Medication Adherence in Cardiovascular Disease:
“Drugs Don’t Work in Patients Who Don’t Take Them”

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Adherence vs. Compliance

“The word adherence is preferred by many health care providers, because compliance suggests that the patient is passively following the doctor’s orders…”
– Osterberg NEJM 2005

“…compliance is preferred because it implies a responsibility shared by both patient and physician”

Why You Should Care

Affordable Care Act of 2010

Accountable Care Organizations (ACO)

Proposed Measures for ACO Quality Standards
– LDL cholesterol <100 mg/dl
– Blood pressure <140/90 mm Hg

Goal: Pay to lower BP and LDL, not to see patients

Outline

Adherence is difficult to measure.

Adherence to cardiovascular medications is poor.

Nonadherence is associated with
– worse outcomes.
– higher costs.

Nonadherence is a complex behavior.

Interventions may improve adherence.

Gregory Roth, MD

DISCLOSURE DECLARATION

FINANCIAL OR OTHER RELATIONSHIP(S) DISCLOSURE:

Dr. Roth has indicated that he has not had financial or other relationships with commercial interests, related to this presentation, within the past 12 months.
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Adherence is difficult to measure

- Direct Methods
  - Direct Observation (Tuberculosis)
  - Measurement of drug in blood
- Indirect Methods
  - Self-report (interview, questionnaire)
  - Patient diaries
  - Pill counts
  - Electronic medication monitors
  - Prescription fill records
  - Clinical response or physiologic markers

Osterberg et al; NEJM 2005

Indirect

C: The last time I saw you was when we started you on your blood pressure medication.
P: Yeah. Uh huh.
C: Okay. Have you noticed any changes since you've started taking that medication?
P: Well, I go to the bathroom quite often.
C: All right. That's a fairly normal effect of the medication.
P: (Laughs) Uh huh.
C: It's a water pill, a diuretic, and it takes some of the extra fluid out of your body. (Topic shift)

Steele DJ et al; J Fam Practice 1990
Simple Direct

C: (After measuring the patient's blood pressure) ... One-twenty over eighty-eight. That's really good.
P: (Laughs)
C: You've been taking your medications?
P: Oh yes, oh yes.
C: Okay. (Topic shift)

Information-Intensive

C: You still taking the Lasix?
P: Yup.
C: Once in the morning, forty milligrams. And the Inderal?
P: Right.
C: How much do you take of that?
P: Twice a day. Morning and evening (laughs).
C: Two tablets? Or is this a forty milligram tablet?
P: Right.
C: Okay. So it's just one tablet.
P: Right.
C: Okay. Okay. Good. (Topic shift)

Does interview style influence detection of nonadherence?

<table>
<thead>
<tr>
<th>Interview Style</th>
<th>Success Rate Detecting Nonadherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indirect</td>
<td>90%</td>
</tr>
<tr>
<td>Simple Direct</td>
<td>62%</td>
</tr>
<tr>
<td>Information-intensive</td>
<td>80%</td>
</tr>
</tbody>
</table>

Morisky Compliance Assessment Score

- Do you ever forget to take your medicine? (1 point)
- Are you careless at times about taking your medicine? (1 point)
- When you feel better do you sometimes stop taking your medicine? (1 point)
- Sometimes if you feel worse when you take the medicine, do you stop taking it? (1 point)
- ↑ Score = less adherent

The Morisky Score Correlates with Blood Pressure Control

<table>
<thead>
<tr>
<th>Predicted Adherence (Morisky Score)</th>
<th>Low (3-4)</th>
<th>Medium (1-2)</th>
<th>High (0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicted Adherence (Morisky Score)</td>
<td>30</td>
<td>50</td>
<td>60</td>
</tr>
</tbody>
</table>
P<0.01

Data for Research Studies

- Prescription Fill Record
  - Proportion Days Covered
  - Medication Possession Ratio
- Medication Event Monitoring System (MEMS)
Outline

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Adherence to Statins

- How long do patients stay on their statins?

Statin Adherence DropsPrecipitously Over 10 years

- Retrospective cohort study 1990-1999
- 34,000 Medicaid enrollees starting a statin
- Proportion of Days Covered

Benner et al.; JAMA 2002

Number of Monthly Statin PrescriptionsFilled in 12 months

- Retrospective cohort study 1996-2004
- 20,000 Medicare enrollees starting a statin

Brookhart et al.; Am J Epidemiol 2007

Adherence to Statins

- Is adherence to statins poor because these people are asymptomatic?

Statin Adherence Drops in both Primary and Secondary Prevention

- Retrospective cohort study 1994-1998
- 140,000 patients in Ontario

Jackevicius et al.; JAMA 2002
Adherence after Acute MI

- How well do these patients fill prescriptions for all of their cardiac medications?

Prospective multicenter cohort study 2003-2005
1,500 patients with acute MI
All were discharged with ASA, beta blocker, and statin

Ho et al; Arch Intern Med 2006

Failure to Fill Clopidogrel and Other Medications is Common after Stent

- Retrospective cohort study
- Medicare Part D
- 16,000 patients with drug-eluting stent
- Any prescription filled within 60 days of discharge

Roth et al; Cinc Cardiovasc Qual Outcomes 2012

How Good Can It Get?

Adherence in COURAGE and STICH
- Frequent nurse visits
- Free medications
- Positive reinforcement

Adherence in COURAGE

Randomized controlled trial
2287 individuals with stable CAD
Percutaneous coronary intervention and optimal medical therapy vs. optimal medical therapy alone

Maron et al; JACC 2010
Adherence in STICH
- Randomized controlled trial
- 2136 individual with
  - CAD amenable to CABG
  - EF <35%
- CABG vs. optimal medical therapy

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CAD, Adherence, and Outcomes
- Does adherence impact outcomes

Discontinuation of Medications after AMI is Associated with Worse Outcome at 1 year

Log-rank test P<0.001
The Cost of Nonadherence

Roebuck et al; Health Affairs 2011

The Healthy Adherer Effect

Does improved adherence really improve outcomes and save money?

Nonadherence with Clopidogrel Associated with Death but Not Acute MI

Retrospective cohort study
Medicare Part D
16,000 patients with drug-eluting stent

Adjusted Odds Ratio

<table>
<thead>
<tr>
<th>No Fill of Clopidogrel in week after discharge</th>
<th>Death</th>
<th>AMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>

Roth et al; AHA Scientific Sessions 2010

CHARM: Healthy Adherers

Randomized Trial
7500 patients with heart failure class II-IV
ARB vs. placebo

Pfeffer et al; Lancet 2003
Granger et al; Lancet 2005

Adherence to Statins Prevents Trauma?

Association Between Adherence to Statin Therapy and Risk of Health-Related Events

Dormuth; Circulation 2009

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- Nonadherence is associated with:
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- Nonadherence is a complex behavior.
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Why is my patient nonadherent?

- **Health Belief Model of Medication Adherence**
  - Patient’s perception of risk
  - Patient’s concerns and priorities
  - Adherence to therapy

  *Urquhart in Patient Compliance in Medical Practice and Clinical Trials, Raven Press, 1991
  *Inui TS, Annals Internal Med 1975

- **Complex Roots of Medication Nonadherence**
  - [Image: Ho et al, Circulation 2009]

- **Depression Predicts Nonadherence with Aspirin after AMI**
  - 172 patients with AMI
  - Depression assessed in hospital
  - Given ASA in electronic pill tracker (MEMS)
  - Followed 3 months

  *Rieckmann et al; JACC 2006

- **Higher Dosing Frequency is Associated with Less Adherence**
  - [Image: Osterberg et al; NEJM 2005]

- **Polypharmacy**
  - Outpatient pharmacy records
  - 1.8 million people on statins
  - New prescription

  *Choudhry et al; Arch Intern Med 2011
Polypharmacies
- Outpatient pharmacy records
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Polyproviders
- Outpatient pharmacy records
- 1.8 million people on statins
- New prescription

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A Physician-led Intervention with Pill Counting
Blood Pressure for Physician-led Intervention vs. Control Groups over 60 months
- 147 physicians randomized
  - Physician pill counting
  - Designated family member supporting adherence
  - Educational handouts
- 5 years of follow-up
- Adherence very high: 83-92%

A Pharmacist-led Intervention with Blister Packs
Medication Adherence During A Trial of Blister Packs vs. Usual Care

Clinician Strategies That May Improve Adherence
- Identify
  - Ask about barriers to adherence
  - Adopt a more information-intensive interviewing style
- Communicate
  - Elicit patient’s feelings about ability to adhere
  - Listen to patient and customize to their wishes
- Dosing
  - Consider more “forgiving” medications
  - Longer half-lives
    - Depot or extended release medications
    - Transdermal medications
System Strategies That May Improve Adherence
- Blister packaging
- Case management
- Education with behavioral support
- Reminder calls
- Pharmacist-led collaboration
- Interdisciplinary assessment
- Decision Aids
- Phone, computer, mail, or video behavioral support or reminders
- Health coaching
- Access to online medical records
- Pharmacist or physician access to adherence data
- Personalized disease risk communication
- Shared decision-making tools

Blister packaging
Case management
Education with behavioral support
Reminder calls
Pharmacist-led collaboration
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Limits to Modifying Standard Care
- 174 primary care practices in UK with 2164 patients with LV dysfunction
- 30 minute pharmacist appointments for medication optimization
- 3-4 follow-up pharmacist visits

Viswanathan et al; Annals of Internal Med 2012

Policy or Structural Strategies That May Improve Adherence
- New Quality Measures
  - Outpatient
  - Reported to Medicare
  - Pharmacy data prescription measures
  - BP and LDL goal measures
  - Pay for performance
- Decreasing out-of-pocket costs
- Novel EHR and mobile technologies

Outlining Adherence
- Adherence is difficult to measure.
- Adherence to cardiovascular medications is poor.
- Nonadherence is associated with
  - worse outcomes.
  - higher costs.
- Nonadherence is a complex behavior.
- Some interventions may improve adherence.

The End of Cowboy Medicine
"Recently, you might be interested to know, I met an actual cowboy. He described to me how cowboys do their job today, herding thousands of cattle. They have tightly organized teams, with everyone assigned specific positions and communicating with each other constantly. They have protocols and checklists for bad weather…"

Atul Gawande MD, Harvard Medical School Commencement, 2011
Acknowledgments

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- American Heart Association
- University of Washington Institute for Translational Health Sciences
- University of Washington Institute for Health Metrics and Evaluation

Adherence With Secondary Prevention Regimen Associated with Improved Outcomes

Adjusted Survival Curves for Adherent vs. Nonadherent

- Ho et al; Am Heart J 2008

Patient Rating their Providers

- 9377 patients in the Diabetes Study of Northern California
- On a hypoglycemic, lipid-lowering, or antihypertensive medication
- Examined sufficiency of medication fills according to patient ratings of their doctors

Higher Rated Items Associated with Better Adherence

- Involved you in decisions
- Understood your problems with treatment
- Had confidence or trust in your PCP

Ratanawongsa, Arch Intern Med. 2012

Adherence Beyond Medications

Yearly Adherence Schedule for a Patient With Well-Controlled Hypertension, Diabetes, and Hyperlipidemia

<table>
<thead>
<tr>
<th>Adherence Behavior</th>
<th>Precocept</th>
<th>Relation to Your Medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Take medication(s)</td>
<td>Daily</td>
<td>Daily or as needed</td>
</tr>
<tr>
<td>Expectations about drug(s)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Initial change in treatment</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Compliance</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Frequency of nonadherence</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Frequency of adherence</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Assessment of treatment effectiveness</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Ability to take medication(s)</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Trust in medication(s)</td>
<td>9</td>
<td>8</td>
</tr>
</tbody>
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Roth et al; Circ Cardiovasc Qual Outcomes 2012

Dementia is the Strongest Predictor of Clopidogrel Nonadherence

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>Dementia</td>
<td>5.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PCI without myocardial infarction</td>
<td>2.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Age &gt; 84 vs age 65-70</td>
<td>1.8</td>
<td>0.03</td>
</tr>
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Roth et al; Circ Cardiovasc Qual Outcomes 2012