Increasing Medication Adherence

JENNA NEGRELLI, PHARMD, BCPS
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Disclosures

• I have no disclosures to report
Objectives

• Understand the current state of medication adherence
• Identify factors influencing medication adherence
• Develop patient specific strategies to increase medication adherence
• Utilize available resources within Intermountain to improve medication adherence
THE CURRENT STATE
Measuring adherence is hard

- Taking ≥ 80% of the doses
- Refill records
- Self-reporting as a yes or no question
- Self-reported Morisky-Green questionnaire (MAQ) ≥ 16
  1. Some people forget to take their medications. How often does this happen to you?
  2. Some people miss out a dose of their medication or adjust it to suit their own needs. How often do you do this?
  3. Some people stop taking their medication when they feel better. How often do you do this?
  4. Some people stop taking their medication when they feel worse. How often do you do this?
Prevalence and Economic Burden of Cardiovascular Disease (CVD)
# Improvements in Long-Term Mortality After Myocardial Infarction (MI) and Increased Use of Cardiovascular (CV) Drugs After Discharge

<table>
<thead>
<tr>
<th>Data source</th>
<th>Pharmacy assistance programs and Medicare in New Jersey and Pennsylvania (1995 to 2004)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study population</td>
<td>Patients with MI who survived 30 days after discharge</td>
</tr>
<tr>
<td>Endpoint</td>
<td>Mortality</td>
</tr>
<tr>
<td>Covariates</td>
<td>Age, gender, race, comorbidities, and coronary interventions during the MI hospitalization and recorded filled prescriptions for statins, BBs, ACEIs/ARBs, or antiplatelet agents within 30 days after discharge</td>
</tr>
</tbody>
</table>
| Results | N = 21,484  
Average age of 80, 73% female, 62% CAD, 66% HF, 46% diabetes, 32% cerebrovascular disease, and 17% CKD  
Showed a 3% reduction in mortality per year from 1995 to 2004 |

CAD = coronary artery disease, HF = heart failure, CKD = chronic kidney disease
Improvements in Long-Term Mortality After MI and Increased Use of CV Drugs After Discharge

<table>
<thead>
<tr>
<th>Medication</th>
<th>1995 (% use)</th>
<th>2004 (% use)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blockers</td>
<td>41.5</td>
<td>71.6</td>
</tr>
<tr>
<td>ACEi/ARBs</td>
<td>39.2</td>
<td>50.0</td>
</tr>
<tr>
<td>Statins</td>
<td>7.6</td>
<td>50.7</td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>2.6</td>
<td>50.9</td>
</tr>
</tbody>
</table>

P values < 0.001 for each medication

ARB = angiotensin receptor blocker
ACEi = angiotensin converting enzyme inhibitor
A poll of your colleagues

What is your profession?

- **Nurse**: 10%
- **Pharmacist**: 60%
- **Provider (MD, NP, PA)**: 20%
- **Other healthcare...**: 0%

How many years have you been in practice?

- **<1**
- **1-5**
- **6-10**
- **11-15**
- **>15**
Why do you think patients are non-compliant?

1. Cost
2. Pill burden
3. Complexity of regimen
4. Side effects
5. Stigma
6. Low health literacy
7. Not told about benefits of the medication
8. Not told about the harms of the disease state
9. Forgetfulness
Survey Results: why do you think your patients are non-compliant with medications?

1. Cost
2. Low health literacy
3. Pill burden
4. Complexity of regimen
5. Side effects
6. Forgetfulness
7. Not told about benefits of the medication
8. Not told about the dangers of an uncontrolled disease state
9. Stigma
Why are you non-compliant?

1. Cost
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5. Stigma
6. Low health literacy
7. Not told about benefits of the medication
8. Not told about the harms of the disease state
9. Forgetfulness
Survey Results: why are you non-compliant to medications?

1. Forgetfulness (6)
2. Cost (1)
3. Side effects (5)
4. Pill burden (3)
5. Complexity of regimen (4)
6. Stigma (9)
7. Not told about the dangers of an uncontrolled disease state (8)
8. Not told about benefits of the medication (7)
9. Low health literacy (2)
POTENTIAL SOLUTIONS
According to this CEO of a pharmaceutical company, raising the cost of a medication from $13.50 per pill to $750 overnight was “altruistic”
### MI FREE: Full Coverage for Preventive Medications After MI

<table>
<thead>
<tr>
<th><strong>Design</strong></th>
<th>Cluster-randomized, controlled trial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inclusion</strong></td>
<td>Patients with Aetna insurance who were discharged post MI and were &lt;65 years old</td>
</tr>
</tbody>
</table>
| **Intervention** | • Full prescription coverage versus usual prescription coverage for statins, β-blockers, and ACEi/ARBs  
• All patients were called to tell them of the importance of taking medications  
• Patients in the full coverage group were also told that their pharmacy benefits had changed and they would receive the above medications at no cost |
| **Primary outcome** | Composite of the first readmission for a major vascular event (fatal or nonfatal MI, unstable angina, stroke, or CHF) or coronary revascularization (CABG or PCI). |

CABG = coronary artery bypass graft, PCI = percutaneous coronary intervention

MI FREE: Full Coverage for Preventive Medications After MI – Adherence

Medication adherence was defined as medication possession of ≥80%

Medication possession = # of days a patient had a supply of the medication ÷ # of days of eligibility for that medication

<table>
<thead>
<tr>
<th>Variable</th>
<th>Full Prescription Coverage</th>
<th>Usual Prescription Coverage</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>789/2845 (27.7)</td>
<td>689/3010 (22.9)</td>
<td>1.31 (1.14–1.49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACE inhibitor or ARB</td>
<td>873/2845 (30.7)</td>
<td>758/3010 (25.2)</td>
<td>1.32 (1.16–1.49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>1097/2845 (38.6)</td>
<td>950/3010 (31.6)</td>
<td>1.37 (1.20–1.56)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Statin</td>
<td>344/2845 (12.1)</td>
<td>268/3010 (8.9)</td>
<td>1.41 (1.18–1.67)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>All three medication classes</td>
<td>344/1385 (24.8)</td>
<td>268/1389 (19.3)</td>
<td>1.36 (1.12–1.65)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Patients who filled at least one prescription

<table>
<thead>
<tr>
<th>Variable</th>
<th>Full Prescription Coverage</th>
<th>Usual Prescription Coverage</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitor or ARB</td>
<td>789/1759 (44.9)</td>
<td>689/1775 (38.8)</td>
<td>1.28 (1.10–1.49)</td>
<td>0.002</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>873/2159 (40.4)</td>
<td>758/2224 (34.1)</td>
<td>1.31 (1.14–1.50)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Statin</td>
<td>1097/2223 (49.3)</td>
<td>950/2267 (41.9)</td>
<td>1.36 (1.18–1.56)</td>
<td>&lt;0.001</td>
</tr>
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<td>All three medication classes</td>
<td>344/1385 (24.8)</td>
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</tr>
</tbody>
</table>
MI FREE: Full Coverage for Preventive Medications After MI – Clinical Outcomes

The mean total spending for the insurance company for all medical costs was $66,008 in the full-coverage group and $71,778 in the usual-coverage group, a non-significant difference (relative spending, 0.89; 95% CI, 0.50 to 1.56; P = 0.68).

Table 3. Clinical Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Full Prescription Coverage (N = 2845)</th>
<th>Usual Prescription Coverage (N = 3010)</th>
<th>Hazard Ratio† (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. rate/100 person-yr</td>
<td>no. rate/100 person-yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First event</td>
<td>493 17.6</td>
<td>562 18.8</td>
<td>0.93 (0.82–1.04)</td>
<td>0.21</td>
</tr>
<tr>
<td>Total events</td>
<td>622 21.5</td>
<td>729 23.3</td>
<td>0.89 (0.80–0.99)</td>
<td>0.03</td>
</tr>
<tr>
<td>First fatal or nonfatal vascular event</td>
<td>329 11.0</td>
<td>405 12.8</td>
<td>0.86 (0.74–0.99)</td>
<td>0.03</td>
</tr>
<tr>
<td>Individual components of outcome‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction or unstable angina</td>
<td>187 6.0</td>
<td>236 7.1</td>
<td>0.84 (0.70–1.02)</td>
<td>0.08</td>
</tr>
<tr>
<td>Stroke</td>
<td>60 1.8</td>
<td>92 2.6</td>
<td>0.69 (0.50–0.96)</td>
<td>0.03</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>150 4.8</td>
<td>182 5.4</td>
<td>0.87 (0.70–1.08)</td>
<td>0.21</td>
</tr>
<tr>
<td>Revascularization</td>
<td>293 9.8</td>
<td>298 9.1</td>
<td>1.06 (0.90–1.24)</td>
<td>0.51</td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>57 1.7</td>
<td>72 2.0</td>
<td>0.85 (0.60–1.21)</td>
<td>0.36</td>
</tr>
</tbody>
</table>
Resources

• **30 day free trial cards**
  – Apixaban, rivaroxaban, prasugrel, ticagrelor

• **Co-pay assistance cards**
  – Apixaban, rivaroxaban, prasugrel, ticagrelor, dofetilide
  – GoodRx app (or website: http://www.goodrx.com)

• **Assistance programs for low income patients without prescription insurance**
  – Many medications via company website based on income and persons in the household
  – Ex: prasugrel: < $47,790 for 2 person household through Lilly TruAssist
  – ticagrelor: < $48,000 for 2 person household through AZ&Me
COUNSELING
Project PhARMD: Pharmacist Assisting at Routine Medical Discharge

- **Standard group**
  A nurse reviewed discharge prescriptions with the patient
  - Discussion of the discharge prescriptions was required, but not standardized between units and nurses

- **Intervention group**
  In addition to standard care, a pharmacist provided
  - Discharge counseling
  - Medication reconciliation on discharge orders
  - Follow up phone call 36-72 hours post discharge

Project PhARMD: Pharmacist Assisting at Routine Medical Discharge

Results

•  N = 279

• Medication adherence (assessed by prescription refill data) was 58.5% and 75.7% in the control and intervention groups, respectively (P = 0.05).

• The intervention group had a significantly higher patient satisfaction score.

• No difference in hospitalization or emergency department (ED) visit.

• The only predictor of ED visit/readmission was previous hospitalization in the past year (odds ratio = 1.27; 95% confidence interval = 1.06-1.51; P = 0.008).

The Effect of Pharmacotherapeutic Counseling on Readmissions and ED Visits

<table>
<thead>
<tr>
<th>Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prospective, randomized, single center controlled trial</td>
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</table>

<table>
<thead>
<tr>
<th>Inclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elderly patients admitted over a 3 month period to a hospital in Croatia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intervention Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard of care vs. physician provided counseling on:</td>
</tr>
<tr>
<td>- Indication, dosage, timing, importance of compliance</td>
</tr>
<tr>
<td>- Consequences of non-compliance and possible ADRs</td>
</tr>
<tr>
<td>- ADRs: Prevention, early detection, and what do to if occurs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcomes at 30 days (N = 130)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Significantly higher compliance rates in intervention group compared to control group, 89% vs. 54% respectively (p &lt;0.001)</td>
</tr>
<tr>
<td>• No difference in readmission rates or ED visits</td>
</tr>
</tbody>
</table>

ADRs: adverse drug reactions
Resources

• Nurses stress medication adherence during “MAWDS” teaching
• Diabetic educators are available for counseling
• Pharmacists are trying to increase the number of patients they counsel on medications prior to discharge. Pharmacists are flagging patients for counseling if they meet one of the following criteria:
  – High risk for readmission heart failure patients
  – A1c >9%
  – New start antiplatelet or anticoagulant medications
  – Digoxin
  – > 10 home medications
  – Patients who get their medications filled at our pharmacy prior to discharge
A tough act to swallow when your pill box looks like this

PILL BURDEN
## “Polypills” studied

<table>
<thead>
<tr>
<th>Study</th>
<th>Antiplatelet</th>
<th>Statin</th>
<th>Diuretic</th>
<th>ACEi/ARB</th>
<th>Beta-blocker</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TIPS</strong></td>
<td>Aspirin 100 mg</td>
<td>Simvastatin 20 mg</td>
<td>HCTZ 12.5 mg</td>
<td>Ramipril 5 mg</td>
<td>Atenolol 50 mg</td>
</tr>
<tr>
<td><strong>PolyIran</strong></td>
<td>Aspirin 81 mg</td>
<td>Atorvastatin 20 mg</td>
<td>HCTZ 12.5 mg</td>
<td>Enalapril 2.5 mg</td>
<td>X</td>
</tr>
<tr>
<td><strong>Combination therapy trial</strong></td>
<td>Aspirin 75 mg</td>
<td>Simvastatin 10 mg</td>
<td>HCTZ 10 mg</td>
<td>Lisinopril 10 mg</td>
<td>X</td>
</tr>
<tr>
<td><strong>IMPACT &amp; UMPIRE</strong></td>
<td>Aspirin 75 mg</td>
<td>Simvastatin 40 mg</td>
<td>HCTZ 12.5 mg or atenolol</td>
<td>Lisinopril 10 mg</td>
<td>Atenolol 50 mg or HCTZ</td>
</tr>
<tr>
<td><strong>HOPE-3</strong></td>
<td>X</td>
<td>Rosuvastatin 10 mg</td>
<td>HCTZ 12.5 mg</td>
<td>Candesartan 16 mg</td>
<td>X</td>
</tr>
<tr>
<td><strong>FOCUS</strong></td>
<td>Aspirin 100 mg</td>
<td>Simvastatin 40 mg</td>
<td>X</td>
<td>Ramipril 2.5, 5 or 10 mg</td>
<td>X</td>
</tr>
</tbody>
</table>
A Polypill Strategy to Improve Global Secondary Cardiovascular Prevention: From Concept to Reality

- Adherent: ≥ 80% of medication taken
- IMPACT and UMPIRE showed small decreases in LDL and BP in polypill arm, Kanyini-GAP showed no difference
FOCUS: A Polypill Strategy to Improve Adherence

| Design          | Phase 1: observational, prospective, cross-sectional study  
<table>
<thead>
<tr>
<th></th>
<th>Phase 2: randomized, open-label, active-controlled trial</th>
</tr>
</thead>
</table>
| Patients        | Argentina, Brazil, Italy, Paraguay, and Spain            
|                 | Phase 1: age ≥ 40 years with a history of acute MI within the last 2 years  
|                 | Phase 2: patients in phase 1 who did not have exclusion criteria including, secondary dyslipidemia, previous PCI with a DES within the previous year, severe CHF, SCr >2 mg/dl, any condition limiting life expectancy <2 years, and pregnancy or pre-menopause |
| Objectives      | Phase 1: identify factors contributing to inadequate adherence to treatment  
|                 | Phase 2: assess the percentage of patients taking medication adequately at 9 months (adherence measured by attendance at the final 9-month visit and the MAQ + pill count methods, simultaneously) |

DES = drug eluting stent, SCr = serum creatinine
FOCUS: A Polypill Strategy to Improve Adherence

**TABLE 3** Multivariable Analysis of Variables That Independently Contribute to Adherence, Phase 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;50 yrs</td>
<td>1.50</td>
<td>1.08-2.09</td>
<td>0.015</td>
</tr>
<tr>
<td>Score depression</td>
<td>1.07</td>
<td>1.04-1.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Score social support</td>
<td>0.94</td>
<td>0.92-0.96</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% insurance coverage</td>
<td>1.00</td>
<td>0.99-1.00</td>
<td>0.025</td>
</tr>
<tr>
<td>Complexity of treatment</td>
<td>1.42</td>
<td>1.00-2.02</td>
<td>0.047</td>
</tr>
</tbody>
</table>

(A) Primary Outcome (ITT)  
\[ p=0.019 \]

(B) Morisky-Green (20)  
\[ p=0.049 \]
Resources

- No cardiovascular “polypills” are available at this time
- Several combination pills are available
- However, most are still brand name only and more expensive than individual generic medications
There’s an app for that

And a website: http://www.goodrx.com/

TECHNOLOGY
Technology

- Currently, one in five American adults use some technology to track health data and the most popular health apps downloaded are related to exercise, counting steps, or heart rate.

- In 2013 a study was conducted by pharmacists assessing available apps to help with medication adherence.
  - Found 160 different apps
  - Article available online: http://www.medscape.com/viewarticle/782609

COMBINATION
Maximizing Medication Adherence in Low-Income Hypertensive Patients

• Hypertensive management program
  – Multidisciplinary staff included attendings, Internal Medicine residents, a pharmacist, psychology students, a nurse and a blood pressure technician
  – Held clinic 2 afternoons weekly

• Interventions
  – Patients were seen biweekly x 4 months then every 4-6 weeks for 6 months total
  – Medications were provided free of charge
  – Education about hypertension and strategies to improve compliance
Maximizing Medication Adherence in Low-Income Hypertensive Patients

- Patients (N=60) only received free medication if they went to clinic appointments.
- Approximately 83% of appointments were kept, providing soft adherence data.
- The percentage of patients whose blood pressure was controlled (<140/90 mmHg) increased drastically at 6 months compared to baseline, 63% versus 12% respectively.

| Age | 47 years |
| Education | 11 years |
| Family income | $830/month |
| Female | 70% |
| African American | 77% |
| Marital Status | |
| Single | 27% |
| Married | 40% |
| Divorced/separated | 25% |
| Widowed | 8% |

BP (mmHg) at Baseline and 6-Months:

- SBP: Baseline 160 mmHg, 6-Months 150 mmHg
- DBP: Baseline 90 mmHg, 6-Months 80 mmHg

Significance: P < 0.001
Summary

• Medication non-adherence is multifaceted
• The following have potential to increase adherence
  – Decreasing cost
  – Decreasing pill burden
  – Increasing counseling/patient education
  – Possibly using technology?
  – Using a multi-disciplinary approach
• Individualize your approach based on the specific patient
When will we completely eliminate non-compliance?
Questions
Pharmacists: Receiving CE Credit

- CE provided by the California Society of Health-System Pharmacists
- Log-in to [http://ihc.cshp.wcea.education](http://ihc.cshp.wcea.education) (First time only: create account)
- *Do not use Internet Explorer as your browser*
- Click ‘Add Live Event’ on left menu
- Enter Secret Code (case-sensitive): 8 c 4 K
- Then ‘Validate Code’
- Answer “No” to exam and upload certificate questions
- Choose ‘Fill Out’ for Evaluation Statement
- Complete evaluation and click ‘Save Changes’