



Allan Showalter, MD

**AlignMap**

*Beyond Patient Compliance*

7716 Crystal Springs Road

Crystal Lake, IL 60012

815 459-3201 ♦ [allan@alignmap.com](mailto:allan@alignmap.com)

## Patient Compliance Myths

By Allan Showalter, MD

### The No-Nonsense Summary Patient Compliance Myths

- 1. The only absolute criterion for patient noncompliance is that a clinician has made a treatment recommendation to a patient. Once that's accomplished, it's a numbers game; as the number of patients receiving the treatment recommendation increases, the likelihood noncompliance will occur approaches certainty, regardless of the treatment, disorder, patient demographics, astrological signs, ... .*
- 2. It is essential not to confuse bullet points (information about noncompliance) with silver bullets (panaceas for noncompliance).*
- 3. If a patient's clinician is well-trained, proficient, & sensitive, his or her accuracy in determining if that patient is compliant or noncompliant with treatment will equal that obtained from flipping a coin. (Note: the heads-or-tails option is less expensive but also less amusing.)*

## **Introduction**

After 20 years of talking about patient compliance with clinicians and civilians, I can report with confidence that the prevailing beliefs about treatment adherence are reasonable, based on common sense, and steadfastly maintained in the face of well documented evidence to the contrary. As H.L. Mencken put it,

*For every complex problem there is an answer that is clear, simple, and wrong.*

## **Myth #1**

### **Noncompliance Is Unusual Except In Certain Groups**

It's only common sense, for example, that noncompliance occurs only occasionally and even then is primarily a problem of the foolish, the recalcitrant, the poorly educated, the psychologically or intellectually impaired, and the poor. After all, when one's health and sometimes one's life is at stake, why wouldn't any reasonable, mentally competent person who is aware of the problem and can afford the treatment follow the physician's advice? Yet, surveys of actual healthcare behavior consistently indicate that significant noncompliance exists throughout healthcare, and, in fact, there are many instances in which noncompliance is routinely more prevalent than compliance; i.e., situations in which ***compliance is the aberration***.

For example, a study completed in 2000 found that 20% of patients given medication prescriptions never filled their prescriptions, and of those who did fill their prescriptions, 50% did not take the medications as directed;<sup>1</sup> for those keeping score, that means the majority – 70% of all patients – were noncompliant. Multiple studies, in fact, calculate the chances that an individual prescribed medication non-acute disorders will satisfactorily adhere to that treatment plan as no better than even money – approximately 50%.<sup>2,3,4,5,6,7,8,9</sup> For impressive noncompliance, it's hard to beat The Nurses' Health Study, a collection of data describing the healthcare behaviors of 84,129 female nurses, which reported that only 3% of the participants adhered to medical advice on diet and exercise.<sup>10</sup>

To paraphrase the *Chickenman's* (AKA "The caped crusader, winged warrior, and day time shoe salesman") catchphrase in regard to patient noncompliance:

*It's Everywhere! It's Everywhere!*

## **Myth #1A** (*The Converse Of Myth #1*)

### **In Those Certain Groups, Noncompliance Is Very Likely**

It turns out there is little that is certain about the "certain groups" that one might suppose are prone to noncompliance. Efforts to correlate noncompliance with demographic, diagnostic, socioeconomic, and psychological features have been numerous and extensive but largely unrequited. Race, amount or quality of schooling, intelligence, and socioeconomic status have little direct effect on patient compliance,<sup>11</sup> except in specific situations.

Further, even statistical trends that may be valid are of little practical use because (1) the flood and flux of variables that influence compliance from moment to moment and situation to situation can easily wash out the effect of any single factor and (2) exceptions to any simple cause-effect generalities are numerous. Patients from low income urban areas, for instance, are often identified as being at high risk for nonadherence, and there is evidence that, all things being equal, patients with more fiscal resources are somewhat more likely to comply with treatment for chronic disorders.<sup>12</sup> On the other hand, a study of impoverished African Americans in East Baltimore with type 2 diabetes demonstrated an adherence rate to diabetic medications of 74%<sup>13</sup> (adherence rates for all patients with type 2 diabetes have been reported to range from 65% to 85% for oral agents and 60% to 80% for insulin<sup>14</sup>). In a similar and perhaps more wrenching example, Bangsberg reported on a study,<sup>15</sup> triggered by the observation that Protease Inhibitors were typically being withheld from impoverished and homeless HIV+ patients, to investigate the validity of the underlying premise – that this population would be unable to adhere to this complex and expensive treatment. The researchers recruited 153 HIV+ patients from San Francisco homeless shelters, free food lunch lines, and single room occupancy (SRO) hotels to begin the program. After 20 months, these patients had attended 91% of all scheduled clinic sessions, hardly a sign of poor adherence to treatment.

At this time, in fact, no associations between noncompliance and any signs, symptoms, qualities, or traits are sufficiently strong and sufficiently free of exceptions to serve as a basis for a clinical or administrative decision such as disqualifying a patient from a transplant program because he is unlikely to adhere to the treatment necessary to prevent rejection of the organ.

## **Myth #2**

### **Doctors In Touch With Their Patients Know Who Is And Who Isn't Compliant**

There is impressive evidence that clinicians, regardless of discipline, years of experience, or specialty, overestimate compliance among their own patients – **by 100%**.<sup>16</sup> Moreover, the level of a given clinician's confidence that he or she can detect noncompliance has little correlation with the actual capacity to do so. Even when primary practice physicians were allowed to stack the deck by predicting the compliance of only those patients they felt they knew well, noncompliance was detected only 10% of the time.<sup>17</sup> Overall, physicians are no more accurate in detecting compliance or noncompliance than relying on the flip of a coin.<sup>18</sup> (Physicians are the profession typically studied; there is no indication that other healthcare professionals predict noncompliance more or less accurately.)

### **Myth #3**

#### **Noncompliance Can Be Eliminated Educating By The Patient, Motivating The Patient, Eradicating Or Relieving Side-effects, Simplifying The Treatment Plan, ...**

This notion differs from its predecessors because it is true – kinda, sorta; i.e., certain interventions, including but not limited to those listed, can indeed ameliorate noncompliance. The danger lies in the erroneous assumption that any of these issues is universally effective or the only key to compliance.

That is, for example, the kind of fallacy that underlies ads that prominently display a new medication's decreased frequency or severity of side-effects alongside the medication noncompliance rates for the drug being replaced to imply that patients will have higher adherence rates with the new medication. There is ample evidence, however, that this is not always the case. Consider these examples. Four studies of cancer chemotherapy,<sup>19,20,21,22</sup> as Partridge noted in his review,<sup>23</sup> "found no relationship between side effects and adherence." A 2002 paper<sup>24</sup> on long-term compliance with treatment for hypercholesterolemia reported similar side-effects rates in both compliant and noncompliant patients. In a review focusing on adherence among patients with schizophrenia, only 1 out of 9 studies found a correlation between side effects and compliance.<sup>25</sup> Studies comparing patients treated with older antipsychotics (e.g., haloperidol), and those medicated with the newer, atypical antipsychotics (e.g., olanzapine), which have fewer and less severe side effects, have reported no significant differences in adherence.<sup>26,27</sup> Of three meta-analyses of studies comparing adherence of patients taking tricyclic antidepressants (known to frequently severe side-effects) cause with those taking selective serotonin reuptake inhibitors (SSRIs) (known to have a much more benign side-effect profile), one found that in 67 studies only 5% more patients terminated treatment while taking tricyclics than while taking SSRIs,<sup>28</sup> another found no significant clinical difference between the two medication groups,<sup>29</sup> and the third suggested that the slight advantage of the SSRIs could be secondary to the use of older tricyclics the early trials, and might dissipate entirely if the studies were repeated with newer varieties of tricyclic medicines.<sup>30</sup>

Easily the most frequently advised and implemented tactic to improve compliance is educating the patient about the disorder, the treatment, and the treatment agents, such as medication. This strategy, however, may have a wider appeal as a concept than effectiveness as a pragmatic intervention. A study of asthmatic patients found that the level of patient knowledge had no significant impact on medication compliance and that, indeed, the individuals with the highest rate of compliance were those respondents who reported never receiving an explanation about the condition. In a 2001 study, diabetic patients who were highly knowledgeable about their disease were no better at managing their treatment than patients with little understanding of diabetes. In fact, when risk factors were measured, both groups, in the words of the study's author, did "exactly the same,"<sup>31</sup> a finding consistent with studies of treatment with antihypertensives<sup>32,33</sup> which found no connection between the patients' knowledge of their disease or therapy and their treatment adherence.

Information about the patient's disease is often provided in the belief that understanding the problem and the value of the treatment will increase his or her motivation to comply with the prescribed regimen. In practice, however, noncompliance is widespread even when it clearly increases the risk of severe consequences, including death, i.e., situations in which motivation would be expected to be highest. Large numbers of HIV patients, for example, fail to take medications as prescribed even though these patients acknowledged that the medications were effective and potentially life-saving.<sup>34 35</sup> About one in five renal transplant patients, all of whom have subjected themselves (and often a donor) to surgery, do not take their prescribed immunosuppressive medications to prevent rejection of the transplanted kidney,<sup>36</sup> more than a third of glaucoma patients in one study were noncompliant *despite already having lost vision in one eye because they failed to use the prescribed medication*,<sup>37</sup> and the majority of diabetics do not follow their treatment regimen although they are aware that they are thus hastening disability and death.<sup>38</sup> We have come to understand that

***Motivation To Recover Is Not Synonymous With  
Motivation To Comply With Treatment***

Further belying the compliance-enhancing impact of both motivation and comprehension of healthcare matters is the earlier referenced fact that among the participants in the Nurses' Health Study – a population which consisted entirely of nurses, healthcare professionals whose grasp of medical information and whose awareness of the importance of lifestyle habits are superior to the general population and, in this case, a specific group of nurses who *volunteered* to be part of research they knew would monitor their health-pertinent behaviors – 97% failed to closely follow the exercise and diet recommendations.<sup>39</sup> (It is sobering that this same study also concluded that 82% of heart disease and infarctions resulted from the failure to follow these recommendations.<sup>23</sup>)

Decreasing the number of times per day a medication has to be taken is a frequently recommended compliance enhancement tactic and one supported by research.<sup>40,41</sup> It is not, however, always the answer. Cheever assessed the level of adherence to once-a-day dosing by patients with *Pneumocystis carinii* pneumonia, whose treatment plan called for them to take one pill (with few side-effects) each day, any time during that day. Under these conditions, 29% of patients took more than 90% of the doses as prescribed, and a total of 54% were adherent at or above the 80% level (believed to be the lowest level at which clinical benefit could be expected).<sup>42</sup> Moreover, a simple regimen is not always an option. While advances have been reported which could soon make single-pill, once-a-day AIDS treatment possible,<sup>43</sup> for example, effective HIV treatment currently requires multiple combinations of medications taken several times a day. It is, in fact, the unusual case in which a physician would arbitrarily choose a more complex schedule when a simpler one is available.

None of this negates, for example, the potential utility of decreasing the number of doses in a given patient's regimen or reducing side-effects when possible. It does mean that there are no simple answers to enhancing compliance.

## References

- <sup>1</sup> Ellickson P., Stern S., Trajtenberg M. Patient Welfare and Compliance: An Empirical Framework for Measuring the Benefits from Pharmaceutical Innovation. 2000; NBER Working Paper No. W6890.
- <sup>2</sup> Matsui DM. Drug compliance in pediatrics. Clinical and research issues. *Pediatr Clin North Am.* 1997;44:1-14.
- <sup>3</sup> Clepper I. Noncompliance, the invisible epidemic. *Drug Topics*, 1992, 17:44-65.
- <sup>4</sup> Sackett DL, Snow JC. The magnitude of compliance and noncompliance. In: Haynes RB, Taylor DW, Sackett DL, eds. *Compliance in Health Care*. Baltimore, Md: John Hopkins University Press; 1979:11-22.
- <sup>5</sup> Bond WS, Hussar DA. Detection methods and strategies for improving medication compliance. *Am J Hosp Pharm.* 1991;48:1978-88.
- <sup>6</sup> World Health Organization. Adherence to Long-Term Therapies: Evidence for Action. Geneva, Switzerland: World Health Organization; 2003. Available at: [http://www.who.int/chronic\\_conditions/en/adherence\\_report.pdf](http://www.who.int/chronic_conditions/en/adherence_report.pdf). Accessed January 6, 2004.
- <sup>7</sup> Meichenbaum D, Turk DC. *Facilitating Treatment Adherence: A Practitioner's Guidebook*. New York, NY: Plenum Press; 1987.
- <sup>8</sup> Dunbar-Jacob J, Erlen JA, Schlenk EA, et al. Adherence in chronic disease. *Annu Rev Nurs Res.* 2000;18:48-90.
- <sup>9</sup> Haynes RB, McKibbin KA, Kanani R. Systematic review of randomized trials of interventions to assist patients to follow prescriptions for medications. *Lancet.* 1996;348:383-6.
- <sup>10</sup> Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC. Primary prevention of coronary heart disease in women through diet and lifestyle. *NEJM.* 2000;343(1):16-22.
- <sup>11</sup> Haynes RB. A critical review of the "determinants" of patient compliance with therapeutic regimens. In: Sackett DL, Haynes RB, editors. *Compliance With Therapeutic Regimens*. Baltimore: The Johns Hopkins University Press; 1976:26-39.
- <sup>12</sup> DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care.* March 2004;42:200-209.
- <sup>13</sup> Hill-Briggs F, Gary TL, Bone LR, Hill MN, Levine DM, Bancati FL. Medication adherence and diabetes control in urban African Americans with type 2 diabetes. *Health Psychol.* 2005;24:349-357.
- <sup>14</sup> Rubin RR. Adherence to pharmacologic therapy in patients with type 2 diabetes mellitus. *Am J Med.* 2005;118:27S-34S.
- <sup>15</sup> Bangsberg D, et al. Session 389/32406: Protease inhibitors (PI) in the HIV+ homeless and marginally housed (h/m): good adherence but rarely prescribed. *12th World AIDS Conference.* July 1, 1998. Available at: <http://www.thebody.com/confs/worldaids698/bangsberg.html>. Accessed February 15, 2006.
- <sup>16</sup> Mushlin A, Appel F. Diagnosing potential noncompliance. *Arch In Medication.* 1977;137:318-321.
- <sup>17</sup> Gilbert J, Evans C, et al. Predicting compliance with a regimen of digoxin therapy in family practice. *Can Med Assoc J.* 1980;123:119-122.
- <sup>18</sup> Caron H, Roth H. Objective assessment of cooperation with an ulcer diet, *Am J Med Sci.* 1971;261:61-67.

- <sup>19</sup> Lebovits AH, Strain JJ, Schleifer SJ, Tanaka JS, Bhardwaj S, Messe MR. Patient noncompliance with self-administered chemotherapy. *Cancer*. 1990;65:17–22.
- <sup>20</sup> Becker MH. Sociobehavioral determinants of compliance. In: Sackett DL, Haynes RB, editors. *Compliance with therapeutic regimens*. Baltimore(MD): The Johns Hopkins University Press; 1976. p. 40–50.
- <sup>21</sup> Richardson JL, Marks G, Levine A. The influence of symptoms of disease and side effects of treatment on compliance with cancer therapy. *J Clin Oncol* 1988;6:1746–52.
- <sup>22</sup> Lee CR, Nicholson PW, Souhami RL, Deshmukh AA. Patient compliance with oral chemotherapy as assessed by a novel electronic technique. *J Clin Oncol* .1992;10:1007–13.
- <sup>23</sup> Partridge AH, Avorn J, Wang PS, Winer EP. Adherence to therapy with oral antineoplastic agents. *J Natl Cancer Inst*. May 1, 2002;94(9):652-61.
- <sup>24</sup> Tatemichi M, Hamaguchi T, Hashira M, Hayashi T, Ito M, Nakatani A. Acceptability and long-term compliance with drug treatment for hypercholesterolemia in Japanese male workers: II. Long-term compliance with drug treatment. *Journal Of Occupational Health*. 2002;44(5):307-314.
- <sup>25</sup> Lacro J, Dunn LB, Dolder CR et al. Prevalence of risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. *Journal of Clinical Psychiatry*. 2002;63:892-909.
- <sup>26</sup> Vanelli M, Burstein P, Cramer J. Refill patterns of atypical and conventional antipsychotic medications at a national retail pharmacy chain. *Psychiatric Services* 2001;52:1248-1250.
- <sup>27</sup> Dolder CR, Lacro JP, Dunn LB et al. Antipsychotic medication adherence: is there a difference between typical and atypical agents? *American Journal of Psychiatry* 2002;159:103-108.
- <sup>28</sup> Montgomery SA, Kasper S. Comparison of compliance between serotonin reuptake inhibitors and tricyclic antidepressants: a meta-analysis. *International Clinical Psychopharmacology*, 1995;9 (Suppl 4):33–40. 17.
- <sup>29</sup> Anderson IM, Tomenson BM. Treatment discontinuation with selective serotonin reuptake inhibitors compared with tricyclic antidepressants: a meta-analysis. *BMJ*. 1995;310:1433–1438.
- <sup>30</sup> Hotopf M, Hardy R, Lewis G. Discontinuation rates of SSRIs and tricyclic antidepressants: a meta-analysis and investigation of heterogeneity. *BMJ*, 1997;170:120–127.
- <sup>31</sup> Sanchez CD et al. Diabetes-related knowledge, atherosclerotic risk factor control, and outcomes in acute coronary syndromes. *Am J Cardiology* 2005;95:1290-1294.
- <sup>32</sup> Sackett DL, Haynes RB, Gibson ES, Hackett BC, Taylor DW, Roberts RS, et al. Randomised clinical trial of strategies for improving medication compliance in primary hypertension. *Lancet* 1975;1:1205–7.
- <sup>33</sup> Wang PS, Bohn RL, Knight E, Glynn RJ, Mogun H, Avorn J. Noncompliance with antihypertensive medications: the impact of depressive symptoms and psychosocial factors. *J Gen Intern Med*. 2002 Jul;17(7):504-11.
- <sup>34</sup> Gallant, J, Block, D. Adherence to antiretroviral regimens in HIV infected patients: Results of a survey among patients and physicians. *International Association of Physicians in AIDS Care*. May 1998.
- <sup>35</sup> Chesney, M. New antiretroviral therapies: adherence challenges and strategies. *HIV/AIDS Treatment Updates*. ICAAC 1997 Satellite Symposium. Evolving HIV Treatments: Advances and the Challenge of Adherence. Available at: <http://hiv.medscape.com/Medscape/HIV/TreatmentUpdate/1997/tu01/tu01-06.html>. Accessed September 21, 1999.
- <sup>36</sup> Butler JA, Roderick P, Mullee M, Mason JC, Peveler RC. Frequency and impact of nonadherence to immunosuppressants after renal transplantation: A systematic review *Transplantation*. 2004;77:769-789.
- <sup>37</sup> Vincent, P. Factors influencing patient noncompliance: A theoretical approach. *Nursing Research*. 1971;20:509-516.

---

<sup>38</sup> Cerkoney, AB & Hart, K. The relationship between the health belief model and compliance of persons with diabetes mellitus. *Diabetes Care*. 1980;3:594-598.

<sup>39</sup> Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC. Primary prevention of coronary heart disease in women through diet and lifestyle. *NEJM*. 2000;343(1):16-22.

<sup>40</sup> Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. *Clin Ther*. 2001;23(8):1296-310.

<sup>41</sup> Cramer, J. The Titanic impact of medication compliance on epilepsy. The Epilepsy.com Web Site. Available at:

[http://www.epilepsy.com/articles/ar\\_1064959019.html](http://www.epilepsy.com/articles/ar_1064959019.html). Accessed Nov. 22, 2004.

<sup>42</sup> *JAMA Newslines*. Adherence to therapy. a background briefing by Dennis Blakeslee. May 19, 1998

<sup>43</sup> Gillis, J. Once-a-day aids pill could be ready soon. *Washington Post* web site. January 19, 2006; A01. Available at:

[http://www.washingtonpost.com/wp-dyn/content/article/2006/01/18/AR2006011802428\\_pf.html](http://www.washingtonpost.com/wp-dyn/content/article/2006/01/18/AR2006011802428_pf.html). Accessed January 24, 2006.