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Postpartum depression in relation to chronic diseases and multimorbidity in women's mid-late life: a prospective cohort study of UK Biobank

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Abstract

Background Maternal short-term outcomes of postpartum depression (PPD) were widely examined, but little is known about its long-term association with multiple chronic diseases (multimorbidity) in women's later life. This study aims to assess the association of PPD with chronic diseases and multimorbidity in women's mid-late life.

Methods This prospective cohort study included female participants in UK Biobank who attended online follow-up assessment and reported their history of PPD. A total of 36 chronic diseases were assessed and multimorbidity was defined as the co-existence of two or more of these diseases. Participants were followed from the baseline recruitment to the onset of two or more chronic diseases, death, or the end of follow-up (2023). Logistic regression models, Cox proportional hazard models, quasi-Poisson mixed effects models, and linear mixed models were conducted to examine the association of PPD with chronic diseases and multimorbidity at baseline and during follow-up.

Results Among all 54,885 participants, 5106 (9.3%) participants experienced PPD, 13,928 (25.4%) participants had multimorbidity at baseline, and 14,135 (25.8%) participants developed two or more diseases during a median follow-up of 15 years. Women with a PPD history had higher odds of having multimorbidity at baseline (odds ratio = 1.35, 95% confidence interval [CI] = 1.27–1.44) and higher risk of developing multimorbidity during follow-up (hazard ratio = 1.13, 95% CI = 1.08–1.20). PPD was associated with increased number of chronic diseases, with the relatively new-onset number of diseases during follow-up being 8% higher for those with PPD (relative risk = 1.08, 95% CI = 1.05–1.12). Chronic diseases also accumulated at a faster annual rate for women with a history of PPD ($b = 0.009$, 95% CI = 0.007–0.011), compared to those without. We observed no interaction or mediation effects of physical activity, smoking, alcohol drinking, and dietary factors on the association between PPD and multimorbidity; however, women's body mass index at baseline contributed to the association, with the mediation proportion of 6.38% (2.56–10.20%).

Conclusions PPD was associated with higher risks of chronic diseases and multimorbidity in women's mid-late life. This finding supports the importance of perinatal and postpartum mental health care, and its role in the prevention of chronic diseases and multimorbidity throughout women's life course.

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Keywords Postpartum depression, Depression, Chronic diseases, Multimorbidity

Background

Depression is twice as common in women than in men across the lifespan, and sex hormones, in particular estradiol and progesterone, are suggested to play an important role in the sex differences in susceptibility [1, 2]. During a critical time of the first five postnatal weeks, these hormones fluctuate, resulting in a three-fold increased risk of depressive episodes for women [3–5]. Postpartum depression (PPD), defined as an episode of major depressive disorder occurring up to one year after childbirth [6], has an estimated prevalence of 17.22% (95% confidence interval [CI]: 16.00–18.51%) worldwide [7]. The clinical symptoms of PPD are similar to depression occurring at other stages over women's lifespan; however, some studies indicated that women with PPD were more likely to comorbid with anxiety than the non-postpartum women [8, 9], exacerbating the burden of maternal mental disorders.

While PPD tends to remit spontaneously, its influence on women could continue for several years and even result in persistent mood disorders, in particular for those inadequately treated [7]. A systematic review synthesized that PPD was associated with higher risks of maternal physical and psychological problems, including weight retention, social relationship problems, persistent depression, and worsen quality of life [10]. For specific chronic diseases, some population-based studies revealed that PPD was associated with higher risks of diabetes [11], cardiovascular disease (CVD) [12], and chronic depression [13]. However, these studies focused on maternal short-term outcomes with the median follow-up time ranging from 6 months to 5 years after childbirth. We found only two prospective studies revealing significant associations of PPD with the long-term risks of CVD up to 23 years of follow-up [14] and elevated depressive symptoms up to 11 years after childbirth [15]. Data on whether mental disorders in women's postpartum period may impact long-term risks of chronic diseases are still lacking.

More importantly, the global burden of multimorbidity (i.e., the coexistence of two or more chronic diseases in an individual) has increased with the population aging [16, 17], affecting nearly 40% women worldwide [18]. Compared to people without multimorbidity, the presence of depression is two to three times more common in those with multimorbidity [19]. Although numerous studies have linked depression with the higher risk of multimorbidity in the general population [20–23], whether and to what extent the depression episode occurring during women's postpartum period is associated with the risk of multimorbidity later in life remains unclear [24]. There is a need of prospective data to disentangle the patterns and trajectories of multimorbidity long-term after childbirth, in particular among women who experienced PPD.

Using data from a large-scale population-based prospective study of UK Biobank, this study aims to investigate whether the history of PPD during maternal reproductive age is associated with long-term risks of chronic diseases and multimorbidity in their mid-to-late life.

Methods

Study design and population

This study used data from UK Biobank, a population-based prospective cohort study which enrolled over half a million participants aged between 40 and 69 years when recruited in 2006–2010 across the UK. Participants have completed touch screen questionnaires about information on their socioeconomic status, lifestyles, and reproductive factors at the baseline recruitment. They were also invited to attend online follow-up surveys on their mental health status in 2016. All participants were followed for their health-related outcomes through linkage to health registers including the Hospital Episode Statistics for England, the Patient Episode Database for Wales, and the Scottish Morbidity Record for Scotland. More information about UK Biobank is available elsewhere [25]. This study followed the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) reporting guideline.

In this study, we initially included women who have attended the online follow-up assessment on mental health status ($n=89,076$). The exclusion criteria included (1) women who were nulliparous or had no information on parity ($n=20,061$); (2) women with no information on whether they had a history of PPD ($n=2589$); (3) women with any of the 36 chronic diseases before pregnancy (computed by subtracting the age when diseases were diagnosed and the age at last live birth for multiparous women or age at first live birth for primiparous women) ($n=11,513$); and (4) women with any of 36 chronic diseases before 20 years ($n=28$). Finally, a total of 54,885 females were included in the following analyses (Fig. 1). The characteristics of the excluded participants can be found in Additional file 1: Table S1.

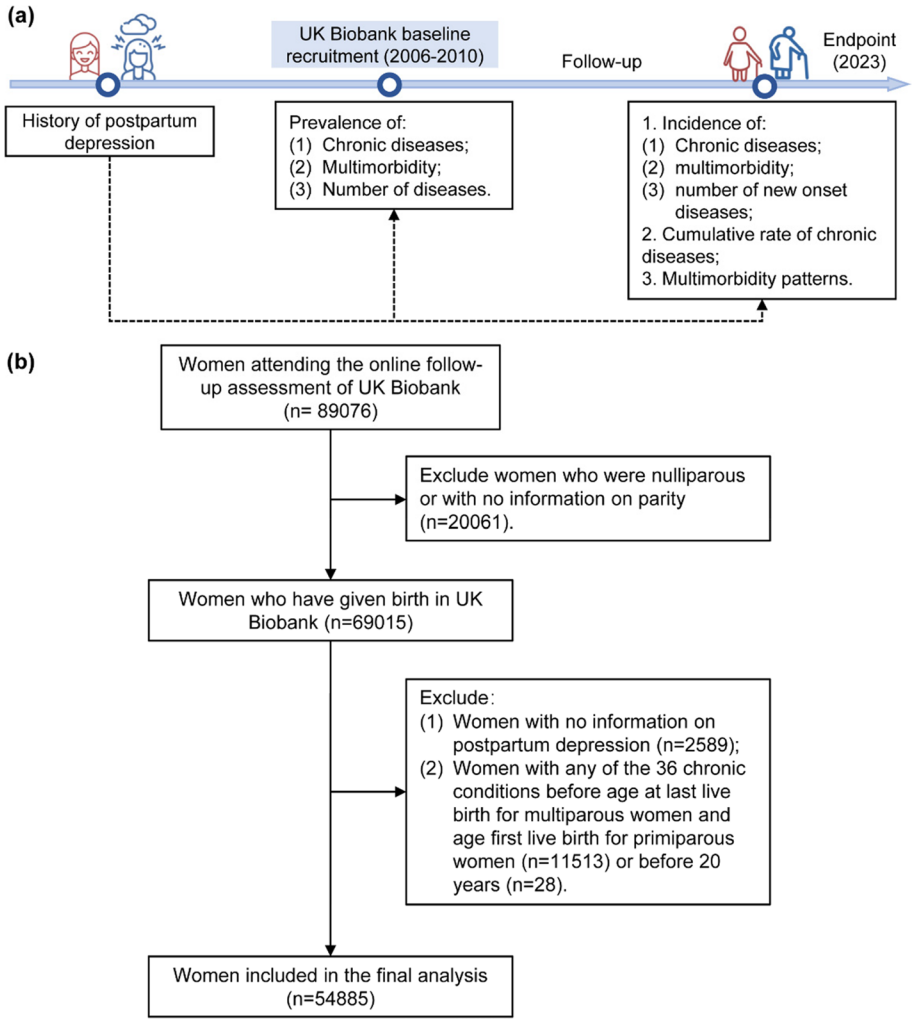

Fig. 1 Diagram of study design and selection process. **a** The concept framework of study design. **b** The selection process of study population

Assessment of postpartum depression

The history of PPD was ascertained through the online follow-up of mental health self-assessment questionnaire which was conducted in 2016. In detail, if female participants reported a history of depressive feeling, they were then asked "Did this depressive episode occur within months of giving birth? Or has it been suggested you had post-natal depression?" Women who answered "Yes" were considered having a PPD history. In addition, disease records (mental and behavioral disorders associated with the puerperium) in the primary care system and hospital inpatient system were extracted as supplements.

Assessment of chronic diseases and multimorbidity

A total of 36 chronic diseases were chosen and used to define multimorbidity in this study according to (1) the UK's primary care pay for performance program—the Quality and Outcomes Framework (QoF)—which introduced the most common chronic diseases in the UK [26]; (2) systematic reviews about multimorbidity which recommended the core diseases for the measurement [27, 28]; (3) a large-scale study in the UK which reported long-term diseases identifying as important by NHS Scotland [29]; and (4) previous studies measuring multimorbidity in UK Biobank [30–33] (Additional file 1: Table S2). Diagnoses of these chronic diseases were ascertained through 4 sources: self-reported medical diseases at the baseline or subsequent assessment of UK Biobank, the primary care data, the hospital inpatient data (according to the codes of International Classification of Diseases [ICD] 9th and 10th version), and death register records (according to the codes of ICD-10). Diagnoses of cancer were also ascertained through cancer register.

Multimorbidity was defined as the presence of two or more chronic diseases in an individual. In this study, the following specific outcomes were measured: (1) the prevalence of multimorbidity at baseline: presence of two or more chronic diseases at the UK Biobank baseline recruitment; (2) the incidence of multimorbidity: the incidence of developing at least two chronic diseases during follow-up; (3) the number of new-onset chronic diseases during follow-up; (4) the cumulative rate of chronic diseases during follow-up; and (5) multimorbidity patterns at the end of follow-up, identified using exploratory factor analysis (Additional file 1: Supplementary Methods).

Assessment of covariates

Covariates ascertained in this study were collected at baseline, including sociodemographic characteristics (age at baseline, ethnicity, educational level, employment status, and total household income before tax), anthropometric information (body mass index [BMI]), lifestyle factors (current smoking status, current alcohol drinking status, physical activity, and alternative healthy eating index [AHEI]), and reproductive factors (menopause status, parity, and ever usage of hormone-replacement therapy). BMI were categorized into four groups of underweight, healthy weight, overweight, and obesity [34]. Physical activity was measured according to Metabolic Equivalent Task minutes per week for moderate and vigorous activity and was divided as tertiles. The AHEI was calculated with the reference of previous studies [35]. Covariates with responses of "do not know" or "prefer not to answer" were considered as missing data and were assigned to the "unknown" group.

Statistical analysis

Baseline characteristics of participants were summarized as mean (standard deviation [SD]) for continuous variables and as number (percentage) for categorical variables according to the history of PPD, number of chronic diseases at baseline, and number of new onset diseases during follow-up. Differences of variables across groups were compared using Student's *t*-test or chi-squared test when appropriate.

At baseline, we used binomial logistic regression models to assess the associations of PPD with the presence of one or more chronic diseases, the prevalence of multimorbidity, and the prevalence of each individual chronic diseases. Also, quasi-Poisson mixed effects models were utilized to assess the association between PPD and number of chronic diseases at baseline (Additional file 1: Supplementary Methods) [36]. The fully adjusted model included age at baseline, ethnicity, educational level, employment status, total household income, current smoking status, current alcohol drinking status, physical activity, BMI, AHEI, menopause status, parity, and ever usage of hormone-replacement therapy.

During follow-up, Cox proportional hazard models were used to evaluate the associations of PPD with the incidence of developing one or more diseases, the incidence of developing two or more diseases, and the incidence of each individual diseases. Years from the baseline recruitment to the new onset of the first or the second chronic diseases, the ascertainment of death, or the end of follow-up (1st September 2023), whichever occurred first, were considered the time scale. The proportional hazard assumption was checked using Schoenfeld's residual methods and no violations were found. Quasi-Poisson mixed effects models were conducted to examine the association between PPD and number of new-onset diseases during follow-up. The models were adjusted for number of chronic diseases at baseline in addition to the aforementioned covariates. We used linear mixed model to examine the association between PPD and the cumulative rate of chronic diseases during follow-up by including interactions between follow-up year and PPD as fixed effects, and including random effects for participants and follow-up year.

At the end of follow-up, we identified five multimorbidity patterns: Cardiometabolic Pattern, Heart Pattern, Respiratory Pattern, Mental Pattern, and Digestive Pattern (Additional file 1: Table S3). Multinomial logistic regression models were then used to assess the association between PPD and the adherence of each multimorbidity pattern.

A series of additional analyses were conducted to test the robustness of our primary results. First, subgroup analyses were conducted to assess the association of PPD with the incidence of multimorbidity stratified by age at baseline, ethnicity, educational level, employment status, total household income, menopause status, and parity. Second, a series of sensitivity analyses were performed by (1) excluding women who have developed multimorbidity during the first 2 years of follow-up; (2) excluding women with missing covariates; (3) imputing missing covariates with multiple imputation; (4) including women without any single of 36 diseases at baseline; (5) including women with one or more diseases at baseline; and (6) using the Fine and Gray's model to account for death as a competing event. Third, to examine the role of lifestyle factors (physical activity, current smoking and alcohol drinking status, BMI, and AHEI) on the association between PPD and the incidence of multimorbidity, we conducted a four-way decomposition analysis, which can decompose the total effect of PPD on multimorbidity into four components: (1) the controlled direct effect: the effect of PPD on multimorbidity caused by neither mediation nor

interaction; (2) reference interaction effect: the effect of PPD on multimorbidity due to the interaction between PPD and lifestyle factors; (3) mediated interaction effect: the component of PPD on multimorbidity that is due to both interaction and mediation of lifestyle factors; and (4) the pure indirect effect: the component of PPD on multimorbidity that is due to the mediation role of lifestyle factors.

Statistical analyses were conducted using SAS (version 9.4, SAS Institute Inc., NC, USA) and R (version 4.3.3, R Foundation for Statistical Computing). Odds ratios (ORs), hazard ratios (HRs), relative risks (RRs), and 95% CIs were reported in this study. Significance tests were evaluated at the 0.05 level using two-sided tests.

Results

Baseline characteristics of participants

Among the 54,885 female participants who have attended the online follow-up assessment on mental health, 9.3% ($n=5106$) of them had a history of PPD. A total of 13,928 (25.4%) participants had multimorbidity at baseline (Additional file 1: Table S4), and 14,135 (25.8%) participants developed two or more diseases during a median follow-up of 15 years (Additional file 1: Table S5). Participants with a history of PPD tended to be younger, white, higher educated, unemployed, smokers, previous drinkers, obese, pre-menopause, ever using hormone-replacement therapy, and have a higher parity at baseline (Table 1). As shown in Fig. 2, participants with a PPD history had a higher rate of having chronic diseases and multimorbidity at baseline and were more likely to develop chronic diseases and multimorbidity during follow-up.

Association of PPD with multimorbidity, number of chronic diseases, cumulative rate of chronic diseases, individual chronic diseases, and multimorbidity patterns

The history of PPD was associated with higher prevalence and incidence of one or more chronic diseases and multimorbidity at baseline and during follow-up (Table 2). The adjusted ORs for the association between PPD and the prevalence of having one or more diseases and multimorbidity at baseline were 1.32 (95% CI = 1.24–1.40) and 1.35 (95% CI = 1.27–1.44), respectively. The adjusted HRs for the association between PPD and the incidence of developing one or more new diseases and multimorbidity were 1.06 (95% CI = 1.02–1.11) and 1.13 (95% CI = 1.08–1.20), respectively. Moreover, PPD was associated with higher number of chronic diseases at baseline and during follow-up, with the relative number of chronic diseases being 19% higher at baseline (adjusted RR = 1.19, 95% CI = 1.16–1.23) and 8% higher during follow-up (adjusted RR = 1.08, 95% CI = 1.05–1.12) for women with a history of PPD, compared to those without. Chronic diseases also accumulated at a faster annual rate for women with a history of PPD ($b=0.009$, 95% CI = 0.007–0.011), compared to those without (Fig. 3).

Similar results were observed for individual chronic diseases. The results showed statistically significant association of the PPD history with the higher prevalence of 11 chronic diseases at baseline (Additional file 1: Fig. S1) and higher incidence of 6 chronic diseases during follow-up (Fig. 4). The history of PPD was associated with higher odds of chronic diseases mapped to the Mental Pattern (adjusted OR = 2.05, 95% CI = 1.89–2.22), followed by the Respiratory Pattern (adjusted OR = 1.22, 95% CI = 1.11–1.33), the Digestive Pattern (adjusted OR = 1.19, 95% CI = 1.08–1.31), and the Heart Pattern (adjusted OR = 1.13, 95% CI = 1.03–1.25) (Table 2).

Additional analyses

Subgroup analyses showed consistent results between PPD and the risk of multimorbidity across sub-populations stratified by age at baseline, ethnicity, educational level, employment status, total household income, menopause status, and parity (Additional file 1: Fig. S2). The four-way decomposition analysis showed no interaction or mediation effects of physical activity, smoking, alcohol drinking, and dietary factors on the association between PPD and multimorbidity (Additional file 1: Table S6). We observed a mediation effect of women's BMI at baseline contributing to the association between PPD and the incidence of multimorbidity, with the mediation proportion of 6.38% (95% CI = 2.56–10.20%). Sensitivity analyses also showed similar results to the main findings (Additional file 1: Table S7).

Discussion

Principle findings

Based on a longitudinal study of 54,885 female participants in the UK, we found that maternal PPD was associated with higher risks and faster accumulative rates of chronic diseases and multimorbidity in women's mid-late life. In particular, PPD was associated with higher risks of chronic diseases mapped to the Mental Pattern, the Respiratory Pattern, the Digestive Pattern, and the Heart Pattern. These relationships were confirmed to be robust according to the sensitivity and subgroup analyses.

Comparison with previous research

We observed 9.3% participants having a history of PPD in our study. This prevalence is similar to a cohort study reporting 11% of the total 206,517 women had a record of PPD based on UK primary care electronic health records [37], but is lower than the global prevalence of

Table 1 Baseline characteristics of participants by postpartum depression

	Total population (*n* = 54,885)	History of postpartum depression		*P* value
		With (*n* = 5106)	Without (*n* = 49,779)	
Age at baseline, mean (SD)	56.6 (7.4)	55.9 (7.6)	56.7 (7.4)	**< 0.001***
Ethnicity, *n* (%)				**0.012***
White	53,284 (97.1)	4967 (97.3)	48,317 (97.1)	
Non-white	1490 (2.7)	121 (2.4)	1369 (2.8)	
Unknown	111 (0.2)	18 (0.4)	93 (0.2)	
Educational level, *n* (%)				**< 0.001***
College or above	21,973 (40.0)	2049 (40.1)	19,924 (40.0)	
Below high school	24,658 (44.9)	2189 (42.9)	22,469 (45.1)	
Unknown	8254 (15.0)	868 (17.0)	7386 (14.8)	
Employment status, *n* (%)				**< 0.001***
Unemployed	3601 (6.6)	412 (8.1)	3189 (6.4)	
Employed	50,964 (92.9)	4665 (91.4)	46,299 (93.0)	
Unknown	320 (0.6)	29 (0.6)	291 (0.6)	
Total household income before tax, *n* (%)				**0.036***
Less than £18,000	7495 (13.7)	709 (13.9)	6786 (13.6)	
£18,000–£30,999	11,811 (21.5)	1070 (21.0)	10,741 (21.6)	
£31,000–£51,999	13,446 (24.5)	1326 (26.0)	12,120 (24.3)	
£52,000–£100,000	11,345 (20.7)	1034 (20.3)	10,311 (20.7)	
> £100,000	3469 (6.3)	331 (6.5)	3138 (6.3)	
Unknown	7319 (13.3)	636 (12.5)	6683 (13.4)	
Current smoking status, *n* (%)				**< 0.001***
Never	33,492 (61.0)	2924 (57.3)	30,568 (61.4)	
Previous	18,173 (33.1)	1849 (36.2)	16,324 (32.8)	
Current	3098 (5.6)	320 (6.3)	2778 (5.6)	
Unknown	122 (0.2)	13 (0.3)	109 (0.2)	
Current alcohol drinking status, *n* (%)				**< 0.001***
Never	1950 (3.6)	158 (3.1)	1792 (3.6)	
Previous	1399 (2.5)	167 (3.3)	1232 (2.5)	
Current	51,504 (93.8)	4776 (93.5)	46,728 (93.9)	
Unknown	32 (0.1)	5 (0.1)	27 (0.1)	
Physical activity, *n* (%)				0.136
Low	7410 (13.5)	681 (13.3)	6729 (13.5)	
Moderate	19,331 (35.2)	1861 (36.4)	17,470 (35.1)	
High	16,750 (30.5)	1494 (29.3)	15,256 (30.6)	
Unknown	11,394 (20.8)	1070 (21.0)	10,324 (20.7)	
Body mass index, *n* (%)				**< 0.001***
Underweight	1924 (3.5)	158 (3.1)	1766 (3.5)	
Healthy weight	22,845 (41.6)	1988 (38.9)	20,857 (41.9)	
Overweight	19,924 (36.3)	1886 (36.9)	18,038 (36.2)	
Obese	10,068 (18.3)	1062 (20.8)	9006 (18.1)	
Unknown	124 (0.2)	12 (0.2)	112 (0.2)	
Alternative healthy eating index, mean (SD)	27.8 (7.4)	27.8 (7.4)	27.8 (7.4)	0.934
Post menopause, *n* (%)				**< 0.001***
No	11,893 (21.7)	1246 (24.4)	10,647 (21.4)	
Yes	40,621 (74.0)	3624 (71.0)	36,997 (74.3)	
Unknown	2371 (4.3)	236 (4.6)	2135 (4.3)	
Ever usage of hormone-replacement therapy, *n* (%)				**< 0.001***
No	33,719 (61.4)	2990 (58.6)	30,729 (61.7)	
Yes	21,069 (38.4)	2101 (41.1)	18,968 (38.1)	
Unknown	97 (0.2)	15 (0.3)	82 (0.2)	
Parity, mean (SD)	2.2 (0.8)	2.3 (0.9)	2.2 (0.8)	**< 0.001***

* Statistical significance

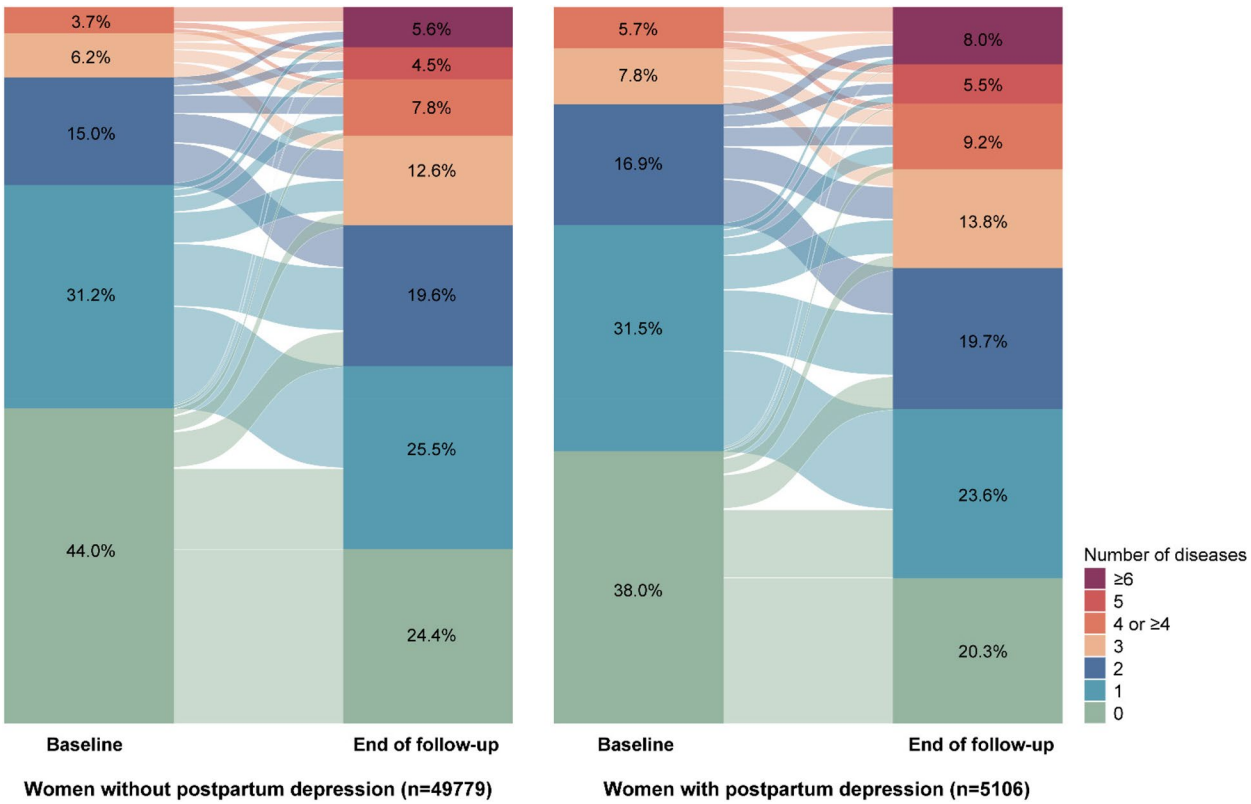

Fig. 2 Sankey plot for the changes of number of chronic diseases from baseline to the end of follow-up among women without or with postpartum depression

17.2% according to a systematic review [7]. These variations in prevalence may partly be explained by the different socioeconomic contexts, as the prevalence of PPD was lower in high-income countries than that of low- or middle-income countries [38]. In addition, information on PPD in our study was collected based on self-reported medical history; therefore, the estimated prevalence may be affected by recall bias. Although we have extracted records from primary care and hospital inpatient data as supplements, some women may not recognize the depressive symptoms, or may be reluctant to seek help to disclose their mental problems, which might result in an underestimate of the PPD prevalence in our study [39].

Previous studies have linked depression with chronic diseases and multimorbidity at older ages in the general population. For example, a cohort study including 4605 Chinese elders suggested that depression was associated with higher odds of developing physical multimorbidity (OR = 1.84, 95% CI = 1.50–2.46) [22]. Another multicohort study based on middle-aged and older adults revealed that the HR for developing cardiometabolic multimorbidity was 1.31 (95% CI: 1.14–1.50) in patients with depression [23]. To date, few studies examined the physical and psychological outcomes of depression occurring at women's early life ages. It was suggested that PPD was associated with higher risks of CVD [12], diabetes [11], and chronic depression [13] shortly after giving birth (the median follow-up time: 6 months to 5 years). However, current evidence on the long-term health outcomes of PPD is limited. We extended the influence of PPD beyond pregnancy and childbirth, taking advantage of the long-term follow-up time of UK Biobank. Our findings are in line with previous longitudinal studies revealing the associations of PPD with long-term risks of CVD and chronic depression [14, 15] and provide further evidence on the associations of PPD with several chronic diseases and multimorbidity in women's mid-to-late life. The faster accumulative rates of multimorbidity in women with a PPD history suggested the accelerated aging processes among these women [40].

For individual chronic diseases, we showed that PPD was associated with 11 chronic diseases at UK Biobank baseline when the women's mean age was 56.6 years. These diseases included depression, anxiety, peripheral vascular disease, irritable bowel syndrome, constipation, angina, chronic sinusitis, rheumatoid arthritis, migraine, endometriosis, and asthma. During follow-up, we found statistically significant associations of PPD with

Table 2 Associations of postpartum depression with number of chronic diseases, multimorbidity, and multimorbidity patterns at baseline (2006–2010) and during follow-up (to 2023)

	Model 1	Model 2	Model 3
Baseline prevalence			
One or more chronic diseases[a]	1.28 (1.21–1.36)	1.33 (1.25–1.41)	1.32 (1.24–1.40)
Multimorbidity[a]	1.32 (1.24–1.41)	1.36 (1.27–1.45)	1.35 (1.27–1.44)
Number of chronic diseases[b]	1.20 (1.16–1.24)	1.20 (1.17–1.24)	1.19 (1.16–1.23)
Follow-up incidence			
One or more chronic diseases[c]	1.08 (1.04–1.13)	1.10 (1.05–1.14)	1.06 (1.02–1.11)
Multimorbidity[c]	1.17 (1.10–1.23)	1.18 (1.12–1.25)	1.13 (1.08–1.20)
Number of chronic diseases[b]	1.11 (1.07–1.15)	1.12 (1.08–1.16)	1.08 (1.05–1.12)
Follow-up patterns			
Cardiometabolic Pattern[a]	1.06 (0.97–1.17)	1.07 (0.97–1.18)	1.05 (0.95–1.17)
Heart Pattern[a]	1.08 (0.98–1.19)	1.14 (1.04–1.26)	1.13 (1.03–1.25)
Respiratory Pattern[a]	1.25 (1.14–1.36)	1.24 (1.13–1.36)	1.22 (1.11–1.33)
Mental Pattern[a]	2.15 (1.98–2.33)	2.07 (1.91–2.24)	2.05 (1.89–2.22)
Digestive Pattern[a]	1.19 (1.08–1.30)	1.21 (1.10–1.33)	1.19 (1.08–1.31)

Model 1: unadjusted

Model 2: adjusted for age at baseline, ethnicity, educational level, employment status, total household income, current smoking status, current alcohol drinking status, physical activity, body mass index, and alternative healthy eating index

Model 3: adjusted for age at baseline, ethnicity, educational level, employment status, total household income, current smoking status, current alcohol drinking status, physical activity, body mass index, alternative healthy eating index, menopausal status, parity, and ever usage of hormone-replacement therapy (and number of chronic diseases at baseline for follow-up incidence)

[a] Odds ratios and 95% confidence interval

[b] Relative risks and 95% confidence interval

[c] Hazard ratios and 95% confidence interval

6 chronic diseases, including schizophrenia, depression, anxiety, heart failure, angina, and constipation. Most of these chronic diseases were related to mental, vascular, and inflammatory disorders, which were consistent with results for the association of PPD with higher adherence to multimorbidity patterns including the Mental Pattern, the Respiratory Pattern, the Digestive Pattern, and the Heart Pattern.

The stronger association of PPD was found in particular with chronic depression, anxiety, and their comorbid Mental Pattern, supporting the hypothesis that women were likely to have persistent (i.e., the risk of depression is persistently high across the lifetime) or a U-shaped form (i.e., the high risk of depression occurs in early adulthood of women's reproductive age, while the risk declines over the midlife period and rises again in later life) of mental health disorders across the life course [41]. The associations of PPD with several heart diseases and the Heart Pattern were also robust at baseline and during follow-up, which was in accord with previous studies linking PPD with long-term risk of CVD [12, 14]. The relationships of depression with respiratory diseases (e.g., asthma) [42] and digestive diseases (e.g., irritable bowel syndrome) [43] have been well-studied in the general population, but less is known about depression in women's perinatal period with the risks of these diseases later in life. The novel finding of the associations between PPD with diseases mapped to the Respiratory Pattern and Digestive Pattern accentuates the demand for further research to verify such relationships.

Several potential mechanisms can explain the long-term health impacts of PPD. First, different from depression occurring in other stages of women's lifespan, the hormonal changes specific to the transition from pregnancy to postpartum is a unique risk factor for PPD [44]. Women who are prone to PPD were also sensitive to depressive symptoms during other times of hormonal perturbations, such as during the peri-menopause stages [45], resulting in persistent depression symptoms across women's life course. Such repeated depressive episodes may accelerate women's aging process [46], leading to higher risks of other comorbid chronic physical diseases and faster accumulative rate of diseases later in life [22, 47]. Second, women who have experienced PPD were more likely to withdraw from favorable lifestyles or maintain unhealthy behaviors, such as unhealthy diets, which would have sustained effects on the development of multiple chronic diseases and multimorbidity in their later life [48–50]. In this case, we conducted four-way decomposition analyses to examine the potential roles

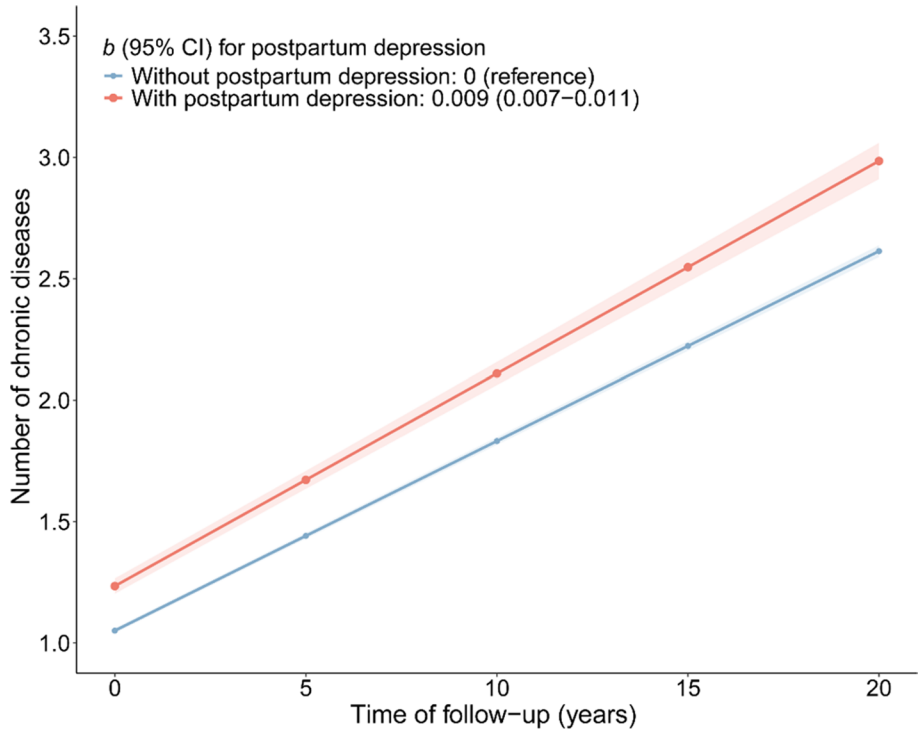

Fig. 3 Association between postpartum depression with chronic disease accumulation over time. The model was adjusted for age at baseline, ethnicity, educational level, employment status, total household income, current smoking status, current alcohol drinking status, physical activity, body mass index, alternative healthy eating index, menopausal status, parity, and ever usage of hormone-replacement therapy

of lifestyle factors in the association between PPD and multimorbidity. Women's BMI at baseline exhibited as a mediator in such association, which suggests that weight management might be a potential efficient strategy to counteract the adverse health outcomes resulting from PPD. However, the information on women's BMI before pregnancy and its dynamic changes after childbirth were not available in our study; future studies are needed to verify such results. Third, women's effort to combat stress after childbirth would increase corticosteroids and adrenaline, resulting in vasoconstriction [11, 51]. These physiological responses were associated with the development of diseases mapped to the Vascular Pattern. In addition, PPD was linked to inflammatory dysregulation and hyperactivation of immune, which would damage neurons and limit neuronal growth and repair [52–55]. These pathophysiology pathways implicate prolonged neurodegenerative changes which would have long-term impact on women's health.

Strengths and limitations

Strengths of this study include the large sample size, the prospective study design, the adjustment of multiple covariates, and the comprehensive diseases information by considering records from primary care, hospital inpatient records, death register, and self-reported medical history. The long-time follow-up of participants also allowed us to explore the long-term effects of PPD on mothers themselves.

There remain some limitations that should be mentioned. First, information on PPD was self-reported by participants, which was vulnerable to recall bias. Although we have extracted records from primary care and hospital inpatient data as supplements, records of PPD in these systems were limited and misclassifications of PPD cases remain a possibility. In addition, the retrospective recall of PPD limited us to follow women from the date of PPD diagnosis to their later life. A continuous surveillance of women from pregnancy and childbirth to their mid- and late-life health is needed. Second, the study design covers a long time span of women's life course from giving birth to mid-late life. Although we have adjusted for a series of covariates in this study, residual confounding is still possible. We used the E-value methodology [56] to assess the robustness of results to unmeasured confounders, indicating that the observed HR of 1.13 for incident multimorbidity could only be explained by an unmeasured confounder that was associated with both PPD and the risk of multimorbidity by a risk ratio of more than 1.40

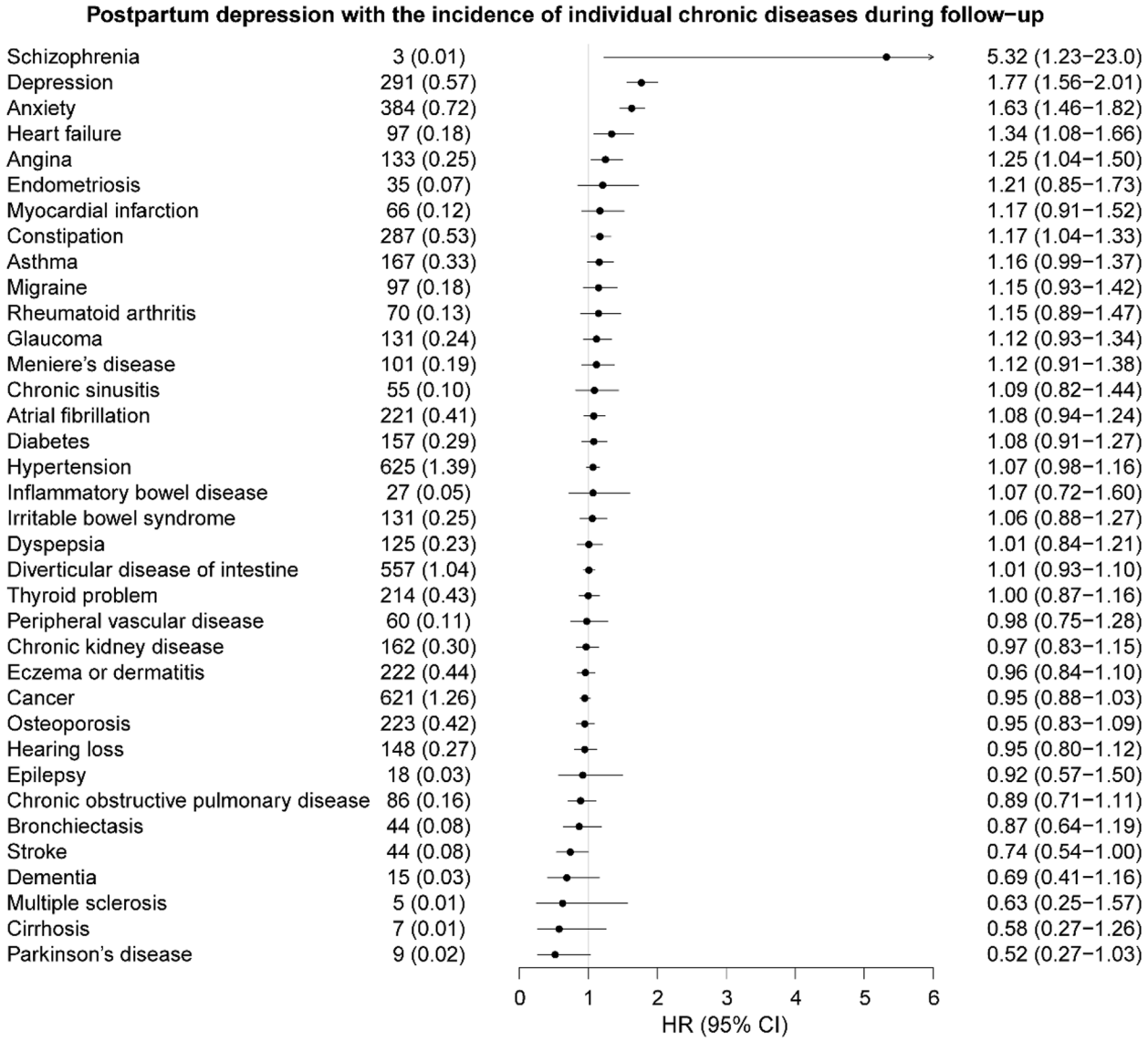

Fig. 4 Hazard ratios for the associations of postpartum depression with the incidence of each individual chronic diseases during follow-up. All models were adjusted for age at baseline, ethnicity, educational level, employment status, total household income, current smoking status, current alcohol drinking status, physical activity, body mass index, alternative healthy eating index, menopausal status, parity, ever usage of hormone-replacement therapy, and number of chronic diseases at baseline

above and beyond that of the confounders measured in this study (upper confidence bound, 1.30). Considering the relatively large E-value, our results may not be influenced by unmeasured confounders. Third, maternal age at childbirth might be an important factor affecting PPD and later risk of multimorbidity. However, the age at each live birth of women was not available in UK Biobank, limiting the consideration of such factor in our models. Finally, only a part of UK Biobank participants attended the online follow-up assessment and reported their information on PPD. When comparing the baseline characteristics of participants included and excluded in the final analyses, we found that women being excluded from the study, due to either the lack of information on PPD or other reasons, were more like to be younger, non-white, higher educated, unemployed, with higher household income, smokers, non-drinkers, physically inactive, underweight or obese, pre-menopause, and never using hormone-replacement therapy. The differences between the excluded and included participants would limit the

representative of our results to the general UK female population. Further studies are warranted to verify such association in other populations.

Implications

The associations of depression with chronic physical diseases and multimorbidity have been widely studied in the general population, but PPD was suggested to be a unique syndrome distinct from major depressive disorders occurring outside the peripartum period [57]. Determining whether the associations of PPD with these adverse health outcomes remain significant has important implications for maternal health surveillance as well as designing and assessing prevention strategies and treatment practices. Previous research mainly focused on the offspring health outcomes followed by PPD, while only a few studies exploring the associations of PPD with mothers' short-term outcomes after childbirth. Our study provides an overview of PPD-related long-term chronic diseases and the profile of multimorbidity. We also showed that PPD was associated with specific multimorbidity patterns, including the Heart Pattern, Respiratory Pattern, Mental Pattern, and Digestive Pattern, which can facilitate future considerations of which disease patterns should be prioritized in future research. However, these findings are novel, which request more large-scale prospective studies and Mendelian randomization studies to verify such relationships, and animal studies to explore potential mechanisms.

For current clinical practice, there remains a gap between the mothers' actual needs and professionals' perceptions of what they need [58]. It was suggested that many mental health issues during the perinatal period were undetected or under-treated [59], which might partly result from the more focus on maternal physical health needs rather than emotional needs [60]. Our study showed a long-term effect of PPD on women's health later in life, suggesting that maternal healthcare system should strengthen mental health care, and that the promotion of maternal health should go beyond shortly after childbirth and continue throughout women's life course [61].

Conclusions

In conclusion, this study found that PPD was associated with higher risks of chronic diseases and multimorbidity in women's mid-late life. Our findings suggest that the promotion of maternal mental health is needed in the perinatal and postpartum periods, and highlight its role in the prevention of chronic diseases and multimorbidity throughout women's life course.

Abbreviations

AHEI Alternative healthy eating index
BMI Body mass index
CVD Cardiovascular diseases
CI Confidence interval
HR Hazard ratio
ICD International Classification of Diseases
OR Odds ratio
PPD Postpartum depression
RR Relative risk
SD Standard deviation

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12916-025-03853-1.

Additional file 1: Table S1. Baseline characteristics of participants included or not included in the final analysis. Table S2. Chronic diseases included in the definition of multimorbidity. Table S3. Factor loadings of each chronic disease for the five multimorbidity patterns. Table S4. Baseline characteristics of participants by number of chronic diseases at baseline. Table S5. Baseline characteristics of participants by number of new onset chronic diseases during follow-up. Table S6. The effect of postpartum depression on the incidence of multimorbidity during follow-up due to mediation and interaction of lifestyle factors. Table S7. Sensitivity analysis of the association between postpartum depression and the incidence of multimorbidity during follow-up. Fig. S1. Odds ratios for the associations of postpartum depression with the prevalence of each individual chronic diseases at baseline. Fig. S2. Subgroup analyses of the associations of postpartum depression and the incidence of multimorbidity. Supplementary Methods. Exploratory factors analysis and quasi-Poisson mixed effects models.

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Authors' contributions

X.X. contributed to the study conceptualization and supervised the whole project. Y.Z. made the analysis plan, conducted the statistical analyses, and drafted the initial manuscript. X.X., Y.C., YG.Z., and H.W. verified the underlying data and statistical analyses. R.C. provided support on the statistical methods and manuscript revision. All authors contributed to and approved the final manuscript. X.X. is the corresponding author, has full access to all the data and has final responsibility for the decision to submit for publication. All authors read and approved the final manuscript.

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Data availability

The original data for the study are available on the website: https://www.ukbiobank.ac.uk/.

Declarations

Ethics approval and consent to participate

The UK Biobank has ethical approval from the North West Multi-centre Research Ethics Committee (reference number 06/MRE08/65). All participants provided informed consent. Institutional review board approval was exempted for this study because of the publicly available and deidentified data.

Competing interests

The authors declare no competing interests.

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