The Efficacy of Adherence Interventions for Chronically Ill Children: A Meta-Analytic Review

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Objectives To provide quantitative information about the overall effectiveness of adherence interventions to improve adherence and health outcomes for children with chronic illnesses. To evaluate statistically the potential moderators. **Methods** A meta-analysis was performed on 71 adherence intervention studies. **Results** Weighted-mean effect size (ES) across all the adherence outcomes for group design studies was in the medium range (mean $d = 0.58$) and for single-subject design studies was in the large range (mean $d = 1.44$). The weighted mean ES across all health outcome measures for studies using group designs was in the medium range (mean $d = 0.40$) and for studies using single-subject designs was in the large range (mean $d = 0.74$). **Conclusions** Adherence interventions for children with chronic illnesses effectively increase adherence and result in some positive health benefits. Intervention and methodological variables had significant impact on ESs. High levels of heterogeneity characterized the data.

Key words adherence; chronic illness; meta-analysis.

Low adherence to medical regimens is common among children with a chronic illness. On average, children take about 50% of the medication prescribed for their chronic illness (Drotar, 2000; Rapoff & Barnard, 1991). The significance of this relatively low level of adherence is particularly salient when considering the evidence of harm due to non-adherence in different chronic illnesses. It is important to determine the effects of interventions on adherence and health outcomes, so that resources can be focused on the most effective techniques. In general, adherence intervention strategies are divided into three groups: behavioral (i.e., modifying the environment to encourage adherence or providing positive and negative consequences), educational (i.e., providing information on physician orders or how to use medical equipment), and organizational (i.e., decreasing barriers to medical care by improving communication with medical staff or reducing the complexity of medical regimens; Rapoff, 1999). Many treatments combine two or more of these techniques. Other strategies include addressing psychological issues that may interfere with adherence, such as family systems problems, depression, or general child behavioral non-compliance. The consensus in literature reviews is that interventions are generally effective for increasing adherence to the treatment regimens for childhood chronic illnesses (La Greca & Mackey, 2009; Lemanek, Kamps, & Chung, 2001; Rapoff, 1999)

The overall quantitative power and effectiveness of adherence interventions cannot be determined from these and other literature reviews. A meta-analysis is the best technique to provide such information (Rosenthal, 1995). Several meta-analytic reviews have been published on adherence interventions for adults examining the relative effectiveness of adherence interventions across many patient conditions and adherence measures (Peterson, Takiya, & Finley, 2003; Roter et al., 1998). The Peterson et al. (2003) meta-analysis concluded that despite being intensive and complex, the effect sizes (ESs) for adherence interventions were generally small. In contrast, the Roter et al. (1998) meta-analysis found that overall ESs for interventions ranged from small to large. Roter and colleagues also concluded that combined-type interventions (e.g., educational and behavioral) were more effective than single-type interventions. This difference in

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conclusions likely resulted from differing inclusion criteria and decision rules which may actually help interpreting treatment effects.

Only one meta-analysis was found in the literature that focused specifically on adherence interventions for children with chronic illnesses. Analyzing 70 studies, Kahana, Drotar, and Frazier (2008) concluded that the mean ES was in the small range for all the included adherence outcomes. Behavioral and multi-component interventions had stronger effects (medium range) than those interventions that just used educational techniques (small range). However, most single-subject design studies were excluded from this meta-analysis and data about health outcomes were not included.

The current meta-analysis provides an expanded view of the adherence intervention research by including more single-subject design studies and health outcome data. Additionally, slightly different decisions were made for this meta-analysis than those made for the Kahana et al. (2008) meta-analysis. Of the studies included in this meta-analysis, only 19 out of 71 were also in the Kahana et al. (2008) meta-analysis. The reason for this difference in studies sampled is most likely due to differences in inclusion and exclusion criteria. For example, we did not include studies on obesity, as the Kahana et al review did, because we viewed obesity as a condition and lifestyle-related variable that contributes to the development of chronic diseases, such as diabetes and hypertension, but not as a chronic disease per se. We also excluded studies that did not have adherence as the primary outcome. Additionally, single-subject design studies were included in this meta-analysis but generally excluded by Kahana et al. Given the recent editorial in the *Journal of Pediatric Psychology* encouraging the use of single-subject methodology (Rapoff & Stark, 2008), we thought it was important to recognize the adherence intervention studies using these designs. Also, single-subject designs are recognized as significant experimental designs that can be used to empirically validate treatments in pediatric psychology (Janicke & Finney, 1999). In our view, these procedural differences do not represent significant flaws in either study, but rather provide somewhat different representations of adherence interventions and help elucidate research approaches in the literature. The present meta-analysis attempted to provide a quantitative summary of the research on adherence interventions for children with chronic illnesses. Additionally, this meta-analysis evaluated the influence of different intervention methods, assessment types, methodological variables, and participant characteristics on study ESs. Health outcome and follow-up data were also analyzed.

Method

Literature Search

Computerized and manual methods were used to identify studies to be included in this meta-analysis. The computer searches were conducted using PubMed and PsycINFO, including psychology dissertation abstracts. The searches included all years in the databases up to November 2006. For each database, a total of thirty-six searches were completed using a $2 \times 6 \times 3$ search pattern. The first two terms ''adherence'' or ''compliance'' were paired with each of the following second keywords: ''treatment,'' ''strategies,'' ''improve,'' ''interventions,'' ''education,'' and ''medication.'' Each of these pairs was combined with the following third keywords: ''child,'' ''adolescent,'' and ''pediatric.'' Manual searches were also conducted using literature reviews and journals expected to publish adherence intervention studies. Only studies or abstracts written in English were retained for review. Dissertations were included in the literature review in order to include unpublished research that had undergone at least some level of rigorous review as recommended by Lipsey and Wilson (2001).

Inclusion and Exclusion Criteria

To be included in the meta-analysis, a study had to meet the following criteria:

(a) The study participants were diagnosed with a chronic illness as defined by the World Health Organization (Sabaté, 2001). If the designation of an illness was in question (i.e., infectious, acute, or chronic), the Center for Disease Control and Prevention's website (www.cdc.gov) was consulted for their classification of the illness. This technique excluded malaria and tuberculosis.
(b) The study reported on interventions that systematically attempted to alter specific behaviors related to carrying out prescribed medical regimens. Medical regimens could include taking medications, following diets, and doing prescribed exercises. The study quantitatively measured adherence, so that the statistical effect of the intervention on adherence could be determined.
(c) The study sought to increase adherence in children (under the age of 21 years). If the study included both children and adults, it had to provide separate data for the children to be included.

The initial literature search identified 340 potential studies for inclusion. All but 71 of these studies were excluded. Studies were excluded for the following reasons: not focused on adherence to specific medical regimen

components ($n = 52$), not chronic illness ($n = 50$), inadequate data ($n = 49$), not an adherence intervention ($n = 43$), included only adults ($n = 28$), correlational study ($n = 21$), review articles ($n = 18$), and data reported in another publication (i.e., dissertation data excluded because published later in a peer-reviewed journal; $n = 8$).

Coding

Two independent raters (M.G. and A.B.) were trained to code the necessary information. Interrater reliability was determined by having both raters code 20% of the included studies. Kappa was calculated as a measure of agreement for categorical data and ranged from 0.96 to 1.0, with a mean kappa of 0.99, indicating a high level of rater agreement (Orwin, 1994). Intercoder corrlation was used for continuous variables and ranged from 0.80 to 1.0, with a mean r^2 of 0.95, indicating a high level of rater agreement.

Coded Variables

The interventions were coded as including any combination of the following intervention techniques: (a) ''educational'' if information or teaching was provided about the chronic illness or medical regimen, (b) ''behavioral'' when interventions used behavioral techniques to encourage adherence, shape adherent behaviors, or provide positive and negative consequences for adherence. (c) ''organizational'' interventions were those that used techniques the health care provider could implement to reduce barriers to adherence, such as reducing the complexity of the regimen, (d) ''psychological/other'' were interventions for psychological diagnoses (e.g., depression) and family therapy that was not primarily focused on the medical regimen, but were hypothesized to increase adherence, (e) ''educational'' and ''behavioral'', and (f) all other combinations. Outcome measures were coded into three categories: (a) direct measures (i.e., blood or urine tests that indicated medication levels), (b) indirect measures (i.e., electronic medication monitors and pill counts), and (c) subjective measures (i.e., self-report measures, medication use record keeping, and 24-h recall). Health outcome data were also collected because the ultimate aim of adherence promotion is to improve the health and quality of life of chronically ill children and adolescents (Rapoff, 1999). Examples of health outcomes reported included blood assays used to determine health status, pain ratings, functional disability, lung function tests, and health care utilization.

Methodological variables were coded both to provide an estimate of the quality of the reviewed literature and because methodological features may be important moderators of the adherence outcomes (Durlak, 2003). The methodological variables that were coded for the purpose of this meta-analysis include type of publication (e.g., journal article, dissertation), treatment attrition rates, length of the treatment, methodological design (e.g., randomized control trial, within-subject, single-subject), and nature of the control group (e.g., treatment as usual, alternative treatment). Other variables were chosen because previous research suggests that they may affect both adherence rates and the efficacy of adherence interventions. These variables included the age, gender, ethnicity, and socioeconomic status (SES) of the participating children.

ES Estimates

Because the outcome variables for this meta-analysis were inherently continuous and each study used different measures or scales, the recommended ES estimate for this meta-analysis is the standardized mean difference ES, also known as the *d* statistic (Lipsey & Wilson, 2001). For small sample sizes ($n < 20$), the Hedges (1981) correction was used to reduce an upward bias in the standardized mean difference ES. Additionally, because studies with larger sample sizes are considered to be a more precise reflection of the population ES, Durlak (2003) has recommended weighting each ES by the inverse of its variance, using an equation by Hedges and Olkin (1985). All of the ESs used in this meta-analysis were reported in weighted form, including the single-subject design data. This also allows for easy comparison between other meta-analyses, since weighting ESs is common practice.

Maintaining Independence

Because independence within data sets is necessary for both statistical purposes and for the integrity of the conclusions drawn from a meta-analysis, several steps were taken to maintain independence. First, if multiple articles were published using the same participants, these articles were combined and considered as one study. Second, many adherence interventions report several different types of outcome, such as self-report, electronic monitoring, and functional disability. In general, there are three ways to handle this situation: (a) using generalized least squares approaches (Gleser & Olkin, 1994), (b) selecting one of the ESs to represent each study, and (c) computing an average ES for each study (Faith, Allison & Gorman, 1996). Although the generalized least squares approach accounts for the most within-study correlation and variance, this approach requires data that are not available for the adherence literature (e.g., the actual variance between two outcome measures). Additionally, this

method is most robust when the studies all use the same treatments and outcome measures (Gleser & Olkin, 1994). Selecting an ES to represent each study is problematic because neither research nor expert consensus have concluded that one form of adherence outcome is a better reflection of true adherence than any other outcome measure. Additionally, the preferred method of measuring adherence outcomes differs depending on the chronic illness group, the medication regimen, and the intervention type (Quittner, Espelage, Ievers-Landis, & Drotar, 2000). Thus, for the purpose of this meta-analysis, ESs were averaged within studies for each of the ES groups reported (i.e., overall adherence, health outcomes, and follow-up data).

Single-Subject Studies

For those studies that did not provide sufficient statistics for calculating ES (e.g., means and standard deviations), measurements were taken from graphs to use as individual data points (Faith et al., 1996). ESs were calculated by finding the difference between the baseline mean scores and treatment mean scores, dividing this difference by the pooled within-phase standard deviations (Busk & Serlin, 1992). Even though all of the ESs used the same metric (*d*), group studies were not combined with single-subject studies, because the two research designs provide fundamentally different estimates (i.e., within-person variation versus averaged change data; Faith et al., 1996).

The random-effects model was used in this meta-analysis whenever combining the results of multiple studies. This model includes both within-group sampling error and between-study error measurements. According to Hedges and Vevea (1998), this model should be chosen when assuming that the studies included in the meta-analysis are a random sample of all possible studies, and that the results of the meta-analysis can be generalized to other studies similar to those included in the analyses.

Homogeneity Testing

Homogeneity tests, using the *Q* statistic, were used to determine whether all of the ESs reflected the same population. The *Q* statistic assessed whether the variability in the ESs was greater than expected based on chance and sampling error (Lipsey & Wilson, 2001). In other words, the *Q* statistic established whether it was appropriate to group all of the studies into one analysis based on the assumption that they all estimated the same effect (Durlak, 2003). The *Q* statistic was also used to perform a statistical test which is analogous to an analysis of variance (ANOVA; Lipsey & Wilson, 2001), thus providing the ability to determine whether the ESs for between groups are significantly different, such as those group design studies that used a pre–post test design versus those that used an experimental versus control group design. Weighted mean ESs and *Q* statistics of homogeneity are presented for potential moderators in the tables.

Interpreting the Results

Two techniques were used to interpret the significance of the ESs. First, because the ESs used are *d* statistics, the generally accepted criteria for small (0.20), medium (0.50), and large (0.80) effects were used (Cohen, 1988). Second, 95% confidence intervals (CI) were calculated for each group of ESs. If a CI included zero, then the ES was considered not statistically significant.

For the analyses of moderator variables, we elected (to conserve space) not to discuss those that failed to show a significant between group difference or when the data were not independent, thus precluding the calculation of a between group *Q*.

Results

Study Design Characteristics

Of the 71 included studies, 34 (48.6%) used a comparison group design (i.e., experimental versus control group), 17 (24.3%) used a within subject design (i.e., pre–post studies), and 20 (28.2%) used a single-subject design. Of the comparison group studies, the control group was assigned an alternative treatment in 11 studies (32.4%), treatment as usual in 20 studies (58.8%), and waitlist in three studies (8.8%). Of all of the group design studies ($n = 51$), 16 studies involved asthma (31.4%), 15 with type-1 diabetes (29.4%), five with cystic fibrosis (CF, 9.8%), three each with HIV/AIDS or post-transplant (5.9% each), two each with hyperlipidemia, juvenile rheumatoid arthritis (JRA), and sickle cell disease (3.9% each), and one each with epilepsy, hemophilia, and phenylketonuria (2% each). The total *N* across all the group design studies was 3027 ($M = 35.6$, $SD = 59.2$). Of the single-subject design studies ($n = 19$), seven studies involved type-1 diabetes (36.8%), three each with JRA and CF (15.8% each), two with asthma (10.5%), and one each with epilepsy, lung disease, various rheumatic diseases, and sickle cell (5.3% each). The total *N* across all the single-subject design studies was 50 ($M = 2.6$, $SD = 1.8$). The percentage of attrition from the beginning of the study to the end of treatment was reported by 36 studies (70.6% of the studies), and attrition rates ranged from 0% to 49% ($M = 13.3$, $SD = 12.8$). For a detailed table of the studies included in this meta-analysis, please see the Appendix, available online.

Nine (12.7%) of the included studies were dissertations. The dissertations had a weighted mean ES of 0.49, with a 95% CI of 0.26–0.72. The remaining published studies had a weighted mean ES of 0.57, with a 95% CI of 0.49–0.63. Although the dissertations had a slightly smaller mean ES, both ESs are considered in the medium range. Additionally, the CIs overlap considerably, suggesting that the dissertations do not represent a significantly different population of studies than the published studies. Thus, they were included in all subsequent analyses.

The remainder of the results will be divided into those pertaining to the group design studies and those of the single-subject studies.

Group Design Studies

Demographic Characteristics

The mean age of the youth included in each study ranged from 2 to 15 years ($M = 9.9$, $SD = 3.7$). Thirty-eight studies provided information about the children's gender. The percentage of males ranged from 24% to 91% ($M = 51.7$, $SD = 14.2$). Only 22 studies (43%) reported quantifiable information about the ethnicity of the participants. Of these studies, the percentage of minority group participants ranged from 0% to 100% ($M = 39.1$, $SD = 31.4$). Fifteen studies (29.4%) reported the average time since diagnosis of a chronic illness for the children in the study. Time since diagnosis ranged from 4 to 125 months ($M = 53.0$, $SD = 33.4$). Eighteen studies (35.3%) provided information about SES of the included samples, but SES was based on a wide range of indices (e.g., Hollingshead index, parental income, etc.). Because so few studies provided SES information and the information was so varied, these data were not aggregated or used in any analyses.

Intervention Characteristics

Almost half of the studies utilized combined educational and behavioral treatment techniques ($n = 24$, 47%). About one fourth utilized a single approach: organizational ($n = 6$, 11.8%), behavioral ($n = 5$, 9.8%), and educational ($n = 2$, 3.9%). The remainder of the studies ($n = 13$, 25.4%) used a variety of combinations (i.e., organizational and educational, psychological and educational, etc.). The length of the treatments ranged from 1 to 1095 days ($M = 167.5$, $SD = 109$).

Regimen Characteristics

The regimens targeted in the group design studies included: medication ($n = 32$, 46.4%), diet ($n = 13$, 18.8%), overall disease management ($n = 10$, 14.5%), monitoring ($n = 10$, 14.5%), and exercise ($n = 4$, 5.8%). Adherence was measured primarily through subjective methods ($n = 40$, 63.5%). These data were obtained through child report ($n = 14$), parent report ($n = 9$), diary ($n = 9$) and 24-h recall ($n = 8$). Twenty-seven percent of the data ($n = 17$) were derived from indirect measures (electronic monitor, $n = 10$; pill count, $n = 7$). The remainder of the data was from direct measures (i.e., blood and urine tests; $n = 6$, 9.5%).

Follow-up and Health Outcome Data

Ten (19.6%) of the included studies reported follow-up adherence data. The average length of follow-up was 8 months, with a range from 3 to 13 months. Thirty-one studies (60.8%) included health outcome data. Most of the health outcome data were direct measures ($n = 27$, 56.3%), which included A1C ($n = 15$), body mass index (BMI; $n = 6$), and pulmonary function tests (PFT; $n = 6$). The remainder of the health outcome data included disease severity estimates ($n = 13$, 27.1%), healthcare utilization ($n = 4$, 8.3%), and quality of life measures ($n = 4$, 8.3%). Of the studies that included health outcome data, 13 provided follow-up health outcome data. Length of follow-up ranged from 0.5 to 24 months, with a mean of 9.2 months. These follow-up data were derived from A1C ($n = 7$), BMI ($n = 3$), PFT ($n = 4$), and disease activity estimates ($n = 3$).

Adherence

The weighted-mean effect across all of the adherence outcomes was in the medium range (Mean $d = 0.58$, 95% CI = 0.51–0.65). However, there was a significant amount of heterogeneity among the ESs ($Q = 194.96$, Table I).

Among the moderators, the only significant between-group Q was found for design control type. Specifically, studies using a waitlist design had a significantly stronger mean ES (Mean $d = 1.09$) than those using an alternative treatment (Mean $d = 0.43$; Table I).

Health Outcome ESs

The weighted-mean effect across all of the health outcomes was in the medium range (Mean $d = 0.40$, 95% CI = 0.31–0.50; see Table II). However, there was a significant amount of heterogeneity ($Q = 182.40$) and thus the data were divided into groups based on potential moderators. The only group of potential moderators that had some homogeneity and exhibited significant group differences was the type design, the diagnosis, and the type of intervention used in the treatment. Specifically, ESs for the health outcomes were higher for studies using a

Table I. Adherence ES estimates for group designs

	Number of ESs	Mean sizes	95% CI	*Q*	Between group *Q*
All adherence effects	51	0.58	0.51–0.65	194.96**	
Methodological design					−12.3
Pre–post	17	0.59	0.46–0.73	76.34**	
Experimental versus control	34	0.53	0.45–0.61	130.92**	
Diagnosis					–9.83
Asthma	16	0.58	0.47–0.69	136.22**	
Type-1 diabetes	15	0.42	0.26–0.58	32.19**	
Others combined	19	0.57	0.45–0.69	36.38**	
Outcome type					+
Direct measures (blood/urine)	6	0.20	−0.08–0.48	7.58	
Indirect measures	17	0.56	0.40–0.72	15.51	
Pill count	7	0.60	0.34–0.86	8.08	
Electronic monitor	10	0.49	0.28–0.70	5.24	
Subjective measures	40	0.56	0.48–0.63	562.79**	
Child report	14	0.35	0.24–0.47	38.78**	
Parent report	9	1.57	1.35–1.79	401.97**	
Diary	9	0.54	0.23–0.84	14.60	
24-hour recall	8	0.45	0.33–0.57	16.83*	

Note. *Q* scores that are statistically significant indicate heterogeneity in ES grouping. + indicates data are not independent, so between group *Q* cannot be calculated.
*$p < .05$, **$p < .01$.

pre–post test design (Mean $d = 1.27$), studies involving patients with asthma (Mean $d = 0.86$), and studies using a combination of educational and behavioral interventions (Mean $d = 0.74$).

Adherence Follow-up ESs

The weighted-mean effect across all of the follow-up adherence data was in the medium range (Mean $d = 0.48$, 95% CI = 0.28–0.69; see Table III). However, there was a significant amount of heterogeneity and thus, the data were divided into groups based on potential moderators. Overall, there was some homogeneity in these data, but no significant between group differences.

Health Outcome Follow-up ESs

The weighted-mean effect across all of the follow-up health outcome data was in the medium range (Mean $d = 0.36$, 95% CI = 0.16–0.56; see Table IV). However there was a significant amount of heterogeneity and thus, the data were divided into groups based on potential moderators. There was some homogeneity in all of the different ways the data were grouped, but no significant between group differences.

Other Moderating Variables

Correlations were calculated between the ESs and various potential moderating variables (Table V). Most of the correlations were not statistically significant. However, the percentage of males included in the study was significantly negatively correlated with adherence ($r^2 = -0.34$) and health outcome ($r^2 = -0.38$) ESs. In other words, the more males in the study the less effective the interventions were at increasing adherence or improving health outcomes. However, this correlation did not remain significant in the follow-up data. Attrition rate was significantly correlated with health outcome ES ($r^2 = 0.42$), such that the higher the attrition, the better the health outcomes. Additionally, the length of treatment was significantly correlated with ES in single-subject follow-up data ($r^2 = 0.71$). So, as the treatment length increased, the effectiveness of the intervention at follow-up increased.

Single-Subject Design Studies

Demographic Characteristics

The mean age of the youth included in each single-subject study ranged from 2 to 17 years ($M = 11.0$, $SD = 4.3$). All of the studies provided information about the participants' gender. The percentage of males ranged from 0% to 100% ($M = 47.1$, $SD = 44.1$). Only four studies (21%) reported information about the ethnicity of the participants. Two studies had 0% minority participants and two studies had 100% minority participants. Seven studies (36.8%) reported the average time since diagnosis of a chronic illness for the children in the study. Time since diagnosis ranged from 7 to 96 months ($M = 48.3$, $SD = 32.1$). None of the studies provided information about SES.

Table II. Health outcome ESs for group designs

	Number of ESs	Mean ES	95% CI	*Q*	Between group *Q*
All health outcome	31	0.40	0.31–0.50	182.40**	
Methodological design					68.82**
Pre–post	8	1.27	1.05–1.50	45.23**	
Experimental versus control	23	0.22	0.12–0.32	68.35**	
Diagnosis					28.46**
Asthma	7	0.86	0.67–1.05	59.20**	
Type-1 diabetes	15	0.29	0.13–0.45	47.58**	
Others combined	9	0.24	0.10–0.39	47.16**	
Intervention type					24.69**
Educational or behavioral only	5	0.16	0.02–0.30	6.20	
Educational and behavioral	15	0.74	0.55–0.94	69.37**	
Others combined	11	0.50	0.34–0.66	82.14**	
Control type					−53.44
Alternative treatment	10	0.43	0.29–0.57	3.15	
Treatment as usual	11	0.56	0.32–0.80	118.64**	
Regimen type					+
Diet	13	0.18	0.07–0.29	88.00**	
Medication	22	0.61	0.49–0.73	208.42**	
Overall disease management	6	0.26	0.01–0.51	14.36*	
Monitoring	7	0.36	0.16–0.55	2.85	
Outcome type					+
Direct measures	27	0.18	0.10–0.27	66.46**	
A1C	15	0.28	0.12–0.44	47.63**	
Body mass index	6	0.10	−0.05–0.26	14.65*	
Pulmonary function test	6	1.01	0.74–1.28	23.71**	
Indirect measures	13	0.70	0.57–0.84	191.16**	
Healthcare utilization	4	1.41	1.01–1.80	16.39**	
Subjective measures	4	0.24	−0.09–0.57	0.48	

Note. + indicates data are not independent, so between group *Q* cannot be calculated.
*$p < .05$, **$p < .01$.

Intervention Characteristics

Almost half of the single-subject studies utilized a combined educational and behavioral treatment and the same number of studies utilized a behavioral approach alone ($n = 9$, 47.4%, respectively). Only one study (5.3%) used another combination (i.e., behavioral and organizational). The length of the treatments ranged from 1 to 112 days ($M = 56.9$, $SD = 33.2$).

Regimen Characteristics

The regimens targeted by the single-subject studies included: medication ($n = 11$, 34.4%), monitoring ($n = 9$, 28.1%), overall disease management ($n = 5$, 15.6%), diet ($n = 4$, 12.5%), and exercise ($n = 3$, 9.4%). Adherence data were obtained primarily through diary methods ($n = 23$, 71.9%). The remainder of the data was obtained through electronic monitoring ($n = 4$, 12.5%), pill count ($n = 3$, 9.4%), and 24-hour recall ($n = 2$, 6.3%). None of the adherence data was collected through direct means (i.e., blood titers).

Follow-up and Health Outcome Data

Most of the single-subject studies ($n = 14$, 70%) included follow-up adherence data. Seven studies (35%) included health outcome data: A1C ($n = 3$), PFT ($n = 3$), quality of life ($n = 2$), BMI ($n = 1$), and disease activity estimates ($n = 1$). Of the studies that included these data, four provided follow-up health outcome data. The follow-up data were derived from A1C ($n = 2$), PFT ($n = 2$), and disease activity estimates ($n = 1$).

Adherence and Health Outcomes

The weighted-mean effect across all of the single-subject adherence data was in the large range (mean $d = 1.53$, 95% CI 1.07–1.98; see Table VI). Because ES is homogeneous, it can be considered an appropriate estimate of the average

Table III. Follow-up adherence ESs for group designs

	Number of ESs	Mean sizes	95% CI	*Q*	Between group *Q*
All follow-up adherence effects	10	0.48	0.28–0.69	20.22*	
Methodological design					0.10
Pre–post	4	0.56	0.04–1.07	17.36**	
Experimental versus control	6	0.47	0.25–0.69	2.76	
Diagnosis					1.02
Type-1 diabetes	4	0.38	0.10–0.66	4.69	
Others combined	6	0.59	0.30–0.89	14.51*	
Intervention type					−0.67
Educational only	6	0.64	0.35–0.93	19.42**	
Others combined	4	0.58	0.34–0.82	1.47	
Control type					0.75
Alternative treatment	2	0.61	0.22–0.99	0.67	
Others combined	4	0.40	0.12–0.67	1.34	
Regimen type					+
Diet	4	0.86	0.35–1.38	15.47**	
Exercise	3	0.79	0.19–1.38	2.59	
Medication	2	0.47	0.09–0.85	0.002	
Overall disease management	6	0.27	0.03–0.51	7.85	
Outcome type					+
Child report	3	0.22	−0.11–0.54	3.06	
Parent report	3	0.35	0.01–0.70	4.67	
Diary	7	0.83	0.44–1.22	18.09**	

Note. + indicates data are not independent, so between group *Q* cannot be calculated.
*$p < .05$, **$p < .01$.

Table IV. Health outcome follow-up ESs for group designs

	Number of ESs	Mean sizes	95% CI	*Q*	Between group *Q*
All health outcome follow-up	13	0.36	0.16 to 0.56	24.02*	
Methodological design					0.01
Pre–post	8	0.36	0.13 to 0.58	18.91**	
Experimental versus control	5	0.38	−0.06 to 0.82	5.10	
Diagnosis					6.48
Type-1 diabetes	8	0.18	−0.06 to 0.42	7.37	
Others combined	5	0.73	0.38 to 1.08	10.17*	
Intervention type					1.04
Educational only	7	0.51	0.16 to 0.85	15.59*	
Others combined	6	0.29	0.04 to 0.53	7.39	
Control type					−10.18
Alternative treatment	4	0.60	0.26 to 0.94	12.17**	
Others combined	4	0.16	−0.13 to 0.46	3.12	
Regimen Type					+
Diet	6	0.60	0.21 to 0.99	51.67**	
Medication	3	0.61	0.20 to 1.01	2.43	
Overall disease management	7	0.09	−0.16 to 0.33	1.34	
Outcome type					+
Direct measures	14	0.17	−0.01 to 0.34	13.75	
A1C	7	0.17	−0.08 to 0.42	6.90	
Body mass index	3	0.11	−0.40 to 0.62	0.92	
Pulmonary function test	4	−0.35	−1.02 to 0.32	4.81	
Disease severity	3	1.01	0.62 to 1.40	32.28**	

Note. + indicates data are not independent, so between group *Q* cannot be calculated.
*$p < .05$, **$p < .01$.

effectiveness of single-subject adherence interventions. The weighted-mean effect of the single-subject follow-up adherence data was also in the large range (mean $d = 1.44$, 95% CI = 0.99–1.89; see Table VI) and homogeneous.

Table V. Correlations between study ESs and moderating variables for group designs

Correlated variables	r^2	Significance
Overall adherence data		
ES: Mean age	−0.12	$t(43) = -0.82$
ES: Attrition rate	0.06	$t(33) = 0.34$
ES: Time since diagnosis	−0.09	$t(13) = -0.34$
ES:% of males	−0.34	$t(35) = -2.12$*
ES:% of minority	−0.14	$t(22) = -0.61$
ES: Length of treatment	−0.14	$t(46) = -0.97$
Follow-up data		
ES: Mean age	−0.28	$t(7) = -0.77$
ES: Attrition rate	−0.32	$t(7) = -0.9$
ES:% of males	−0.32	$t(6) = -0.83$
ES: Length of treatment	−0.13	$t(8) = -0.36$
ES: Length of follow-up	−0.07	$t(8) = -0.21$
Health outcome data		
ES: Mean age	−0.06	$t(26) = -0.31$
ES: Attrition rate	0.42	$t(23) = 2.13$*
ES: Time since diagnosis	−0.10	$t(9) = -0.31$
ES:% of males	−0.38	$t(24) = -2.04$*
ES:% of minority	0.06	$t(12) = 0.06$
ES: Length of treatment	−0.05	$t(28) = -0.26$
Health outcome follow-up		
ES: Mean age	−0.27	$t(10) = -0.90$
ES: Attrition rate	0.24	$t(8) = 0.70$
ES:% of males	–0.56	$t(10) = -2.13$
ES: Length of treatment	−0.17	$t(10) = -0.17$
ES: Length of follow-up	0.61	$t(11) = 0.61$
Single-subject data		
ES: Mean age	−0.15	$t(16) = -0.59$
ES:% of males	− 0.12	$t(17) = -0.51$
ES: Length of treatment	0.36	$t(13) = 1.41$
Single-subject follow-up data		
ES: Mean age	−0.22	$t(11) = -0.73$
ES: Attrition rate	0.41	$t(12) = 1.54$
ES: Length of treatment	.071	$t(10) = 3.16$*

*$p < .05$.

The single-subject health outcome mean effect was in the large range (Mean $d = 0.74$, 95% CI = 0.19–1.29; see Table VI) and homogeneous. The follow-up single-subject health outcome mean effect was in the large range (mean $d = 0.87$, 95% CI = 0.17–1.58; see Table VI) and homogeneous.

Fail-Safe N-statistic

In order to evaluate the possible problem of publication bias, Rosenthal's ''file drawer'' statistic was calculated (Rosenthal, 1991). Rosenthal's statistic suggests that the overall mean ES of this meta-analysis is likely not the result of publication sampling bias, because 245 400 null result studies would have to be in ''file drawers'' to reduce this ES to a nonsignificant result.

Discussion

The results of this meta-analysis suggest that adherence interventions not only increase adherence, but also generally lead to improved health outcomes, both at the completion of the intervention and at follow-up, with the average length of follow-up being 8 and 9 months, respectively. Methodological variables seemed to have some effect on the ES estimates of studies. Specifically, adherence ESs were significantly higher when group design studies used waitlist control groups compared to alternative treatments. This makes sense in that a waitlist control is a less stringent comparison group compared to an alternative and potentially effective treatment.

The health outcome analyses revealed some interesting trends. Specifically, health outcomes were significantly better for studies using a pre–post test design, those involving patients with asthma, and for studies using a combination of educational and behavioral interventions. Improving adherence to regimens for asthma (such as increasing adherence to inhaled daily steroids) may impact more directly a highly reversible disease such as asthma. Also, the combination of behavioral and

Table VI. Single-subject adherence and health outcome ESs

	Number of ESs	Mean sizes	95% CI	*Q*	Between group *Q*
All single-subject adherence	20	1.53	1.07–1.98	9.94	
Intervention type					0.63
Behavioral only	9	1.41	0.81–2.01	5.01	
Educational and behavioral	9	1.74	1.01–2.46	4.30	
Single-subject follow-up	14	1.44	0.99–1.89	21.85	
Single-subject health outcome	7	0.74	0.19–1.29	8.05	
Single -subject health outcome follow-up	4	0.87	0.17–1.58	0.41	

educational strategies may be more potent in impacting health outcomes than either strategy used alone.

Significant levels of heterogeneity (except in the case of single-subject studies) hampered attempts to summarize the information by combining the data into a single ES. Heterogeneity persisted even when the ESs were divided in ways that were suggested by previous research. This heterogeneity does not indicate that the mean ES estimates are meaningless, but does cast serious doubt on the usefulness of combining all adherence intervention research as though they represent a single construct. For example, the tasks required for children and families to successfully follow asthma treatment regimens are quite different than the tasks required to correctly follow treatment regimens for cystic fibrosis. On the other hand, understanding gained about enhancing adherence in diabetes can inform research about increasing adherence to post-transplant medications.

Single-subject studies presented no problems with heterogeneity, possibly due to characteristics of these studies. First, variance in the type of intervention was much smaller in the single-subject designs, because almost half of the studies used behavioral techniques alone and almost all of the other studies used educational and behavioral techniques combined. The single-subject studies had a similarly lower variance in the kinds of outcome assessment techniques used and the diagnoses of the patients studied. Thus, overall mean ES estimates appear to be larger when there is less variance in the characteristics of the included studies. In addition, single-subject designs are more subject to Type II error rates as visual inspection of the data has to produce consensus among reviewers that a treatment has had a robust, obvious, and reliable effect (Baer, 1977). Thus, single-subject interventions judged to be effective are much more likely to be published.

Despite the significant methodological differences between this meta-analysis and the Kahana et al. (2008) meta-analysis, the general conclusions are the same. First, adherence interventions are generally successful at increasing adherence (overall adherence ES for this meta-analysis = 0.58, 95% CI = 0.51–0.65; Kahana et al. overall adherence ES = 0.34, 95% CI = 0.30–0.38). Second, methodological and participant characteristics seem to have an effect on intervention effectiveness. Third, a significant amount of heterogeneity exists in the data sets.

Clinical Implications

Clinicians might consider using combination educational and behavioral interventions as they yielded higher ESs on health outcomes in this meta-analysis, which is the ultimate aim of adherence promotion efforts. Also because participant characteristics (e.g., age, gender, diagnosis) seem to significantly impact the effectiveness of adherence interventions overall, it is likely necessary for clinicians to consider these characteristics and adapt interventions to meet the specific needs of each patient.

Future Directions

Based on the results of this meta-analysis, some recommendations can be made for future research. First, in order to provide useful information about what kinds of adherence interventions are most effective, basic research on adherence interventions will need to continue. As the research base grows, then more focused meta-analyses can be conducted that evaluate specific areas of adherence interventions, such as interventions for adolescents with asthma or school-age children with diabetes. Second, the ability to summarize and evaluate research would be significantly enhanced if important data were uniformly reported in all intervention research, such as by using guidelines for the Consolidated Standards of Reporting Trials (CONSORT; Moher, Schultz, & Altman, 2001). Third, health outcomes need to be routinely assessed in adherence intervention studies. The ultimate goal of adherence interventions is to help children get better, feel better, and have an improved quality of life. Fourth, because different measures of adherence may produce different results, researchers need to measure adherence using multiple methods from multiple sources (Quittner et al., 2000), and include direct measures because these data appear to provide unique information about adherence.

Supplementary data

Supplementary data can be found at:
http://www.jpepsy.oxfordjournals.org/

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* Indicates the publication was included in the meta-analysis.

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