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PSYCHIATRY IN PRIMARY CARE (BN GAYNES, SECTION EDITOR)

# Psychiatric and Medical Comorbidity in the Primary Care Geriatric Patient—An Update

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**Abstract** The mental health needs of older primary care patients are now widely recognized if not widely addressed. The range of behavioral health approaches including co-locating psychiatrists and integrating mental health professionals as care managers into primary care sites is extensive and growing. Nonetheless the primary care provider remains the first line of defense against mental disorders, most commonly depression and anxiety that accompany and exacerbate common physical conditions. The excess, potentially avoidable disability that results from comorbidity makes it imperative that early recognition and evidence based intervention occur. Multimorbidity and polypharmacy make intervention a challenge. Psychotherapy can help overcome comorbidity depression however the most accessible intervention would be an antidepressant FDA approved for both anxiety and depressive disorders. For all these reasons, a focus on physical conditions most commonly associated with mental disorders can foster early recognition before the older patient's care becomes overwhelmingly complicated.

**Keywords** Comorbidity · Geriatric · Depression · Anxiety · Dementia · Neurocognitive

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## Introduction

The mental health needs of older primary care patients are now widely recognized if not widely addressed. The range of behavioral health approaches including co-locating or integrating mental health professionals as care managers into primary care sites is extensive and growing. Nonetheless, the primary care provider remains the first line of defense against mental disorders that accompany and exacerbate common physical conditions. The excess, potentially avoidable disability that results from comorbidity makes it imperative that early recognition and evidence based intervention occur. Multimorbidity and polypharmacy make intervention a challenge. In addition, a number of chronic conditions are associated with impairments in cognition that do not manifest as memory problems. Executive dysfunction or impaired cognitive control disrupts planning and problem solving making adherence difficult despite good intentions. If memory is intact, persons with impaired executive function can learn work-around strategies to improve adherence. For all these reasons, a focus on physical conditions most commonly associated with mental disorders can foster early recognition before the older patient's condition becomes overwhelmingly complicated.

## Depression and Mortality

Gallo et al. [1] sought to provide an estimate of the number of deaths that could be prevented in the population if the influence of depression could be mitigated in older care patients. After adjusting for the presence of cardiovascular disease and diabetes at baseline, patients with depression were 1.75 times as likely to die after the 2-year follow-up period. The population attributable fraction due to depression on mortality was estimated to be 13 % compared to 9 % diabetes and 18 % for

any cardiovascular disease. Depression and depression-related mortality may be even higher than reported, given that many older adults minimize reports of sadness, anhedonia, and other psychological symptoms of depression secondary to physical health conditions. Similarly, cognitive impairment may lead to under-reporting of depression. Lastly, the authors estimate that 1 in 10 deaths would be prevented if the influence of depression could be eliminated from the primary care population. Practices incorporating a depression care manager, achieved survival rates among depressed patients with high multi-morbidity scores comparable to those with low scores. In contrast, depressed patients with high multi-morbidity scores in usual care practices without depression management staff experienced a threefold increase in mortality risk compared to those with low morbidity scores [2••].

## Models of Mental Health Care

Older primary care patients encounter both acute and chronically debilitating illnesses that are associated with depression. In each, depression degrades self-care and the process of recovery but the circumstances differ. In acute illness, both the older patient's independence and the caring ecosystem of family and social supports are disrupted. Recovery requires rehabilitative efforts by the patient and an enhanced supportive environment both of which need to become active in the immediate aftermath of the acute event. Reliance on others is crucial for rehabilitation requiring family routines to change even as rehabilitation specialists enter the field. Avari and Alexopoulos [3•] argue that a four element "ecosystems-focused therapy" model be adopted following acute illness. First, the patient needs to acquire a new adaptive perspective to regain independence. Second, a structure needs to arise to enhance adherence to the prescribed regimen of medications and physical activity. Third, a problem solving approach needs to evolve to reduce obstacles to recovery, adherence, and interdependence. Fourth, family plans and goals need to be reengineered to support all of the above. And finally, care coordination between the primary physician, rehabilitation specialists, and family needs to be established. What follows is an update on the most prevalent conditions in which mental and physical disorders are comorbid.

## Chronic Obstructive Pulmonary Disease

Exacerbations of chronic obstructive pulmonary disease (COPD) especially those requiring hospitalization are associated with an increased risk of post-traumatic stress disorder symptoms. Severe dyspnea has been likened to a near-death experience [4]. Among Medicare beneficiaries, 23 % with an incident diagnosis of COPD were subsequently diagnosed with depression. The risk of depression was elevated fourfold among those with a COPD-related hospitalization [5]. COPD may also increase risk for dementia [6]. And depending on the extent of patient dependency, caregivers of persons with COPD have elevated rates of health-related problems [7]. A 2015 review of studies of depression and COPD found both exacerbations of respiratory distress and all-cause mortality were increased among patients with depression. In addition, recognition of depressive disorders was infrequent despite their contribution to morbidity [8].

Avari and Alexopoulos [3•] describe a specialized care management exemplified by the personalized adherence intervention for depression and chronic obstructive pulmonary disease (PID-C). Here, the core elements of intervention are first the identification of treatment barriers which could be logistical, emotional, cognitive, or behavioral. Misconceptions, hopelessness, helplessness, and misattribution of symptoms are addressed to insure that patents are taking their antidepressant and maintaining the prescribed regimen of exercise. Adherences to treatment, for example, participating in physical rehabilitation, as well as course of the illness are monitored. The authors acknowledge that "The last things a depressed, demoralized, cognitively compromised, and weak COPD patient wants to do are to follow a tiring exercise program, visit treatment centers, and increase social activities." Nonetheless, PID-C compared to treatment as usual reduced depressive symptoms and dyspnea-related disability with benefits sustained 6 months after the end of the intervention. Their physicians were notified of their patients' depressed status but those in the intervention group also received telephone care management by specially trained social workers [9].

PID-C is particularly promising because patient activation has gained support for a number of chronic conditions where anxiety and depression compromise the patient's capacity for self-management [10]. However, antidepressants may be more accessible. Unfortunately, published placebo-controlled trials of antidepressants with COPD patients are few. Among COPD patients diagnosed with either major depression or dysthymia, nortriptyline was superior to placebo in reducing both depression and anxiety. Daily function, physical comfort, and respiratory symptoms also improved [11]. In addition to nortriptyline, antidepressants with proven antianxiety properties but little sedation (paroxetine, escitalopram, sertraline, bupropion, duloxetine) may be worthwhile [12].

## Acute Coronary Syndromes

Myocardial infarction and unstable angina are comorbid with major depressive disorder (MDD) almost 20 % of the time. Depression is often persistent, impairs health status more than heart disease itself [13], and substantially increases cardiac morbidity and mortality [14]. Factors that have been discussed

to underlie the association between depression and cardiovascular disorders comprise risk taking and a lifestyle characterized by low exercise, increased volumes of visceral fat, and low glucose disposal rates [15]. The Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) was designed to evaluate the safety and efficacy of sertraline for treatment of major depression. No evidence of harm was seen, and sertraline had an overall beneficial effect on mood that occurred primarily in patients with a prior history of MDD. Depression with onset after hospitalization showed a high placebo response rate (69 vs 60 %, respectively). The onset of MDD immediately following acute coronary syndrome (ACS) onset is more likely to remit spontaneously whereas onset before the ACS episode, like recurrent MDD, identifies cases that are more persistent and less likely to remit without treatment. Although involving fewer than 400 patients, the SADHART found a 23 % reduction in life-threatening events for patients treated with sertraline [16••].

### Congestive Heart Failure

Depression and related poor self-care increase rates of hospitalization and mortality in patients with heart failure [17]. A 2015 meta-analysis found that depression but not anxiety is an important and independent predictor of all-cause mortality among patients with heart failure [18]. However, treating depression in the context of heart failure with antidepressant therapy has not been shown to improve survival. In a study of more than 100,000 patients with heart failure, those taking antidepressants had an increased risk for cardiovascular and all-cause mortality. However, more than 80 % of those prescribed an antidepressant did not have a diagnosis of depression [19•]. In the Sertraline Against Depression and Heart Disease in Chronic Heart Failure (SADHART-CHF) trial sertraline in doses of 50–200 mg was safe but compared to placebo did not provide greater reduction in depression or improved cardiovascular status among heart failure patients with depression [20•]. Cognitive behavioral therapy focused on both depression and heart failure self-care is effective for depression but does not improve self-care or physical functioning compared to usual care enhanced with an education program delivered by a cardiology nurse. However, cognitive behavioral therapy was associated with reduced anxiety, fatigue, improved social functioning, and health-related quality of life [21]. Exercise training also significantly reduced depression in heart failure patients under and over 65 years [22]. Newhouse and Jaing [23] offer a treatment algorithm for depression in heart failure that begins with education and exercise, progressing to SSRI antidepressant prescriptions and referral to psychiatry after two failed trials of antidepressants or the presence of psychosis, mania, or suicidal ideation.

### Hypertension

Scazufa et al. [24] compared the depression identification and treatment rates with those of diabetes and hypertension among elderly individuals served in primary care [25]. Of 1558 participants, 4.8 % were diagnosed with depression based on ICD-10 criteria. Of these patients, only 12.3 % were receiving appropriate treatment. In contrast, 23.2 and 79.3 % of the patients had a diagnosis of DM and HTN, respectively, of which 72.4 and 77.4 %, respectively, were receiving appropriate treatment for DM and HTN. Levels of treatment rates of depression are very low compared to those of DM and HTN. The barriers to treatment identified were, (1) difficulty identifying depression without diagnostic and standardized instruments, (2) lack of registries track of treatment outcomes, and (3) lack of financial support.

### Diabetes

A positive association between depression and diabetes has been reported but the direction and nature of this association is unclear. Depression may be associated more with diabetes in men than in women. Older men with clinically significant depressive symptoms are more likely to have higher insulin resistance [26]. Although depression is a comorbid condition in many physical health problems, people with diabetes who are depressed report the greatest decrements in perceived health compared with those with any other chronic illness. People with diabetes and major and minor depression have a 2.3- and 1.67-fold increase in mortality, respectively, compared to those without depression. There is strong evidence of an increased risk of depression in people with diabetes as well as increased risk of developing diabetes in people with depression [27]. More importantly, there is a body of evidence that collaborative care for depression improves glycemic control [28, 29].

### Stroke

The prevalence in generalized anxiety disorder (GAD) in the first 6 months post-stroke is 21.3 %, and although GAD is often comorbid with depression, the prevalence without depression is still 10.7 %. Late-life anxiety disorders are frequently associated with physical disability [30], memory impairment [31, 32], poor quality of life [33, 34], increased risk of medical illness [35], and increased use of healthcare resources [30].

Although one study found escitalopram may prevent the onset of depression following stroke [36], a meta-analysis of 13 antidepressants showed a weak effect on post-stroke depression. Four studies of psychotherapies including problem

solving therapy, cognitive behavioral therapy, and motivational interviewing showed no evidence of benefit for post-stroke depression [37]. One large study found an increased risk of subsequent stroke associated with antidepressants suggesting that risks may outweigh benefits [38].

More recently, Mikami et al. [39•] demonstrated that development of GAD can be effectively prevented over the first year after an acute stroke by either escitalopram or problem solving therapy. Study participants given placebo over 12 months were 4.95 times more likely to develop GAD than patients given escitalopram and 4.00 times more likely to develop GAD than patients given problem solving therapy. Preliminary results from 24 post-stroke depressed patients who received home delivered ecosystems-focused therapy demonstrated greater rates of depression remission and lessened disability compared to treatment as usual [3•].

## Cancer

Up to a third of elderly cancer patients experience psychological distress [40]. Geriatric assessments for frailty and low cognitive reserve are valuable for identifying older patients at risk of cognitive decline after cancer and its treatments [41]. Independent predictors of depression include younger age (<65), employment status, proximity to family, and multiple symptoms due to cancer or treatment [42]. Almost 25 % of 112 newly diagnosed cancer patients (≥65 years) followed for 12 months experienced clinically relevant decline in quality of life [43]. Identifying depressive disorders among older adults with cancer is challenging due to both the symptoms associated with the burden of illness as well as those associated with advanced age. Saracino et al. [44] examined criteria from The Diagnostic and Statistical Manual for Mental Disorders (DSM) and found anhedonia, concentration difficulties, sleep disturbances, psychomotor retardation/agitation, and loss of energy were relevant to both depressed older adults and cancer patients. Alternative criteria not listed in DSM included irritability, loneliness, and loss of purpose in older persons. Tearfulness, social withdrawal, and failure to participate in treatment despite ability to do so were identified as important indicators of depression among those with cancer.

## Impairments in Vision and Hearing

Decrements in vision and hearing can impair activities of daily living as well as interpersonal relations [45]. Combined visual and hearing loss compounded effects of either alone on ADLs or social engagement [46]. Visually impaired individuals are significantly more likely to have mental and physical health conditions. As visual loss may lead to depression from decreased function and complicated management of comorbidities, clinicians should be alert to also screen for depression and hearing loss in this population [47]. Meuleners et al. [48] found the number of mental health contacts for depression and/or anxiety declined substantially the year after cataract surgery. In patients with optic neuropathies, those with less subjective visual loss had less mental distress. If vision cannot be restored or maintained, coping strategies and supportive therapy should be offered [49]. In one study, a program of low vision rehabilitation combined with behavioral activation halved the incidence of depressive disorders compared to standard vision rehabilitation among outpatients with age-related macular degeneration [50•].

### Chronic Kidney Disease

Depression ascertained by trained interviewers as opposed to self-reports approaches 20 % of persons with chronic kidney disease (CKD). Depression is associated with reduced treatment adherence and quality of life as well as elevated rates of hospitalization and mortality. The interaction of CKD and depression is reciprocal with one condition worsening the other [51]. Anxiety symptoms are also common among CKD patients but when they accompany symptoms of depression do not add to the risk of poor clinical outcomes beyond that associated with depression alone [52]. Major depression may also be associated with greater risk of microalbuminuria independent of differences in self-care [53]. Although depression is common in CRD, randomized controlled trials of antidepressant among these patients are not. A 2012 meta-analysis recommended that major depression be treated with an SSRI in CKD stages 3–5 but could not determine which SSRI might be preferred. Agents to be avoided due to markedly reduced drug clearance included venlafaxine, desvenlafaxine, bupropion, reboxetine, tianeptine, and selegiline [54].

## Arthritis

Older community residents with arthritis and depression are likely to be less physically active, more disabled, less socially active, and in greater pain compared to those without depression [55]. Among persons with osteoarthritis, a 19 % increased odds of self-reported depression is associated with each additional symptomatic joint even after adjusting for age, gender, and comorbidity [56]. Excess health burden and health care expenditures are observed when depression is comorbid with osteoarthritis and is related to associated anxiety, other chronic conditions, and poor health status [57]. Of those with anxiety and depression, 70 % suffer from chronic pain. However, anxiety, depression, and pain are rarely the patient's chief complaint leading to under-recognition and undertreatment [58]. Rheumatoid arthritis elevates the incidence

rate of depression 1.74-fold with female gender, older age, and comorbid chronic conditions adding to the risk profile [59]. Symptoms of anxiety and depression were also associated with a 50 % reduction in the effects of prenisolone treatment. Persistent anxiety and depression are associated with reduced odds of achieving rheumatoid remission [60].

A number of investigators have studied the effects of antidepressants on mood, pain, and physical function among persons with major depressive disorders and rheumatoid arthritis [61, 62]. Although the effects on function are less clear, often both pain and depression are reduced by antidepressant therapy. In the Improving Mood: Promoting Access to Collaborative Treatment (IMPACT) trial, more than a thousand arthritis patients aged 60 and older, most of who had osteoarthritis with major depression or dysthymia were randomized to either antidepressant medication with or without problem solving psychotherapy or to treatment as usual. Quality of life, physical function pain, and depressive symptoms were all significantly improved with the intervention [59]. A 2015 meta-analysis of arthritis studies found that prescribed exercise was associated with a statistically significant reduction in depressive symptoms with an effect size such that the number needed to treat to demonstrate benefit was seven [63].

## Neuropsychiatric Symptoms of Dementia (Neurocognitive Disorders)

Close to a third of patients with neurodegenerative disease will have some psychiatric condition resulting in impaired quality of life and reduced time until institutionalization [64, 65••, 66, 67]. Anxiety, depression, or apathy as well as disinhibition, hallucinations, or delusions are more common in males [68]. NPS occurrence tends to increase as neurocognitive disorder progresses [69]. Neuropsychiatric symptoms (NPS) tend to segregate into clusters in Alzheimer's disease. The most preponderant is an apathetic syndrome seen across all stages of disease. An affective syndrome (anxiety, depression) follows in prevalence, with nearly one third of patients manifesting symptoms of clinical significance [70]. A psychotic syndrome of delusions, less commonly with hallucinations, is third. The relationship between neurocognitive disorders and depression is described as a dynamic of three components. First depression is a prodromal phase in many neurocognitive disorders [71]. Second depression lowers the threshold for manifesting symptoms associated with neurocognitive decline [72]. Third depression induces hippocampal damage leading to the neurocognitive findings associated with dementing illnesses [66].

Sudden onset NPS should trigger the search for reversible causes. These include infection, anemia, hyperglycemia, hypothyroidism, metabolic derangements, pain, constipation, dehydration, visual or hearing impairment, and side effects of medications, both prescribed and over the counter, with anticholinergic properties such as sedative antihistamines labeled "PM." The use of alcohol, nicotine, caffeine, marijuana, and stimulants should be queried. One study found that more than a third of community-residing older adults with neurocognitive disorders were found to have undiagnosed illness, most commonly bacteriuria, and followed by hyperglycemia and anemia [73•]. Resisting/refusing care was the most common behavioral disturbance among those found to have undiagnosed illness.

In most instances, management of NPS should be non-pharmacological. Management is based on how interactions among different factors contribute to NPS which the patient, the caregiver, and the environment. Patient factors include pre-morbid mental illness, sensory impairments, and unmet needs. Caregiver factors may include lack of education about management strategies, unrealistic expectations and exhaustion. Environmental factors include too little or too much stimulation and lack of structure in a patient's day.

Caregiver interventions typically include a series of supportive help sessions individualized to patient and caregiver. The caregiver is taught stress reduction as well as cognitive reframing techniques. Though psychosis has not been found to be responsive to the results of such an approach, aggression, agitation, and depression have all shown to respond [74•]. Regular assessment of unmet needs (pain, toileting, sensory deprivation, loneliness, boredom) has also been shown to improve outcomes [75]. Finally, there are reports of acupressure/massage or music therapy mitigating aggression [76].

There are no currently FDA-approved pharmacological treatments for NPS in the setting of neurocognitive disorders, but there is a body of evidence that explores distinct pharmacological approaches for different NPS [77]. The HTA-SADD trial demonstrated no difference between sertraline or mirtazapine and placebo with respect to efficacy though there were higher numbers of drug-related adverse events [78]. Though repeated studies of second generation antipsychotics have demonstrated efficacy for NPS, these same studies have found that an associated serious adverse events including increased cerebrovascular accidents, extrapyramidal symptoms, and all-cause mortality trumped the benefits [79, 80]. Consequently, these medications should be reserved for situations requiring emergent symptomatic improvement due to safety considerations such as psychosis causing harm or with potential to cause harm to self or others, treatment-resistant major depression with or without suicidal ideation, or aggression/agitation causing risk to self or others.

More recent research supports the use of SSRIs to manage agitation. The CitAD trial found that among patients with Alzheimer's disease receiving psychosocial interventions for caregivers, citalopram significantly reduced agitation [81•]. Another study found citalopram worked as well as risperidone

with respect to agitation or psychotic symptoms [82]. More recently, the combination of dextromethorphan and quinidine at doses up to 30/10 mg twice daily significantly reduced agitation/aggression scores compared to placebo among persons with dementia [83•]. Notably, another study found that implementing a systematic approach to pain management in nursing homes led to significantly reduced agitation [84]. With respect to the treatment of apathy, two small studies suggest benefits from methylphenidate though accompanied by the expected adverse effects such as elevated blood pressure [85, 86].

## Alcohol Use Disorders

Of all substance use disorders, alcohol is the most common among older adults. The "Baby Boomer" cohort of aging adults indicates that they use alcohol at a higher rate than their parent's generation [87•]. One third of older persons with an alcohol use disorder developed the problem in later life, while the other two thirds grew older with the medical and psychosocial sequella of early-onset alcoholism [88]. Being 65 to 74 years old, white, divorced/widowed, and male were associated with increased risks of lifetime alcohol use disorders (AUD). Financial strain also places older adults, especially older women, at higher risk for heavy drinking [89]. Alcohol use can have significant effects on many chronic diseases seen in older adults. Due to the collective effect of exacerbating hypertension and hyperlipidemia, chronic alcohol use increases the risk of myocardial infarction and cardiomyopathy. In patients with chronic obstructive pulmonary disease, alcohol can cause mental confusion owing to its depressive effect on respiratory drive. Moreover, rates of dementia are higher in older individuals with chronic alcohol use. Cerebellar damage increases ataxia and risk of falls. Lastly, risk of osteomalacia is also increased due to alcohol's inhibitory effect on the hydroxylation of vitamin D. Of older adults who use alcohol, the overall death rates are the lowest among men and women reporting about one drink daily [90]. And simply sharing the facts that more than one drink a day has deleterious health consequences can have a significant impact on patient alcohol intake [87•].

## Conclusion

Mental health professionals are taking a greater role in primary care and this trend will likely continue. Nonetheless primary care providers will remain the first to encounter the signs of an emerging mental illness that if left untreated will lead to excess morbidity and mortality. In addition, comorbid mental and physical illness can lead to polypharmacy and multi-morbidity that are overwhelmingly complex. Early intervention requires early recognition. An awareness of conditions among older primary care patients that are more frequently associated with mental illness gives the primary care provider the preparation needed to intervene. Whether the salient feature is anxiety or depression, the most accessible intervention would be an antidepressant FDA approved for both anxiety and depressive disorders. These include sertraline, paroxetine, escitalopram, and duloxetine [12]. In as much as the growth of the older adult population will outpace any proposed increase in mental health practitioners, the need for behavioral health competence among primary care providers is obvious.

### Compliance with Ethical Standards

**Conflict of Interest** The authors declare that they have no conflict of interest.

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