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A protocol to evaluate the efficacy, perceptions, and cost of a cholesterol packaging approach to improve medication adherence

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ABSTRACT

Purpose: Elevated low-density lipoprotein cholesterol (LDL-C) is a major modifiable risk factor for cardiovascular disease (CVD), a leading cause of death in the United States. Despite clinical practice guidelines aimed at facilitating LDL-C control, many Veterans do not achieve guideline-recommended LDL-C levels.

Methods: We describe a study focused on VA healthcare system users at risk for CVD (i.e., LDL-C level >130 mg/dl and/or <80% cholesterol pill refill adherence in the last 12 months). We are conducting a two and a half year randomized controlled trial (i.e., intervention administered over 12 months) among Veterans with uncontrolled cholesterol receiving care at select VA-affiliated primary care clinics in North Carolina. We anticipate enrolling 250 diverse patients (10% women; 40% African American). Patients are randomized to an educational control group or intervention group. Intervention group participants' medication is provided in special blister packaging labeled for daily use that includes reminders; MeadWestvaco Corporation's pre-filled DosePak® contains standard doses of statins in accordance with the existing prescriptions.

Conclusions: Pre-filled blister packaging may provide an inexpensive solution to improve medication adherence. Our study enrolls a diverse sample and provides information about whether an adherence packaging intervention can: 1) improve medication adherence; 2) improve patients' LDL-C levels; 3) be well received by patients and providers; and 4) provide a cost effective solution to improve medication adherence.

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1. Introduction

Elevated low-density lipoprotein cholesterol (LDL-C) is a modifiable risk factor for cardiovascular disease (CVD). In 2013 the American Heart Association, in collaboration with the National Heart, Lung, and Blood Institute and others, released revised guidelines for cardiovascular risk reduction including LDL-C management [1]. This guideline changed recommendations about which patients are at high cardiovascular risk and should be prescribed a statin medication. Based on the new guidelines, most older Americans will be recommended to take statin drugs. The guidelines also removed target cholesterol levels from treatment recommendations (i.e., treat to target and lower is better strategy are not evidence-based).

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Because of the health implications of hyperlipidemia, the Centers for Medicare and Medicaid Services (CMS) established a quality goal. The goal ensured that Medicare Part D members who were prescribed statin medication for hyperlipidemia would fill their prescription often enough to cover 80% or more of the time they are supposed to be taking the medication. Not properly adhering to prescribed medications is associated with higher LDL-C, increased all-cause hospitalization, and increased all-cause mortality [2]. To improve LDL-C control, it is essential to improve medication adherence. The objective of this prescription medication refill goal is to facilitate patients' LDL-C control. Similarly, the Department of Veterans Affairs (VA) healthcare system has adopted the pill refill quality guideline, noting that the overarching goal is to properly treat each individual patient. Unfortunately, many Veterans are not achieving preferred LDL-C levels [3]. Because elevated LDL-C is a major modifiable risk factor for CVD, developing strategies to reduce LDL-C is critical. Reduction of LDL-C in high-risk patients is associated with a substantial reduction in morbidity, mortality, and costs.

Our study seeks to evaluate efficacy, clinical effectiveness, patient and provider perceptions, and cost effectiveness of an innovation prescription medication packaging approach. We posit that this special packaging will improve medication adherence rates among Veterans by addressing the modifiable risk factor of LDL-C. To achieve LDL-C risk reduction, we are conducting a clinical trial that tests the innovative adherence packaging relative to usual care. Specifically, we assess MeadWestvaco (MWV) Corporation's pre-filled DosePak® (i.e., a blister package system).

Innovative packaging of prescription medication could improve medication adherence through several mechanisms. The simple daily labeling may make it is easier to determine whether medications were taken, if there were any missed or skipped doses, and when missed doses occurred. Blister packaging may make medication-taking more convenient for patients by eliminating issues associated with traveling with medication, forgetting whether medications have been taken on a particular day, and other common problems of medication non-adherence. Additionally, this packaging approach may streamline professional monitoring of patients' adherence. Patient's provider or pharmacy staff could examine patient's DosePak® and straightforwardly assess whether and when patients have taken their medication. In general, our study addresses: 1) whether there are benefits of the special blister packaging that, despite additional costs, make it advantageous over a typical amber vial; and 2) for which patients the packaging is most beneficial.

2. Materials and methods

2.1. Study overview

The study that we describe is focused on the users of the VA healthcare system at risk for cardiovascular disease (CVD). Patients are considered to be at risk for CVD if the LDL-C level is greater than 130 mg/dl and/or they have less than 80% medication adherence in the last 12 months. We concentrate on the VHA and LDL-C risk reduction because, despite the availability of effective therapies for dyslipidemia in the VHA, many VA patients fail to meet cholesterol control recommendations [2,3]; only approximately 53% of VA patients who have concomitant diabetes mellitus and hypertension attain appropriate LDL-C values [3].

Patients are followed for 12 months and the study will be a two and a half year (i.e., the intervention will be administered over 12 months, but patients are monitored for up to 30 months to allow for longer-term assessment of whether improvements in medication adherence and LDL-C are sustained after the intervention is complete). This is a randomized controlled trial among Veterans with uncontrolled cholesterol receiving care at the Raleigh Community-based Outpatient Clinic (CBOC) and hospital-based primary care clinics associated with Durham VAMC to improve their CVD risk profile. This study is sponsored by a grant from MeadWestvaco (MWV) and is approved by the Durham VA Medical Center Institutional Review Board (clinicaltrials.gov registration number: NCT01744977).

2.2. Sample identification and eligibility criteria

Potential participants are identified through a data extraction from the VA electronic health record. In order to be eligible for inclusion in the study, patients must meet all of the following criteria: be enrolled in one of the three primary care clinics affiliated with the Durham VA Medical Center (e.g., the Durham VA Medical Center, Hillandale Outpatient Clinic, or Raleigh Community-Based Outpatient Clinic) for at least one year; had at least one visit to their primary care provider in the previous 12 months; have an outpatient diagnostic code for hypercholesterolemia; have uncontrolled LCL-C in the last 12 months (average >130 mg/dl) and/or poor LDL refill defined as <80% medication adherence in the last 12 months; and be prescribed simvastatin, rosuvastatin or pravastatin (e.g., 20 mg or 40 mg as described below). The study statistician identifies patients meeting initial inclusion criteria and randomly samples potential participants for additional screening and study recruitment. Patients are also screened for exclusion criteria at several stages throughout the recruitment process (Table 1).

2.3. Recruitment and randomization procedure

Patient recruitment takes place over the course of 18 months, with the goal of recruiting 8–10 patients weekly. Based on appointment information available in the electronic health record, study staff identify participants who have an upcoming medical appointment scheduled in the next two to three weeks. If insufficient patients are identified, additional patients meeting eligibility criteria who do not have an immediately scheduled upcoming appointment are contacted. An introductory recruitment letter signed by patient's provider is sent to participants that have been identified. Approximately one to two weeks after the introductory letter is mailed, study staff call potential participants to assess patient's interest in the study and determine whether they meet eligibility criteria. For patients interested and eligible, an in-person interview is scheduled. Patients are sent reminder letters up to three weeks prior to their scheduled appointments (e.g., six and 12 month follow-up appointments). During the initial in-person interview, patients are provided with full details of the study and provide written informed consent. Should a consented