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A literature review of clinical outcomes associated with antipsychotic medication use in North American nursing home residents

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ABSTRACT

The benefits and harms of antipsychotic medication (APM) use in nursing home residents need to be examined because, although commonly used, APMs are considered an off-label use by the Food and Drug Administration for residents with dementia and behavioral problems. The objective of this study was to provide a realist literature review, summarizing original research studies on the clinical effects of conventional and atypical APM use in nursing home residents. Searches of multiple databases identified 424 potentially relevant research articles, of which 25 met the inclusion criteria. Antipsychotic medication use in nursing home residents was found to have variable efficacy when used off-label with an increased risk of many adverse events, including mortality, hip fractures, thrombotic events, cardiovascular events and hospitalizations. Findings suggested certain APM dosing regimens (e.g. fixed-dose) and shorter duration of use might have fewer adverse events. Non-pharmacological interventions should still be considered the first-line treatment option for nursing home residents with dementia related behavioral disturbances, as more studies are needed to establish safer criteria for APM use in nursing homes residents.

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1. Introduction

Antipsychotic medications (APMs) have been used frequently in nursing home residents, especially for those with dementia and behavioral or psychological problems [1]. Slightly more than one in four nursing home residents in the United States (US) and Canada receive an APM [2]. The appropriateness of APM use in this population is often questioned because of efficacy and safety concerns. In addition, frequent APM use has been noted to be an indicator of suboptimal care and insufficient staffing in nursing homes [3–5]. There have been ongoing regulatory efforts to reduce unnecessary APM use in nursing homes, especially over the last several years [6]. However, few reviews have investigated the impact of APM use specifically on nursing home residents.

Antipsychotic medications are approved by the US Food and Drug Administration (FDA) primarily for the treatment of psychosis and mood disturbances associated with schizophrenia or bipolar disorders [7], but are often used off-label. Safety concerns with the conventional and atypical categories of APMs include higher risk of movement disorders and cardiac issues with the conventional APMs [8,9]; and increased risk of metabolic disturbances such as weight gain or diabetes with the atypical APMs [10–12]. An increased risk of death in the elderly with dementia was observed with the use of both categories of APMs, which led to the FDA mandated class Black Box Warning in 2008 [10–14]. Other safety concerns with APM use in the elderly included cerebrovascular events, hyperprolactinemia, pneumonia, cardiovascular events and thromboembolism among others [15]. Medication-related adverse events (AE) are concerning because nursing home residents are generally already frail with multiple comorbidities [16,17].

Despite FDA warnings, a survey conducted by the Office of Inspector General in 2011 still found that 86 to 95% of nursing home residents who received APMs were given the drugs for off-label indications, e.g., to manage dementia associated behavioral disturbances [18] and often in contravention of the black box warning in the dementia population [19]. While it has been recognized that certain specific situations may warrant off-label APM treatment, it should not replace assessments of unmet needs, and non-pharmacological behavioral interventions are preferred over pharmacological alternatives [20–22].

According to the Nursing Home Reform Act in the Omnibus Budget Reconciliation Act (OBRA) of 1987, the restriction on the use of unnecessary and inappropriate medications included limiting APM use only for specific clinical conditions as diagnosed, for the shortest duration possible, and while incorporating behavioral interventions [23,24]. Nursing homes are regulated by the Centers for Medicare and Medicaid Services (CMS); they are inspected annually by each state's survey agency for compliance with state licensure regulations and federal certification requirements. In the past, data on APM use was not made available to the public on Nursing Home Compare. However, in response to widespread concern about the use of APMs in nursing home residents, CMS made nursing home APM utilization available to the public in July 2012, and soon will be adopting it as a star quality measure [25,26]. Since APM utilization data was made available publically, the overall use of APMs in nursing homes has decreased, but it still remains to be seen if public information and oversight will be sufficient to lead to optimal use of APMs use in the long term [28].

There are many factors that influence APM use besides medication effects (e.g., efficacy, adverse events (AE)), such as individual variability (e.g., resident comorbidities, prescriber habits) and system differences (e.g., staffing, regulatory). Given the complexity with APM use, studies conducted to measure effects are often heterogeneous in design focusing on particular outcome(s) of interest. Additionally, the funding source of these studies is often the manufacturers of the APMs, which poses a potential conflict of interest and is associated with results and conclusions that favor the sponsor, even when controlling for other study design features [29]. In order to appropriately reduce APM use in nursing homes, we need to be informed about how the interplay of the various factors affects overall usage.

1.1. New contribution

We chose to adopt a realist-review approach to our analysis [30], instead of the qualitative or quantitative summary typically found in a systematic review. A realist review is more useful because it provides rich, detailed, and highly practical information and understanding of an intervention (use of APMs) within the nursing home environment rather than a more traditional systematic review [30]. Based on our expertise, we selected and assessed published literature on APM use in nursing homes in Canada and United States over the last ten years.

The summary table was constructed based on APM use with specific focuses to explore and discuss the following issues: what are the outcomes associated with the use of APMs in nursing home residents; are there any special considerations for APM use that should be adopted based on population being treated or the pharmacological characteristics of the drugs; is there a difference in outcomes between studies funded by industry and those with other types of funding; where are the gaps in the current literature on harms and benefits associated with APMs in the nursing home population. In addition, the evidence table generated through this review should serve as a summary reference for policy makers, practitioners, nursing home providers, and residents and their family members. Such information can be useful in policy discussions and in developing educational tools regarding APM use in nursing homes.

2. Methods and data analysis

2.1. Data sources and searches

We searched for original studies that measured clinical outcomes of APM use in nursing home residents. Searches were conducted in Medline, Cochrane Database, PsychInfo, CINAHL, and Web of Science for the period of 2002–2012. The MESH search terms *antipsychotic agents* and *nursing*