

Electronic Subject Diaries in Clinical Trials

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Subject diaries are an essential component of certain clinical studies, particularly those that assess the occurrence and intensity of symptoms, effects of medication, frequency of target behaviors, or perceived quality of life. Despite many years of experience with paper diaries in clinical studies, uncertainties persist about the timeliness, currency, completeness, and accuracy of diary data collected by conventional pencil-and-paper methods. Some strengths and weaknesses of written diary data are summarized in Table 1.



Electronic diaries are small, portable electronic devices that are capable of presenting text and/or graphics to the subject, recording and electronically storing subjects' responses, and transmitting stored data to a computer, where data from several such devices can be pooled and analyzed (Table 2). Electronic diaries have contributed significantly to the technology of diary-based clinical studies as a result of two simple but important attributes: they can time stamp (automatically record date and time) each entry as it is made, and they can make it very simple to enter a data point.¹

Here we discuss diary data in clinical research and present the case that electronic subject diaries offer some key advantages. We illustrate the points discussed with a specific example using an electronic diary in a chronic pain study and suggest how it is possible to increase—by technical means—the quality of self-reported information and data.

Issues common to paper and electronic diaries

Several years ago, N.K. Aaronson examined the methodological issues surrounding quality-of-life assessment.^{2, 3}

His analysis applies as well to the more general issues of diary data in clinical trials. In particular, he raised questions about who should make the assessment, what should be assessed, how data should be collected, and what time frame should be specified for the subjects' responses.

Who should assess. Studies that Aaronson summarized show that physicians do not agree with each other in their assessments of a patient's quality of life—nor is agreement between physicians and patients themselves statistically reliable. In short, he found that individual patients are the best experts on how they feel.

Other studies indicate that data concerning drug efficacy and safety in subjects is most pertinent when it is obtained from the subjects themselves. It is also most revealing when subjects do their self-assessments as they live and work, and at the same moment to which the self-assessment applies. Saul Shiffman at the University of Pittsburgh coined the term *ecological momentary assessment* (EMA) to refer to such autobiographical reporting, and EMA has become an important part of the literature in health psychology. Most modern EMA studies rely on electronic diaries.⁴

What to assess. Global health status questions (great breadth but little depth) are appropriate if the research goal is to find a summary health-status statistic to correlate with, for example, another summary statistic (for example, cost of care). Aaronson says,

If, however, the expected difference in event rates between the treatment arms in a clinical trial is small, it may be necessary to employ a more detailed instrument that is highly sensitive to either intra-individual change or intergroup differences in selective quality-of-life domains.³



Electronic diaries that are simple to use can record compliance and have advantages when studies require frequent measures.

TABLE 1 Strengths and weaknesses of paper diaries**Strengths**

Behavioral equivalent of a monitor of physiologic status
 Only way to assess subject's status when the condition being treated has a subjective or behavioral dimension (e.g., measurement of symptoms like pain or airway status, evaluation of compliance with prescribed drug regimen)
 Statistically dense sampling allows tracking changes in parameters over time
 Furnishes information on the significance of symptoms and relief to subjects, which may be at least as important as the symptoms
 Available for entry concerning current symptoms, medication consumption, episodes
 Data handwritten on paper by marking selections, entering numbers or text

Weaknesses

Construction and validation of the test instruments
 Logistic problems of maintaining subject compliance in completing and returning diary
 Quality of data compromised by problems with subject compliance
 Few, if any, ways to monitor the integrity of subject-supplied data
 No controls for retrospective entry of "current" data
 Effort and cost of data entry, data management, database correction; no checks for completeness or range

For this purpose, the repeated longitudinal tracking possible with subject diaries is particularly appealing.

The appetite for data. In studies of chronic relapsing disorders, investigators yearn for a record that measures symptoms several times daily over a course of months or years.⁵ Such investigators often design written diary requirements that burden subjects, medical staff, and institutional support staff. A study of the effectiveness of acrivistine, acrivistine plus pseudoephedrine, pseudoephedrine alone, or placebo in the treatment of seasonal allergic rhinitis serves as an example. In that study, 676 subjects sensitive to white cedar pollen were expected to record their allergy symptoms on written diary cards twice daily for two weeks.⁶ In a similar study, allergic rhinitis subjects sensitive to ragweed pollen were expected to record their symptoms three times daily on written diary cards.⁷ In a pain study, 227 migraine subjects were randomized to receive either zolmitriptan or placebo and to maintain a written symptom diary for more than a year, recording all headache symptoms, the response of the headache to treatment after two and four hours, any recurrence of headaches, and all adverse responses to medication.⁸ (This, incidentally, while the subject was in the throes of a migraine headache.)

In another study, Eich and colleagues instructed chronic headache subjects to keep an hourly written record of their symptoms for six weeks.⁹ In a study of ibuprofen in control of

pain associated with dental impaction, subjects were to record their pain in a diary hourly for 12 hours.¹⁰ Compliance with these difficult requirements is generally poor, or, if good, is suspect because subjects are known to fill in diary cards retrospectively.

Reducing the data burden. Paper diaries lack the means to prevent missing data or to check for out-of-range data at the time of entry. Some studies have relied upon staff to elicit and record the diary data in an effort to minimize the burden on the subject and to increase the accuracy of diary data. Telephone-administered questionnaires have been used in many studies, including a study of the possible effects of stress on subjects with unstable angina¹¹ and one on the effect of percutaneous transluminal coronary angioplasty on quality of life.¹² Such telephone-administered questionnaires yield more reliable subject responses and cleaner data, but these improvements require the commitment of trained staff to actually perform the work of contacting the subjects and transcribing their observations. This approach can be especially effective when telephone interview data is entered not on paper but directly into the study database, either automatically or by manual transcription during the interview.¹³

Dense data. Electronic diaries may elicit more data and sometimes more clinically appropriate data than paper diaries. The statistical power of studies is increased by dense sampling of key parameters, according to J.R. Trout (professor emeritus of

TABLE 2 Strengths and weaknesses of electronic diary data**Strengths**

Includes all the strengths of written diary data
 Greater subject compliance because of ease of entry; possibility of monitoring compliance
 Enhanced data integrity because of internal validity checks, time stamps
 Possibility of interim access to diary data—direct transfer from subject's device to central database aids in subject and trial management
 Little or no need for study staff to enter data, actively manage database, or clean data
 Dynamic display permits a variety of user-friendly data entry elements and formats
 Permits comments by subjects

Weaknesses

Requires training to familiarize subjects with use of the technology
 Cost of the device and communication of data
 Possible errors in local time settings or programming requires pretrial testing
 Logistics of distribution, maintenance, and recovery of devices and communications infrastructure
 Design, implementation, validation of a system to collect, display, and deliver data
 Each data entry element or format requires programming and planning
 Reading and transcription of comments may require user to have a computer

statistics at Rutgers University and a statistical consultant to FDA and pharmaceutical companies). Dense sampling reduces the component of variance in statistical analyses contributed by intrasubject variability and allows the tracking of varying parameters. New approaches to the analysis of tracking data may be required to obtain full benefit of dense sampling.¹⁴

How often and when to assess. A diary entry is a record of a memory—but memory is unreliable. Aaronson advocates short intervals between entries “to avoid confounding specific symptom experience with a more generalized tendency to complain.”

Evidence from psychological studies of autobiographical memory indicates that recollection is not a process that degrades uniformly in time as if holes were appearing at random in an archive. Instead, people rely on heuristic strategies and reconstruct the past from cues (such as “we usually don’t go to restaurants except on Fridays”). Long-term (weeks, months) recall of dates, events, symptoms, and overall status is known to be grossly inaccurate.¹⁵

A study of mechanisms for coping with pain in fibromyalgia, for example, relied upon self-reported measures of pain and psychosocial functioning at baseline and then at the end of a three-month treatment period.¹⁶ At weekly office visits in the chronic

Entering time-sensitive diary data at the wrong time invalidates the entry, and studies suggest that this problem cannot be successfully managed with paper diaries.

headache study, subjects were asked to rate their present pain intensity and to recall their maximum, usual, and minimum pain intensity over the previous week.⁹ In both studies, recalled pain correlated strongly with present pain severity, indicating that subjects rated past pain higher when asked about it while they were hurting. Smith and Safer confirmed this finding by having subjects record in an electronic diary their chronic pain symptoms and use of medications. As in Eich’s headache study, subjects recalled their pain and need for medication on the previous day and week in a way that was biased by their present pain intensity.¹⁷ The inverse is also true; an extremely intense experience in the past will strongly bias a present pain assessment.^{4,15}

The cognitive demands of indicating how much one hurts *now* do not appear to involve such complex cognitive reconstruction. For this reason and because of increasing interest in moment-to-moment correlations among variables, interest is also increasing in repeated, simple assessments of current status instead of asking people retrospective questions that may exceed the capability of autobiographical memory.⁴

Contrasting paper and electronic diaries

Subject identity. The FDA (Food and Drug Administration) mandates that data entry not be anonymous. Practices vary for how subjects acknowledge responsibility for the content of diary data on paper, but regulations governing computerized clinical data (21 CFR 11) apply to electronic subject diaries. It is clear that all such data must, therefore, be linked to the author and acknowl-

edged by the author’s signature. FDA guidance documents also advise that any person entering clinical data be able to make a parenthetical comment.

Subject experiences. The above considerations indicate the value of tracking a subject’s experience by making multiple samples of the subject’s present status. But attempting to do so with paper is difficult. Sampling theory dictates that to represent the time behavior of a changing parameter, sampling must be done at twice the frequency of the change one wants to track. Frequent monitoring with paper diaries is burdensome, in part because any recording of unscheduled sample times must be written by hand. Yet indications are that subjects can make rather frequent samples when they are easy to do. In a study of subjects’ pain using an electronic pain recording device, for example, subjects changed the electromechanical slide setting on the device an average of every 2.6 hours.¹⁷ Pain subjects do not consistently log the time and severity of their symptoms on handwritten diary cards. Electronic diary entries, on the other hand, can be very fast, and, with thoughtful design, can be simplified to a series of selections made by single touches of a stylus to a screen.

Attempts at frequent sampling have been made using paper diaries by prompting momentary assessments. In one such study, treated alcoholics were beeped using a randomized alarm programmed into special wristwatches. Eight times a day such alarms prompted the subjects to complete a paper assessment card concerning craving for a drink, mood, recent alcohol use, and current situation. Although compliance seemed high, debriefing revealed

that 70% of the subjects had faked at least some entries every day by writing in the time of the alarm, but actually completing the assessment later at a more convenient time. Thus, a substantial number of retrospective entries had been entered under the guise of current entries.¹⁸ Obviously, in the case of momentary assessments, the time of entry is at least as important as the accuracy of the entry itself. Entering time-sensitive diary data at the wrong time invalidates the entry, and studies suggest that this problem cannot be successfully managed with paper diaries. Electronic subject diaries can confirm when entries are made by time stamping them.

Data accuracy. When investigators use unobtrusive duplicate measures to check the accuracy of subject-kept written diaries, they find that subjects’ compliance with instructions is notoriously poor. Reports on the events of interest—compliance with drug regimens, peak expiratory flow rates, blood glucose levels—are often inaccurate. Such simple tasks as reporting nocturnal coughing on written diary cards¹⁹ or the date and time that the subject entered a particular room in the house²⁰ have provided unreliable and inconsistent data.

In a study of compliance with peak flow monitoring in asthmatic children, subjects were given either a mechanical mini-Wright peak flow meter and instructions to measure peak expiratory flow rate (PEFR) at least twice a day for three weeks and to complete a manual diary card logging each of the two required daily measurements. Subjects also used an electronic meter that automatically recorded the time of PEFR measure-

ment along with the date.²¹ The electronic monitor data indicated that 52% of the expected twice daily measurements were missing, while the manual diary card data indicated only 15% of the twice daily values were missing. The investigators concluded that manual diaries overestimated use of the peak flow meter, and that in general, written diary records would distort value toward the more desirable outcomes.

Researchers in a similar study gave 20 adult asthmatic subjects a modified mini-Wright peak flow meter that recorded PEFV values, date, and time in its electronic memory, but subjects were not told that the device was time stamping their PEFV measurements.²² Subjects were instructed to measure PEFV and to record the values morning and evening. Only 1897 (54%) of the values were recorded in the diary card, but even fewer (1533, or 44% of the total) were stored in the electronic device. In other words, of the 1897 values written in the diary card, the subjects invented 425 (22%). Straka and colleagues compared the accuracy of self-reported use of isosorbide dinitrate for the management of ischemic heart disease with data from a com-

Numerous anecdotes describe subjects completing a week's or a month's worth of diaries in the parking lot before delivering them to sites.

puterized medication event monitoring system.²³ In written diary entries, 67% of the subjects overestimated their compliance, and 30% of the diary entries were in error.

Similarly, Milgrom found that written diary data on subject compliance for treatment of asthma in children agreed poorly with data collected electronically by metered-dose inhalers.²⁴ Subjects reported a median use of inhaled corticosteroids 95.4% of the time in written diaries while electronic data collection showed a median use of 58.4%. Comparison with electronic data collection showed that more than 90% of subjects exaggerated their use of inhaled corticosteroids.

Compliance and acceptance

A sizable proportion of subjects in a clinical trial fail to complete written diary cards. In a study of the effectiveness of various treatments on low back pain, for example, 22 of 85 subjects (26%) failed to complete both the initial and final questionnaires.²⁵ In a study of incontinence in women undergoing vaginal reconstructive surgery, 9 of 32 subjects (28%) failed to complete urinary diary and quality-of-life evaluations after a mean of 2.9 years. In a two-week study of omeprazole and famotidine for the treatment of duodenal ulcers, 33% of subjects failed to complete their diary cards.²⁶ In a study of low-dose levonorgestrel ring contraception in 1005 women, 30% failed to return the required menstrual diary.²⁷

The "parking lot problem." Sites urge subjects to complete diaries faithfully. Occasionally, sites also arrange for financial incentives. With paper diaries, however, data can be entered retrospectively even if the protocol requires entry of current data in a timely and progressive fashion. Thus, there are numerous

anecdotes (though we have found no published data) about subjects entering a week's or a month's worth of diaries in the parking lot before delivering them to sites. To avoid such faked data, trial planners experienced with paper diaries have told us they like to keep incentives weak. As noted, electronic diaries can be configured so as to enable only the entry of current data where such data is required. An interesting consequence is that incentives can be increased without risking "parking lot" data, which restores the potency of tools to increase compliance—such as hounding subjects.

Subject comparisons. Subjects readily accept electronic diaries²⁸ and are more likely to comply with data collection procedures when using them.²⁹ A study of 166 migraine subjects using nonsteroidal anti-inflammatory (NSAID) drugs in at-home self-medication demonstrated the acceptability and utility of a computerized electronic subject diary for assessment of headache.³⁰ Subjects recorded visual analog scales of headache severity, headache relief scales, and time of taking analgesics. Bolten compared electronic and written pain diaries and found that the two were comparable, but that subjects were more likely to report significant drug-related adverse experiences on the electronic diary than on the written diary.³¹ There was an increased volume of data and greater subject compliance in reporting episodes of urinary incontinence when women used the computerized voiding diary than when using the conventional written diary.^{32, 33}

Studies report high compliance in the use of electronic diaries. When 20 psychiatric subjects with panic disorder were given an electronic diary—with instructions to answer 19 or more questions on the hour from 7 a.m. to 11 p.m. or when they were having a panic attack—they completed an average of 88% of all hourly ratings.³⁴ Heart-lung transplant patients at the University of Minnesota were given a paperless electronic spirometry and diary instrument as part of the home monitoring program to detect the earliest signs of rejection or infection.³⁵ They were instructed to use the device daily to measure lung function and to complete a symptom diary, and then to transmit data weekly by telephone. Over the one-year review period, 82% of patients transmitted records every week, an average of 4.5 records per week. Spirometry data were always present and vital sign and symptom data were missing in only 2% of cases.

Women with urinary incontinence preferred an electronic, computerized voiding diary to a written diary: 90% of the women with a variety of voiding dysfunctions and 79% of normal control women.³⁶ The electronic device provided more information and better data than the written diary. In this crossover study, subjects were randomly assigned to groups that got either the electronic diary or the manual diary, and then they crossed over after two weeks. Subjects preferred the electronic diary. One remarkable finding in this study is that only 14.3% of the subjects who received the handwritten diary before the electronic diary found this manual method tedious. After having used the electronic diary, however, 61.9% of the subjects reported finding the written diary tedious. Tiplady and colleagues also made a comparison of an electronic diary and paper questionnaire among 22 adult patients with chronic obstructive airways disease; 13 of

them (59%) found it “easy” or “very easy” to use the electronic device, and 5 (23%) reported that the two were equivalent.³⁷

In cases where unauthorized access to a subject’s data may be embarrassing or harmful, electronic privacy controls on a diary device can make it impossible to read previously entered data. With paper diaries, on the other hand, subjects are vulnerable to snooping if they lose physical control of the handwritten pages.

Data reduction

Data reduction from manual diaries requires several steps. In the NSABP (National Surgical Adjuvant Breast and Bowel Project) Breast Cancer Prevention Trial, for example, questionnaires were first logged into the computer, then digitally scanned and electronically checked for missing, contradictory, and impossible entries. Questionnaires with dubious responses were placed in an electronic holding file while a letter of inquiry was sent to the investigative center where the problematic ques-

on one screen be completed before the subject could advance to the next screen. Multiple reports could be filed each day, but one report completed for the waking hours of a day was the standard of full compliance. Although the device was portable and could be used to enter data on battery power, most subjects kept the device powered by means of a recharger and connected to a telephone line at home.

The device supported two-way messaging. In accordance with 21 CFR 11 concerning electronic source data, subjects signed each report and could handwrite a short on-screen note



or comment. After transmission of diary data to the central network computer via telephone, which took about one or two minutes of connect time, the study coordinator could view such messages on a computer—either at home or at the office—and respond appropriately. The study coordinator’s outgoing messages to subjects appeared on the device’s screen during

the next reporting session.

Data entry. Subjects could enter data in several ways.

Body diagram. The report included a diagram of the human body, which the subject could mark by touching the screen with the stylus to indicate the location of pain. In this study, only pain regions that included the lower back were part of the data analyzed. Pain sites were coded for data retrieval and analysis.

Visual analog scale (VAS). A visual analog scale was marked by touching a line (2 mm wide by 5.7 cm long) on the screen. A mark appeared on the line and a score was posted in a box beside the line. The score ranged from 0 (none) to 10 (worst), and was used by the subject to rate the “intensity of pain at this site NOW.”

Pain history. For each pain site, the subject recorded hourly pain ratings for up to 16 waking hours preceding the report time by marking 16 vertical VAS columns each representing one hour. Subjects noted below the columns whether they had been asleep during that hour. In order to move to the next screen, the subject had to complete all 16 hours (unless a prior report had already covered part of the time).

Medications. Subjects were asked to log each medication taken (including 2 opioids and 2 NSAIDs as well as some 20 over-the-counter medications for pain, anxiety, or muscle relaxation). The subjects selected medications from a list and tapped on “hour columns” spanning the 16 hours prior to the time of the report. They recorded time of consumption to the nearest minute (if taken “now”) or to the nearest 10 minutes if entered retrospectively.

Activity average. Subjects used a VAS ranging from 0 (lying still but not asleep) to 10 (hard physical labor) to record their “average activity over the last 16 hours” and to mark their activity for each waking hour in that period.

Mood. Subjects were required to use the VAS marked from “none” to “worst” to rate their current severity of depression, anxiety, and irritability.

It requires a firm effort of the will to remember quite how inchoate European regulatory affairs were as recently as the early 1990s.

tionnaire originated. If issues were resolved, data were corrected and entered into the database.³⁸ Data reduction from

Data from electronic diaries can be entered unambiguously by capture, subjected to completeness and logic checks on entry, and parsed directly into the database.

electronic diaries can avoid most of this process because data can be entered unambiguously by capture, subjected to completeness and logic checks on entry or submission, and can be automatically parsed directly into the database.

Interim access to data

The hardware platforms that qualify as electronic subject diaries vary widely—from tiny special-purpose devices for collecting one measure by button push or physical manipulation to pen-based multifunctional portable computers. Even interactive voice response systems (IVRS) can serve as electronic subject diaries. Reviewing available devices is beyond the scope of this article, but a case study illustrates our discussion and shows how access to diary data can assist trial management.

In a study done at Brigham and Women’s Hospital (Boston) and Harvard Medical School to assess the suitability of opioid therapy for chronic low back pain, 21 subjects used an electronic diary to furnish hourly pain and physical activity scores every day for a year. Apple Newtons were converted into subject diaries called LogPads (Personal Health Technologies, Boston, MA), which were programmed to require that all data elements

Symptoms. Subjects could select from a list of 8 on-screen symptoms or call up an expandable library of some 30 others. They rated any selected symptom for severity using a VAS ranging from “none” to “worst.”

Messages. Short (1–3 sentences) messages to the subject appeared in typescript above a series of yes or no questions that could be written by the study coordinator or selected from a library of all questions asked over the course of the study. Messages from the subject were recorded as pen strokes on an 8-cm by 5-cm area of the screen encoded as a vector map and displayed in LinkManager (PHT Corporation, Boston, MA) as an image. The study coordinator routinely transcribed such messages.

Subjects were instructed to enter and send at least one report per day at the end of their wake cycle. They were encouraged to submit more reports if they wanted to document changes in their pain level, medication consumption, or symptoms. Most subjects submitted a report each day. The electronic diary time

Pain, mood, attitude toward illness or treatment, and perceived quality of life cannot be measured mechanically. The only way to measure these is to ask the subject.

stamped all data, field by field. It also logged the report submission time and transmission session duration.

Compliance was satisfactory (all 21 subjects missed fewer than one report per week on average, usually because of postmidnight reporting on weekends). Subjects entered data on average 6.75 times per week and showed 89.9% compliance with daily monitoring over the year. None dropped out. For comparison, 16 pain subjects participating in the study did not use the LogPad and were asked to fill in paper diaries for one week each month. Compliance ratings for device users exceeded 99% for ratings of activity, medication, and pain, but 33%, 53%, and 56% for subjects filing information on those parameters via paper diaries. In exit interviews, 5 of the 21 subjects (24%) complained about the effort to fill in the long questionnaires (SF 36 Health Status Questionnaire, CPEQ Comprehensive Pain Evaluation Questionnaire), but reported that the daily task of entering the LogPad data was no trouble. Several subjects expressed regret that they would no longer be monitored by device, which had given them an important link to the pain management clinic. They expressed a global preference (100%) for electronic data entry.³⁹

Observations

The subject diary in a clinical trial is a way of measuring aspects of the subject's status that cannot otherwise be measured. Blood pressure, heart rate, lung function, and blood glucose, for example, can all be measured by attaching appropriate instruments to the subject. Pain, mood, attitude toward illness or treatment, and perceived quality of life, on the other hand, cannot be measured mechanically. The only way to measure changes in parameters

such as these is to ask the subject.

Technical advances now solve key problems in capturing meaningful diary data. They enable simple, frequent sampling needed for capturing a series of momentary measures, thus avoiding bias and error in recollected autobiographical reports. And they ensure the authenticity of such momentary ratings as current. These two deceptively simple achievements convert an error-prone, low-compliance, low-quality instrument (a hand-written diary) into a dependable device capable of providing a data stream that reveals and documents a subject's experience in compelling detail. Researchers and regulators who have avoided diary data in the past because of its known problems need to re-evaluate that decision now that reliable, dense data can be generated directly by subjects or their caretakers.

References

1. H.E. Drummond, S. Ghosh, D. Ferguson, D. Brackenridge, and B. Tiplady, “Electronic Quality of Life Questionnaires: A Comparison of Pen-Based Electronic Questionnaires with Conventional Paper in a Gastrointestinal Study,” *Quality of Life Research*, 4, 21–26 (1995).
2. N.K. Aaronson, “Methodologic Issues in Assessing the Quality of Life in Cancer Patients,” *Cancer*, 67 (supplement 3) 844–850 (1991).
3. N.K. Aaronson, “Quality of Life Assessment in Clinical Trials: Methodologic Issues,” *Controlled Clinical Trials*, 10 (supplement 4) 195S–208S (1989).
4. S. Shiffman and A.A. Stone, “Introduction to the Special Section: Ecological Momentary Assessment in Health Psychology,” *Health Psychology*, 17, 3–5 (1998).
5. B.J. Marshall, S.R. Hoffman, V. Babadzov, et al., “The Automatic Patient Symptom Monitor (PASM): A Voice Mail System for Clinical Research,” *Proceedings of The Annual Symposium on Computer Applications in Medical Care*, 32–36 (1993).
6. B.O. Williams, H. Hull, P. McSorley, et al., “Efficacy of Acrivastine plus Pseudoephedrine for Symptomatic Relief of Seasonal Allergic Rhinitis Due to Mountain Cedar,” *Annals of Allergy, Asthma, and Immunology*, 76, 432–438 (1996).
7. R.J. Dockhorn, B.O. Williams, and R.L. Sanders, “Efficacy of Acrivastine with Pseudoephedrine in Treatment of Allergic Rhinitis Due to Ragweed,” *Annals of Allergy, Asthma, and Immunology*, 76, 204–208 (1996).
8. G.D. Solomon, R.K. Cady, J.A. Klapper, et al., “Clinical Efficacy and Tolerability of 2.5 mg Zolmitriptan for the Acute Treatment of Migraine: The 042 Clinical Trial Study Group,” *Neurology*, 49, 1219–1225 (1997).
9. E. Eich, J.L. Reeves, B. Jaeger, and S.B. Graff-Radford, “Memory for Pain: Relation between Past and Present Pain Intensity,” *Pain*, 23, 375–379 (1985).
10. S.A. Cooper, P.D. Quinn, K. MacAfee, et al., “Ibuprofen Controlled-Release Formulation: A Clinical Trial in Dental Impaction Pain,” *Oral Surgery, Oral Medicine, and Oral Pathology*, 75, 677–683 (1993).
11. N. Frasure-Smith and F. Lesperance, “Differential Long-Term Impact of In-Hospital Symptoms of Psychological Stress after Non-Q-wave and Q-wave Acute Myocardial Infarction,” *American Journal of Cardiology*, 69, 1128–1134 (1992).
12. P.D. Cleary, A.M. Epstein, G. Oster, et al., “Health-Related Quality of Life Among Patients Undergoing Percutaneous Transluminal Coronary Angioplasty,” *Medical Care*, 29, 939–950 (1991).

13. R.N. Jamison, S.A. Raymond, E.A. Slawsby, S.S. Nedeljkovic, and N.P. Katz, "Opioid Therapy for Noncancer Back Pain: A Randomized Prospective Study," *Spine*, 23, 2591-2600 (1998).
14. J.E. Schwartz and A.A. Stone, "Strategies for Analyzing Ecological Momentary Assessment Data," *Health Psychology*, 17, 6-16 (1998).
15. D. Eisenhower, N.A. Mathiowetz, and D. Morganstein, "Recall Error: Sources and Bias Reduction Techniques," In P.P. Biemer, R.M. Groves, L.E. Lyberg, N.A. Mathiowetz, and S. Sudman (Eds.), *Measurement Errors in Surveys* (Wiley, New York, 1991) pp. 127-144.
16. P.M. Nicassio, K. Schoenfeld-Smith, V. Radojevic, et al., "Pain Coping Mechanisms in Fibromyalgia: Relation to Pain and Functional Outcomes," *Journal of Rheumatology*, 22, 1552-1558 (1995).
17. W.B. Smith and M.A. Safer, "Effects of Present Pain Level on Recall of Chronic Pain and Medication Use," *Pain*, 55, 355-361 (1993).
18. M.D. Litt, N.L. Cooney, and P. Morse, "Ecological Momentary Assessment (EMA) with Treated Alcoholics: Methodological Problems and Potential Solutions," *Health Psychology*, 17, 48-52 (1998).
19. P. Munyard, C. Busst, R. Logan-Sinclair, and A. Bush, "A New Device for Ambulatory Cough Recording," *Pediatric Pulmonology*, 18, 178-186 (1994).
20. J.M. Waldman, S.M. Bilder, N.C. Freeman, and M. Friedman, "A Portable Datalogger to Evaluate Recall-Based Time-Use Measures," *Journal of Exposure Analysis and Environmental Epidemiology*, 3, 39-48 (1993).
21. S. Redline, E.C. Wright, M. Kattan, et al., "Short-term Compliance with Peak Flow Monitoring: Results from a Study of Inner City Children with Asthma," *Pediatric Pulmonology*, 21, 203-210 (1996).
22. P. Verschelden, A. Cartier, J. L'Archeveque, et al., "Compliance and Accuracy of Daily Self-Assessment of Peak Expiratory Flows (PEF) in Asthmatic Subjects over a Three Month Period," *European Respiratory Journal*, 9, 880-885 (1996).
23. R.J. Straka, J.T. Fish, S.R. Benson, and J.T. Suh, "Patient Self-Reporting of Compliance Does Not Correspond with Electronic Monitoring: An Evaluation Using Isosorbide Dinitrate as a Model Drug," *Pharmacotherapy*, 17, 126-132 (1997).
24. H. Milgrom, B. Bender, L. Ackerson, et al., "Noncompliance and Treatment Failure in Children with Asthma," *Journal of Allergy and Clinical Immunology*, 98, 1051-1057 (1996).
25. C.Y. Hsieh, R.B. Phillips, A.H. Adams, et al., "Functional Outcomes of Low Back Pain: Comparison of Four Treatment Groups," *Journal of Manipulative and Physiological Therapeutics*, 15, 4-9 (1992).
26. T.R. Kumar, M.U. Naidu, J.C. Shobha, et al., "Comparative Study of Omeprazole and Famotidine in the Treatment of Duodenal Ulcer," *Indian Journal of Gastroenterology*, 11, 73-75 (1992).
27. S. Koetsawang, G. Ji, U. Krishna, et al., "Microdose Intravaginal Levonorgestrel Contraception: A Multicenter Clinical Trial: IV. Bleeding Patterns," *Contraception*, 41, 151-167 (1990).
28. I. Godschalk, H.J. Brackel, J.C. Peters, and J.M. Bogaard, "Assessment of Accuracy and Applicability of a Portable Electronic Diary Card Spirometer for Asthma Treatment," *Respiratory Medicine*, 90, 619-622 (1996).
29. M.E. Hyland, C.A. Kenyon, R. Allen, and P. Howarth, "Diary Keeping in Asthma: Comparison of Written and Electronic Methods," *British Medical Journal*, 306 (6876), 487-489 (1993).
30. J.M. van Gerven, R.C. Schoemaker, L.D. Jacobs, et al., "Self-Medication of a Single Headache Episode with Ketoprofen, Ibuprofen or Placebo, Home-Monitored with an Electronic Patient Diary," *British Journal of Clinical Pharmacology*, 42, 475-481 (1996).
31. W. Bolten, M. Emmerich, E. Weber, and N. Fassmeyer, "Validierung Elektronischer an Konventionellen Schmerztagebuchern," *Zeitschrift fur Rheumatologie*, 50 (supplement 1) 55-64 (1991).
32. J.M. Rabin, J. McNett, and G.H. Badlani, "A Computerized Voiding Diary," *Journal of Reproductive Medicine*, 41, 801-806 (1996).
33. J.M. Rabin, J. McNett, and G.H. Badlani, "Compu-Void II: The Computerized Voiding Diary," *Journal of Medical Systems*, 20, 19-34 (1996).
34. C.B. Taylor, L. Fried, and J. Kenardy, "The Use of a Real-Time Computer Diary for Data Acquisition and Processing," *Behaviour Research and Therapy*, 28, 93-97 (1990).
35. S.M. Finkelstein, M. Snyder, C. Edin-Stibbe, et al., "Monitoring Progress after Lung Transplantation from Home-Patient Adherence," *Journal of Medical Engineering and Technology*, 20, 203-210 (1996).
36. J.M. Rabin, J. McNett, and G.H. Badlani, "Computerized Voiding Diary," *Neurourology and Urodynamics*, 12, 541-553 (1993).
37. B. Tiplady, G.K. Crompton, M.H. Dewar, et al., "The Use of Electronic Diaries in Respiratory Studies," *Drug Information Journal*, 31, 759-764 (1997).
38. P.A. Ganz, R. Day, J.E. Ware, Jr., et al., "Base-Line Quality-of-Life Assessment in the National Surgical Adjuvant Breast and Bowel Project Breast Cancer Prevention Trial," *Journal of the National Cancer Institute*, 87, 1372-1382 (1995).
39. R.N. Jamison, S.A. Raymond, E. Slawsby, S. Nedeljkovic, and N. Katz, "Assessment of Pain Using Electronic Diary vs. Paper Diary in Patients with Back Pain," *IASP World Congress Proceedings*, (in press, 1999).

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