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Short Communication

The effect of interactive reminders on medication adherence: A randomized trial

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ABSTRACT

Expanding on evidence that interventions to improve health are more effective when informed by behavioral science, we explore whether reminders designed to harness behavioral science principles can improve medication adherence. We conducted a randomized controlled trial with 46,581 U.S. participants with commercial or Medicare Advantage insurance from Humana. Participants were randomly assigned to one of four experimental conditions. Participants in the *usual care* condition only received standard mailings that the insurer usually sends. In addition to the standard mailings, participants in the other three conditions also received (1) mailings that reminded them to take a target medication (*basic reminder* condition), (2) reminders that prompted them to predict their medication adherence in the next 30 days (*prediction* condition), or (3) reminders that prompted them to commit to a self-determined level of adherence for the next 30 days (*commitment* condition). We sent these mailings once a month for three months from November, 2014 through January, 2015, and tracked prescription refills. We find that, during the mailing period, reminders increased adherence by 0.95 percentage points ($p < 0.05$), and this effect was driven by the *prediction* and *commitment* conditions; during the three-month post-mailing period, reminders increased adherence by 0.98 percentage points ($p < 0.05$), and this effect was driven by the *basic reminder* and *commitment* conditions. The reminders increased medication adherence by 0.7 pills per dollar spent over our 181 day study period.
Trial registry name: Effect of Reminders on Adherence.
Registration identification number: NCT02411006
URL for the registry: https://clinicaltrials.gov/ct2/show/NCT02411006

1. Introduction

The low rate of medication adherence in the United States is estimated to cost Americans between $100 billion and $289 billion annually (Viswanathan et al., 2012). Forgetfulness is considered to be a key contributor to patients' failure to take their medications as prescribed (Gadkari and McHorney, 2012). To overcome forgetfulness, a number of recent studies have examined whether devices that remind people to take their prescribed medication improve medication adherence. We conducted a large randomized controlled trial (RCT) to examine the efficacy of not only basic reminders that simply tackle forgetfulness but also reminders that are designed to tackle another barrier of adherence—procrastination and lack of motivation (George et al., 2006; Israni et al., 2016). We evaluated their impact on medication adherence over a three-month intervention period and three-month post-intervention period using data on prescription refills.

Our basic reminders tackle forgetfulness by simply encouraging people to take pills regularly. Inspired by the potential of behavioral science for promoting health behavior (Mogler et al., 2013; Li and Chapman, 2013), our interactive reminders are designed to leverage several behavioral science principles that may increase patients' motivation to refill prescriptions and take medicines as prescribed. First, past research has shown that merely asking people about their intentions and plans to engage in a behavior (e.g., to make blood donations, to get vaccinations) can increase actual engagement (Godin et al., 2008; Milkman et al., 2011). One explanation for this effect is that people prefer to behave consistently with intentions that they have stated, even when their intentions are private (Milkman et al., 2011; Cialdini, 2006). Second, research has shown that setting specific goals motivates people to work harder and achieve better performance than they would in the absence of such goals (Locke and Latham, 1990). Building on these insights, we

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designed two types of interactive reminders that prompted people to form intentions about taking medications and encouraged them to set specific adherence goals. One type of reminder prompted participants to *predict* their future medication adherence levels, and another type of reminder prompted participants to *commit* to a medication adherence level. Our RCT compares receiving no reminders with receiving reminders and explores whether interactive reminders are particularly impactful.

2. Methods

2.1. Study design, population, and procedures

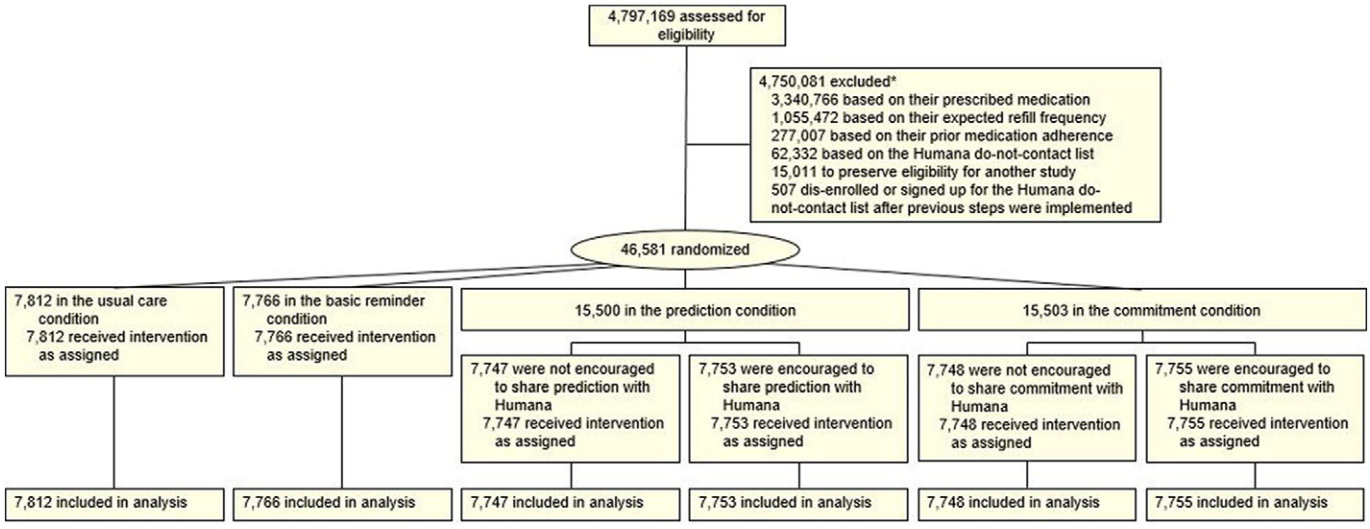
In November 2014, 46,581 participants with employer-sponsored commercial or Medicare Advantage insurance from Humana were deemed eligible for inclusion in our randomized controlled trial. These participants were taking oral medication for cholesterol, diabetes, or blood pressure control, were expected to refill their medication every 30 days, and had 40–80% medication adherence in the 12 months prior to randomization (Fig. 1). Participants were enrolled by Humana.

This study involved four primary experimental conditions. After consulting with Humana, we set our intervention period to three months—a reasonable starting point for examining the impact of our intervention on adherence among participants with 30-day scripts. Participants in the *usual care* condition received standard engagement messages that the insurer regularly sends. Participants in the other three conditions received three additional reminder mailings, with each mailing sent around the 15th of each month from November, 2014 through January, 2015. In the *basic reminder* condition, these mailings simply reminded participants to take a target medication (for cholesterol, diabetes, or blood pressure) (Szilagyi et al., 2000). In the *prediction* condition, our mailings prompted participants to predict the number of days in the next 30 when they would take their medication (Godin et al., 2008; Milkman et al., 2011; Cialdini, 2006; Locke and Latham, 1990). In the *commitment* condition, the mailings prompted participants to commit to a self-determined number of days over the next 30 to take their medication (Godin et al., 2008; Milkman et al., 2011; Cialdini, 2006; Locke and Latham, 1990). All reminder mailings included a sticky note that participants could place somewhere (e.g. on a refrigerator) as a reminder, and those in the prediction and commitment conditions were encouraged to record their prediction or commitment on the sticky note.

Furthermore, inspired by past research showing that people are more likely to follow through on plans that are made public (Cialdini, 2006), we randomly assigned half of the participants in the prediction and commitment conditions to receive encouragement to share their prediction or commitment with Humana online, via text, or via postcard. Thus, both the prediction and commitment conditions consisted of two sub-groups. After institutional review board waiver of informed consent, researchers at the University of Pennsylvania used R, version 3.1.1 (R Core Team) to randomly assign participants in a 1:1:1:1:1:1 ratio to one of six groups, without blocking or other restrictions (Fig. 1).

2.2. Study outcomes and statistical analysis

We used pharmacy claims data to calculate each participant's proportion of days covered (PDC), defined as the number of days when he/she had any pills in the medication category listed on his/her mailing divided by the number of days in the observation period. In our primary analysis, we use PDC as our proxy for adherence, a continuous measure that is widely used by researchers to measure medication adherence (Lee et al, 2006; Lin et al., 2006; Osterberg and Blaschke, 2005; Choudhry et al., 2011). We used ordinary least squares regressions in STATA, version 14 (StataCorp) to predict PDCs on an intent-to-treat basis, controlling for PDC during the six months prior to the start of our experiment (May 15, 2014 to November 14, 2014), gender, ethnicity, the linear and squared terms of age, log-transformed income, and the type of medication that was listed on the reminders. The regressions had an 80% power to detect a minimum of a 1.2-percentage-point difference between the usual care and each treatment condition with $\alpha = 0.05$. We also evaluated adherence using a binary measure of optimal adherence which was set equal to one if a patient's PDC in a given period was equal to or >80%, and zero otherwise. This less sensitive measure of adherence has also been widely used in past research, and we used logistic regressions to predict



* Exclusions were done sequentially:
1. Humana identified people who were prescribed any of the following medications: (a) Statin, (b) Metformin, (c) Sulfonylureas (including glipizide and gliclazide), (d) Meglitinides (including repaglinide and nateglinide), (e) Thiazolidinediones (including rosiglitazone and pioglitazone), (f) DPP-4 inhibitors (including sitagliptin, saxagliptin, linagliptin, and alogliptin), (g) Glucagon-like peptide 1 agonists (including exenatide and liraglutide), and (h) ACE/ARB/DRI.
2. Humana identified people who were prescribed a 30-day supply of medication.
3. Humana identified people who had 40%-80% compliance for relevant medications in the 12 months prior to sample selection.
4. Humana excluded people who were on the do-not-contact list at the time.
5. We then selected the first 47,088 people identified by Humana to preserve the eligibility of the remaining 15,011 people for another study.
6. At the start of our RCT, Humana excluded people who dis-enrolled or signed up for the Humana do-not-contact list after previous steps were implemented.
After these steps, 46,581 participants were eligible for inclusion in our RCT, included in our randomization, targeted by our RCT, and included in our analysis.

Fig. 1. CONSORT Flow diagram of study blocks and sample sizes.