Letters

RESEARCH LETTER

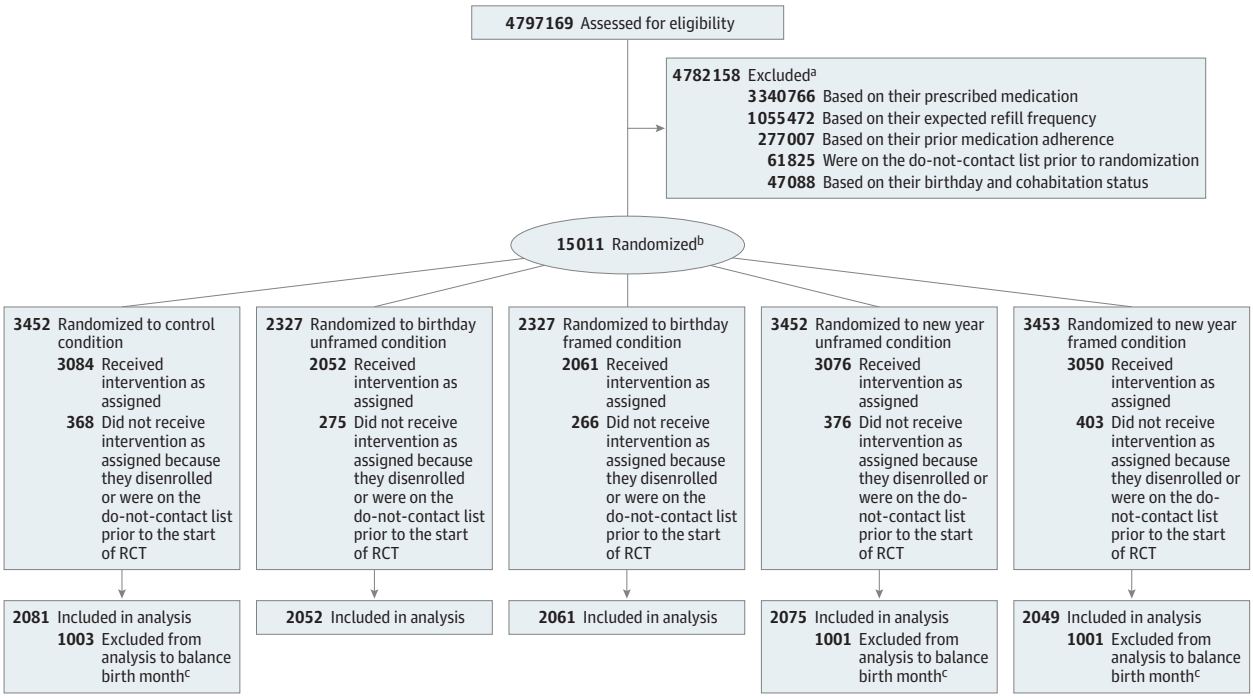
Effectiveness of Medication Adherence Reminders Tied to "Fresh Start" Dates: A Randomized Clinical Trial

Low medication adherence is problematic.[1] Well-designed reminders can increase adherence,[2] but when should reminders be sent to maximize their effect? Prior observational studies[3] and laboratory experiments[4] have shown that engagement in healthy activities increases considerably following *fresh-start* dates: life and calendar events signaling the beginning of new cycles (eg, birthdays or New Year's Day).[3,4] Extending this insight, we conducted what is, to our knowledge, the first randomized clinical trial examining whether sending medication adherence reminders around fresh-start dates and highlighting these dates as an opportunity for positive changes could boost reminders' effectiveness.

Supplemental content

Methods | Between January 21, 2015, and March 25, 2015, we mailed reminders to 13 323 participants (5970 men [45%]; 40%-80% adherence in the past 12 months) with commercial or Medicare Advantage insurance with Humana, encouraging them to regularly take their cholesterol, diabetes, or blood pressure medications. Participants were randomly assigned to 1 of 5 mailing conditions (**Figure 1**). In the birthday unframed and birthday framed conditions, reminders were sent within 1 week

Figure 1. Flow of Study Participants



[a] Exclusions were done sequentially. We included participants who were prescribed any of the following medications: (1) statin; (2) metformin; (3) sulfonylureas (including glipizide and gliclazide); (4) meglitinides (including repaglinide and nateglinide); (5) thiazolidinediones (including rosiglitazone and pioglitazone); (6) dipeptidyl peptidase–4 inhibitors (including sitagliptin, saxagliptin, linagliptin, and alogliptin); (7) glucagon-like peptide 1 agonists (including exenatide and liraglutide); and (8) angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and direct renin inhibitors; were prescribed a 30-day supply of medication; had a 40% to 80% compliance for relevant medications in the 12 months prior to randomization; were not on the do-not-contact list prior to randomization; had a birthday from January 21 to April 21; and were not living with any other participant in our sample.

[b] Researchers at the University of Pennsylvania used R, version 3.1.1 (R Core Team) to randomly assign participants to conditions. Participants whose birthdays were between January 21 and March 31 were assigned to 1 of 5 conditions under a 1:1:1:1:1 allocation ratio. Participants who birthdays were between April 1 and April 21 were assigned to the control, new year unframed, or new year framed condition under a 1:1:1 allocation ratio. Participants were enrolled by Humana. All conditions were balanced on available demographic variables (age, sex, race/ethnicity, and income) and proportion of days covered prior to our randomized clinical trial (RCT), suggesting that our randomization was successful.

[c] We excluded 3005 participants born in April from our analysis to make conditions comparable. The birthday unframed and birthday framed conditions did not include anyone with April birthdays because our last mailing date was March 25.

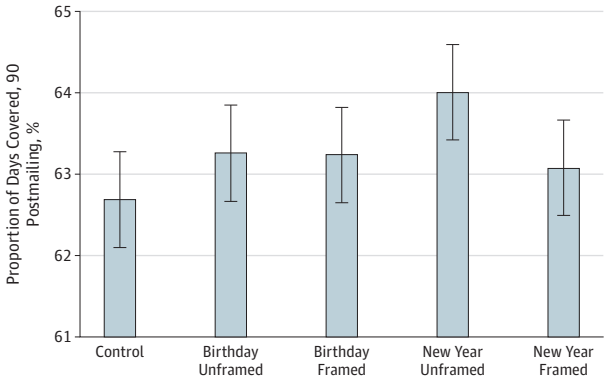
before each participant's birthday. In the new year unframed and new year framed conditions, reminders were sent 3 weeks after New Year's Day. Reminders in the birthday framed and new year framed conditions highlighted the participants' birthday or New Year's Day, respectively, as an opportunity to make a fresh start and begin taking medications regularly. In the control condition, reminders without any reference to fresh-start dates were sent on a randomly selected day that was at least 1 month after New Year's Day and 1 week away from the participant's birthday. The institutional review board of the University of Pennsylvania approved a waiver of informed consent requirements because the research presented no more than minimal risk of harm to participants and involved no procedures for which written consent is normally required outside of the research context. The formal trial protocol can be found in the Supplement.

For each participant, we used pharmacy claims data to calculate the proportion of days covered during our 90-day postmailing observation period, defined as the number of days he/she had any pills in the medication category listed on his/her reminder divided by 90 days. Ordinary least squares regressions to estimate treatment effects in STATA, version 14 (StataCorp) had an 80% power to detect a difference of at least 2 percentage points between the control and each treatment condition with $\alpha = .05$.

Results | Mean proportion of days covered among participants was 63.3% over 90 days postmailing. Compared with the control condition, proportion of days covered did not significantly differ in the birthday unframed (mean difference, 0.56%; 95% CI, −1.09% to 2.19%), birthday framed (mean difference, 0.55%; 95% CI, −1.08% to 2.20%), new year unframed (mean difference, 1.32%; 95% CI, −0.32% to 2.95%), or new year framed condition (mean difference, 0.38%; 95% CI, −1.26% to 2.03%). The difference in proportion of days covered was also insignificant comparing the birthday unframed and birthday framed conditions (mean difference, −0.02%; 95% CI, −1.66% to 1.63) or the new year unframed and new year framed conditions (mean difference, −0.93%; 95% CI, −2.57% to 0.71%). **Figure 2** depicts these results.

Discussion | Contrary to our expectations, sending reminders following fresh-start dates was not associated with increased medication adherence, and fresh-start-based framing was not associated with increased reminder effectiveness. We encourage further study before concluding that the psychology of fresh starts does not apply to medication adherence. Because fresh-start dates motivate individuals wishing to initiate goal pursuit,[3,4] our timing- and framing-based treatments may increase the effectiveness of reminders when reminders involve goal-setting activities. Additionally, there is often a delay between a target fresh-start date and the date when treatment-condition reminders were actually received; in the New Year conditions, reminders often arrived in late January. Reminders received immediately after the target date could be more effective. Further investigation into alternative ways to leverage fresh starts[5] and compel patients to attend to public health messaging would be valuable.

Figure 2. Ordinary Least Squares Regression–Adjusted Proportion of Days Covered by Different Mailing Conditions



Error bars represent standard error. For each participant, our ordinary least squares regression controls for his or her proportion of days covered during the 90 days prior to the mailing date, sex, race/ethnicity, the linear and squared terms of age, log-transformed income, and the type of medication that was listed on the reminder (ie, diabetes, cholesterol, or blood pressure). By design, any differences between the control and treatment conditions reflect a combination of the time of year and the potential treatment effect of receiving a fresh-start reminder.

This study has several limitations. The insurer sent some customers medication adherence reminders outside of the randomized clinical trial, and we were unable to include a condition without reminders. Also, many participants were involved in another randomized clinical trial comparing reminders that ended shortly before this randomized clinical trial. Furthermore, our participants had lower medication adherence levels than those in other adherence studies (eg, a multisite study published in 2015[6]), possibly because of our selection criteria.

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Drafting of the manuscript: Dai, Mao.
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Statistical analysis: Dai, Mao.
Obtained funding: Volpp, Relish, Milkman.
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