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#### Review

# Antidepressants in elderly: Metaregression of double-blind, randomized clinical trials



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#### ABSTRACT

*Background:* Depression is common in the elderly and in the last few years this led to a significant increase in antidepressant prescription rates. However, little is known about antidepressant efficacy profile in relation with socio-demographic and clinical features in this population.

The aim of the present study was to define the most suitable socio-demographic and clinical profile for the use of antidepressant treatments in late-life depression.

Methods: MEDLINE, EMBASE and PsycINFO were searched for randomized controlled trials (RCTs) focused on efficacy of antidepressants of all classes in major depressed elderly subjects ( > 60 years old). Reviews and meta-analyses focusing on this topic have been considered as well. Thirty-four RCTs were included and socio-demographic and clinical features were investigated via meta-regression analysis as moderators of efficacy measures (standardized mean difference based on Hamilton Depressive Rating Scale and Montgomery–Asberg Depression Rating Scale).

Results: A lower rate of response to antidepressants of all classes was found in patients of male gender, of older age, and with a longer mean duration of the current episode. On the contrary, a higher rate of response was found in patients with a higher baseline severity and at their first episode of illness. Subsamples treated with selective serotonin reuptake inhibitors alone yielded similar results.

Limitations: RCTs only have been included.

Conclusions: A number of socio-demographic and clinical features have been found to moderate antidepressant efficacy in elderly population. Those variables could help clinicians for a more individualized treatment.

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#### **Contents**

1.	. Introduction	
2.	Methods	
	2.1.	Search strategy and eligibility criteria
	2.2.	Data extraction.
	2.3.	Data analysis
3.	Results	
4.	Discus	ssion
Role of funding source		
Conflict of interest		
Appendix A		
References		

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#### 1. Introduction

Major depressive disorder (MDD) is the most prevalent psychiatric disorder among elderly patients (Hybels and Blazer, 2003). Its prevalence ranges from 6% to 18% among geriatric primary care patients, and it is higher on medical inpatient services or in nursing homes (Lyness et al., 2009; Park and Unutzer, 2011). Despite the high MDD prevalence in this population, it is estimated that clinically significant depression is often under-recognized, and goes untreated or not adequately treated in 40–60% of cases (Wilson et al., 1999; Steffens et al., 2000; Richardson et al., 2012).

A number of reviews and meta-analyses focused on antidepressant efficacy in late-life depression have been published (Mittmann et al., 1997; Taylor and Doraiswamy, 2004; Nelson et al., 2008; Tedeschini et al., 2011; Kok et al., 2012), also in long-term treatment (Kok et al., 2011) or in subgroups of elderly people like nursing home residents (Boyce et al., 2011). Antidepressants have been reported to have a higher efficacy in comparison with placebo in elderly patients, response rate of patients treated with antidepressants being 48.0% versus 38.6% and remission rate being 33.7% versus 27.2% (Kok et al., 2012).

Studies comparing different classes of antidepressants did not indicate differences in achieving response or remission between tricyclics (TCAs) and selective serotonin reuptake inhibitors (SSRIs) or other antidepressants (Mittmann et al., 1997; Nelson et al., 2008; Mukai and Tampi, 2009; Kok et al., 2012).

However, late-life depressed patients were found to respond to all classes of antidepressants, but with a small effect (Kok et al., 2012; Nelson et al., 2008), especially when they were compared

with MDD adults (Tedeschini et al., 2011). In particular, it is well known that specific clinical features (e.g., concomitant presence of physical illness (Wilkins et al., 2010), concomitant medications (Caughey et al., 2010), and deficit in executive functions (Pimontel et al., 2011)) could influence administration, compliance (Barry et al., 2012) and treatment response in elderly patients (Tedeschini et al., 2011). Nevertheless, the outcome prediction on the basis of socio-demographical and clinical variables remains elusive even when empirically derived decision trees for the treatment of late-life depression have been applied (Andreescu et al., 2008).

Consequently, the definition of a socio-demographic and clinical profile of responsiveness to antidepressants in older patients may help clinicians in the choice of more effective therapeutic strategies. So, the aim of this study was to investigate the role of socio-demographic and clinical features as moderators of antidepressant outcome in elderly depressed patients via the tool of meta-regression. We firstly considered several antidepressant classes together (TCAs, SSRIs, serotonin-noradrenaline reuptake inhibitors (SNRIs)) and then we focused on the SSRI class alone.

#### 2. Methods

#### 2.1. Search strategy and eligibility criteria

We searched in PubMed/MEDLINE, EMBASE, and PsycINFO for "elderly" (or older, old age, late-life, aged, geriatric or senile) AND "major depressive disorder" (or depressive disorder, mood disorder, dysthymic disorder, minor depressive disorder, clinical

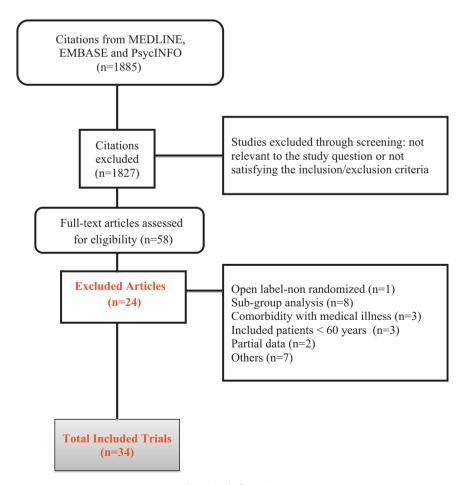


Fig. 1. Study flow chart.

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