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Subsyndromal Depression and Anxiety in Older Adults: Health Related, Functional, Cognitive and Diagnostic Implications

JW Kasckow^{1,2,*}, JF Karp², E Whyte², M Butters², C Brown², A Begley², S Bensasi², and CF Reynolds III²

¹VA Pittsburgh MIRECC and Behavioral Health, 7180 Highland Dr (116a), Pittsburgh, PA 15206

²Department of Psychiatry, University of Pittsburgh School of Medicine, 3811 O'Hara St, Pittsburgh, PA 15213

Abstract

Subsyndromal depression in later life is common in primary care. Comorbid anxiety disorders could exacerbate the negative effect of subsyndromal depression on functioning, health-related quality of life, comorbidity and/or cognition. We examined anxiety disorders coexisting with subsyndromal depression in participants age 50 in an NIH trial of Problem Solving Therapy for Primary Care for indicated prevention of major depression. There were 247 participants, with Centers for Epidemiologic Studies - Depression scores 11. Participants could have multiple psychiatric diagnoses: 22% of the sample had no DSM IV diagnosis; 39% of the sample had only 1 DSM IV diagnosis; 28% had 2 diagnoses; 6% had 3 DSM IV diagnoses; 4% had 4 DSM IV diagnoses; and 1% had 5 diagnoses. Furthermore, 34% of participants had a current comorbid DSM IV diagnosis of a syndromal anxiety disorder. We hypothesized that those with subsyndromal depression, alone relative to those with coexisting anxiety disorders, would report better health-related quality of life, less disability, less medical comorbidity and less cognitive impairment. However, there were no differences in quality of life based on the SF 12 nor in disability based on Late Life Function and Disability Instrument scores. There were no differences in medical comorbidity based on the Cumulative Illness Scale-Geriatrics scale scores nor in cognitive function based on the Executive Interview (EXIT), Hopkins Verbal Learning Test-Revised and Mini Mental Status Exam. Our findings suggest that about one third of participants 50 years and older with subsyndromal depression have comorbid anxiety disorders; however, this does not appear to be associated with worse quality of life, functioning, disability, cognitive function or medical comorbidity.

Keywords

comorbidity; subsyndromal depression; anxiety; prevention; cognition; functioning

*Corresponding Author John Kasckow, MD, PhD, VA Pittsburgh Health Care System Behavioral Health, 7180 Highland Dr (116a), Pittsburgh, PA 15206, Ph: (412) 954-4344, kasckowjw@upmc.edu.

Conflicts of Interest

Dr. Reynolds has received pharmaceutical supplies from Forest Laboratories, Pfizer, Lilly, and BMS for his NIH sponsored research. Dr. Kasckow has served as a consultant for Bristol Meyers Squibb and Forest and has also received grant support from Astra Zeneca. Dr. Karp is a stock owner of Corcept. In addition, he has received medication supplies for an Investigator Initiated Trial from Pfizer, Eli Lilly, and Reckitt Benckiser.

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Objectives

Subsyndromal depressive symptoms are common, and already symptomatic individuals are at high risk for developing depressive and anxiety disorders. This enhanced risk occurs in both younger (Karsten et al 2011; Shankman et al 2009) and older populations (i.e., 65; Lyness et al 2007). However, the degree of psychiatric comorbidity in individuals with subsyndromal depression has not been well studied.

It is not known how the presence of a syndromal comorbid anxiety disorder in those with subthreshold depression affects functioning, medical comorbidity, quality of life or cognitive function. Kessler et al (1999) demonstrated that individuals with comorbid Major Depression and Generalized Anxiety Disorder have a greater odds of perceiving their mental health as fair or poor; in addition, those with both conditions are more likely to exhibit greater work impairment and social role impairment compared to individuals with Major Depression which is not comorbid with anxiety disorders.

Furthermore, individuals with both comorbid depression and anxiety have greater rates of hospitalization for cardiovascular disease as well as a greater risk of death from cardiovascular disease (Chamberlin et al 2011; Doerng et al 2010). With regard to cognitive status, it has been demonstrated that older patients with both major depression and a comorbid anxiety disorder have worse outcomes with regard to cognitive status compared with major depression alone. For instance, DeLuca et al (2005) determined that individuals age > 55 with comorbid major depression and either generalized anxiety disorder or panic disorder have a greater decline in memory than those with major depression alone. Our research team wondered whether comorbid anxiety disorders in individuals with subthreshold depression could exacerbate the negative effect that subthreshold depression exerts on functioning, health-related quality of life, comorbid medical illnesses or cognitive functioning. If these outcomes were worse in individuals with both subthreshold depression and an accompanying anxiety disorder, it would suggest that this subpopulation might require specialized treatment or preventive strategies.

In the parent study from which this sample was drawn (Sriwattanakomen et al 2008; 2010; Kasckow et al 2010; 2012), we had reported the spectrum of co-existing current and past psychiatric disorders among adults aged 50 and older having subthreshold depressive symptoms who participated in a randomized, single-blind trial of Problem Solving Therapy-Primary Care for indicated prevention of major depression. The current study extends these findings by initially characterizing the number of different diagnoses that all randomized participants exhibited and testing the hypothesis that participants with subsyndromal depressive symptoms and comorbid anxiety disorders would have worse health-related quality of life, greater medical comorbidity, greater functional disability and/or worse cognitive status. In addition, we conducted exploratory analyses aimed at determining what demographic and clinical factors would be associated with depression severity.

Methods

Sample

Participants took part in an ongoing NIH- sponsored, randomized single-blind clinical trial comparing Problem Solving Therapy in Primary Care (PST-PC; Arean et al 2008) vs a dietary education condition to prevent or delay episodes of major depression in individuals with subsyndromal symptoms of depression. "Subthreshold depression" was defined by a score of 11 or greater on the Center for Epidemiologic Studies-Depression (CES-D) Scale, in the absence of a SCID/DSM IV defined episode of major depression within the past year. The CES-D score of 11 or greater was based on its performance characteristics in the

PROSPECT trial (Bruce et al 2004) where it was used to identify primary care patients aged 60 and greater with mild depressive symptoms.

We have described the parent study previously (Sriwattanakomen et al 2008; 2010). Here, we report baseline, data acquired for all randomized subjects of the parent study (August 2006-October 2010). Participants were screened with the CES-D under the authority of a University of Pittsburgh IRB approved 'Waiver of Informed Consent' and 'Waiver of Documentation of Informed Consent'. Participants aged 50 and older with scores of 11 and higher on the CES-D scale were then asked to come to the medical center to learn more about the study and to provide written informed consent.

The parent study excluded potential participants with a history of a major depressive episode within the past 12 months and/or already taking antidepressant medication or currently engaged in any other mental health treatment, those with a Mini Mental Status Score < 24 (Folstein et al 1975) and/or already diagnosed with a neurodegenerative disorder. In participants meeting the inclusion and exclusion criteria for the parent study, we assessed past and present psychiatric comorbidity using the Structured Clinical Interview for DSM-IV of the American Psychiatric Association (First et al 1994).

Scales/Measures

To test our hypothesis, we then divided the study group into those with a) no anxiety or those with b.) a current DSM IV syndromal anxiety disorder. Syndromal anxiety disorders included specific phobia, generalized anxiety disorder, anxiety disorder NOS, agoraphobia without panic, panic disorder without agoraphobia, obsessive compulsive disorder, post traumatic stress disorder and social phobia. We compared the 2 groups on demographic measures, health-related quality of life (SF 12; Ware et al 1996), social and physical functioning (Late Life Function and Disability Instrument, LL-FDI; Karp et al 2009; Sayers et al 2004) and medical comorbidity (Cumulative Illness Rating Scale – Geriatrics, CIRS-G; Miller et al 1992). In addition, we compared the 2 groups with regards to cognitive status using the following measures: Mini Mental Status Exam (Folstein et al 1975), Hopkins Verbal Learning Test-Revised (Shapiro et al 1999) and Executive Interview (EXIT; Royal et al 1992).

Demographic variables included age, gender, self-reported race, employment status, marital status, and residential status. Additional clinical assessments included the 17-item Hamilton Depression Rating Scale (Hamilton, 1960) and the anxiety subscale of the Brief Symptom Inventory (Derogatis and Melisaratos, 1983).

Statistical Analysis

We generated descriptive data to characterize the presenting psychiatric diagnoses of 247 randomized subjects. For hypothesis testing, we then excluded 4 participants because after signing consent and being randomized, they were determined to have current major depression (n=2), current alcohol abuse (n=1), or a mood disorder secondary to substance use (n=1).

We generated group measures (means, standard deviations and %, n) to characterize the remaining N=243 subjects with respect to demographic and clinical variables. We compared 2 groups: those with 'subthreshold depression' only vs. those with 'subthreshold depression + a current DSM IV anxiety disorder'. We used t-tests to examine differences in the means and standard deviations of continuous variables. In the case of unequal variances, we used the Satterthwaite method. Fisher's exact test was used to examine frequency differences (%) in categorical variables. Pearson correlation coefficients were used to examine which demographic and clinical factors were related to depression severity. Any variable correlated

with CES-D at $p < 0.10$ was included in a multiple linear regression model. Prior to all analyses, we examined data for normality. All tests were considered significant at $p < 0.05$ (2-tailed).

Results

All 247 subjects were considered to have subthreshold depression given the recruitment definition of CES-D 11. We first present an updated summary of our sample relative to our earlier report (Sriwattanakomen et al 2010) with regard to diagnoses. There were a total of 32 different diagnoses and a subject could present with multiple diagnoses. The types of current DSM-IV diagnoses for the 247 participants were grouped into those with depression, anxiety, adjustment disorders and other.

Subjects in the depression subgroup included those with depressive disorder NOS ($n = 55$; 22%), Major Depression, single episode in full remission ($n = 52$; 21%), major depression, recurrent episode, in full remission ($n = 18$; 7.2%), dysthymic disorder ($n = 15$; 6.1%), major depression, single episode in partial remission ($n = 6$; 2.4%), major depression, recurrent episode in partial remission ($n = 5$; 2.0%), major depression, recurrent episode, mild ($n = 1$; 0.4%), major depression, recurrent episode, mild ($n = 1$; 0.4%), major depression, single episode, moderate ($n = 1$; 0.4%).

Subjects in the Anxiety disorder group included those with specific phobia ($n = 32$; 13.0%), generalized anxiety disorder ($n = 30$; 12.1%), anxiety disorder NOS ($n = 19$; 7.6%), social phobia ($n = 11$; 4.5%), panic disorder without agoraphobia ($n = 9$; 3.6%), post traumatic stress disorder ($n = 6$; 2.5%), agoraphobia without a history of panic disorder ($n = 2$; 0.8%) or obsessive compulsive disorder ($n = 2$; 0.8%).

Those with Adjustment Disorder diagnoses included subjects with adjustment disorder with anxiety ($n = 3$; 1.2%), those with adjustment disorder with mixed anxiety and depressed mood ($n = 9$; 3.6%), and those with adjustment disorder with depressed mood ($n = 7$; 2.8%) and adjustment disorder unspecified ($n = 4$; 1.6%). Finally, the 'Other' category included those with primary insomnia or insomnia related to another disorder ($n = 17$; 6.9%), cognitive disorder NOS or dementia due to HIV disease ($n = 2$; 0.8%), eating disorder NOS ($n = 2$; 0.8%), alcohol abuse ($n = 1$; 0.4%), attention deficit/hyperactivity disorder NOS ($n = 1$; 0.4%), breathing related sleep disorder or sleep disorder due to a general health condition, mixed type or parasomnia type ($n = 1$; 0.4%), diagnosis or condition deferred on Axis I ($n = 1$; 0.4%), relational problem NOS ($n = 1$; 0.4%), stuttering ($n = 1$; 0.4%), substance induced mood disorder ($n = 1$; 0.4%), unspecified mental disorder (nonpsychotic; $n = 1$; 0.4%), bereavement ($n = 7$; 2.8%).

Of the 247 subjects, 84 (34%) also had a current DSM IV diagnosis of an anxiety disorder. The most common comorbid anxiety disorder was specific phobia ($n = 32$; 13.0%) followed by generalized anxiety disorder ($n = 30$; 12.1%). The Table compares the demographic and clinical characteristics of the 2 groups: those with no current anxiety vs those with a current anxiety disorder. We observed significant differences in age, i.e. a higher age in the subthreshold group without current anxiety (66.77 ± 11.64 vs 63.33 ± 9.24). There were no differences in race, gender, years of education, employment status, marital status nor living status. As expected, the group with a comorbid anxiety disorder had higher anxiety scores on the Brief Symptom Inventory, a higher rate of a history of a DSM IV syndromal anxiety disorder and higher Hamilton Depression Rating Scale scores than the group without a comorbid anxiety disorder.

We observed no group differences in current depressive symptoms (i.e. CES-D scores), burden of comorbid medical illness (CIRS-G), nor in mental and physical health-related

quality of life (SF 12). In addition, there were no differences in the Social, Personal, Management and Instrumental subscales of the Late Life Function and Disability Instrument nor in scores from the 3 cognitive measures: the Mini Mental Status Exam, the Hopkins Verbal Learning Test-Revised and the EXIT.

Pearson correlation showed that the anxiety scores from the Brief Symptom Inventory, mental health component scores from the SF12 and the personal role scaled score, the social role scaled score and the management role scaled score from the LL-FDI were correlated with depression severity at $p < 0.10$. Results from a multiple regression model including these variables showed that significant predictors of CES-D depression severity included the mental health component score (standardized beta = -0.38 , $t = -5.22$, $p < 0.0001$) from the SF12 and the personal role scaled score from the LL-FDI (standardized beta = 0.23 , $t = 3.12$, $p = 0.002$). Decreased SF 12 mental health scores and increased LL-FDI personal role scaled scores predicted higher depression severity. The model was significant [$F(2,174) = 15.09$, $p < 0.0001$, $R^2 = 0.15$].

Discussion

Our results demonstrate that individuals age 50 and older with subthreshold depression exhibit a broad range of psychiatric comorbidity. Indeed, approximately 78% of the participants had 2 or more DSM IV current psychiatric diagnoses. The degree of psychiatric comorbidity in individuals in this age range with subthreshold depressive disorders has not been well studied. The few studies available in geriatric samples have examined comorbid anxiety disorders. For instance, Lenze et al (2000) examined individuals from primary care clinics age 60 with subthreshold depressive symptoms (also defined as Center for Epidemiologic Scale-Depression scores ≥ 11) and without current major depression; 23% had a current anxiety disorder. In our sample, 34% of individuals with subthreshold depression had a comorbid current anxiety disorder.

Kvaal et al (2007) surveyed 2535 community dwellers age ≥ 65 in the United Kingdom and determined that only 4% of individuals with subthreshold depression also had a syndromal anxiety disorder; thus the sample in this study included individuals with comorbid anxiety disorders exhibiting rates much higher than has been observed in the community. It is important to note that our study specifically included individuals who chose to undergo a psychosocial intervention for their emotional distress. Furthermore, the subset of individuals in our sample which had a comorbid syndromal anxiety disorder displayed no differences in quality of life, functioning, disability, cognition or medical comorbidity. However, there were differences in depression scores between groups; the group with anxiety had significantly higher Hamilton Depression scores; in addition, the group with anxiety also had higher CES-D scores although these differences were not significant.

When examining predictors of depression severity, we found that mental health scores from the SF 12 were negatively associated with CES-D severity. In addition, we found that LL-FDI personal role scores were positively associated with CES-D scores. Lyness et al (2007) reported previously that patients with subsyndromal depression had more functional disability relative to a group with no depression. Our findings with the SF 12 scores but not personal role scores are consistent with this finding. The finding with personal role scores could reflect variability in functional status associated with mild depression and/or measurement issues, such as differences in the approach in measuring functional status.

Various approaches have been utilized to define the “subsyndrome” of ‘less than Major Depression.’ Experts have not yet decided how the ‘gold standard’ for this diagnosis should be determined; this is also true when considering the elderly population. Much of the

preliminary work in this area has focused on establishing criterion validity. For instance, studies by Lyness et al (2007) determined in individuals age 65 and older that the functional consequences of having subthreshold depression were as marked as those with major depression. In addition they determined that this older group of individuals with subthreshold depression had more medical disability compared to a non-depressed group.

Subthreshold depressive disorders can progress to more severe conditions over time (Lyness et al 2006). Over a 2 year period, Karsten et al (2011) examined a group of individuals with subthreshold depression with a mean age of 42.6 +/- 13.9. These individuals were more likely to develop an anxiety disorder (odds ratio = 3.5) as well as a depressive disorder (odds ratio = 6.2). In an older group of individuals age 60 with subthreshold depression, Lyness et al (2006) demonstrated that 10% of these individuals convert to Major Depression within a year. Thus not treating subthreshold disorders can lead to negative consequences. In our sample, those with Comorbid anxiety had higher Hamilton Depression Rating Scale scores. This suggests the comorbid group may be at higher risk of conversion to Major Depressive Disorder.

Our study was limited by its cross sectional design. Future studies will determine how the presence of comorbid anxiety in individuals with subthreshold depression affects overall prognosis in the long term. In addition, future studies will determine whether the presence of comorbid anxiety moderates outcome when these individuals participate in treatment interventions.

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Table 1

Clinical and Demographic Differences between those with Subthreshold Depression and those with Subthreshold Depression + Current DSM IV Anxiety

	Whole Group [243]	No Current Anxiety [159] (a)	Current Anxiety [84] (b)	
Age	65.58 (10.97)	66.77 (11.64)	63.33 (9.24)	# $t(204.9)=2.51$
%Female	71.19 [173]	70.44 [112]	72.62 [61]	$\chi^2_{(1)}=0.13$
%Caucasian	62.14 [151]	61.64 [98]	63.10 [53]	$\chi^2_{(1)}=0.05$
%Employed	40.74 [99]	40.88 [65]	40.48 [34]	$\chi^2_{(1)}=0.00$
Marital				$\chi^2_{(3)}=1.36$
%Co-habiting/Married	46.50 (113)	45.28 (72)	48.81 (41)	
%Divorced/Separated	19.75 [48]	20.13 [32]	19.05 [16]	
%Never Married	11.11 [27]	10.06 [16]	13.10 [11]	
%Widowed	22.63 [55]	24.53 [39]	19.05 [16]	
%Living at home with no supervision	92.18 [224]	93.08 [148]	90.48 [76]	$\chi^2_{(1)}=0.52$
Education	14.54 (2.74)	14.50 (2.63)	14.62 (2.94)	$t(241)=-0.33$
CIRS-G	7.85 (3.89) [241]	7.70 (3.85) [158]	8.13 (3.97) [83]	$t(239)=-0.81$
HRS17	11.13 (3.78) [242]	10.35 (3.89) [159]	12.61 (3.09) [83]	*** $t(202.0)=-4.94$
CES-D	21.10 (7.92)	20.66 (7.89)	21.94 (7.97)	$t(241)=-1.20$
BSI anxiety	0.51 (0.50) [233]	0.37 (0.35) [156]	0.81 (0.63) [77]	*** $t(99.6)=-5.76$
%History of anxiety	21.40 [52]	11.95 [19]	39.29 [33]	$\chi^2=24.42$
SF 12				$t(203)=0.49$
Physical	42.06 (11.80) [205]	42.34 (11.65) [138]	41.48 (12.18) [67]	
Mental	47.39 (9.69) [205]	48.04 (9.81) [138]	46.06 (9.36) [67]	$t(203)=1.38$
LL-FDI Scaled				$t(199)=0.53$
Personal	64.95 (15.84) [201]	65.38 (16.58) [132]	64.13 (14.39) [69]	
Social	46.79 (8.96) [199]	47.42 (8.64) [132]	45.55 (9.49) [67]	$t(197)=1.40$
Instrumental	66.97 (14.47) [199]	67.33 (14.75) [132]	66.28 (13.97) [67]	$t(197)=0.48$
Management	79.07 (15.87) [201]	79.64 (15.45) [132]	77.97 (16.71) [69]	$t(199)=0.71$
Mini-Mental Status Examination (MMSE)	28.22 (1.65) [242]	28.20 (1.70) [159]	28.28 (1.56) [83]	$t(240)=-0.37$

	Whole Group [243]	No Current Anxiety [159] (a)	Current Anxiety [84] (b)	
Executive Interview (EXIT)	6.92 (4.54) [214]	6.97 (4.93) [142]	6.82 (3.68) [72]	# $t(183.0)=0.25$
Hopkins Verbal Learning Test- Revised (HVLTR)				$t(213)= -1.41$
Total Trial 1–3	22.80 (5.69) [215]	22.41 (5.92) [143]	23.57 (5.16) [72]	
Trial 4	7.26 (3.38) [215]	7.16 (3.37) [143]	7.44 (3.42) [72]	$t(213)= -0.58$
Percent Retained	78.84 (32.59) [216]	78.11 (31.37) [144]	80.31 (35.09) [72]	$t(214)= -0.47$
Recognition Discriminability Index	9.43 (2.31) [215]	9.34 (2.43) [143]	9.63 (2.06) [72]	$t(213)= -0.87$

Satterthwaite reported due to unequal variances; Brackets indicate number per group while parentheses indicate standard deviation if applicable;

* indicates $p < 0.05$;

** indicates $p < 0.01$.

The ranges of the scales are as follows: Cumulative Illness Rating Scale – Geriatrics (CIRS-G); 0–52; higher score worse; 17 item Hamilton Depression Rating Scale (HRS17); 0–52 higher score worse; Center for Epidemiologic Studies - Depression (CES-D); 0–60; higher score worse; Brief Symptom Inventory-Anxiety (BSI anxiety); 0–4; higher score worse; SF 12 physical; 17.32–58.51; higher score better; SF 12 mental; 16.34–67.29; higher score better; Late Life Function and Disability Instrument scaled scores (LL-FDI); 0–100; higher score better; Mini Mental Status Exam (MMSE); 1–30; higher score better; Executive Interview (EXIT); 0–50; higher score worse; Hopkins Verbal Learning Test-Revised (HVLTR); Total Trial 1–3; 0–36; higher better; Trial 4; 0–12; higher score better; Percent Retained; 0–1200%; interpretation of score depends on Trial 3; Recognition Discriminability Index; 0–12; higher score better.