with support from their mother during pregnancy and after the delivery.

According to our data analysis, the prevalence of MB (measured by Stein's Scale) was highest on the first day; it then decreased on the second day, but increased on the third to the fourth day; then it decreased again on the fifth day. In the previous studies, there was no consensus about the prevalence of MB [9,29]; clearly, the differences in results might be due to the differences in the scales used, the sampling period, and the elimination of the group of women who had already shown signs of depression before delivery. In order to calculate the rate of women suffering from pure MB (as indicated by Stein's Scale), we have analyzed separately the women who experienced only MB and those who experienced depressive mood throughout their pregnancy and remained depressed following the birth of their child.

Our longitudinal study also confirms the possibility of predicting subsequent postpartum depressive mood (above EPDS cutoff of 8/9) if a depressive mood during pregnancy and/or maternity blues is present. This outcome was consistent with prior studies [17,18,30–34]. However, compared with previous studies, we observed different sequences over time regarding mood state, which might indicate a different etiology of depression during pregnancy and postpartum depression. These differences were not recognized in previous studies, because the previously used postpartum depressive group included women who belonged to the continuous depressive group. However, the women who were in the latter group did not suffer from pure and simple postpartum depression, as they appeared to have experienced depression before pregnancy and should therefore be considered separately. Furthermore, the association that we observed between maternal blues and high EPDS scores at 1 month shown by longitudinal ratings might of course be an indicator of postnatal depression. Moreover, there might be an overlap between the maternity blues and the onset of postnatal depression. One of the clinical implications of this finding is that if women with maternity blues were followed up for longer periods of time, fewer cases of postnatal depression would be overlooked.

There were several limitations in this study that should be considered. We evaluated the women's mental states only with self-administered questionnaires, and we did not use a psychiatric interview to establish the diagnosis of depression. These limitations may have led to the following four problems: (1) we did not check for false positives; (2) we could not confirm the women's clinical history; thus we could not know whether the women who were identified as belonging to the continuous depressive and temporary gestational depressive groups had or had not been clinically depressed before pregnancy; (3) we did not validate the definition of MB in a clinical setting; and (4) as significant changes have been found in physiological and psychological functions in different trimesters of pregnancy [35,36], time-specific threshold might be appropriate [37]; however, as these data are not validated in the Japanese population, we used the same cutoff (8/9) in the present study.

As postpartum depression is an extremely important potential risk factor, not only for the mother but also for the newborn child, we hope that our study can shed light on how women at risk can be identified. As the results of our study suggested that there might be different pathoethiological mechanisms of MB and/or postpartum depression regarding the continuous depressive and the pure postpartum depressive groups, our opinion is that, in order to better understand the aforementioned differences and clarify the risks related to postpartum depression, additional research regarding psychosocial factors is needed.

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Prospective Study on the Association between Harm Avoidance and Postpartum Depressive State in a Maternal Cohort of Japanese Women

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Abstract

Background: Recent studies have displayed increased interest in examining the relationship between personality traits and the onset, treatment response patterns, and relapse of depression. This study aimed to examine whether or not harm avoidance (HA) was a risk factor for postpartum depression measured by the Edinburgh Postnatal Depression Scale (EPDS) and the state dependency of HA.

Methods: Pregnant women (n = 460; mean age 31.9±4.2 years) who participated in a prenatal program completed the EPDS as a measure of depressive state and the Temperament and Character Inventory (TCI) as a measure of HA during three periods: early pregnancy (T1), late pregnancy (around 36 weeks), and 1 month postpartum (T2). Changes in EPDS and HA scores from T1 to T2 were compared between the non depressive (ND) group and the postpartum depressive (PD) group.

Results: There was no significant difference in the level of HA between the ND and PD groups at T1. In the ND group, EPDS and HA scores did not change significantly from T1 to T2. In the PD group, both scores increased significantly from T1 to T2 (EPDS, $p<0.0001$; HA, $p<0.048$). In the ND and PD groups, a significant positive correlation was observed in changes in EPDS and HA scores from T1 to T2 ($r = 0.31$, $p = 0.002$).

Conclusions: These results suggest that HA cannot be considered a risk factor for the development of postpartum depression measured by EPDS. Furthermore, HA may be state dependent.

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Introduction

Recent studies have displayed increased interest in examining the relationship between personality traits and the onset, treatment response patterns, and relapse of depression [1,2,3]. Personality traits have been demonstrated to play an important role in the onset of major depression, and have been considered useful as a possible outcome for the prevention and early detection of and intervention for symptoms of depression. A recent study demonstrated that psychosocial adversity interacts with neuroticism in the etiology of major depression, and the impact of neuroticism on illness risk is greater at high than at low levels of adversity [4].

On the other hand, previous studies have examined the relationship between depression and personality as well as changes in personality traits due to the onset of depression and have demonstrated a significant association [5,6,7,8]. In a previous study, our colleagues examined the state dependency of the Temperament and Character Inventory (TCI) [9] in patients with major depression [7] and reported that harm avoidance (HA), an anxiety-related trait associated with neuroticism, decreased as symptoms of depression improved in patients with major depressive disorder (MDD). However, these patients were

medicated with antidepressants; therefore, there may be state dependency of personality traits regarding depression [7].

Most previous studies that have explored the relationship between personality traits and depression have done so after the onset of depression or when medical intervention was already underway. To date, only a handful of studies have examined the association between personality and symptoms of depression before the onset of depression. Thus, studies examining the relationship between personality and the development of depression within a prospective cohort design should consider the following three points: 1) the longitudinal changes in personality traits through measured assessments or observations; 2) the effects of changes in depression or symptoms of depression within a continuous spectrum in order to capture individuals that fall underneath beneath the threshold); and 3) the heterogeneity in the pathophysiology of depression within individuals diagnosed with having MDD.

However, previous prospective cohort studies that examined the relationship between personality and depression did not take into account the instability of personality within a longitudinal timeframe, and assessed depression using a categorical (mental disorder present or not present) approach. Additionally, previous studies did not explore the heterogeneity found in participants diagnosed with MDD, for example, by examining qualitative differences within individuals diagnosed with MDD.

Postpartum depression is a specific type of depression used to describe a continuum of depressive symptoms and diagnosis that occur from several weeks to several months after childbirth. The operational definition given in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision* uses a time frame of 4 weeks after childbirth for the onset of symptoms. We previously conducted a prospective study on a maternal cohort of Japanese women using a longitudinal design and a questionnaire to elucidate the prevalence of postpartum depression (measured by the EPDS), changes in depression symptoms, and biopsychosocial factors affecting the onset of depressive state during pregnancy and postpartum period [10].

The present study using a maternal cohort of pregnant Japanese women is suitable to study personality traits associated with the onset of depressive symptoms for the following three reasons: 1) we can evaluate whether or not participants had postpartum depression within a relatively short period (about 1 year) because pregnant women are susceptible to the development of postpartum depression and the incidence of postpartum depression is high (approximately 10–15%) [11,12,13,14,15,16,17]; 2) we can investigate how changes in depressive symptoms in unaffected participants affects personality traits because using prospective design we can detect depressive symptoms and personality traits before onset of depression; and 3) in our cohort, subjects who presented with depressive symptoms were more homogeneous than MDD patients from previous studies because life events influencing the onset of depression included common biopsychosocial events (pregnancy and childbirth). To the best of our knowledge, there have been no prospective cohort studies that have investigated the role of personality in the onset of postpartum depression.

Thus, the present study aimed to examine the relationship between personality and depressive state to elucidate 1) whether HA was a risk factor for postpartum depression and 2) whether or not mean levels in HA changed before and after the onset of depressive state, that is, to investigate the state dependency of HA.

Results

Participant profiles are shown in Table 1. No significant differences in age were found across the four groups ($p = 0.81$, ANOVA). There was no significant difference in HA during T1 (early pregnancy) between the ND and PD groups (Table 2). Changes in EPDS from T1 to T2 are shown in Table 3 and Figure S1. In the PD group, EPDS score increased significantly from T1 to T2. Changes in HA from T1 to T2 are shown in Table 4 and Figure S2. In the PD group, HA score also increased significantly from T1 to T2. The effect size of the HA change was smaller than the EPDS change. Correlations between changes in scores on the EPDS and HA are shown in Table 5 and Figure S3. Correlations between changes in scores on the EPDS and HA were significant ($r = 0.31$, $p = 0.002$). Regarding the HA subscales, only changes in fatigability and asthenia was significantly correlated with changes in EPDS scores ($r = 0.29$, $p = 0.003$) (Table 5).

Discussion

This study is the first to investigate the relationship between HA and postpartum depression measured by EPDS prospectively in a cohort of pregnant Japanese women. The systematic, longitudinally collected information and subsequent analysis in the current study brings new information regarding the understanding the mental state dynamics of women from pregnancy to postpartum.

We investigated HA levels and depressive state before and after childbirth to assess the role of HA as a risk factor for the development of depressive symptoms prospectively. Moreover, we assessed the levels of HA among mothers that experienced depressive state only after delivery (ie, the TG and CD groups were excluded). We observed different sequences over time regarding the depressive state that might indicate a different etiology of depression during pregnancy and postpartum depression. These differences were not recognized in previous studies, because the previously used postpartum depressive group included women who belonged to the CD group. In addition, as the women included in TG and CD groups may have suffered from mood disorders including MDD or bipolar disorder, we excluded those groups from the current analyses. This exclusion was one of the strengths of our study.

The sample size used in the current study was large and bias effects (ie, recall/reporting bias) were relatively small as prospective design was used in the current study. Moreover, as all subjects were Japanese, genetic and cultural confounders were negligible.

Results demonstrated that there were no differences in mean levels of HA between the ND and PD groups at T1. Thus, our results suggest that HA may not be a significant risk factor for the development of postpartum depression measured by EPDS. Furthermore, our findings indicated that HA may increase according to increase of severity of depressive symptoms (the state dependency of HA) due to significantly positive correlations in changes of EPDS and HA from T1 to T2. In addition, we observed the most significant correlation between EPDS change and Fatigue/Asthenia subscale of HA. Although in order to explore this findings it may be necessary to have additional covariables that could contribute to the association between Fatigue and Asthenia and EPDS, it is of note that the levels of Fatigue and Asthenia may be elevated due to the pregnancy and child birth experience [18]. Therefore, we speculate that this may result in the strongest association between EPDS and Fatigue/Asthenia.

This study had several limitations. First, we evaluated women's mental states only with a self-administered questionnaire. Additionally, histories regarding mood disorders before pregnancy

Table 1. Participant profiles in the four groups.

	period							
	pregnancy		postpartum					
groups	T1	late	T2	n	%	age		p-value[a]
						mean	SD	
Non depressive (ND) group	−	−	−	331	72.0	31.9	4.1	0.81
Postpartum depressive (PD) group	−	−	+	48	10.4	32.0	3.9	
Temporary gestational depressive (TG) group	+	+	−	52	11.3	31.8	5.1	
	+	−	−					
	−	+	−					
Continuous depressive (CD) group	+	+	+	29	6.3	31.1	4.7	
	+	−	+					
	−	+	+					
All				460	100.0	31.9	4.2	

+: EPDS>8, −: EPDS<9.
T1: early pregnancy (before 25 weeks).
late: late pregnancy (around 36 weeks).
T2: postpartum (1 month).
[a]: ANOVA was used to test the mean differences of age within the four groups.
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were not assessed, and the ND and PD group also might include people with bipolar disorder [19,20]. Future studies may find it helpful to assess histories of mood disorders using diagnostic tools such as the SCID in groups with postpartum depression.

In conclusion, this prospective study suggests that high HA, a personality trait, observed during pregnancy may not be a significant risk factor for the development of postpartum depression measured by EPDS. Furthermore, our findings demonstrate that levels of HA may increase according to the onset of depressive symptoms (the state dependency of HA), and decrease as a result of improvement in symptoms of depression. Additional investigations into the state dependency of additional personality traits that are purported to be linked to the onset of MDD are needed.

Materials and Methods

Participants

This study was approved by the Ethics Committees of the Nagoya University Graduate School of Medicine and associated institutes and hospitals. Written informed consent was obtained from all participants after the study was described to them in full detail. Participants in this study consisted of women who attended the prenatal program during pregnancy (starting before the 25th week) at two obstetrical hospitals between August 2004 and October 2010. The hospitals were located in the local administrative center of the city of Nagoya (with a population of approximately 2 million people). Participants were randomly selected from the obstetric hospital. Mothers with previous history of mental problems or current treatment for mental problems were excluded from the study, as well as mothers suffering from neonatal pathology, born before 32 weeks of pregnancy. The follow-up period was 6 months after the delivery [10]. Participants were asked to complete self-reported questionnaires about depression and personality (namely, HA traits) at home according to a predetermined schedule.

A total of 647 adults (≥20 years) were recruited for the study. All subjects were Japanese. Several participants were excluded for various reasons including lack of information on age (n = 4); incomplete data on HA scores on the TCI (n = 7); incomplete EPDS (n = 160); and incomplete other data (n = 16). Thus, a total of 460 participants (mean age, 31.9±4.2 years; range, 20–44 years) were included.

Table 2. HA scores in the ND and PD groups at T1.

	n	mean	SD	p-value[a]
ND group	331	10.2	4.5	0.60
PD group	48	11.0	4.6	
All	379	10.3	4.5	

ND group: non depressive group.
PD group: postpartum depressive group.
SD: standard deviation.
[a]: Student's t-test was conducted in HA scores between the ND and PD groups at T1.
doi:10.1371/journal.pone.0034725.t002

Table 3. EPDS scores in the ND and PD groups.

		T1		T2		p-value[a]	Cohen's d
	n	mean	SD	mean	SD		
ND group	331	2.8	2.4	2.6	2.3	0.27	−0.09
PD group	48	4.0	2.2	12.2	3.4	**<0.0001**	2.86
All	379	2.9	2.4	3.8	4.0		

EPDS: Edinburgh Postnatal Depression Scale.
T1: early pregnancy (before 25 weeks).
T2: postpartum (1 month).
ND group: non depressive group.
PD group: postpartum depressive group.
SD: standard deviation.
[a]: Paired t-test in EPDS between T1 and T2 in the ND and PD groups.
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Table 4. HA scores in the ND and PD groups.

		T1		T2		p-value[a]	Cohen's d
	n	mean	SD	mean	SD		
ND group	81	10.4	4.3	10.1	3.8	0.27	−0.07
PD group	18	11.1	5.0	12.3	4.2	**0.048**	0.26
All	99	10.6	4.4	10.5	3.9		

HA: harm avoidance.
T1: early pregnancy (before 25 weeks).
T2: postpartum (1 month).
[a]: Paired t-test in HA scores between T1 and T2 in the ND and PD groups.
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Study design

Depressive state (measured by EPDS) and HA were evaluated from early pregnancy to 1 month after postpartum. Depressive state (measured by EPDS) and HA were measured using the EPDS and TCI, respectively. Participants were divided into the following four groups according to severity of depressive symptoms from early pregnancy to 1 month after childbirth as same as our previous study [10]: group 1, non depressive (ND) group (mothers scoring below EPDS threshold in all 3 time points) (n = 331); group 2, postpartum depressive (PD) group (mothers scoring above EPDS threshold only at T2) (n = 48); group 3, temporary gestational depressive (TG) group (mothers scoring above EPDS threshold only during pregnancy) (n = 52); and group 4, continuous depressive (CD) group (mothers scoring above EPDS threshold during both pregnancy and postpartum) (n = 29) (Table 1).

EPDS scores obtained during the following three periods were used to classify participants into the four aforementioned groups: early pregnancy (before 25 weeks, T1), late pregnancy (around 36 weeks), and 1 month postpartum (T2). The merit of this classification is to distinguish groups that did not present with symptoms of depression during pregnancy (ND and PD groups) from groups that presented with depressive symptoms during pregnancy (TG and CD groups). Because depressive symptoms were evaluated only at postpartum in most previous studies, the NG and TG groups were combined into a single group and the PD and CD groups were combined into a single group.

Differences in HA scores during T1 were compared between the ND and PD groups to evaluate whether levels of HA in pregnant women served as a risk factor for postpartum depression. The present study did not use structured interviews such as the Structured Clinical Interview for DSM Disorders (SCID) to confirm a history of mood disorders. The TG and CD groups were excluded from these analyses because these groups may include people with mood disorders, including MDD or bipolar disorder. A total of 379 participants (ND, n = 331; PD, n = 48) were included in these analyses.

Next, the association in the change between EPDS and HA scores was examined in the ND and PD groups to evaluate whether HA levels increased as EPDS increased from T1 to T2, that is, we measured the state dependency of HA. In this analysis we included 99 participants (ND, n = 81; PD, n = 18; mean age, 32.2±4.1 years; range, 24–44) who submitted HA scores both at T1 and T2. To note, there was a discrepancy in the number of subjects with HA scores between T1 and T2 due to the fact that HA was not assessed during the launch of this cohort study at T2.

Table 5. Correlations between HA and EPDS score changes from T1 to T2 in the ND and PD groups.

	ND and PD groups (n = 99)	r	p-value
HA total		0.31	**0.002**
HA subscale	Anticipatory worry	0.16	0.12
	Fear of uncertainty	0.17	0.10
	Shyness with strangers	0.13	0.21
	Fatigability and asthenia	0.29	**0.003**

r: Pearson's r.
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Measures

We investigated the mental state of the participants with two self-administered questionnaires. EPDS is a well-known screening tool for depression in women during pregnancy and postpartum. The TCI is used to assess four dimensions of temperament including HA and three dimensions of character. We examined EPDS and TCI scores during early pregnancy (that is, before 25 weeks at T1) and at 1 month postpartum (at T2).

The Edinburgh Postnatal Depression Scale. We evaluated the depressive state (measured by EPDS) of participants during the period right after childbirth using the EPDS [21,22]. The EPDS is a self-reported questionnaire that includes 10 items designed to screen for postpartum depression in community samples. Each item is scored on a four-point Likert scale (from 0 to 3), with scores ranging from 0 to 30. This scale focuses on the cognitive and affective features of depression, rather than on somatic symptoms. Its sensitivity and specificity in a Japanese community sample were 75% and 93%, respectively, using a cut-off point of 8/9 [23]. The 8/9 cut-off point to screen for depressive women was also used in the present analyses. This questionnaire has also been validated as a screening instrument for use throughout pregnancy and is comparable to other screening scales for depression for use in community samples. When used in community settings, this scale is referred to as the Edinburgh Depression Scale [24].

The Temperament and Character Inventory. Personality traits including HA were measured with the TCI. The TCI is a self-reported questionnaire that includes 125 items that tap into four dimensions of temperament (novelty seeking, HA, reward dependence, and persistence) and three dimensions of character (self-directedness, cooperativeness, and self-transcendence). HA was originally assumed to be influenced by the serotonergic system [25]. We used the Japanese version of the TCI-125, which includes 125 questions including 20 items pertaining to HA [26]. HA scores ranged from 0 to 20 and consisted of the following four subscales, anticipatory worry (0–5), fear of uncertainty (0–5), shyness with strangers (0–5), and fatigability and asthenia (0–5).

Statistical analysis

Analysis of variance (ANOVA) was used to test the mean differences within the four groups divided by EPDS (Table 1). The student t-test was used to compare HA scores between the ND and PD groups at T1 (Table 2). Paired t-test was used to calculate changes in EPDS scores and HA scores between T1 and T2 in the ND and PD group (Table 3 and 4). Cohen's d was used to show the differences in HA and EPDS from T1 to T2 as effect size in the ND and PD group (Table 3 and 4). Cohen's d was calculated from means, standard deviations and sample size in two groups. Correlations between EPDS and HA scores at T1, T2, and

changes in EPDS score and HA total score/subscores from T1 to T2 were evaluated based on Pearson's coefficients (r) within the ND+PD group (Table 5). Significance levels were set at $p<0.05$. All p-values were two-tailed p-values. IBM SPSS Statistics Version 19 (IBM Japan, Tokyo) was used for all analyses.

Supporting Information

Figure S1 Changes in EPDS score in ND and PD group.
(TIF)

Figure S2 Changes in HA score in ND and PD group.
(TIF)

Figure S3 HA and EPDS score changes from T1 to T2 in the ND and PD groups.
(TIF)

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Author Contributions

Conceived and designed the experiments: KF TK TO SM SG AK T. Masuda NO. Analyzed the data: KF TK TO BA NO. Contributed reagents/materials/analysis tools: KF NH TS YN AT NI HO HU NB T. Morita SG AK T. Masuda NO. Wrote the paper: KF TK TO BA.

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The Postpartum Depressive State in Relation to Perceived Rearing: A Prospective Cohort Study

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Abstract

Background: The relationship between perceived rearing and the postpartum depressive state remains unclear. We aimed to examine whether perceived rearing is a risk factor for postpartum depression as measured by the Edinburgh Postnatal Depression Scale (EPDS), and whether the score of perceived rearing is affected by depressive mood (the state dependency of perceived rearing).

Methods: Pregnant women (n = 448, mean age 31.8±4.2 years) completed the EPDS as a measure of depressive state in early pregnancy (T1), late pregnancy (around 36 weeks), and at 1 month postpartum (T2), and the Parental Bonding Instrument (PBI) at T1 as a measure of perceived rearing. Changes in the EPDS and the PBI scores from T1 to T2 were compared between the non depressive (ND) group and the postpartum depressive (PD) group.

Results: There were no significant differences in any PBI category for perceived rearing between the ND and PD groups at T1. EPDS scores did not change significantly from T1 to T2 in the ND group but increased significantly in the PD group. The PBI maternal care score increased significantly in the ND group ($p<0.01$), while decreasing in the PD group ($p<0.05$). Additionally, in both the ND and PD groups, significant negative correlation was observed regarding change in the EPDS and PBI maternal care scores from T1 to T2 ($r = -0.28$, $p = 0.013$).

Conclusions: The present study suggests that perceived rearing is not a strong risk factor for postpartum depression as measured by the EPDS. Furthermore, the results indicated the state dependency of the PBI maternal care score.

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Introduction

Postpartum depression, which is observed in about 13% of postpartum women, is defined as a depressive disorder occurring within four weeks after delivery [1]. Postpartum depression not only leads to substantial impairment of the patient's daily life, but also has huge impact on the patient's family members including promotion of depressive tendencies in the husband, abuse or neglect of the child [2], and delayed cognitive development or increase in psychopathological problems in the child [3,4,5]. Consequently, identification of the risk factors in postpartum depression is important, so that appropriate preventive and early intervention measures may be taken for pregnant and postpartum women.

There have been recent studies attempting to establish the relationship between postpartum depression and perceived rearing (own memories of being raised) in women. For example, Boyce *et al.* [6] have reported that the onset of postpartum depression is associated with parental rearing styles manifested in the form of low care or high overprotection, as well as high interpersonal sensitivity regarding the relationship with the husband. Similar findings by Matthey *et al.* [7] revealed that the onset of postpartum depression 4 months after delivery in patients showing no signs of depression during pregnancy depended on the relationship with their partners, the high interpersonal sensitivity, and quality of

early parent-child relationships characterized by low care and high overprotection. However, in their study, depression at 12 months after delivery was not linked to early relationships with parents, but only to relationships with the partner. On the other hand, McMahon *et al.* [8] have reported low maternal care as a cause of persistent depressive symptoms even at 12 months after delivery.

Historically, Gotlib *et al.* [9], examining the influence of depressed mood in postpartum depression on perceived rearing using the Parental Bonding Instrument (PBI), concluded that perceived rearing, evaluated retrospectively, was independent of the state of depression at the time of evaluation. It was also reported that scale scores regarding perceived rearing had long-term stability and that scores were not skewed by mood states at the time of evaluation [10,11,12,13]. On the contrary, a more recent report [14] suggests that depressed mood might influence the evaluation of perceived rearing, indicating the relationship between depression and perceived rearing is as yet unclear.

A prospective cohort study was performed in women during pregnancy and the postpartum to examine the prevalence and course of depressive mood occurring during these periods, and to identify the risk factors involved in the development of depression as measured by the Edinburgh Postnatal Depression Scale (EPDS) [15]. The results indicated that the clinical course of postpartum depressive state could be classified into four patterns based on scores of the Japanese version of the EPDS in early pregnancy, late pregnancy, and at 1 month postpartum [16,17]. Thus, the current study was designed to investigate the state of depressive mood and perceived rearing among women using the questionnaire longitudinally from pregnancy through the postpartum. This approach allowed for evaluation of the effects of perceived rearing during pregnancy on onset of postpartum depression as measured by the EPDS, and whether the perception of rearing changes through onset of depressive mood.

In the manner described above, depressive mood and perceived rearing was investigated prospectively over time to: 1) compare and verify the influence of perceived rearing on the pattern of depressive states during pregnancy and the postpartum, and 2) to examine whether the evaluation of perceived rearing is affected by depressive mood at the time of evaluation.

Materials and Methods

Ethics Statement

The study was explained to the participants both verbally and in writing, and written consent was obtained from all participants. Study protocol was approved by the Ethics Committees of Nagoya University Graduate School of Medicine and the institutes and hospitals involved, and the study itself was conducted in conformity with the established ethical standards of all institutions.

Participants

Female participants were recruited from prenatal classes for pregnant women (starting before the 25th week of pregnancy) at two obstetric hospitals located in central Nagoya, Japan (with a population of approximately 2 million) between August 2004 and October 2010. The participants were randomly sampled at these institutions. The follow-up period was 6 months after delivery [16]. Mothers with current or past histories of mental problems were excluded from the study, as well as mothers with children born before the 36th week of gestation.

A total of 643 Japanese women (20 years and older) agreed to participate in the study. Of this total, 467 (72.6%) completed the EPDS at all time points (T1: early pregnancy before the 25th week of pregnancy; late pregnancy: around week 36 of pregnancy; and T2:1 month after delivery), and 558 (86.8%) completed the PBI without omission at T1. This amounted to 448 women (69.7%) completing the EPDS at all time points and the PBI without omission at T1 (mean age 31.8±4.2, range 22–44 years of age).

Measures

The Edinburgh Postnatal Depression Scale (EPDS). The EPDS is a self-report questionnaire consisting of ten items to evaluate depressive states after delivery [15], employing a four-point assay (0–3 points) yielding a total score ranging from a minimum of 0 to a maximum of 30. The scale focuses on the cognitive and affective aspects of depression, excluding the physical symptoms such as loss of appetite. The reliability and validity of the scale in a Japanese general population sample has been reported at 75% and 93% (cut-off ≥9 points), respectively [18]. It's efficacy as a screening scale for depression during pregnancy has also been demonstrated [19]. Thus, a score of 9 points on the EPDS was selected as the cut-off point for screening the depression groups in this study. This screening was repeated three times: in early pregnancy before the 25th week: T1), late pregnancy (around week 36), and at 1 month after delivery (T2).

The Parental Bonding Instrument (PBI). The PBI was used to evaluate perceived rearing [20]. The PBI is a self-report questionnaire evaluating perception of how one was raised by recalling the parents' child-rearing attitudes before one reached 16 years of age. The scale consists of 25 items each for the father figure, and the mother figure. The child-rearing attitudes are evaluated on a four-point scale (0–3 points), regarding 12 care category items and 13 overprotection category items. Possible scores for the care category ranges from 0 to 36 points– higher scores indicating more acceptive and more affectionate rearing attitudes on the part of the parents; a lower score indicating apathy and rejection. The overprotection category ranges from 0 to 39 points–higher scores indicating the parents' rearing attitudes as being overprotective and excessively interfering; a lower score indicating respect for self-subsistence. Overall, the evaluation consists of four categories: paternal care, paternal overprotection, maternal care, and maternal overprotection, and scores were obtained for each category. Kitamura and Suzuki translated the PBI into Japanese incorporating back-translation in 1993 to confirm the validity of this Japanese edition [21].

As part of this study, the Japanese version of the PBI was administered in early pregnancy (T1) and again at 1 month postpartum (T2) in some participants to examine whether the PBI scores were subject to change in accordance with transition in EPDS scores. A point of note is the discrepancy in number of subjects regarding PBI scores at T1 and T2, due to the fact that the PBI was not initially assessed at T2 in launching the cohort study.

Study Design

Pregnant women participating in prenatal classes were provided detailed verbal and written explanations about the nature and scope of this study. Subjects consenting to partake in the study were given a demographic questionnaire, the EPDS, and the PBI, with instructions to complete the forms at home, and returned by mail.

In line with a preceding analysis of the EPDS results by Ishikawa *et al.* [16], the 448 subjects of this study were initially divided according to the timing of exhibiting depression into 4 groups as follows: 1) a non depressive (ND) group, with EPDS scores below the cut-off point at all time points; 2) a postpartum depressive (PD) group, with EPDS scores exceeding the cut-off point only at 1 month postpartum; 3) a temporary gestational

Table 1. Participant profiles in the four initial subject categories.

	period							
	pregnancy		postpartum					
groups	T1	late	T2	n	%	age		p-value[a]
						mean	SD	
non depressive (ND) group	–	–	–	321	71.7	31.9	4.0	0.97
postpartum depressive (PD) group	–	–	+	49	10.9	32	3.9	
temporary gestational depressive (TG) group	+	+	–	50	11.2	31.7	5.2	
	+	–	–					
	–	+	–					
continuous depressive (CD) group	+	+	+	28	6.3	31.5	4.3	
	+	–	+					
	–	+	+					
All				448	100	31.8	4.2	

T1: early pregnancy (before 25 weeks).
late: late pregnancy (around 36 weeks).
T2: postpartum (1 month).
+: EPDS >8, – : EPDS <9.
a: ANOVA was used to test the mean differences of age within the four groups.
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depressive (TG) group, with EPDS scores exceeding the cut-off point only during pregnancy; and 4) a continuous depressive (CD) group, exhibiting EPDS scores above the cut-off point during both pregnancy and the postpartum (Table 1). The merit of classifying the participants into these four groups was that it enabled distinction between those who did not present with symptoms of depression during pregnancy (ND and PD groups) from those who did (TG and CD groups). The TG and CD groups were excluded from subsequent analyses to preclude subjects with possibly unidentified mood disorders, including MDD or bipolar disorder, as the present study did not employ structured interviews (such as the Structured Clinical Interview for DSM Disorders) to rule out such mood disorders.

As the first step in this study, difference in PBI scores at T1 were compared between the ND and PD groups to examine whether levels of PBI in pregnant women was an indicator for risk of postpartum depression. Thus, the remaining 370 participants (ND, $n = 321$; PD, $n = 49$) were selected as the subjects for the current analysis.

Next, association in the change between EPDS and PBI scores was examined in the 80 subjects submitting PBI scores at T2 in addition to T1 (ND, $n = 63$; PD, $n = 17$) to evaluate whether PBI scores increase with increase in EPDS scores from T1 to T2–i.e., measurement of the state dependency of PBI scores. As noted previously, there is a discrepancy in the number of subjects with PBI scores at T1 ($n = 448$) and T2 ($n = 80$), due to the fact that the PBI was not administered at T2 at the start of this cohort study.

Statistical Analysis

Analysis of variance (ANOVA) was used to test the mean difference of age within the four initial EPDS groups (Table 1). The Student's t-test was used to compare PBI scores between the ND and PD groups at T1 (Table 2). The paired t-test was used to compare change in EPDS score and PBI score from T1 to T2 in the ND and PD groups (Tables 3 and 4). Correlation between changes in EPDS and PBI scores from T1 to T2 was examined based on Pearson's coefficients (r) within the ND and PD groups (Table 5). Significance levels were set at $p<0.05$. All p-values were two-tailed. IBM SPSS Statistics Version 19 (IBM Japan, Tokyo) was used in all analyses.

Results

Participant profiles are shown in Table 1. No significant differences in age were found across the initial four subject groups ($p = 0.97$, ANOVA) (Table 1). There were no significant differences in any PBI category (paternal care, paternal overprotection, maternal care, and maternal overprotection) between the non depressive (ND) group and postpartum depressive (PD) group at T1 (Table 2). Changes in EPDS scores in the ND and PD groups from T1 to T2 are shown in Table 3. The EPDS scores did not change significantly from T1 to T2 in the ND group ($p = 0.45$), but significantly increased in the PD group ($p<0.0001$). Changes in PBI scores in the ND and PD groups are shown in Table 4. In both ND and PD groups, there were no significant differences in

Table 2. PBI scores in the ND and PD groups at T1.

	ND group		PD group		[a]P-value
	n = 321		n = 49		
Category of PBI	mean	SD	mean	SD	
Paternal care	24.6	8	22.3	9.5	0.07
Paternal overprotection	11.1	6.9	12.2	9.6	0.33
Maternal care	29.6	7.2	28.5	8.1	0.31
Maternal overprotection	10.9	7.5	10.2	7.5	0.71

PBI: Parental Bonding Instrument.
T1: early pregnancy (before 25 weeks).
ND group: non depressive group.
PD group: postpartum depressive group.
SD: standard deviation.
a: Student's t-test between the ND and PD group.
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scores for paternal care, paternal overprotection, and maternal overprotection between T1 and T2 (all $p>0.05$). However, the scores for maternal care significantly increased in the ND group ($p=0.008$) while significantly decreasing in the PD group ($p=0.044$). A weak but significant correlation was confirmed between the change in maternal care score and change in EPDS score in the ND and PD groups ($r=-0.28$, $p=0.013$) (Table 5). No correlation was noted between the EPDS and any of the other PBI scores (all $p>0.05$) (Table 5).

Discussion

Principal Findings

The present study is the first prospective investigation on the relationship between depressive mood and perceived rearing through pregnancy and the postpartum in a cohort of pregnant Japanese women. The findings revealed absence of any significant difference in perceived rearing between the ND and PD groups during pregnancy. This appears to indicate that perceived rearing is not a strong risk factor for postpartum depression as measured by the EPDS. On the other hand, significant correlation was found between changes in maternal care score and EPDS score from T1 to T2 in the ND and PD groups, suggesting state dependency of the PBI maternal care score.

Many studies have examined the relationship between perceived rearing and postpartum depression. The results have been inconsistent, although this might be due at least in part to the inclusion of subjects with persistent depression in the 'postpartum depression' group in those previous studies. We observed different sequences over time regarding the depressive state possibly indicating a different etiology for depression during pregnancy and the postpartum. The possibility of such differences were not addressed in the previous studies conducted on postpartum depression groups including women who would have belonged to a CD (continuous depression) group had that distinction been made, not to mention women falling into a TG (temporary gestational depressive) group who may have suffered from mood disorders including major depressive disorder or bipolar disorder. In the present study, analysis of the EPDS results were conducted excluding such subjects (groups TG and CD) from the ND and PD groups. This exclusion is one of the strengths of our study. In addition, the sample size used in the current study was large and bias effects were relatively small given the prospective design. Moreover, all subjects were Japanese, making the genetic and cultural confounders negligible.

Table 3. EPDS scores in the ND and PD groups.

		T1		T2		[a]P-value
	n	mean	SD	mean	SD	
ND group	321	2.8	2.4	2.6	2.3	0.45
PD group	49	4.0	2.2	12.2	3.4	<0.0001
All	370	2.9	2.4	3.9	4.1	

EPDS: Edinburgh Postnatal Depression Scale.
ND group: non depressive group.
PD group: postpartum depressive group.
T1: early pregnancy (before 25 weeks).
T2: postpartum (1 month).
SD: standard deviation.
a: Paired t-test.
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Table 4. PBI scores in the ND and PD groups.

			T1		T2		[a]P-value
	group	n	mean	SD	mean	SD	
Paternal care	ND group	63	25.3	7.6	26.1	7.4	0.13
	PD group	17	21.2	10.6	20.3	10.8	0.15
Paternal overprotection	ND group	63	12.1	6	11.4	6.3	0.17
	PD group	17	10.5	7.8	10.7	6.5	0.85
Maternal care	ND group	63	29.7	6.8	30.7	6.3	**0.008**
	PD group	17	27.8	10.6	26.5	10.8	**0.044**
Maternal overprotection	ND group	62	11.6	7.1	11.3	7.6	0.54
	PD group	17	10.7	7.6	11.9	8.7	0.37

PBI: Parental Bonding Instrument.
ND group: non depressive group.
PD group: postpartum depressive group.
T1: early pregnancy (before 25 weeks).
T2: postpartum (1 month).
SD: standard deviation.
a: Paired t-test between T1 and T2.
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Depressive symptoms were observed in 28.3% of the initial sample of 448 subjects at least one of the three time points between early pregnancy and 1 month postpartum. Prevalence during pregnancy (17.5%) and the postpartum (17.2%) was similar to that reported in previous studies [22,23,24,25]. Regarding the course of depressive state, only 10.9% of the subjects were examined in this analysis as constituting the PD group, i.e., subjects exhibiting depressive states measured by the EPDS only after delivery.

As a result of this maneuver, no significant differences were found in mean scores for each PBI category between the ND and PD groups at T1. This result is inconsistent with previous studies suggesting a relationship between perceived rearing and postpartum depression. A probable cause for this discrepancy is the inclusion of subject groups with different psychopathologies in the previous studies. The previous studies using the PBI have revealed relationships between onset of eating disorders [26]/obsessive-compulsive disorder [27]/borderline personality disorder [26]/depression [28,29,30,31], and parents' inappropriate rearing styles characterized by low care and/or high overprotection. It is well known that patients with these psychiatric disorders frequently exhibit depression during the course of illness. Thus, datasets

Table 5. Correlations between PBI and EPDS score changes from T1 to T2 in the ND and PD groups.

	n	r	P-value
Parental care	80	−0.21	0.06
Parental overprotection	80	−0.02	0.85
Maternal care	80	−0.28	**0.013**
Maternal overprotection	79	0.04	0.69

PBI: Parental Bonding Instrument.
EPDS: Edinburgh Postnatal Depression Scale.
T1: early pregnancy (before 25 weeks).
T2: postpartum (1 month).
ND group: non depressive group.
PD group: postpartum depressive group.
r: Pearson's r.
doi:10.1371/journal.pone.0050220.t005

including such subjects may have affected the results of such previous investigations.

Our findings also showed significant increase in maternal care scores in the ND group, in contrast to its significant decrease in the PD group. In addition, significant correlation was found between maternal care and EPDS score changes from T1 to T2 in both ND and PD groups. This may be due to the experience of childbirth and depressive state possibly distorting the perception of rearing. As pointed out in previous studies, depressed patients exhibit a tendency for negative recollections [32,33]. A previous study has reported correlation of the PBI score with the Beck Depression Inventory [34], although most longitudinal studies have indicated consistency of the PBI regardless of fluctuations in mood [9,10,11,12,13,35,36]. Our results were in line with such studies demonstrating the state dependency of perceived rearing [31,37,38].

Limitations

Lastly, this study has its limitations. The mental states of the subjects were evaluated only with self-administered questionnaires (EPDS and PBI). The EPDS is usually used as a screening scale for depression during the perinatal period and there is no consensus of its validity as an index for indicating the degree of depression. As we adopted 9 as the EPDS cutoff (sensitivity: around 77%, specificity: 69%, area under the ROC curve: 75%), 25% of the subjects may not have been correctly classified [18,39]. Thus, the initial classification of subjects into four groups (ND, PD, TG and CD) by the EPDS might be different from the classification by structured clinical interviews such as the SCID. Additionally, histories regarding mood disorders before pregnancy were not assessed, and even after excluding the TG and CD groups, it is possible the ND and PD groups might still include subjects with, for example, bipolar disorder [40]. In future, it may be helpful to assess histories of mood disorders using diagnostic tools such as the SCID. It should also be useful to take into account the effects of repetitive measurement using the same questionnaire during a short period of time, as well as the effects of various psychosocial factors, including the relationship with partners, socioeconomic factors, relevant demographical data (number of family members, age and gender of children) because these factors are likely to influence the results. Additionally, previous studies have shown significant changes in physiological and psychological functions during the different trimesters of pregnancy [41,42]. Such changes could predispose women to develop depression to a certain degree, suggesting a time-specific threshold might be appropriate [43]. However, as these thresholds have not been validated in the Japanese population, a single cutoff score was adopted for this study. And with regards to the multiple comparison problem, we did not adjust the threshold of significance in the current study. After the Bonferonni correction, several p-values were not under the threshold of significance. Thus, our results need to be replicated in independent studies.

Conclusions

We examined how the experience of being raised as evaluated by the PBI influences the onset of postpartum depressive mood, and how the onset of depressive state influences the recall of perceived rearing. Several findings were obtained through this study: 1) no significant differences were noted in perceived rearing between ND and PD groups; 2) the PBI score for maternal care increased significantly in the ND group, while significantly decreasing in the PD group; 3) significant correlation was noted between changes in the EPDS and the PBI maternal care score from T1 to T2. This study suggests that perceived rearing during pregnancy is apparently not a strong risk factor for postpartum depression as measured by the EPDS, while demonstrating the state dependency of perceived maternal care assessed by the PBI.

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RESEARCH ARTICLE Open Access

Multiple barriers against successful care provision for depressed patients in general internal medicine in a Japanese rural hospital: a cross-sectional study

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Abstract

Background: A general internist has an important role in primary care, especially for the elderly in rural areas of Japan. Although effective intervention models for depressed patients in general practice and primary care settings have been developed in the US and UK medical systems, there is little information regarding even the recognition rate and prescription rate of psychotropic medication by general internists in Japan. The present study surveyed these data cross-sectionally in a general internal medicine outpatient clinic of a Japanese rural hospital.

Methods: Patients were consecutively recruited and evaluated for major depressive disorder or any mood disorder using the Patient Health Questionnaire (PHQ). Physicians who were blinded to the results of the PHQ were asked to diagnose whether the patients had any mental disorders, and if so, whether they had mood disorders or not. Data regarding prescription of psychotropic medicines were collected from medical records.

Results: Among 312 patients, 27 (8.7%) and 52 (16.7%) were identified with major depressive disorder and any mood disorder using the PHQ, respectively. Among those with major depressive disorder, 21 (77.8%) were recognized by physicians as having a mental disorder, but only three (11.1%) were diagnosed as having a mood disorder.

Only two patients with major depressive disorder (7.4%) had been prescribed antidepressants. Even among those (n = 15) whom physicians diagnosed with a mood disorder irrespective of the PHQ results, only four (26.7%) were prescribed an antidepressant.

Conclusions: Despite a high prevalence of depression, physicians did not often recognize depression in patients. In addition, most patients who were diagnosed by physicians as having a mood disorder were not prescribed antidepressants. Multiple barriers to providing appropriate care for depressed patients exist, such as recognizing depression, prescribing appropriate medications, and appropriately referring patients to mental health specialists.

Background

Depression is a common and chronic psychiatric disorder. It is estimated that depression will become the leading cause of disability worldwide in 2030 [1]. In middle-income and high-income countries including Japan, depression was the leading cause of disability in 2004 [1]. Depression is associated with impaired quality of life, yet many depressed patients do not receive appropriate care [2]. The importance of early detection and appropriate care for depressed patients has only recently been recognized.

In the United States and United Kingdom, primary care physicians and general practitioners (GPs) have an important role in diagnosing and treating depressed patients [3,4]. In countries with a primary care system, the importance of developing effective depression management models for primary care settings has been emphasized to provide appropriate care for depressed patients. Collaborative care has emerged as a potentially effective intervention for improving the quality of primary care and patient outcomes, primarily in the US. The effectiveness of collaborative care has been shown in a

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meta-analysis of US and UK studies [5]. Effective depression management models have been developed and introduced on site in these countries. These models are developed based on situation-specific parameters such as prevalence of depression, recognition rate of depressed patients by physicians, prescription rate of antidepressants to depressed patients, and referral rate to mental health specialists. However, little information necessary for developing effective intervention models is available in Japan.

In Japan, there are few specialists for primary care or general practice because the Japanese medical system has no clear definition regarding the role of primary care and the specific provider responsible. Patients do not need to consult with assigned primary care providers as in the UK medical system. In the Japanese system, patients select hospitals using their own judgment and usually consult general internists, as well as any other specialist, directly. In rural areas, most patients consult a general internist who plays a role similar to that of a primary care physician in the UK. It has been reported that depressed patients in Japanese communities tend to consult not only mental health specialists, but also other specialists such as a general internists because of their somatization in addition to the stigmatization of psychiatric disorders and services [6,7]. The importance of primary care provided by general internists in the management of depressed patients has been stated recently in the Comprehensive Suicide Prevention Initiative published by the Japanese Government. This publication was based on effective intervention models and guidelines for depression care in primary care settings and general practice developed in the US and UK medical systems [8].

A survey examining the prevalence of depression and the recognition rate of depressed patients by physicians was performed nearly 20 years ago. The survey was conducted at general internal medicine outpatient clinics in general hospitals in medium-sized cities of Japan and the patients in the survey were 15-65 years old. The recognition rate of depression by physicians in this survey was lower than in other countries at 19.3% [9]. However, the situation has changed recently as the number of depressed patients receiving medical care has increased [10]. Because of this change in situation, there are no usable data suitable for developing intervention models reflecting the role of primary care in a general internal medicine outpatient clinic in Japanese rural areas.

Meanwhile, the prevalence of chronic medical illness in the elderly is high. Given that a higher prevalence of depression has been reported in patients with chronic medical illnesses [11], general internists have an important role in diagnosing depression among older people, especially in rural areas with a high population aging rate. Also from this perspective, information regarding general internal medicine in rural areas is important.

In the present study, we conducted a survey investigating the prevalence of depression in addition to the ability to recognize depression and rates of psychotropic prescription at a general internal medicine outpatient clinic in a rural hospital. These rates are important indices of each step - diagnosis, judging the care that is necessary, and treating and/or referring the patient to mental health specialists - in the provision of appropriate care for depressed patients by general internists in Japanese rural areas.

Methods

Setting

This study was approved by the ethics committee of the National Center of Neurology and Psychiatry in Japan. The researchers provided all participants with detailed information of the study in the form of a written document. The study was performed after obtaining the patients' oral informed consent.

This study was conducted on 6 of 10 consultation days between June 15 and 26, 2009, at a general internal medicine outpatient clinic in a general hospital having no mental health services. This hospital is located in Oshu City, Iwate Prefecture in the Tohoku region of Japan. The hospital is functioning as a regional public hospital and is funded by the National Health Insurance Society at Oshu City. Oshu City is a typical rural area about 500 km north of Tokyo with low influx and efflux of the population. There are high proportions of elderly people and people engaged in primary industry [12].

Participants

All patients aged 20 or older who visited the outpatient clinic to consult a physician were recruited consecutively. Visitors who consulted for family members or others and patients who had already participated in the survey were excluded. Patients with significant cognitive impairment, those who were unable to understand Japanese, and those who had physical or mental conditions too severe to participate in the survey were excluded. Cognitive impairment was judged by research staff (trained psychiatric nurses, psychiatrists, or trained investigators), based on a semi-structured interview that including asking patients questions such as, "What is the date today?" and "Did you come here by yourself?". The staff sometimes conducted an additional interview regarding the patients' life style and history of dementia if accompanying persons were present.

Figure 1 shows the number of patients included and excluded at each stage of the present study. Of 427 patients who consulted the general internal medicine

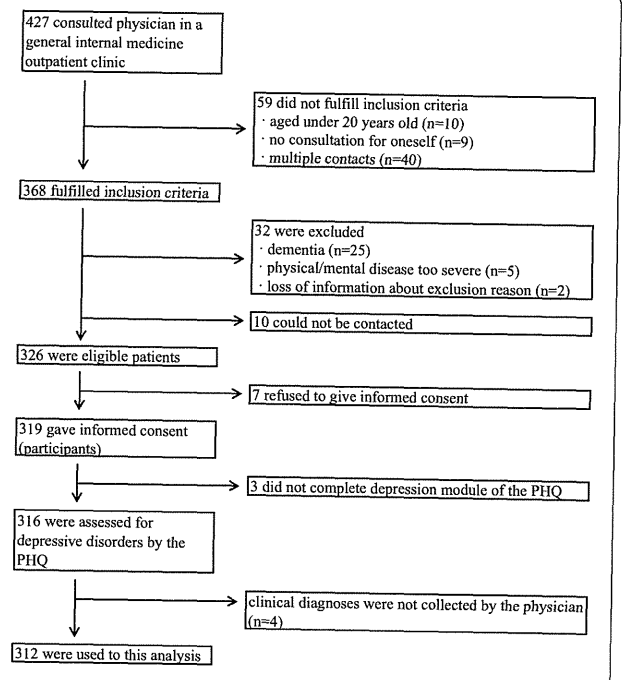

Figure 1 Sampling Process.

outpatient clinic during the survey period, 319 patients fulfilled the inclusion criteria and gave informed consent. Three patients had deficits in one or several items of the Patient Health Questionnaire (PHQ: described below) that were needed to evaluate depressive disorders. The questionnaires regarding physician recognition of mental disorders (described below) could not be collected for 4 patients. As a result, we used information from 312 patients in our analyses. The number (%) of patients who could not be contacted, and the number of patients who refused to participate or dropped out from the study were 10 (3.0%) and 14 (4.2%), respectively. The information about sex and age of patients who refused to participate was not collected. Among the seven patients who dropped out from the study, five (71.4%) were female. Age of one patient was unknown, and the mean (standard deviation: SD) age of the six patients was 73.2 (8.4) years.

Five male physicians (mean (SD) age, 44.4 (10.6) years), all of whom had their clinical duties at the outpatient clinic, examined patients at the general internal medicine department in the hospital. Each day, two physicians worked at the routine outpatient clinic in the morning and two others worked there in the afternoon. Each physician saw approximately 15-20 patients, with the four physicians seeing a total of about 60-80 patients in one day.

Procedure

We approached outpatients visiting the department of general internal medicine during the survey days listed above. Candidate participants who provided informed consent answered several self-report questionnaires during the waiting period for consultation as described in the Measures section below. These questionnaires were used to assess psychiatric disorders, and to survey sociodemographic information and treatment history of mental disorders. Physicians who were blinded to the results of the questionnaires were asked about the diagnosis of primary illness and recognition of mental disorders for each patient after consultation. The history of psychotropic medicine prescription for each patient was collected after the consultation day.

Measures

Clinical diagnosis of primary illness

The clinical diagnosis of primary illness for each patient was made by physicians using a questionnaire that allowed multiple answers and the freedom to provide description.

Recognition of mental disorders by physicians

We evaluated the recognition of mental disorders by physicians for each patient using a questionnaire. If any mental disorders were recognized by the physician, a clinical psychiatric diagnosis and the impression of severity were determined by the physician using the following procedure. Clinical psychiatric diagnoses were selected from the following terms: mood disorder, anxiety disorder, alcohol-related disorder, insomnia, dementia, other, and uncategorizable. Multiple selections were allowed. The "other" category included psychiatric disorders or symptoms other than those listed above, and "uncategorizable" indicated that physicians could not clinically diagnose the psychiatric disorder. These terms were determined during a discussion among physicians and researchers prior to the survey period. Because recognition of mental disorders by physicians was intended to reflect clinical diagnoses used daily, not only clinical psychiatric diagnoses but any psychiatric symptoms observed were included as recognition of mental disorders. We defined the severity of mental disorders as the degree of influence on daily life, similar in concept to the Global Assessment of Functioning (GAF) scale in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) [13]. The physician's judgment concerning the severity of mental disorders was recorded using a 5-point scale ranging from "5 = extremely severe" to "1 = mild," with patients having no mental disorders scored as a zero.

Prescription of psychotropic medicine

Data regarding history of psychotropic medicine prescription for all patients on the consultation (survey) day and during the previous 6 months were collected from medical records after the consultation day by two researchers including a psychiatrist (MI and TO).

Referral to mental health specialists

History of referral to mental health specialists during the previous 6 months was surveyed from medical records after the consultation day for all patients evaluated as having any mood disorder using the PHQ described below.

Depressive disorders and other psychiatric comorbidities

We used the Japanese version of the Patient Health Questionnaire (PHQ) to assess depressive disorders [14]. The PHQ is a self-report version of the Primary Care Evaluation of Mental Disorders (PRIME-MD) [15] that was developed as a primary care screening tool for common mental disorders, including major depressive disorder and probable alcohol abuse or dependence [16,17]. The PHQ has been used in studies all over the world [18,19]. The Japanese PHQ was developed and its validity was assessed using the Mini-International Neuropsychiatric Interview-Plus [14]. We used a 9-item depression module of the Japanese PHQ to assess major depressive disorder and other depressive disorders. Clinical significance of major depressive disorder and other depressive disorders was assessed using a categorical algorithm for the PHQ depressive module. Patients were assessed as having major depressive disorder if they responded "more than half the days" or higher to five or more of the nine items (Questions 1a-1i). Question 1i was included in this total if their response was at least "several days." In addition, the five items had to include either Question 1a or 1b. A patient was considered to have another depressive disorder if they responded with at least "more than half the days" to two, three, or four of the nine items. Again, Question 1i was included in the total items if it received at least "several days", and one of the items had to include either Question 1a or 1b. Patients were considered to have "any mood disorder" when evidence for both major depressive disorder and another depressive disorder was present. The sensitivity and specificity of major depressive disorder were 84% and 95%, respectively [14]. The sensitivity and specificity of any mood disorder were 75% and 94%, respectively (unpublished data analyzed from the data set used in the reference [14]). The severity of depressive disorder was assessed using the summary score (0-27) of each item of the depressive module of the PHQ.

As additional information, we assessed three psychiatric comorbidities: panic disorder, alcohol-related disorder, and generalized anxiety disorder. We used the panic disorder module of the brief PHQ, a simplified version of the PHQ, to assess panic disorder [16]. Although a Japanese version of the brief PHQ has been developed by reverse translation, the validity data have not been reported. We used the probable alcohol abuse or dependence module of the PHQ to assess alcohol-related disorder. The sensitivity and specificity of probable alcohol abuse or dependence in Japanese were 100% and 95%, respectively [14]. We used the Japanese version of the 7-item generalized anxiety disorder scale (GAD-7) to assess generalized anxiety disorder. The GAD-7 is a brief self-report questionnaire used as a screening tool for GAD in clinical practice [20]. Similar to the PHQ, the Japanese version GAD-7 has been developed by reverse translation. Sensitivity and specificity of the Japanese version GAD-7 are 88% and 82%, respectively [21].

Analysis

We calculated the prevalence and 95% confidence intervals of major depressive disorder and any mood disorder. The recognition rate of mood disorder by physicians and the prescription rate of psychotropic medicine were each calculated as a ratio among patients evaluated as having major depressive disorder and any mood disorder using the PHQ.

We assessed the relationship between the severity of depressive disorder evaluated by the PHQ and the severity of mental disorders based on the physician's judgment using Pearson's correlation coefficient. A two-sided P-value < 0.05 was considered significant. We performed statistical analyses using SPSS version 17.0J (SPSS Japan Inc.)

Results

Characteristics of the patients who participated in the present study

Among the 312 patients, 193 (61.9%) were female. The median (range) and mean (SD) age were 75 (21-98) and 72.9 (12.5) years. The most common diagnosis of primary illness was hypertension, followed by hyperlipidemia and diabetes (Table 1). Five patients consulted the physician only for mental disorders.

The number and prevalence of patients with major depressive disorder and any mood disorder as assessed by the PHQ are shown in Table 2. The number and prevalence of patients diagnosed with panic disorder, alcohol-related disorder, and GAD were 3 (1.0%), 23 (7.4%), and 16 (5.2%), respectively.

The number and prevalence of patients with major depressive disorder comorbid with panic disorder, alcohol-related disorders, and GAD were 2 (7.7%), 1 (4.0%), and 5 (19.2%), respectively. For patients with any mood disorder comorbid with panic disorder, alcohol-related disorders, and GAD, the number and prevalence were 2 (4.0%), 3 (6.4%), and 9 (18.4%), respectively.

Recognition of mental disorders by physicians

Physicians clinically diagnosed 85 patients as having a mental disorder. The clinical psychiatric diagnoses (number of patients) made by the physicians included the following: mood disorder (15), anxiety disorder (17),

Table 1: Clinical diagnosis of primary illness (n = 312).

Diagnosis	n	% of patients
Hypertension	165	52.9
Hyperlipidemia	37	11.9
Diabetes	33	10.6
Reflux Esophagitis	17	5.4
Gastritis/Gastric ulcer	14	4.5
Other	132	42.3

Multiple clinical diagnoses were allowed for each patient. The total number of clinical diagnosis for all patients was 398.
Five mental disorders as the primary illness are included in "Other".

alcohol-related disorder (5), insomnia (48), dementia (6), other (13) and uncategorizable (4).

Among the 27 patients identified with major depressive disorder using the PHQ, physicians recognized 21 patients (77.8%) as having a mental disorder. The clinical psychiatric diagnoses made by the physicians for these 21 patients are shown in Table 3. Among the 27 patients with major depressive disorder, only three patients (11.1%) were correctly recognized by physicians as having a mood disorder. Many patients with major depressive disorder were clinically diagnosed with insomnia by physicians.

Meanwhile, among the 52 patients diagnosed with any mood disorder using the PHQ, physicians recognized 31 patients (59.6%) as having a mental disorder. The clinical psychiatric diagnoses made by the physicians for these 31 patients are shown in Table 4. Among the 52 patients with any mood disorder, physicians recognized only seven patients (13.5%) as having a mood disorder.

Among the 85 patients who were recognized by physicians as having a mental disorder, the physicians judged the severity of the mental disorders (number of patients) as follows: extremely severe (1), moderately severe (7), moderate (20), moderately mild (30), or mild (24). The severity scores for three patients were blank.

Among patients identified with any mood disorder using the PHQ, the relationship between depression severity using the PHQ summary score and the severity of the mental disorder as judged by the physician was significant (Pearson's correlation coefficient r = 0.346, p = 0.012). Among the 27 patients with major depressive disorder, 12 patients had moderately severe depression (summary score of the PHQ: 15-19) or severe depression (20-27). Among these, physicians judged seven patients (58.3%) as having a moderately mild or a mild mental disorder, or no mental disorders. In short, physicians underestimated the severity of their disorders.

Table 2: Prevalence of depressive disorders.

	n	%	95% CI
Major depressive disorder	27	8.7	5.5-11.8
Any mood disorder	52	16.7	12.5-20.8

Major depressive disorder and any mood disorder, which was defined to include both major depressive disorder and other depressive disorders, were assessed by the PHQ.
CI: confidence interval

Prescription of psychotropic medicine by physicians

The survey of psychotropic prescription history showed that 13 (4.2%) patients were prescribed any antidepressant including sulpiride, which is permitted by insurance as a drug for depression in the Japanese health system, and 72 (23.1%) were prescribed an anxiolytic or hypnotic. Two patients had been prescribed an antiepileptic. The numbers (%) of psychotropic medicine prescriptions in patients identified with major depressive disorder and any mood disorder using the PHQ are shown in Table 5. Among the 27 patients with major depressive disorder, only one patient had been prescribed an antidepressant by a physician and another patient was prescribed an antidepressant by another outpatient clinic (orthopedic department) in the same hospital. In addition to the two patients prescribed antidepressants by physicians, one patient had been prescribed an antidepressant from another hospital. As a result, only three patients with major depressive disorder had received any antidepressants.

Even among those who were clinically diagnosed as having mood disorders by physicians irrespective of the PHQ depression score (n = 15: three with major depressive disorder, four with other depressive disorder, and eight without any mood disorder), only four (26.7%) were prescribed an antidepressant.

Additionally, according to medical records, none of the patients identified with any mood disorder using the PHQ had been referred to a mental health specialist.

Discussion

PHQ results from patients visiting a general internal medicine outpatient clinic of a rural hospital showed that the prevalence of major depressive disorder and any mood disorder were 8.7% and 16.7%, respectively, in this population. However, among the patients with major depressive disorder, the physician recognition rate of mood disorder was 11.1%. The prescription rate of antidepressants to patients with major depressive disorder was 7.4%. Even in patients who were clinically diagnosed by physicians as having a mood disorder, the prescription rate of antidepressants was only 26.7%.

Prevalence

In a survey performed nearly 20 years ago using the Composite International Diagnostic Interview (CIDI) at general internal medicine outpatient clinics in Japanese general hospitals, the prevalence of depression was 3.0% [9]. The prevalence of major depressive disorder in the present study was higher than that in the previous study. The previous survey included patients 15-65 years old, while most of the participants in this study were older (mean age: 72.9 years old). In addition, the study sites of the previous survey were located in medium-sized cities in Nagasaki Prefecture, but the present study was performed in a rural hospital. These differences in patient characteristics and hospital settings may partly explain the higher prevalence of depression in the present study.

A meta-analysis of several studies in other countries showed that the prevalence of depression in primary care settings for people aged 65 or older is 15.9% [22]. The prevalence of major depressive disorder in this study was 8.7%, lower than in other countries. This may be partially due to a difference in medical systems because patients can directly consult mental health specialists in Japan rather than being required to consult primary care physicians, as is common in other countries. Meanwhile, in a previous epidemiological study of people in a Japanese community, the 12-month prevalence of major depressive disorder was 2.9% [23]. The lower prevalence in the community may be reflective of the lower prevalence of depression diagnosed in a general internal medicine outpatient clinic. Although a direct comparison is limited by differences in response rate, age distribution, and survey method, the prevalence of depression in a general internal medicine outpatient clinic of a rural hospital in the present study was higher than the prevalence in the community. This is consistent with results reported from the US and UK showing the prevalence of depression in primary care settings is higher than in the community [22,24]. This means that depressed patients who have not received appropriate treatment have consulted general internists in spite of Japan's medical system that allows direct consultation to specialists. It is important that physicians appropriately recognize depressed patients and treat and/or refer them to mental health specialists. These physicians can play a role in gatekeeping unrecognized and untreated depressed patients to provide them with appropriate care.

Recognition

The recognition rate (11.1%) of major depressive disorder in the present study was lower than the rate of depression reported in the previous Japanese study (19.3%) [9]. Hospitals in the previous study had their own psychiatric units, and thus physicians in those hospitals may have frequently examined patients with psychiatric disorders and become proficient in diagnosing depression. However, the hospital in the present study did not have a psychiatry department and no mental health services were provided by mental health specialists. Despite this difference between the Japanese studies, both recognition rates in Japan were much lower than those in other countries as shown by a meta-analysis (47.3%) [22]. Therefore, as a first step, it is necessary to increase the recognition rate of depressed patients by physicians in Japan. Effective screening of depression [18,19] may be a key activity for improving depression care.

A simulation in the meta-analysis suggested that when the prevalence is 10%, there are more false positives (n = 16.8) than either missed (n = 5) or identified cases (n = 5) for every 100 unselected cases seen in primary care. There was concern that false positives would increase as the prevalence decreased [22]. In the present study, not only the physician recognition rate of depressed patients was low, but also the false positive rate of was low (3.1%). This may mean that physicians do not pay attention to depressive disorder. General internists may think that care of depression is not "their business" in the Japanese medical system and that depressed patients should directly consult mental health specialists. To introduce an effective screening system, education to increase awareness and to change physician attitudes toward depression may be important.

Although the severity of mental disorders judged by physicians correlated with the severity of depression assessed by the PHQ (Pearson's correlation coefficient r = 0.346, p = 0.012), more than half of the patients with severe depression were misjudged as having depression of mild to moderate severity, or having no mental disorder (58.3%). This result suggests that appropriate care for depression was not provided even to severely depressed patients who really needed care. In addition to constructing and implementing a system of screening for depression, a referral system to mental health specialists and/or an increase in physician diagnostic and treatment skills is needed.

Many patients identified with major depressive disorder using the PHQ were recognized as having a mental disorder by physicians, but physicians often clinically diagnosed the disorder as insomnia, which is a common symptom of depressive disorders. The higher physician recognition rate of any mental disorder, such as insomnia, may be useful in prompting the suspicion of depression. When a physician notes insomnia and/or a mental disorder in a patient, they should at least screen for depression using a validated screening tool. This step will increase the recognition rate of probable depression by physicians.

Of patients with major depressive disorder, only two were prescribed antidepressants and many were prescribed anxiolytics or hypnotics. This may be creating a

Table 3: Recognition of mental disorders by physicians among patients with major depressive disorder (n = 27) as evaluated by the PHQ.

Recognition by physician	Clinical diagnosis by physician	n	% of patients with major depressive disorder	n	% of patients with major depressive disorder
Any mental disorder		21	77.8		
	Mood disorder			3	11.1
	Anxiety disorder			3[a]	11.1
	Alcohol-related disorder			1	3.7
	Insomnia			14[b]	51.9
	Dementia			1	3.7
	Other			4	14.8
	Uncategorizable			2	7.4
No mental disorder		6	22.2		

Because multiple answers were allowed in the clinical psychiatric diagnosis, the total number of diagnoses was 28 and the number of diagnoses per patient was 1.33 for patients with major depressive disorder. Also, the numbers for anxiety and insomnia include patients diagnosed with a mood disorder: [a]1, [b]2.

further significant problem of likely dependence on the medication. In addition, no patients were referred to mental health specialists. These results seem consistent with the higher rate of insomnia clinically diagnosed by physicians, the lower rate of correct clinical diagnosis of depression, and the lower estimate of the severity of mental disorders. Even for patients judged by physicians as having a mood disorder, the prescription rate of antidepressants by physicians was low (26.7%). Although it is controversial whether antidepressants should be prescribed to patients with mild depression in primary care settings [3,25], the results of the present study suggest that appropriate care may not always be provided for depressed patients even when physicians become able to accurately diagnose depression. Given such a situation, physicians must at least recognize and monitor depressive disorders to judge the necessity of care and referral to mental health specialists.

Advantages of the study

No prior study has surveyed recent data of depression prevalence and physicians' recognition rate of depression at a general internal medicine outpatient clinic in Japan.

Table 4: Recognition of mental disorders by physicians among patients with any mood disorder (n = 52) as evaluated by the PHQ

Recognition by physician	Clinical diagnosis by physician	n	% of patients with any mood disorder	n	% of patients with any mood disorder
Any mental disorder		31	59.6		
	Mood disorder			7	13.5
	Anxiety disorder			5[a]	9.6
	Alcohol-related disorder			2	3.8
	Insomnia			18[a]	34.6
	Dementia			1	1.9
	Other			6	11.5
	Uncategorizable			2	3.8
No mental disorder		21	40.4		

Because multiple answers were allowed in the clinical psychiatric diagnosis, the total number of diagnoses was 41 and the number of diagnoses per patient was 1.32 for patients with any mood disorder. Also, the numbers for anxiety and insomnia include patients diagnosed with a mood disorder: [a]3.