Cost-Effectiveness of Intensive Exercise Therapy Directly Following Hospital Discharge in Patients With Arthritis: Results of a Randomized Controlled Clinical Trial

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Objective. To estimate the cost-utility and cost-effectiveness of a 3-week intensive exercise training (IET) program directly following hospital discharge in patients with rheumatic diseases.

Methods. Patients with arthritis who were admitted to the hospital because of a disease activity flare or for elective hip or knee arthroplasty were randomly assigned to either the IET group or usual care (UC) group. Followup lasted 1 year. Quality-adjusted life years (QALYs) were derived from Short Form 6D scores and a visual analog scale (VAS) rating personal health. Function-related outcome was measured using the Health Assessment Questionnaire, the McMaster Toronto Arthritis (MACTAR) Patient Preference Disability Questionnaire, and the Escola Paulista de Medicina Range of Motion scale (EPMROM). Costs were reported from a societal perspective. Differences in costs and incremental cost-effectiveness ratios (ICERs) were estimated.

Results. Data from 85 patients (50 IET and 35 UC) could be used for health-economic analysis. VAS personal health–based QALYs were in favor of IET. Function-related outcome showed statistically significant improvements in favor of IET over the first 6 months, according to the MACTAR ($P < 0.05$) and the EPMROM ($P < 0.01$). At 1-year followup, IET was €718 less per patient. The ICER showed a reduction in mean total costs per QALY. In 70% of cases the intervention was cost-saving.

Conclusion. IET results in better quality of life at lower costs after 1 year. Thus, IET is the dominant strategy compared with UC. This highlights the need for implementation of IET after hospital discharge in patients with arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) and osteoarthritis (OA) have a different pathophysiologic basis. However, patients who have either form of arthritis experience pain and a gradual decline in muscle strength, eventually resulting in loss of function and quality of life. Hospitalization is indicated in patients with arthritis who experience a disease activity flare or who require elective joint replacement. During hospitalization, an increased decline of function is observed (1). Recently, in the Disabled Arthritis Patients Post-hospitalisation Intensive Exercise Rehabilitation (DAPPER) study (2), we have shown the beneficial effects of intensive exercise training (IET) directly following hospital discharge of arthritis patients with disease flare or after elective joint replacement. This finding is in line with earlier studies in patients with arthritis that evaluated IET on an inpatient basis and on an ambulatory basis (3–5).

Usual care for patients with arthritis following hospitalization due to a flare of disease activity or for joint replacement is not standardized and depends upon local custom, health care system, and preferences of the patient, among other things. Nowadays, health care policy is based on evidence of effectiveness and, conversely, on health economic considerations. Thus the implementation of novel treatment strategies should be based on evidence of effectiveness as well as on an acceptable balance between costs.
and effectiveness. Up to now, only a limited number of studies have reported the cost-effectiveness of exercise in patients with arthritis (6–10). However, patients with active disease were excluded.

This report addresses the health economic aspects of an IET program compared with usual care (UC) for patients with arthritis following hospitalization due to a flare in disease activity or for elective knee or hip replacement. The cost-effectiveness analysis was performed alongside the randomized controlled clinical trial.

PATIENTS AND METHODS

Patients. Patients were recruited from 4 Dutch hospitals (Medisch Spectrum Twente, Enschede; Twenteborg ziekenhuis, Almelo; Sint Maartenskliniek, Nijmegen; and Isala klinieken, Zwolle). Patients were eligible when they were admitted either due to a flare in disease activity or for elective knee or hip replacement. Additional inclusion criteria were age >18 years and either RA according to the American College of Rheumatology (formerly the American Rheumatism Association) 1987 criteria (11) or polyarticular OA. Exclusion criteria were presence of serious cardiac disease (New York Heart Association criteria class III and IV) (12), incapacitating pulmonary disease (Gold stage IV) (13), serious hypertension (diastolic blood pressure >110 mm Hg), pregnancy, insufficient understanding of the Dutch language, and functional incapacity (Steinbrocker functional class 4) (14). A signed consent form was obtained from all participants.

Design. The DAPPER study is a randomized controlled clinical trial. In summary, consecutive eligible patients who gave informed consent were included and randomized blockwise to either the intervention group (IET) or the control group (UC). Directly following discharge, patients in the IET group were referred to a dedicated convalescent resort to receive 3 weeks of intensive exercise training. Thereafter, the IET group received regular care only.

In contrast, after discharge the patients in the UC group received usual care at the discretion of their attending physician only. Standard usual care after an elective joint replacement often consists of physical therapy once or twice weekly at a home-based setting. In case of comorbidity or polyarticular OA complication, rehabilitation referral to a nursing home is customary. Usual care after a disease flare is diverse, ranging from no additional therapy to physical therapy and ergotherapy at home. Outcome assessments were performed at baseline and after 3, 13, 26, and 52 weeks. Costs were measured prospectively by monthly questionnaires.

Intervention. Directly following discharge, the IET group received a 3-week intensive exercise program at the European Care Residence and Resort “Groot Stokkert,” which offers hotel facilities and professional care for disabled persons. During their 3-week stay, patients from the IET group were trained twice a day by physical therapists for 75 minutes per session. The goals of the training were improvement of range of motion, muscle strength, aerobic capacity, physical function, and daily activities. The therapy sessions were administered individually and in groups. In the first 2 weeks, treatment focused on individual limitations (range of motion, strength, balance, aerobic capacity, and simple functionality). Aerobic capacity training occurred daily on a submaximal level. Hydrotherapy was applied after sufficient wound healing. During the third week, the training focused on the functional capacities as prioritized by the patient. A group education program was administered twice per week. This program was based on the self-management training for patients with arthritis developed by Lorig et al (15) and modified for The Netherlands by Taal et al (16).

Health outcome. Utilities. Utilities refer to the preferences individuals or society may have for any particular health state (17) and a valuation of the health of the patient ranging from 0 (equivalent to death) to 1 (full health). Utilities are used to calculate quality-adjusted life years (QALYs). A QALY is a composite index that includes effects in terms of both quality of life (utility) and the duration of time in such a health state (17). QALYs are an accepted measure for resource allocation decisions involving diverse treatments and patient populations (18).

For the present study, utilities were assessed using the Short Form 6D (SF-6D) and a 100-mm visual analog scale (VAS). The SF-6D utility index was calculated from the RAND 36-item health survey 1.0 (RAND-36) questionnaire (19). The RAND-36 includes the same items as those in the Short Form 36 (SF-36) and measures general health status. The RAND-36 comprises 36 items on physical and social functioning, role limitations, mental health, vitality, pain, and general health perception (20). The VAS score ranges from 0 (worst imaginable health) to 100 (best imaginable health).

Functional ability. Outcome expressed as functional ability was calculated according to the Health Assessment Questionnaire (HAQ) (21,22), the McMaster Toronto Arthritis (MACTAR) Patient Preference Disability Questionnaire (23,24), and the Escola Paulista de Medicina Range of Motion scale (EPMROM) (25). The HAQ score ranges from 0 (no disability) to 3 (severe disability); the MACTAR followup score ranges from 21 to 77 points (lower scores reflect better functional ability). The followup assessments focus on change in ability to perform impaired activities and evaluate the patient’s health status by asking questions on general health; quality of life; and physical, social, and emotional well-being. The EPMROM evaluates 10 distinct movements of joints on both sides of the body, and the score varies from 0 (no limitation) to 30 (severe limitation).

Costs. Costs were assessed using the societal perspective and were valued in accordance with the Dutch guidelines for pharmacoeconomic research (26) including direct and indirect medical costs and indirect nonmedical costs. All unit cost prices were based on the year 2003 and were expressed in euros (€).

To estimate the costs of the convalescence program (IET), College Tarieven Gezondheidszorg/Zorgautoriteit
in oprichting (CTG/ZAio) charges were used (www.ctg-zaio.nl). The cost per day of the IET program was composed as follows: 1) accommodation €90, 2) nursing care €10.50, 3) individual physical therapy €21.50, and 4) group therapy €37.25. During the weekend no therapy was administered. The cost per weekday per IET patient was valued at €159.25. The cost per weekend day per IET patient was €100.50. The total cost of the intervention was estimated at €2,991 per patient.

Medical costs were based on the 2003 Dutch governmental charges (CTG/ZAio) or, whenever applicable, on the market prices. The general practitioner was valued at €20.20 per visit. Medical specialist visits were valued at an average charge of €57.65. The physical therapist was valued at €21.50 per visit. All other paramedical and alternative therapists (such as occupational therapists and social workers) were separately valued according to average market prices of the professions in The Netherlands. The average price was €32.60 per visit. Medication was valued according to the Dutch Pharmacotherapeutic Compass (27) including the 6% price per prescription to cover pharmacist fees.

For hospital admissions, the number of days spent in the hospital and the type of hospital were recorded. Hospitalization days were valued according to the prices declared by the financial administration of the hospitals. The aids used for physical restrictions were recorded as were the actual costs incurred by the patients.

Nonmedical costs were based on Dutch standard prices reflecting societal costs for economic evaluations (28). These costs included travel costs required to obtain health care, the costs of absenteeism from work, professional domestic care, paid domestic help, and informal care (the number of hours per week patients received help from family or friends). Absenteeism was valued using the human-capital method in which productivity costs are calculated for the entire absent period. Absenteeism from paid work was recorded on a per-day basis. Monthly income and regular working hours were recalculated to value a day’s income (28,29).

Professional domestic care was valued at €30.70 per hour. The costs of paid domestic help and informal care were valued as reported by the patients with a maximum of 28 hours per week in order to prevent overreporting. When actual costs were unavailable, an average cost per hour of €8.00 was imputed.

Statistical analysis. Results were analyzed for patients who completed at least 6 of the 12 monthly questionnaires on costs. Results are expressed as QALYs and measures of physical function. The time-integrated summary score (the area under the curve [AUC]) of the utilities was calculated to define the quality of life per period (0–6 months and 0–1 year).

The scores of the HAQ, MACTAR, and EPMROM were presented as change scores from baseline. Between-group differences in outcome measurements were analyzed per period by Student’s t-test for unpaired observations.

The costs are presented as the arithmetic mean ± SD per patient per group. The between-group differences in resource use were analyzed per period by Mann-Whitney U test. Mean incremental costs per patient and study period were calculated and 95% confidence intervals (95% CIs) were calculated using double-sided bootstrapping.

The incremental cost-utility ratio (ICER) was calculated by dividing the incremental costs for the IET group by the gained QALYs derived from IET. The ICER is expressed as costs per QALY gained. The incremental cost-effectiveness ratio (ICER) for function measures was calculated by dividing the extra costs for the IET group by the gained units of effectiveness. These ICERs are expressed as costs per score points. The 95% CIs of the ratios were estimated with bootstrapping. ICERs were only calculated when group differences were significantly different. Costs and health outcome were not discounted because the time horizon of this study was less than 1 year and no modeling beyond the observed period was performed.

RESULTS

Study participants. The DAPPER trial included 114 patients with arthritis who were admitted to the hospital because of a flare in disease activity or for elective joint replacement of the hip or knee. Cost questionnaires were completed by 85 of the patients (75%; 50 IET and 35 UC). Twenty-nine of the patients (10 IET and 19 UC) did not complete the questionnaires, but they did not differ from the other patients in the DAPPER trial with respect to sex, age, work, or education.

The demographic and baseline disease characteristics of the patients in this health economic analysis are presented in Table 1. Differences between groups were not statistically significant.

Health outcome results. SF-6D–based QALYs were similar in both groups. VAS-based QALYs were in favor of IET (P < 0.05) for both periods (Table 2).

Function-related outcome was similar according to the HAQ. However, the MACTAR (P < 0.05) and the EPM-ROM (P < 0.01) showed statistically significant improvements in favor of IET during the first 6 months (Table 2).

Cost results. The amount of medical and nonmedical resource use during the followup is presented in Table 3. For both periods, a difference in favor of the IET group was observed in the number of visits for paramedical treatments (P < 0.01). Patients from the UC group visited physical therapists 1.8 times more frequently compared with the IET group. For the other variables, including hospitalization, no significant differences in the amount of resource use were found.

Mean costs per patient per year by cost category and treatment group are listed in Table 4. Mean total costs from a societal perspective were €7,18 lower per patient per year (95% CI −€7,553, €3,660) for the IET group compared with the UC group. When excluding the price of the IET program, mean incremental costs per patient were €3,709 lower for IET. After 6 months of followup, the mean incremental costs per patient was €804 higher for IET (95% CI −€2,595, €3,996). When excluding the price of the IET
program, the mean incremental costs per patient was €2,068 lower for IET (data not shown).

The observed difference in costs between groups was mainly generated by the cost of hospitalization. Therefore, further specification of these costs was explored. The main difference in hospitalization costs could be explained by a small group of patients from the UC group. Immediately after initial discharge from the hospital, these patients (mainly diagnosed with OA) were referred to a nursing home for an average of 47 days. This resulted in €31,000 extra costs for the UC group. In addition, during followup patients from the UC group who were hospitalized because of a second elective hip or knee arthroplasty stayed in the hospital longer on average compared with patients from the IET group, which explains a difference in total costs of €21,000 between groups (results not shown).

Cost-utility. The incremental cost-utility ratio (based on the AUC of the VAS personal health) after 6 months of followup was €20,100 (€804/0.04) per QALY gained (95% confidence interval: €15,700 to €28,500).
CI –€235,000, €293,000). In 49% of the cases the intervention was cost-saving. After 1 year of followup, the intervention was cost-saving and IET was the dominant strategy. The uncertainty around the ratio was estimated with bootstrapping and is presented graphically by the cost-utility plane (Figure 1). This plane shows in which quadrant the bootstrapped ratios were situated in the lower-right quadrant (signifying lower costs and better quality of life) whereas 30% were situated in the upper-right quadrant (signifying higher costs). Because the SF-6D did not show differences in QALYs between groups, the ICER was not calculated based on this instrument.

**Cost-effectiveness.** The ICER was calculated based on the MACTAR and EPMROM score over the first 6 months because significant differences between groups in terms of effectiveness were found with these instruments. The ICER based on the MACTAR over the first 6 months was €142 (€804/5.7) per score point (95% CI –€2.328, €2.829); in 38% of the cases the intervention was cost-saving. The ICER based on the EPMROM over the first 6 months was

| Table 3. Amount of medical and nonmedical resource use over the 0–6-month and 0–1-year study period comparing patients in the intensive exercise therapy (IET) and usual care (UC) groups* |
|---------------------------------|-----|-----|-----|-----|
| **0–6 months**                  |     |     |     |     |
| IET                             | UC  | IET  | UC  |
| General practitioner visits     | 2.5 ± 2.7 | 3.7 ± 4.8 | 4.9 ± 4.2 | 7.6 ± 8.9 |
| Specialist visits               | 3.9 ± 2.8 | 4.8 ± 2.8 | 7.2 ± 5.2 | 8.2 ± 4.7 |
| Physical therapist visits       | 14.5 ± 15.4† | 27.4 ± 15.1 | 25.1 ± 28.2† | 41.5 ± 25.6 |
| Other paramedical professional visits | 2.3 ± 6.7 | 1.3 ± 3.5 | 3.4 ± 8.5 | 3.3 ± 7.2 |
| Hospitalization, no. of days§   | 15.7 ± 13.9 | 21.3 ± 19.7 | 17.2 ± 14.1 | 27.9 ± 34.0 |
| No. of aids used                | 1.7 ± 1.6 | 2.5 ± 2.3 | 2.7 ± 2.6 | 3.2 ± 2.9 |
| Professional domestic care, hours | 46.1 ± 58.0 | 44.1 ± 74.4 | 79.7 ± 105.1 | 72.5 ± 122.1 |
| Paid domestic help, hours       | 15.5 ± 35.2 | 20 ± 34.9 | 33.9 ± 76.1 | 47.8 ± 82.5 |
| Informal care, hours            | 121 ± 189.3 | 209 ± 291.0 | 196 ± 281.9 | 233 ± 313.4 |

* Values are the mean ± SD number per patient per period.
† P < 0.01 for differences between groups (Mann-Whitney U test).
§ Hospitalization includes hospital (academic or general), rehabilitation center, and nursing home.

| Table 4. Mean total costs in euros per patient per year by cost category comparing patients in the intensive exercise therapy (IET) and usual care (UC) groups* |
|---------------------------------|-----|-----|-----|-----|
| **IET (n = 50)**                | UC  (n = 35) | Difference | 95% CI† |
| Medical costs                   |     |     |     |     |
| IET program‡                   | 2,991 ± 256 | NA | 2,991 |     |
| General practitioner            | 99 ± 84 | 153 ± 182 | −54 |     |
| Specialist                      | 426 ± 372 | 489 ± 354 | −63 |     |
| Paramedical treatments          | 623 ± 709 | 1,005 ± 648 | −382 |     |
| Alternative medicine            | 58 ± 239 | 66 ± 227 | −8 |     |
| Hospitalization§                | 9,363 ± 7,389 | 12,444 ± 9,927 | −3,081 |     |
| Aids used                       | 458 ± 885 | 554 ± 943 | −96 |     |
| Medication                      | 1,093 ± 2,171 | 1,271 ± 2,393 | −178 |     |
| Total medical costs             | 15,111 ± 8,462 | 15,983 ± 11,327 | −872 | −6,210, 2,930 |
| Direct nonmedical costs         |     |     |     |     |
| Travel costs                    | 133 ± 327 | 133 ± 191 | 0 |     |
| Indirect nonmedical costs       |     |     |     |     |
| Absenteeism                     | 350 ± 1,555 | 50 ± 294 | 300 |     |
| Domestic help                   | 2,447 ± 3,227 | 2,227 ± 3,749 | 220 |     |
| Formal care                     | 252 ± 565 | 322 ± 570 | −70 |     |
| Informal care                   | 1,568 ± 2,255 | 1,867 ± 2,507 | −299 |     |
| Total nonmedical costs          | 4,752 ± 3,882 | 4,599 ± 3,868 | 153 | −1,993, 1,620 |
| Total costs                     | 19,863 ± 10,147 | 20,581 ± 13,665 | −718 | −7,553, 3,660 |
| Total costs (excluding IET program) | 16,872 ± 10,209 | 20,581 ± 13,665 | −3,709 | −10,171, 1,120 |

* Values are the mean ± SD costs per patient in 2003 euros. 95% CI = 95% confidence interval; NA = not applicable.
† Double-sided bootstrapping.
‡ IET program = 3 weeks of intensive exercise training in a dedicated convalescent hotel.
§ Hospitalization includes hospital (academic or general), rehabilitation center, and nursing home.
This health-economic analysis demonstrates that after 1 year of followup, the IET program for patients with arthritis immediately after hospital discharge is the dominant strategy. It is associated with lower costs and better effectiveness expressed as VAS personal health–based QALYs gained compared with UC. After 6 months of followup, IET is associated with slightly higher costs but a better quality of life and improved gain in function compared with UC.

The 2 QALY measures used in this study led to different conclusions on the effectiveness of the intervention. This can be explained by the fact that conceptual differences exist in the measurement of utilities using the VAS and SF-6D because they are based on different elicitation methods. The VAS general health is a direct measure of utility representing the individual valuation of a single health state on a rating scale, whereas the SF-6D is a preference-based indirect utility measure in which the general public is the source of values, representing a summary score of 6 health states (19). The VAS is preferable to the SF-6D as a measure of patient-reported outcomes because the SF-6D uses preferences from the general public. In health-economic evaluation, however, the SF-6D is preferable as a standardized measure of QALYs representing the societal perspective. Both instruments have some disadvantages. Rating scales such as the VAS have been found to be subject to measurement bias (30) and should not be used alone in a study (31). The SF-6D, however, might not be sensitive to changes in the current study population. According to Stucki et al (32), the responsiveness of the SF-36 for patients undergoing total hip arthroplasty is rather moderate, because many items from the physical ability scale of the SF-36 reflect intermediate rather than extreme levels of difficulty. This floor effect was also demonstrated for the SF-6D: although the SF-6D has been shown to be a responsive measure in diseases of mild to moderate severity, it struggles to distinguish between states of severe health (33).

Although the MACTAR measures primary functional ability, it combines information on functional limitations with information on health-related quality of life. A key advantage of using the MACTAR is the ability to detect the impact of treatment on functional outcomes that are of most importance to the patient. A limitation of this instrument is that it is not widely used; little information on other patients is available for comparison (34). Therefore, the interpretation of the MACTAR results is rather difficult.

An improvement of 3 points on the MACTAR can be interpreted to represent 1 less functional problem (7). In the current study, patients in the IET group showed improved functional ability as measured with the MACTAR. The estimated score difference of 4.2 after 1 year in the DAPPER study can be interpreted to indicate that patients receiving IET had at least 1 less relevant individual activity problem after 1 year of followup, at €718 lower costs.

The DAPPER study demonstrates that IET reduces the mean total health care costs of patients with arthritis from a societal perspective in the first year after hospitalization. The main difference was caused by the costs of hospitalization. However, no statistically significant difference between groups was found in amount expressed as total days of hospitalization. Nevertheless, a trend showed that patients from the UC group stayed in the hospital longer immediately after study start as well as during followup because of (another) hospital admission. Essentially, high hospitalization costs in the UC group in the first months were caused by a small group of patients who were referred to a nursing home for a long period. During followup, differences in costs between groups were mainly caused by another small group of patients with extremely long periods of hospitalization. In other words, it is noteworthy that patients from the IET group did not need nursing home care and were able to return home. Moreover, these patients needed less hospitalization in the year of followup, which could be due to a higher level of physical fitness. Because the UC group initially had more patients with RA and less with OA compared with the IET group, one should consider selection bias. However, this is unlikely as all patients sent to a nursing home were diagnosed with OA.

Although not of great impact for the cost difference between groups, a significant difference in favor of the IET group was observed in the number of visits for physical therapy. Obviously, the IET program included physical therapy, which influenced the difference in the first 6 months of followup. Nevertheless, the number of visits to the physical therapist continued to be lower in the IET group during the entire year. A possible explanation might be the instant favorable recovery.

This is the first study that addresses the difference in total costs between usual care and an intensive convalescence treatment program in patients with arthritis who were hospitalized because of a flare in disease activity or for elective joint replacement. The results of the DAPPER study are of great interest because the population is aging and resources are limited. There are only a few studies on
cost-effectiveness of exercise in patients with arthritis (6–10). However, except for the study by Mitchell et al (8), patients scheduled for joint replacement surgery or patients with total knee or hip replacements were excluded in these studies. Moreover, the definition of exercise differed greatly among the studies. Most authors concluded that exercise therapy provided insufficient improvement in health to justify the additional costs (6–8). Only Richardson et al (10) found that group-based exercise is likely to be cost-effective compared with home-based exercise. However, this 8-week, twice-weekly, group-based program was only suitable for patients with knee OA.

This economic evaluation was conducted alongside a randomized clinical trial. Therefore, all resource use and health outcomes data were fully stochastic and were collected prospectively over the 1-year study period. This is an important strength of the current study because many economic evaluations use modeling techniques that are often based on indirect data and best guesses. Furthermore, the analysis was conducted from a societal perspective, which implies that all relevant costs (including the indirect costs) were taken into account.

There are some limitations to the current study. First, as described before, VAS personal health–based preferences are not preferable as a standardized measure of QALYs for use in societal-perspective economic evaluation; therefore, caution should be taken with the interpretation of the ICER. Furthermore, the number of patients lost to followup was quite high: only 75% of the eligible patients could be excluded in the analysis. Nevertheless, there were no significant differences in baseline characteristics between the evaluable and nonevaluable patients. Finally, when considering the human-capital method, there is a possibility of overestimating the true societal costs. However, because only 4 patients reported absenteeism from work, it probably had a limited effect on the results.

The results from this study demonstrate that IET therapy is designated for all patients with arthritis (with the emphasis on those with polyarticular arthritis symptoms) after hospital discharge. Implementation of IET therapy should include the combination of intensive exercise and group-based patient education in arthritis-dedicated facilities in the presence of experienced care givers.

In conclusion, IET after hospitalization for patients with arthritis due to a flare of disease activity or for elective joint replacement results in better quality of life at lower costs after 1 year compared with UC. This highlights the need for implementation of IET after hospital discharge in patients with arthritis.

**AUTHOR CONTRIBUTION**

Dr. Braakman-Jansen had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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**REFERENCES**


20. VanderZee KI, Sanderman R, Heyink JW, de Haes H. Psycho-metric qualities of the RAND 36-Item Health Survey 1.0: a


