Title: Anxiety disorders in late life – why are we not more worried?

Short Running Title: Anxiety disorders in late life – why are we not more worried?

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Late life anxiety disorders and subthreshold anxiety disorders are highly prevalent conditions that cause significant disability, yet they receive very little research attention when compared with late life depression. In 2008, Beekman observed that anxiety in later life had "only very recently become the subject of systematic investigation."[1] Given that this comment was made over a decade ago, it is timely to examine how much systematic investigation there has been into late life anxiety since then.

One approach to address this question is to quantify how much research attention has been paid to late life anxiety over the years and whether this has changed. Further, the use of a comparator such as late life depression can provide an indication of the relative research attention that late life anxiety receives in the broader context of geriatric psychiatry research.

As described below, at the end of August 2019, there were 5,738 MEDLINE indexed publications relating to late life anxiety. In comparison, the number of MEDLINE indexed publications relating to late life depression passed this number almost a quarter of a century ago in 1995! In 1995, a review article about late life depression concluded that "depression in old age presents considerable problems in diagnosis and is frequently neither detected not adequately managed… Its aetiology, and, in particular, the contribution of the aging process, remain poorly understood".[2] Furthermore, the relationship between cognitive impairment and depression was described as not yet clear.[2] We suggest that there are some parallels between late life depression research in 1995 and late life anxiety depression research in 2020.

To compare the research attention on late life anxiety with late life depression, we used number of MEDLINE publications as a proxy for amount of research attention.   The number of publications related to late life anxiety was compared to late life depression in Ovid MEDLINE and Epub ahead of Print, In-Process & Other Non-indexed Citations, Daily and Versions from 1946. The Medical Subject Heading (MeSH) terms deemed most appropriate in Ovid MEDLINE were "Anxiety Disorders", "Depressive Disorder" and "Aged". The searches were deliberately broad to be inclusive and were not limited except by year when looking at trends over time. The search strategy is included in Appendix One. The search was conducted on 31 August 2019 and yielded:

"Anxiety Disorders" (MeSH term) and "Aged" (MeSH term) = 5,738 publications

"Depressive Disorder" (MeSH term) and "Aged" (MeSH term) = 18,119 publications

As shown in Figures 1-4, there was a significant difference in the number of publications related to late life anxiety compared to depressive disorders with the difference in absolute numbers continuing to grow. When examining new publications (Figures 3-4), the ratio appeared to be

narrowing with an initial ratio in favour of depressive over anxiety disorders ranging from almost nine to one in 1991 to the most recent ratio of around two to one. The most recent ratio still meant that each year, there were twice as many new publications about depressive disorders compared with anxiety disorders in late life when using the MeSH terms in Ovid MEDLINE above.

Insert Figures 1-4 here

There are many possible explanations for the difference in research attention being paid to late life anxiety as compared with late life depression. This may reflect differences in priorities of researchers, funding bodies and journals. There may also be misperceptions about the relative prevalence and burden of late life anxiety disorders as compared with late life depression. We will explore some of these possible explanations, including:

1. The relatively early age of onset of anxiety disorders may lead to the belief that anxiety disorders in late life are less important to research than anxiety disorders in younger adults.
2. The prevalence of late life anxiety disorders might be under-estimated when using diagnostic tools that are not adapted for use in late life, and thus felt to not require as much research attention.
3. There may be a perception that anxiety disorders are less "severe" and less disabling than some other mental health conditions, and consequently considered as lower priority for research attention.
4. There may be a perception that late life anxiety is usually part of "mixed anxiety-depression" implying that it is part of depression, rather than needing to be researched in its own right.
5. When compared with the interaction between depression and cognition, our understanding of the potential detrimental effects of anxiety on cognition is at a less advanced stage, and thus we may not yet appreciate the importance of focusing on this interaction.

An Ovid MEDLINE ALL search of publications up to and including 2019 that relate to the MeSH terms "Anxiety Disorders" and "Depressive Disorder" without combining with the MeSH team "Aged" was conducted on 8 March 2020. This search resulted in 32,993 and 72,024 publications respectively. In 2018, the number of new publications related to Anxiety was 1,487 and Depression was 2,140 when not combining with the term "Aged". While publication numbers without the "Aged" focus still favour depression over anxiety, the difference appears to be less than publications focused on late life. These observations may suggest that there are two factors at play: the first being a relative general lack of attention being paid to anxiety compared with depression across the lifespan, and the second being a greater attention being paid to anxiety in younger adults rather than in late life.

Age of Onset and Prevalence of Anxiety Disorders

The US National Comorbidity Survey Replication (NCS-R) study examined lifetime prevalence and age of onset distributions in Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) disorders.[3] This survey found that anxiety disorders were the most prevalent class of disorders with a lifetime prevalence of 28.8%. They found a median age of onset for anxiety disorders of 11 years with an interquartile range (IQR) of 6-21 years. There was variation within anxiety disorders with specific phobia and separation anxiety disorder having a median age of onset of 7 years, social phobia 13 years and other anxiety disorders 19-31 years.[3] A more recent meta-analysis found a mean age of onset of anxiety disorders to be 21.3 years which varies from separation anxiety disorders 10.6 years to GAD 34.9 years.[4]

This early age of onset may result in the belief that late life anxiety disorders are less important to research compared with anxiety disorders in younger people. Despite the age of onset being generally earlier in life, it has been demonstrated that anxiety disorders and subthreshold anxiety disorders are highly prevalent in late life with a 12-month prevalence of 17.2% in the MentDis_ICF65+ study,[5] a cross-sectional survey of 3,142 community dwelling adults aged between 65 and 84 years in five European cities and Israel. The study used the Composite International Diagnostic Interview (CIDI) 65+, an adaptation of the CIDI to this age-group. The authors found that the 12-month prevalence of anxiety disorder was 17.2%, with prevalence for specific disorders being Agoraphobia 4.9%, Panic Disorder 3.8%, GAD 3.1%, Post-Traumatic Stress Disorder (PTSD) 1.4%, Social Anxiety Disorder 1.3% and Obsessive-Compulsive Disorder (OCD) 0.8%. They further reported a gender difference with females having higher prevalence rates of any anxiety disorder (OR=2.96), agoraphobia (OR=2.44) and GAD (OR=3.48). There was a linear reduction in prevalence with age: prevalence of 20% in those aged 65-70 years, reducing to 12% in those aged 80-84 years.[5] The NCS-R study in the United States found a 12-month prevalence of 7.0% for DSM-IV anxiety disorders,[6] which was lower than that found in the MentDis_ICF65+ study, but still relatively common.

It is possible that the adaptation of the CIDI65+ in the MentDis_ICF65+ study contributed to the difference in estimations of prevalence, compared with the NCS-R study. There has been ongoing discussion about the shortcomings of diagnostic criteria such as those of DSM-IV when applied without modification to a late life population.[7-9] Canuto and colleagues have suggested that "uncertainty remains about whether lower rates in old age reflect a true decline in anxiety disorders, or whether they result from methodological biases or the insufficiency of current diagnostic instruments in detecting and diagnosing anxiety disorders in old age."[5] Furthermore, Grenier and colleagues have postulated that the DSM-IV clinical significance criterion may lead to false negatives in older adults as they are usually less active and less likely to perceive themselves as disabled compared to younger adults, and are more likely to present with somatic symptoms rather than the emotional disturbance symptoms, making it more difficult to meet diagnostic criteria.[10]

In addition to the higher prevalence of anxiety disorders in late life when age modified diagnostic criteria were applied, there were also studies of late life GAD that found an approximately even split between early and late onset of the condition,[11-13] with these episodes often being chronic as 36%

last longer than ten years.[12] This is in contrast to other studies finding that most anxiety disorders have onset in adolescence or early adulthood.

Subthreshold anxiety disorders in late life are even more prevalent than anxiety disorders. There is no consensus definition for subthreshold anxiety disorder. Most studies have defined subthreshold anxiety disorder by reducing the threshold of one or more of the diagnostic criteria for anxiety disorders as defined by the DSM or the International Statistical Classification of Diseases and Related Health Problems (ICD). It is clear, however, that significant disability and distress is caused by subthreshold anxiety disorders.[14]   The Enquete sur las Sante des Aines (ESA) Study in Canada found 12-month prevalence of subthreshold anxiety disorder of 26.2%.[10] Focusing on GAD specifically, the National Epidemiological Survey of Alcohol and Related Conditions (NESARC) in the US included 13,420 participants aged 55 – 98 years with this group having a 12-month prevalence of subthreshold GAD of 3.3-7.1%, compared with GAD at 1.4-2.4%.[15]

Consequences of Anxiety Disorders

Another possible explanation for the relative neglect of anxiety disorders compared to depressive disorders is that historically, it was thought that anxiety disorders were associated with less functional impairment than depressive disorders. For example, a study of adults presenting to primary care with unrecognised anxiety and major depressive disorder found that major depressive disorder was associated with greater reduction in function than anxiety disorders.[16] Furthermore, the World Health Organization and some research publications have utilised a definition of "severe mental disorders" that encompasses schizophrenia and related conditions, bipolar disorder and moderate and severe depression.[17,18]

In fact, individuals with anxiety were found generally to experience increased mortality risk with a nationwide Danish prospective cohort registry study finding a mortality rate ratio (MRR) of 1.39 for natural causes and 2.46 for unnatural causes when comparing individuals with anxiety disorders with the general population.[19] This ratio was adjusted for confounders including demographic variables, somatic comorbidity and depression. Furthermore, individuals with comorbid anxiety and depression experienced a greater increase in mortality risk than those with either anxiety or depression alone.[19]

When the negative effects of late life GAD on quality of life have been compared with other conditions, the effect of late life GAD is actually comparable to that of depression and greater than that of recent acute myocardial infarction or type II diabetes.[20] Anxiety and depression have been shown to have similar associations with increased levels of physical disability which increase with age.[21] When anxiety disorders are comorbid with depression in late life, they worsen prognosis[12] and are associated with a higher prevalence of several risk factors for suicide (longer illness duration, more emotional distress at last contact with professional, more prescriptions of psychotropic

medication) in depressed older patients who died by suicide.[22] Furthermore, late life anxiety disorders are even more prevalent in clinical settings, with deleterious effects on illness recovery, quality of life and levels of function.[9]

Late life anxiety disorders impact significantly on health services as individuals with late-life GAD have increased healthcare utilisation compared to non-anxious individuals[23] with a review finding greater economic cost to the healthcare system ranging from $-116 to $19,003 per person per year in 2016 US dollar terms.[24]

Subthreshold anxiety disorders, such as subthreshold GAD, are also associated with increased distress and functional impairment, being reported by at least 75% of older adults with these disorders.[14] Subthreshold GAD is also associated with more sleep disturbance and fatigue, more suicide attempts, poorer perceived physical health, more somatic diagnoses, higher primary healthcare use and greater benzodiazepine use.[14]

A review by Wolitzky-Taylor and colleagues discussed that a number of review articles have suggested that the typical presentation of late life anxiety is "mixed anxiety-depression", however they observed that none of these articles have provided data to support this suggestion.[25] It has been postulated that the suggestion that late life anxiety is part of "mixed anxiety-depression" rather than commonly presenting as an entity in its own right, may have contributed to the relative lack of research attention towards late life anxiety.[26]   Furthermore, in the Epidemiological Catchment Area (ECA) study, 20% of adults aged 18-54 years with an anxiety disorder had comorbid depression, while in late life, studies have estimated comorbidity rates that range from 13-29%.[25] This suggests that comorbidity is not specific to late life, and in fact, the majority of people with late life anxiety disorders do not actually have comorbid depression. In addition, one study reported that late life GAD and major depressive disorder do not have simultaneous onset and offset with the former tending to be a single chronic episode and the latter being recurrent in pattern.[12] Late life GAD also appears to precede major depressive disorder and not remit despite remission of depression.[12] The evidence thus supports a pattern of late life anxiety often occurring independently of late life depression, potentially preceding depression and not remitting despite remission of depression. The implication of this pattern is that late life anxiety should have more research attention in its own right and not be subsumed into "mixed anxiety-depression" or depression research.

Anxiety and Cognition

Compounding the direct disability and costs caused by late life anxiety disorders, there is increasing evidence to suggest that anxiety may be detrimental to cognitive functioning and associated with neuropathological changes linked with Alzheimer's dementia. It is informative that the putative underlying neurobiological changes in depression and anxiety may overlap, and there is clear

evidence that depression is a risk factor for dementia.[27] The link between anxiety and dementia has only been examined quite recently, which again reflects the neglect of anxiety in research. Data from at least two large longitudinal cohorts provide some support to the link between anxiety and dementia, after adjusting for the effect of depression:

- The Alzheimer's Disease Neuroimaging Initiative (ADNI) study followed-up 376 participants aged 55 years and above with amnestic Mild Cognitive Impairment (aMCI) for 36 months and found that anxiety severity increased the rate of conversion to Alzheimer's dementia (AD) and predicted greater decrease in entorhinal cortex volume.[28]
- The Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing (AIBL) followed-up 333 healthy participants aged over 60 years for 54 months and found that slope of cognitive decline were significantly more pronounced in the beta amyloid positive plus high anxiety group compared to beta amyloid positive plus low anxiety group.[29]

In addition to being associated with accelerating cognitive decline trajectory, there is increasing evidence from systematic reviews that anxiety disorders may be a modifiable risk factor for developing dementia. Becker and colleagues found anxiety predicted risk of AD with a hazard ratio of 1.53 (seven studies) and Vascular Dementia with a hazard ratio of 1.88 (two studies).[30] Similarly, Gulpers and colleagues found a relative risk of 1.77 for incident cognitive impairment (four studies) and 1.57 for incident dementia (six studies) in community settings.[31] The authors discussed whether anxiety may be a prodromal symptom of dementia given that increasing age appeared to increase the strength of the associations. In contrast, anxiety was not shown to predict conversion to dementia in the studies of participants with aMCI. Li and Li, however, found that anxiety increased risk of conversion from aMCI to dementia with a hazard ratio of 1.18 (seven studies).[32] Gimson and colleagues conducted a systematic review of studies where the anxiety diagnosis preceded the dementia diagnosis by at least 10 years.[33] Their review found four eligible studies with a combined sample size of 29,819 and odds ratios of developing dementia ranging from 1.48-7.4.[33]

This "chicken and egg" question of whether anxiety is a risk factor for dementia or a prodromal symptom of dementia is important and unresolved, and parallels the debate in the late life depression literature. Relatedly, there is increasing research into the concept of Mild Behavioural Impairment (MBI) which is strongly associated with risk of dementia. MBI has been estimated in a population-based sample of 1,377 participants aged 72-79 years to have a prevalence of 34.1% with a gradient that increases with cognitive impairment.[34] In the same sample, anxiety, as defined using the Neuropsychiatric Inventory (NPI), had a prevalence of 3.4% in cognitively healthy, 5% in "cognitively normal, but at risk" and 6% in MCI.[34]

Conclusions

It is clear that anxiety and subthreshold anxiety disorders are highly prevalent in late life and cause significant distress, disability and cost. Excess mortality due to both natural and unnatural causes that can be attributed to anxiety disorders suggests that anxiety disorders are a "silent killer". In addition, there is emerging evidence to suggest that anxiety may be associated with worsening dementia trajectories, is potentially a modifiable risk factor for dementia and/or an early clinical marker of dementia. The evidence presented provides compelling reasons for us to be more worried about anxiety in late life, and to consider that similar to moderate and severe depression, moderate and severe anxiety could also be categorised as a "severe mental disorder".

Despite this growing evidence base, there is still insufficient research attention paid to this important area, particularly when compared to late life depression. We have explored some possible explanations for this difference, and strongly advocate for an increase in research attention. It is promising that the gap appears to be closing, but new research publications in late life depression still outnumber late life anxiety by a ratio of two to one.

The relative lack of focus on research in late life anxiety has myriad clinical implications, that potentially include poorer detection of late life anxiety due to lack of awareness of its prevalence, severity and the most appropriate diagnostic tools. This then can lead to delayed diagnosis, increased morbidity and mortality, poorer prognosis and a more limited range of effective evidence-based treatments being available. Unfortunately, it can also be a missed opportunity to utilise existing effective treatments and target a potential risk factor or prodromal symptom of dementia.

A review of late life anxiety in 2008 authored by Bryant and colleagues, raised key issues which included questions about its prevalence and whether this changes with ageing, whether it is qualitatively different in older adults and the nature of its comorbidity with depression.[26] More than a decade after Beekman's observation about the then recent beginning of systematic investigation into late life anxiety[1], we point out that the key issues raised by Bryant and colleagues[26] around the same time remain largely unresolved.

Critical areas of research that we believe to have the potential to make a meaningful difference to individuals living with late life anxiety, and their communities include:

- Detection of late life anxiety, including subthreshold anxiety – research relating to design and validation of age-appropriate tools and diagnostic criteria, increased clinician attention and reduction of stigma.
- Interactions with dementia and depression – research relating to the effect of anxiety on dementia risk, the potential utility of anxiety as a clinical marker for dementia and the interaction between anxiety and depression.
- Effective treatments – increased research into treatment effectiveness in late life anxiety with the aim to expand the repertoire of available treatments, improve access to treatment and consequently reduce excess mortality attributed to anxiety.

We call for researchers, clinicians and funders to be more worried about anxiety in late life during this new decade and beyond.

References

1. Beekman ATF. Anxiety in aging: a newly chartered territory. Am J Geriatr Psychiatry 2008;16:787-789.
2. Katona CLE, Watkin V. Depression in old age. Rev Clin Gerontol 1995;5:427-441.
3. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005;62:593-602.
4. De Lijster JM, Dierckx B, Utens EMWJ et al. The age of onset of anxiety disorders: a meta-analysis. Canadian J Psychiatry 2017;62:237-246.
5. Canuto A, Weber K, Baertschi M, Andreas S, Volkert J, Dehoust MC. Anxiety disorders in old age: psychiatric comorbidities, quality of life, and prevalence according to age, gender, and country. Am J Geriatr Psychiatry 2018;26:174-185.
6. Gum AM, King-Kallimanis MS, Kohn R. Prevalence of mood, anxiety, and substance-abuse disorders for older Americans in the National Comorbidity Survey-Replication. Am J Geriatr Psychiatry 2009;17:769-781.
7. Jeste DV, Blazer DG, First M. Aging-related diagnostic variations: need for diagnostic criteria appropriate for elderly psychiatric patients. Biol Psychiatry 2005;58:265-271.
8. Mohlman J, Bryant C, Lenze EJ et al. Improving recognition of late life anxiety disorders in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition: observations and recommendations of the Advisory Committee to the Lifespan Disorders Work Group. Int J Geriatr Psychiatry 2012;27:549-556.
9. Bryant C, Mohlman J, Gum A, Stanley M, Beekman ATF, Wetherell JL. Anxiety disorders in older adults: Looking to DSM5 and beyond… Am J Geriatr Psychiatry 2013;21(9):872-876.
10. Grenier S, Preville M, Boyer R et al. The impact of DSM-IV symptoms and clinical significance criteria on the prevalence estimates of subthreshold and threshold anxiety in the older adult population. Am J Geriatr Psychiatry 2011;19:316-326.
11. Chou K. Age at onset of generalized anxiety disorder in older adults. Am J Geriatr Psychiatry 2009;17:455-464.
12. Lenze EJ, Mulsant BH, Mohlman J et al. Generalized anxiety disorder in late life: lifetime course and comorbidity with major depressive disorder. Am J Geriatr Psychiatry 2005;13:77-80.
13. Le Roux H, Gatz M, Wetherell JL. Age at onset of generalized anxiety disorder in older adults. Am J Geriatr Psychiatry 2005;13:23-30.
14. Haller H, Cramer H, Lauche R, Gass F, Dobos GJ. The prevalence and burden of subthreshold generalized anxiety disorder: a systematic review. BMC Psychiatry 2014;14:128.
15. Miloyan B, Byrne GJ, Pachana NA. Threshold and subthreshold generalized anxiety disorder in later life. Am J Geriatr Psychiatry 2015;23:633-641.

16. Schonfeld WH, Verboncoeur CJ, Fifer SK, Lipschutz RC, Lubeck DP, Buesching DP. The functioning and well-being of patients with unrecognized anxiety disorders and major depressive disorder. J Affect Disord 1997;43:105-119.

17. World Health Organization (WHO). Helping people with severe mental disorders live longer and healthier lives: policy brief 2017. Geneva: World Health Organization; (WHO/MSD/MER/17.7). Licence: CC BY-NC-SA 3.0 IGO. https://apps.who.int/iris/bitstream/handle/10665/259575/WHO-MSD-MER-17.7-eng.pdf;jsessionid=78CDA1EB565B0C803DF0D83D6DA5E7B9?sequence=1. Accessed December 2, 2019.

18. Liu NH, Daumit, GL, Dua T, et al. Excess mortality in persons with severe mental disorders: a multilevel intervention framework and priorities for clinical practice, policy and research agendas. World Psychiatry 2017;16:30-40.

19. Meier SM, Mattheisen M, Mors O et al. Increased mortality among people with anxiety disorders: total population study. Br J Psychiatry, 2016;209:216-221.

20. Wetherell JL, Thorp SR, Patterson TL, Golshan S, Jeste DV, Gatz M. Quality of life in geriatric generalized anxiety disorder: a preliminary investigation. J Psychiatr Res 2004;38:305-312.

21. Brenes GA, Penninx BWJH, Judd PH, Rockwell E, Sewell DD, Wetherell JL. Anxiety, depression and disability across the lifespan. Aging Ment Health 2008;12:158-63.

22. Oude Voshaar RC, van der Veen DC, Hunt I, Kapur N. Suicide in late-life depression with and without comorbid anxiety disorders. Int J Geriatr Psychiatry 2016;31:146-152.

23. Porensky EK, Dew MA, Karp JF et al. The burden of late-life generalized anxiety disorder: effects on disability, health-related quality of life, and healthcare utilization. Am J Geriatr Psychiatry 2009;17:473-482.

24. Hohls JK, Konig H, Raynik YI, Hajek A. A systematic review of the association of anxiety with health care utilization and costs in people aged 65 years and older. J Affect Disord 2018;232:163-176.

25. Wolitzky-Taylor KB, Castriotta N, Lenze EJ, Stanley MA, Craske MG. Anxiety disorders in older adults: a comprehensive review. Depress Anxiety 2010;27:190-211.

26. Bryant C, Jackson H, Ames D. The prevalence of anxiety in older adults: methodological issues and a review of the literature. J Affect Disord 2008;109:233-250.

27. Livingston G, Sommerlad A, Orgeta V et al. Dementia prevention, intervention, and care. Lancet 2017;390:2673-2734.

28. Mah L, Binns MA, Steffens DC. Anxiety symptoms in amnestic mild cognitive impairment are associated with medial temporal atrophy and predict conversion to Alzheimer disease. Am J Geriatr Psychiatry 2015;23:466-476.

29. Pietzrak RH, Lim YY, Neumeister A et al. (2015) Amyloid-β, anxiety, and cognitive decline in preclinical Alzheimer disease – a multicenter, prospective cohort study. JAMA Psychiatry 2015;72:284-291.

30. Becker E, Rios CLO, Lahmann C, Rucker G, Bauer J, Boeker M. Anxiety as a risk factor of Alzheimer's disease and vascular dementia. Br J Psychiatry 2018;213:654-660.

31. Gulpers B, Ramakers I, Hamel R, Kohler S, Voshaar RO, Verhey F. Anxiety as a predictor for cognitive decline and dementia: a systematic review and meta-analysis. Am J Geriatr Psychiatry 2016;24:823-842.

32. Li Z, Li Z. The impact of anxiety on the progression of mild cognitive impairment to dementia in Chinese and English data bases: a systematic review and meta-analysis. Int J Geriatr Psychiatry2018;33:131-140.

33. Gimson A, Schlosser M, Huntley D, Marchant NL. Support for midlife anxiety diagnosis as an independent risk factor for dementia: a systematic review. BMJ Open 2018;8:e019399.

34. Mortby ME, Ismail Z, Anstey KJ. Prevalence estimates of mild behavioural impairment in a population-based sample of pre-dementia states and cognitively healthy older adults. Int Psychogeriatr 2018;30:221-232.

Figure Legends

Figure 1: Cumulative Number of Publications identified by MeSH terms of Anxiety vs Depressive Disorders and Aged Population (MEDLINE)

Figure 2: Figure 2: Cumulative Publication Ratio for Depressive vs Anxiety Disorders in Aged Population (MEDLINE)
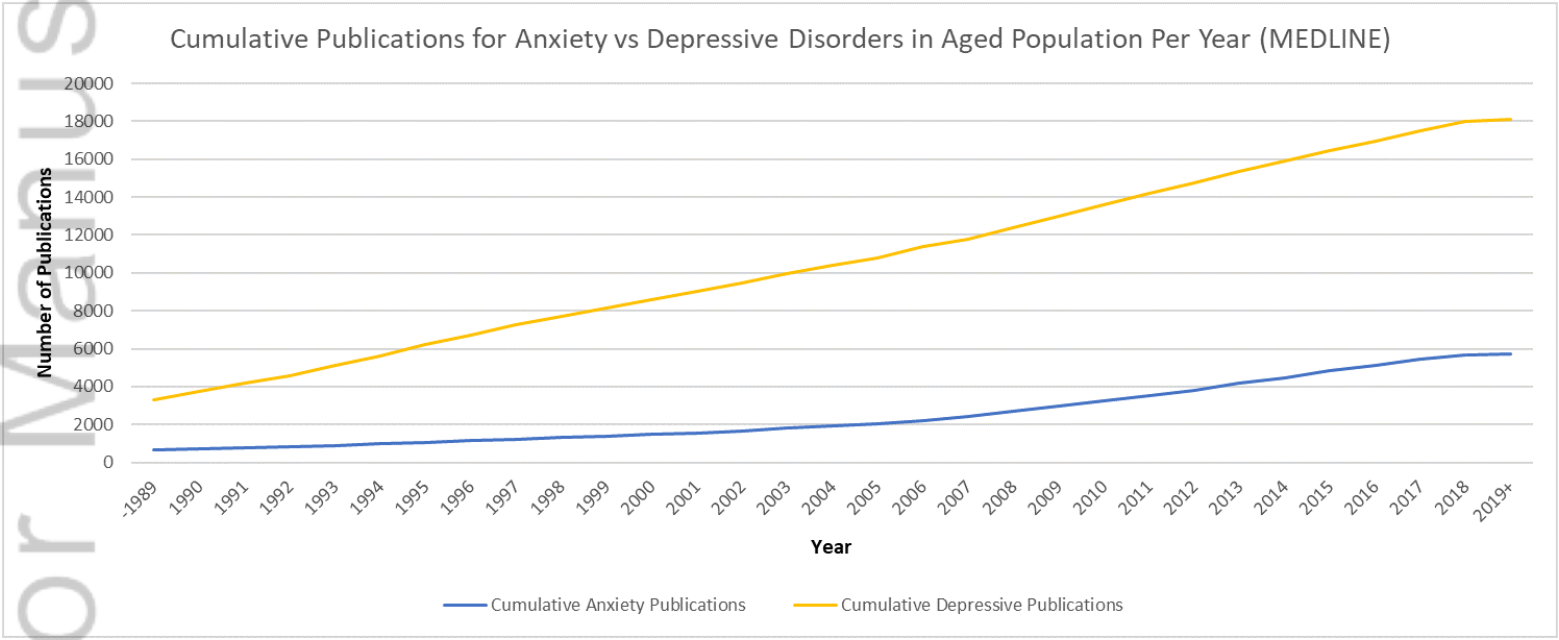
Figure 3: New Publications for Anxiety vs Depressive Disorders in Aged Population (MEDLINE)

Figure 4: New Publication Ratio for Depressive vs Anxiety Disorders in Aged Population (MEDLINE)
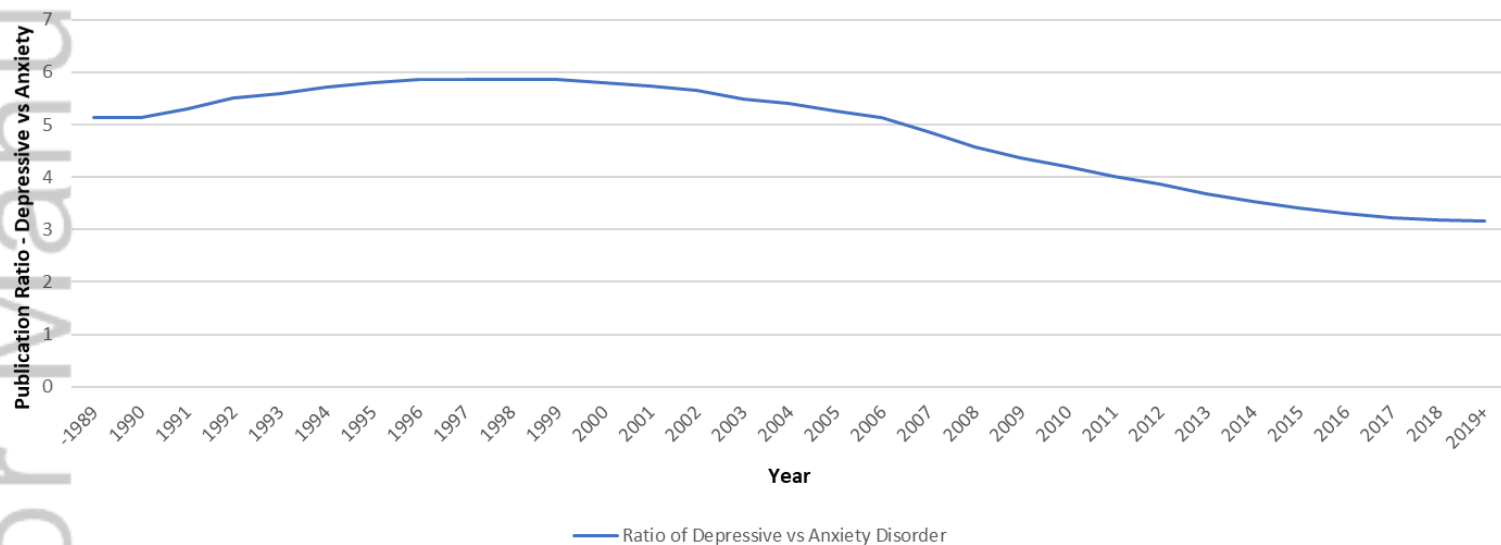

Appendices:

Appendix One: Search Strategy for Ovid MEDLINE and Epub ahead of Print, In-Process & Other Non-indexed Citations, Daily and Versions from 1946, conducted on 31 August 2019.

Appendix Two: Late Life Anxiety and Late Life Depression Publications from search of Ovid MEDLINE and Epub ahead of Print, In-Process & Other Non-indexed Citations, Daily and Versions from 1946, conducted on 31 August 2019.
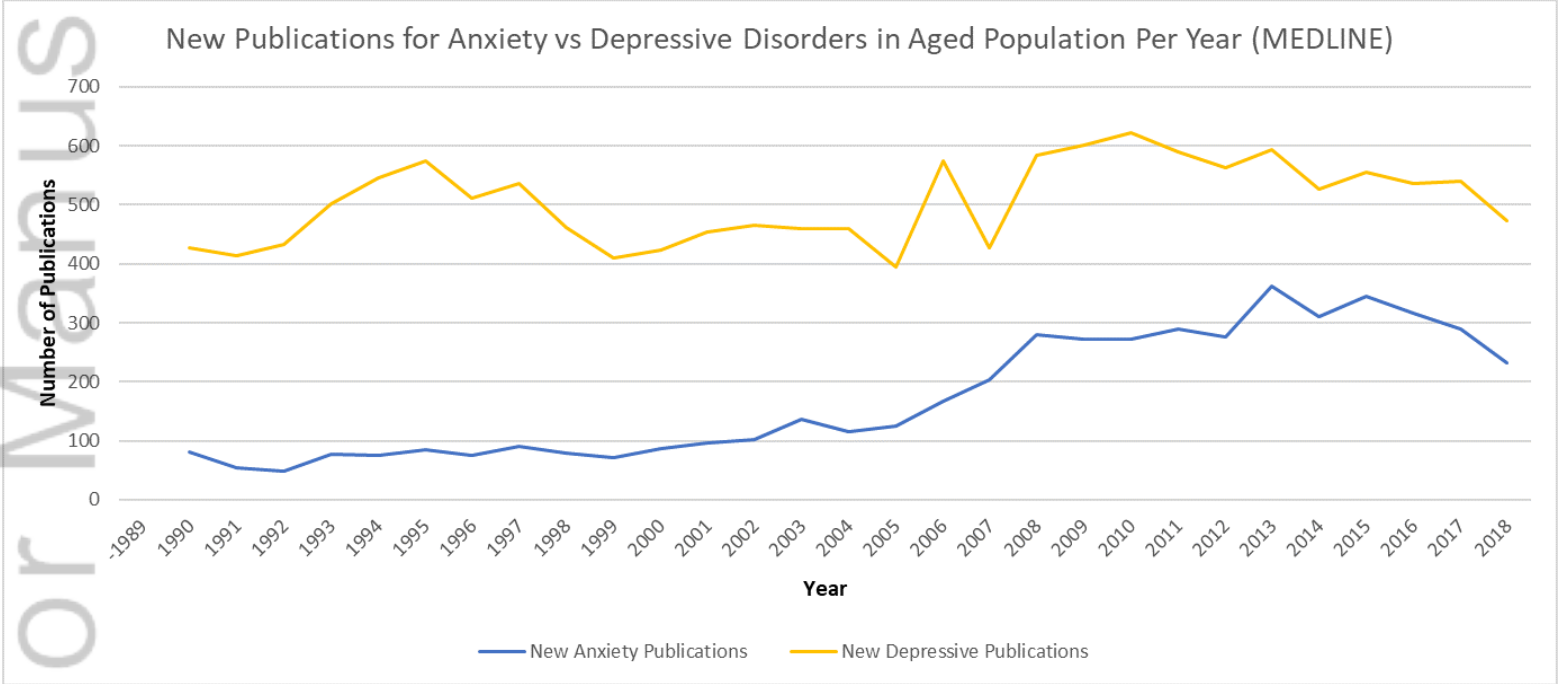
Cumulative Publications for Anxiety vs Depressive Disorders in Aged Population Per Year (MEDLINE)

GPS_5300_Figure 1 anxiety editorial.tif

Cumulative Publication Ratio for Depressive vs Anxiety Disorders in Aged Population (MEDLINE)

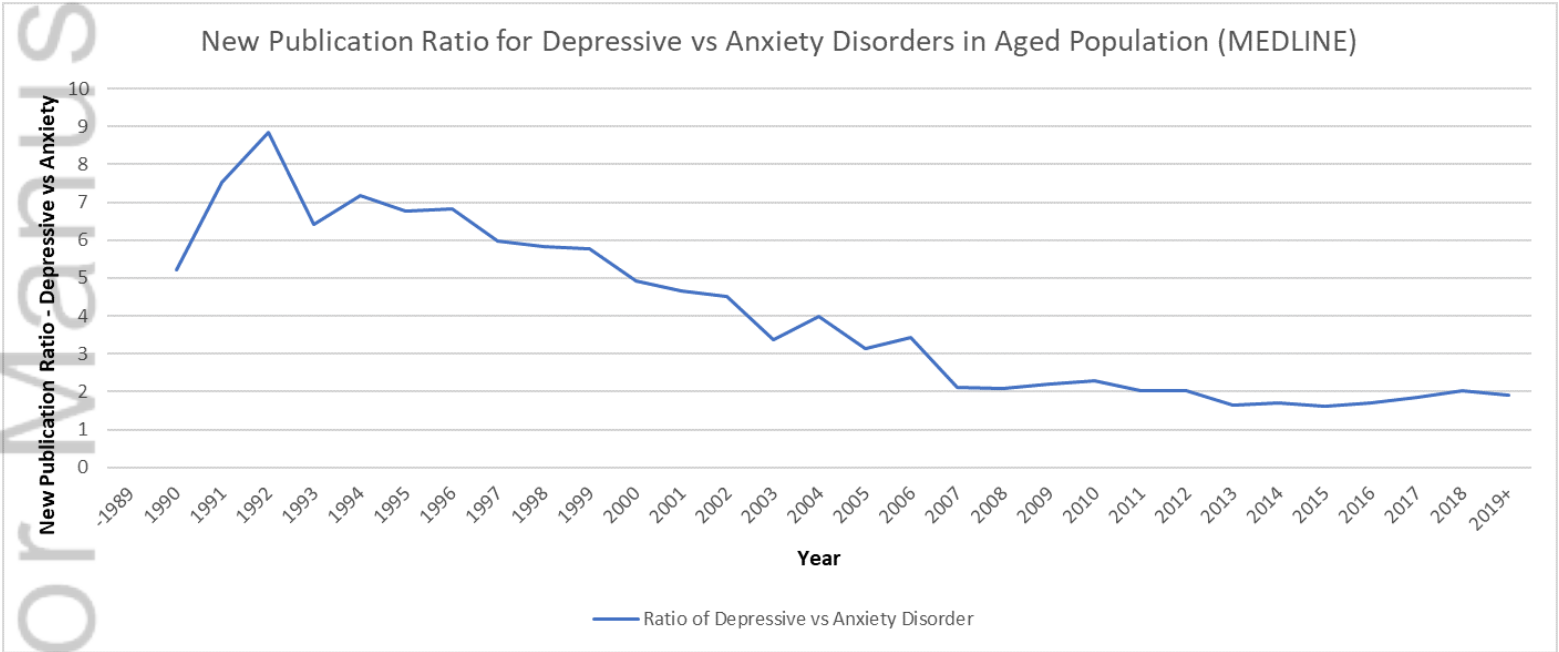GPS_5300_Figure 2 anxiety editorial.tif

New Publications for Anxiety vs Depressive Disorders in Aged Population Per Year (MEDLINE)

GPS_5300_Figure 3 anxiety editorial.tif

New Publication Ratio for Depressive vs Anxiety Disorders in Aged Population (MEDLINE)

GPS_5300_Figure 4 anxiety editorial.tif