Published in final edited form as:

Am J Kidney Dis. 2010 September ; 56(3): 423–426. doi:10.1053/j.ajkd.2010.05.006.

Kidney Disease and Antihypertensive Medication Adherence: The Need for Improved Measurement Tools

Tara I. Chang, MD, MS and Wolfgang C. Winkelmayer, MD, MPH, ScD

Stanford University School of Medicine Palo Alto, California

In 2000, the Department of Health and Human Services launched the Healthy People 2010 campaign, a comprehensive initiative designed to improve the overall health of the United States.¹ Among the stated objectives was to decrease the prevalence of hypertension and improve blood pressure control and hypertension awareness. Despite the campaign, during the last decade, the prevalence of hypertension has continued to increase and now affects a staggering 1 in 3 adults² in the United States. The costs of uncontrolled hypertension are high in terms of both disease burden and dollars. Hypertension accounts for 1 of every 6 deaths in the United States³ and is the leading modifiable risk factor for cardiovascular disease morbidity and mortality; sustained reductions in blood pressure significantly decrease the incidence of stroke, myocardial infarction, and death.⁴ In 2009, the estimated cost of hypertension was \$73.4 billion,⁵ with antihypertensive medications accounting for nearly half those costs.⁶

Although billions of dollars are spent each year on antihypertensive medication in the United States, less than one-third of patients who have been prescribed antihypertensive medication have adequately controlled blood pressure.² Several studies have supported poor medication adherence as 1 reason for the high rates of poor blood pressure control.^{7–11} For example, a recent study using data from a large US managed care organization showed that participants with inadequate blood pressure control, despite intensification of their antihypertensive treatment regimens, more often were medication nonadherent. In contrast, participants who achieved adequate blood pressure control also had their antihypertensive treatment regimens intensified, but importantly, more often were medication adherent.¹¹ This study emphasized that no matter how much money is spent on antihypertensive medication, if patients cannot or will not use the medications correctly, blood pressure targets will not be reached.

Achieving medication adherence is a complex process. First, the patient must fill the prescription (primary adherence), then take the medication at the correct dose and times (secondary adherence), and finally continue taking the medication until otherwise instructed by the provider (persistence). Even if each step proceeds flawlessly, a proportion of patients may not respond adequately to the medication because of various physiologic issues or other

issues (nonresponse), necessitating adjustments to the antihypertensive regimen and repetition of the entire sequence. Failures can occur anywhere along the way, and it is clinically important to distinguish between nonresponse and nonadherence because the therapeutic approach obviously will differ.

In this issue of the *American Journal of Kidney Diseases*, Muntner et al¹² conducted a cross-sectional analysis of data from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study. In this study, participants with chronic kidney disease (CKD) were no more likely to be medication nonadherent than participants without CKD. For those of us who take care of patients with CKD, this may provide a modicum of reassurance, especially because participants in this study with CKD were older and more often were using 3 or 4 different classes of antihypertensive medications. However, far from providing cause for celebration, Muntner et al¹² describe an overall medication adherence rate of only 69%, drawing attention to the important issue of secondary medication adherence in patients with CKD, a population particularly vulnerable to the adverse consequences of poor medication adherence and blood pressure control. Not only are patients with CKD at higher risk of cardiovascular disease compared with the non-CKD population, but also poorly controlled hypertension can hasten progression of kidney disease and increase the risk of endstage renal disease.¹³

Similar to previous studies of antihypertensive medication adherence, participants in the study by Muntner et al¹² with greater nonadherence had higher odds of uncontrolled hypertension. However, even in participants considered adherent, 25% of the non-CKD cohort and 34.6% of the CKD cohort had uncontrolled hypertension, defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg. These numbers increased to 60.4% and 66.9% when using the cutoff of 130/80 mm Hg, respectively. Although the high rate of poor blood pressure control in presumably adherent participants could reflect nonresponse to the medications, alternatively, it could stem from inaccuracies with the measure of adherence, which may not reflect true medication-taking behaviors. The issue of how best to measure medication adherence remains unresolved. Some studies have used a medication event monitoring system as the gold standard, consisting of an electronic bottle cap that records each time the bottle is opened as a marker of medication adherence. However, this technique is imperfect because some patients may remove multiple doses at once or open the bottle multiple times out of curiosity or to give the impression of adherence, especially if they are aware of the monitoring device.¹⁴ In addition, such electronic devices are costly, may get lost, and are difficult to implement outside of a research setting.

Self-report questionnaires, although subject to recall bias, are the easiest and least expensive methods to use in the clinical setting. Muntner et al¹² used the 4-item Morisky Scale,¹⁵ a self-report questionnaire frequently used in studies of medication adherence. The Morisky Scale can illuminate some of the reasons for medication nonadherence, such as forgetfulness or carelessness, but does not address other reasons, such as cost, personal beliefs, or discontinuation because of side effects. The dichotomous nature of the response choices (yes/no) does not allow much flexibility, labeling a person as nonadherent after forgetting to take medications just once, and as noted by the investigators, the Morisky Scale was not

constructed to address antihypertensive medication adherence specifically. Although this scale originally showed relatively high internal consistency (as reflected in Cronbach $\alpha = 0.61$),¹⁵ a recent reassessment of its performance in assessing antihypertensive medication adherence showed much lower internal consistency (Cronbach $\alpha = 0.25$).¹⁶ Another study using a modified Morisky Scale (which added an additional question, “Do you think you are taking your medications as intended, i.e. on schedule and regularly” to the original 4 questions) found that the modified Morisky scale had only 67.2% positive predictive value and 50.8% negative predictive value, using a medication event monitoring system as the gold standard of adherence.¹⁷ Of note, the 4-item Morisky Scale was updated recently to an 8-item scale⁹ designed specifically to assess antihypertensive medication adherence, which may improve its performance.

In addition to self-report questionnaires, the 2 other most common methods used to measure adherence are pill count and pharmacy claims data,¹⁸ objective measures of medication adherence that circumvent many of the subjective biases associated with self-report. Pill counts, like medication event monitoring systems, can be manipulated by patients to improve apparent adherence and may be inaccurate if patients combine several pills into a single bottle. Pharmacy claims data have an added benefit over pill counts in that they can pinpoint which medication was dispensed, how much, and when. However, patients may pick up medications but then choose to not take them, and pharmacy claims data cannot distinguish between nonadherence and discontinuation by the prescriber. Additionally, neither of these 2 methods provides information about patients’ reasons for medication nonadherence.

Despite thousands of articles published in the last few decades regarding medication adherence, current methods used to measure adherence each have weaknesses, and no true gold standard exists. However, with technologic and computing advances, the future holds great promise for improved ways to measure medication adherence. For example, Fischer et al¹⁹ cleverly leveraged information available through electronic prescriptions and pharmacy claims data to directly assess primary adherence in a community health care setting, which in the previous era of paper prescriptions was nearly impossible to assess. At present, analyzing pharmacy claims data necessitates extensive computer programming and a delay of at least several months and thus remains useful mostly for retrospective research studies. However, as more and more health systems move toward real-time health data and claims processing, medication adherence information may become available to the clinician for immediate use in counseling or medical decision making. Currently, many physicians intensify antihypertensive medication treatments without regard for or assessment of the patient’s history of medication adherence.⁸ An integrated electronic medication record system could alert the physician if a prescription is never filled or the timing of medication refills does not match the expected refill rate, thereby boosting the low rates of provider recognition of medication nonadherence.^{20,21}

Whether technologic tools will improve medication adherence remains to be seen, but one thing is certain: improved methods of measuring medication adherence are needed if we hope to improve it. The stated hypertension goals of Healthy People 2010 unfortunately

were not achieved, but armed with better technology and improved adherence strategies, perhaps there will be better news to report by 2020.

Acknowledgments

Support: None.

REFERENCES

- Centers for Disease Control and Prevention. [Accessed April 30, 2010] About Healthy People 2010. http://www.cdc.gov/nchs/healthy_people/hp2010.htm.
- Ostchega, Y.; Yoon, S.; Hughes, J.; Louis, T., editors. Hypertension Awareness, Treatment, and Control—Continued Disparities in Adults: United States, 2005–2006. Hyattsville, MD: National Center for Health Statistics; 2008.
- Washington, DC: The National Academic Press; 2010. Committee on Public Health Priorities to Reduce and Control Hypertension in the U.S. Population Institute of Medicine. A Population-Based Policy and Systems Change Approach to Prevent and Control Hypertension.
- Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003; 289:2560–2572. [PubMed: 12748199]
- Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics—2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2009; 119:480–486. [PubMed: 19171871]
- Balu S, Thomas J. Incremental expenditure of treating hypertension in the United States. *Am J Hypertens*. 2006; 19:810–816. [PubMed: 16876679]
- Wu PH, Yang CY, Yao ZL, Lin WZ, Wu LW, Chang CC. Relationship of blood pressure control and hospitalization risk to medication adherence among patients with hypertension in Taiwan. *Am J Hypertens*. 2010; 23:155–160. [PubMed: 19927135]
- Heisler M, Hogan MM, Hofer TP, Schmittiel JA, Pladevall M, Kerr EA. When more is not better: treatment intensification among hypertensive patients with poor medication adherence. *Circulation*. 2008; 117:2884–2892. [PubMed: 18506011]
- Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. *J Clin Hypertens (Greenwich)*. 2008; 10:348–354. [PubMed: 18453793]
- Krousel-Wood MA, Muntner P, Islam T, Morisky DE, Webber LS. Barriers to and determinants of medication adherence in hypertension management: perspective of the cohort study of medication adherence among older adults. *Med Clin North Am*. 2009; 93:753–769. [PubMed: 19427503]
- Ho PM, Magid DJ, Shetterly SM, et al. Importance of therapy intensification and medication nonadherence for blood pressure control in patients with coronary disease. *Arch Intern Med*. 2008; 168:271–276. [PubMed: 18268167]
- Muntner P, Judd SE, Krousel-Wood M, McClellan WM, Safford MM. Low medication adherence and hypertension control among adults with CKD: data from the REGARDS (Reasons for Geographic and Racial Differences in Stroke) Study. *Am J Kidney Dis*. 2010; 56(3):447–457. [PubMed: 20471734]
- Klag MJ, Whelton PK, Randall BL, et al. Blood pressure and end-stage renal disease in men. *N Engl J Med*. 1996; 334:13–18. [PubMed: 7494564]
- Wetzels GE, Nelemans P, Schouten JS, Prins MH. Facts and fiction of poor compliance as a cause of inadequate blood pressure control: a systematic review. *J Hypertens*. 2004; 22:1849–1855. [PubMed: 15361751]
- Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care*. 1986; 24:67–74. [PubMed: 3945130]

16. Koschack J, Marx G, Schnakenberg J, Kochen MM, Himmel W. Comparison of two self-rating instruments for medication adherence assessment in hypertension revealed insufficient psychometric properties. *J Clin Epidemiol.* 2010; 63:299–306. [PubMed: 19762213]
17. Hansen RA, Kim MM, Song L, Tu W, Wu J, Murray MD. Comparison of methods to assess medication adherence and classify nonadherence. *Ann Pharmacother.* 2009; 43:413–422. [PubMed: 19261962]
18. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care.* 2004; 42:200–209. [PubMed: 15076819]
19. Fischer MA, Stedman MR, Lii J, et al. Primary medication non-adherence: analysis of 195,930 electronic prescriptions. *J Gen Intern Med.* 2010; 25:284–290. [PubMed: 20131023]
20. Copher R, Buzinec P, Zartosky V, Kazis L, Iqbal SU, Macarios D. Physician perception of patient adherence compared to patient adherence of osteoporosis medications from pharmacy claims. *Cur Med Res Opin.* 2010; 26:777–785.
21. Miller LG, Liu H, Hays RD, et al. How well do clinicians estimate patients' adherence to combination anti-retroviral therapy? *J Gen Intern Med.* 2002; 17:1–11. [PubMed: 11903770]