



VU Research Portal

Cost-effectiveness of physiotherapy, manual therapy and general practitioner care for neck pain: economic evaluation alongside a randomised controlled trial

Korthals-de Bos, I.B.C.; Hoving, J.L.; van Tulder, M.S.; Rutten-van Molken, M.P.M.H.; Ader, H.F.; de Vet, H.C.W.; Koes, B.W.; Vondeling, H.; Bouter, L.M.

published in

British Medical Journal
2003

document version

Publisher's PDF, also known as Version of record

[Link to publication in VU Research Portal](#)

citation for published version (APA)

Korthals-de Bos, I. B. C., Hoving, J. L., van Tulder, M. S., Rutten-van Molken, M. P. M. H., Ader, H. F., de Vet, H. C. W., Koes, B. W., Vondeling, H., & Bouter, L. M. (2003). Cost-effectiveness of physiotherapy, manual therapy and general practitioner care for neck pain: economic evaluation alongside a randomised controlled trial. *British Medical Journal*, 326, 911-916.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

E-mail address:

vuresearchportal.ub@vu.nl

Primary care

Cost effectiveness of physiotherapy, manual therapy, and general practitioner care for neck pain: economic evaluation alongside a randomised controlled trial

Ingeborg B C Korthals-de Bos, Jan L Hoving, Maurits W van Tulder, Maureen P M H Rutten-van Mólken, Herman J Adèr, Henrica C W de Vet, Bart W Koes, Hindrik Vondeling, Lex M Bouter

Abstract

Objective To evaluate the cost effectiveness of physiotherapy, manual therapy, and care by a general practitioner for patients with neck pain.

Design Economic evaluation alongside a randomised controlled trial.

Setting Primary care.

Participants 183 patients with neck pain for at least two weeks recruited by 42 general practitioners and randomly allocated to manual therapy (n=60, spinal mobilisation), physiotherapy (n=59, mainly exercise), or general practitioner care (n=64, counselling, education, and drugs).

Main outcome measures Clinical outcomes were perceived recovery, intensity of pain, functional disability, and quality of life. Direct and indirect costs were measured by means of cost diaries that were kept by patients for one year. Differences in mean costs between groups, cost effectiveness, and cost utility ratios were evaluated by applying non-parametric bootstrapping techniques.

Results The manual therapy group showed a faster improvement than the physiotherapy group and the general practitioner care group up to 26 weeks, but differences were negligible by follow up at 52 weeks. The total costs of manual therapy (€447; £273; \$402) were around one third of the costs of physiotherapy (€1297) and general practitioner care (€1379). These differences were significant: $P < 0.01$ for manual therapy versus physiotherapy and manual therapy versus general practitioner care and $P = 0.55$ for general practitioner care versus physiotherapy. The cost effectiveness ratios and the cost utility ratios showed that manual therapy was less costly and more effective than physiotherapy or general practitioner care.

Conclusions Manual therapy (spinal mobilisation) is more effective and less costly for treating neck pain than physiotherapy or care by a general practitioner.

Introduction

Neck pain is a common condition, affecting around a sixth of men and a quarter of women in the Netherlands.¹ Neck problems are not life threatening,

but they do cause pain and stiffness, often resulting in utilisation of healthcare resources, absenteeism from work, and disability.² The total costs of neck pain in the Netherlands are estimated at \$686m a year (£437m and €540m, according to 1996 costs). Therefore there is a need to determine the most cost effective intervention for neck pain.

Many conservative interventions are available for treating neck pain, including analgesics prescribed by general practitioners, physiotherapy, and manual therapy.^{3,4} Little information is available from randomised controlled trials on the effectiveness of these treatments.^{4,5} We performed an economic evaluation alongside a randomised controlled trial to evaluate the cost effectiveness of manual therapy, physiotherapy, and care by a general practitioner for patients with non-specific neck pain. An evaluation of the short term clinical effects has been reported elsewhere.⁶

Methods

Participants and randomisation

Forty two general practitioners recruited patients in 1997 and 1998.⁶ The general practitioners were randomly selected from a representative group of general practitioners. Inclusion criteria were neck pain for at least two weeks (confirmed during a physical examination at baseline), age 18-70, and willingness to comply with treatment and follow up measurements. Exclusion criteria were physiotherapy or manual therapy for neck pain in the previous six months, surgery of the neck, or a specific cause for the neck pain (for example, malignancy, fracture, inflammation). Eligible patients were enrolled who gave their written informed consent after physical examination and baseline assessment.

Our sample size was based on the ability to detect a clinically important difference of 25% in perceived recovery between groups. We estimated that 60 patients in each group would give a power of 80% and an α of 5%.

A blinded administrative assistant allocated patients to one of the three intervention groups using a computer generated random sequence table. Allocation, concealed in opaque sealed envelopes, was on the basis of block randomisation (block size 6), after

Institute for Research in Extramural Medicine, VU University Medical Centre, Van der Boechorstraat 7, 1081 BT Amsterdam, Netherlands
Ingeborg B C Korthals-de Bos
research fellow
Jan L Hoving
research fellow
Maurits W van Tulder
senior investigator
Herman J Adèr
biostatistician
Henrica C W de Vet
professor in clinimetrics
Hindrik Vondeling
senior investigator
Lex M Bouter
professor in epidemiology

Institute for Medical Technology Assessment, Erasmus University, Rotterdam, Netherlands
Maureen P M H Rutten-van Mólken
senior investigator
Department of General Practice, Erasmus Medical Centre, Rotterdam, Netherlands
Bart W Koes
professor of general practice research

Correspondence to: I B C Korthals-de Bos
ibc.korthals-de_bos@med.vu.nl
emgo@med.vu.nl

bmj.com 2003;326:911

prestratification for severity of symptoms (0-6 points low severity, 7-10 points high severity), age (<40 years, ≥40 years) and, for practical reasons, the research centre (4).

Interventions

Within the boundaries of the protocol, each method of treatment could be adapted to the patient's condition. Patients were allowed to perform home exercises and to continue with the drug they were taking at baseline or to take over the counter drugs during the intervention period of six weeks. Patient education was included in each intervention.

Manual therapy

Manual therapy consisted of a range of interventions, including hands-on techniques (muscular mobilisation, specific articular mobilisation, coordination or stabilisation). Spinal mobilisation was defined as low velocity passive movements within or at the limit of joint range of motion. Spinal manipulation (low amplitude, high velocity techniques) was not provided. Chiropractors, osteopaths, and physiotherapists use mobilisation and manipulation techniques. In our trial, manual therapy was applied by six registered manual therapists who had followed a 3 year curriculum in manual therapy after training in physiotherapy. Treatment sessions lasting 45 minutes were scheduled once a week, with a maximum of six sessions.

Physiotherapy

Physiotherapy was applied by five physiotherapists and consisted of individualised exercise therapy, including active and postural or relaxation exercises, stretching, and functional exercises. Additional massage and manual traction were optional, but specific manual mobilisation techniques (as applied in the manual therapy group) were discouraged. Treatment sessions lasting 30 minutes were scheduled twice a week, with a maximum of 12 sessions.

General practitioner care

General practitioner care (42 general practitioners) consisted of standardised care provided by a general practitioner. Follow up visits for 10 minutes, once a fortnight, were optional. Advice consisted of discussing the prognosis and factors that aggravated the condition, self care (heat application, home exercises), and ergonomic considerations. The patients were also encouraged to await spontaneous recovery. In addition, patients were given an educational booklet.⁷ If necessary, drugs such as paracetamol or non-steroidal anti-inflammatory drugs were prescribed on a time contingent basis.

Outcomes

Clinical outcomes were perceived recovery, intensity of pain, functional disability, and utility. Patients rated their perceived recovery on a six point scale ranging from "much worse" to "completely recovered" compared with baseline. This scale was used to estimate the percentage of patients with a successful outcome, which was defined as "much improved" or "completely recovered." Mean pain during the preceding week was indicated by the patient on an 11 point scale. Functional status was measured according to the neck disability index, a scale comprising 10 items for activi-

ties of daily life, with a 5 point score.⁸⁻¹⁰ Utility was measured with the EuroQol.¹¹ Effects of the primary outcome measures were expressed as differences within each intervention group between baseline and 52 weeks. Perceived recovery was rated as the percentage of patients with a successful outcome.

Outcome measures were assessed at baseline and at 3, 7, 13, and 52 weeks after randomisation. At 26 weeks' follow up, patients received a postal questionnaire instead of attending an appointment. They were asked not to reveal their treatment to the research assistants (experienced manual therapists and physiotherapists). After each assessment, the research assistant was asked to guess the allocated treatment and to state the reasons for his or her assumption.⁶

Costs were collected from a societal viewpoint. Patients completed cost diaries for 52 weeks.¹² Direct healthcare costs were: the costs of manual therapy, physiotherapy, or general practitioner care; additional visits to other healthcare providers; drugs; professional home care; and hospitalisation. Direct non-healthcare costs included out of pocket expenses, costs of paid and unpaid help, and travel expenses. Also included were indirect costs of loss of production owing to absenteeism from work or days of inactivity for patients with or without a paid job. Table 1 provides an overview of the costs.^{13 14} The costs of drugs were estimated on the basis of prices charged by the Royal Dutch Society for Pharmacy.¹⁵

We calculated indirect costs for paid work by using the friction cost approach (friction period 122 days) based on the mean income of the Dutch population according to age and sex.^{13 16} For unpaid work, such as housework, costs were estimated at a shadow price of €7.94 an hour.¹³

Analysis was performed according to the intention to treat principle. Bootstrapping was used for pair wise comparison of the mean costs between the groups. Confidence intervals for the mean differences in costs were obtained by bias corrected and accelerated bootstrapping (500 replications).¹⁷ The cost effectiveness

Table 1 Costs applied in economic evaluation of treatments for patients with neck pain

Costs	Cost (€)
Direct healthcare costs:	
General practitioner (≤20 min visit)*	16.60
Manual therapist (≤45 min visit)†	25.90
Physiotherapist (≤30 min visit)*	18.15
Outpatient appointment*	40.85
Hospitalisation (per day)*	235.95
Cesar or Mensendieck exercise therapist (per visit)*	17.70
Professional home care (per hour)*	22.70
Direct non-healthcare costs:	
Alternative therapist (per visit)‡	27.20
Home care (per hour)*	7.94
Help from partner or friends (per hour)*	7.94
Travel expenses (per km)*	0.11
Indirect costs:	
Absenteeism from paid work (per day)§	—
Absenteeism from unpaid work (per hour)*	7.94

€1.00=£0.60, \$0.90.

*Guideline price according to Dutch guidelines.¹³

†Tariff of Dutch Central Organisation for Health Care Charges.¹⁴

‡Price according to professional association.

§Indirect costs for paid work calculated on basis of mean income of Dutch population according to age and sex.¹³

and cost utility ratios were also calculated with bootstrapping (5000 replications) according to the bias corrected percentile method, by using the clinical outcomes.¹⁸ The bootstrapped cost-effect pairs were graphically represented on a cost effectiveness plane. Acceptability curves were calculated, which show the probability that a treatment is cost effective at a specific ceiling ratio.^{19 20}

Results

The 183 patients were randomised to manual therapy (60 patients), physiotherapy (59), and general practitioner care (64). Overall, 178 patients (97%) completed the follow up measurement at one year (fig 1). All data of patients who withdrew from the trial were included in the analysis until the time of withdrawal, after which we used the group mean to impute the missing data. Similarly, group means substituted occasional missing values. Complete cost data were available for 56 (93%) patients in the manual therapy group, 56 (95%) in the physiotherapy group, and 61 (95%) in the general practitioner care group. At baseline, minor differences in prognostic factors were found between the three groups (table 2). As confounding scarcely influenced the results, we present only the unadjusted differences between interventions.⁶

Effects of interventions

Manual therapy was the most effective treatment. Recovery rates after seven weeks in the manual therapy group, physiotherapy group, and general practitioner care group were 68%, 51%, and 36%, respectively.⁶ The number needed to treat was 3—that is, every third patient referred to manual therapy would make a complete recovery within seven weeks compared with patients referred to continued care by a general practitioner.⁶ This percentage remained stable in the manual therapy group during the follow up period, whereas both the physiotherapy group and general practitioner care group showed a slight increase in recovery rate over 52 weeks. Differences in recovery rates between groups were still statistically significant after 26 weeks but not at 52 weeks (table 3). Differences in pain intensity were small but statistically significant between the manual therapy group and the physiotherapy group at 52 weeks. The differences in disability scores at long term follow up remained small and were not statistically significant. Minor benign short term adverse reactions such as headache, pain and tingling in the upper extremities, and dizziness were reported more often for manual therapy and physiotherapy than for general practitioner care. Eleven patients (18%) who received manual therapy reported an increase in neck pain shortly after treatment.

Healthcare utilisation and absenteeism from work

Table 4 shows the utilisation of healthcare resources by the groups. The number of manual therapy and physiotherapy treatments was substantial in the general practitioner care group, and most of these sessions took place after the intervention period. During the follow up period of 52 weeks relatively more patients (41/64; 64%) in the general practitioner care group took prescription drugs than patients in the manual therapy group (22/60; 37%) or physiotherapy group (23/59; 39%). Overall, 37% of the patients in the manual

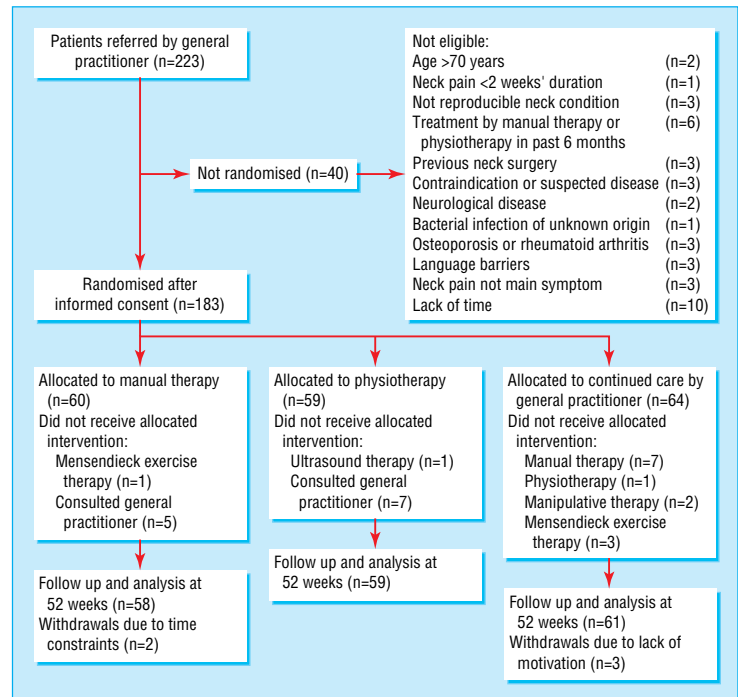


Fig 1 Progress of patients through trial

therapy group took over the counter drugs compared with almost 50% of patients in both the physiotherapy group and the general practitioner care group. Only nine patients reported the utilisation of other healthcare resources, such as radiography and professional home care (n=2). During the trial, only two patients were hospitalised for neck pain—one for additional neurological testing (physiotherapy group) and one for hernia of a cervical disc (general practitioner care group)—whereas six visited a chiropractor.

Only nine patients in the manual therapy group reported absenteeism from paid work owing to neck pain compared with 12 patients in the physiotherapy group and 15 patients in the general practitioner care group. Absenteeism from unpaid work was reported by 11 patients in the manual therapy group, 18 patients in the physiotherapy group, and 15 patients in the general practitioner care group.

Costs

Table 5 shows the mean (standard deviation) costs for each intervention. Direct healthcare costs in the manual therapy and physiotherapy groups consisted

Table 2 Baseline characteristics of patients allocated manual therapy, physiotherapy, or general practitioner care for neck pain. Values are numbers (percentages) of patients unless stated otherwise

Outcome measure	Manual therapy (n=60)	Physiotherapy (n=59)	General practitioner care (n=64)
Mean (SD) age (years)	44.6 (12.4)	45.9 (11.9)	45.9 (10.5)
Female	34 (57)	41 (70)	36 (56)
In paid work	47 (78)	42 (71)	46 (72)
Duration of neck pain:			
2-6 weeks	29 (48)	27 (46)	32 (50)
7-12 weeks	13 (22)	15 (25)	20 (31)
≥13 weeks	18 (30)	17 (29)	12 (19)
Previous neck pain	38 (63)	35 (59)	46 (72)
Previous treatment for neck pain	42 (70)	34 (58)	43 (67)

Table 3 Improvement in primary outcome measures after 52 weeks

Outcome measure	Mean (SD) effects			Difference (95% CI)		
	Manual therapy	Physiotherapy	General practitioner care	Manual therapy v physiotherapy	Manual therapy v general practitioner care	Physiotherapy v general practitioner care
Perceived recovery	71.7 (43)	62.7 (37)	56.3 (36)	9.0 (-7.9 to 25.8)	15.4 (-1.3 to 32.1)	6.5 (-10.9 to 23.8)
Pain intensity*	4.2 (2.4)	3.1 (2.9)	4.1 (2.9)	1.2 (0.1 to 2.1)	0.1 (-0.8 to 1.1)	-1.0 (-2.0 to 0.002)
Functional disability*	7.2 (7.5)	6.3 (8.0)	8.5 (7.4)	0.9 (-1.9 to 3.6)	-1.4 (-4.1 to 1.3)	-2.2 (-5.0 to 0.5)
Utility	0.82 (0.13)	0.79 (0.14)	0.77 (0.16)	0.03 (-0.04 to 0.09)	0.05 (-0.01 to 0.11)	0.02 (-0.04 to 0.09)

*Differences in mean effects within each intervention between baseline and 52 weeks.

mainly of the costs of the intervention treatment. The general practitioner care group showed an increase in utilisation of manual therapy, physiotherapy, and drugs after the intervention period. The total costs in the manual therapy group were around one third of the costs in the physiotherapy and general practitioner care groups. Total direct, indirect, and total costs were statistically significantly lower in the manual therapy group than in the physiotherapy and general practitioner care groups (table 5).

Cost effectiveness and cost utility analyses

Table 6 presents the cost effectiveness and cost utility ratios of all three comparisons. Figure 2 shows the cost effectiveness plane for pain intensity when comparing manual therapy and physiotherapy groups. The graph represents 5000 bootstrap replications of the cost effectiveness ratio for pain intensity comparing manual therapy with physiotherapy. Most cost-effect pairs

(98%) are located in the bottom right quadrant suggesting that manual therapy is dominant over physiotherapy—that is, manual therapy is associated with a larger improvement in pain and lower costs. The cost effectiveness planes showed similar dominance of manual therapy over physiotherapy on recovery and quality of life (with most bootstrapped ratios in the bottom right quadrant, 85% and 87%, respectively).

Also, a similar dominance was shown for the cost effectiveness planes for manual therapy over general practitioner care on perceived recovery and quality of life (96% and 97%, respectively, of bootstrapped ratios in the bottom right quadrant; fig 3). The cost effectiveness planes for pain intensity and functional disability showed similar percentages of ratios in the bottom two quadrants, which confirms that there was no difference in these outcome measures between manual therapy and general practitioner care but lower costs for manual therapy.

We found no statistically significant differences in costs and effects between physiotherapy and general practitioner care, and the cost effectiveness planes for this comparison confirmed this finding. The acceptability curve for pain intensity comparing manual therapy with physiotherapy showed that at a ceiling ratio of zero there was still a 98% probability that manual therapy was cost effective.

Sensitivity analysis

Only two patients (physiotherapy and general practitioner care groups) were admitted to hospital. These patients were excluded in a sensitivity analysis (data not shown). In this analysis the mean costs in both therapy

Table 4 Utilisation of healthcare resources and absenteeism from work for intervention group during follow up of 52 weeks. Values are means (standard deviations)

Type of utilisation	Manual therapy (n=60)	Physiotherapy (n=59)	General practitioner care (n=64)
General practice (No of visits)*	0.5 (1.3)	0.7 (1.3)	3.0 (1.6)
Manual therapy (No of sessions)*	7.3 (4.4)	1.5 (3.0)	7.2 (9.2)
Physiotherapy (No of sessions)*	1.2 (3.3)	14.7 (11.1)	3.0 (6.3)
Medical specialist care (No of outpatient visits)	0.2 (0.7)	0.7 (2.3)	0.4 (1.1)
Professional home care (hours)	0 (0)	0.3 (2.1)	0.1 (1.1)
Help from partner or friends (hours)	3.2 (9.1)	14.0 (63.6)	6.4 (23.8)
Absenteeism from paid work (days)	1.3 (4.1)	7.5 (31.4)	10.4 (30.1)
Absenteeism from unpaid work (hours)	5.4 (14.9)	23.8 (85.1)	15.7 (51.3)

*Includes standard number of visits conforming with protocol.

Table 5 Mean (standard deviation) total costs (€) and differences in mean total costs (95% confidence intervals)* during follow up of 52 weeks for three interventions for neck pain

Costs	Mean (SD) total costs			Difference in mean (95% CI) total costs		
	Manual therapy (n=60)	Physiotherapy (n=59)	General practitioner care (n=64)	Manual therapy v general practitioner care	Manual therapy v physiotherapy	Physiotherapy v general practitioner care
Direct healthcare costs	222 (141)	390 (353)	316 (473)	-94 (-342 to -9)	-168 (-264 to -84)	74 (-83 to 196)
Direct non-healthcare costs	50 (139)	127 (509)	74 (213)	-24 (-95 to 34)	-77 (-315 to 7)	53 (-41 to 262)
Total direct costs	271 (222)	517 (677)	390 (544)	-119 (-290 to -4)	-246 (-498 to -115)	127 (-79 to 352)
Indirect costs	177 (447)	780 (2999)	989 (2788)	-812 (-1998 to -280)	-603 (-2076 to -116)	-209 (-921 to 1245)
Total costs	447 (525)	1297 (3475)	1379 (3104)	-932 (-1932 to -283)	-850 (-2258 to -239)	-82 (-1063 to 1446)

€1.00=£0.60, \$0.90.

*95% confidence interval obtained by bias corrected and accelerated bootstrapping.

Table 6 Cost effectiveness and cost utility ratios (€) for perceived recovery, pain intensity, functional disability, and utility for neck pain

Outcome measure	Manual therapy: general practitioner care	Manual therapy: physiotherapy	Physiotherapy: general practitioner care
Perceived recovery (%)	Manual therapy -6041	Manual therapy -9488	Physiotherapy -1265
Pain intensity* (0-10 scale)	Manual therapy -6652	Manual therapy -757	General practitioner care 83
Functional disability* (neck disability index; 0-50)	General practitioner care 682†	Manual therapy -967	General practitioner care 36
Utility* (EuroQol; 0-1)	Manual therapy -15 505	Manual therapy -31 144	Physiotherapy 2688

€1.00=£0.60, \$0.90.

*Higher scores indicate more favourable outcome.

†Costs €682 to get improvement of one point in pain intensity.

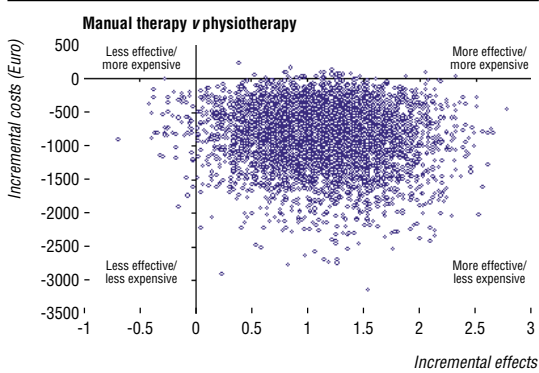


Fig 2 Cost effectiveness plane for pain intensity after manual therapy or physiotherapy for neck pain

groups decreased, but this had no impact on the statistical significance of differences between groups.

Discussion

Manual therapy for the treatment of neck pain was more cost effective than physiotherapy or care by a general practitioner. Manual therapy had significantly lower costs and slightly better effects at 52 weeks compared with physiotherapy and general practitioner care. The clinical outcome measures showed that manual therapy resulted in faster recovery than physiotherapy and general practitioner care up to 26 weeks.⁶

The direct healthcare costs were, as expected, highest during the intervention period. The number of patients in the general practitioner care group who visited a manual therapist was high. A recent study showed that general practitioners in the Netherlands refer most patients with neck pain to physiotherapists instead of manual therapists.² A possible explanation for the high referral rate to manual therapy may be that patients and general practitioners who participated in this study were better informed about the possibility of manual therapy as an alternative to physiotherapy.

Systematic reviews of trials on conservative treatments for acute, subacute, and chronic neck pain provide little evidence of one treatment being more effective than another.^{4 21 22} Some evidence has shown that staying active is beneficial and that active exercises

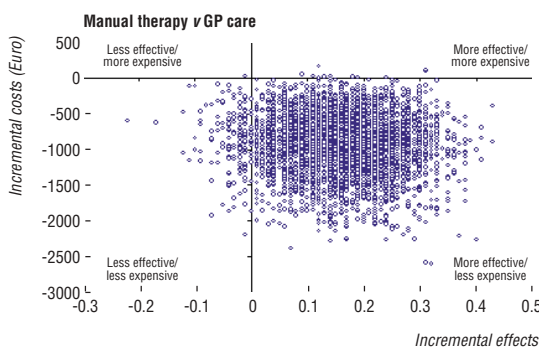


Fig 3 Cost effectiveness plane for perceived recovery after manual therapy or care by a general practitioner for neck pain

What is already known on this topic

The cost of treating neck pain is considerable

Many conservative interventions are available, such as prescription drugs, yet their cost effectiveness has not been evaluated

No randomised trials of conservative treatment for neck pain have so far included an economic evaluation

What this study adds

Manual therapy is more effective and less costly than physiotherapy or care by a general practitioner for treating neck pain

Patients undergoing manual therapy recovered more quickly than those undergoing the other interventions

are more effective than passive modalities such as massage, heat, and traction.²¹ Trials on neck pain vary in methodological quality, study populations, interventions, reference treatments, and outcome measures, leading the reviewers to conclude that no one type of treatment can be favoured over another.²²

None of the randomised trials evaluating conservative treatment for neck pain published so far included an economic evaluation. One study, comparing chiropractic and physiotherapy for patients with low back pain and neck pain, included a cost measurement but did not conduct a full economic evaluation.⁵ Our economic evaluation alongside a pragmatic randomised controlled trial showed manual therapy to be more cost effective than physiotherapy and continued care provided by a general practitioner in the treatment of non-specific neck pain.

Contributors: IBCK-deB, JLH, MWvanT, MPMH R-vanM, HJA, HCWdeV, BWK, HV, and LMB conceived and designed the study and critically revised the manuscript. IBCK-deB, MWvanT, MPMHR-vanM, and HJA analysed and interpreted the data. IBCK-deB and MWvanT drafted the manuscript. JLH was responsible for provision of the study materials or patients. IBCK-deB and HJA provided statistical help. BWK and LMB obtained funding. JLH and HCWdeV provided administrative, technical, or logistic support. IBCKdeB and JLH collected and assembled the data. All authors will act as guarantor for the paper.

Funding: Netherlands Organization for Scientific Research (904-66-068) and the Health Insurance Council's fund for investigative medicine (OG95-008).

Competing interests: None declared.

Ethical approval: The medical ethics committee of the VU University Medical Centre approved the study protocol.

- 1 Picavet HS, van Gils HW, Schouten JS. *Klachten van het bewegingsapparaat in de Nederlandse bevolking: prevalenties, consequenties en risicogroepen*. [Musculoskeletal complaints in the Dutch population: prevalence, consequences and people at risk.] RIVM report No 266807 002. Netherlands; National Institute of Public Health and the Environment, 2000. (In Dutch.)
- 2 Borghouts JA, Koes BW, Vondeling H, Bouter LM. Cost-of-illness of neck pain in the Netherlands in 1996. *Pain* 1999;80:629-36.
- 3 Borghouts JA. *Neck pain in general practice; prognosis, management and costs*. Wageningen: Ponsen and Looijen, 2000. (Thesis.)
- 4 Gross AR, Aker PD, Goldsmith CH, Peloso P. Conservative management of mechanical neck disorders. A systematic overview and meta-analysis. *Online J Curr Clin Trials* Document No 200-1, 1996.
- 5 Skargren EI, Carlsson PG, Oberg BE. One-year follow-up comparison of the cost and effectiveness of chiropractic and physiotherapy as primary management for back pain. *Spine* 1998;17:1875-84.

- 6 Hoving JL, Koes BW, De Vet HC, Assendelft WJ, Van der Windt DA, Van Mameren H, et al. Manual therapy, physical therapy or continued care by the general practitioner for patients with neck pain: short-term results from a pragmatic randomized trial. *Ann Intern Med* 2002;136:713-22.
- 7 Lanser K. *Nekklachten voorkomen, wat doe ik er zelf aan*, [The neck school: prevention of neck pain, what can I do about it myself.] 3 ed. Hardinxveld-Giessendam, Netherlands: Lanser, 1994. (In Dutch.)
- 8 Hains F, Waalen J, Mior S. Psychometric properties of the neck disability index. *J Manipulative Physiol Ther* 1998;21:75-80.
- 9 Stratford PW, Riddle DL, Binkley JM, Spadoni G, Wetsaway MD, Padfield B. Using the neck disability index to make decisions concerning individual patients. *Physiother Can* 1999;51:107-12.
- 10 Vernon H, Mior S. The neck disability index: a study of reliability and validity. *J Manipulative Physiol Ther* 1991;14:409-15.
- 11 Dolan P. Modelling valuations for EuroQol health states. *Med Care* 1997;35:1095-108.
- 12 Goossens ME, Rutten-van Mölken MP, Vlaeyen JW, van der Linden SM. The cost diary: a method to measure direct and indirect costs in cost-effectiveness research. *J Clin Epidemiol* 2000;53:688-95.
- 13 Oostenbrink JB, Koopmanschap MA, Rutten FF. *Handleiding voor kostenonderzoek, methoden en richtlijnrijzen voor economische evaluaties in de gezondheidszorg*. [Handbook for cost studies, methods and guidelines for economic evaluation in health care.] Hague, Netherlands: Health Care Insurance Council, 2000. (In Dutch.)
- 14 Dutch Central Organisation for Health Care Charges. *Tarieven voor medisch specialist, exclusief psychiaters. Bijlage bij tariefbeschikking nummer 5600-1900-97*. [Tariffs for medical specialist, excluding psychiatrists. Supplement to tariffs decision No 5600-1900-97-1 from 21 Oct 1996.] Utrecht: CTG, 1996. (In Dutch.)
- 15 *Taxe report*. Hague, Netherlands: Z-index, 2000. (In Dutch.)
- 16 Koopmanschap MA, Rutten FF. A practical guide for calculating indirect costs of disease. *Pharmacoeconomics* 1996;10:460-6.
- 17 Efron B, Tibshirani RJ. *An introduction to the bootstrap*. New York: Chapman and Hall, 1993.
- 18 Chaudhary MA, Stearns SC. Estimating confidence intervals for cost-effectiveness ratios: an example from a randomised trial. *Stat Med* 1996;15:1447-58.
- 19 Van Hout BA, Al MJ, Gordon GS, Rutten FF. Cost, effects and c/e ratios alongside a clinical trial. *Health Econ* 1994;3:309-19.
- 20 Stinnett AA, Mullahy J. Net health benefits: a new framework for the analysis of uncertainty in cost-effectiveness analysis. *Med Decis Making* 1998;18 suppl:68-80S.
- 21 Harms-Ringdahl K, Nachemson A. Acute and subacute neck pain: nonsurgical treatment. In: Nachemson AL, Jonsson E, eds. *Neck and back pain: the scientific evidence of causes, diagnosis and treatment*. Philadelphia: Lippincott, Williams and Wilkins, 2000:327-38.
- 22 Van Tulder MW, Goossens ME, Hoving JL. Nonsurgical treatment of chronic neck pain. In: Nachemson AL, Jonsson E, eds. *Neck and back pain: the scientific evidence of causes, diagnosis and treatment*. Philadelphia: Lippincott, Williams and Wilkins, 2000:339-54.

(Accepted 26 February 2003)

Commentary: Bootstrapping simplifies appreciation of statistical inferences

Marcus Müllerner

Universitätsklinik
für Notfallmedizin,
Allgemeines
Krankenhaus Wien,
Währinger Gürtel
18-20/6D, A-1090
Vienna, Austria
Marcus Müllerner
clinical epidemiologist
marcus.muellner@
univie.ac.at

Many conventional statistical methods of analysis make assumptions about normality, including correlation, regression, *t* tests, and analysis of variance. When these assumptions are violated, such methods may fail. Costs are often severely non-normal in distribution because there are always a few patients who use a lot of resources. Korthals-de Bos et al used bootstrapped estimates of costs and effectiveness to construct a convincing graph: compared with physiotherapy, manual therapy is most likely more effective and cheaper. A scenario where manual therapy is less effective while being more expensive is unlikely.

The process of bootstrapping seems simple: after completion of the study, patients, or any other units, are randomly drawn from the study population, usually as many as there are participating in the study. Sampling is performed with replacement. This means that each patient can be drawn once, more than once, or not at all until the required number of patients is reached. From this sample the main effect, such as costs, is calculated. Sampling with replacement is then repeated, and a new effect is calculated. This is done several hundred or even several thousand times. The resulting sample of effects then may be used to calculate the confidence interval.¹ Fifty to 200 repetitions are usually enough for such an estimate of the confidence interval. Alternatively, confidence inter-

vals may be extracted almost directly from the simulated data. In this case, several thousand repetitions may be necessary. Even though this method is a form of simulation, it is based on the observed data.

The process can be simplified as follows. A study has two arms of 60 patients each. One patient is randomly selected out of the 120, and treatment allocation, costs, and effects—say costs and effects for this example—are recorded. The patient is then returned to the study population (replaced), and another patient is selected from the sample of 120. This continues until 120 samples are collected. Theoretically any patient can be drawn not at all or even several times. This is repeated 5000 times. The summary estimates for costs and effects for each repetition then can be represented graphically.

Bootstrap methods are not necessarily better than conventional methods, but they do allow a direct appreciation of probabilistic phenomena. Bootstrapping is intended to simplify the calculation of statistical inferences even in situations much more complicated than the present study; sometimes situations where no analytical answer can be obtained at all.

1 Gardner MJ, Altman DG, eds. *Statistics with confidence*. London: BMJ, 1989.