Supplement_F_PICO_4_Non-adherence on outcome

PICO 4: Effect of non-adherence on outcome.

Assuming non-adherence has a negative impact on treatment outcome, the question remains what are the effects of adherence interventions on the clinical outcome?

All interventions included in the selected systematic reviews were reviewed. The primary outcome in the studies were adherence. Only studies that measured clinical outcomes (disease activity [DAS-28, CDAI], data on patient’s perspective [QoL, function, and fatigue]) in addition to adherence were included.

Summary

In total, 5 reviews, including 15 RCT studies, describing interventions, which had a significantly positive effect on adherent behaviour were included in this analysis (9 studies[1-9] on medication adherence; 6 on non-pharmacological/exercise adherence[10-15]). Studies were excluded, if they did not reach significance[16-23], if the intervention only focused on rheumatologists[24], focused on health literacy only[25], or the study was not a RCT[26-28], interventions to improve adherence was not an object of the study[29-44], or if the study did not focus on RMDs (ulcerative colitis[45-49], inflammatory bowel diseases[50]).

Medication adherence

Patients in the 9 included studies regarding medication adherence, patients were diagnosed with rheumatoid arthritis (RA)[2-5, 8], psoriasis[1], systemic lupus erythematosus (SLE)[6, 9], juvenile rheumatoid arthritis (JRA)[7]. Changes in clinical outcomes due to a change in adherence were seen in:

1) Decrease in disease severity[1/activity[9], pain[1, 3, 4], PGA[1, 3, 4], functional disability[1, 3, 4, 8], DAS-28[3, 4], fatigue[8].
2) Increase in quality of life[1, 3, 4], knowledge[6], active coping with stress[8].
3) Decrease of helplessness[4], medicine related problems[5], depression[8].
4) Increase in quality of patient–physician communication[1].

Exercise adherence

In the 6 included studies dealing with exercise adherence, patients were diagnosed with osteoarthritis[10, 12, 15], low back pain[11], and RA[13, 14]. The group that was significantly more adherent, had also significant improvements in:

physical activity[10, 12-14], functioning[11, 15], quality of life[11], proxy efficacy (refers to patients' confidence in their therapists' ability to function effectively on their behalf)[11], working alliance[11], treatment expectancy[11], and a decrease in pain[15] and weight[10].
Table 1. Individual studies exploring effective communication and SDM components of interventions proven effective.

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<tr>
<th>Study, Design, medication</th>
<th>Review, IG, CG</th>
<th>Intervention</th>
<th>Outcome measures</th>
<th>Results</th>
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<tr>
<td>Balato, Megna [1]; Pilot RCT; medication</td>
<td>Depont, Berenbaum [51]</td>
<td>Psoriasis IG n=20 CG n=20</td>
<td>IG: Daily text messages (TM), providing reminders and educational tools CG: not clear</td>
<td>At the beginning and end of the study, the following assessments were performed: Psoriasis Area Severity Index (PASI), Self-Administered Psoriasis Area Severity Index (SAPASI), body surface area (BSA), Physician Global Assessment (PGA), Dermatology Life Quality Index (DLQI), evaluation of patient-physician relationship and adherence to therapy. The intervention group reported a significantly better improvement of disease severity as well as quality of life, showing lower values of PASI, SAPASI, BSA, PGA and DLQI compared to the control group (P&lt;0.05) (values are not reported, can only be estimated from the figures). Adherence to therapy improved significantly (98.0 to 91.6% at week 4; 97.4 to 85.0% at week 12; 96.2 to 78.0% at week 24; 94.9 to 69.0% at week 36). TM led to an optimization of patient-physician communication.</td>
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<td>Hill, Bird [2]; RCT; medication</td>
<td>Depont, Berenbaum [51]</td>
<td>RA IG n=51 CG n=49</td>
<td>IG: patient education programme: information about the types of drugs used for RA, the disease process, physical exercise, joint protection, pain control, and coping strategies. Written information, including a DPA drug information leaflet developed especially for the study, was provided as back up. CG: same DPA drug information leaflet</td>
<td>Primary measure of adherence was by pharmacological marker (dosage of DPA) (The ratio of phenobarbitone level in the blood to prescribed dose (LDR) was calculated for each patient at each study visit: (phenobarbitone concentration (mg/l))/(daily phenobarbitone dose (mg/kg body weight))). Pharmacological marker showed the EG to be significantly more adherent on more occasions than the CG (p&lt;0.05). Patterns of adherence over time showed that at 12 weeks 86% (38/44) of those in the EG compared with 64% (29/45) of the CG remained adherent (p=0.01). These trends continued and by the end of the study 85% (29/34) of the EG compared with 55% (23/42) of the CG were taking their DPA as prescribed.</td>
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<td>El Miedany, El Gaafary [3]; Pilot RCT; medication</td>
<td>Depont, Berenbaum [51]</td>
<td>Early RA IG n=55 CG n=56</td>
<td>IG: visual feedback facility (visualization of computer charts showing the disease progression) CG: Usual care</td>
<td>Primary outcome: change in the patients’ adherence to their medications, disease activity score (DAS-28), and PROMs domains: pain score, patient global assessment, functional disability, and quality of life. Adherence: IG 47/54 (87%) patients in were adherent to their drug therapy, whereas 23/54 (43%) in CG to their drug therapy (P &lt; 0.01). Pain (IG 4.48 (1.4) vs CG 3.39 (1.1), p &lt;0.001), PGA (IG 4.22 (1.2), CG 3.41 (1.1), p &lt;0.001), functional disability (IG 1.75 (0.3), CG 1.21 (0.3), p &lt;0.001), QoL (IG 1.77 (0.2), CG 1.30 (0.2), p &lt;0.001), DAS28 (IG 1.79 (0.4), CG 1.23 (0.3), p &lt;0.001)</td>
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<td>El Miedany, El Gaafary [4]; RCT;</td>
<td>Depont, Berenbaum [51]</td>
<td>RA IG n=74 CG n=73</td>
<td>IG: Joint-fitness programme combined with discussion/review of PROMs and patient education; The programme includes 4 main components: a) educational – joint-learn, b) behavioural – joint-change, c) information – joint act and d) joint-exercise.</td>
<td>At 3, 12 and 18 months: The primary outcome was the change in the patients’ adherence to their medications, disease activity score (DAS-28) and PROMs (pain score, patient global assessment, functional significant reduction DAS-28 score, as well as improvement of the patients’ adherence to therapy (p&lt;0.01), improvement of disease activity was associated with improvement in functional disability and quality of life scores. At 18 months: Pain (IG 4.49 (1.3) vs CG 3.38 (1.1), p &lt;0.001), PGA (IG 4.25 (1.1), CG 3.43 (1.2), p...</td>
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<td>Study, Design, med/non-pharma</td>
<td>Review</td>
<td>Dig., IG, CG</td>
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<td>Clifford, Barber [5]; RCT; medication</td>
<td>Galo, Mehat [52]</td>
<td>RA IG n=261 CG n=239</td>
<td>IG: telephone-based, patient-tailored pharmacy advisory service delivered by community pharmacists to elderly patients which included RA. The pharmacist gave information, advice or reassurance in response to the patients’ expressed needs. CG: usual care</td>
<td>Primary Outcome: Incidence of non-adherence Secondary outcome: problems with the new medicine, beliefs about the new medicine, safety and usefulness of the interventions.</td>
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<td>Galacho and Almas [6]; RCT; medication</td>
<td>Galo, Mehat [52]</td>
<td>SLE IG n=21 CG n=20</td>
<td>IG: education regarding SLE and its management by clinical pharmacist: including lifestyle modifications, via the distribution of patient information CG: usual care</td>
<td>Knowledge Assessment Questionnaire, Medication Adherence Questionnaire</td>
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<td>Rapoff, Belmont [7]; RCT; medication</td>
<td>Galo, Mehat [52]</td>
<td>Juvenile Rheumatoid Arthritis IG n=19 CG n=15</td>
<td>IG: educational and behavioral strategies for enhancing adherence: 10-min audiovisual program and received abooklet which described adherence-enhancement strategies: cueing(e.g., pairing medication taking with an established behavior such as brushing teeth), monitoring (e.g., using a calendar to track medication taking), positive reinforcement (e.g., praising and rewarding with tokens that are exchanged for special privileges), and discipline (e.g., using time-out for defiant refusals to take medications). Nurse reviewed and rehearsed strategies, gave answers CG: received a general educational on JRA</td>
<td>Adherence: Medication Event Monitoring System (MEMS), Disease activity and functional status (standard clinical indices, number of active joints, minutes of morning stiffness, and global disease activity rating), Childhood Health Assessment Questionnaire (CHAQ),</td>
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<td>Evers, Kraaimaat [8];</td>
<td>Deponent, Beren</td>
<td>Early RA IG n=32 CG n=32</td>
<td>IG: cognitive-behavioural therapy (CBT): consisted of individual treatment with two out of the four treatment modules:</td>
<td>Disease activity: Disease Activity Score (DAS); Functional disability: Mobility and Self-care scales of</td>
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<td>RCT; medication</td>
<td>baum [51]</td>
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<td>pain and functional disability, fatigue, negative mood and social relationships. CG: usual care</td>
<td>the Impact of Rheumatic Diseases on General Health and Lifestyle (IRGL); Pain: IRGL Pain scale (six items); Fatigue: Checklist Individual Strength (CIS); Psychological functioning: IRGL Anxiety and Negative Mood scales; Social functioning: IRGL social functioning scales; Illness cognitions: Illness Cognition Questionnaire; Coping with stress: Utrechtse Coping Lijst (UCL); Coping with pain: Pain Coping Inventory (PCI); Compliance with RA medication: 3-point scale by a single item, inquiring about the frequency of failing to take the prescribed RA medication during the previous month (1=once a week or more, 2=less than once a week, 3=never).</td>
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<td>Ting, Kudalkar [9]</td>
<td>Galo, Mehat [52]</td>
<td>childhood-onset SLE</td>
<td>IG: cellular text messaging reminders (CTMR) to remind taking medication and to remind for CG: usual care</td>
<td>Systemic Lupus International Collaborating Clinics/American College of RheumatologyDamage Index (SDI), the Systemic Lupus Erythematosus Disease ActivityIndex (SLEDAI), and the physician assessment of disease activity (by visu-al analog scale; range 0–10, 0 = inactive disease, 10 = very active disease).The number of emergency room (ER)</td>
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<td>visits and the number of hospital admissions were monitored among patients participating in clinic visit adherence.</td>
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<td><strong>Studies with significant effects on non-pharmacological intervention adherence</strong></td>
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<td>Ravaud, Flipo [10]; RCT; Non-pharma</td>
<td>Ezzat, MacPherson [53]</td>
<td>OA/knee, IG n=154 CG n=182</td>
<td>IG: Standardised consultation during three goal oriented visits: education on osteoarthritis and treatment management, information on physical exercises, information on weight loss. CG: usual care</td>
<td>Change in (1) body weight; (2) time spent on physical exercises (Baecke index)</td>
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<td>Vong, Cheing [11]; RCT; Non-pharma</td>
<td>Nicolson, Bennell [54]</td>
<td>Low Back Pain IG n=38 CG n=38</td>
<td>IG: motivational enhancement treatment (MET) including supporting appropriate behaviour change and increasing self-efficacy PLUS PT CG: conventional physical therapy (PT)</td>
<td>Motivational-enhancing factors (PRES and PSEQ), pain intensity (VAS), physical functions (trunk motion and RMDQ), and exercise compliance (exercise log book).</td>
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<td>Halbert, Crotty [12]; RCT; Non-pharma</td>
<td>Ezzat, MacPherson [53]</td>
<td>OA IG n=37 CG n=32</td>
<td>IG: individualized physical activity advice CG: received a pamphlet on good nutrition</td>
<td>Intention to exercise was: self-reported questionnaire Physical activity outcomes included frequency of walking per week, minutes of walking per session, frequency of vigorous exercise per week, and minutes of vigorous exercise per session. Intention to exercise was measured using a stages-of-change model.</td>
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<td>Brus, Van De Laar [13] RCT; medicatio n</td>
<td>Depont, Beren baum [51]</td>
<td>RA IG n=25 CG n=30</td>
<td>IC: education programme focused on compliance with sulphasalazine therapy, physical exercises, endurance activities (walking, swimming, and bicycling), advice on energy conservation, and joint protection, training was given in proper execution of physical exercises. Patients were encouraged to plan their treatment regimens. Their intentions were discussed and help was given in recasting unrealistic ones. Patients made contracts with themselves regarding their intentions. Feedback on the eventual implementation of therapeutic advice was included in each meeting.</td>
<td>Physical exercise and with endurance activity regimens (walking, swimming, bicycling) were measured by questionnaire; patients were asked how many times a week and how many minutes average each time they performed these activities. Time spent on endurance activities were added.</td>
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<td>Pisters, Veenhof [14]</td>
<td>Ezzat, MacPh erson [53]</td>
<td>OA/hip, knee</td>
<td>IG: individually tailored graded exercise program to teach the patient that it is safe to move while increasing the level of activity. CG: usual care</td>
<td>Exercise adherence was measured using a questionnaire and physical activity was measured using the SQUASH questionnaire at baseline, 13, and 65 weeks.</td>
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<td>Tüzün, Ciftçi [15] Nicholas, Bennelli [54]</td>
<td>Knee OA</td>
<td>IG: Photos displaying these exercises were taken, and explanatory information was written next to the relevant photo using large fonts. CG: usual care</td>
<td>The compliance of the participant: logs and weekly follow-up via phone call performed by a blind investigator. Effectiveness of the therapy: (1) WOMAC score (2) Quadriceps measurements 15 cm proximal to the tuberositas tibiae</td>
<td>These analyses revealed that 100% of the participants in the IG were compliant with all assessments, and 80% of the participants in the SCG were compliant in the first week, and the rate of compliance decreased to 70% at Week 5 and to 55% at Week 10 (p=0.0001). The CEP in the SCG was 80% at Week 1 (55.0 – 100.0), 70% at Week 5 (55.0 – 93.75), and 55% at Week 10 (17.5 – 70) (p=0.001), and the most significant decrease in the CEP occurred between Weeks 5 and 10 (p=0.0001). The median WOMAC values of the participants in the IG and SCG were 43.5 (25.75 – 50.25) and 36.0 (23.5 - 42.25) (p=0.276), and the final WOMAC values decreased by 9.5 (5.0 - 18.0) and 27.0 (15.25 - 39.0), respectively. The analysis of WOMAC measurements revealed that the decrease was significant in both groups, yielding a p value of 0.037 in the SCG and 0.0001 in the IG. The comparison of the decrease in WOMAC values between the groups: yielded a value of p=0.0001. The evaluation of the median BMI values between the initial and final assessment revealed a significant decrease (p=0.005). When the participants were evaluated according to their randomization groups, the decrease was significant in SCG (p=0.012) and insignificant in the IG (p=0.179). Furthermore, there was no significant difference between the groups in terms of the measurement of the quadriceps circumference.</td>
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REFERENCES


