Two Randomized Controlled Trials of Nudges to Encourage Referrals to Centralized Pharmacy Services for Evidence-Based Statin Initiation in High-Risk Patients: The SUPER LIPID Program

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Disclosures

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Gaps in evidence-based statin prescriptions

• In patients with or at high risk for ASCVD, statins reduce major adverse cardiovascular events by 33-50%

• > 50% of U.S. adults with an indication are not prescribed statins at guideline-recommended intensity

• In hypothetical patient scenarios, the vast majority of clinicians indicate they would prescribe statins to patients for whom they’re indicated

• Physicians have limited time to cover acute and preventive needs in office visits, and do not have time allocated to population health management

• Pharmacists can be used to increase statin prescriptions to appropriate patients as part of a population health management strategy, but it is uncertain how to optimize referrals of appropriate patients
Objectives

• To test two strategies for integration of centralized pharmacy services for lipid management into clinician workflow:
  • Interruptive, pop-up EHR notification strategy (visit-based)
  • Asynchronous strategy (non-visit-based)
Methods

• Two parallel clinical trials:
  • Stepped wedge trial of visit-based interruptive pop-up EHR notification with recommendation to refer patients to centralized pharmacy for consideration of statin initiation versus usual care
  • Cluster randomized trial of non-visit-based, automatically-placed orders for referral to centralized pharmacy for consideration of statin initiation versus usual care
Patient population

• Eligible patients identified via EHR algorithms
• Patients assigned a primary care provider at participating clinics who were not prescribed a high- or moderate-intensity statin, despite an indication:
  • ASCVD risk > 10% by pooled cohort equation
  • Diabetes mellitus
  • LDL-C > 190 mg/dl
  • Familial hyperlipidemia
  • Established ASCVD

• Exclusion criteria:
  • Documented allergy or intolerance to statins
  • GFR < 30 ml/min or on hemodialysis
  • Prescribed PCSK9 inhibitor
  • Pregnant or breast-feeding
  • Hospice
Trial sites
Methods – pharmacist protocol

• Upon receiving a referral, pharmacists reviewed the chart and confirmed that the patient was appropriate for treatment with statin
  • Patients with contraindications to statin initiation and those who had declined statins when offered by a clinician within the past 2 years were not contacted

• Pharmacists then called the patients, discussed initiation of statins, and (if the patient agreed) prescribed a statin and ordered follow-up labs as indicated
Methods – stepped wedge RCT of visit-based intervention

- Patients with an indication for high- or moderate-dose statin but not treated
- 16 PCPs randomly assigned
  - Group 2
  - Group 1

- Usual care
  - Month 0-3

- Interruptive pop-up during patient encounters for pharmacist referral for statin initiation
  - Month 3-6
  - Month 6-9

- 9-month primary outcome: % of patients prescribed statin
- Secondary outcomes:
  - % of patients prescribed statin at appropriate dose
  - % of patients who fill statin prescriptions
Methods – stepped wedge RCT of visit-based intervention

Statistical analyses and power calculation

• Analyses conducted under the intention-to-treat principle, including all patients for whom the interruptive pop-up notification appeared or would have appeared at the time of their visit

• Generalized estimating equations to compare intervention and usual care arms, with terms to account for clustering by PCP

• Assuming each PCP sees an average of 60 eligible patients per 3-month block (total n = 2880), ICC of 0.05, and baseline prescription rate of 30% in the usual care arm  ➔ 80% power to detect an OR 1.6, corresponding to a 10.7% absolute increase in statin prescriptions
## Results – stepped wedge RCT of visit-based intervention

### Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 970)</th>
<th>Group 2 (n = 672)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BPA started</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>68.9 ± 10.1</td>
<td>67.8 ± 9.2</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Female sex</strong></td>
<td>35.9%</td>
<td>55.4%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Black race</strong></td>
<td>1.0%</td>
<td>1.0%</td>
<td>0.69</td>
</tr>
<tr>
<td><strong>Hispanic</strong></td>
<td>0.8%</td>
<td>0.9%</td>
<td>0.83</td>
</tr>
<tr>
<td><strong>ASCVD risk by PCE</strong></td>
<td>19.7 ± 10.8%</td>
<td>18.4 ± 10.1%</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>Baseline LDL</strong></td>
<td>101 ± 33</td>
<td>111 ± 34</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>74.8%</td>
<td>70.8%</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>Current smoker</strong></td>
<td>12.9%</td>
<td>12.6%</td>
<td>0.39</td>
</tr>
</tbody>
</table>
Results – stepped wedge RCT of visit-based intervention

Response to notification

• PCPs saw the notification ~ 11.5 times per month

• Overall notification fired 3579 times in 913 patients over 6 months

• An order was entered in response to the notification 165 times (4.6% of all BPA firings, 18% of all patients)
Results – stepped wedge RCT of visit-based intervention

Any statin prescription

<table>
<thead>
<tr>
<th>Group</th>
<th>Notification active</th>
<th>Usual care</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months 1-3</td>
<td>14.9</td>
<td>10.9</td>
<td>14.6</td>
</tr>
<tr>
<td>Months 4-6</td>
<td>17.6</td>
<td>10.6</td>
<td></td>
</tr>
<tr>
<td>Months 7-9</td>
<td>16.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Months: 1-3, 4-6, 7-9

Group 1: Notification active

Group 2: Usual care, Intervention
Results – stepped wedge RCT of visit-based intervention

Any statin prescription

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<th>Group 2</th>
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<tr>
<td>Months 7-9</td>
<td>16.5</td>
<td>10.6</td>
</tr>
</tbody>
</table>

OR 1.43 (95% CI 1.02-2.00) for intervention vs. usual care
Results – stepped wedge RCT of visit-based intervention

Statin prescription at appropriate dose

<table>
<thead>
<tr>
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<th>Group 2</th>
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<tbody>
<tr>
<td>Months 1-3</td>
<td>Notification active</td>
<td>Notification active</td>
</tr>
<tr>
<td>Months 4-6</td>
<td>8.0</td>
<td>8.9</td>
</tr>
<tr>
<td>Months 7-9</td>
<td>9.3</td>
<td>4.3</td>
</tr>
<tr>
<td></td>
<td>9.0</td>
<td>5.2</td>
</tr>
</tbody>
</table>

% prescribed any statin

Group 1: Usual care vs. Intervention
Group 2: Usual care vs. Intervention
Results – stepped wedge RCT of visit-based intervention
Statin prescription at appropriate dose

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<tbody>
<tr>
<td>Months 1-3</td>
<td>8.0</td>
<td>4.3</td>
</tr>
<tr>
<td>Months 4-6</td>
<td>9.3</td>
<td>5.2</td>
</tr>
<tr>
<td>Months 7-9</td>
<td>9.0</td>
<td>8.9</td>
</tr>
</tbody>
</table>

- Notification active

OR 1.47 (95% CI 0.85-1.47) for intervention vs. usual care
Methods – cluster RCT of non-visit-based intervention

1950 patients with an indication for high- or moderate-dose statin but not treated

10 primary care practices randomly assigned

Usual care

Pended orders entered for referral to pharmacist for statin initiation, independent of in-person visit

6-month primary outcome: % of patients prescribed statin

Secondary outcomes:
- % of patients prescribed statin at appropriate dose
- % of patients who fill statin prescriptions
Methods – cluster RCT of non-visit-based intervention

Statistical analyses and power calculation

• Analyses conducted under the intention-to-treat principle: eligible patients were identified prior to the start of the intervention period, and were analyzed in the group to which they were assigned (even if they became ineligible prior to being contacted by pharmacy)

• Generalized estimating equations to compare intervention and usual care arms, with terms to account for clustering by practice

• 10 practices with ~ 195 patients per practice (n = 1950), ICC of 0.05, and baseline prescription rate of 30% in the usual care arm 80% power to detect a 12.1% absolute increase in statin prescriptions
## Results – cluster RCT of non-visit-based intervention

### Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n = 975)</th>
<th>Usual care (n = 975)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63.3 ± 10.3</td>
<td>64.6 ± 9.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Female sex</td>
<td>45.6%</td>
<td>41.8%</td>
<td>0.09</td>
</tr>
<tr>
<td>Black race</td>
<td>5.6%</td>
<td>5.2%</td>
<td>0.006</td>
</tr>
<tr>
<td>Hispanic</td>
<td>6.2%</td>
<td>7.9%</td>
<td>0.26</td>
</tr>
<tr>
<td>ASCVD risk by PCE</td>
<td>17.4 ± 9.2%</td>
<td>16.7 ± 8.4%</td>
<td>0.23</td>
</tr>
<tr>
<td>Baseline LDL</td>
<td>118 ± 33</td>
<td>115 ± 43</td>
<td>0.005</td>
</tr>
<tr>
<td>Hypertension</td>
<td>63.4%</td>
<td>57.0%</td>
<td>0.004</td>
</tr>
<tr>
<td>Current smoker</td>
<td>24.1%</td>
<td>15.0%</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
Results – cluster RCT of non-visit-based intervention
Response to orders placed for cosign

- 719 orders cosigned (73.7%) and referral to centralized pharmacy initiated

- Target dose statin started: 28%
- Patient declined statin: 19%
- Patient not reached: 18%
- Patient considering statin: 12%
- Statin contraindicated: 10%
- Patient previously declined statin: 8%
- Other: 6%
Results – cluster RCT of non-visit-based intervention
Any statin prescription

- Usual care: 15.2%
- Intervention: 31.6%

% prescribed any statin

50
45
40
35
30
25
20
15
10
5
0

Usual care
Intervention
Results – cluster RCT of non-visit-based intervention
Any statin prescription

- Usual care: 15.2%
- Intervention: 31.6%

OR 2.22 (95% CI 1.47-3.37) for intervention vs. usual care
Results – cluster RCT of non-visit-based intervention
Appropriate dose statin prescription

% prescribed statin at appropriate dose

Usual care | Intervention
---|---
7.7 | 24.8
Results – cluster RCT of non-visit-based intervention

Appropriate dose statin prescription

OR 6.79
(95% CI 4.00-11.53)
for intervention vs. usual care
Limitations

• Visit-based trial did not reach enrollment goal
• Randomization at the level of practice and physician imbalance between groups
• No direct comparison between BPA and pended order strategies
• No data collected on statin adherence or effects on longer-term cardiovascular event rates
Conclusions

• In two simultaneous pragmatic trials:
  • An asynchronous strategy of orders to centralized pharmacy placed for cosign increased prescriptions of any statin by 16 percentage points versus usual care, and of appropriate dose statin by 17 percentage points
  • An interruptive EHR notification strategy had a smaller effect on statin prescriptions and no effect on appropriate dose statin prescription
• A centralized asynchronous model could be an effective adjunct to visit-based clinical interactions in increasing statin prescribing for high-risk patients
Thanks to the team!

PennMedicine downtown
• Kayla Clark, MPH
• Laurie Norton, MPH
• Srinath Adusumalli, MD
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• Kevin Volpp, MD, PhD

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• Wendell Kellum, MD
• Dwight Eichelberger, MD
• John Wood, MD
• Zachary Bricker, MSN, RN
• Andrea Dooley-Wood, PharmD
• Greta Kemmer, PharmD
• Jennifer Smith, PharmD
ASCVD Risk Reduction Initiative

Innovation in Heart Disease Prevention
ASCVD RISK REDUCTION INITIATIVE

Extra slides
Implications

• What are the clinical implications of a 17 percentage point increase in prescriptions of statins in high-risk patients?
100 patients with an indication for a statin, not prescribed a statin...
75 not prescribed a statin
8 prescribed a statin in the course of usual care
17 prescribed a statin by involving centralized pharmacy
ASCVD risk = 17% risk of CV death, MI, stroke over 10 years
Relative risk reduction from statins = 33%
ASCVD risk of this group, after statin initiation = ~ 11%
Absolute risk reduction = ~ 6%
Number needed to treat = ~ 17
ASCVD risk = 17% risk of CV death, MI, stroke over 10 years
Relative risk reduction from statins = 33%
ASCVD risk of this group, after statin initiation = ~ 11%
Absolute risk reduction = ~ 6%
Number needed to treat = ~ 17

1 cardiovascular event saved per 100 orders placed