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REVIEW ARTICLE

The Effects of Feedback on Adherence to Treatment: A Systematic Review and Meta-analysis of RCTs

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Context: The aim of this systematic review is to determine whether providing feedback, guided by subjective or objective measures of adherence, improves adherence to treatment.

Evidence acquisition: Data sources included MEDLINE, Embase, CINAHL, and PsycINFO, and reference lists of retrieved articles. Only RCTs comparing the effect of feedback on adherence outcome were included. Three independent reviewers extracted data for all potentially eligible studies using an adaptation of the Cochrane Library data extraction sheet. The primary outcome, change in adherence, was obtained by measuring the difference between adherence at baseline visit (prior to feedback) and at the last visit (post-feedback).

Evidence synthesis: Twenty-four studies were included in the systematic review, and 16 found a significant improvement in adherence in the intervention group (change in adherence range, −13% to +22%), whereas adherence worsened in the control group (change in adherence range, −32% to 10.2%). Meta-analysis included six studies, and the pooled effect showed that mean percentage adherence increased by 10.02% (95% CI=3.15%, 16.89%, p=0.004) more between baseline and follow-up in the intervention groups compared with control groups. Meta-regression confirmed that study quality, form of monitoring adherence, delivery of feedback, or study duration did not influence effect size.

Conclusions: Feedback guided by objective or subjective measures of adherence improves adherence and, perhaps more importantly, prevents worsening of adherence over time even when only small absolute improvements in adherence were noted. Increased use of feedback to improve treatment adherence has the potential to reduce avoidable healthcare costs caused by non-adherence.

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CONTEXT

Adherence is defined as "the extent to which a patient's behavior coincides with medical and health advice."[1] Subjective and objective methods have been employed to monitor adherence in both clinical trials and clinical practice.[2] These include self-report, drug level monitoring, Medication Event Monitoring System (MEMS) caps; pill counts; and surrogate markers of adherence (serum carboxy-terminal collagen crosslinks [CTX] bone marker level and Disease Activity Score).[2] It is estimated that up to half of medications prescribed for long-term conditions are not taken as recommended.[3] Non-adherence has both medical and economic implications.[3] Approximately 57% of avoidable healthcare cost incurred by suboptimal medicine use is due to non-adherence.[4]

Non-adherence can be classified into two categories: intentional and unintentional non-adherence.[3] The latter describes an individual willing to adhere to treatment but

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unable to do so owing to factors beyond their control (e.g., reduced understanding).[3] Intentional non-adherence defines when an individual chooses not to follow the recommended treatment.[3] It is important to understand a patient's view of the need for treatment, concerns, and expectations in order to address non-adherence.[3,4] As such, there is no intervention that will address non-adherence in all patients; it is ideal to take into account individual needs when implementing an intervention.[3–5] Reported interventions include enhanced support from family, peers, or allied health professionals such as pharmacists, who often delivered education, counseling, or daily treatment support.[6]

Several studies have employed feedback interventions to improve adherence based upon patients' individual needs.[7–30] Studies have monitored adherence either subjectively or objectively. Obtained adherence measures were used as guides to explore reasons for non-adherence and provided specific feedback based on the information given by participants. The aim of this systematic review is to explore whether feedback, guided by subjective or objective adherence measures, improves adherence.

EVIDENCE ACQUISITION

Literature Search, Study Selection, and Data Extraction

Four major databases were searched: MEDLINE (1946–2016), Embase (1974–2016), CINAHL, and PsycINFO. Key words included *feedback*, *patient adherence*, *patient compliance*, *patient concordance*, *treatment adherence*, and *non-adherence* (Appendix 1, available online). Searches were limited to RCTs.

Studies were assessed for eligibility based on the following inclusion criteria: (1) patients of all ages; (2) use of objective or subjective measures of adherence as a guide to provide specific feedback on improving adherence; (3) RCTs; and (4) reporting of adherence as an outcome. There were no language restrictions. Studies giving general advice or reminders as an intervention were excluded. All abstracts were reviewed independently by three reviewers (MDS, RJM, and GDEM). Full-text articles were evaluated for all potentially eligible studies.

The Delphi Tool was used for quality assessment.[31] Studies with a score $<3/9$ were excluded. Owing to the nature of these studies, masking of investigators and patients was not possible, resulting in lower quality scores (Table 1).

The data extraction sheet was adapted from Cochrane Library (Appendix 2, available online)[32] and was performed independently by the three reviewers above. The chosen primary outcome measure was change in adherence (CA) from baseline, calculated by subtracting adherence at baseline from adherence at the last visit. Analyses were carried out in Stata, version 13.1.

Meta-analysis

Studies presenting raw data with SD or SE values, on adherence in both intervention and control groups, allowed data to be extracted for a meta-analysis. CA was calculated for both intervention and control groups, and the effect size included in the meta-analysis was the difference in this change (intervention – control). As the SE of the difference in change was not reported, this was calculated conservatively as square root of [(SD1\widehat2 / n1) + (SD2 \widehat2 / n2)], therefore, assuming a covariance of 0.[33] A random effects meta-analysis was used to pool study results. Meta-regression analyses were performed assessing if effectiveness of the intervention varied by study characteristics (i.e., study quality); form of monitoring adherence (self-reported or electronic); who administered the feedback (treating clinician or someone else); and study duration. The analysis was also stratified by form of monitoring adherence, by running separate meta-analyses for those who self-reported and those who were monitored electronically. A funnel plot was used to assess the potential publication bias of included studies.

EVIDENCE SYNTHESIS

Literature Search

The authors identified 3,041 citations and removal of duplicates left 3,008 studies, of which 96 were related to the area of interest. Reference lists revealed no new articles. Altogether, 24 studies met the inclusion criteria (Figure 1).

Feedback has been evaluated as an intervention in 12 healthcare areas. Forms of monitoring included electronic monitoring such as MEMS or electronic dose monitors (devices recording the date/time of bottle opening); the pill count method; and subjective approaches (i.e., self-report diaries). Study characteristics and main outcomes are summarized in Table 1. CA could only be calculated for 12 studies. The remaining studies did not specify adherence either at the beginning or end of the study. A total of six studies were included in the meta-analysis as these provided both the baseline and final visit adherence along with the SD/SE data needed for pooled analysis.

Asthma

Two studies explored feedback on adherence for use of preventative inhalers in asthma.[7,8] Burgess and colleagues[7] objectively monitored adherence in children using the Smart inhaler, which calculated the date/time of inhaler actuation and number of dispensed doses. Parents and children in the intervention group viewed their monitor results monthly for 4 months, whereas controls were masked to their monitor recordings. A significant difference in adherence between the two groups ($p<0.01$) was reported. CA was +6.7% in the intervention group and –2.7% for controls.

Oniyirimba et al.[8] evaluated a similar intervention in an adult population using metered dose inhaler chronologs. Adherence improved from 61% to 70% for the intervention group but declined in the controls ($p<0.0001$; CA of +15% and –24%, respectively).

Table 1. Main Characteristics of All 24 Studies Included in the Systematic Review

Author	Condition	Mean age (years)		Number randomized	Monitoring	Study duration, outcome measure	Quality score	Baseline % adherence		Final visit % adherence		Change in adherence (%)		*p*-value	% effect size
		I	C					I	C	I	C	I	C		
Burgess[7,a]	Asthma	9.1	9.3	26	Electronic	12 weeks, mean %	6	77.50	58.00	84.20	55.30	6.7	−2.7	<**0.01**	9.40[a]
Oniyirimba[8,a]	Asthma	45.0	53.0	30	Electronic	10 weeks, mean %	5	61.00	51.00	76.00	27.00	15	−24	<**0.0001**	39.00[a]
Smith[9,b]	HIV/AIDS	Not provided[c]		43	Electronic	12 weeks, mean %	4	74.00	70.00	96.00	38.00	22	−32	**0.0017**	54.00[b]
Sabin[10,a]	HIV/AIDS	36.1	35.1	68	Electronic	12 months, mean %	5	86.80	83.8	96.50	84.50	9.7	0.7	**0.0030**	9.00[a]
Rigsby[11,b]	HIV/AIDS	44.6	47.2	55	Electronic	12 weeks, mean %	4	68.00	68.00	55.00	65.00	−13	−3	0.79	−10.00[b]
Rosen[12,a]	HIV/AIDS	45.8	42.2	56	Electronic	32 weeks, mean %	4	62.00	60.00	65.00	47.00	3	−13	**0.01**	16.00[a]
Kalichman[13,a]	HIV/AIDS	51.1	50.9	40	Pill count	12 weeks, mean	6	87.40	91.00	94.10	87.80	6.7	−3.2	<**0.01**	9.90[a]
Mooney[14]	Smoking	42.1[d]		55	Electronic	7 weeks	5	–	–	–	–	–	–	<**0.0001**	–
Schmitz[15]	Smoking	48.9	48.1	97	Electronic	7 weeks	4	–	–	–	–	–	–	**0.0001**	–
Elixhauser[16,b]	Mental Health	49.1[d]		93	Electronic	4–8 months, percentage complied	4	50.00	52.00	48.40	62.20	−1.6	10.2	>0.05	−11.80[b]
Kozuki[17,b]	Mental Health	46.5[d]		30	Electronic	12 weeks, mean rate	5	78.40	88.50	87.90	68.40	9.5	−20.1	**0.026**	29.60[b]
Cramer[18]	Mental Health	46	48	81	Electronic	6 months	3	–	–	–	–	–	–	0.08	–
Russell[19]	Post-transplant surgery	51.5	44.0	15	Electronic	9 months	4	–	–	–	–	–	–	**0.03**	–
Hardstaff[20]	Post-transplant surgery	Not provided		48	Electronic	12 months	3	–	–	–	–	–	–	**–**[e]	–
Ruppar[21,b]	Hypertension	72.5	73.0	15	Electronic	20 weeks, median adherence	4	75.50	34.10	94.30	40.00	18.8	5.9	**0.01**	12.90[b]
Wu[22,b]	Heart failure	63.6	58.6	82	Electronic	10 months, mean rate	4	96.00	94.00	94.00	84.00	−2	−10	**0.021**	8.00[b]
Duncan[23]	Heart failure	66.0[d]		13	Subjective	12 weeks	3	–	–	–	–	–	–	<**0.05**	–
Kung[24]	Osteoporosis	65.6	66.3	596	Subjective	12 months	5	–	–	–	–	–	–	0.16	–
Lai[25,a]	Osteoporosis	65.3	67.1	198	Subjective	12 months, mean	5	96.85	97.38	97.97	96.17	1.12	−1.21	<**0.05**	2.33[a]
El Miedany[26]	Rheumatoid arthritis	50.5	51.0	111	Subjective	12 months	5	–	–	–	–	–	–	<**0.01**	–
Nadeem[27]	Sleep apnea	57.3	55.5	40	Electronic	1 month	4	–	–	–	–	–	–	0.61	–
Watson[28]	Exercise	44.1	40.6	70	Electronic	12 weeks	3	–	–	–	–	–	–	0.07	–
Shakudo[29]	Exercise	39.3	40.4	105	Electronic	12 weeks	5	–	–	–	–	–	–	0.36	–
Reddy[30]	Statin	65.6	64.1	126	Electronic	13 weeks	7	–	–	–	–	–	–	**0.001**	–

Note: Boldface indicates statistical significance ($p<0.05$). The % effect size is the difference between the intervention and control arms, in the change in % adherence of baseline and follow-up. Columns with no values are where baseline and final visit adherence were not reported in the paper but statistical analysis was performed.
[a]Included in meta-analysis.
[b]Not included in meta-analysis as no SD or SE values were reported.
[c]Age range = 20–50 years.
[d]Mean age of all participants.
[e]Statistical analysis not performed.

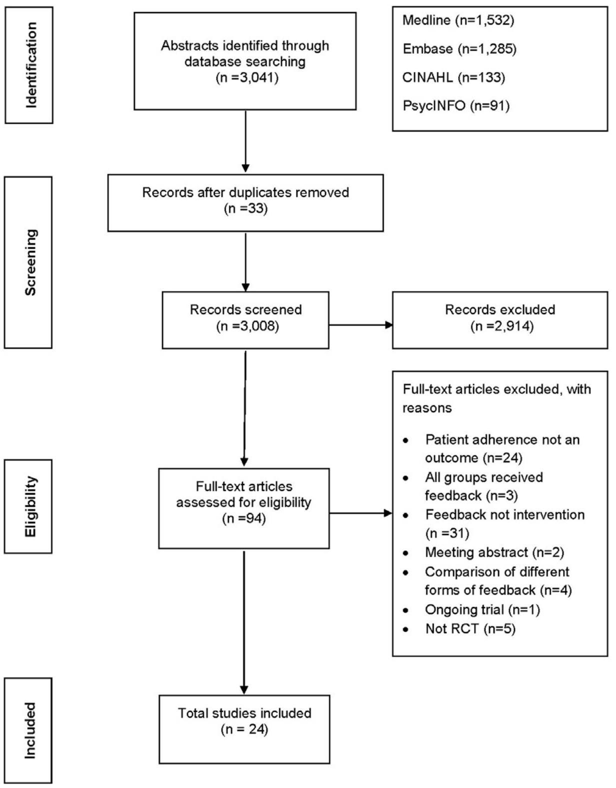

Figure 1. PRISMA study inclusion flowchart.
CINAHL, Cumulative Index to Nursing and Allied Health Literature.

HIV/AIDS

Five studies explored the effects of feedback in HIV/AIDS medication adherence.[9–13] Smith and colleagues[9] measured adherence to anti-retroviral medication using MEMS, with the intervention group viewing results monthly. Adherence in the intervention group was higher throughout the study (p=0.0017). CA was +22% in the intervention group and −32% for controls.

Sabin et al.[10] used a similar approach, although consisting of a pre-intervention period (allowing participants for stratification into high/low adherence before randomization) and a 6-month intervention period. A significant increase in adherence in the intervention group, who viewed and discussed their data, was reported, with controls remaining unchanged at 12 weeks (p=0.003). CA was +9.7% and +0.7%, respectively. Participants were considered non-adherent if medications were not taken within 1 hour of scheduled dose time; this is a stricter adherence measure than other studies and may result in an underestimate of actual adherence.

Rigsby and colleagues[11] explored feedback effects with and without rewards. Three groups were assessed: control; MEMs feedback (intervention); and MEMs feedback plus cash reinforcement. The latter group viewed their MEMS results, discussed any problems with adherence, and received cash for each dose taken within 2 hours of the scheduled time. Adherence in all groups worsened over time. CA showed better results with reward (control, −1%; intervention, −13%; intervention plus cash, −3%). Feedback alone had no effect on adherence.

Rosen et al.[12] similarly evaluated the effects of rewards together with feedback. One medication became the reinforced medication (RM) for which rewards were given whereas the remainder were non-RM. MEMS feedback for medication adherence to both RM and non-RM were provided to the intervention group. By Week 16, adherence had improved 15% for RM in the intervention group, with similar results for non-RM. Medication adherence significantly decreased in controls for both RM and non-RM (p=0.01).[12] CA values were 0% for intervention RM, +3% for intervention non-RM, −13% for control RM, and −13% for control non-RM. MEMS feedback improved adherence during the first 16 weeks (p=0.01), but RM did not increase adherence (p=0.09).[12]

Kalichman and colleagues[13] monitored adherence by undertaking unannounced pill counts in all participants. Phone calls informed the intervention group of their adherence. Increase in adherence from 87.4% to 94.1% at 4-month follow-up was noted ($p<0.01$), with the controls decreasing from 91% to 87.8% (CA of +6.7% and −3.2%, respectively).

Smoking

Mooney et al.[14] explored the role of MEMS feedback on adherence to bupropion for smoking cessation. The intervention group received their MEMS adherence weekly in graphical form. Adherence was reported as greater in the intervention group (77%) compared with controls (54%) at all time points. Schmitz and colleagues[15] used a similar approach, and adherence in the intervention group remained relatively stable (73%) with a decrease in adherence in controls (48%) (p=0.0001).

Mental Health

Elixhauser et al.[16] assessed adherence to lithium medication for bipolar disorder with MEMS. The intervention group received feedback based on MEMS recorded adherence and serum lithium levels. Controls received information of their serum lithium levels alone. Adherence was calculated from self-reported diaries provided to all participants. CA was −1.6% in the intervention group and +10.2% in controls ($p>0.05$). Kozuki and colleagues[17] used electronic pill bottles with an electronic chip in the cap (similar to MEMS) to monitor adherence to antipsychotic medications. The intervention group viewed a graphical display of their adherence at each visit and were encouraged to discuss any concerns with adherence. Controls received supportive counseling only. Adherence improved in the interventional group but declined for controls (CA of +9.5% and −20.5%, respectively; p=0.026).[17] Cramer et al.[18] also investigated effects of visual feedback from MEMS on adherence to antipsychotic medications. Overall adherence was 76% in the intervention group and 57% in controls (p=0.08).

Post-transplant Surgery

Two studies assessed feedback using MEMs recordings on adherence to immunosuppressive medication post-kidney transplant surgery.[19,20] Russell and colleagues[19] provided MEMs feedback to intervention participants at each follow-up visit and reported a significant improvement in adherence (intervention group CA, +0.128; control CA, +0.065; adherence was reported as an adherence score; p=0.03). Hardstaff et al.[20] delivered feedback at the first follow-up visit only (four total) and found no significant difference (adherence worsened by 48% for intervention and 52% for control).

Hypertension

Ruppar and colleagues[21] recorded adherence to antihypertensive medication using MEMs over 20 weeks. A higher increase in adherence was noted in the intervention group compared with controls (CA of +18.8% and +5.9%, respectively; p=0.008).[21]

Heart Failure

Wu et al.[22] recruited participants with poor adherence (<88% considered non-adherent) after an initial trial of MEMS recording without feedback. Selected study participants were randomized into one of three groups: control; counseling (LITE) group; and counseling plus feedback (PLUS) group. The PLUS group was shown a visual display of adherence from the MEMS report, missed doses were identified, and barriers to medication adherence discussed. The LITE group received information about the importance of medication but no MEMS recording data. Controls received standard care. The authors concluded that adherence was better in the PLUS group compared with the controls at all time points (CA of −2% and −10%, respectively; p=0.021) but no significant difference was noted between the PLUS and LITE groups (CA of −2% and +1%, respectively; p=0.804).

Duncan and colleagues[23] explored the effect of feedback on exercise adherence in patients undergoing cardiac rehabilitation. All participants completed weekly diaries regarding their exercise frequency/duration. Individuals were independently assessed and given exercise targets. The intervention group received regular e-mails with graphs depicting their exercise progress (from diary information) followed by feedback in the form of problem-solving guidance to achieve preset exercise targets.[23] A significant increase in exercise duration was noted (intervention group CA, +6.9; control CA, +2.8; $p<0.05$). Similar results were reported for exercise frequency (intervention CA, −0.7; control CA, −1.2; $p<0.01$). Although minimal changes, the results were significant as adherence was reported as the mean of preset exercise duration and frequency targets achieved. The intervention group achieved a mean of 108.7% and 104.6% for exercise duration and frequency, respectively. Controls achieved a mean of 84.9% and 64% for exercise duration and frequency, respectively.[23]

Osteoporosis and Rheumatoid Arthritis

Kung et al.[24] assessed the impact of bone marker CTX (measure of disease activity, an indirect measure of adherence), feedback on adherence to monthly bisphosphonate medication in the treatment of osteoporosis. The intervention group reviewed CTX levels rather than medication adherence. Medication adherence was self-reported using the Osteoporosis Patient Treatment Satisfaction Questionnaire (OPSAT-Q). No significant difference in adherence between the intervention and controls was reported (proportion of adherent participants were 92.6% for intervention 96.0% for control, p=0.16).

Lai and colleagues[25] used a similar approach and concluded that adherence was higher in the intervention group compared with controls but this change did not lead to a significant decrease in bone marker levels (intervention CA, +1.12%; control CA, −1.21%; $p<0.05$).

El Miedany et al.[26] studied the effect of visual feedback of disease marker parameters on adherence to disease-modifying antirheumatic drugs in rheumatoid arthritis. The intervention group viewed a graphical display of their disease marker parameters, with controls being given this result verbally as routine care. A significantly higher overall medication adherence in the intervention group (percentage adherence, 92.7%) compared with controls (percentage adherence, 69.6%) ($p<0.01$) was reported.[26]

Sleep Apnea

Nadeem and colleagues[27] evaluated the effects of showing patient polysomnographic data on adherence to continuous positive airway pressure therapy in sleep apnea. The intervention group viewed a graphic display of their polysomnograph on a computer screen, whereas the control group received a three-page report used in standard practice. Adherence was monitored using an adherence data card attached to the continuous positive airway pressure device. No significant improvement in adherence to therapy was reported, with overall adherence of 38% for the intervention group and 47% in controls (p=0.61).

Exercise

Watson et al.[28] investigated the role of feedback guided by pedometer results to improve adherence to physical activity in overweight/obese adults. Step-counting pedometers were worn continuously on shoes for a total of 12 weeks. The intervention group received personalized feedback, including problem solving based on their current pedometer result, which was compared to preset targets. The controls were able to view activity levels but did not receive personalized feedback. No significant difference was noted in percentage change in step counts between the two groups (p=0.07).[28] Shakudo and colleagues[29] applied a similar approach and reported that percentage achievement of target exercise level was 26.5% in the intervention group and 17.4% in controls (p=0.36).

Statins

Reddy et al.[30] investigated the effect of guided feedback (GlowCap Bottle) on adherence to statin medication. There were three groups: intervention group, control group, and a partner intervention group, whereby the report from the GlowCap Bottle was also sent to a designated family member/friend of the participant. A significant difference in overall adherence was noted between the two intervention groups (individual and partner feedback) and controls (89% and 86% vs 67%, respectively; p=0.001).[30] The authors continued to monitor adherence once the 13-week intervention period was over. The higher adherence rates achieved in the intervention groups were not sustained once intervention was stopped.[30]

Meta-analysis Results

Of the 24 identified studies, six presented raw data with SD or SE values on adherence in both an intervention and a control group, allowing data to be extracted for a meta-analysis.[7,8,10,12,13,25] Six other studies reported mean adherences but without SD or SE values, and therefore could not be included in the meta-analysis.[9,11,18,19,22] Meta-analysis of the six studies showed a significant difference in change in mean percentage adherence between the intervention and control groups, with the intervention groups showing a greater improvement (p=0.004). The pooled effect of the six studies estimates that mean percentage adherence increased by 10.02 (95% CI=3.15, 16.89) more between baseline and follow-up in the intervention groups compared with controls (Figure 2). Of the 12 studies that

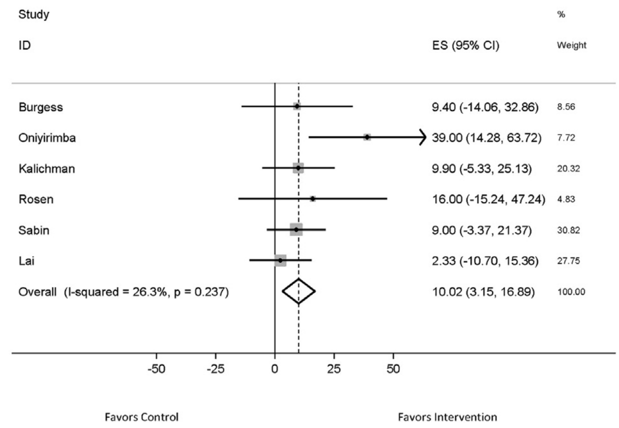

Figure 2. Results of random-effects meta-analysis of the effects of feedback on change in mean percentage adherence between intervention and control groups.

reported an effect size, one reported median values (Wu and colleagues[22]) and one reported the percentage of patients who complied (Elixhauer et al.[16]). For the ten studies reporting a mean percentage adherence, a weighted mean was calculated to investigate if studies that could be included in the meta-analysis differed from those that could not. The weighted mean was 11.29, similar to the main meta-analysis result.

The I^2 value from the random effects meta-analysis of the six studies, showing the amount of variation in the effect size attributable to study heterogeneity, was small (26.3%, p= −0.237, Figure 2). This was also reflected in the between-study SD (τ=5.335), demonstrating a small, non-significant effect of study heterogeneity. Meta-regression analysis indicated that the study effect size was not significantly associated with study quality, form of monitoring adherence, delivery of feedback, or study duration (p=0.818, 0.335, 0.348, and 0.0.226, respectively). However, when the analysis was stratified by electronic monitoring (four studies) and self-report (two studies), the pooled effect size was higher in studies with electronic monitoring: 14.175 (95% CI=4.64, 23.70) and 5.53 (95% CI= −4.37, 15.43), respectively, although this was not a statistically significant difference.

A funnel plot was produced to assess potential publication bias, but difficult to interpret given the small number of studies. No clear evidence of publication bias was found with the funnel plot, showing relatively good balance (Appendix 3, available online).

DISCUSSION

In total, 16 studies found significant improvements in adherence in the intervention group, compared with controls, across a range of medical conditions.[7–10,12,14,19,21–23,25,26] Although feedback did not result in a considerable increase in adherence in three of these studies, no decline in adherence in the intervention group occurred as with controls.[7,12,25]

Meta-analysis

Six studies were included in the meta-analysis, which all showed a significantly greater increase in adherence in the intervention group (overall effect size, 10.02; 95% CI=3.15, 16.89). Oniyirimba and colleagues[8] showed the greatest increase, with an effect size of 39. In this study, feedback was given on two occasions in face-to-face consultations by the treating clinician as opposed to other members of the research team. Meta-regression analysis showed study effect size was not associated with the professional background of the person giving feedback; therefore, reasons for a greater improvement in adherence in this study is unclear. The I^2 value of 26.3% also shows low heterogeneity between the studies, indicating the effect sizes are comparable.[34] Given the heterogeneity in the reporting of results, a limitation of this study was that only six studies could be included in the meta-analysis. Owing to this small number, the results of the meta-analysis should be interpreted with caution. More emphasis should be placed on the narrative synthesis of the review.

Factors Influencing Effects of Feedback

Two studies reported an improvement in adherence in controls, while adherence worsened in the intervention group.[18,27] Although not statistically significant, it is important to explore factors that may have influenced the results. In the study by Elixahauser et al.[16] exploring feedback in bipolar disorder, it may be that the feedback group recorded their adherence more accurately in diaries being aware adherence measures from MEMS containers were available to the research team. Controls, who did not receive MEMS containers, may have over-reported adherence (often the case with self-reported measures).[35] Three studies exploring feedback in HIV, post-transplant, and heart failure medication adherence reported decreases in adherence in both the intervention and control groups.[11,20,22] However, other studies exploring the effect of feedback in the same diseases found a significant increase in adherence.[9,10,12,13,19,21] This indicates subtle differences between similar studies may influence the effects of feedback on adherence.

Surrogate Adherence Markers

Feedback using surrogate markers as an indirect measure of adherence resulted in mixed results.[24–27] Kung and colleagues[24] reported no significant difference in adherence to bisphosphonates when CTX bone marker levels were given as a form of feedback. By contrast, two other studies concluded that adherence was significantly higher in the intervention group compared with controls.[25,26] Although Lai et al.[25] reported an increase in adherence (self-reported) to taking bisphosphonate in the intervention group, this improvement did not correlate with a decrease in bone marker levels. Therefore, surrogate markers do not appear to be an appropriate method of quantifying adherence, particularly if they do not change immediately with adherence to medication. In addition, as adherence was self-reported in these studies, adherence may have been overestimated.

Use of Counseling/Incentives to Improve Adherence

Wu and colleagues[22] used a different approach whereby participants were allocated to one of three groups: control, counseling, and counseling plus intervention. Although adherence was significantly higher in the counseling plus intervention group compared with the controls, difference in adherence was not noted between the counseling and counseling plus feedback group. It is not necessarily feedback alone that improves adherence but also education of patients regarding their medical condition and encouraging positive behavioral beliefs. Increased attention by health professionals may contribute to improvements in adherence also.

Two studies explored the effect of feedback with and without rewards (monetary incentives).[11,12] Both concluded that simultaneous use of rewards did not modify the effects obtained with feedback alone. Informing patients about their adherence and educating them on ways to improve adherence is more effective than rewards.

Influence of Individual Providing Feedback

In two studies, feedback was provided by the treating clinician as opposed to other research staff.[8,10] In the study by Sabin et al.,[10] adherence improved by 9.7% in the feedback group. However, other HIV studies in which feedback was given by research staff also found similar improvements, with one study reporting a 30% increase in adherence.[9,12,13] There is no evidence, including from the meta-regression analysis, that the effect of feedback is influenced by the provider's professional background.

Effect of Feedback on Different Ages

Only one study explored the effect of feedback on adherence in children.[7] Burgess and colleagues[7] reported a CA of 6.7% when parents of asthmatic children received feedback regarding their child's adherence. Oniyirimba et al.[8] noted a CA of 15% in adult asthmatics who received feedback. The authors postulate that children may feel less involved in the feedback discussions and are unable to understand the advice given, resulting in poor cooperation with parents and, therefore, less improvement in adherence compared with adults. Further studies are needed to explore the impact of feedback adherence in children and identify strategies to engage children of various ages in feedback. In children, feedback with rewards may be more beneficial.

Visualization of Results

Two main methods of feedback were used in the studies. A total of seven studies provided MEMS/electronic dose monitors and indirect markers of adherence data verbally.[7,8,13,18,20,24,25] The remaining studies provided adherence data graphically where participants were able to visualize the MEMS/electronic dose monitor recordings as a graph and discuss missed doses at specific times.[9–12,14,19,21–24,28] In general, studies allowing visualization of adherence data reported a higher improvement in adherence, with five studies showing a CA >10% in the intervention group.[9,10,12,19,23] Only one study using verbal reporting found similar improvements.[8] Graphical display of MEMS data gives more in-depth information regarding timing/frequency of missed medication doses, allowing for more detailed discussion with the examiner. Participants can also view their progression over the study period.

Limitations

The main strength of this study is that only RCTs were included—the most reliable method of determining whether a causal relationship exists between treatment and outcome.[36] A robust selection process was applied; all studies were reviewed and quality assessed by three independent reviewers. This review was not limited to any particular field of health care and covered a broad range of conditions. Other strengths included no limitation of language or age and bibliography hand searches.

Limited data were available from some studies, which resulted in only six studies being suitable for the meta-analysis. Moreover, some studies reported data qualitatively and it was not possible to calculate CA from available data, making comparisons more difficult. Also, some RCTs included in the review used self-reporting methods, which may not be a reliable measure of adherence.

CONCLUSIONS

Overall, this systematic review shows that feedback of adherence can influence adherence outcomes. In most studies, a significant improvement in adherence was reported, whereas in some feedback was shown to prevent worsening of adherence over time. Greater improvements were reported when feedback was given in a graphical form versus verbal feedback. The current review shows adherence was not influenced by the provider's professional background; therefore, it is not necessary for feedback to be given by a clinician. This systematic review shows that feedback on adherence has significant potential to improve treatment. Non-adherence costs are both personal and economic, not only resulting in a lack of improvement or deterioration in health for the patient, but also financial costs of wasted medication and increased demands for health care when health deteriorates. Administering feedback to patients has the potential to reduce both personal and economic healthcare costs. Feedback is an important element to be incorporated in treatment and future studies.

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SUPPLEMENTAL MATERIAL

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