Medication Adherence and Stroke/TIA Risk in Treated Hypertensives: National Results from the REGARDS Study

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Case Study

- Ms. KB is a 66 year old female with diabetes, hypertension, obesity, and hyperlipidemia who presents for a follow-up visit.
- She complains today of arthritis pain in her knee and a stye in her eyelid. She asks about a new herbal preparation for lowering sugar.
- Despite your advice, her weight is unchanged, her HbA1c & LDL remain elevated, and her BP today is 146/83 mmHg on lisinopril and HCTZ.
- Careful questioning reveals that **she sometimes forgets her medications**

Inadequate Adherence and High BP: Do I counsel or do I intensify meds or both?

Key Points in our Understanding

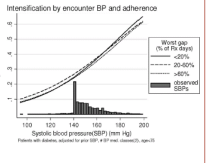
•Intensification only occurs 20-30% of time

•Decision often based on BP or BP pattern

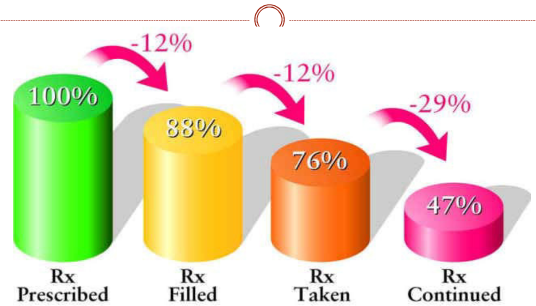
•Adherence usually not all or none

•**Heisler et al**: Patients' adherence had little impact on decisions about intensifying medications, even at very high levels of poor adherence. ***Circulation 2008;117:2884-2892***

•**Rose et al: "**In this observational study (n=819), treatment intensification was associated with similar BP improvement regardless of the patient's level of adherence." ***Hypertension. 2009;54:524-529***



Long-term Medication Adherence



Greater prescribing /filling complexity was associated with lower levels of adherence

Consequences of Non-adherence in High Risk Patients

- 1015 Patients with Hx stable CAD
- Single question about adherence
- Followed for 4 yr
- **4.4x risk of stroke, 3.8 x risk of death**

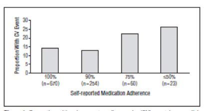


Figure 1. Proportion with subsequent cardiovascular (CV) event (myocardial infarction, stroke, or coronary heart disease death) by the percentage of time in the past month when participants reported taking medications as prescribed ($P=.20$ for proportion with events across all 4 adherence categories; $P=.03$ for proportion with events in patients with adherence ≤75% vs >75% of the time).

Table 2. Association of Medication Nonadherence With CHD Death, Myocardial Infarction, and Stroke in 1007 Participants With Stable CHD

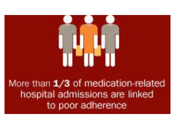
Variable	Unadjusted HR (95% Confidence Interval)	*P* Value	Adjusted HR[a] (95% Confidence Interval)	*P* Value
CHD death	2.0 (0.8-4.8)	.12	3.8 (1.3-10.7)	.01
Myocardial infarction	1.4 (0.7-2.6)	.34	1.5 (0.7-3.6)	.33
Stroke	2.8 (1.2-6.9)	.02	4.4 (1.4-13.9)	.01
Any of the above	1.8 (1.1-3.0)	.03	2.3 (1.3-4.3)	.006

Abbreviations: CHD, coronary heart disease; HR, hazards ratio.
[a]Adjusted for age, sex, race, educational level, smoking, depressive symptoms, diabetes mellitus, hypertension, number of cardiovascular medications, use of β-blocker, use of statin, left ventricular ejection fraction, weekly angina, high-density lipoprotein cholesterol level, low-density lipoprotein cholesterol level.

Gehi et al: Arch Int Med 2007; 167:1798-1803

The Cost of Non-Adherence

Poor medication adherence estimated to cost the US ***$ 105.8*** **billion**, or an average of **$453 per adult**, in 2010.



Reference: *Am J Pharm Benefits.* 2012;4(2):e41-e47

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Medication Non-Adherence in HTN

- Non-adherence worse with advanced age, polypharmacy, low SES, regimen complexity
- **Measurement challenges**
  - Non-structured self-report
  - Structured self-report
  - Pill counts
  - Pharmacy fill/refill information
  - MEMs Caps

However.....Questions Remain

- Which non-adherent are at risk?
- What is the role of other CV risk factors in risk w/ non-adherence
- How do race, geography, and other socioeconomic factors influence non-adherence and risk
- Is increased BP the mediator of risk in the non-adherent?
- How does this inform how we intervene in primary care?

Most research is in single health systems and in urban settings

Enter.....the REGARDS Study

REGARDS Study (n=30,239)

- Population based, age ≥ 45 yr; 45% Male/55% Female
- Race: 40% AA/60% W
- Cohort – avg 5yr f/u
- Stroke-belt/rest of the US
- Risk factors for stroke

Our Sub-Study (n= 15,071)

- Treated **hypertensives**
- 51% black, 57% Stroke Belt
- Measured BP at home visit
- Morisky adherence scale
- Physician adjudicated stroke and TIA events

DOES ↓ ADHERENCE →  → 

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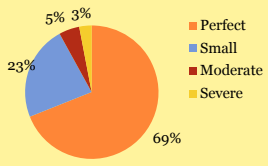
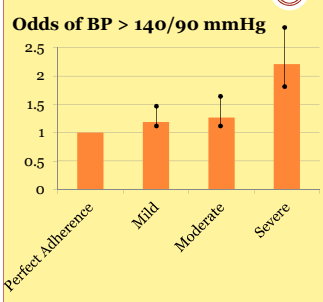
Self-reported Medication Adherence



Parameter	Morisky 0 -2 affirmative responses	Morisky 3 or 4 affirmative responses
Age, mean	66.2	65.0
Black, %	50.3	67.2
Female, %	56.9	66.9
Education level, %		
Less than HS	15.5	19.2
HS graduate	27.6	30.8
Some college	26.6	26.9
College graduate	30.3	23.1
Income level, %		
less than $20k	21.5	31.1
$20k-$34k	26.0	26.6
$35k-$74k	28.1	19.5
$75k and above	12.0	7.7
Refused	12.3	15.1

Logistic Regression: Odds of Inadequate BP Control by Adherence Category



Reference: Morisky - 0 affirmative	Fully Adjusted n=13924
Morisky - 1 affirmative	1.20 (1.10, 1.31)
Morisky - 2 affirmative	1.27 (1.08, 1.49)
Morisky - 3 or 4 affirmative	2.21 (1.75, 2.78)

Medication Adherence and Risk of Stroke/TIA

Cox Hazards Model using Mediation Analysis - Indirect Effects HR (95% CI) *

Reference: Morisky - 0 affirmative	Unadjusted	Fully Adjusted
Morisky - 1 affirmative	1.02 (1.00, 1.03)	1.01 (1.00, 1.02)
Morisky - 2 affirmative	1.03 (1.01, 1.06)	1.02 (1.00, 1.04)
Morisky - 3 or 4 affirmative	1.12 (1.06, 1.17)	1.08 (1.03, 1.12)

*Note: used SBP as mediating variable

Summary of Findings from REGARDS

- Reduced medication adherence was reported by about 30% of participants; more common among African Americans, females, and reduced income folks
- Reduced medication adherence was associated with more than a **2-fold increased risk of uncontrolled BP**
- Reduced medication adherence was associated with a small but significant **increase in the risk for stroke/TIA via increased BP** in fully adjusted models
- Neither race nor geographic location (stroke-belt) were independent predictors of stroke/TIA risk in fully adjusted models.

Implications: We Need To Address Medication Adherence in Primary Care: 4 Top Reasons for Non-adherence

- Cost of medications
- Side effects/fear of side effects
- Forget/can't keep track of meds/complexity
- Don't think it works/don't need it

Key Point: While cost is important, it's **not just about cost**. Medication taking is an **important health behavior** that is influenced by knowledge, attitudes, beliefs, and skills. These behavioral challenges may respond to targeted intervention.

Using the Gehi et al Adherence Question

Medication Adherence Question:

Many patients tell us it is difficult to take their blood pressure medications exactly as recommended. In the past 2 weeks, how often did you take medications as prescribed?

	Please check appropriate box				
	All of the time (100%)	Nearly all of the time (90%)	Most of the time (75%)	About half the time (50%)	Less than half the time (<50%)

If any of the shaded boxes are checked, flag provider & have patient answer "adherence" questions on back of this sheet

If "Most of the time" or less....

Medication Adherence Question:

Many patients tell us it is difficult to take their blood pressure medications exactly as recommended. In the past 2 weeks, how often did you take medications as prescribed?

	Please check appropriate box				
	All of the time (100%)	Nearly all of the time (90%)	Most of the time (75%)	About half the time (50%)	Less than half the time (<50%)
				✓	

If any of the shaded boxes are checked, flag provider & have patient answer "adherence" questions on back of this sheet

✓ Turn form over and ask additional questions

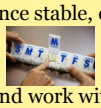
For those less adherent

Some patients find it difficult taking their medication for many different reasons. Do any of the following sound like something you may do?

- ☐ I have trouble keeping track of when I need to take my medicines.
- ☐ I do not take my medications exactly as I am supposed to because of the side effects or bad experiences that I know about.
- ☐ The costs of the medications keep me from taking them as prescribed.
- ☐ I don't think the medicine helps me or that I need it.
- ☐ I intend to take my medications, but forget them
- ☐ Other reason _____

What Can I Do to Help Adherence?

- Avoid dropping out of care; keep patient coming for office visits – reminder systems
- Home BP monitoring improves BP control
- Use low-cost generic meds but discuss efficacy/safety
- Limit # pills/regimen complexity; once stable, consider 90-day supply for chronic meds



- Blister Packaging and pill boxes
- Discern reason for non-adherence and work with staff/pharmacy to address/educate; then follow-up
- Health coaching –ongoing monitoring and feedback

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