Overcoming Barriers to Medication Adherence for Chronic Diseases
Understanding Barriers to Medication Adherence

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Extent of Nonadherence Across the Population

At any given time ~50% of patients are non-adherent.

For every 100 prescriptions written:
- Filled by the pharmacy: 100
- Picked up from the pharmacy: 50-70
- Taken properly: 48-66
- Refilled as prescribed: 25-30

15-20

Adherence is the process by which patients take their medications as prescribed.

- **Initiate**
  - Patient does not initiate treatment
  - *Binary (yes/no)*

- **Implement**
  - Patient delays, omits or takes extra doses
  - *Dosing history*

- **Persist**
  - Patient discontinues treatment
  - *Time to event*

Different forms of nonadherence

Medication nonadherence in the U.S. costs $100 billion–$300 billion per year

33%–69% of hospital admissions are due to nonadherence

Good adherence reduces adverse events and mortality

PDC = Proportion of days covered (adherence measured with pharmacy refill data)
Nonadherence is multifactorial

- **Socioeconomic factors**
  - Lower social economic status associated with lower adherence

- **Health care system factors**
  - Team-based care and post-hospital follow-up improve adherence

- **Medical condition-related disease factors**
  - Concomitant conditions and comorbidities can impact adherence

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More Factors that Impact Adherence

- **Therapy-related factors**
  - Side effects of medications
  - Number and different types of pills to be taken
  - Complexity or changes to regimen

- **Patient-related factors**
  - Understanding of disease, its course and possible complications
  - Expectations of improvement on medication
  - Perceptions of symptoms, either improving or worsening

Medication Adherence Interventions Can Impact Nonadherence

Meta-Analyses of Medication Adherence Intervention Outcomes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Studies</th>
<th>Total Number of Patients</th>
<th>Effect size</th>
<th>95% C.I.</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>112</td>
<td>34,272</td>
<td>0.42</td>
<td>0.32, 0.52</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>28</td>
<td>18,839</td>
<td>0.23</td>
<td>0.14, 0.32</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Heart failure</td>
<td>29</td>
<td>4,285</td>
<td>0.29</td>
<td>0.09, 0.48</td>
<td>.004</td>
</tr>
</tbody>
</table>


Understanding Interventions Impact on Nonadherence

- Evaluating the effect of an intervention on adherence
  - Medication adherence needs to be measured in valid, reliable and cost-effective ways
  - Lack of valid, reliable, and cost-effective ways to measure the impact of an intervention on medication adherence prevents scale-up of interventions to wider clinical practice

Adherence intervention studies often include a mix of adherent and non-adherent patients

For patients with good adherence, little or no room to improve
- Limits the effect when measuring outcomes
- Allocates intervention resources poorly
Unintentional vs. Intentional Nonadherence

- Most interventions are not designed to assess the reasons for nonadherence
- Unintentional nonadherence will require a different approach than intentional nonadherence
Intervention Effects Will Vary Based on Intervention Type

- Education and cognitive-focused interventions tend not to change behavior
- Need more innovative social support interventions
- Need better understanding of variation in adherence by diseases and type of patients
Intervention Effects Will Vary Based on Intervention Type

- **Multilevel interventions are needed**
- **Focus beyond providers**
- **Barriers exist at patient, provider, and systems levels**

**Cognitive**
- Knowledge
- Attitudes
- Beliefs
- Norms

**Behavioral**
- Skills, abilities
- Reminders, cues
- Contractual obligations

**Motivation/Intention**
- Motivation to change
- Intent to change
- Reward/Benefit (level-specific)

**Environment/Policy**
- National/state/local policies
- Institutional policies
- Home/Work environment
- Resources

Overcoming Unintentional Nonadherence

- For patients with unintentional nonadherence, packaging interventions are cost-effective first steps
  - Pillboxes
  - Blister packs
- Integrating medication taking into existing habits and routines can be helpful
  - Uses behavior prompt to remember medication
  - Can be external reminder, phone alarm or medication log
Larger Intervention Doses Tend to Be More Effective

- **Intervention delivery method matters**
  - Face-to-face are more effective, but more expensive
  - Trials of face-to-face with mobile health follow-up may be more effective than just making mobile health tools available

- **Intervention dose makes a difference**
  - Measured as either number of times or length of time meeting with patient

- **How to sustain improved adherence beyond the intervention?**
Challenges

➢ Need interventions that incorporate health disparities
  ● Same disparities seen in disease are seen in adherence

➢ Further distinguish between reasons for nonadherence
  ● Unintentional vs. intentional
  ● Social determinants of health

One year of blister packs for one patient
Next Steps

➢ Need better ways to measure adherence, especially for clinical settings
  ● Integration of pharmacy data and patient-reported data
  ● Communication between electronic monitoring and electronic health records

➢ Move from interventions to long-term solutions that support patients
Multifaceted Interventions Improve Adherence

P. Michael Ho, MD, PhD
Staff Cardiologist, VA Eastern Colorado Health Care System
Professor of Medicine, University of Colorado Anschutz Medical Campus
Patient Case: Mr. A

- Dec 2010: Presents with initial heart attack; stent placed and started on antiplatelet medication
- May 2011: Second heart attack; different stent type placed
- Nov 2011: Third heart attack; switched to different antiplatelet medication
- June 2012: Fourth heart attack

Angiograms from May 2011
Medication Discontinuation Occurs Earlier Than Expected

Rates of Medication Use for the Entire Cohort, By Drug Type and All 3 Medications

% of Population Adherent to Medication

Drug Type

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Discharge</th>
<th>1-month</th>
<th>6-month</th>
<th>12-month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>~9%</td>
<td>~9%</td>
<td>~9%</td>
<td>~9%</td>
</tr>
<tr>
<td>Beta-Blocker</td>
<td>~13%</td>
<td>~13%</td>
<td>~13%</td>
<td>~13%</td>
</tr>
<tr>
<td>Statin</td>
<td>~20%</td>
<td>~20%</td>
<td>~20%</td>
<td>~20%</td>
</tr>
<tr>
<td>All 3 meds</td>
<td>~30%</td>
<td>~30%</td>
<td>~30%</td>
<td>~30%</td>
</tr>
</tbody>
</table>

Prematurely Stopping Therapy Is Associated with Subsequent Mortality

1 in 7 patients with heart attack who receive a stent are no longer taking clopidogrel by 30 days.

1 in 6 patients who receive a stent do not fill clopidogrel prescription.

Kaplan-Meier Mortality Curves 1 to 12 months after MI, By Thienopyridine Therapy at 1 Month after MI

<table>
<thead>
<tr>
<th>N at Risk</th>
<th>Continued</th>
<th>Discontinued</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>431</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>431</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>430</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td>429</td>
<td>65</td>
</tr>
<tr>
<td></td>
<td>420</td>
<td>62</td>
</tr>
</tbody>
</table>
Eliminating Co-pays and Costs Can Improve Adherence BUT Still There is Room for Improvement

Drug Type

ACEi or ARB  Beta-Blocker  Statins  All 3 Classes

Medication Adherence During Follow-up Among Patients Filling At Least One Prescription, 2008–2010

Percent of Patients

Full Coverage  Usual Care

ACEi: Angiotensin-converting-enzyme inhibitors
ARB: Angiotensin-receptor blockers
Intentional and Unintentional Reasons for Nonadherence

Self-Reported Reasons for Nonadherence

- Forgot: 42%
- Ran out: 34%
- Away from home: 27%
- Trying to save money: 22%
- Had side effects: 21%
- Was too busy: 17%
- Rx wasn't working: 17%
- Didn't think Rx was needed: 16%
- Didn't like taking it: 12%

Multifaceted Intervention to Improve Cardiac Medication Adherence and Secondary Prevention Measures (MEDICATION) Study

Hospitalization for acute myocardial infarction or unstable angina

Higher Adherence in Patients Receiving Multifaceted Intervention

**Proportion of Patients Adherent to Medications**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Intervention</th>
<th>Usual Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined</td>
<td>90</td>
<td>70*</td>
</tr>
<tr>
<td>Statin</td>
<td>90</td>
<td>70*</td>
</tr>
<tr>
<td>ACE/ARB</td>
<td>90</td>
<td>70*</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>90</td>
<td>70*</td>
</tr>
<tr>
<td>B-blocker</td>
<td>90</td>
<td>70</td>
</tr>
</tbody>
</table>

**PDC**: Proportion of days covered. The number of days the member is covered by at least one medication prescription of appropriate intensity, divided by the number of days in the treatment period. * p<0.05

## Modest Intervention Costs and Similar Total Costs at 12 Months

<table>
<thead>
<tr>
<th>Costs</th>
<th>Usual Care</th>
<th>Intervention</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>$0</td>
<td>$360</td>
<td></td>
</tr>
<tr>
<td>Cardiac medications</td>
<td>$663</td>
<td>$722</td>
<td>0.70</td>
</tr>
<tr>
<td>Total medications</td>
<td>$2,724</td>
<td>$2,887</td>
<td>0.43</td>
</tr>
<tr>
<td>Total outpatient</td>
<td>$11,691</td>
<td>$13,086</td>
<td>0.53</td>
</tr>
<tr>
<td>Total inpatient</td>
<td>$14,287</td>
<td>$11,294</td>
<td>0.68</td>
</tr>
<tr>
<td><strong>Total (intervention, medication, outpatient, and inpatient)</strong></td>
<td><strong>$19,989</strong></td>
<td><strong>$19,901</strong></td>
<td><strong>0.56</strong></td>
</tr>
</tbody>
</table>

Positive Relationships With Providers
Bidirectional Communication Key to Improving Adherence

- Mutually respectful collaboration with their providers
- Importance of hearing the patients’ perspectives and concerns
- Patients became comfortable disagreeing with the providers’ recommendations or asking clarifying questions
- Patients became active participants in the development of their treatment plan, which they believed was essential for high-quality care

Frequent Interactions With Study Pharmacists and Medication Refill Reminder Calls Improved Adherence

Two-thirds of the intervention arm had positive experiences, specifically with the study pharmacists, who were seen as supportive providers and caring people.

“... it made me think that it musta’ been more important than I thought it was ... to have these people contact me on a regular basis to make sure I was takin’ it.”

Additional Factors That Improved Adherence

➢ Important in improving their lives
  • Social support from family and friends
  • Medication-taking routines
  • Specific adherence tools

Multimodal and Team-based Interventions Can Improve Adherence

- Medication non-adherence is common
- Reasons for non-adherence are multifactorial and change over time
- Multimodal and team-based interventions that address different reasons for nonadherence are more likely to be successful
- Mutually respectful collaborations encourage patients to become active participants in the development of their treatment plan, and led to better adherence
- Interventions leveraging data and technology are needed to improve adherence while remaining cost-effective
Promoting Medication Adherence Through High-Tech and High-Touch

Larry Garber, MD  
*Medical Director, Informatics*  
*Associate Medical Director for Research*  
Reliant Medical Group
Over 500 provider multi-specialty group practice in central Massachusetts
- Not affiliated with any hospitals and not-for-profit
- Over 50% Pay-for-Performance

20,000 hypertensive patients
- In 2011, only 68% of hypertensive patients were under control, but nationally 90<sup>th</sup> percentile for control was over 72% of patients
- In 2012, Reliant initiated a hypertension control program
- Included focus on medication adherence
How to Promote Medication Adherence

- Ensure that patient understands the benefits
- Choose lower cost medications and ones that are easier to take
- Minimize medication side effects
- Show the effectiveness of the medications in lowering blood pressure
- Monitor medication adherence
Empower the Patient Through Education

- Educate on the **harms** of uncontrolled hypertension and the **benefits** of controlling hypertension
- Make education materials widely available
  - On Reliant’s trusted website
  - Automatically print on the After-Visit Summary if diagnosis of hypertension
  - Available within EHR and adjustable computer monitors designed to be visible to the patient
- Demonstrate that alternatives have failed
  - Graph of blood pressure trends within EHR prior to medications
Empower the Provider to Choose Appropriate and Lower Cost Medications

- **Use step-therapy protocols**
  - Developed by multidisciplinary team
  - Standardized across organization

- **Control access to pharmaceutical marketing**

- **Show patient’s payer-specific formulary in EHR**

- **Generic substitution mandated in state**

<table>
<thead>
<tr>
<th>Hypertension Medication Protocol Pathways</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient Characteristic</strong></td>
<td><strong>Path to Follow</strong></td>
</tr>
<tr>
<td>Black (unless presents with fluid overload)</td>
<td>Path #1</td>
</tr>
<tr>
<td>Clinical fluid overload at presentation</td>
<td>Path #2</td>
</tr>
<tr>
<td>&gt;60 years old</td>
<td>Path #3</td>
</tr>
<tr>
<td>&lt;60 or Diabetes or Renal disease (if fluid overload - go to pathway #5)</td>
<td>Path #4</td>
</tr>
<tr>
<td>Diabetic/Renal disease with fluid overload initially</td>
<td>Path #5</td>
</tr>
</tbody>
</table>

EHR: Electronic health record
Empower the Provider to Minimize Medication Complexity and Expense

- Choose once-a-day and combos for convenience
- Engage in dialogue about costs vs convenience
  - Pill-splitting can reduce cost but can be inconvenient for patient to split them
- Provide assistance in paying for medications
  - RxAssist.org website hyperlink within EHR
  - Consult Reliant’s social workers

EHR: Electronic health record
Minimize Medication Side Effects

➢ Be creative in addressing concerns
  • Concern about swollen feet ➔ use a diuretic
  • Concern about medication causing too high or too low potassium level ➔ combine ACE-Inhibitor + diuretic to normalize potassium

➢ Monitor side effects
  • At visits
  • At renewals, using standard template
  • After hospital discharge – automated warnings

➢ Consult Reliant’s pharmacists
  • Complex medication regimens or problems
  • After hospital discharge

ACE: Angiotensin Converting Enzyme
Show Effectiveness of Medications in Lowering Blood Pressure

- **Empower patient to record BPs at home**
  - Provide booklets to record readings
  - For financial hardship, give out free monitors
- **Free BP clinics at Reliant**
- **Automatically upload BP readings into EHR via Microsoft HealthVault®**
- **Show graphs of trends in EHR**
- **Patients can view graphs of trends at home**

**BP:** Blood pressure  
**EHR:** Electronic health records
Monitor Medication Adherence

- Surescripts® medication fill history
- Payer medication claims
  - Loaded into EHR nightly
  - Shows dates and days of supply picked up
- Review during visits
  - Knowing that clinician can be watching adherence is at least as important as seeing the results
- Automate compliance monitoring?

Display of Pharmacy Refills

EHR: Electronic health records
Hypertension Interventions’ Outcome

Reliant Medical Group
Hypertension Control

Blood Pressure Interventions
Lessons Learned

- Educate and empower patients
- Make medication adherence and BP monitoring easy for the patient
- Offload work from physician to other team members
- Patients knowing that you can monitor medication adherence may be more important than actually monitoring medication adherence
Next Steps

- Expand home BP monitoring options to include smartphone authentication and aggregation
- Consider financial incentives to patients and care team for hypertension control
Looking to the Future: Personalize Health Risk

Patient-friendly Health Risk Assessment Tools

Cardiovascular Risk | Effective Age | Cancer Risk
---|---|---
BMI | 63 | 
Cholesterol | 
Blood Pressure | 
Tobacco | 
Exercise | 
Stress | 
Seatbelts | 

Cardiovascular Risk | Effective Age | Cancer Risk
---|---|---
BMI | 58 | 
Cholesterol | 
Blood Pressure | 
Tobacco | 
Exercise | 
Stress | 
Seatbelts |

BMI: Body mass index
Broadening Public Health Approaches to Medication Adherence for HIV

CAPT Paul J Weidle, PharmD, MPH
Team Lead, Health Services Research for Prevention with HIV Positive Persons
Division of HIV/AIDS Prevention
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Medication Adherence Is Important for Treatment and Prevention in HIV Disease

- Antiretroviral treatment reduces the amount of HIV virus circulating in the blood
  - Improve immune function and health of people with HIV
  - Reduce transmission by 90% or more
  - Since 2012, recommended for all persons living with HIV in the United States

- To maximize health and prevent HIV transmission, medication adherence must achieve viral suppression
  - HIV viral load is a direct proxy for adherence to treatment and is typically tested at least twice per year
HIV Treatment That Leads to Viral Suppression Reduces HIV Transmission

- 3 out of every 5 new HIV infections can be attributed to people who have been diagnosed with HIV but are not in care.

- Few HIV transmissions occur when care is optimized and viral suppression is achieved.

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ART: Antiretroviral treatment
National HIV/AIDS Strategy Goals by 2020

- Reduce new HIV infections
- Increase access to HIV care and improve health outcomes for people living with HIV
- Reduce HIV-related health disparities and health inequities

NATIONAL HIV/AIDS STRATEGY for the UNITED STATES:

UPDATED TO 2020

JULY 2015

aids.gov/federal-resources/national-hiv-aids-strategy/nhas-update.pdf
Goal: At least 85 percent of newly diagnosed persons are linked to HIV medical care within one month of their HIV diagnosis

- In 2014, 74.5% of persons newly diagnosed with HIV were linked to HIV medical care within one month of diagnosis
Goals by 2020 for Retention in Care and Viral Suppression

- **Goal:** At least 90 percent of persons with diagnosed HIV infection are retained in HIV medical care
  - In 2013, more than half (56.5%) of persons with diagnosed HIV infection were retained in HIV medical care

- **Goal:** At least 80 percent of persons with diagnosed HIV infection are virally suppressed
  - In 2013, more than half (54.7%) of persons with diagnosed HIV infection were virally suppressed
Health departments collect laboratory data to monitor progress towards goals

- HIV diagnostic tests
- CD4+ cell counts
- HIV viral load
- HIV resistance tests

As of December 2015, in 33 jurisdictions, at least 95% of tests are reported
The Data to Care Strategy aims to use HIV surveillance data to identify persons diagnosed with HIV who are not receiving HIV care and link them to care

- Persons who either never linked to care after diagnosis
- Persons who did not continue to receive care
Three Models to Connect Individuals to HIV Care

- **Health Department Model**
  - Health department-initiated linkage and re-engagement outreach

- **Healthcare Provider Model**
  - Healthcare provider-initiated linkage and re-engagement outreach

- **Combination Health Department and Healthcare Provider Model**
Using health department HIV surveillance database to identify individuals who are probably not in HIV medical care currently:

- Vital records status “Alive”
- Currently residing in jurisdiction
- HIV diagnosis at or before the end of a specified time period

No CD4+ cell count or viral load result during a specified time period:

- Time interval can be as short as 6 months
Finding and Connecting People to HIV Care

- **Investigate out-of-care list**
  - Fill in important information that might be missing from an individual’s record (e.g., current telephone number or address)
  - Check with the last known care provider
  - Match out-of-care list to databases internal and external to health department

- **Share key data with field services staff and care providers**

- **Reach out to individuals on the out-of-care list**
  - Identify barriers and link or re-engage into care
Evidence That the Data to Care Strategy Can Improve Re-linkage to Care

- Combined healthcare provider and health department model
- Largest HIV clinic in Washington State
  - Criteria: No visit > 12 months
- Outreach
  - Clinic-based linkage specialist
    - Phone call x 3, email x 1, call emergency contact
  - Department of health re-linkage team
- Shorter time to re-link and more re-linked to care
  - Compared to historical controls

Data to Care Strategy
Cooperative Re-engagement in Care Controlled Trial (CoRECT)

- Establish a data-sharing partnership between health departments and HIV care providers to identify HIV-infected persons who are out of care
  - Necessary to share and protect data
- Implement a health department field services intervention and identify barriers to care
  - Link to an HIV clinic within 90 days
  - Remain in HIV medical care at least 12 months
  - Achieve HIV viral load suppression within 12 months
  - Achieve durable HIV viral load suppression for 12–18 months
  - Sites in Connecticut, Philadelphia, Massachusetts

clinicaltrials.gov/ct2/show/NCT02693145?term=corect&rank=1
Multi-agency federal partnership

- Co-led by CDC and HRSA’s Bureau of Primary Health Care

Use HIV surveillance data and health-center EHR to improve HIV health outcomes for persons living with HIV who are not in care

- Sites in Florida, Maryland, Massachusetts, New York State
Data to Care Strategy
Targeted Highly Effective Intervention to Reverse the HIV Epidemic

- Implements comprehensive HIV prevention and care services for men who have sex with men
  - Includes a Data to Care strategy to re-engage them in care
  - Sites in Alabama, Baltimore, District of Columbia, Louisiana, New York City, Philadelphia, Virginia

cdc.gov/hiv/funding/announcements/ps15-1509/index.html
Data to Care Strategy
Project PrIDE

- Supports men who have sex with men and transgender persons not in HIV care and re-engage them in care
- Implementing Data to Care demonstration projects
  - Sites in Baltimore, Chicago, Houston, Louisiana, San Francisco

cdc.gov/hiv/research/demonstration/projectpride.html
By Re-engaging Persons Living with HIV In Care, Public Health Can Improve Their Health and Prevent HIV Transmission

“HIV, life’s a game, and with treatment, I’m winning it day by day.”

Christopher - Washington, DC
Living with HIV since 1987.
Hear his story >

“HIV, you may have tried to take my life, but with treatment I took it back.”

Katrina - Decatur, GA
Living with HIV since 2007.
Hear her story>


cdc.gov/actagainstaids/campaigns/hivtreatmentworks
Together We Can Overcome Barriers to Medication Adherence and Improve Lives

- Adhering to medications improves the lives of people with chronic diseases
- Nonadherence is common and multifactorial
  - Up to half of persons on medications are non-adherent
- Many ways to reduce barriers exist, but more ways are needed
  - Along with better understanding of what works, and with whom
- Working together, we can reduce these barriers and improve adherence and peoples lives
Overcoming Barriers to Medication Adherence for Chronic Diseases