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Impact of Interventions on Medication Adherence and Blood Pressure Control in Patients with Essential Hypertension: A Systematic Review by the ISPOR Medication Adherence and Persistence Special Interest Group

Femida H. Gwadry-Sridhar, BSc, Pharm, MSc(Epi), PhD[1,2,], Elizabeth Manias, RN, CertCritCare, BPharm, MPharm, MNStud, PhD, FRCNA[3], Lincy Lal, PharmD, PhD[4], Maribel Salas, MSc, DSc, MD[5,6], Dyfrig A. Hughes, BPharm, MSc, PhD, MRPharmS[7], Alexandria Ratzki-Leewing, BHSc[2], Maja Grubisic, BSc, MSc[6,8]*

[1]*Faculty of Science, Department of Computer Science, The University of Western Ontario, London, Ontario, Canada;* [2]*I-THINK Research, Lawson Health Research Institute, London, Ontario, Canada;* [3]*Melbourne School of Health Sciences, The University of Melbourne, Melbourne, Victoria, Australia;* [4]*Ingenix Consulting, Ingenix, Houston, TX, USA;* [5]*Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Philadelphia, PA, USA;* [6]*AstraZeneca, Wilmington, DE, USA;* [7]*Centre for Economics and Policy in Health, Bangor University, Wales, UK;* [8]*Centre for Health Evaluation and Outcome Sciences, Providence Health Care, Vancouver, BC, Canada*

ABSTRACT

Objectives: To systematically review the evidence on the impact of interventions to improve medication adherence in adults prescribed antihypertensive medications. **Methods:** An electronic search was undertaken of articles published between 1979 and 2009, without language restriction, that focused on interventions to improve antihypertensive medication adherence among patients (≥18 years) with essential hypertension. Studies must have measured adherence as an outcome of the intervention. We followed standard guidelines for the conduct and reporting of the review and conducted a narrative synthesis of reported data. **Results:** Ninety-seven articles were identified for inclusion; 35 (35 of 97, 36.1%) examined interventions to directly improve medication adherence, and the majority (58 of 97, 59.8%) were randomized controlled trials. Thirty-four (34 of 97, 35.1%) studies reported a statistically significant improvement in medication adherence. **Discussion/Conclusions:** Interventions aimed at improving patients' knowledge of medications possess the greatest potential clinical value in improving adherence with antihypertensive therapy. However, we identified several limitations of these studies, and advise future researchers to focus on using validated adherence measures, well-designed randomized controlled trials with relevant adherence and clinical outcomes, and guidelines on the appropriate design and analysis of adherence research.

Keywords: hypertension, intervention, medication adherence, uncontrolled blood pressure.

Introduction

Nonadherence to medications is well established as an important contributor to poorly controlled hypertension [1–4]. However, despite the convenience of once-daily dosing schedules of antihypertensives, the relative lack of adverse effects, and the many interventions developed to improve medicine taking [5], adherence to antihypertensives remains suboptimal, resulting in persisting rates of uncontrolled blood pressure (BP) among hypertensive patients (BP below 140/90 mmHg) [6,7]. In the United States, only 50% of the patients have good control of their BP [8]. Poor medication adherence has been widely identified as the main cause of failure to control hypertension [9].

A quarter of patients who are newly initiated on antihypertensive therapy fail to fill their first prescription [2,3]. During the first year of treatment, the average patient has possession of antihypertensive medications for only 50% of the time, and only one patient in five has sufficiently high adherence during this period to achieve the benefits observed in clinical trials [10]. Consequently, suboptimal implementation of a daily-dosing regimen and a lack of adherence to antihypertensive agents [2,3,5,11,12] constitute major barriers to reductions in cardiovascular mortality [10,13]. A study by Nelson et al. [14] found that hypertensive patients who reported forgetting to take their medication were significantly more likely to experience a cardiovascular event or death than those who reported never forgetting to take their medication. In 2010, hypertension cost the United States $93.5 billion in health care services, medications, and missed days of work [15]; improving adherence could represent a major source of health and economic improvement from a societal, institutional, and employers' perspective [16–19].

A significant proportion of nonadherence is intentional, and despite the existence of patient-centered behavioral theories and models developed to understand reasons for poor adherence [20–24], there has been limited work focusing on the doctor-patient relationship and patient health beliefs [18]. Interventions aimed at promoting adherence are variably effective [5], a likely consequence of large intraindividual variability in the factors that influence patients' behavior to take their medicines. An important criterion for any adherence-enhancing intervention is that it

* *Address correspondence to:* Femida H. Gwadry-Sridhar, 268 Grosvenor Street, Room FB-112, London, Ontario N6A4V2, Canada.
E-mail: femida.gwadry-sridhar@lhsc.on.ca.

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should be tailored to address the root causes of nonadherence [21–28].

While a Cochrane review has been previously published on interventions aimed at improving medication adherence in hypertension [29], it included randomized controlled trials (RCTs) published only up to 2002, of interventions directly geared at patients. The aims of this systematic review were to update previous reviews on examining interventions geared toward improving medication adherence in hypertension and to broaden the coverage of studies and interventions to be included. This latter aim was achieved by not restricting research designs or specifying for whom the intervention is to be directed. Our consideration of studies besides RCTs is aligned with the notion that different forms of evidence should be valued, in contrast to the traditional concept of an evidence hierarchy [30].

Definition of Adherence

For the purposes of this article, dichotomous and continuous measures of medication adherence are defined as the process by which patients take their medications as prescribed, composed of initiation, implementation, and discontinuation [12,31–34]. We also draw distinction between adherence and persistence according to Vrijens et al. [12], where persistence describes the length of time between initiation and the last dose immediately preceding discontinuation. This article will focus on adherence to antihypertensive medication only. Although medication adherence seems to be the more preferred term, patient compliance is recognized as a synonym for adherence provided the term is used to describe the process by which patients take their medications as prescribed [35]. Medication adherence will be operationally defined as dose taking in relation to what was prescribed [35].

Methods

Authors followed the Centre for Reviews and Dissemination's guidance for undertaking reviews in health care, and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [36] guidelines that have also adopted the definitions of systematic reviews and meta-analysis used by the COCHRANE collaboration [37]. Owing to the diverse nature of interventions and study designs considered, a meta-analysis (quantitative synthesis) was not conducted.

Literature Search

A literature search of articles published between January 1979 (when the first article on adherence research was published) and February 2009 was conducted using four electronic databases: CINAHL, EMBASE, all EBM reviews, and MEDLINE. Databases were selected on the basis of relevancy to the subject area (i.e., medicine and health) and available publication type (i.e., journal articles). The search strategy focused on four key elements: study design (e.g., RCTs, comparison study), sample (e.g., age of study population), measurements of adherence and BP (self-reporting, medication event monitoring systems), and findings (e.g., improvement in clinical outcomes). Search terms were determined by the research team's own expertise and by examining previous literature in the area. These were refined iteratively on the basis of a sample of articles identified previously as being suitable for inclusion (Table 1).

Relevant citations and abstracts were examined independently by eight reviewers (E.M., M.G., L.L., M.S., C.H., F.G.S., A.R.L., and S.G.). Studies were examined to determine whether the adherence-enhancing intervention 1) directly improved medication adherence, 2) indirectly improved medication adherence via the involvement of a single health care provider or a multidisciplinary team, or 3) indirectly improved adherence through an intervention directed at the health care provider of the multidisciplinary team. Interventions could constitute a number of different approaches, including behavioral change techniques, case management, counseling, disease management, family therapy, patient education, or reminders for patients or for health professionals.

Reviewers also hand-searched references found in included publications for additional articles of relevance. Any duplicate and redundant articles were flagged and eliminated from the review.

Study inclusion criteria

Studies that focused on interventions to improve medication adherence to antihypertensives in adult (≥18 years) patients with

Table 1 – Search strategy using PubMed, EMBASE, EBM reviews, and MEDLINE.

	PubMed MeSH heading search strategy				
	Patient adherence	***AND***	**Disease**	***AND***	**Intervention**
	Patient adherence		Hypertension		Case management
OR	Medication adherence				Counseling
OR	Treatment refusal				Disease management
OR	Patient dropout				Health promotion
OR					Family therapy
OR					Patient education
OR					Reminder system*
	EMBASE, EBM reviews, and MEDLINE keyword search strategy				
	Patient adherence	***AND***	**Disease**	***AND***	**Intervention**
	Adherence		Hypertension		Behavior
OR	Persistence				Behavior
OR					Communication
OR					Intervention

* The wildcard character.