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Clinical Pain Research

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A cost-utility analysis of multimodal pain rehabilitation in primary healthcare

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Abstract

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Objectives: Multimodal rehabilitation programs (MMRPs) have been shown to be both cost-effective and an effective method for managing chronic pain in specialist care. However, while the vast majority of patients are treated in primary healthcare, MMRPs are rarely practiced in these settings. Limited time and resources for everyday activities alongside the complexity of chronic pain makes the management of chronic pain challenging in primary healthcare and the focus is on unimodal treatment. In order to increase the use of MMRPs incentives such as cost savings and improved health status in the patient group are needed. The aim of this study was to evaluate the costeffectiveness of MMRPs for patients with chronic pain in primary healthcare in two Swedish regions. The aim of this study was to evaluate the cost-effectiveness of MMRPs at one-year follow-up in comparison with care as usual for patients with chronic pain in primary healthcare in two Swedish regions.

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Methods: A cost-utility analysis was performed alongside a prospective cohort study comparing the MMRP with the alternative of continuing with care as usual. The health-related quality of life (HRQoL), using EQ5D, and working situation of 234 participants were assessed at baseline and one-year follow-up. The primary outcome was cost per quality-adjusted life year (QALY) gained while the secondary outcome was sickness absence. An extrapolation of costs was performed based on previous long-term studies in order to evaluate the effects of the MMRP over a five-year time period.

Results: The mean (SD) EQ5D index, which measures HRQoL, increased significantly (p<0.001) from 0.34 (0.32) to 0.44 (0.32) at one-year follow-up. Sickness absence decreased by 15%. The cost-utility analysis showed a cost per QALY gained of 18 $704 \in$ at one-year follow-up.

Conclusions: The results indicate that the MMRP significantly improves the HRQoL of the participants and is a cost-effective treatment for patients with chronic pain in primary healthcare when a newly suggested cost-effectiveness threshold of 19 734 € is implemented. The extrapolation indicates that considerable cost savings in terms of reduced loss of production and gained QALYs may be generated if the effects of the MMRP are maintained beyond one-year follow-up. The study demonstrates potential benefits of MMRPs in primary healthcare for both the patient with chronic pain and the society as a whole. The cost-effectiveness of MMRPs in primary healthcare has scarcely been studied and further long-term studies are needed in these settings.

Keywords: chronic pain; cost-utility analysis; multimodal rehabilitation; primary healthcare; sickness absence.

Introduction

Chronic non-malignant pain, defined as a persistent or recurrent pain that lasts more than three months [1, 2], is a major public health challenge that causes both individual suffering and inflicts a heavy economic burden on society

[3–5]. A large survey of chronic pain in Europe showed that nearly 20% of adult Europeans suffer from moderate to severe chronic pain that affects their social and working lives considerably [5]. One out of three patients in Swedish primary healthcare seeks care due to pain and of these, almost 40% suffer from chronic pain [6]. Similarly, a crossnational study found that 22% of primary healthcare patients had chronic pain and that the odds of work disability are doubled for these patients compared with those not affected by chronic pain [7]. In Sweden, chronic pain is one of the most common reasons for long-term sickness absence [8] leading to considerable costs in terms of loss of production. Moreover, chronic pain is associated with increased healthcare consumption [4, 8-10]. In 2003, the Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) estimated that the costs for chronic pain of at least moderate intensity amounted to 87.5 billion SEK of which around 90% accounted for costs due to loss of production [8].

Multimodal rehabilitation is a team-based intervention with a biopsychosocial approach that has been developed to address the widespread impact of chronic pain on the physical, mental and social condition of the patient [11, 12]. Multimodal rehabilitation programs (MMRPs) have been shown to be more effective for reducing pain and disability than care as usual [8, 11, 13, 14]. MMRPs have also been shown to reduce sickness absence [15–17]. Systematic reviews have demonstrated the cost-effectiveness of MMRPs in specialist care [18, 19].

MMRPs have primarily been offered in specialist care for patients with complex chronic pain. The launch of the national rehabilitation warranty by the Swedish government in 2009 [20] made it possible for patients with less complex chronic pain to access MMRPs in primary healthcare settings with the help of economic compensation. The aim of the rehabilitation warranty was to reduce sickness absence and support return to work by offering access to evidence-based rehabilitation as an early intervention for persons suffering from chronic musculoskeletal pain. The effectiveness of MMRPs explicitly in primary healthcare has scarcely been studied. A few studies have shown that MMRPs for patients with chronic pain contributed to increased work capacity and decreased healthcare consumption [21–24]. One of them, a long-term study, also showed that MMRPs have positive effects on pain intensity, functional impairment and quality of life [21].

Limited time and resources alongside the complexity of pain conditions makes the assessment and management of chronic pain in primary healthcare challenging [25–27]. MMRPs have high initial costs in terms of time and

resources [11], which may be one of the reasons for the intervention being under-utilized in primary healthcare [27, 28]. Considering that the vast majority of patients with chronic pain are treated at primary healthcare level, there is a need for more research on the economic consequences of MMRPs in these settings [24, 26, 29, 30]. Hence, the aim of this study was to evaluate the cost-effectiveness of multimodal rehabilitation programs for patients with chronic pain compared with care as usual in primary healthcare.

Methods

Design

This was a prospective cohort study of patients attending MMRPs in primary healthcare in two Swedish regions. The observations were at baseline, after termination of the MMRP and after one year. In the study, we compared the effects of the MMRP with the alternative of continuing with care as usual. A cost-utility analysis was executed, the focus being on the health-economic effects of MMRPs. The study covered the MMRPs financed by the rehabilitation warranty between the years 2012 and 2015 when the primary healthcare centers received financial compensation for the MMRP.

Participants and setting

Participants attended the MMRPs between August 29 2012 and December 16 2015. In total, 11 primary healthcare centers participated, five in the northern part of Sweden and six in the southern part. The participants were consecutively assessed and referred to participate in the MMRP before participation in the program. The inclusion criteria were 1) disabling chronic pain that had lasted more than three months, 2) age between 18 and 65 years, 3) no further medical assessments needed, 4) sufficient knowledge of the Swedish language, 5) agreements not to participate in other parallel treatments. The exclusion criteria were 1) ongoing major somatic or psychiatric disease, 2) a history of significant substance abuse and 3) state of acute crisis.

General aims of the MMRP are to enhance the daily and emotional function and quality of life of the patient as well as to promote return to work [1]. The MMRPs included physical exercises and activities, relaxation, coping strategies and pain education. The program lasted over a period of 6–10 weeks with $1\frac{1}{2}-3\frac{1}{2}$ h/week during office hours. In most cases, the sessions were held at the local primary healthcare center of the patient, thus the majority of the patients were able to avoid long-distance travel. Most sessions were group interventions or a combination of group intervention and individual activity. The multi-professional MMRP teams differed between primary healthcare centers but always included a physiotherapist and an occupational therapist. At least one of them was trained in cognitive behavioral therapy, since that is a key element of the MMRP [31]. The team members were offered a two-day training course on team work, chronic pain and consequences related to living with this condition. There is an array of unimodal chronic pain treatments such as pharmaceutical, surgical, neuro-augmentative, somatic, behavioral,

rehabilitative, complementary and alternative treatment [8, 32, 33]. Nevertheless, MMRP with its biopsychosocial approach to the complexity of chronic pain has the strongest evidence and is therefore the first-line recommendation in Swedish healthcare [33].

Procedure and questionnaires

Data were gathered from participating primary healthcare centers using a comprehensive questionnaire with patient-reported outcome measures (PROM) combined with standardized instruments from the Swedish Quality Registry for Pain Rehabilitation (SQRP) (www.ucr.uu. se/nrs/) and a number of additional variables in order to adapt the questionnaire to primary healthcare settings. The instruments included were the numeric pain rating scale (NPRS) [34], the hospital anxiety and depression scale (HADS) [35], the functional rating index (FRI) [36], the chronic pain acceptance questionnaire (CPAQ) [37], the pain catastrophizing scale (PCS) [38], two variables from the life satisfaction questionnaire (LiSat-11) [39], the european quality of life instrument (EQ5D-3L) [40] and one item from the work ability index (WAI) [41]. The questionnaire was filled in by the patient before assessment, immediately after MMRP and one year later.

The outcome measures of the questionnaire were chosen in accordance with recommended core outcome domains by the initiative on methods, measurement, and pain assessment in clinical trials: IMMPACT recommendations [42]. At the end of 2015, the data from the primary healthcare centers were gathered into one common registry which in turn was connected to the SQRP. The SQRP has evaluated the effects of MMRPs at specialist clinics since 1998. The primary healthcare version was named the Swedish Quality Registry for Pain Rehabilitation for primary healthcare (SQRP-PC).

In the present study, data at baseline and one-year follow-up were evaluated with a focus on the EQ5D descriptive system and self-reported sickness absence according to the percentages used by the Swedish Social Insurance Agency (25, 50, 75 or 100%). The EQ5D is a generic preference-based instrument developed by the EuroQol group. It consists of two parts: a descriptive part which measures health-related quality of life (HRQoL) on five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and the EQ VAS, a visual analogue scale that generates a self-rating HRQoL. When the dimensions from the descriptive system are combined, a utility score or EQ5D index between 0 and 1 is generated (1=full health and 0=worst imaginable health state/death). The EQ5D index reflects the health status of the individual at the measured time point [40].

Outcome measures

The primary outcome measure was cost per gained quality-adjusted life year (QALY) measured using EQ5D. The secondary outcome measure was sickness absence at one-year follow-up compared with baseline.

Economic evaluation

Continuously rising healthcare expenditure and restricted budgets makes it more difficult to prioritize and make choices in healthcare [43]. Information about the cost-effectiveness of a treatment can support decision-makers in allocating limited healthcare resources fairly and to achieve maximum value [40, 44]. The purpose of an

economic evaluation is to compare two or more alternative courses of action considering both costs and consequences [44, 45]. According to Torrance [45], the comparative intervention can sometimes be whatever would have happened in the absence of the intervention being considered. In this study, the results of the patients who were enrolled for MMRP were compared with the baseline data for the same patient group, as if they would have continued receiving care as usual without participation in the MMRP. In so doing, we assumed that the average mean of the EQ5D index and working situation would remain unchanged without participation in the MMRP. Care as usual was standard medical treatment offered by the primary healthcare center, e.g. pharmacological treatment or unimodal treatment by physiotherapist or occupational therapist. The economic evaluation consisted of a cost-utility analysis (CUA) with cost per QALY gained as outcome [44]. The economic evaluation is described according to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement [46].

Cost data: The CUA was conducted from a partial societal perspective including costs for the intervention and costs in terms of loss of production due to sickness absence. The intervention costs were set as equal to the financial compensation that the primary healthcare centers received within the rehabilitation warranty, that was 25,000 SEK per patient treated.

The costs resulting from loss of production were evaluated by assuming that the contribution to overall production of an employee is equal to the cost of employing him or her, including wages plus additional costs incurred by the employer to employ the person, according to the human capital approach [44]. The average salary (all professional categories included) in Sweden 2012 was 29,800 SEK (in 2015, the average net salary was 32,000 SEK) and the general payroll tax 31.42% [47, 48]. The average yearly salary was 4,69,958 SEK (29,800*12*1.3142) and was interpreted as being equal to the annual cost of loss of production for a patient on full-time sickness absence. Other healthcare costs, other sector costs, and costs for the patient and families were not included because they were assumed not to differ between the two alternatives being compared. Drummond et al. [44] argue that costs common to the two options being compared can be excluded as they would not affect the choice between the two alternatives. Costs derived from sickness benefits were not included since they, from a societal perspective, are considered to be an income transfer from those who work to those who are on sick leave, thus they do not change the aggregated resources of the society [49]. Costs are presented in Swedish crowns (SEK) (1 SEK=0.09397 EUR [50]). No discounting of costs was made in the cost calculations since the follow-up was only one year.

Cost-utility: QALY is the most commonly used utility value in CUA [43]. The advantages with QALY as a measure of health gain are that it incorporates both reduced morbidity (quality gains) and reduced mortality (quantity gains) in one single measure. QALY also allows a comparison of economic evaluations across different healthcare areas and is widely used as a decision-making foundation for prioritizing scarce resources [44]. One QALY is defined as a year of full or "optimal" health. The QALY gain is the difference in utility score between two or more measurement points multiplied by the time (in years) spent in the particular health state. The results of the CUA are presented as the incremental cost-utility ratio (ICUR) which is the ratio of the incremental cost and the incremental QALY. The ICUR stands for

the additional cost per QALY gained associated with the new intervention in comparison with treatment as usual or alternative treatment [43].

Extrapolation of costs: The CUA presents a one-off benefit with the time horizon applied in the economic evaluation, which in this study was one year after treatment. The MMRP aim to make permanent changes in the patients' ability to both cope with and understand their pain and to enhance participation in work and social life. Taking this into consideration a period of one year may not be long enough to capture the major health and economic consequences of MMRP. One way to evaluate the effectiveness of an intervention over a longer time period is to extrapolate the effects by implementing results from previous long-term studies in the same field [21, 51, 52]. The extrapolation serves as a way of addressing the unavoidable uncertainty about expected costs and effects when assessing cost-effectiveness [44]. A discount rate of 3.5% was applied in the extrapolation in accordance with the recommendation of Drummond et al. that the rate should be between 3 and 5% [44].

Cost-effectiveness threshold: The cost-effectiveness threshold for one gained QALY was set at 2,10,000 SEK or 19,734 € which is a newly advocated estimation based on the work of Claxton et al. on behalf of The National Institute of Health and Care Excellence (NICE) [53, 54]. This cost-effectiveness threshold is based on a marginal productivity approach, where the threshold is a measure of the opportunity cost in terms of the health produced by the least cost-effective intervention that the new intervention will replace [53]. Thus, theoretically, in a healthcare system with a fixed budget, an intervention with a cost per QALY below the given threshold is favorable [43].

Statistical analysis

The data analysis was conducted according to the per protocol principle, accounting for those persons who filled out the questionnaire both at baseline and at one-year follow-up. The analyses were carried out with IBM SPSS version 24.0 (Chicago, IL) with the significance level set at p<0.05 (two-tailed) and 95% confidence intervals (CI). Data were first summarized and examined with the help of descriptive statistics. A comparison within groups was carried out at baseline and one-year follow-up using a parametric paired sample t-test. No imputation was used for missing values. Cohen's d effect size (ES) was calculated with the help of a psychometric webpage [55]. Absolute ES of 0.0-0.2 was interpreted as non-significant, 0.2-0.49 as small, 0.5-0.79 as medium, and ≥0.8 as large [56].

Results

In total, 503 patients were examined for participation (Figure 1). Of these, 31 patients did not fulfill the inclusion criteria and were thereby excluded from the study. Five patients declined to fill in the questionnaire and were not included. Another 39 patients did not complete the MMRP and 194 did not fill in the questionnaire at one-year followup, which left in total 234 patients for further analysis. The

Table 1: Baseline descriptive data of the participants in the multimodal rehabilitation program. Continuous variables are given as mean and standard deviation (SD) and categorical variables as numbers and percentages (%).

	All patients n=234	Women	Men
Sex		n=200	n=34
		(85.5)	(14.5)
Age, years	43.6 (10.8)	43.5 (10.7)	44.7
Country of origin			(11.7)
Sweden	206 (88.0)	177 (88.5)	29 (85.3)
Other country	28 (12.0)	23 (11.5)	5 (14.7)
Education	28 (12.0)	25 (11.5)	5 (14.7)
Compulsory school	40 (17.4)	33 (16.5)	7 (20.6)
Upper secondary school	141 (61.3)	119 (59.5)	22 (64.7)
University/College	45 (19.6)	40 (20.0)	5 (14.7)
Pain location variation	, ,	, ,	, ,
Constant	180 (76.9)	152 (77.9)	28 (90.3)
Varies	46 (19.7)	43 (22.1)	3 (9.7)
Pain duration, years	9.8 (9.1)	8.9 (9.6)	10.0 (9.0)
Pain intensity last week	6.5 (1.8)	6.5 (1.8)	6.7 (1.5)
Current pain intensity	6.0 (2.0)	6.0 (2.0)	6.0 (1.9)
Number of pain sites	14.6 (8.1)	15.2 (8.4)	11.3 (6.5)
Anxiety, HADS ^a ≥11	93 (40.3)	83 (41.9)	10 (30.3)
Depression, HADS ^a ≥11	42 (18.3)	38 (19.2)	4 (12.5)
Self-reported work ability	3.7 (2.7)	3.7 (2.9)	3.7 (2.7)
FRI ^b	57.8 (16.1)	57.3 (16.4)	60.8
110	37.0 (10.1)	37.3 (10.4)	(13.9)
CPAQ-AE ^c	29.0 (11.4)	29.2 (11.5)	28.1
CITIQITE	27.0 (11.4)	27.2 (11.3)	(10.8)
CPAQ-PW ^c	23.4 (8.8)	23.4 (8.8)	23.6 (9.3)
Pain catastrophizing	23.3 (10.7)	23.5 (10.9)	20.5
scale	25.5 (10.7)	23.3 (10.7)	(10.1)
LiSat-life ^d	3.63 (1.33)	3.63 (1.35)	3.62
	2102 (2122)	2112 (2122)	(1.23)
LiSat-vocationd	2.94 (1.50)	2.92 (1.48)	3.09
		_,, _ (_, ,_,	(1.64)
Health-related quality of life			(=== //
EQ5D index ^e	0.34 (0.32)	0.34 (0.32)	0.30
	(0.52)	(0.52)	(0.30)
EQ VAS ^e	46.1 (19.3)	46.4 (19.5)	44.4
.	(=2.3)	(=, .,)	(18.4)
			,

^aThe hospital anxiety and depression scale (HADS).

only significant differences in baseline characteristics between those who did and did not complete MMRP were that the patients who completed the program had a higher educational level and those who completed the one-year

The functional rating index (FRI).

^{&#}x27;The chronic pain acceptance questionnaire (CPAQ), activity engagement (AE), and pain willingness (PW).

The life satisfaction questionnaire (LiSat-11).

eThe European quality of life instrument contains the EQ5D descriptive system and a visual analogue scale.

follow-up scored two points lower on the pain catastrophizing scale.

Hence, 234 participants were included in the study. Table 1 illustrates the baseline characteristics of the study participants. The variation in pain duration was large: between 12 and 480 months (40 years). The median (interquartile range, IQR) pain duration was 72 months (six years). An examination of quartiles showed that less than 5% had a pain duration of more than 351 months (29.25 years) and 25% more than 180 months (15 years). Half of the participants had a pain duration under 75 months (6.25 years).

Sickness absence

A 15% reduction in sickness absence was seen at one-year follow-up (Table 2). Both the group of participants on parttime and on full-time sickness absence decreased with 17 and 12% respectively. Two of the participants had retired at follow-up (marked as missing in Table 2). The net reduction of sickness absence corresponded to 11.25 full-time employments, including sickness absence due to disability pension. The disability pension rate (full-time or part-time) was 8.6% at baseline and 11.2% at one-year follow-up (Table 3).

Loss of production

The annual cost of loss of production for a person on fulltime sickness absence was estimated to be 4,69,058 SEK (see Cost data in methods section). As demonstrated in Table 4 the costs resulting from loss of production was the heaviest cost item in the cost calculation for the different treatment options compared. Gains in terms of reduced loss of production attributable to return to work were estimated using a previous Swedish study on return to work after multi-professional rehabilitation by Kärrholm

Table 2: Patients on sickness absence (including disability pension).

Total n=234	Baseline (%)	One-year follow- up (%)	
No sickness absence	96 (41.0)	110 (47.0)	+14 (15)
Part-time sickness absence	59 (25.2)	49 (20.9)	-10 (17)
Full-time sickness absence	52 (22.2)	46 (19.7)	-6 (12)
Missing	27 (11.6)	29 (12.4)	NA

Table 3: Disability pension amongst the participants.

	Baseline (%)	One-year follow-up (%)	Difference
Full-time (100%)	4 (1.9)	6 (2.9)	+2
Part-time (75%)	1 (0.5)	1 (0.5)	0
Part-time (50%)	9 (4.3)	14 (6.8)	+5
Part-time (25%)	4 (1.9)	2 (1.0)	-2
Total	18 (8.6)	23 (11.2)	+5

et al. [57]. In the study, it was shown that the effect on return to work after rehabilitation occurred during the second six-month period after the end of the intervention, seen in a one-year follow-up [57]. Applying these results, we assumed that those who reported being full-time or part-time at work at one-year follow-up had returned to work nine months after baseline. In other words, the length of time back at work was three months during the follow-up period. It was not possible to determine at which point in time the return to work took place based on the data analyzed in this study.

Cost-utility analysis

There was a statistically significant increase in the mean (SD) EQ5D index (p<0.001) from 0.34 (0.32) to 0.44 (0.32). Similarly, the EQ VAS score increased significantly (Table 5).

The QALY gain was calculated using the area under the curve (AUC) method and the trapezium rule [43, 58]. The AUC in the present study consisted of the area T1 representing the time between baseline and after treatment and T2 corresponding to the time from after treatment to oneyear follow-up (Figure 2). For n + 1 measurements y_i at time

Table 4: Costs calculations for multimodal rehabilitation program (MMRP) and care as usual group for the first year after MMRP.

Costs (SEK) (n=234)	MMRP	Care as usual
Healthcare costs	Х	Х
Intervention costs	5 850 000 (25 000*234)	0
Social care costs	X	Χ
Informal costs	X	Χ
Productivity loss	[(81°*469 958*1)–(11.25*469	(81*469 958
the first year	958*(3/12)] 36 744 841	*1) 38 066 598
Total costs	42 594 841	38 066 598
Total mean cost per participant	182 029	162 678

^aThe total amount of sickness absence at baseline was equal to 81 fulltime employments.

Table 5: EQ5D^a and EQ VAS at baseline and one-year follow-up.

	Baseline (SD)	One-year follow-up (SD)	p- Value	ES
EQ5D index	0.34 (0.32)	0.44 (0.32)	<0.001	0.314
EQ VAS	46.1 (19.3)	53.1 (22.8)	<0.001	0.328

^aThe European Quality of Life instrument with five dimensions (EQ5D).

point t_i (after intervention and at one-year follow-up), the AUC is [58]:

$$AUC = \frac{1}{2} \sum_{i=0}^{n-1} (t_{i+0} - t_i) (y_i + y_{i+1}) \rightarrow AUC_{MMRP}$$
$$= 0.156 \times \frac{0.11}{2} + (1 - 0.156) \times \frac{0.1 + 0.11}{2}$$

The QALY gain was 0.097 QALYs per patient, which corresponds to about 1.2 months or 35 days of spared life time in perfect health for each patient or 22.75 QALYs gained for all the 234 participants. The incremental costs were 45.28.243 SEK and the incremental OALY gains 22.75 QALYs (Table 4). Hence, the ICUR at one-year follow-up was 45,28,243/22.75=1,99,044 SEK or 18,704 €.

Long-term costs and effects

To estimate future costs and effects of MMRPs, we extrapolated our results using results from previous long-term studies described below (Table 6). There were not enough studies to make an extrapolation based solely on studies originating from primary healthcare, hence specialist care was also included. The extrapolation comprised three studies on the long-term effects of MMRPs. In the study by Rivano-Fischer et al. [51], the effects on sick-leave after MMRPs were evaluated and a long-term reduction of sick leave was shown. In the study, the number of patients not on sick leave increased from baseline (34%) to one-year follow-up and continued to increase (63%) at two-year follow-up. In a study by Norrefalk et al. [52] where workrelated interdisciplinary rehabilitation was evaluated for long-term pain, findings showed that 49% of the 63% of patients who had returned to work at one-year follow-up were still working after three years. In a five-year follow-up on early MMRP for patients with musculoskeletal pain and disability by Westman et al. [21], the authors found that the group of patients that had gone from full-time sick leave to part-time or full-time work dropped from 81% at one-year to 58% at five-year follow-up. We could not find a study with a four-year follow-up. Therefore, we estimated an increase in sickness absence as a mean of the increased

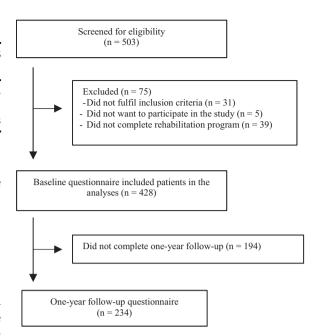


Figure 1: Flow-chart.

percentage at three-year and five-year follow-up. All percentages of decrease/increase were calculated in relation to one-year follow-up.

We could only find one study reporting long-term effects on HRQoL after an MMRP in primary healthcare. Westman et al. (2006) studied the quality of life after early multimodal rehabilitation for patients with musculoskeletal pain and disability and could see significant improvements at five-year follow-up [21]. If we apply these results and assume that the HRQoL of the participants persists at the level of one-year follow-up, an extrapolation with a five-year perspective would generate 121 QALYs gained for all 234 participants and an ICUR of 37,424 SEK or 3,517 €. If we, in turn, assumed that the HRQoL would decrease by half during a five-year period,

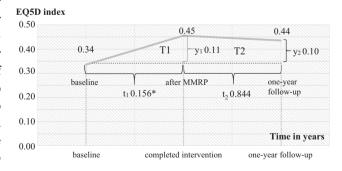


Figure 2: Calculations of quality-adjusted life year (QALY) gain using the trapezium rule. * The time point "after MMRP" is the average intervention duration of eightweeks (56 days or approximately 0.156 vears).

Table 6: An extrapolation of cost savings generated by MMRP in a long-term perspective.

Follow-up	Intervention cost	Cost savings (reduced productivity loss)		Total cumulative discounted value (discount rate 3.5%)
One-year	(234* 25 000) 5 850 000	[11.25*469 958* (3/12)] ^a 1 321 757	1 321 757	-4 528 243
Two-year	0	(14.51*469 958) ^b 6 820 266	8 142 023	2 139 628 (2 292 023/1.035²)
Three- year	0	(9.675*469 958) ^c 4 546 844	12 688 867	6 030 814 (6 686 472/1.035³)
Four-year	0	(9.225*469 958) ^d 4 335 363	17 024 230	9 033 524 (10 366 177/1.0354)
Five-year	0	(8.6625*469 958)° 4 071 011	21 095 241	11 033 667 (13 104 535/1.0355)

^a11.25 full-time employment gained, 4,69,958 SEK yearly salary, three months of return to work.

the ICUR would amount to 50,325 SEK or 4,729 €. The extrapolated ICURs are ½-1/5 of the ICUR at one-year follow-up which is explained by the high initial costs of MMRPs that burden the costs of year one and part of year two after MMRPs. Independently of which of these assumptions is implemented, MMRP must be considered cost-effective. The extrapolation of cost savings demonstrated that the total cumulative discounted value of the MMRPs amount to around one million euros after five years (Table 6).

Discussion

The aim of this study was to evaluate the cost-effectiveness of MMRPs in Swedish primary healthcare in the light of the heavy socio-economic burden inflicted by chronic pain. The cost-effectiveness was evaluated from a partial societal perspective. The CUA demonstrated an ICUR of 18,704 € at one-year follow-up which indicates that MMRPs within the rehabilitation warranty were cost-effective compared with care as usual when implementing a common costeffectiveness threshold of 19,734 € [53, 54]. The HRQoL of the participants increased significantly. The number of patients not on sickness absence increased by 15% and contributed to cost savings in terms of reduced loss of production. The results of our CUA were in line with the only CUA found in earlier research by Whitehurst et al. [22]. They showed that stratified primary healthcare management was cost-effective for low back pain patients at high risk of persistent disability compared with care as usual. In addition, the authors found that the intervention reduced work absence and improved quality of life. According to a study by Lang et al. [59], multidisciplinary rehabilitation for chronic low back pain in primary healthcare improved

HRQoL significantly compared with care as usual, which is also in line with our results. In addition, Lang et al., together with a number of studies on multidisciplinary rehabilitation for chronic pain patients in primary health-care settings, conclude that the intervention increases work capacity [21, 23, 24].

Two recently published papers concerning the effects of MMRP on pain-related sickness absence in Sweden and within the rehabilitation warranty presented differing results. Busch et al. [60] compared participants of MMRPs with matched controls and found that MMRPs were not effective in reducing sickness absence compared with care as usual. MMRP was, nevertheless, effective in reducing the risk of future disability pension. Rivano Fischer et al. [51] found that MMRPs had a favorable effect on sick leave patterns for the participants. There are a few notable differences between these two studies and our study. Busch et al. [60] included patients at two different time periods at both specialist and primary healthcare from the last quarter of 2009 until the end of 2010 and retrieved data from the Swedish Social Insurance Agency. Rivano Fischer et al. [51] included data from specialist care reported to the SQRP during 2007–2011 supplemented with sickness absence data from the Swedish Social Insurance Agency. Busch et al. [60] and Rivano Fischer et al. [51] included data on a national level. The present study was based on data gathered during the second half of 2012 to the end of 2015 and was restricted to primary healthcare in two Swedish regions. Our results are in agreement with the results of Rivano Fischer and al [51]. A shared feature was that the studies included more recent data than the study by Busch et al. [60]. The more positive results in terms of sickness absence may be related to the fact that the units offering MMRP within the rehabilitation warranty had gained more experience and had evolved associated

^bA 29 % (63-34%) decrease in sickness absence at two-year-follow-up; 11.25*1.29≈13.2 employments.

^{&#}x27;A 14% (63-49%) increase in sickness absence at three-year-follow-up; 11.25*0.86≈9.675 employments.

dA 18% ((13% + 23%)/2) increase in sickness absence at four-year-follow-up; 11.25*0.82≈9.225 employments.

A 23% (81-58%) increase in sickness absence at five-year-follow-up; 11.25*0.77≈8.6625 employments.

routines. Nevertheless, the phase of implementation of MMRPs was still ongoing in the two county councils when the data for the present study were gathered.

When healthcare policy makers decide how limited resources should be used in order to maximize health outcomes, the focus should, according to Drummond et al. [44], rather be on the predicted health benefits and costs offered by the intervention than on the traditional rules of statistical significance. Our study demonstrates that even small improvements in sickness absence contribute to large economic savings in the long term. In addition to these financial aspects, the observed increase in the HRQoL score indicated that MMRP also improve the health status of the patient. These gains are important, bearing in mind the severe clinical condition of the patients illustrated by Table 1 and that the patients constitute a selection of patients that have already tried various unimodal treatments with no manifest improvements in their condition. These findings are reinforced by a recent study [61] based on the same data as the present study from SQRP-PC as well as the yearly report from the SQRP-PC [62]. Both conclude that MMRPs in primary healthcare contribute to significant improvements in pain, function, daily activity and HRQoL.

Future directions

Little research has been done on the cost-effectiveness of MMRP in primary healthcare and problems of methodological heterogeneity make it difficult to draw conclusions from the results [30]. There is a need for consensus and standardization of the MMRPs and how the effectiveness of MMRP can be measured. This applies not only when it comes to the selection of participants, team set-up and program content but also regarding the design of the economic evaluation, the perspective, the time-horizon and how costs are valued [23, 30]. Another challenge is the implementation of MMRP in primary healthcare which will require considerable investments in both time and effort from an already tightly scheduled primary healthcare personnel [25, 31] in terms of reorganization and changing ways of working and thinking. To argue for such changes, it is necessary to demonstrate the health benefits and cost sayings of MMRP for the healthcare sector, the patient and society with a focus on long-term evaluations.

Strengths and limitations

Our study contributes new and valuable insights regarding research on MMRPs in primary healthcare. One of the strengths of this study is its execution in real-life clinical settings with regular primary healthcare staff. The study was carried out on a cross-national level, representing both the north and south parts of Sweden, which enhances the generalizability of the results. The costs and cost savings in the economic evaluation as well as the extrapolation were calculated from the lower bottom limit. There are other studies with more optimistic findings. For example, the study by Busch et al. published in 2011 [63] reports a tendency of decrease in sick leave of at least three years after inclusion in multidisciplinary chronic pain interventions. In the study, the improvements in all-cause sickness absence decline slowly but benefits still exist at 10-year follow-up, at which point sickness absence had not yet reached baseline levels. The calculations in the current study are presented with transparency in order to make it easy for the reader to understand and follow how the results were reached.

It is important to point out the methodological limitations of the study when drawing conclusions from the results. This was a prospective cohort study where detailed information about costs and intervention content could not be retrieved. The study design was adapted to these circumstances and we were unable to complete a CUA with competing alternatives, as is recommended in health economic literature. Therefore, we could not present the relative effectiveness of MMRPs and the CUA in itself cannot be used to support decision-making concerning resource allocation.

Randomized controlled studies (RCT) are often called for to minimize bias and strengthen the empirical evidence in an economic evaluation [64]. Our design and access to data did not allow us to perform an RCT which can be regarded as a limitation. Moreover, we have made several assumptions which imply that the results should be regarded with caution. We assumed that the average mean of the EQ5D measurements and working situation of the participants would remain unchanged without participation in the MMRP. In addition, the intervention costs were set as equal to the financial compensation to primary healthcare centers, which might be a reason for both under- and overestimation. The extrapolation relies on assumptions based on results from prior long-term studies and should also be regarded with care. The generalizability of the results is reduced due to the low response rate at follow-up. An explanation for this can be that the MMRP as an intervention was new for the primary healthcare centers and the professionals lacked experience of a structured follow-up of patients. The non-response analysis showed that the participants who did not fulfill the MMRPs had a lower educational level and scored two points lower on the

pain catastrophizing scale. We cannot rule out that the participants who experienced less satisfactory effects after MMRP did not feel motivated to answer the follow-up questionnaire.

Conclusions

In conclusion, our study shows that MMRP is a costeffective intervention for treating patients with chronic pain in primary healthcare. Considerable societal cost savings and improved health-related quality of life may be generated if the effects of the multimodal rehabilitation program are maintained beyond one-year follow-up. If the decrease in sickness absence continued for another 10 months after one-year follow-up, the intervention costs for all studied participants would be balanced by cost savings due to reduced loss of production. After that, the additional cost savings generated would be a pure economic gain for the society. Our results may serve as a platform for further discussion on the socioeconomic implications of MMRP in primary healthcare and as incentive for future and more profound research in these settings.

Data security and management

The authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. All personal data collected are stored in accordance with applicable regulatory requirements. Data are stored securely to maintain confidentiality. To preserve participant anonymity, only allocated trial numbers are recorded on trial documentation or computer software except for the consent form and contact details. Documents with identifiable information are stored separately to other study documents.

Data availability statement

The datasets generated and/or analyzed in this study are not publicly available as the Ethical Review Board has not approved the public availability of these data.

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interpretation, writing of the report, or the decision to submit for publication.

Author contributions: All authors listed qualify for authorship and have participated sufficiently in the work to take public responsibility for appropriate portions of the content. KE takes responsibility for the integrity of the work as a whole, from inception to published article. KE analyzed the data, BMS, GS, PE, BG, and KGS have contributed substantially to conception and design. All authors have contributed to the interpretation of data, revising it critically for important intellectual content and approval of the final version to be published.

Informed consent: Written informed consent was obtained from all individuals included in this study.

Ethical approval: The Research Ethics Committee at Umeå University has approved the present study (Dnr 2017-438-32M).

Conflict of interest: The authors have no known conflicts of interest to declare.

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