

# Clinical effectiveness of interventions for treatment-resistant anxiety in older people: a systematic review

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## Scientific summary

### Interventions for treatment-resistant anxiety

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# Scientific summary

## Background

Anxiety disorders can affect people of all ages. In contrast to the appearance of anxiety that might be experienced during a stressful event, for example when taking a driving test, an anxiety disorder persists for a longer period of time and symptoms can progressively worsen if not treated. The onset of anxiety disorders is typically between childhood and young adulthood, with relatively few people (< 1%) developing an anxiety disorder for the first time after the age of 65 years. Recognition of the difficulties in differentiating symptoms of anxiety from physiological and physical changes (e.g. changes in sleep pattern) arising from the ageing process, together with the reluctance of many people to acknowledge psychological difficulties, has led to the realisation that anxiety in older people tends to be under-detected and under-treated. Many people with an anxiety disorder also suffer from various comorbidities, both physical and psychological, that can further complicate diagnosis and worsen the outcome of the disorder. Therefore, a comprehensive evaluation by an experienced clinician is needed. Disorders affecting physical health are common in older adults, and older adults often attribute symptoms of anxiety to their physical illness, which could result in non-diagnosis of their anxiety disorder.

The specific cause of symptoms in each anxiety disorder is not well established and the underlying aetiology of the disorders is yet to be fully elucidated. Treatments offered for an anxiety disorder are determined by the presumed underlying cause, though initial treatment might involve education and active monitoring. People whose symptoms of anxiety do not improve might subsequently be recommended to undergo psychological therapy or be prescribed a pharmacological treatment. Despite initial treatment, many people will continue to have symptoms of anxiety. Although there is no accepted definition of treatment resistance in anxiety disorders, people are generally considered to be resistant to treatment if they have made an inadequate response (either no response or only a partial response) or do not respond (refractory) to first-line treatment, irrespective of whether the first-line treatment was a psychological or pharmacological intervention.

As with younger adults, the course of anxiety disorders in older people is typically chronic or episodic in nature, and most disorders are unlikely to remit completely, even with long-term treatment. Compared with people of the same age and with what would be categorised as normal worries, older people with an anxiety disorder frequently experience greater difficulty in managing their day-to-day lives and are at an increased risk of comorbid depressive disorders, falls, physical and functional disability, and loneliness. Furthermore, the presence of an anxiety disorder is associated with reduced adherence with medical treatment, and long-term medical conditions are potentially exacerbated, which can result in a further loss of independence and increased reliance on family or carers. Anxiety has a considerable detrimental effect on quality of life (QoL) for both the older person with an anxiety disorder and that of any carers.

## Objectives

The aim of the review was to evaluate the clinical effectiveness of medical, psychological and alternative therapies for treatment-resistant anxiety in older people.

## Methods

A systematic review of the clinical effectiveness of treatments for treatment-resistant anxiety in older adults was carried out. Electronic databases (MEDLINE, MEDLINE In-Process and Other Non-Indexed citations, EMBASE, The Cochrane Library databases, PsycINFO and Web of Science) were searched from inception to September 2013. Bibliographies of relevant systematic reviews were hand-searched to identify additional potentially relevant studies. ClinicalTrials.gov was searched for ongoing and planned studies.

Studies eligible for inclusion in the review were randomised controlled trials (RCTs) and prospective comparative observational studies (matched control studies, case series and case-control studies) evaluating pharmacological, psychological and alternative therapies for treatment-resistant anxiety in older people. Study selection was carried out independently by two reviewers. Studies were eligible for inclusion in the review if they evaluated at least one intervention of interest, included only people aged  $\geq 65$  years or reported data for a subgroup of patients aged  $\geq 65$  years, compared the intervention with another intervention of interest and reported at least one of the following outcomes: reduction in symptoms of anxiety; response defined as proportion of people experiencing  $\geq 50\%$  reduction in symptom score from baseline); remission; functional disability; sleep quality; development of, or change in, symptoms of depression; adherence to treatment; QoL; carer outcomes; and adverse effects.

## Summary of findings of included studies

No RCT or prospective comparative observational study was identified meeting the prespecified inclusion criteria. Therefore, it was not possible to draw conclusions on clinical effectiveness of interventions for treatment-resistant anxiety in older people.

## Discussion

As no study was identified evaluating treatments in older adults, there is uncertainty as to which treatments are clinically effective for older adults with an anxiety disorder that has not responded to prior treatment. Older adults present with manifestations of anxiety different from those of younger adults. Taken together with the observation that response to treatment is often poorer in later life, it is probably inappropriate to extrapolate results of clinical effectiveness of interventions in anxiety disorders in younger adults to older adults.

## Strengths and limitations

To our knowledge, the review reported here is the first systematic review of interventions for treatment-resistant anxiety in older adults. The comprehensive methods implemented to carry out the review are a key strength of the research presented. However, the review highlights the lack of research in this area, identifying no comparative studies, which is a limitation. Although multiple RCTs were identified that evaluated clinical effectiveness of interventions for treatment-resistant anxiety disorders, many limited inclusion to adults aged  $\leq 65$  years. Of those studies that included people  $\geq 65$  years, the mean ages reported at baseline suggest that most included people were much younger than 65 years. The potentially small number of people likely to be aged 65 years and over in the studies identified restricts the practicality and feasibility of carrying out a meta-analysis based on individual patient data. In addition, as the studies identified evaluated a range of treatments across various anxiety disorders, it is likely that the number of events for each treatment would be low, which would probably lead to considerable uncertainty in the results.

## Conclusions

Studies evaluating interventions in older adults with an anxiety disorder that has not responded to first-line treatment are needed to address the lack of evidence in this area. This lack of evidence means that older adults are perhaps receiving inappropriate treatment, or are not receiving a particular treatment because there is no evidence to support its use. There is scope to develop guidance on service provision and, as a consequence, to advance the standard of care received by older adults with a treatment-resistant anxiety disorder in the primary and secondary settings.

## Study registration

The protocol for the systematic review is registered on PROSPERO (registration number CRD42013005612).

## Funding

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