment scale[18,19,21,25]. Logistic regression models were used to assess the association between the exposures and new-onset mental disorders post-pandemic. The exposures were analyzed individually, with adjustments made for age, sex, BMI, smoking status, alcohol consumption, hypertension, diabetes, hemoglobin, serum glucose, and creatinine-based eGFR at baseline. Participants with missing covariates were excluded from the analysis.

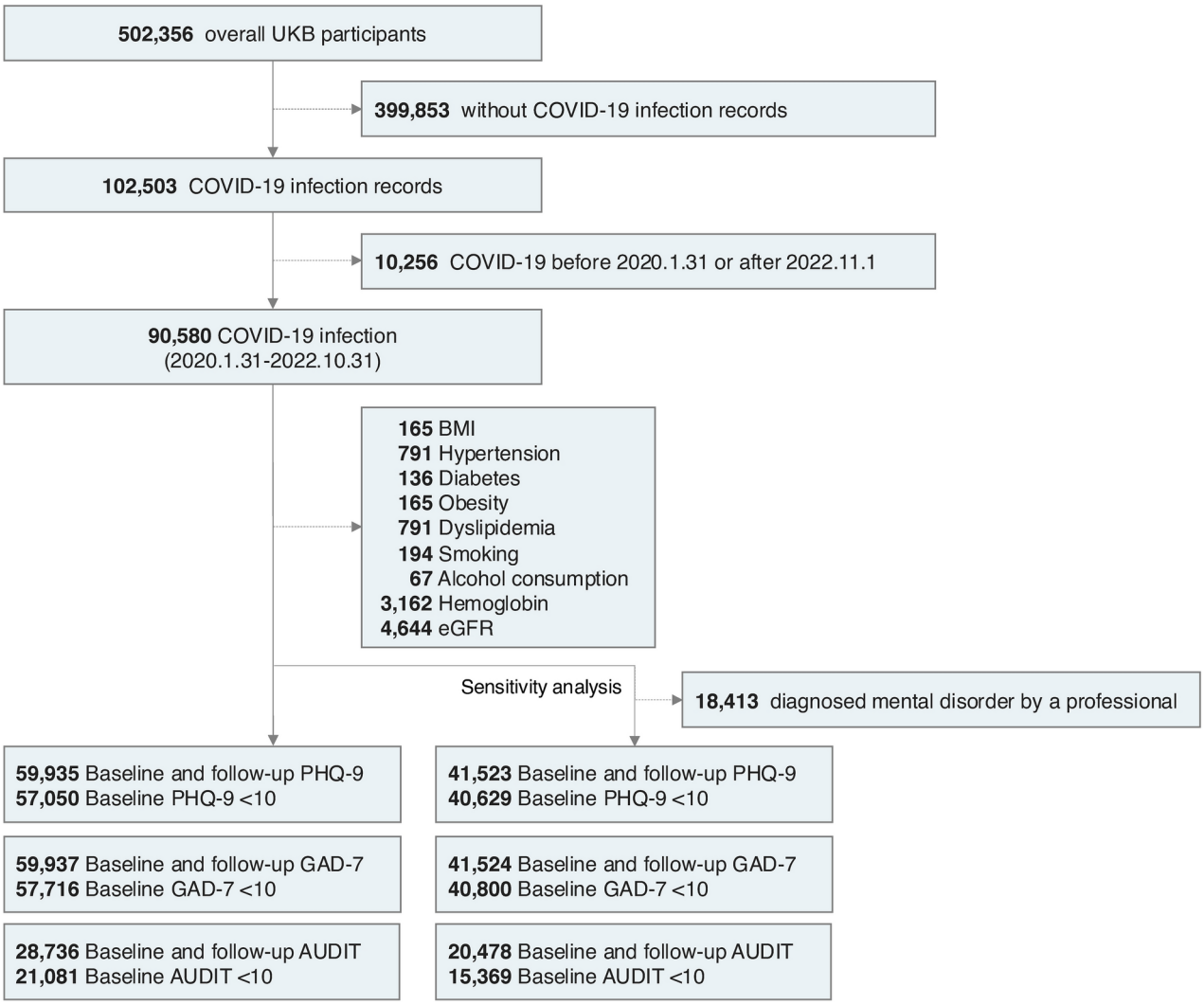


Fig. 1. Study flowchart. UKB, UK Biobank; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder 7-item; AUDIT, Alcohol Use Disorders Identification Test.

The longitudinal changes of mental health-assessment scales across the COVID-19 pandemic were assessed using linear regression models. Time was determined as a binary variable (baseline, follow-up). Worsening of mental health was defined as the significant increase in PHQ-9, GAD-7, or AUDIT score. Then, to test whether there were subgroups of distinct mental health changes over the course of the COVID-19 pandemic, linear regression models were fitted in subgroups (Supplementary Data 3). The rate of change over the COVID-19 pandemic was assessed using interaction term between the variable of interest and time. To ensure the robustness of the main analysis, sensitivity analyses were conducted after excluding participants who had been diagnosed with a mental disorder by a professional at baseline. Statistical significance was set at $P < 0.05$. All statistical analyses were performed using R software (version 4.2.3).

Results

Characteristics of participants

Of 502,356 UKB participants, 90,580 participants diagnosed with COVID-19 in Jan 2020–Oct 2022 were included in the study. Characteristics of the study population are provided in Table 1. Briefly, participants were aged 55 (48–60) year-old and 58.8% were male, with prevalence of hypertension (13.5%), diabetes (2.5%), obesity (10.8%), depression (11.2%), and anxiety disorder (3.9%). Among the participants who completed both baseline and follow-up assessments for the PHQ-9, GAD-7, and AUDIT questionnaires (59,935 [66.1%], 59,937 [66.1%], and 28,736 [31.7%], respectively), the proportion with the scores less than 10 accounted for 95.2%, 96.3%, and 73.4% on each scale at baseline. In the follow-up, participants with a PHQ-9 score less than 10 slightly decreased (95.2% to 94.6%), while those with a GAD-7 score less than 10 remained stable at 96.3%, and participants with an AUDIT score less than 10 were increased over time (73.4% to 76.3%).

Characteristic	Participants, n = 90,580
Age, y	55 (48–60)
Sex	
Female	37,320 (41.2)
Male	53,260 (58.8)
BMI, kg/m^2	25.9 (23.5–28.8)
Comorbidity at baseline	
Hypertension	12,075 (13.3)
Diabetes	2,235 (2.5)
Obesity	16,504 (18.2)
Dyslipidemia	9,655 (10.7)
Employment and lifestyle factors	
Smoking status	
Never smoker	53,890 (59.5)
Former smoker	30,741 (33.9)
Current smoker	5,755 (6.4)
Alcohol consumption, times/week	
Less than once a week	20,924 (23.1)
1–2	23,743 (26.2)
3–4	25,385 (28.0)
7	20,461 (22.6)
Job involves shift work	
Never/rarely	55,896 (61.7)
Sometimes/usually/always	8,489 (9.4)
Current employment status	
Employed	64,472 (71.2)
Retired	20,307 (22.4)
Social interaction, loneliness, and resilience	
Frequency of seeing friends and family in person	
At least once within a month	86,787 (95.8)
Once every few months	3,265 (3.6)
Never	395 (0.4)
Frequency of feeling "in tune" with the people	
Hardly ever	1,456 (1.6)
Some of the time	19,366 (21.4)
Often	68,342 (75.4)
Frequency of feeling that lacks companionship	
Hardly ever	62,141 (68.6)
Some of the time	22,940 (25.3)
Often	5,073 (5.6)
Frequency of feeling left out	
Hardly ever	63,975 (70.6)
Some of the time	22,819 (25.2)
Often	3,062 (3.4)
Quick recovery from stressful events	
Hardly ever	12,803 (14.1)
Some of the time	24,362 (26.9)
Often	53,353 (58.9)
Clinical variables	
Systolic blood pressure, mmHg	135.0 (123.0–148.0)
Hemoglobin, g/dL	14.0 (13.3–14.9)
Albumin, g/L	45.4 (43.7–47.1)
Serum glucose, mmol/L	4.9 (4.6–5.2)
Glycated hemoglobin, mmol/mol	34.5 (32.2–36.9)
LDL-cholesterol, mmol/L	3.5 (3.0–4.1)
eGFR, ml/min/1.73 m^2	94.2 (84.7–101.2)
Mental health screening scales[a]	
Continued	

Characteristic	Participants, n = 90,580
Time from first COVID-19 infection to complete MHQ	243 (145–426)
PHQ-9	
Baseline score	2.6 ± 3.4
< 10	57,050 (95.2)
≥ 10	2,885 (4.8)
Follow-up score	2.7 ± 3.7
< 10	56,680 (94.6)
≥ 10	3,255 (5.4)
GAD-7	
Baseline score	2.0 ± 3.2
< 10	57,716 (96.3)
≥ 10	2,221 (3.7)
Follow-up score	2.1 ± 3.3
< 10	57,712 (96.3)
≥ 10	2,225 (3.7)
AUDIT	
Baseline score	7.4 ± 4.0
< 10	21,081 (73.4)
≥ 10	7,655 (26.6)
Follow-up score	7.3 ± 4.0
< 10	21,936 (76.3)
≥ 10	6,800 (23.7)

Table 1. Baseline characteristics of study population2. Statistics were presented as percentages for categorical variables, means with SDs, or medians with interquartile ranges. [a]59,935, 59,937, and 28,736 participants completed both baseline and follow-up PHQ-9, GAD-7, and AUDIT scores, respectively. Participants with baseline PHQ-9, GAD-7, or AUDIT score ≥ 10, respectively, were excluded from the following analyses. BMI, body mass index; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder 7-item; AUDIT, Alcohol Use Disorders Identification Test.

Associated factors of new-onset depression, anxiety, and alcohol use disorder

The associations of the factors and new-onset depression, anxiety, or alcohol use disorder are examined. In the multivariable-adjusted models, being 60 years or younger (OR [95% CI], 1.4 [1.18–1.66]), being female (OR 1.64 [1.41–1.92]), being current or former smoker (OR 1.36 [1.21–1.54]), being obese (OR 1.66 [1.43–1.92]), prevalent hypertension (OR 1.22 [1.01–1.47]), diabetes (OR 1.8 [1.25–2.6]), and current main job involving shift work (OR 1.56 [1.3–1.87]) were significantly associated with a higher risk of new-onset depression following COVID-19 pandemic (Figs. 2 and 3). Risk factors of new-onset anxiety also included the factors mentioned above, as well as being retired (OR 1.45 [1.18–1.79]). Younger age (OR 1.52 [1.33–1.74]), being male (OR 1.43 [1.25–1.63], being current or former smoker (OR 1.5 [1.35–1.66]), being obese (OR 1.17 [1.02–1.35]), and prevalent hypertension (OR 1.2 [1.02–1.42]) were significantly associated with higher risk of new-onset alcohol use disorder.

Next, we examined whether the patterns of social interaction, loneliness and resilience were associated with the risk of new-onset mental disorder (Fig. 4). Participants who have not had regular contact with their friends and family were associated with higher risk of new-onset depression (OR 2.45 [1.69–3.55]) and anxiety (OR 2.81 [1.86–4.24]). Frequent feeling of being left out was markedly associated with a higher risk of new-onset depression (OR 28 [20.8–37.7]), anxiety (OR 15.8 [11.3–22.2]), and alcohol use disorder (OR 1.7 [1.12–2.57]); frequent feeling of "in tune" with the people around was associated with lower risk of all three mental disorders (depression, OR 0.08 [0.05–0.12]; anxiety, OR 0.1 [0.06–0.17]; alcohol use disorder, OR 0.47 [0.27–0.82]). Regarding resilience, participants who reported difficulty recovering from stressful events or who tended to take a long time to recover were more likely to develop mental disorders post-pandemic, while those who reported quick recovery from stressful events had a significantly lower risk of those.

Factors related to accelerated worsening of mental health

Multivariable-adjusted linear regression models demonstrated the increase of PHQ-9 (beta [95% CI], 0.32 [0.29–0.35]) and GAD-7 scores (beta, 0.10 [0.06–0.13]) throughout the COVID-19 pandemic, while AUDIT score decreased over time (beta, -0.24 [-0.30– -0.18]) (Table 2).

Several factors, particularly baseline comorbidity, were associated with the rate of worsening mental health during the era (Table 3 and Fig. 5). Participants with hypertension showed significant increase of both PHQ-9 and GAD-7 scores over time, showing greater degree of increase compared to those without hypertension (hypertension vs. those without, beta [95% CI]; PHQ-9, 0.43 [0.34–0.53] vs. 0.3 [0.27–0.34]; GAD-7, 0.19 [0.1–

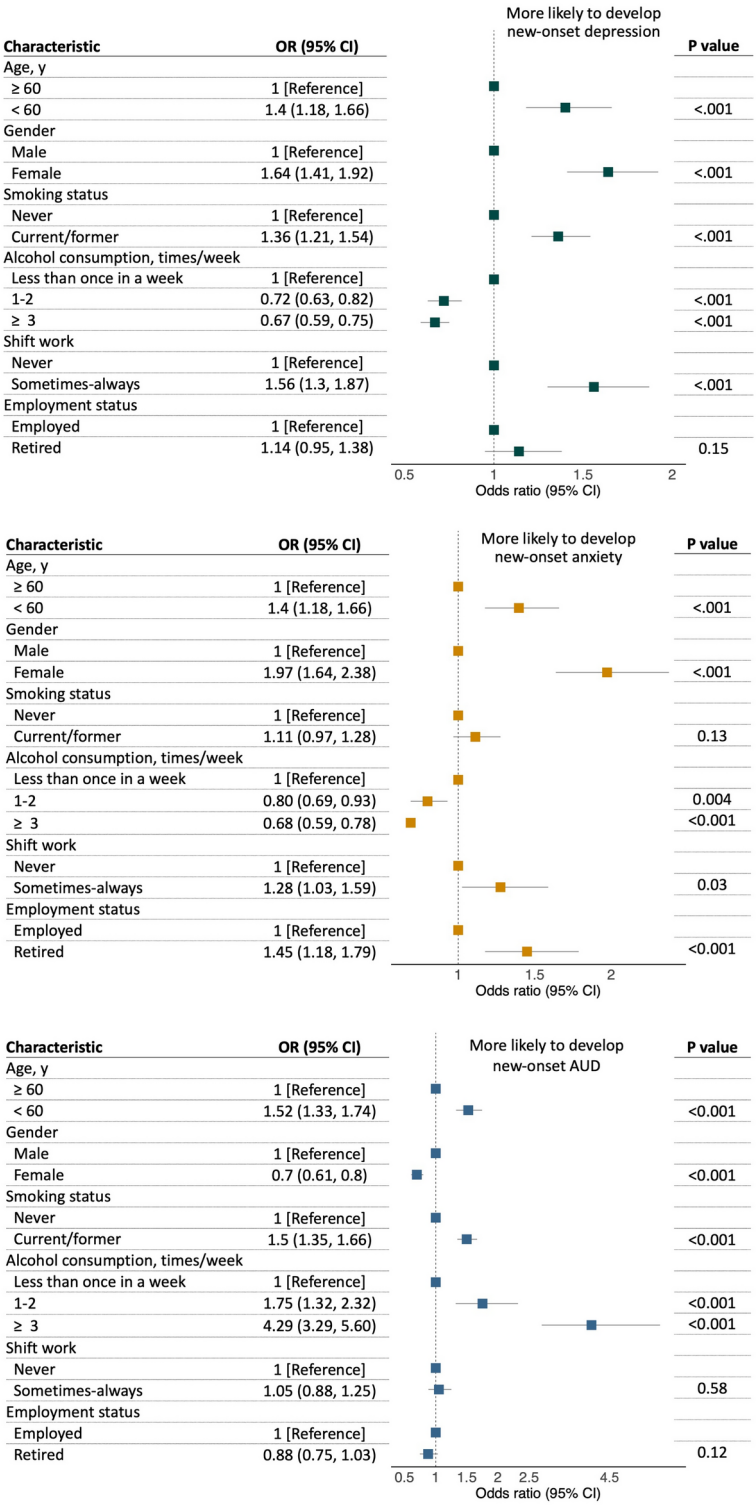
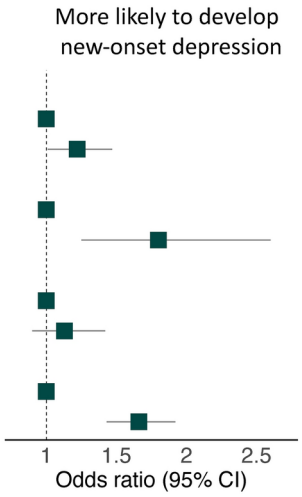


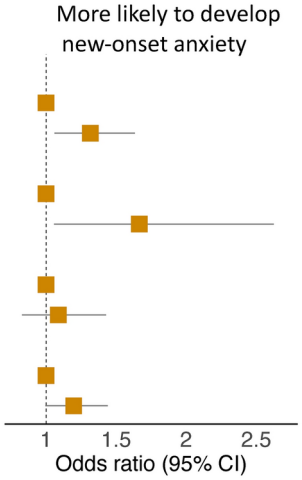
Fig. 2. Multivariable-adjusted results of the association between demographic factors and new-onset mental disorders. Models were adjusted for age, sex, body mass index, smoking status, alcohol consumption, prevalent hypertension, diabetes, hemoglobin, serum glucose, and creatinine-based eGFR at baseline. AUD, alcohol use disorder; OR odds ratio; 95% CI, 95% confidence interval.

0.29] vs. 0.08 [0.05–0.12]; P for interaction, < 0.001). Obese participants also exhibited a steeply increasing slope of PHQ-9 (obesity vs. those without, beta [95% CI]; 0.49 [0.4–0.58] vs. 0.28 [0.25–0.32]; P for interaction, < 0.001) and GAD-7 scores over time (obesity, those without, beta [95% CI]; 0.16 [0.08–0.25] vs. 0.08 [0.05–0.12]; P for interaction, 0.20) compared to those without obesity. Similar patterns were identified in participants with

Comorbidity	OR (95% CI)	P value
Hypertension		
No	1 [Reference]	
Yes	1.22 (1.01, 1.47)	0.03
Diabetes		
No	1 [Reference]	
Yes	1.8 (1.25, 2.6)	0.002
Dyslipidemia		
No	1 [Reference]	
Yes	1.13 (0.9, 1.42)	0.28
Obesity		
No	1 [Reference]	
Yes	1.66 (1.43, 1.92)	<0.001



Comorbidity	OR (95% CI)	P value
Hypertension		
No	1 [Reference]	
Yes	1.32 (1.06, 1.63)	0.01
Diabetes		
No	1 [Reference]	
Yes	1.66 (1.06, 2.62)	0.03
Dyslipidemia		
No	1 [Reference]	
Yes	1.09 (0.83, 1.43)	0.54
Obesity		
No	1 [Reference]	
Yes	1.2 (0.99, 1.44)	0.05



Comorbidity	OR (95% CI)	P value
Hypertension		
No	1 [Reference]	
Yes	1.2 (1.02, 1.42)	0.03
Diabetes		
No	1 [Reference]	
Yes	0.85 (0.58, 1.25)	0.41
Dyslipidemia		
No	1 [Reference]	
Yes	0.96 (0.79, 1.18)	0.7
Obesity		
No	1 [Reference]	
Yes	1.17 (1.02, 1.35)	0.03

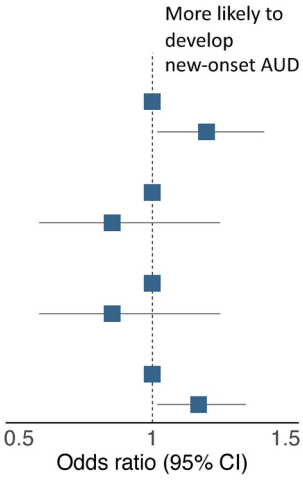


Fig. 3. Multivariable-adjusted results of the associations between comorbidity and new-onset mental disorders. Obesity was defined as baseline body mass index > 30 kg/m^2. Models were adjusted for age, sex, body mass index, smoking status, alcohol consumption, prevalent hypertension, diabetes, hemoglobin, serum glucose, and creatinine-based eGFR at baseline. AUD, alcohol use disorder; OR, odds ratio; 95% CI, 95% confidence interval.

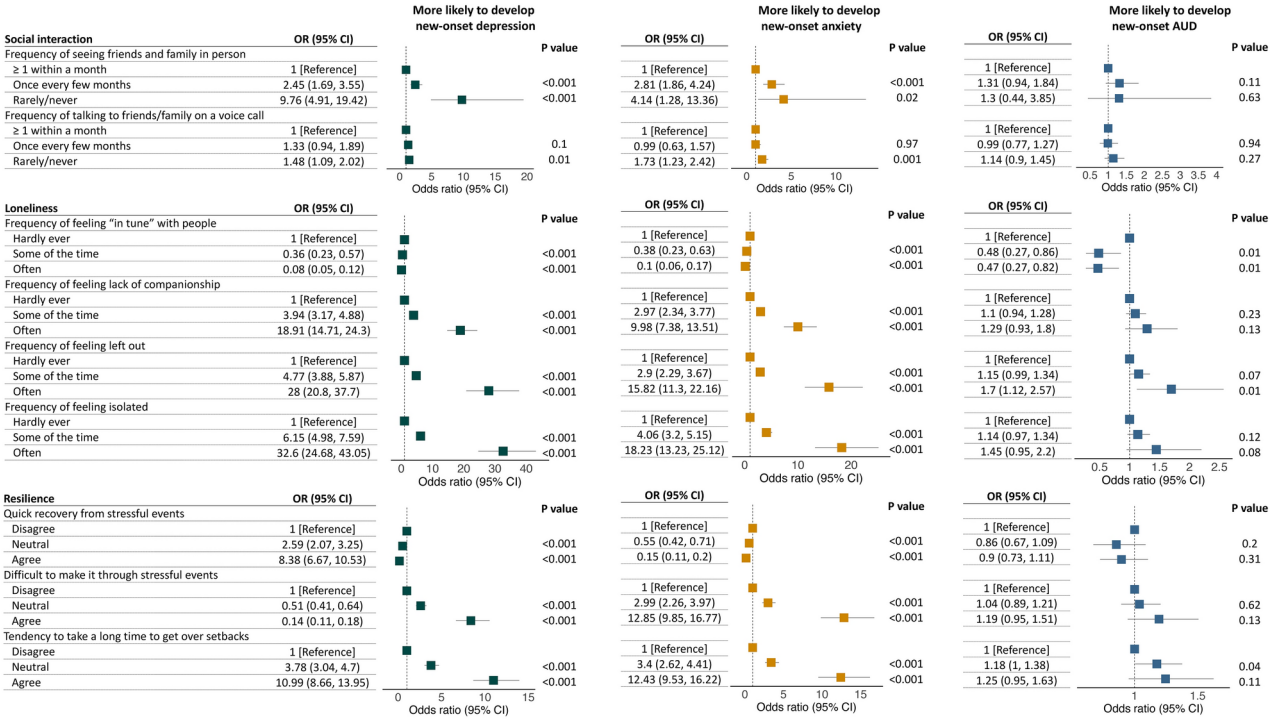


Fig. 4. Association between social interaction, loneliness, and resilience and new-onset mental disorders. Models were adjusted for age, sex, body mass index, smoking status, alcohol consumption, prevalent hypertension, diabetes, hemoglobin, serum glucose, and creatinine-based eGFR at baseline. AUD, alcohol use disorder; OR, odds ratio; 95% CI, 95% confidence interval.

	Univariable		Multivariable 1		Multivariable 2	
Scale	Beta coefficient (95% CI)	P	Beta coefficient (95% CI)	P	Beta coefficient (95% CI)	P
PHQ-9	0.32 (0.29, 0.35)	< .001	0.32 (0.29, 0.35)	< .001	0.32 (0.29, 0.35)	< .001
GAD-7	0.09 (0.06, 0.12)	< .001	0.09 (0.06, 0.12)	< .001	0.1 (0.06, 0.13)	< .001
AUDIT	− 0.19 (− 0.25, − 0.14)	< .001	− 0.21 (− 0.27, − 0.15)	< .001	− 0.24 (− 0.3, − 0.18)	< .001

Table 2. Change in PHQ-9, GAD-7, and AUDIT scores following the COVID-19 pandemic. In participants who completed baseline and follow-up questionnaires for each scale, linear regression was conducted between baseline and follow-up to identify the change in PHQ-9, GAD-7, and AUDIT scores after the COVID-19 pandemic. Participants with baseline PHQ-9, GAD-7, or AUDIT score ≥ 10, respectively, were excluded from the analyses. Model 1 was adjusted for age and sex. Model 2 was additionally adjusted for body mass index, smoking status, alcohol consumption, prevalent hypertension, diabetes, hemoglobin, serum glucose, and creatinine-based eGFR at baseline. Unit of change in each score, score per time-interval between visits. 95% CI, 95% confidence interval; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder 7-item; AUDIT, Alcohol Use Disorders Identification Test.

diabetes and dyslipidemia, while no significant interaction was observed between subgroups in each group with respect to GAD-7.

In adjusted models, participants who lacked regular contact with friends or family and frequently experienced a sense of companionship or isolation showed a greater increase in both PHQ-9 and GAD-7 scores. Conversely, participants who responded they often feel "in tune" with others or exhibit quick recovery from stressful events showed a significantly lower degree of increase in these scores.

Sensitivity analysis

To test the robustness of the relationship between the change in mental health and several factors across the COVID-19 pandemic, we conducted sensitivity analysis for the subset of 72,167 participants who were free of mental disorders at baseline. The associations between new-onset mental disorder and the factors examined in the main analysis mostly remained significant in the fully-adjusted models (Supplementary Table 1). The patterns of change in mental health assessment scores, such as the increase in PHQ-9 and GAD-7 scores and the decrease in AUDIT scores, were consistently observed in the sensitivity analysis (Supplementary Table 2).

Subgroups	PHQ-9 Beta (95% CI)	P	P for interaction	GAD-7 Beta (95% CI)	P	P for interaction	AUDIT Beta (95% CI)	P	P for interaction
Gender									
Male	0.22 (0.17, 0.27)	< .001	< .001	0.03 (− 0.02, 0.07)	0.26	< .001	− 0.25 (− 0.34, − 0.17)	< .001	0.75
Female	0.39 (0.35, 0.44)	< .001		0.15 (0.1, 0.2)	< .001		− 0.23 (− 0.31, − 0.15)	< .001	
Age, y									
≥ 60	0.4 (0.35, 0.46)	< .001	0.64	0.21 (0.16, 0.27)	< .001	< .001	− 0.32 (− 0.43, − 0.21)	< .001	0.01
< 60	0.28 (0.24, 0.32)	< .001		0.05 (0, 0.09)	0.03		− 0.21 (− 0.28, − 0.15)	< .001	
Smoking status									
Never smoker	0.27 (0.23, 0.32)	< .001	0.002	0.08 (0.04, 0.12)	< .001	0.19	− 0.18 (− 0.25, − 0.11)	< .001	0.07
Current/former smoker	0.39 (0.33, 0.44)	< .001		0.13 (0.07, 0.18)	< .001		− 0.3 (− 0.4, − 0.21)	< .001	
Obesity									
No	0.28 (0.25, 0.32)	< .001	< .001	0.08 (0.05, 0.12)	< .001	0.20	− 0.22 (− 0.28, − 0.16)	< .001	0.30
Yes	0.49 (0.4, 0.58)	< .001		0.16 (0.08, 0.25)	< .001		− 0.34 (− 0.49, − 0.19)	< .001	
Hypertension									
No	0.3 (0.27, 0.34)	< .001	0.01	0.08 (0.05, 0.12)	< .001	0.03	− 0.24 (− 0.3, − 0.18)	< .001	0.68
Yes	0.43 (0.34, 0.53)	< .001		0.19 (0.1, 0.29)	< .001		− 0.29 (− 0.46, − 0.12)	0.001	
Diabetes									
No	0.31 (0.28, 0.34)	< .001	< .001	0.1 (0.06, 0.13)	< .001	0.45	− 0.24 (− 0.3, − 0.18)	< .001	0.99
Yes	0.69 (0.44, 0.95)	< .001		0.18 (− 0.06, 0.43)	0.14		− 0.25 (− 0.65, 0.15)	0.22	
Dyslipidemia									
No	0.3 (0.27, 0.34)	< .001	0.01	0.09 (0.05, 0.13)	< .001	0.19	− 0.24 (− 0.3, − 0.17)	< .001	0.60
Yes	0.45 (0.35, 0.56)	< .001		0.16 (0.06, 0.27)	0.002		− 0.31 (− 0.49, − 0.13)	< .001	
Shift job									
Never	0.26 (0.22, 0.3)	< .001	< .001	0.03 (− 0.01, 0.07)	0.17	< .001	− 0.22 (− 0.29, − 0.15)	< .001	< .001
Sometimes–always	0.43 (0.31, 0.56)	< .001		0.12 (0, 0.25)	0.04		− 0.15 (− 0.35, 0.04)	0.13	
Frequency of seeing friends and family in person									
Within a month	0.26 (0.22, 0.3)	< .001	< .001	0.08 (0.04, 0.12)	< .001	0.01	− 0.27 (− 0.33, − 0.2)	< .001	0.17
Once every few months	0.6 (0.36, 0.85)	< .001		0.3 (0.05, 0.55)	0.01		− 0.16 (− 0.54, 0.23)	0.42	
Hardly ever	2.28 (1.13, 3.42)	< .001		0.56 (− 0.4, 1.53)	0.25		0.74 (− 0.67, 2.15)	0.30	
Frequency of feeling "in tune" with the people									
Hardly ever	2.36 (1.8, 2.93)	< .001	< .001	1.11 (0.57, 1.66)	< .001	< .001	− 0.12 (− 0.83, 0.6)	0.74	0.99
Some of the time	0.26 (0.22, 0.3)	< .001		0.08 (0.04, 0.12)	< .001		− 0.27 (− 0.33, − 0.2)	< .001	
Often	0.11 (0.07, 0.14)	< .001		− 0.03 (− 0.07, 0.01)	0.14		− 0.26 (− 0.33, − 0.19)	< .001	
Frequency of feeling that lacks companionship									
Hardly ever	0.05 (0.02, 0.09)	0.005	< .001	− 0.06 (− 0.1, − 0.02)	0.003	< .001	− 0.27 (− 0.34, − 0.2)	< .001	0.37
Some of the time	0.59 (0.5, 0.67)	< .001		0.31 (0.23, 0.4)	< .001		− 0.25 (− 0.39, − 0.11)	< .001	
Often	2.27 (2, 2.54)	< .001		1.19 (0.93, 1.44)	< .001		− 0.11 (− 0.48, 0.25)	0.54	
Frequency of feeling isolated from others									
Hardly ever	0.04 (0.01, 0.07)	0.02	< .001	− 0.07 (− 0.1, − 0.03)	< .001	< .001	− 0.27 (− 0.34, − 0.21)	< .001	0.29
Some of the time	0.84 (0.74, 0.94)	< .001		0.45 (0.35, 0.56)	< .001		− 0.23 (− 0.39, − 0.07)	0.004	
Often	3.21 (2.84, 3.59)	< .001		1.86 (1.5, 2.23)	< .001		− 0.04 (− 0.54, 0.46)	0.87	
Quick recovery from stressful events									
Disagree	1.06 (0.93, 1.2)	< .001	< .001	0.71 (0.56, 0.85)	< .001	< .001	− 0.12 (− 0.31, 0.07)	0.23	0.01
Neutral	0.49 (0.41, 0.57)	< .001		0.22 (0.14, 0.3)	< .001		− 0.19 (− 0.32, − 0.07)	0.003	
Agree	0.03 (− 0.01, 0.07)	0.17		− 0.1 (− 0.14, − 0.06)	< .001		− 0.32 (− 0.39, − 0.24)	< .001	

Table 3. Subgroup analyses for the change in mental score following the COVID-19 pandemic. Participants with baseline PHQ-9, GAD-7, or AUDIT score ≥ 10, respectively, were excluded from the analyses. Models were adjusted for age, sex, body mass index, smoking status, alcohol consumption, prevalent hypertension, diabetes, hemoglobin, serum glucose, and creatinine-based eGFR at baseline. PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder 7-item; AUDIT, Alcohol Use Disorders Identification Test.

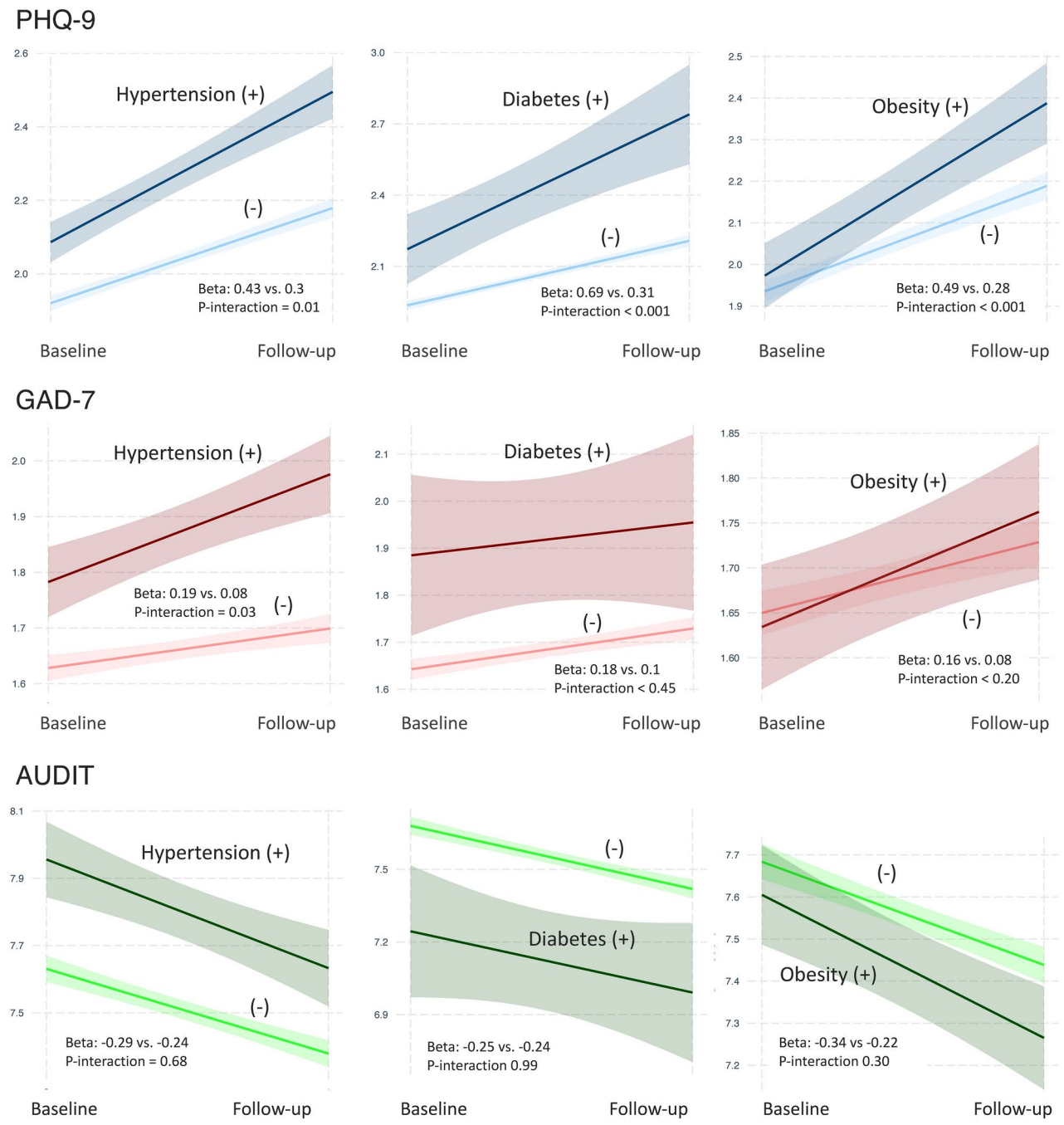


Fig. 5. The change in average mental health scores over time in subgroups of metabolic diseases. The interaction plots show the change in average PHQ-9, GAD-7, and AUDIT scores (y-axis) across baseline and follow-up timepoints (x-axis) within each comorbidity subgroups. Beta coefficients, indicating the slope between the average mental health scores at the specified timepoints, and P-values for these associations (P for interaction) are presented as indicators of statistical significance in each subgroup. Models were adjusted for age, sex, body mass index, smoking status, alcohol consumption, prevalent hypertension, diabetes, hemoglobin, serum glucose, and creatinine-based eGFR at baseline. PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7; AUDIT, Alcohol Use Disorder Identification Test.

In the interaction term analysis, participants being female, current/former smokers, engaged in shift work, having prevalent comorbidities, and being emotionally vulnerable had greater increases in PHQ-9 scores (Supplementary Table 3).

Discussion

In this study, we explored the change in mental health following the COVID-19 pandemic, the factors associated with new-onset depression, anxiety, and alcohol use disorder, as well as the accelerated worsening of mental health in ~ 60,000 participants diagnosed with COVID-19 in the UK Biobank. We identified that adults with prevalent metabolic diseases, including hypertension, diabetes, and obesity, were more likely to develop new-onset depression, anxiety, and alcohol use disorder across the pandemic, compared to those without such comorbidities. On average, PHQ-9 and GAD-7 scores increased over time, while AUDIT scores were decreased. Patients with metabolic disease presented a marked increase in the rate of deterioration of PHQ-9 and GAD-7 scores. Social interactions, loneliness, and resilience were significantly linked to a reduced risk of new-onset mental disorder and worsening of mental health.

The COVID-19 pandemic reshaped the global landscape of mental health, causing significant increases in the prevalence of depression and anxiety compared to pre-pandemic era[26–29]. Accumulating evidence on the impact of the COVID-19 pandemic on the mental health indicates an association between comorbidities and an increased risk of mental illness[12,30–32]. Particularly, patients with preexisting comorbidities are more exposed to a burden from social disconnection and financial instabilities, which can lead to much detrimental effects on mental health[33,34]. The people with metabolic diseases are not only at a higher risk of mental disorders in peri-pandemic era[35–38], but being complicated with mental disorders in these patients exacerbates adverse biological responses, such as elevated blood pressure[39,40], insulin resistance[41,42], and activation of inflammatory and stress signaling[43], potentially leading to unfavorable outcomes. As the world is slowly recovering from the aftermath of the pandemic, it is necessary to demonstrate the longitudinal change of mental health throughout the COVID-19 era, identify high-risk groups and modifiable risk factors of new-onset mental disorders to risk-stratify the population, conduct effective interventions, and establish post-pandemic public health strategies.

Our study has several strengths. First, several studies and systematic reviews focused on the short-term consequences of COVID-19 on mental health or were conducted in a cross-sectional design[11,12,44,45]; we observed longitudinal patterns of mental health in a large population over an extended period (2016–2017 to 2022–2023) in the UK Biobank dataset to broaden the scope in understanding the change in mental health pre- and post-COVID-19 era. Second, we used well-established scales, including PHQ-9 (depression)[19], GAD-7 (anxiety disorder),[18] and AUDIT (alcohol use disorder)[21], and employed validated cut-off values in defining cases of mental disorders, as in previous studies. Measure for loneliness and resilience were also taken form established scoring system, such as 3-item UCLA loneliness scale[22,23] and Brief Resilience Scales[24]. Third, in addition to observing a change in the overall mental health of the study population, we also focused on the rate of worsening mental health in several subgroups—females, adults aged < 60-year-old, those with comorbidities, shift workers, those vulnerable to loneliness, and those lacking resilience—to determine whether these subgroups require interventions at an earlier stage than those who do not.

In this study, females and participants aged < 60-year-old were associated with a greater risk of depression and anxiety compared to males and those with older age, which was in line with the previous observations[30,44,46]. Remarkably, we identified that prevalent hypertension, diabetes, and obesity were associated with an increased risk of new-onset depression and anxiety post-pandemic. These patients were already at higher preexisting risks for mental disorders before the pandemic; it is noticeable that the preexisting risks significantly accelerated during the pandemic, leading to substantial deterioration in mental health and an increase in new-onset mental disorders following the pandemic. Patients with metabolic diseases are more predisposed to developing severe diseases and increased mortality rates associated with COVID-19[47]. Obese individuals are 1.75 times more likely to be hospitalized in the intensive care unit[48], and patients with type 2 diabetes and hypertension have a 2.88 and 1.74 times higher likelihood, respectively, of developing severe COVID-19[49,50]. They face unprecedented somatic and social challenges, which significantly complicate the management of the preexisting comorbidities[30,42,47]. These findings support that post-pandemic mental health management strategies should be initiated at an earlier stage for patients with metabolic diseases. In addition, through an analysis of the association between mental health, social interactions with family or friends, and self-perceived emotional states, our study demonstrated that these factors are significantly associated with post-pandemic changes in mental well-being. Individuals diagnosed with COVID-19 often experience social isolation and disruptions in interpersonal connections. However, even within this cohort, differences in the extent of social interaction were linked to varying risks of mental disorders. These findings underscore the critical role of social engagement and self-perceived emotional status in mitigating psychological distress and highlighting the need for tailored interventions to support mental well-being in affected populations.

During the early period of the COVID-19 pandemic, several studies reported a significant rise in alcohol use disorder and related mortality[51,52]. The greatest increase in high-risk drinking was observed among individuals who were under lockdown or stay-at-home restrictions, potentially because of the increased emotional strains due to confinement with other family members[53]; however, our study shows a contradictory results of a decrease in AUDIT score throughout the pandemic. This could be explained by the different timing of data collection, as most studies were implemented during the lockdown period or when social restrictions were stringent. In contrast, the current study examined the longitudinal change in alcohol misuse between pre- and post-pandemic. Our study suggests, while the risk of alcohol use disorder was increased during the pandemic, relaxation of social restrictions and public efforts to improve alcohol-related disorders may have contributed to the overall decrease of alcohol use disorder following the pandemic.

There are some limitations to this study. First, it should be noted that the findings may not be representative of global changes in mental health, as the study only included participants from the UK Biobank. Second, using mental health-assessment scales in defining cases of mental illnesses can possibly overestimate the prevalence of mental disorders in patients with metabolic diseases to some extent[9]. However, considering the cohort size of over 300,000 participants who completed the MHQ from the UK Biobank, and given the diagnostic validity of using a cut-off score of 10 or higher[18–21], our study effectively demonstrates a population-based longitudinal patterns of mental health change following the COVID-19 pandemic. Additionally, the reciprocal impact of mental disorders on the progression of metabolic diseases was not examined in the present study. Given the well-established associations between mental and metabolic disorders—mediated by behavioral[54,55], pharmacological[56], genetic[57], and healthcare factors[58]—it is plausible that the new-onset mental disorders may exacerbate the severity of preexisting metabolic diseases and contribute to adverse health outcomes. However, further research is warranted to elucidate the bidirectional relationship between these conditions.

In summary, we found that patients with metabolic diseases showed an increased risk for new-onset depression and anxiety disorders and accelerated rate of mental health worsening following the COVID-19 pandemic. Modifiable risk factors include social interactions, as well as self-perceived emotional status. Increased attention to the risk stratification and intervention for mental health in these patients is a public health priority.

Data availability

The datasets generated and analysed during the current study are available in the UK Biobank (www.ukbiobank.ac.uk; study accession no, 53,799).

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Author contributions

The corresponding author attests that all of the listed authors meet the authorship criteria and that no others meeting the criteria have been omitted. JMC, JO, JHK, MK, SGK, SC, SL, YK, YCK, SSH, and HL performed the main statistical analysis including data curation, formal analysis, and investigation. JMC, JO, JHK, MK, and

SGK contributed to the investigation and methodology. KWJ, YSK, DKK, and SP contributed to the conceptualization and design of the study. SP advised on statistical aspects and interpreted the data. DKK and SP offer advice regarding the data interpretation and supervised. SP supervised the overall project. All of the authors participated in drafting the manuscript. All of the authors reviewed the manuscript and approved the final version to be published.

Declarations

Competing interests
The authors declare no competing interests.

Ethical approval
The study was conducted in accordance with the Declaration of Helsinki and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline. UK Biobank (no. 53799) and Institutional Review Board of Seoul National University Hospital (IRB No. 2402-003-1506) approved this study. Written informed consent was obtained from the study participants before collecting any bio-specimens or clinical information.

Additional information
Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-99280-6.

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