

PSYCHOSOCIAL INTERVENTIONS TO IMPROVE MEDICATION COMPLIANCE: A META-ANALYSIS

Paul F. Cook, Ph.D.

ScriptAssist Medication Compliance Programs

Selection of Studies for Review

Patient non-adherence to prescribed medical treatment is a known problem, albeit one that may be overlooked in conventional treatment settings (Meichenbaum & Turk, 1987). The topic generated much empirical research in the 1970s and 1980s, and patient compliance is generating a current resurgence of interest among both researchers and clinicians. Despite renewed interest in the topic, no systematic review of compliance-enhancing interventions has been conducted since 1985 (Mullen, Green, & Persinger, 1985). Therefore, the current meta-analytic review was undertaken to evaluate the overall efficacy of interventions to improve medication compliance.

Empirical studies of compliance-enhancing interventions were identified from searches on both PsycINFO and MedLine, using the keywords “medication compliance” and “medication adherence.” In MedLine searches, results were limited to the outcomes of randomized trials. Additional citations were gathered from published reviews of this literature (Cameron & Best, 1987; Haynes, Wang & Gomes, 1987; Meichenbaum & Turk, 1987; Mullen, Green, & Persinger, 1985) and from reference trails in studies located. On-line article abstracts were reviewed to determine whether studies met criteria for inclusion in the meta-analysis (see below). In cases where a determination could not be made from the abstract alone, the full text was reviewed.

Inclusion criteria for studies were as follows: (a) the study was published in English in a professional journal (psychology or medicine) after 1970; (b) the study provided enough statistical detail to permit meta-analytic calculations (this required, at minimum, a p value for between-group differences); (c) the study included an experimental intervention designed to improve medication compliance in some targeted population; (d) the study focused on adult patients (this was required because pediatric and adolescent compliance seemed to involve different psychological issues), and (e) the study provided data on compliance rates (% of medication taken) for both experimental and control groups, or else data on a biochemical or psychosocial outcome measure that was clearly related to medication compliance. Studies where the intervention consisted only of patient education were excluded, because patient education alone has not been found more efficacious than standard care (e.g., Wolfe & Schirm, 1992). However, studies that claimed to use an “improved” or “enhanced” patient education technique were included. A total of 43 articles were included in the review on the basis of these criteria (see Table 1: the total number of studies is 44 because one article tested two separate interventions in a 2 x 2 design). Most excluded studies were removed from consideration because they evaluated compliance rates, but did not attempt to improve medication compliance in any way. The second most common reason for exclusion was a lack of statistical detail in the results section.

The studies included in this review are of varying quality, including both randomized clinical trials (RCTs) and a few studies with simple pre/post experimental designs. In all cases, standard medical care (including patient education by physicians or nurses) served as the benchmark for compliance. Therefore, the effect sizes reported in Table 1 represent “value added” to standard medical care, rather than gains compared to no treatment at all.

Table 1. Studies Included in Meta-Analytic Review

Authors & Date	Participants (number)	Treatments	Findings (measure)	Effect on compliance	Effect Size
Sackett, et al. (1975, study 1)	hypertensive pts (N = 144)	1. work-site based disease mgt. (RS) 2. standard care	RS = SC (pill count)	up 3 points (to 54%)	$d = 0.12$ $r = 0.06$ $z = 0.06$
Sackett, et al. (1975, study 2)	hypertensive pts (N = 144)	1. "mastery learning" (CBT) 2. standard care	CBT = SC (pill count)	up 5 points (to 56%)	$d = 0.18$ $r = 0.09$ $z = 0.09$
Haynes, et al. (1976)	previously noncompliant hypertensive pts (N = 38)	1. self-monitoring and feedback 2. standard care	SM > SC (pill count)	up 41 points (to 80%)	$d = 2.98$ $r = 0.83$ $z = 1.19$
Wandless & Davie (1977)	older adults on 2 rehabilitation units (N = 46)	1. tear-off pill calendar (SM) 2. pill identification card (AP) 3. standard care	SM > AP > SC (pill count)	significant drop in med errors ($p < 0.0005$)	$d = 1.50$ $r = 0.60$ $z = 0.69$
Johnson, et al. (1978)	hypertensive pts suspected of past noncompliance (N = 140)	1. self-monitoring 2. self-monitoring + home visits 3. home visits (RS) 4. standard care	SM = SM+RS = RS = SC (pill count)	SM+RS: up 15 points (to 76%) SM: up 6 points (to 67%) RS: down 5 points (to 56%)	$d = 0.63$ $r = 0.30$ $z = 0.31$ $d = 0.26$ $r = 0.13$ $z = 0.13$ $d = -0.22$ $r = -0.11$ $z = -0.11$ <i>(RS only)</i>
Levine, et al. (1979)	hypertensive pts (N = 400)	1. home visit to gain family support (FC) 2. standard care	FC > SC (self-report)	up 13 points (to 53%)	$d = 0.56$ $r = 0.27$ $z = 0.28$
Logan, et al. (1979)	hypertensive pts (N = 457)	1. work-site based disease mgt. (RS) 2. standard care	RS > SC (pill count)	up 19 points (to 68%)	$d = 0.80$ $r = 0.37$ $z = 0.39$
Takala, Niemela, Rosti, & Sievers (1979)	hypertensive pts (N = 202)	1. reminder mailing with individual feedback (RS) 2. standard care	RS > SC (blood pressure)	up 17 points (to 81%)	$d = 0.77$ $r = 0.36$ $z = 0.38$
Nessmen, Carnahan, & Nugent (1980)	previously noncompliant pts w/ hypertension (N = 52)	1. 8 weekly 90-min sessions of CBT 2. standard care	CBT > SC (pill count)	up 26 points (to 88%)	$d = 1.32$ $r = 0.55$ $z = 0.62$

Table 1. (cont'd).

Authors & Date	Participants (number)	Treatments	Findings (measure)	Effect on compliance	Effect Size
Rehder, McCoy, Blackwell, Whitehead, & Robinson (1980)	pts attending a hypertension clinic ($N = 72$)	1. DOSETT pill dispenser (AP) 2. pharmacist counseling (CBT) 3. counseling plus pill dispenser 4. standard care	CBT+AP > AP > CBT > SC (pill count)	CBT+AP: up 11 points (to 99%) AP: up 7 points (to 95%) CBT: up 3 points (to 91%)	$d = 0.72$ $r = 0.34$ $z = 0.35$ (CBT+AP) $d = 0.45$ $r = 0.22$ $z = 0.22$ (AP) $d = 0.18$ $r = 0.09$ $z = 0.09$ (CBT)
Swain & Steckel (1981)	hypertensive pts ($N = 77$)	1. contingency contracting (CBT) 2. standard care	CBT > SC (blood pressure)	significant drop in blood pressure ($p < 0.05$)	$d = 1.12$ $r = 0.49$ $z = 0.54$
Martin & Mead (1982)	ambulatory older adults ($N = 101$)	1. color-coded bottles & pill tray 2. standard care	AP > SC (pill count)	up 15 points (to 98%)	$d = 0.77$ $r = 0.36$ $z = 0.38$
Cochran (1984)	bipolar pts ($N = 28$)	1. 6 weeks CBT 2. standard care	CBT > SC (judge rating)	up 19 points (to 92%)	$d = 1.01$ $r = 0.45$ $z = 0.48$
Peterson, McLean, & Millingen (1984)	outpatients with epilepsy ($N = 53$)	1. counseling, pill container, self-monitoring & reminder mail 2. standard care	RS+AP+SM > SC (prescription refills)	up 38 points (to 88%)	$d = 2.41$ $r = 0.77$ $z = 1.02$
Becker, et al. (1986)	hypertensive pts ($N = 180$)	1. blister-pak 2. standard care	AP > SC (pill count)	up 9 points (to 84%)	$d = 0.45$ $r = 0.22$ $z = 0.22$
Rimer, Levy, Keintz, Roz, Engstrom, & MacElwee (1987)	cancer patients ($N = 230$)	1. personalized nurse counseling (CBT & SM) 2. standard care	CBT+SM > SC (self-report)	up 19 points (to 62%)	$d = 0.82$ $r = 0.38$ $z = 0.40$
Sau Mei Wong & Norman (1987)	pts >66 yrs ($N = 44$)	1. blister-pak 2. standard care	AP > SC (pill count)	up 7 points (to 98%)	$d = 0.49$ $r = 0.24$ $z = 0.24$
Leirer, Morow, Pariante, & Sheikh (1988)	older adults at a community center ($N = 16$)	1. computer-taught memory training (CBT) 2. standard care	CBT > SC (simulated practice task)	up 22 points (to 90%)	$d = 1.46$ $r = 0.59$ $z = 0.68$
Tucker (1989)	chronic hemodialysis pts ($N = 51$)	1. self-monitoring, self-reward, and \$ rewards (SR) 2. tx. #1 + behavior feedback (CBT) 3. tx. #2 + family support (FC) 4. self-monitoring	SR = SM; CBT = FC; CBT & FC > SR & SM (fluid weight gain)	SR, CBT, & FC produced significantly less weight gain than SM alone (all $ps < 0.05$)	$d = 1.57\uparrow$ $r = 0.62\uparrow$ $z = 0.72\uparrow$ (CBT, FC) $d = 0.67^*$ $r = 0.32^*$ $z = 0.33^*$ (SR, SM)

Table 1. (cont'd).

Authors & Date	Participants (number)	Treatments	Findings (measure)	Effect on compliance	Effect Size
Morisky, et al. (1990)	pts with tuberculosis (N = 88)	1. 1/mo counseling with rewards 2. standard care	SR > SC (chemical marker)	up 3 points (to 93%)	$d = 0.22$ $r = 0.11$ $z = 0.11$
Dow, Verdi, & Sacco (1991)	CMI inpatients (N = 48)	1. assertiveness training 2. standard care	AT > SC (test of pts' assertiveness)	greater assertiveness ($p < 0.05$)	$d = 0.87$ $r = 0.40$ $z = 0.42$
Ware, Holford, Davison, & Harris (1991)	older adults on a geriatrics ward (N = 84)	1. unit-dose calendar package plus counseling (AP & CBT) 2. standard care	AP+CBT > SC (pill count)	up 26 points (to 49%)	$d = 1.54$ $r = 0.61$ $z = 0.71$
Cargill (1992)	pts > 60 yrs old (N = 70)	1. patient education and pill cassette 2. pill cassette with follow-up phone call from nurse 3. standard care	RS > AP & SC (pill count)	AP: up 14 points (to 86%) RS: up 11 points (to 83%)	$d = 0.65$ $r = 0.31$ $z = 0.32$ (AP) $d = 0.49$ $r = 0.24$ $z = 0.24$ (RS)
McKenney, et al. (1992)	pts >50 yrs with hypertension (N = 36)	1. medication cap reminder device 2. standard care	AP > SC (blood pressure)	up 42 points (to 92%)	$d = 2.49$ $r = 0.78$ $z = 1.05$
Matsuyama, et al. (1993)	veterans with poor control over diabetes mellitus (N = 47)	1. medication cap monitor & clinical feedback 2. standard care	SM = SC (pill count)	up 25 points (to 60%)	$d = 1.28$ $r = 0.54$ $z = 0.60$
Murray, et al. (1993)	pts > 60 yrs. who take 3 or more medications (N = 31)	1. BID dosing 2. BID dosing plus unit-of-dose packaging 3. standard care	AP+BID dosing > SC & BID dosing (pill count)	up 3.6 points (to 82.6%)	$d = 0.04$ $r = 0.02$ $z = 0.02$ (AP)
Nides, Tashkin, Simmons, Wise, Li, & Rand (1993)	pts with asthma (N = 251)	1. individualized feedback from electronic monitor (SM) 2. standard care	SM > SC (electronic monitor)	up 20 points (to 89%)	$d = 0.95$ $r = 0.43$ $z = 0.46$
Raynor, Booth, & Blenkinsopp (1993)	pts who were taking two or more drugs at the time of hospital discharge (N = 197)	1. computer-generated reminder chart 2. chart + advice from pharmacist 3. standard care	CBT > RS > SC (pill count)	CBT: up 9 points (to 95%) RS: up 5 points (to 91%)	$d = 0.54$ $r = 0.26$ $z = 0.27$ (CBT) $d = 0.16$ $r = 0.08$ $z = 0.08$ (RS)
Putnam, et al. (1994)	college students given antibiotics (N = 60)	1. counseling to increase pts' motivation (MI) 2. standard care	MI > SC (pill count)	up 11 points (to 92%)	$d = 0.56$ $r = 0.27$ $z = 0.28$
Guimon (1995)	schizophrenic day tx. pts (N = 10)	1. 8-session group treatment (CBT)	CBT was efficacious (self-report)	from start: up 37 points (to 85%)	$d = 0.49$ $r = 0.24$ $z = 0.24$

Table 1. (cont'd).

Authors & Date	Participants (number)	Treatments	Findings (measure)	Effect on compliance	Effect Size
Kemp, Hayward, Applewhaite, Everitt, & David (1996)	psychotic pts in inner-city ward (N = 47)	1. brief CBT "compliance counseling" 2. standard care	CBT > SC (nurse rating)	up 18 points (to 79%)	d = 0.80 r = 0.37 z = 0.39
Maisiak, Austin, & Heck (1996)	pts with arthritis (N = 405)	1. standard care 2. regular check-in appointments with a counselor 3. self-monitoring + assertiveness training	RS = SC; SM+AT > RS SM+AT > SC (functional impairment)	AT + SM improved overall health and functioning (p < 0.01)	d = 0.43 r = 0.21 z = 0.21 (RS) d = 0.70 r = 0.33 z = 0.34 (SM+AT)
Mittelman, Ferris, Shulman, Steinberg, & Levin (1996)	older adults with Alzheimer's disease (N = 206)	1. special training & support group for caregivers 2. standard care	FC > SC (nursing home placement rate)	pts at home for 1 extra year before placement	d = 0.32 r = 0.16 z = 0.16
Rich, et al. (1996)	pts with CHF (N = 156)	1. nurse reminder service contacts 2. standard care	RS > SC (pill count)	up 7 points (to 88%)	d = 0.39 r = 0.19 z = 0.19
Dixon, Weiden, Torres, & Lehman (1997)	homeless CMI pts (N = 77)	1. assertive community treatment (ACT: CBT + FC)	ACT was efficacious (provider rating)	from start: up 28 points (to 57%)	d = 1.58 r = 0.62 z = 0.73
Azrin & Teichner (1998)	CMI pts (N = 39)	1. CBT with pt 2. CBT with pt and family (FC) 3. standard care	CBT = FC; CBT & FC > SC (pill count)	CBT: up 22 points (to 95%) FC: up 19 points (to 92%)	d = 1.12 r = 0.49 z = 0.54 (CBT) d = 0.80 r = 0.37 z = 0.39 (FC)
Keder, Rulin, & Gruss (1998)	women receiving progesterone injections for birth control (N = 206)	1. appointment reminders by mail and telephone (RS) 2. standard care	RS = SC (appointment keeping)	down 2.5 points (to 43%)	d = -0.10 r = -0.05 z = -0.05
Shah, et al. (1998)	pts with CHF (N = 54)	1. weekly phone calls, pager reminders, self-monitoring, mailings, & a 24-hr hotline	CBT+SM+RS was efficacious (hospital days)	intervention group had significantly fewer hospital days (p < 0.05)	d = 0.80 r = 0.37 z = 0.39
Cramer (1999)	CMI pts with any Axis I diagnosis (N = 60)	1. monitor bottle cap & self-monitoring 2. standard care	AP+SM > SC (electronic monitor)	up 19 points (to 76%)	d = 0.87 r = 0.40 z = 0.42

Table 1. (cont'd).

Authors & Date	Participants (number)	Treatments	Findings (measure)	Effect on compliance	Effect Size
Fulmer, et al. (1999)	pts > 65 yrs. with CHF (N = 50)	1. daily telephone reminder calls 2. daily videophone reminder calls 3. standard care	RS > SC, with both types of calls working equally well (electronic monitor)	telephone: up 17 points (to 74%) videophone: up 27 points (to 84%)	$d = 0.85$ $r = 0.39$ $z = 0.41$ $d = 1.19$ $r = 0.51$ $z = 0.56$ (videoph.)
Lang, Davidson, Bailey, & Levine (1999)	CMI pts with hx. of serious mental illness (N = 45)	1. assertive community treatment (CBT + FC)	ACT was efficacious (self-rating & clinician rating)	from start: up 38% (to 49%)	$d = 1.58$ $r = 0.62$ $z = 0.73$
Faulkner, Wadibia, Hilleman, & Lucas (2000)	pts taking lipid-lowering drugs after heart surgery (N = 30)	1. pharmacist outreach calls (CBT) 2. standard care	CBT > SC (pill count)	up 26 points (to 63%)	
Hunkeler, et al. (2000)	depressed pts in primary care (N = 302)	1. nurse outreach calls (CBT), w/ or w/out peer support group 2. standard care	CBT = SC (pharmacy refill data)	up 2 points (to 56%)	$d = 0.08$ $r = 0.04$ $z = 0.04$
Katzelnick, et al. (2000)	depressed pts in primary care (N = 407)	1. nurse outreach calls (CBT) & educational patient mailings 2. standard care	CBT > SC (pharmacy refill data)	up 50 points (to 69%)	$d = 1.58$ $r = 0.62$ $z = 0.73$

Note. BID = twice daily; ACT = Assertive Community Treatment (a form of CBT + FC); AP = alternative packaging of medications; SC = standard care; SM = self-monitoring and feedback; RS = external reminders and support; CBT = cognitive behavioral treatment focusing on the participant's beliefs and on environmental cues; SR = self-reward (or external reward); FC = family counseling; AT = assertiveness training; MI = motivational interviewing techniques.

† = calculated based on additional gain over alternate tx in same study (study lacked a standard-care control).

* = calculated based on average effect size for similar treatments (study lacked a standard-care control).

Explanation of Effect Size Statistics

Three effect size statistics were calculated for each of the studies reviewed above. The first, Cohen's d , is a measure of how many standard deviation units the experimental group mean has moved away from the control group mean. (This analysis pools the variance of treatment and control groups to determine the size of the standard deviation units). Therefore, a score of $d = 1.00$ can be interpreted to mean "the experimental group mean is one standard deviation higher on this measure than the mean score for the control group." In studies with a pre/post design, the same effect size would mean "participants' scores were one standard deviation higher after the intervention than they were before the intervention."

The second measure of effect size, r , is a familiar correlation coefficient, with possible values ranging between 0 and 1. In this case, r represents the correlation between the presence of the experimental intervention and the desired effect on compliance outcomes. (In studies where a chi-squared test rather than a t test served as the measure of statistical significance, the statistic given as r actually represents the phi [ϕ] coefficient for nominal-level data. All correlation coefficients are reported as r for the sake of consistency).

The final measure of effect size, z , is a standardized correlation coefficient calculated from r using Fisher's z transformation (for details, see Rosenthal, 1991). This statistic is not readily interpretable on its own, but its standard normal distribution makes it ideal for meta-analytic calculations. This statistic should not be confused with the z -test of statistical significance, as it is not dependent on sample size. For a complete discussion of meta-analytic statistical techniques, the reader is referred to Rosenthal's (1991) cogent summary.

Do Compliance-Enhancing Interventions Help?

The first question asked of this literature was "can psychosocial interventions increase people's medication compliance?" The answer to this question is an unqualified "yes." Meta-analytic statistical procedures allow us to consider all published studies in this area as if they were replications of one another (Rosenthal, 1991). This strategy permits us to determine whether compliance-enhancing interventions produce better outcomes than standard care in terms of patient compliance. The overall findings regarding compliance-enhancing procedures were statistically significant ($Z = 11.61, p < 0.001$), indicating that overall positive findings for compliance-enhancing interventions were probably not due to chance. This conclusion might be challenged only if a large number of studies *not* included in the above review found non-significant results, a situation that might result in part from the fact that studies finding no differences between groups are less likely to be published (Rosenthal, 1991). A "file drawer" analysis to control for this problem reveals that it would take more than 145,000 other studies, each finding no difference between experimental groups and standard care, to suggest that the positive effects observed for compliance-enhancing interventions are due to publication bias. Therefore, the results obtained in these studies are robust to the file drawer problem. It seems highly likely that psychosocial interventions to improve medication compliance are indeed efficacious.

Are All Compliance Interventions Created Equal?

The weighted average effect size for all studies reviewed was $z = 0.36$, which translates to an average change of 0.74 standard deviation units between treatment and control group means (Cohen's d). This relationship can also be expressed as an average correlation of $r = 0.35$ between the presence of the treatment condition and improvement in patients' compliance. This

effect size might be characterized as small- to medium-sized when compared with others in the social science literature, and is within the range of effect sizes that most psychotherapeutic procedures produce on their target outcomes.

Before making too much of this average effect size, it is necessary to determine whether effect sizes were similar across all studies included in the review. Psychosocial interventions to enhance compliance are no more a single, unified set of procedures than are the various modes of psychotherapy. In the current review, meta-analysis revealed significant variability among the effect sizes obtained in the various studies ($\chi^2(1, k = 54) = 61.8, p < .001$). The results of this omnibus test suggest that compliance-enhancing interventions are heterogeneous in terms of their results. Therefore, it makes sense to ask whether some compliance-enhancing interventions are more efficacious than others.

Which Techniques to Enhance Compliance Work Best?

Descriptive statistics on effect sizes can tell us something about the relative efficacy of different interventions. Effect sizes in the current set of studies ranged from $d = -0.22$ to $d = 2.98$, a difference of 3.2 standard deviation units. The treatment that produced the smallest effect size (and one of only two treatments that actually produced a *decrease* in compliance) involved home visits by nurses to provide education and emotional support (Johnson et al., 1978). It is possible that this treatment was counterproductive because it decreased participants' sense of responsibility for their own medications. In fact, within the same study, a home visit program with a focused goal—giving patients behavioral feedback—produced much more positive results ($d = 0.63$). The treatment yielding the largest single effect size ($d = 2.98$) used self-monitoring and feedback for patients who were known noncompliers with an antihypertensive treatment regimen (Haynes et al., 1976). This intervention's effects are particularly impressive considering the recalcitrant group on which the procedure was tested. However, other self-monitoring interventions have produced smaller effect sizes, with an average $d = 1.09$.

Single vs. Combined Techniques

One way to subdivide compliance studies is to compare treatments that offer a single intervention to those which include multiple components. Previous reviewers have suggested that combined interventions are most helpful in improving compliance (e.g., Cameron & Best, 1987). This hypothesis was supported by the current analysis, which found that combined treatments produced significantly larger effects than treatments containing only a single therapeutic element ($Z = 2.56, p = 0.005$). This suggests that interventions including a range of techniques will be more efficacious than interventions relying on one strategy alone. Although combined techniques produced fairly homogenous effects ($\chi^2(1, k = 8) = 0.43, p = .99$), there was still significant variability among the effect sizes of single-component interventions ($\chi^2(1, k = 48) = 3.58, p < .001$). Therefore, it made sense to extend this analysis by asking which particular techniques produce the largest effects. Particularly efficacious techniques can then be combined into a “package” treatment offering a range of appropriate options.

Usefulness of Personal Contact with Participants

A second way to subdivide compliance studies is to separate those that involve personal contact with a counselor from those that involve mailings, electronic reminders, special pillboxes, and other self-help solutions. It is of interest whether interpersonal (or “psychological”) interventions are more efficacious than mechanical (or “technological”) interventions. In the current set of studies, 34 techniques could be classified as clearly “psychological” and 15 as clearly “technological.” Four procedures used both types of technique, and two procedures were difficult to classify (e.g., an “interpersonal”-type procedure that was delivered by computer).

Meta-analysis indicates that psychological and technological interventions do differ significantly in terms of efficacy ($Z = 1.75, p = 0.04$), with psychological interventions producing better results (average $r = 0.38$) than purely technological ones (average $r = 0.32$). Strategies such as mass mailings, pillboxes, and self-help materials may be inexpensive ways to intervene, and do produce better compliance rates than standard care alone. However, more resource-intensive strategies that include interpersonal contact seem to offer additional benefits in terms of compliance. Again, our confidence in these assertions is limited by significant heterogeneity of effect sizes among the psychological techniques. On the other hand, technological interventions seemed to be fairly homogenous in terms of their effects.¹

Specific Elements of Package Treatments

As a final step, compliance-enhancing interventions were categorized based on the therapeutic “ingredients” contained in each one. Treatment strategies evaluated in the literature include: alternative packaging of medications (AP), self-monitoring and feedback (SM), external reminders and support (RS), cognitive-behavioral counseling focusing on beliefs and environmental cues for behavior (CBT), self-reward or external reward strategies (SR), counseling to enlist family members’ support (FC), assertiveness training (AT), and motivational interviewing tactics (MI). “Package” interventions that included more than one of these strategies were included in both categories. The following table gives average effect sizes and heterogeneity statistics for each category of treatment:

Table 2. Average Effect Sizes for Interventions

Intervention Strategy	No. of studies	Average E.S.	Heterogeneity
Self-Monitoring (SM)	12	$d = 1.09$	$\chi^2 = 1.04$
Cognitive-Behavioral Tx (CBT)	20	$d = 0.97$	$\chi^2 = 1.01$
Alternative Packaging (AP)	11	$d = 0.93$	$\chi^2 = 1.12$
Family Counseling (FC)	4	$d = 0.79$	$\chi^2 = 0.17$
Assertiveness Training (AT)	2	$d = 0.78$	$\chi^2 = 0.003$
Reminders and Support (RS)	14	$d = 0.59$	$\chi^2 = 1.04$
Motivational Interviewing (MI)	1	$d = 0.57$	N/A
Self- (or External) Reward (SR)	2	$d = 0.44$	$\chi^2 = 0.02$

It can be seen that interventions producing the strongest effects asked participants to monitor their own medication habits and used cognitive-behavioral techniques to target patients’ problematic beliefs and behaviors. Self-reward strategies emerged as the least efficacious form of treatment, although it should be remembered that these strategies were still significantly better than standard medical care. Although reward strategies have been praised in the compliance literature (e.g., Cameron & Best, 1987; Haynes et al., 1987), it has also been noted that rewards promote compliance only for as long as the participant is being rewarded. It may be that rapid declines in compliance after the cessation of reward are partly responsible for the smaller effects observed in self-reward interventions. Although various medication reminder strategies (e.g., calendars, pagers, e-mail reminders) have also been hailed as important innovations, these methods of enhancing compliance were found to be less efficacious than behavioral, family-oriented, and cognitive interventions. Alternative packaging was only slightly less efficacious than cognitive-

¹ for psychological interventions, $\chi^2 (1, k = 34) = 3.27, p < 0.001$; for technological interventions, $\chi^2 (1, k = 15) = 1.11, p = 0.99$.

behavioral techniques, supporting the cognitive-behavioral principle that changes in patients' medication-taking routines are an effective way to promote compliance.

Some cautions are in order for interpreting these results: First, the results on motivational interviewing come from just one study, while the results on self-reward and assertiveness training come from two studies each. Therefore, the stability of these findings is unknown: Further research might reveal these techniques to be either more or less efficacious than is suggested here. For this reason, motivational interviewing, assertiveness training, and self-reward should still be considered experimental techniques for enhancing compliance. Second, it is important to remember that earlier analyses found combinations of techniques to be more efficacious than single strategies alone. This finding argues for using several of the more efficacious intervention strategies (e.g., self-monitoring, cognitive-behavioral counseling, alternative packaging, and family counseling) in combination. Taken together, these more-efficacious strategies produce an average effect size of about $r = 0.44$. Therefore, a well-designed intervention incorporating these strategies might be expected to yield about a 44% decrease in noncompliance.

Summary and Conclusions

This meta-analytic investigation of the literature on psychosocial interventions to enhance medication compliance provided support for opinions that have been offered in traditional reviews. First, this analysis provides definite evidence that psychosocial interventions can improve medication compliance beyond the level achieved through standard patient education and medical care. The size of this effect, on average, was $d = 0.74$, which translates to about a 35% decrease in noncompliance following the intervention. The most efficacious techniques in the literature produced an average effect size of $d = 0.98$, which translates to about a 44% decrease in the rate of noncompliance. Therefore, for a medication with a base rate of 50% noncompliance, an average intervention might be able to improve compliance to 67%. A more efficacious intervention might improve compliance with the same medication to 72%.

The current review included several analyses to determine which compliance-enhancing interventions produced the best results. First, this analysis confirmed past reviewers' opinions that combined, multicomponent treatments are more helpful than single-component interventions. Therefore, any intervention to improve compliance should probably draw on multiple strategies in order to provide any individual patient with the most appropriate intervention. Second, the current analysis revealed that interventions involving personal contact with a counselor were more efficacious than purely "technological" interventions involving efficient packaging or automatic reminders. Therefore, interventions that incorporate human interaction should produce greater compliance improvement than interventions delivered electronically or in an automated way. Finally, this review found that particular techniques—including self-monitoring, family counseling, cognitive-behavioral strategies, and alternative packaging—are the most likely candidates for producing therapeutic effects. These are the type of techniques that should be combined in multi-component interventions in order to have the greatest chance of producing the desired effect. Other strategies—motivational interviewing, assertiveness training, and self-reward—merit further investigation before solid conclusions about them can be drawn. Given that this review found no single "state-of-the-art" intervention for improving compliance, further empirical work is needed to refine and develop medication compliance interventions.

References

- Cameron, R., & Best, J.A. (1987). Promoting adherence to health behavior change interventions: Recent findings from behavioral research. *Patient Education and Counseling, 10*, 139-154.
- Haynes, R.B., Wang, E., & Gomes, M.D.M. (1987). A critical review of interventions to improve compliance with prescribed medications. *Patient Education and Counseling, 10*, 155-166.
- Meichenbaum, D., & Turk, D.C. (1987). *Facilitating treatment adherence: A practitioner's guidebook*. New York: Plenum Press.
- Mullen, P. D., Green, L. W., & Persinger, G. S. (1985). Clinical trials of patient education for chronic conditions: A comparative meta-analysis of intervention types. *Preventive Medicine, 14*, 753-781.
- Rosenthal, R. (1991). Meta-analysis: A review. *Psychosomatic Medicine, 53*, 247-271.
- Wolfe, S.C. & Schirm, V. (1992). Medication counseling for the elderly: Effects on knowledge and compliance after hospital discharge. *Geriatric Nursing, 13*, 134-138.

Studies Included in Meta-Analysis

- Azrin, N.H. & Teichner, G. (1998). Evaluation of an instructional program for improving medication compliance for chronically mentally ill outpatients. *Behaviour Research and Therapy, 36*, 849-861.
- Becker, L.A., Glanz, K., Sobel, E., Mossey, J., Zinn, S.L., & Knott, K.A. (1986). A randomized trial of special packaging of antihypertensive medications. *Journal of Family Practice, 22*, 357-361.
- Cargill, J.M. (1992). Medication compliance in elderly people: influencing variables and interventions. *Journal of Advanced Nursing, 17*, 422-426.
- Cochran, S.D. (1984). Preventing medical noncompliance in the outpatient treatment of bipolar affective disorders. *Journal of Consulting and Clinical Psychology, 52*, 873-878.
- Cramer, J.A. (1999). Enhancing medication compliance for people with serious mental illness. *Journal of Nervous and Mental Disease, 187*, 53-55.
- Dixon, L., Weiden, P., Torres, M., & Lehman, A. (1997). Assertive Community Treatment and medication compliance in the homeless mentally ill. *American Journal of Psychiatry, 154*, 1302-1304.
- Dow, M.G., Verdi, M.B., & Sacco, W.P. (1991). Training psychiatric patients to discuss medication issues. *Behavior Modification, 15*, 3-21.
- Fulmer, T., Hollander Feldman, P., Kim, T.S., Carty, B., Beers, M., Molina, M., & Putnam, M. (1999). An intervention study to enhance medication compliance in community-dwelling elderly individuals. *Journal of Gerontological Nursing, August 1999*, 6-14.
- Guimon, J. (1995). The use of group programs to improve medication compliance in patients with chronic diseases. *Patient Education and Counseling, 26*, 189-193.
- Haynes, R.B., Gibson, E.S., Hackett, B.C., Sackett, D.L., Taylor, D.W., Roberts, R.S., & Johnson, A.L. (1976). Improvement of medication compliance in uncontrolled hypertension. *The Lancet, 1976*, 1265-1268.
- Hunkeler, E. M., Meresman, J. F., Hargreaves, W. A., Fireman, B., Berman, W. H., Kirsch, A. J., Groebe, J., Hurt, S. W., Braden, P., Getzell, M., Feigenbaum, P. A., Peng, T., & Salzer, M. (2000). Efficacy of nurse telehealth care and peer support in augmenting treatment of depression in primary care. *Archives of Family Medicine, 9*, 700-708.
- Johnson, A.L., Taylor, D.W., Sackett, D.L., Dunnett, C.W., & Shimizu, A.G. (1978). Self-recording of blood pressure in the management of hypertension. *Canadian Medical Association Journal, 119*, 1034-1039.

- Katzelnick, D. J., Simon, G. E., Pearson, S. D., Manning, W. G., Helstad, C. P., Henk, H. J., Cole, S. M., Lin, E. H. B., Taylor, L. H., & Kobak, K. A. (2000). Randomized trial of a depression management program in high utilizers of medical care. *Archives of Family Medicine*, 9, 345-351.
- Kemp, R., Hayward, P., Applewhaite, G., Everitt, B., & David, A. (1996). Compliance therapy in psychotic patients: Randomised controlled trial. *British Medical Journal*, 312, 345-349.
- Lang, M. A., Davidson, L., Bailey, P., & Levine, M. S. (1999). Clinicians' and clients' perspectives on the impact of Assertive Community Treatment. *Psychiatric Services*, 50, 1331-1340.
- Leirer, V. O., Morrow, D. G., Pariente, G. M., & Sheikh, J. I. (1988). Elders' nonadherence, its assessment, and computer assisted instruction for medication recall training. *Journal of the American Geriatrics Society*, 36, 877-884.
- Levine, D.M., Green, L.W., Deeds, S.G., Chwalow, J., Russell, R.P., & Finlay, J. (1979). Health education for hypertensive patients. *Journal of the American Medical Association*, 241, 1700-1703.
- Logan, A.G., Achber, C., Milne, B.J., Campbell, W.P., & Haynes, R.B. (1979). Work-site treatment of hypertension by specially trained nurses. *The Lancet*, 1979, 1175-1178.
- Maisiak, R., Austin, J., & Heck, L. (1996). Health outcomes of two telephone interventions for patients with rheumatoid arthritis or osteoarthritis. *Arthritis and Rheumatism*, 39.
- Martin, D. C., & Mead, K. (1982). Reducing medication errors in a geriatric population. *Journal of the American Geriatrics Society*, 30, 258-260.
- Matsuyama, J.R., Mason, B.J. & Jue, S.G. (1993). Pharmacists' interventions using an electronic medication-event monitoring device's adherence data versus pill counts. *Annals of Pharmacotherapy*, 27, 851-855.
- McKenney, J.M., Munroe, W.P., & Wright, J.T. (1992). Impace of an electronic medication compliance aid on long-term blood pressure control. *Journal of Clinical Pharmacology*, 32, 277-283.
- Mittelman, M. S., Ferris, S. H., Shulman, E., Steinberg, G., & Levin, B. (1996). A family intervention to delay nursing home placement of patients with Alzheimer disease: A randomized controlled trial. *Journal of the American Medical Association*, 276, 1725-1731.
- Morisky, D.E., Malotte, C.K., Choi, P., Davidson, P., Rigler, S., Sugland, B., & Langer, M. (1990). A patient education program to improve adherence rates with antituberculosis drug regimens. *Health Education Quarterly*, 17, 253-267.
- Murray, M.D., Birt, J.A., Manatunga, A.K., & Darnell, J.C. (1993). Medication compliance in elderly outpatients using twice-daily dosing and unit-of-use packaging. *Annals of Pharmacotherapy*, 27, 616-621.
- Nessman, D.G., Carnahan, J.E., & Nugent, C.A. (1980). Increasing compliance: Patient-operated hypertension groups. *Archives of Internal Medicine*, 140, 1427-1430.
- Nides, M. A., Tashkin, D. P., Simmons, M. S., Wise, R. A., Li, V. C., & Rand, C. S. (1993). Improving inhaler adherence in a clinical trial through the use of the nebulizer chronolog. *Chest*, 104, 501-507.
- Norell, S. E. (1979). Improving medication compliance: A randomised clinical trial. *British Medical Journal*, 295 (2), 1031-1033.
- Peterson, G.M., McLean, S., & Millingen, K.S. (1984). A randomised trial of strategies to improve patient compliance with anticonvulsant therapy. *Epilepsia*, 25, 412-417.
- Putnam, D.E., Finney, J.W., Barkley, P.L., & Bonner, M.J. (1994). Enhancing commitment improves adherence to a medical regimen. *Journal of Consulting and Clinical Psychology*, 62, 191-194.

- Raynor, D.K., Booth, T.G., & Blenkinsopp, A. (1993). Effects of computer generated reminder charts on patients' compliance with drug regimens. *British Medical Journal*, 306, 1158-1161.
- Rich, M.W., Baldus Gray, D., Beckham, V., Wittenberg, C., & Luther, P. (1996). Effect of a multidisciplinary investigation on medication compliance in elderly patients with congestive heart failure. *American Journal of Medicine*, 101, 270-276.
- Rimer, B., Levy, M. H., Keintz, M. K., Fox, L., Engstrom, P. F., & MacElwee, N. (1987). Enhancing cancer pain control regimens through patient education. *Patient Education and Counseling*, 10, 267-277.
- Sackett, D.L., Gibson, E.S., Taylor, D.W., Haynes, R.B., Hackett, B.C., Roberts, R.S., & Johnson, A.L. (1975). Randomised clinical trial of strategies for improving medication compliance in primary hypertension. *The Lancet*, 1975, 1205-1207.
- Shah, N.B., Der, E., Ruggerio, C., Heidenreich, P.A., & Massie, B.M. (1998). Prevention of hospitalizations for heart failure with an interactive home monitoring program. *American Heart Journal*, 135.
- Swain, M.A. & Steckel, S.B. (1981). Influencing adherence among hypertensives. *Research in Nursing and Health*, 4, 213-222.
- Takala, J., Niemela, N., Rosti, J., & Sievers, K. (1979). Improving compliance with therapeutic regimens in hypertensive patients in a community health center. *Circulation*, 59, 540-543.
- Tucker, C.M. (1989). The effects of behavioral intervention with patients, nurses, and family members on dietary noncompliance in chronic hemodialysis patients. *Transplantation Proceedings*, 21, 3985-3988.
- Wandless, I., & Davie, J. W. (1977). Can drug compliance in the elderly be improved? *British Medical Journal*, 293 (1), 359-361.
- Ware, G. J., Holford, N. H. G., Davison, J. G., & Harris, R. G. (1991). Unit dose calendar packaging and elderly patient compliance. *New Zealand Medical Journal*, 104, 495-497.
- Wong, B.S.M., & Norman, D. C. (1987). Evaluation of a novel medication aid, the calendar blister-pak, and its effect on drug compliance in a geriatric outpatient clinic. *Journal of the American Geriatrics Society*, 35, 21-26.

Original Draft: December, 1999
Revised and Updated: September, 2000