Medication Adherence

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NPTC :
Raising the health of American Indians and Alaska Natives by increasing access to highly effective medications through robust formulary management and education of clinicians within the Indian Health Systems.

Objectives

- Review the clinical and economic impact of medication non-adherence.
- Compare and contrast compliance and adherence in terms of the physician-patient relationship.
- Determine factors which influence medication non-adherence and its measurement.
- Assess potential solutions to the problem of medication non-adherence.

One of the first duties of the physician is to educate the masses not to take medicine.

-Sir William Osler

Evidence for Action

WHO Adherence to Long Term Therapies Project

- In the last 50 years, there has been a shift in disease burden from acute infectious illness to chronic disease.
- At most, 50% of people with chronic disease comply with their doctor's recommendations, irrespective of disease type, treatment, or age.
- Half of people with hypertension discontinue their medications within the first year of treatment.
- Median time to discontinuing drugs is 90 days.
- Non-adherence is the leading cause of poor BP control.

Bloom BS.Daily regimen and compliance with treatment. *British Medical Journal,* 2001, 323:647.
WHO 2003 Evidence for Action Report, Adherence to Long Term Therapies Project

The Costs of Non Adherence

Waste

Disease complications

- Direct costs
- Indirect costs

Herman WH, Eastman RC. The effects of treatment on the direct costs of diabetes. *Diabetes Care,* 1998, 21 (Suppl 3):C19-C24.
Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005;353(5):487-497.

Costs to Health

- 125, 000 annual deaths in the United States.
- Hospitalizations: 33-69% of medication-related admissions.
- WHO 2003: Global Impact

Bosworth, Hayden, et al, Medication adherence: A call for action. Am Heart J 2011;162:412-24.

Race/Ethnicity

- Medicare 2007-2009: 5% random sample (149,893)
- Heart failure diagnosis
- One drug: B-bl, Diuretic, or ACE/ARB
- Adherence: Medication possession rate >75%
- Ethnicity:
  - White: 63%
  - Asian: 57%
  - Hispanic: 53%
  - Black: 52%
  - American Indian: 50%

Zhang, Y et al, Race/Ethnicity, Disability, and Medication Adherence Among Medicare Beneficiaries with Heart Failure. J Gen Intern Med 29(4):602–7.

Epidemiology
AI/AN Adherence vs. Outcome

- **SUPREME-DM**: Insured cohort 300,000 in 9 commercial health delivery systems, 1.8% AI/AN.
- Glycemic control (A1c > 9.0) and adherence to medication (pharmacy dispensing data).
- Comparing AI/AN with non-Hispanic Caucasians
  - A1c > 9.0% (Risk Ratio 1.41, 95% CI 1.31-1.51) $p < 0.0001$
  - Non-adherence oral DM meds (RR 0.9, 95% CI 0.88-0.93) $p < 0.0001$
  - Insulin use (26% vs 24%, $p < 0.0001$)

Schmittdiel, Julie A et al; Diabetes care and outcomes for American Indians and Alaska natives in commercial integrated delivery systems: a SUrveillance, PREvention, and ManagEment of Diabetes Mellitus (SUPREME-DM) Study; BMJ Open Diabetes Research and Care 2014;2:e000043.

The I.H.S. Experience

- Retrospective cohort analysis
- Coronary Heart Disease and Statin Use
- Phoenix Area
- Adherence 60%

Cooke, CE et al, Statin use in American Indians and Alaska Natives with coronary artery disease. Am J Health-Syst Pharm—Vol 63 Sep 15, 2006

Performance Measures

- “The next frontier in quality improvement.”
- Metrics
- Meeting performance targets
- Performance-based compensation

Heidenreich PA. Patient adherence: the next frontier in quality improvement. *Am J Med*. 2004;117:130–132.

Hippocrates, *Decorum*

Keep a watch…on the faults of the patients, which often make them lie about the taking of things prescribed. For through not taking disagreeable drinks, purgative or other, they sometimes die.

Medical Ethics 101

What are the Four Pillars of Medical Ethics?

- Non-Maleficence
- Beneficence
- Autonomy
- Distributive Justice

Autonomy

- The patient's right to self-determination
- Based on respect for individual and value of a person as an end in itself
- Pre-Conditions for Autonomy
  - Liberty or freedom to choose
  - Agency or capacity to choose
- Informed consent: A communication process between the physician and patient whereby a fully informed patient can participate in healthcare decision-making.

Charles Ellington, MD, JD; The Pillars of Medical Ethics and the Ethical Basis for Law, SIU School of Medicine, Accessed Google 4/28/15

Paternalism

- Deciding what is best for another person and overriding their preferences or choices
- At tension with autonomy.

Charles Ellington, MD, JD; The Pillars of Medical Ethics and the Ethical Basis for Law, SIU School of Medicine, Accessed Google 4/28/15.

Dx: Non-compliant Patient

Compliance vs. Adherence

Compliance

- Following the recommendations of the healthcare provider.
- Paternalistic, condescending

Adherence

- The extent to which a person's behavior corresponds with agreed recommendations from a health care provider.
- Patient empowered; co-equal with doctor

Adherence to Long-term Therapies- Evidence for Action. A report of the World Health Organization, January 2003.

Compliance vs. Adherence

Compliance

- Clinician-centered
- Clinician dominance
- Information is dictated
- Goal: patient obedience
- Activities are dictated
- Rules are dictated
- Persuade, coerce
- Resistance is not tolerated

Adherence

- Patient-centered
- Clinician–patient collaboration
- Information is exchanged
- Goal: patient self-mastery
- Activities are negotiated
- Rules matched to lifestyle
- Discuss, negotiate, motivate
- Resistance provides information for adaptation

Gould, E. Mitty, E.; Medication Adherence is a Partnership, Medication Compliance is Not. Geriatric Nursing, Volume 31, Number 4, pp 290-298.

Adherence Behaviors

- Adherence
  - Taking medications as prescribed.
  - “Intensity” of drug use.

- Persistence
  - Continuing to take prescribed medications.
  - Overall “duration of therapy.”

Ho, P. Michael et al, Medication Adherence Its Importance in Cardiovascular Outcomes. *Circulation*. 2009;119:3028-3035.

Medication Non-Adherence

Taking less than 80% of prescribed doses.

Measuring Adherence

“Clinician judgment is no better than flipping a coin.”

Stephenson, BJ et al. The rational clinical examination. Is this patient taking the treatment as prescribed? JAMA. 1993;269(21):2779

Measuring Adherence

Indirect Measures

- Subjective
  - Providers tend to overestimate patient adherence.
  - Only patients that report non-adherence have been shown to be accurate.
- Objective
  - Remaining dosage units: “Pill counts” have been shown to be inaccurate due to counting errors.
  - Pharmacy databases (MPR, PDC, Gap): Data mining limited by other variables
  - MEMS: Effective but expensive

WHO 2003 Evidence for Action Report, Adherence to Long Term Therapies Project
Ho, P. Michael et al., Medication Adherence, It’s Importance in Cardiovascular Outcomes, ***Circulation*. 2009;119:3028-3035.**

Measuring Adherence

Direct Measures

- Directly observed therapy
- Measurement of medication/metabolites in blood
- Measurement of blood biomarkers

Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005;353:487– 497.

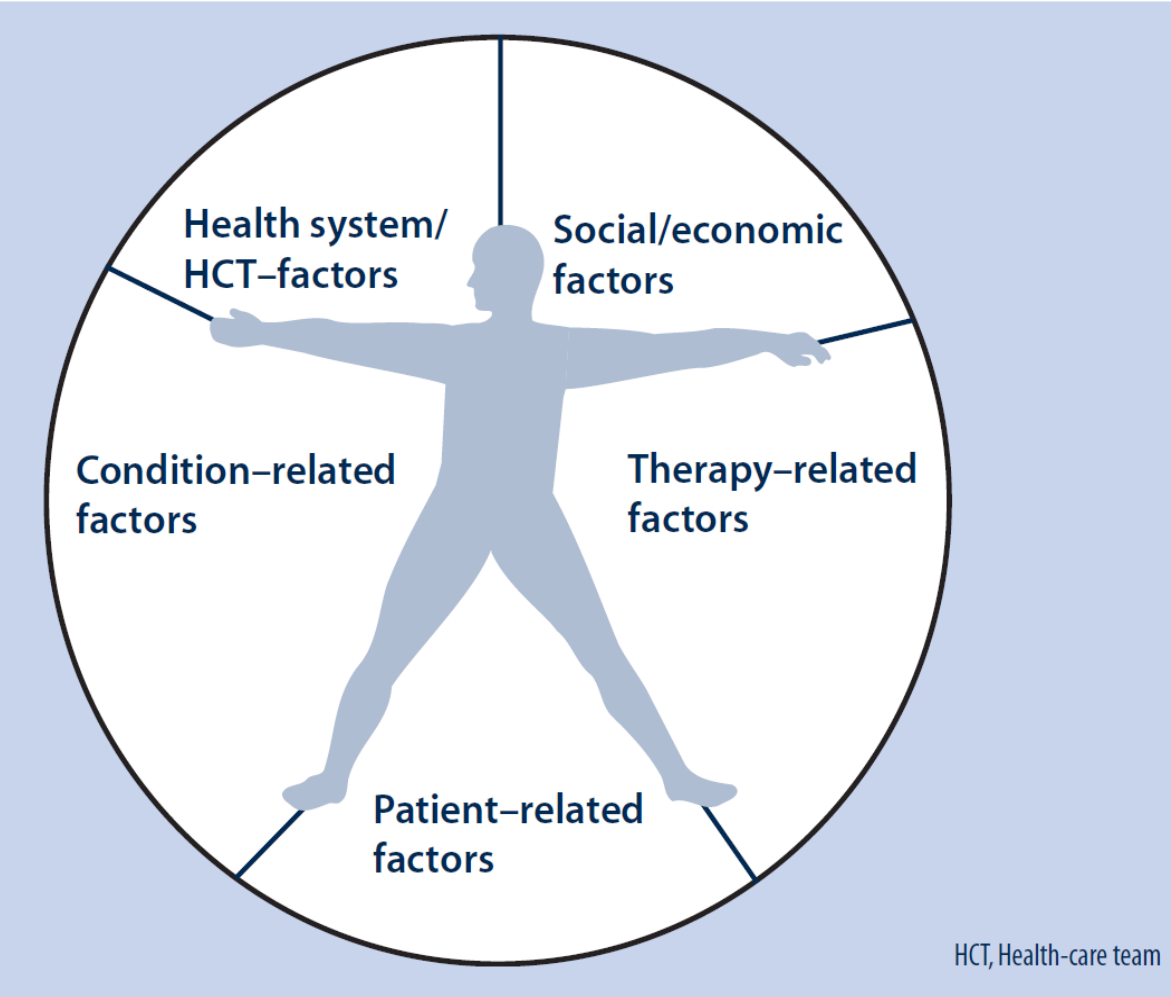
Understanding Non-Adherence
NICE 2009

Framework

- Practical Factors (Unintentional)
  - Lack of access, forgetting, lack of understanding
- Perceptual Factors (Intentional)
  - Beliefs, Preferences, Motivation

Medication Adherence. Involving patients in decisions about prescribed medicines and supporting adherence. NICE clinical guideline 76. January 2009.

The 5 Dimensions of Adherence



Source: WHO 2003 Evidence for Action Report, Adherence to Long Term Therapies Project

Non-Adherence: Factors

Patient/Social Factors

- Asymptomatic
- Health Beliefs/Literacy
- Motivation for Treatment
- Denial
- Mental Illness
- Cognitive Impairment
- Physical Factors
- Therapeutic Alliance w/Clinician
- Lack of follow up
- Lack of social support
- Lifestyle barriers (job, etc)

Treatment/Economic Factors

- Side effects
- Complexity of regimen
- Duration of therapy
- Medication/Access cost

Condition Factors

- Severity of Symptoms
- Level of Disability
- Rate of Disease Progression

System Factors

- Medication discrepancies
- Lack of communication
- Health Care Team
  - Provider knowledge/competence
  - Workload
  - Educational resources

Makaryus AN, Friedman EA. Patients' understanding of their treatment plans and diagnosis at discharge. *Mayo Clin Proc*. 2005;80:991–994.
Coleman EA, Smith JD, Raha D, Min SJ. Posthospital medication discrepancies: prevalence and contributing factors. *Arch Intern Med*. 2005; 165:1842–1847.

I Want a New Drug

Huey Lewis and The News, 1984

Adverse Effects

- Side effect profile
- Drug interactions
- Inappropriate prescribing
- Multiple prescribers
- Nocebo Effect

The Nocebo Effect

- Negative response due to expectation for adverse effects.
- Migraine management (drop-out on placebo v. treatment)
  - Symptomatic therapy: 18.45% (vs. 0.33%)
  - Preventive therapy: 42.78% (vs. 4.75%)

Mitsikostas, R, Nocebo is the enemy, not placebo. A meta-analysis of reported side effects after placebo treatment in headaches. Cephalalgia, Jan 2011.

Adverse Effects and Patient Perceptions

PAXIL

- **Suicidal thoughts or behavior** may occur whether or not you are taking antidepressants. In some children and teens, antidepressants increase suicidal thoughts or actions. You and your family should watch closely and call the doctor right away, if you have **worsening depression**, **thoughts of suicide, or sudden or severe changes in mood or behavior (for example feeling anxious, agitated, panicky, irritable, hostile, aggressive, impulsive, severely restless, hyperactive, overly excited, or not being able to sleep)**, especially at the beginning of treatment or after any change in dose.

DOES PAXIL CAUSE SIDE EFFECTS?

- **nausea**, which may be lessened by taking it with food. Other side effects may include **infection, diarrhea, dry mouth, constipation, decreased appetite, sleepiness, dizziness, sexual side effects, nervousness, tremor, yawning, sweating, weakness or insomnia**.

Rational Non-adherence

"The cessation of a prescribed therapy because of concern for, or the presence of, medication side effects."

- Nearly impossible to circumvent if a patient's specific side-effect concerns are not substantially addressed.
- Adverse effect profiles must be;
  - Considered when prescribing a medication, and;
  - Discussed with the patient before the initial prescription and at every visit thereafter.

Garner JB. Problems of nonadherence in cardiology and proposals to improve outcomes. *Am J Cardiol*. 2010;105(10):1495-1501.

The Problem of Polypharmacy

- 50 percent of Medicare beneficiaries receive 5 or more drugs
- Increased risk of ADEs, hospitalization, medication non-adherence, and death. Increased healthcare costs.
- "Prescribing cascades" describes the inappropriate prescription of additional drug therapies when an adverse drug event is misinterpreted as a new condition.

Tinetti ME et al, Potential pitfalls of disease-specific guidelines for patients with multiple conditions. N Engl J Med. 2004;351(27):2870.

The young physician starts life with 20 drugs for each disease, and the old physician ends life with one drug for 20 diseases.

Sir William Osler

Goal of Treatment

Treatment

Adherence

Outcome

The “Healthy Adherer” Effect

- **The observation that low adherence, even to placebo, increases the risk of death.**

- Adherence appears to favorably influence outcomes over-and-above the expected merits of prescribed medications.

Nieuwlaat R, et al; **Interventions for enhancing medication adherence (Review). The Cochrane Collaboration, Nov. 2014.**

"The Lord hath created medicines out of the earth; and he that is wise will not abhor them."

-- Ecclesiasticus 38:4

AHRQ Evidence Report 2012

Comparative Effectiveness

- MEDLINE Search 1994-December 2011: 62 studies
- Heterogeneity of interventions.
- Evidence for improvement in adherence with policy level interventions:
  - Reduce out-of-pocket expenses
  - Case management
  - Education
- Improved adherence not linked to morbidity/mortality outcomes.
- Risk of bias (small numbers, short/complex interventions)

Medication Adherence Interventions: Comparative Effectiveness. Evidence Report/Technology Assessment Number 208, AHRQ, September 2012.
Viswanathan, M et al, Interventions to Improve Adherence to Self-administered Medications for Chronic Diseases in the United States A Systematic Review. *Ann Intern Med.* 2012;157:785-795.

Pharmacy Care Program

- WRAMC, Age > 65, >4 meds, 200 patients
- Intervention:
  - Standard medication education
  - Regular pharmacist follow-up
  - Time specific medication packs
- Primary Outcome: Pills taken
- Secondary outcomes: BP and LDL-C
- Results: Adherence rose from 61.2% to 96.9%, Modest improvement in BP (6 points), and no change in LDL-c.
- Study limitations: Drop-out, small size, pill counts

Lee, Jeannie, et al, Effect of a Pharmacy Care Program on Medication Adherence and Persistence, Blood Pressure, and Low-Density Lipoprotein Cholesterol: A Randomized Controlled Trial. *JAMA*. 2006;296(21):2563-2571.

Pharmacy Interventions

- Centralized Mail Order Pharmacy
- Automated Medication Refills
- Medication Synchronization

NCPA, National Adherence Survey: The Promise and Prospects of Medication Synchronization, August 2014.

The Polypill

- Secondary Prevention of Cardiovascular Disease
- Statin, anti-platelet, and anti-HTN meds
- Long term RCTs: IMPACT, UMPIRE, and Kanyini-GAP
  - Improved adherence
  - No measureable change in BP, LDL-C
  - Small studies, limited statistical power
- On-going: TIPS-3, HOPE-3, PolyIran, and FOCUS

Castellano, J et al, A Polypill Strategy to Improve Global Secondary Cardiovascular Prevention From Concept to Reality. J Am Coll Cardiol 2014;64:613–21.

Cochrane Review 2014

- 182 RCTs met inclusion criteria
- Most common conditions: DM, HTN, cardiovascular disease, COPD, HIV/AIDS, and psychiatric disorders.
- Heterogeneity limited strength of conclusions.
- Complex interventions
- Only 5 studies showed improved adherence & outcomes.
- No common characteristics.

Nieuwlaat R, et al, Interventions for enhancing medication adherence (Review), Cochrane Collaboration, November 2014.

Potential Solutions

- Education
  - Self management skills
- Counseling
  - Motivational Interviewing
  - Cognitive Behavioral Therapy
- Daily treatment support

Nieuwlaat R, et al, Interventions for enhancing medication adherence (Review), Cochrane Collaboration, November 2014.

Other Strategies

- “Blame free” environment
- Less frequent dosing
- Patient education
- Assessing health literacy
- Paying attention to rational non-adherence

Brown, Marie et al, Medication Adherence: WHO Cares? *Mayo Clin Proc*. 2011;86(4):304-314

HealthNHand, MemoText, Accessed 4/1/15

Digital Technology

Medicaid Health Plan Offers Personalized Medication Adherence Platform for Asthma Patients

BEST Evidence Statement, 2012 Cincinnati Children's Hospital Medical Center , March 2012.
Vollmer, W et al, Improving Adherence to Cardiovascular Disease Medications With Information Technology. AJMC, Nov 2014, Vol 20.

Provider Communication

- Meta-Analysis, 2009
- Relationship between physician communication and medication adherence
- 1949-2008 Literature Review
- 106 studies, 21 investigational interventions
- 19% better adherence with good physician communication

Zolnierek, Kelly et al, Physician Communication and Patient Adherence to Treatment, A Meta-Analysis, Med Care Aug 2009, 47(8), 826-834.

NICE 2009

- "Evidence supporting interventions to increase adherence is inconclusive."

- Recommendations
  - Tailor interventions to individual patient need.
  - Focus interventions on resolving practical problems.

Medication Adherence. Involving patients in decisions about prescribed medicines and supporting adherence. NICE clinical guideline 76. January 2009.

It is easy to get a thousand prescriptions but hard to get one single remedy."

-- Chinese Proverb

ACPM

- **S** implify regimen
- **I** mpart knowledge
- **M** odify patient beliefs and human behavior
- **P** rovide communication and trust
- **L** eave the bias
- **E** valuate adherence

Source: acpm.org

Summary Points

WHO 2003 Evidence for Action Report

- Poor adherence to treatment of chronic diseases is a worldwide problem of striking magnitude.
- The impact of poor adherence grows as the burden of chronic disease grows worldwide.
- The consequences of poor adherence to long-term therapies are poor health outcomes and increased health care costs.
- Improving adherence also enhances patients' safety.

WHO 2003 Evidence for Action Report, Adherence to Long Term Therapies Project

Summary Points

WHO 2003 Evidence for Action Report

- Adherence is an important modifier of health system effectiveness.
- Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments.
- Health systems must evolve to meet new challenges.
- Patients need to be supported, not blamed

WHO 2003 Evidence for Action Report, Adherence to Long Term Therapies Project

Summary Points

WHO 2003 Evidence for Action Report

- Adherence is simultaneously influenced by several factors.
- Patient-tailored interventions are required.
- Adherence is a dynamic process that needs to be followed up.
- Health professionals need to be trained in adherence.
- A multidisciplinary approach towards adherence is needed.

WHO 2003 Evidence for Action Report, Adherence to Long Term Therapies Project

Conclusions

- Medication non-adherence is generally defined as taking less than 80% of prescribed doses.
- Medication adherence rates average around 50%.
- Non-adherence accounts for $100 billion in excess medical costs annually in the U.S. (and over $170 million annually in I.H.S.).
- Non-adherence is associated with poor health, adverse clinical effects, and mortality.
- Efforts to measure non-adherence are notoriously inaccurate.
- An effective strategy to systematically improve adherence would likely have greater impact than improvements in therapy.
- No single intervention or group of interventions has been proven to improve adherence.

Conclusions

- Respect patient autonomy
- Form a therapeutic alliance with the patient
- Educate and counsel
- Collaborate
- Communicate
- Consider adverse effects
- Eliminate inappropriate prescribing
- Keep it simple

Next Steps

- Education and advocacy for provider education and system change to promote better adherence.

“Drugs don’t work in patients who don’t take them.”

-- C. Everett Koop

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- Bloom BS.Daily regimen and compliance with treatment. *British Medical Journal,* 2001, 323:647.
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