Diagnostic Accuracy of Tools to Identify Anxiety Symptoms and Disorders in Persons with Dementia: a Systematic Review Update[a]

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https://doi.org/10.5770/cgj.28.875

ABSTRACT

Limited anxiety tools validated against a diagnostic gold standard in the context of dementia have been identified. A systematic review update was completed to identify publications since 2017 describing tools to detect anxiety in persons with dementia compared to a diagnostic gold standard. The original search strategy was replicated in MEDLINE, Embase, and PsycINFO. Pooled prevalence and diagnostic accuracy estimates were calculated based on three or more studies presenting comparable information from either the original or updated review search. No pooled estimates were calculated in the original review given limited evidence. One study evaluating the Rating Anxiety in Dementia (RAID) scale, Neuropsychiatric Inventory, and Hamilton Anxiety Rating Scale met review inclusion criteria. The pooled prevalence of generalized anxiety disorder (GAD) (n=3, 36.7%, 95% Confidence Interval (CI): 24.3–49.2%) and diagnostic accuracy outcomes for the RAID scale (≥11 cut-off) to detect GAD (n=3, sensitivity: 89%, 95% CI: 78–95%; specificity: 73%, 95% CI: 60–82%) were calculated using data from two studies identified in the original review and the newly included study from the review update. The RAID scale has the most evidence and adequate sensitivity to support its use in identifying anxiety in persons with dementia. Validated tools to detect anxiety in persons with dementia remain understudied.

Key words: anxiety, dementia, detection, systematic review, diagnostic accuracy, generalized anxiety disorder, neuropsychiatric symptoms

INTRODUCTION

Anxiety is common in persons with dementia and is associated with poor outcomes and quality of life.(1) In persons with dementia, anxiety can be hard to detect due to overlapping presentation with dementia symptoms or with other neuropsychiatric symptoms such as depression or agitation.(1) Diagnosing anxiety disorders in the context of dementia can be difficult as standardized diagnostic criteria (e.g., Diagnostic and Statistical Manual of Mental Disorders (DSM)) fail to address anxiety in the setting of dementia as a diagnostic category.(2)

There is a need for clinicians to be able to accurately detect anxiety symptoms and disorders in persons with dementia. The original systematic review, completed on February 1, 2017, sought to identify anxiety tools compared to a diagnostic gold standard to detect anxiety symptoms or disorders in persons with dementia.(3) Four studies examining three anxiety tools were identified. All studies used the DSM-IV/5 to identify either generalized anxiety disorder (GAD) or anxiety disorders inclusive of GAD, panic disorder, anxiety not otherwise specified, and post-traumatic stress disorder (PTSD). Findings from the Geriatric Anxiety Inventory (GAI), Penn State Worry Questionnaire (PSWQ) abbreviated version, and Rating Anxiety in Dementia (RAID) scale were descriptively reported.

Given the limited anxiety tool findings of the original review, the review must be updated with current literature to identify any recent publications of tools to detect anxiety that have been compared to a diagnostic gold standard. An update of the existing systematic review was completed to evaluate the diagnostic accuracy of tools to detect any anxiety symptoms or any type of anxiety disorders (e.g., GAD, social anxiety disorder, panic disorder, specific phobias) in persons with dementia.

[a] *The present manuscript is an update of a previously completed systematic review completed by our team. Data from the original review has been updated in the present analysis. The original review has been cited throughout the present analysis.*

METHODS

The original review[3] search strategy, screening, data extraction, and summary methods were followed for the search update (PROSPERO: CRD42016042123). The original search was replicated in Medline, Embase, and PsycINFO on June 19, 2023, to identify articles published in or after January 2017 using the search concepts anxiety, dementia, and diagnostic accuracy. Two independent reviewers screened all articles at the level of title/abstract and full text.

Any article outlining the use of a tool to detect anxiety symptoms or disorders in persons with dementia was included at the level of title/abstract review. Articles that described an anxiety tool that was compared to a gold standard (i.e., clinical interview or criterion interview based on DSM or International Classification of Disease (ICD) criteria) were included at the level of full text review. No limits were placed on participant ages, inpatient/outpatient settings, or type of dementia. Articles had to include diagnostic accuracy outcomes (e.g., sensitivity and specificity) or provide data conducive to calculating such values.

The Quality Assessment for Diagnostic Accuracy Studies-2 tool was used to assess the quality of included studies by two independent reviewers.[4] Sample characteristics (sample size, dementia type and severity, age, percent female, anxiety prevalence), anxiety tool description (clinical location, anxiety tool cut-offs used, author-identified optimal cut-off, anxiety tool rater, type of anxiety examined), gold standard criterion description (gold standard criterion used to diagnose anxiety, gold standard criterion rater), and diagnostic accuracy outcomes (sensitivity, specificity, likelihood ratios, area under the curve (AUC)) were extracted.

Meta-analyses for anxiety prevalence and anxiety tool sensitivity and specificity were completed if at least three studies from the original or updated review could be compared. All quantitative analyses were completed in Stata V.17.0 (StataCorp, College Station, TX). A pooled prevalence estimate was calculated with metan using a random-effects (DerSimonian Laird) model. Pooled sensitivity and specificity estimates were calculated using metadta using a bivariate random-effects model. Between-study heterogeneity was assessed using the I^2 statistic and Cochran's Q-statistic[5] for prevalence estimates and the I^2 statistic[6] for pooled diagnostic accuracy outcomes. Forest plots were produced for pooled estimates.

RESULTS

Five thousand, eight hundred and fifty-two articles were eligible for title/abstract screening after duplicates were removed. One article met the review inclusion criteria of the 267 screened in full text, bringing the total number of articles included in the review to five (Figure 1). The two reviewers had 91.6% agreement at the level of full text review.

The newly added study had a high rating of risk of bias in the patient selection and patient flow and timing domains, as well as an unclear rating of risk of bias for the index test domain (Appendix Table A1). High or unclear risk of bias resulted from a lack of a consecutive or random sampling used to enroll patients, unclear use of a pre-specified anxiety tool cut-off, and not all patients having received the gold reference standard.

The added study was conducted in Lebanon in residential and nursing homes, and included 136 patients with a mean age of 83.3, of which 61% were female (Appendix Table A2). The majority (84.6%) of participants had Alzheimer's disease among other types, comparable to the studies included in the original review (Appendix Table A3). Dementia severity was not reported. A structured clinical interview based on DSM-5 criteria was administered by a clinical psychologist as the gold standard assessment to 51 of the 136 patients (Table 1). The prevalence of GAD was 45.1% in the study sample receiving the gold standard assessment.

The publication added in the review update examined the RAID scale, Hamilton Anxiety Rating Scale (HAM-A), and Neuropsychiatric Inventory-Anxiety items (NPI-A) to identify GAD.[7] The articles included in the original review examined the GAI,[8] PSWQ-abbreviated,[8] and RAID[9] scale to identify any anxiety disorder (i.e., GAD, anxiety not otherwise specified, panic disorder, and PTSD), and the RAID[10,11] scale to identify GAD. Compared to the four studies included in the original review, the new article using the Arabic version of the RAID scale reported the highest sensitivity (91%) across optimal cut-offs balancing sensitivity and specificity. The PSWQ-abbreviated remained the highest reported specificity (93%).[8] Across all included studies and tools, the optimal sensitivity ranged from 58–91% and the specificity ranged from 56–93%. The AUC was highest for the RAID scale (0.92)[7] and HAM-A (0.87)[7] (Table 1) compared to the AUC described previously for the GAI (0.81)[8] and RAID scale (0.80).[9,11]

The pooled prevalence estimate of GAD calculated from three studies[7,10,11] was 36.7% (95% Confidence Interval (CI): 24.3–49.2%, I^2=61%, p=.077) (Appendix Figure B1). A pooled prevalence estimate for any anxiety disorder could not be completed due to insufficient studies (n=2). A meta-analysis of the diagnostic accuracy of the RAID scale to detect GAD was completed with three studies.[7,10,11] The pooled sensitivity and specificity estimates of the RAID scale at a cut-off of ≥11 were 89% (95% CI: 78–95%, I^2=1.68%) and 73% (95% CI: 60–82%, I^2=7.58%) (Figure 2).

DISCUSSION

The review update furthers our understanding of anxiety detection in the context of dementia, as it identified two new tools and allowed for the completion of a pooled GAD prevalence estimate and pooled diagnostic accuracy estimates for the RAID scale. Few diagnostic accuracy studies are specific to persons living with dementia; therefore, it is important to widely disseminate new findings to improve the level of evidence available to support clinical decision-making. The

RAID scale, a clinician-rated measure developed specifically for use with persons with dementia,[11] continues to have the most evidence of validity and the highest reported sensitivity (91%) among all tools identified. The HAM-A,[12] a fourteen-item, semi-structured interview and the NPI-A,[13] a single-item, clinician-rated measure, were newly identified tools but lacked diagnostic accuracy outcome data apart from AUC values. The AUC values for the HAM-A (0.87) and NPI-A (0.75) showed promising diagnostic accuracy performance, indicating these tools should be further studied to determine optimal cut-offs, and the resulting sensitivity and specificity for detecting anxiety in dementia. The inclusion of the NPI-A demonstrates that general neuropsychiatric symptom questionnaires have been studied specifically for use with anxiety.

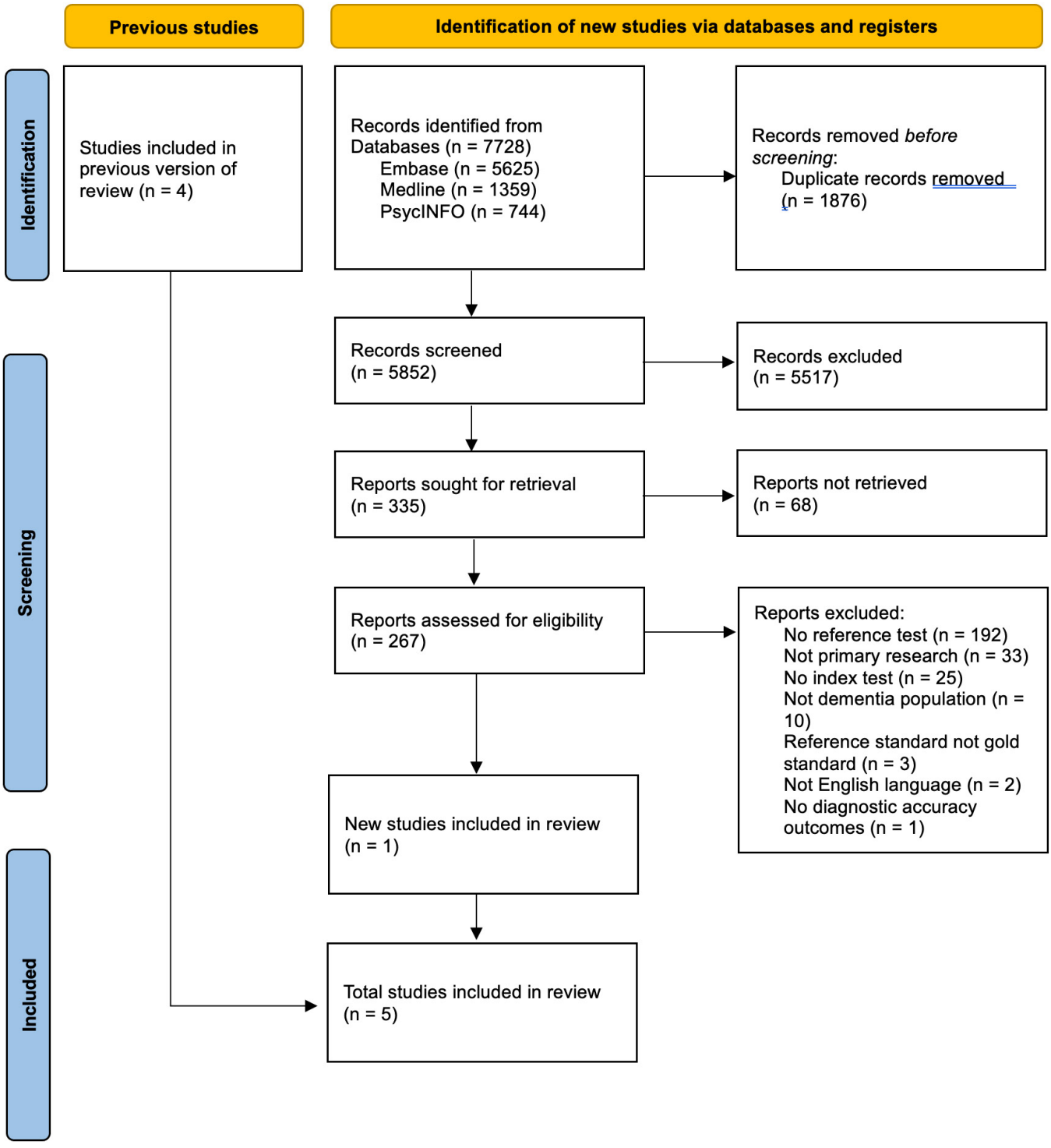

FIGURE 1. PRISMA flow diagram of study inclusion for the updated systematic review

TABLE 1.
Index and reference standard tool descriptions and diagnostic accuracy outcomes (i.e., sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, area under the curve) of index tool compared to reference standard.

Study (First Author, Year, Country)	*Index Tool Rater; Masked to Reference Standard Results?*	*Reference Standard Rater; Masked to Index Tool Results?*	*Evaluation Location*	*Index Tool*	*Index Test Score (mean (SD))*	*Reference Standard*	*Cut-off*	*SN*	*SP*	*LR+*	*LR-*	*AUC*	*Author-Identified Optimal Cut-Off*
Feghali et al.[7] 2020 Lebanon	Primary caregiver of patient; Yes	Clinical psychologist; Yes	NR	RAID-Arabic Version	14.3 (10.3)	DSM-5	≥11	0.91	0.82	5.06	0.11	0.92	≥11
				HAM-Anxiety	NR	DSM-5	NR	-	-	-	-	0.87	
				NPI-Anxiety	NR	DSM-5	NR	-	-	-	-	0.75	
Goyal et al.[10][a] 2017 Norway	Patient's primary nurse; Yes	Clinician; Yes	Nursing homes	RAID-Norwegian Version	10.80 (7.20)	DSM-5	≥11	0.86	0..67	2.60	0.20	0.80	≥10
Shankar et al.[11][a] 1999 UK	Clinician; Unclear	Clinician; Unclear	Acute inpatient, day hospital/day centre, long-stay continuing care	RAID	9.30 (7.10) [from total n=83 sample]	DSM-IV	≥11	0.90	0.79	4.29	0.13	NR	≥11

[a]Included in original review but displayed in Table to show data used for pooled diagnostic accuracy estimates

AUC = area under the curve; DSM-5 = Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition; HAM-A = Hamilton Anxiety Rating Scale; LR+ = positive likelihood ratio; NPI-Anxiety = Neuropsychiatric Inventory-anxiety items; NR- = negative likelihood ratio; NR = not reported; RAID = Rating Anxiety in Dementia Scale; SD = standard deviation; SN = sensitivity; SP = specificity.

In addition to diagnostic accuracy, it is important to consider the target population for whom the tool was developed, who administers the tool, and the cost associated with tool use when selecting a tool. The RAID and NPI-A were designed for persons with dementia and are clinician-rated tools that rely on collateral or clinical report. The self-report GAI was developed for persons 60 years and older (copyright restrictions), while the HAM-A (clinician rated) and PSWQ (self-report) were developed for the general adult population. Diagnostic accuracy findings from this review, compared to synthesized findings for the general older adult population, suggest the GAI, HAM-A, and PSWQ-abbreviated have reduced performance when used with populations with dementia.[14]

A limitation of the present systematic review update is that a substantial degree of heterogeneity was detected in the pooled GAD prevalence estimate which may be explained by differences in participant characteristics or clinical settings. The pooled GAD prevalence estimate may seem high compared to existing GAD estimates in community-dwelling or older adult populations; however, the present estimate focused on clinical populations and may be impacted by dementia severity or type.[15] The three studies included in the pooled diagnostic accuracy estimates for the RAID scale had sample sizes ranging from 21 to 101 participants. Smaller sample sizes may increase the potential for error; however, completing a pooled estimate may help to provide a more accurate estimate. It is possible relevant studies may have been missed despite a comprehensive search strategy. Grey literature sources were not searched as part of the review update, given limited resources of the research team. The lack of detailed reporting, reflected in the assessed quality of the included studies, prevents further discussion on the impact of dementia type and severity, comorbidities, and clinical setting. It is important for future studies to evaluate and report the severity and type of dementia as it has been found to impact the prevalence of anxiety symptoms.[16,17]

The review update identified two additional tools to detect anxiety compared to a gold standard (HAM-A and NPI-A) in addition to the GAI, PSWQ-abbreviated, and RAID scale previously identified. Validated tools to detect anxiety symptoms and disorders in persons with dementia remain under-studied. The RAID scale continues to have the most evidence and adequate sensitivity to support its use in identifying anxiety symptoms in persons with dementia. There is a need for primary validation studies that investigate a variety of anxiety tools inclusive of anxiety specific tools (e.g., RAID) and global measures of neuropsychiatric symptoms (e.g., NPI) and that use clinician-based assessments as gold standard measures to capture both syndrome and subsyndromal presentations of anxiety. Further, there is a need for validation studies to report diagnostic accuracy values (e.g., sensitivity, specificity) for all types of anxiety disorders, and describe the clinical setting and demographic details of participants (e.g., dementia type and severity, comorbidities, race and ethnicity).

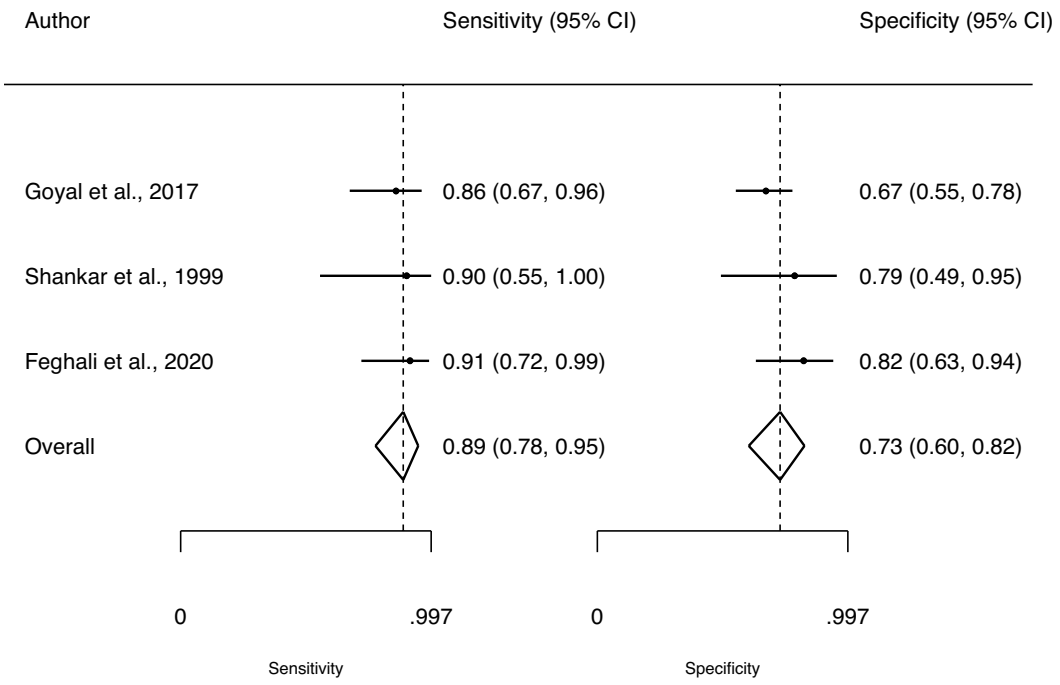

FIGURE 2. Forest plot of the sensitivity and specificity of the Rating Anxiety in Dementia Scale at the cut-off of ≥11 from three included studies

ACKNOWLEDGEMENTS

Not applicable.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood the *Canadian Geriatrics Journal's* policy on disclosing conflicts of interest and declare that we have none.

FUNDING

This work was supported by the Canadian Coalition for Seniors' Mental Health. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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APPENDIX A. Additional tables

TABLE A1.
Quality assessment of included studies based on the Quality Assessment of Diagnostic Accuracy Studies-2 Tool

Study (First Author, Year, Country)	*Domain 1*		*Domain 2*		*Domain 3*		*Domain 4*
	Could selection of patients have introduced bias?	Is there concern that the included patients do not match the review question?	Could the conduct or interpretation of the index test have introduced bias?	Is there concern that the index test, its conduct, or interpretation differ from the review question?	Could the reference standard, its conduct, or its interpretation have introduced bias?	Is there concern that the target condition as defined by the reference standard does not match the review question?	Could the patient flow have introduced bias?
Feghali et al.[7] 2020 Lebanon	High	Low	Unclear	Low	Low	Low	High

TABLE A2.
Demographic information of participants included in studies

Study (First Author, Year, Country)	*Age (mean (SD))*	*Total Participants*	*% Female*	*Anxiety Disorder Being Diagnosed*	*Prevalence of Anxiety Disorder (%)*	*MMSE Score (mean (SD))*	*Dementia Type*	*Marital Status*	*Recruitment Setting*
Feghali et al.[7] 2020 Lebanon	83.3 (7.7)	136[a]	61.0%	GAD	45.1	NR	AD: 84.6% Vascular Dementia: 5.1% Frontotemporal Dementia: 1.5% Parkinson's Disease: 1.5%, Other: 7.4%	NR	Residential and nursing homes

[a]There were 136 patients in the study but only 51 completed the DSM assessment.
AD = Alzheimer's disease; GAD = generalized anxiety disorder; MMSE = Mini Mental Status Examination; NR = not reported; SD = standard deviation.

TABLE A3.
Information on anxiety and dementia type across all studies included in the review

Study (First Author, Year, Country)	*Total Participants*	*Anxiety Disorder Being Diagnosed*	*Prevalence of Anxiety Disorder (%)*	*Dementia Type*	*Dementia Severity*
Feghali et al.[7] 2020 Lebanon	136[a]	GAD	45.1	AD: 84.6% Vascular dementia: 5.1% Frontotemporal Dementia: 1.5% Parkinson's Disease: 1.5% Other: 7.4%	NR
Goyal et al.[10][b] 2017 Norway	101	GAD	27.7	AD: 69.3% Vascular dementia: 17.8% Frontotemporal dementia: 2.0% Mixed: 5.0% Unspecified: 5.0% Lewy body dementia: 1.0%	Mild to moderate
Shankar et al.[11][b] 1999 United Kingdom	24	GAD	41.7	AD: 66.3% Vascular dementia: 13.3% Other: 20.5%	NR
Bradford et al.[8][b] 2013 USA	41	Any (GAD, Anxiety not otherwise specified, panic disorder, PTSD)	63.4	NR	Mild to moderate
Snow et al.[9][b] 2012 USA	32	Any (GAD, Anxiety not otherwise specified, panic disorder, PTSD)	62.5	AD: 62.5% Lewy body dementia: 3.1% Dementia not otherwise specified: 25.0% Vascular dementia: 9.4%	Mild to moderate

[a]There were 136 patients in the study but only 51 completed the DSM assessment.
[b]Included in the original review publication.
AD = Alzheimer's disease; GAD = generalized anxiety disorder; NR = not reported; PTSD = post-traumatic stress disorder.

APPENDIX B. Additional figures

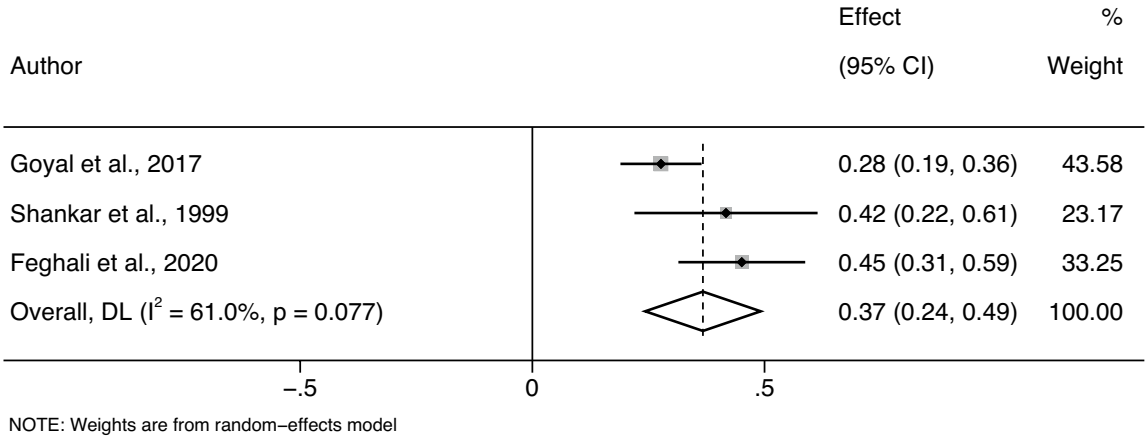

FIGURE B1. Forest plot of the prevalence of generalized anxiety disorder from three included studies