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Beyond Patient Compliance

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Incidence & Prevalence Of Patient Noncompliance

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***Abstract:** Calculating the incidence and prevalence of patient noncompliance is an arduous, uncertain, and all too often unrewarding task. Variations in the definition of compliance, the patient populations under consideration, and research methodologies impair reliability and preclude precision. Further, noncompliance is underreported, typically hidden, and rarely detected by clinicians. Nonetheless, research studies consistently (to the point of near-unanimity) and unambiguously reveal high levels of inadequate adherence to treatment recommendations throughout the healthcare spectrum, including cases of life-threatening illnesses. The indisputable conclusions are that medical noncompliance is, by any measure and from any perspective, pervasive and that healthcare's failure to successfully address such a problem comes at the cost of diminished outcomes, unnecessary expense, and avoidable patient morbidity and mortality.*

The No-Nonsense Summary Incidence & Prevalence Of Patient Noncompliance

- 1. Patient Noncompliance is pervasive*
- 2. Any patient in any practice is at high risk for noncompliance*
- 3. Clinical instinct cannot detect noncompliance*
- 4. No methodology accurately predicts which patients will and will not adhere to a treatment plan*

1. Noncompliance Is Pervasive The Research Tells Us So

Even a cursory scan of the research completed in the past 20-30 years provides an abundance of studies demonstrating that noncompliance is ubiquitous. The following assortment of statistics is representative and could be expanded a hundredfold:

- Chewing et al found that one-third of arthritis patients studied had unilaterally adjusted their medications in the preceding week, approximately 60% of these changes were intentional while the remainder were attributed to forgetfulness.¹
- Among patients receiving oral hypoglycemic drugs for type 2 diabetes, only 31% of those taking sulfonylurea, 34% of those taking metformin, and 13% of patients receiving both sulfonylurea and metformin adhered to the regimen over a one year course.²
- In one survey, 12-20% of adults attested to having taken other people's medications.³
- Up to 40% of patients in mainstream cancer therapy who were concomitantly using nontraditional treatments (e.g., St. John's Wort and shark cartilage) had not volunteered this information to their treating physicians.⁴
- Another study found that 50% of patients did not follow referral advice, 75% did not keep follow-up appointments, and 50% suffering from chronic illnesses dropped out of treatment within a year.⁵
- In multiple countries less than 25% of patients treated for hypertension followed their treatment plans sufficiently to reach their targeted blood pressure levels.⁶
- Fifteen percent of hospital readmissions for heart failure were secondary to underutilization of prescribed medication.⁷
- Although twice-daily chest physiotherapy (CPT) is key to combating pulmonary deterioration in cystic fibrosis, a 1998 study found 74% of patients received no more than two CPT treatments per week.⁸
- Richardson and colleagues found that adherence to clinic attendance did not assure adherence with medication. Of patients keeping more than 60% of appointments, 40% were found to be noncompliant with medication, as determined by urine metabolite measurement⁹
- Only 43% of Australian patients with asthma adhere to their medication regimen; only 28% use preventive medication prescribed them.¹⁰
- Patients prescribed exercise programs have dropout rates that peak during the first three months, with one year dropout rates of approximately 50%.¹¹
- On average, for all dosing schedules of anti-epileptics, patients took the correct prescribed daily dose 75% of the time. For once a day dosing, the compliance rate was 85%; for twice a day dosing, 80%; for three times a day dosing, 75%; and for four times a day dosing, less than 50%.¹²
- In 1977, Mattar et al analyzed 300 pediatric patients receiving prescribed acute otitis media medication from their parents. Of those, 36% received an insufficient number of doses, 37% did not receive a complete course of antibiotic because the parents unilaterally discontinued the medication early, and 20% received the wrong dosage because of incorrect labeling, misunderstood instructions, and other unintentional errors. Only 7% of the children received the medication exactly as prescribed.¹³

Other patient compliance indicators have been studied in great quantity: adherence to diet and stop smoking programs, use of seat belts, fulfillment of immunization recommendations, regularity of dental check-ups, continuation of rehabilitation, addiction, and psychotherapy programs, appropriate use of CPAP instruments, and many others, all with comparable results. An overview of one category, surveys identifying unfilled prescriptions, is instructive. According to the *1985 National Prescription Buyers Survey* conducted for The Upjohn Company by Market Facts, Inc. of Kalamazoo, Michigan, 14% of patients receiving prescriptions never had them filled, and 30% of refillable prescriptions were never refilled. A British study held that 25% of prescriptions for oral contraceptives were not filled.¹⁴ Of the 2000 patients interviewed for the *Schering Report* in 1992, 8.7% reported that they did not fill their initial prescriptions.¹⁵ Levy calculated that 30% or more of refillable prescriptions are abandoned¹⁶ while Fedder, in a 1990 study, found that 77% of authorized refills were never filled.¹⁷ Still other studies found that the percentage of patients who did not have initial prescriptions filled ranged from 6–44%.^{18,19, 20, 21, 22, 23}

In summary, while results may vary and legitimate criticisms of research technique may be raised, the overwhelming preponderance of research demonstrates that that noncompliance with treatment is massive and widespread – regardless of the disorder, the nature of the treatment, the cultural or ethnic background of the patient, the personality of the clinician, the cost of the treatment, or any other studied factors.

2. Noncompliance Is Pervasive Regardless Of The Patient Population

Although common sense suggests that certain groups of patient would more careful than others about following treatment instructions, there is little support for this notion. If patients who require guardianship-level assistance in making significant decisions (e.g., children, clients with severe cognitive impairments, and grossly psychotic patients) are withdrawn from the population under consideration, there are, in fact, few demographic or situational factors that have a dramatic impact on compliance. Intelligence, age, and healthcare experience, for example, have little correlation with compliance. As is true in so many cases, adolescence is an exception to the rule with some studies attributing an impressive recalcitrance among a noteworthy fraction of this age group.²⁴

3. Noncompliance Is Pervasive Even Among Knowledgeable Patients

In a salient study, 36 medical students were assigned to a 14 day regimen of either twice daily or thrice daily ingestion of a medication proxy (Tic Tacs®) from pill bottles that electronically recorded the removal of the medication.²⁵ The results were impressive:

- 14% of the students did not turn in their electronic recording devices
- Overall adherence was about 70% — mirroring the rates found in AZT and anticonvulsant studies
- Only 46.5% of the doses were taken at the prescribed dosing frequency
- Only 28.5% were taken at the prescribed intervals
- When subjects were asked the reasons for being less than 100% adherent, the most common responses had to do with scheduling, the medical students pleading a hectic daily activity list or an irregular routine.

In a similar study, medical students who attended a conference on patient compliance were assigned to take a medication proxy (Vitamin C) for one week, to follow dietary restrictions, and to complete an attitude and health beliefs questionnaire. Based on the results of compliance studies for patients with non-symptomatic disorders (e.g., hypertension), the authors prospectively — and correctly — predicted the students' noncompliance rates.²⁶

Most compelling, at least to me, is the case of my incredibly intelligent and capable wife (successful businesswoman, published author, life-long inhabitant of the 99th percentile intellectually), who was plagued with recurrent cystitis despite apparently successful (repeated) treatment with antibiotics. When yet another episode (perhaps her 5th or 6th) struck, she decided to treat the problem immediately and call her doctor later. She then pulled out four partially-filled bottles of the antibiotic left over from previous prescriptions. When I asked where the medications came from, she explained that happily her physician always gave her a seven day supply although her symptoms typically disappeared after taking only two or three days worth of medications. She responded to my recommendation that she take the entire seven-day supply by pointing out the obvious — that one had to hoard any extra pills possible since the cystitis would inevitably recur.

IMPLICATIONS OF TIC TACS®

UTILIZATION IN MEDICAL RESEARCH

Given the necessity of placebos for use in double-blind clinical studies, Tic Tacs®, used in this case as an openly recognizable proxy for medication, make an intriguing candidate for the more covert role as placebo. Tic Tacs® are readily available in a variety of colors, carry no tell-tale markings, and are competitively priced. At the time of publication, Tic Tacs® were available [wholesale](#) at \$0.60 per unit of 24 packs. At approximately 0.5 grams per piece, they also possess a mass approximating that of most medication tablets. Potential buyers, however, should be aware that beneath that thin candy veneer lurks complexities such that the Food and Drug Administration required six years of study to determine the appropriate weight of a “serving” of Tic Tacs® and competing breath mints in order to comply with the Nutrition Labeling and Education Act.

Cindy Skrzycki, "Sizing Up Breath Mints Leaves a Bad Taste in Some Mouths," *Washington Post*, January 16, 1998.



4. Noncompliance Is Pervasive Even When The Stakes Are High

Still more strikingly counterintuitive is the existence of noncompliance in the face of disorders with especially dire consequences, including death, if treatment is unsuccessful. Examples follow:

- Approximately half of the patients who chose to undergo the pain, risk, and emotional trauma of a kidney transplant do not adequately follow their medication regimen prescribed to prevent rejection, and 25% **regularly** miss doses of prescribed medications.^{27,28} Didlake and colleagues judged noncompliance the third most common cause of rejection of renal transplants.²⁹
- In one study, 58% of patients with glaucoma who were told that failure to use their medication would result in blindness were noncompliant; 42% of patients **who had already lost sight in one eye** after they failed to comply with their medications persisted in their noncompliance.³⁰
- Only 7% of diabetics comply with the regimen necessary to control their glucose levels, which in turn determines the severity of the disease's long term effects.³¹
- A recent study of HIV patients on antiretroviral treatment demonstrated that 43% admitted to not taking their medications as prescribed and 6% never even fill their prescriptions.³² Another study estimated that half of those surveyed had missed doses in the two weeks prior to the survey, although they believed the medication to be effective and potentially life-saving.³³

5. Noncompliance Is Pervasive Whether The Clinician Detects It Or Not

Clinical judgment re compliance, independent of measurements such blood tests, interviews, pill counts, etc. has a spectacular record – for inaccuracy. There is impressive evidence that clinicians, regardless of discipline, years of experience, or specialty, overestimate compliance among their own patients by 100%.³⁴ 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.³⁵ Overall, physicians are no more accurate in detecting compliance or noncompliance than relying on the flip of a coin.³⁶ (Physicians are the profession typically studied; there is no indication that other healthcare professionals predict noncompliance with greater or less accuracy.)

Detection and measurement of noncompliance by the most frequently used methodologies may severely underestimate the rate of adherence failures. Patients, for whatever reason, do regularly overestimate their compliance with treatment, whether they claim 100% compliance or they report partial compliance.^{37,38,39,40} In one study, patients who admitted to missing one or more recent doses still claimed a compliance rate 17% (on average) higher

than their actual rate.⁴¹ While monitoring of medication use by electronic means and by plasma assays of chemical markers incorporated into the medications may promise more routinely accurate results, these methods are expensive and often impractical for day to day clinical use. And, none of these technologies are perfect. Biochemical measurements might, for example, indicate that the subject ingested the medication but not be able to specify whether the patient took the right amount at the right time. Electronic pill bottles may only demonstrate that a vial was opened at a given time without indicating whether a pill was actually removed and taken at that same time.

Further, positive outcomes in the face of poor adherence can also distort the apparent rate of noncompliance. According to one study⁴² of prostate cancer patients in treatment, one patient in six was absolutely compliant. Of the remaining patients,

- Half made errors too small to modify the actions of all but the most unforgiving medicines
- A third delayed or omitted enough doses to modify the actions of all but the most forgiving drugs
- One-sixth took little medicine, but had outcomes that camouflaged them as good compliers

6. Noncompliance Is Pervasive: That Is All We Know On Earth & All We Need To Know

The knowledge that large percentages of any patient group will be noncompliant with any treatment recommendations is useful. Knowing, for example, that the average adherence to medication recommendations for non-acute disorders is approximately 50% in both the pediatric⁴³ and adult^{44,45,46, 47,48,49,50} populations will prompt the thoughtful clinician to maintain a congruently high index level of suspicion re the potential for noncompliance among those she treats.

Beyond such awareness, however, incidence and prevalence research contributes little to the evaluation and management of a specific patient. In general, the utility of incidence and prevalence data diminishes logarithmically as the clinician approaches a real, live, distinctly individual patient. The variations in compliance research methodology and the lack of a gold standard for measuring compliance further restrict the pragmatic usefulness of this data. As Stephenson et al noted in a 1998 *JAMA* article,⁵¹ "This average compliance rate of 50% provides only the most limited picture of compliance" In the same article, the authors also pointedly observed, "There is a wide range of compliance among patients, from 0% to over 100%."⁵² I confess that, on first reading, this quotation seemed silly, but on reflection, I now view it as a handy tool for putting compliance research findings into perspective.

In a similar vein, DiMatteo straightforwardly concludes, in a meta-analysis of patient compliance studies published from 1948-1998, that, "Clinical decisions and research programs ultimately depend on the reliable and valid measurement of adherence. Yet, 50 years of research in this field have not provided the data necessary to answer critical measurement questions."⁵³

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