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# Effectiveness and Content Analysis of Interventions to Enhance Oral Antidiabetic Drug Adherence in Adults with Type 2 Diabetes: Systematic Review and Meta-Analysis

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ABSTRACT

**Objectives:** To estimate the pooled effect size of oral antidiabetic drug (OAD) adherence-enhancing interventions and to explore which of the behavior change techniques (BCTs) applied in the intervention groups modified this pooled intervention effect size. **Methods:** We searched relevant studies published until September 3, 2013, on MEDLINE, Embase, PsycInfo, the Cochrane Library, CINAHL, Current Contents Connect, and Web of Science. Selected studies were qualitatively synthesized, and those of at least medium quality were included in the meta-analysis. A random-effects model was used to pool effectiveness (Hedges's *g*) and to examine heterogeneity (Higgins $I^2$). We also explored the influence on the pooled effectiveness of unique intervention BCTs (those delivered to the intervention groups but not control groups in a trial) by estimating their modifying effects. **Results:** Fourteen studies were selected for the qualitative synthesis and 10 were included in the meta-analysis. The pooled effectiveness of the interventions was 0.21 (95% confidence interval −0.05 to 0.47; $I^2$ = 82%). Eight unique BCTs were analyzed. "Cope with side effects" ($P$ = 0.003) and "general intention formation" ($P$ = 0.006) had a modifying effect on the pooled effectiveness. The pooled effectiveness of the interventions in which "cope with side effects" was applied was moderate (0.64; 95% confidence interval 0.31–0.96; $I^2$ = 56%). **Conclusions:** The overall effectiveness of OAD adherence-enhancing interventions that have been tested is small. Helping patients cope with side effects or formulate desired treatment outcomes could have an impact on the effectiveness of OAD adherence-enhancing interventions. Only those interventions that include helping patients to cope with side effects appear to be particularly effective in improving OAD adherence.

*Keywords:* adherence, diabetes, oral antidiabetic drug, meta-analysis, intervention.



## Introduction

In 2011, approximately 366 million people worldwide suffered from diabetes, and this number could reach 552 million by 2030 [1,2]. In 2011, the global diabetes burden was estimated to be at least US $465 billion, and this represented 11% of adult health care costs worldwide [2]. A large proportion of this burden is attributed to type 2 diabetes, which accounts for more than 90% of all diabetes cases [3].

To prevent microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (cardiovascular and cerebrovascular diseases and leg amputations) diabetes complications, patients with type 2 diabetes should achieve certain target blood glucose levels (typically, glycated hemoglobin level of <7%) through regular physical activity, a healthy diet with low carbohydrate intake, and appropriate use of drug treatment [4]. Oral antidiabetic drugs (OADs), when taken as recommended, can substantially contribute to achieving metabolic control [5,6], which thereby improves quality of life [5]. Even though insulin can be used alone or in combination with OADs, nearly 60% of the individuals with type 2 diabetes use only OADs to control their diabetes [7]. Unfortunately, patient adherence to OAD treatment is often poor [8,9], which contributes to suboptimal metabolic control [10,11], increased diabetes complications and hospitalizations [12,13], and increased health care expenditures [14].

Adherence to OAD treatment could be optimized by exposing patients to effective behavior change interventions. Two systematic reviews [15,16] have been previously conducted, but these focused on only OAD adherence-enhancing interventions delivered by pharmacists and did not assess the overall effectiveness of the interventions. In addition, recent advances in the coding of published behavior change interventions have made it possible to

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conduct more rigorous, standardized analyses of intervention components [17]. Moreover, there is growing evidence that not only intervention groups but also control groups in adherence-enhancing interventions are exposed to effective behavioral support (e.g., as part of usual care) that can vary between studies and have an impact on intervention effects. Hence, we performed a systematic review and a meta-analysis of the effectiveness of interventions aimed at enhancing OAD adherence in adults with type 2 diabetes. The aim was to identify the behavior change techniques (BCTs) delivered to both the intervention and the control groups, estimate the pooled intervention effect size, and explore which of the BCTs that were applied in the intervention groups (but not the control groups) modified this pooled effect size.

## Methods

The present study was performed according to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses [18,19].

### *Literature Search*

We conducted a literature search of studies using MEDLINE (via PubMed), Embase, PsychInfo, the Cochrane Library, CINAHL PLUS with Full Text, Current Contents Connect (Social & Behavioral Sciences [from 1998 to present], Clinical Medicine [from 1998 to present], Engineering, Computing & Technology [from 1998 to present]), and Web of Science. We searched databases from their start dates through September 3, 2013 (see search strategies in Appendix Table S1 in Supplemental Materials found at 10.1016/j.jval.2015.02.017 and the results in Fig. 1). Search results were downloaded and imported directly into EndNote, version X4 [20]. No language restriction was applied. An information scientist (F. B.) assisted us in developing an optimal search strategy.

### *Eligibility Criteria and Study Selection*

We defined eligibility criteria on the basis of PICOS (participants, intervention, comparator, outcomes, and study design) [18].

#### *Types of Participants*

All studies that focused on adults 18 years or older with type 2 diabetes who used OADs.

#### *Types of Interventions*

Interventions with at least one component aimed at improving OAD adherence, regardless of the methods or techniques used.

#### *Comparator*

Individuals with type 2 diabetes who were exposed to usual care and/or to an intervention of any sort.

#### *Outcomes*

The main outcome was OAD adherence. We included original studies in which OAD adherence was measured both before and after the intervention.

#### *Study Designs*

We included randomized controlled trials, quasi-experimental studies, and controlled pre-/posttest studies.

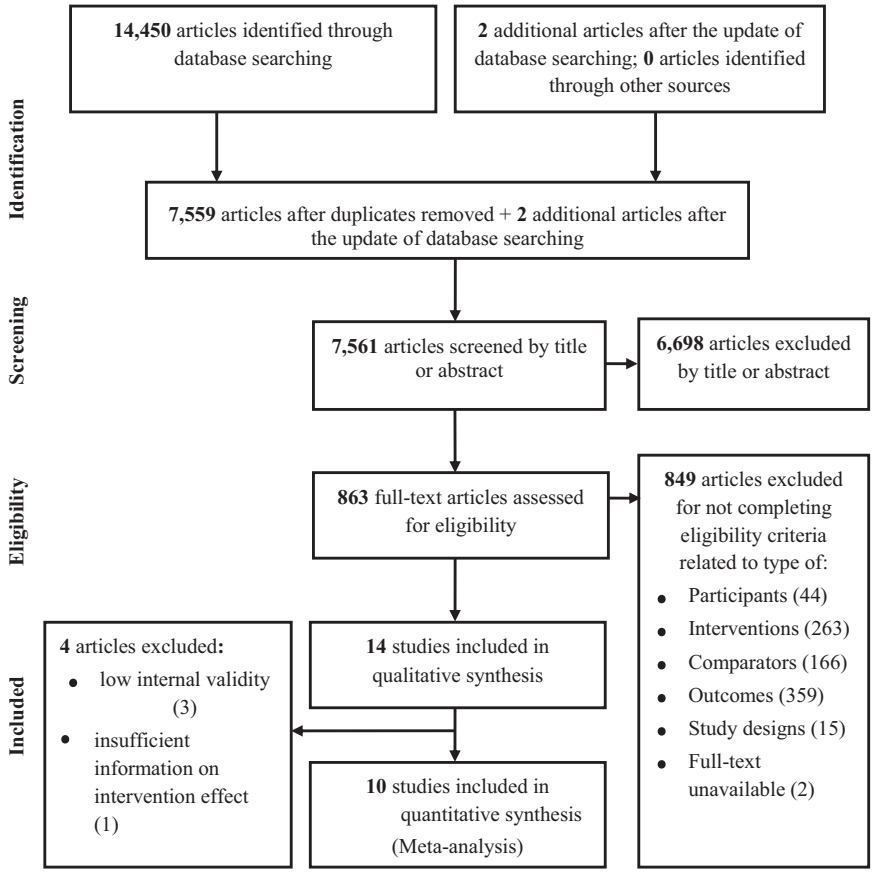


**Fig. 1 – Flow chart of article selection in the systematic review and meta-analysis.**