Personalized Patient Data and Behavioral Nudges to Improve Adherence to Chronic Cardiovascular Medications (The Nudge Study)

Grand Rounds, Rethinking Clinical Trials
11/17/2023
P. Michael Ho, MD, PhD & Sheana Bull, MPH, PhD
Agenda

• Study introduction
• Initial findings from the UG3 Pilot
• Learning from the opt out consent process
• Findings from the UH3 trial
• Pharmacist-patient interactions
• Patient perspectives of the study
• Lessons learned
Introduction

• Medication non-adherence associated with poor health outcomes, high healthcare costs, and preventable deaths.

• Up to half (50%) of patients with cardiovascular conditions don’t take their medications as prescribed.

• Previous adherence interventions have been resource intensive, high-burden, inconsistent, and produced mixed results.
What is a Nudge?

- A strategic reminder can help people adopt healthy behaviors
  - Uses principles from behavioral economics and cognitive psychology
    - Behavior commitments
    - Communicating social norms
    - Narrative stories
- Can help patients improve medication adherence by promoting behavioral change through positive reinforcement.
- Should be delivered close to the timing of the desired behavior.
Specific Aims

• **Year 1 (UG3 Phase)**
  - **Aim 1.** Develop and program a nudge message library using iterative N of 1 studies to optimize content for a range of diverse patients.
  - **Aim 2.** Conduct a pilot intervention to demonstrate feasibility of delivering the intervention and preliminary effects in all 3 HCS. Engage patient, provider and health systems stakeholders in designing, refining, and implementing the pilot intervention.

• **Years 2-5 (UH3 Phase)**
  - **Aim 1.** Conduct a pragmatic patient-level randomized intervention across three health care systems (HCS) to improve adherence to chronic CV medications.
  - **Aim 2.** Evaluate the intervention effectiveness using a mixed methods approach and applying the RE-AIM (reach, effectiveness, adoption, implementation, and maintenance) framework.
Patient Population

Inclusion criteria

- Adult patients diagnosed with ≥ 1 cardiovascular condition of interest, prescribed ≥ 1 medication of interest, with a refill gap of at least 7 days

<table>
<thead>
<tr>
<th>Condition</th>
<th>Classes of medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Beta-blockers (B-blockers), Calcium Channel Blocker (CCB), Angiotensin converting enzyme inhibitors (ACEi), Angiotensin Receptor Blockers (ARB), Thiazide diuretic</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>HMG CoA reductase inhibitor (Statins)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Alpha-glucosidase inhibitors, Biguanides, DPP-4 inhibitors, Sodium glucose transport inhibitor, Meglitinides, Sulfonylureas, Thiazolidinediones, and statins</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>PGY-2 inhibitor (Clopidogrel, Ticagrelor, Prasugrel, Ticlopidine), B-blockers, ACEi or ARB and statins</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Direct oral anticoagulants, B-blockers, CCB</td>
</tr>
</tbody>
</table>

Exclusion criteria

- Patients with neither a landline or cellphone
- Enrolled in hospice or palliative care
- Non-English or Spanish speaking
- Residing out of the state of Colorado.
STUDY SETTING

- UCHealth Clinics
- Denver Health Clinics
- VA Eastern Colorado HCS Clinics
Opt out approach

• Opt out approach
  • Low risk intervention
  • Having patients consent may enroll more adherent patients
  • Challenges of consenting large patient population

• Our opt out process included:
  • Mailed packet with information sheet, opt out sheet, and a self addressed stamped envelope
  • Optional survey seeking to understand why patients do not participate in low-risk, opt out studies
  • Materials were signed by Site PI respective to their HCS
  • 4-week deadline to return opt-out form

• A secondary opt-out opportunity was included in subsequent texts
You are due for a refill on your meds

[Name] Congrats! You’ve filled meds on time at least 60% of the time. Make it 100%!

What problems do you have getting refills? Text
1=transport
2=cost
3=time
Initial findings from the UG3 Pilot
Creation of culturally appropriate nudges

Community Advisory Panel

A Nudge-specific Advisory Panel provided additional input on both the messages and the opt out packets.

- Panel included patients, providers, health care leaders, and pharmacists
- Panel recommendations led to:
  - Added an option for patients to indicate they had leftover medications (responding “Done”)
  - Improved the interactive voice response (IVR) messages by using a robotic voice rather than human voice
  - Provided specific suggestions of way to disseminate findings, including identifying communications platforms at the HCS
Creation of culturally appropriate nudges

**Nof1 interviews**

- 35 patients provided their perspectives of our messages, creating an iterative message design process
  - Disliked messages with humor and emojis
  - Preference for direct and simple communications

**Example of message evolution**

<table>
<thead>
<tr>
<th>Original</th>
<th>Intermediate</th>
<th>Final</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tell us your best strategy to make getting refills a habit! Text 1 = set my alarm; 2 = rely on my family; 3 = make it part of my weekly routine; 4 = other or unknown.</td>
<td>We noticed you didn’t refill some of your meds. Tell us why! Text 1 = too expensive; 2 = I forgot; 3 = I don’t like taking them; 4 = Other.</td>
<td>Hi (FIRST NAME) We noticed you haven’t refilled your (DRUG NAME). Reply 1 = you’ll get them refilled in the next 2 days 2 = I’m still working on a plan to get this done.</td>
</tr>
</tbody>
</table>
## UG3 Patient Characteristics

<table>
<thead>
<tr>
<th>PATIENT CHARACTERISTICS</th>
<th>DENVER HEALTH (N=181)</th>
<th>VA (N=163)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, Mean (SD)</strong></td>
<td>57.8 (12.6)</td>
<td>66.0 (8.6)</td>
</tr>
<tr>
<td><strong>Male, % (n)</strong></td>
<td>47% (85)</td>
<td>93.3% (152)</td>
</tr>
<tr>
<td><strong>Race, % (n)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black/African American</td>
<td>17.7% (32)</td>
<td>23.3% (38)</td>
</tr>
<tr>
<td>White</td>
<td>11.6% (21)</td>
<td>68.1% (111)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>68.5% (124)</td>
<td>9.8% (16)</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>4.3% (7)</td>
</tr>
<tr>
<td><strong>Condition, % (n)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4.4% (8)</td>
<td>11.0% (18)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>14.4% (26)</td>
<td>22.7% (37)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>66.9% (121)</td>
<td>38.7% (63)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>43.1% (78)</td>
<td>41.1% (67)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>80.1% (145)</td>
<td>78.5% (128)</td>
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</table>
Message responses

<table>
<thead>
<tr>
<th></th>
<th>DH</th>
<th>VA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient opt out rate</td>
<td>6.5% (13)</td>
<td>18.5% (37)</td>
</tr>
<tr>
<td>Patients with 7-day gap</td>
<td>63.0% (115)</td>
<td>57.7% (94)</td>
</tr>
<tr>
<td>Spanish language</td>
<td>11.6% (10)</td>
<td>0</td>
</tr>
<tr>
<td>Texted “Done”</td>
<td>15.6% (14)</td>
<td>21.1% (19)</td>
</tr>
<tr>
<td>Texted “Stop”</td>
<td>3.3% (3)</td>
<td>1.1% (1)</td>
</tr>
</tbody>
</table>
Medication refill rates

<table>
<thead>
<tr>
<th></th>
<th>Arm 1 Usual Care</th>
<th>Arm 2 Generic</th>
<th>Arm 3 Optimized</th>
<th>Arm 4 Optimized + Chatbot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total N</td>
<td>50</td>
<td>53</td>
<td>52</td>
<td>52</td>
</tr>
<tr>
<td>N Medications Gapping at Baseline - Median (IQR)</td>
<td>2 (1, 3)</td>
<td>1 (1, 3)</td>
<td>1 (1, 2)</td>
<td>2 (1, 3)</td>
</tr>
<tr>
<td>Filled at Least 1 Gapping Medication - %(n)</td>
<td>18.0% (9)</td>
<td>32.1% (17)</td>
<td>32.7% (17)</td>
<td>26.9% (14)</td>
</tr>
<tr>
<td>Filled All Gapping Medications - %(n)</td>
<td>10.0% (5)</td>
<td>17.0% (9)</td>
<td>21.2% (11)</td>
<td>15.4% (8)</td>
</tr>
</tbody>
</table>
Pilot Study Final Conclusions

- Patient feedback important to refine text message content
- Opt-out rates lower than expected
  - Primary opt out rate (12.5%)
  - Secondary opt-out rate (1.2%) (responding with “STOP”)
- Real time identification of patients who have not refilled medications is feasible
- Sending text messages is feasible and shows potential for improving refill adherence.
Learning from the opt out consent process
OPT-OUT STUDY DESIGN

1. Identify patients with CV disease and prescribed medication
2. Send opt-out packets to eligible patients
3. Patients who do not return opt-out form are eligible for enrollment
4. Monitor for gaps with medication refills
5. Once gap occurs, patient randomized to a study arm
6. Secondary opt out option for those receiving texts by replying ‘STOP’
Comparing patients who opt out vs did not opt out

- Goal of study was to better understand characteristics of patients who opted out, and reasons for doing so:
  - 9,046 patients receiving packets
    - 906 patients (10.0%) returned opt out forms
    - Of those, 451 (49.8%) returned the opt out survey.
  - Patients who opted out were more likely to be older, white, and non-Hispanic.
  - Those who opted out and completed the opt out survey expressed high levels of trust in their health care providers, research, and system.
Reasons that contributed to patients opting out

- I am worried that it will take too much time to participate: 46.6%
- I am worried that participating would be risky to my health: 8.4%
- I am worried about privacy: 10.9%
- I don’t trust the people doing this research: 6.9%
- I am uncomfortable using technology*: 18.6%
- Reported to not need a reminder*: 19.5%
- Other: 26.3%
Studying patient populations who opted out via replying ‘STOP’ to text messaging

- Of 5,707 patients enrolled, 8.3% opted out by text after receiving a text
  - Median time to opt out was 83 days
  - Black and Hispanic patients, and primary Spanish speakers were less likely to opt out.
  - No significant differences were observed in age, gender, medical condition, or health system between patients remaining in study versus opting out.

- In a low-risk intervention, patients who identified as Black, Hispanic, and primary Spanish speakers were more likely to remain in the study

- An opt out approach in the appropriate clinical trial context may be a way to diversify clinical trial populations and improve external validity of results
Patients that remained in study vs opted out

**Ethnicity**
- **Remained in study**: Hispanic, 55%; Non-Hispanic, 45%
- **Opted out**: Hispanic, 40%; Non-Hispanic, 60%

**Language**
- **Remained in study**: Spanish, 32%; English, 68%
- **Opted out**: Spanish, 16%; English, 84%
Findings from the UH3 trial
Patient flow

Assessed for eligibility and sent an opt out consent form (n=13,444)

Did not have a medication gap (n=2,132)
Opted out during consent period (n=1,396)
Returned by USPS (n=415)

Randomized (n=9,501)

Allocated to Arm 1, Usual Care (n=2,376)
Opted out of intervention (n=1)
Other Exclusions (n=54)
Analyzed (n=2,321)

Allocated to Arm 2, Generic texts (n=2,377)
Opted out of intervention (n=6)
Other Exclusions (n=47)
Analyzed (n=2,324)

Allocated to Arm 3, Optimized texts (n=2,373)
Opted out of intervention (n=5)
Other Exclusions (n=47)
Analyzed (n=2,305)

Allocated to Arm 4, Optimized texts + Chatbot (n=2,375)
Opted out of intervention (n=5)
Other Exclusions (n=51)
Analyzed (n=2,319)

Opted out of intervention (n=5)
Other Exclusions (n=63)
Analyzed (n=2,305)

Other Exclusions (n=51)
Analyzed (n=2,319)
# Demographic Characteristics of the Study Population

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Usual Care</th>
<th>Generic</th>
<th>Optimized</th>
<th>Optimized + Chatbot</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>N = 9269</td>
<td>N = 2321</td>
<td>N = 2324</td>
<td>N = 2305</td>
<td>N = 2319</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>60.1% (12.7)</td>
<td>60% (12.6)</td>
<td>60% (12.5)</td>
<td>60% (12.9)</td>
<td>60% (12.7)</td>
<td>0.99</td>
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<tr>
<td><strong>Female</strong></td>
<td>47.0% (4351)</td>
<td>47% (1088)</td>
<td>47% (1087)</td>
<td>47% (1075)</td>
<td>47% (1101)</td>
<td>0.94</td>
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<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.58</td>
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<tr>
<td>White</td>
<td>70% (6460)</td>
<td>69% (1598)</td>
<td>69% (1601)</td>
<td>70% (1615)</td>
<td>71% (1646)</td>
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<tr>
<td>Black/AA</td>
<td>16% (1517)</td>
<td>17% (392)</td>
<td>17% (391)</td>
<td>16% (378)</td>
<td>15% (356)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3% (280)</td>
<td>3% (76)</td>
<td>3% (64)</td>
<td>3% (74)</td>
<td>3% (66)</td>
<td></td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>0.46</td>
</tr>
<tr>
<td>Hispanic</td>
<td>49% (4564)</td>
<td>50% (1149)</td>
<td>47% (1100)</td>
<td>50% (1147)</td>
<td>50% (1168)</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>50% (4629)</td>
<td>50% (1150)</td>
<td>52% (1204)</td>
<td>50% (1141)</td>
<td>49% (1134)</td>
<td></td>
</tr>
<tr>
<td><strong>Spanish Speaking</strong></td>
<td>28% (2605)</td>
<td>28% (654)</td>
<td>27% (619)</td>
<td>28% (650)</td>
<td>29% (682)</td>
<td>0.22</td>
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HCS & Qualifying conditions

<table>
<thead>
<tr>
<th>Health Care System</th>
<th>All</th>
<th>Usual Care</th>
<th>Generic</th>
<th>Optimized</th>
<th>Optimized + Chatbot</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 9269</td>
<td>N = 2321</td>
<td>N = 2324</td>
<td>N = 2305</td>
<td>N = 2319</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td><strong>Denver Health</strong></td>
<td>77% (7127)</td>
<td>77% (1785)</td>
<td>77% (1786)</td>
<td>77% (1781)</td>
<td>77% (1775)</td>
<td></td>
</tr>
<tr>
<td><strong>UCHealth</strong></td>
<td>10% (939)</td>
<td>10% (235)</td>
<td>10% (239)</td>
<td>10% (225)</td>
<td>10% (240)</td>
<td></td>
</tr>
<tr>
<td><strong>VA</strong></td>
<td>13% (1203)</td>
<td>13% (301)</td>
<td>13% (299)</td>
<td>13% (299)</td>
<td>13% (304)</td>
<td></td>
</tr>
<tr>
<td><strong>QUALIFYING CONDITION(S)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>6% (548)</td>
<td>6% (134)</td>
<td>6% (132)</td>
<td>7% (152)</td>
<td>6% (130)</td>
<td>0.45</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>14% (1310)</td>
<td>14% (328)</td>
<td>13% (305)</td>
<td>14% (325)</td>
<td>15% (352)</td>
<td>0.26</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>50% (4623)</td>
<td>50% (1149)</td>
<td>50% (1148)</td>
<td>50% (1164)</td>
<td>50% (1162)</td>
<td>0.86</td>
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<tr>
<td>Hyperlipidemia</td>
<td>46% (4267)</td>
<td>45% (1054)</td>
<td>46% (1072)</td>
<td>46% (1052)</td>
<td>47% (1089)</td>
<td>0.73</td>
</tr>
<tr>
<td>Hypertension</td>
<td>79% (7351)</td>
<td>80% (1864)</td>
<td>79% (1837)</td>
<td>79% (1829)</td>
<td>79% (1821)</td>
<td>0.5</td>
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</tbody>
</table>
Usual Care Generic Optimized Opt + Chatbot

<table>
<thead>
<tr>
<th></th>
<th>Usual Care</th>
<th>Generic</th>
<th>Optimized</th>
<th>Opt + Chatbot</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDC at 3 months</td>
<td>56.2%</td>
<td>61.4%</td>
<td>61.1%</td>
<td>61.6%</td>
</tr>
<tr>
<td>PDC at 12 months</td>
<td>60.6%</td>
<td>62.0%</td>
<td>62.3%</td>
<td>63.0%</td>
</tr>
</tbody>
</table>
SUBGROUP ANALYSES

Difference in PDC between generic text and usual care groups at 3-months
Clinical Events

**Death**

Est. 1-Year Death, Perc. (95% CI):
- Usual Care: 3.3 [2.5, 4.1]
- Generic: 3.1 [2.3, 3.8]
- Optimized: 2.6 [1.9, 3.3]
- Opt + Chatbot: 2.7 [2, 3.4]

**Hospitalization**

Est. 1-Year Hosp, Perc. (95% CI):
- Usual Care: 14.3 [12.6, 16.1]
- Optimized: 13.8 [11.9, 15.3]
- Opt + Chatbot: 13.6 [11.9, 15.3]

**Emergency Department**

Est. 1-Year ED Visit, Perc. (95% CI):
- Usual Care: 30.1 [27.3, 32.9]
- Generic: 29.2 [26.4, 31.9]
- Optimized: 28.5 [25.8, 31.3]
- Opt + Chatbot: 29.4 [26.6, 32.2]
Interactions with Clinical Pharmacists
Pharmacist-patient interactions

- Over half of patients receiving messages (52.5%) responded to at least one text. Of those, 305 (9.2%) responded with a question for a clinical pharmacist.

- Patient factors associated with sending a text:
  - More likely to be enrolled at DHHA
  - More likely to be older (45-64 years, or 65-74 years)
  - Have hypertension

- 20% of patients that had questions for a clinical pharmacist had multiple questions.
Questions received by pharmacists

- Medication Related: 48.2%
- Refill Logistics: 38.4%
- Cost: 9.2%
- Other: 17.7%
Patient satisfaction
Patient satisfaction

- A sample of participants (n=1,526) were sent a post-implementation satisfaction survey via text. We received 100 survey responses (response rate = 6.5%; 76 English speakers and 24 Spanish speakers).

- The survey revealed high levels of satisfaction with the intervention, especially among Spanish speaking populations.
  - Spanish-preferring patients were more likely to rate messages as helpful and to indicate that they would participate in a similar intervention in the future
  - There were no language-based differences in privacy concerns or confusion regarding messages
Patient satisfaction

- **Satisfaction**: 64% were mostly or completely satisfied with the messages.
- **Utility**: 43% reported the nudges helped them remember to refill medications.
- **Trust**: 27% had concerns about privacy.
- **Clarity**: 28% were confused by the messages.
General lessons learned

- Text message intervention improved medication refill adherence
- Effectiveness consistent regardless of type of message delivered
- Differential impact of intervention across some patient groups
- Opt out approach is feasible and drop out rate was lower than expected
- Patients generally satisfied with text messages
- Patients who identified as non-white and Hispanic were more likely to remain in the study.
- Text messages can be implemented as a low cost intervention to improve medication refill adherence across different HCS with disparate EHR systems