APPENDIX A

Request Form for Board of Trustee Consideration of a Change to SHP Benefits

This form is to be used by individuals or groups that would like to propose new benefits coverage or request changes to benefits already covered by the State Health Plan. Please read the Procedure – Requests for Benefits Changes, SHP-PRO-7001-SHPfor more information regarding these types of requests.

Please submit completed forms by email to SHP.Board@nctreasurer.com or mail to NCState Health Plan Board of Trustees, 4901 Glenwood Avenue, Suite 300, Raleigh, NC 27612-3638.

Name of Requestor: **North Carolina Association of Acupuncture and Oriental Medicine**

Contact Information (*phone, email, mailing address):*

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Requested Change in Benefits Coverage:
The inclusion of acupuncture as a covered benefit for state employees.

Reason for Request: **Scientific studies have shown that acupuncture is effective for a variety of ailments, from treating osteoarthritis and nausea to pain relief and addiction at a cost reduction in comparison to other treatment plans. State employees have requested the inclusion of acupuncture.**

Proposed Effective Date of Change: **January 1, 2016**

Supporting Documentation (*Please provide documents to support your request; examples include research or studies regarding medical services, treatment or procedures, fiscal impact analyses if available, or petitions from members.*):
In addition to Appendix A, we are providing the Board of Trustees with two studies illustrating outcome and cost effectiveness.

Would you like to speak with the Board of Trustees about this issue at a Board of Trustees meeting? **We respectfully request the opportunity to present before the Board of Trustees, a presentation highlighting the research and fiscal analysis to support the addition of acupuncture into the state health plan.**

The Board of Trustees reviews select requests annually at a regularly scheduled Board of Trustee meeting. For calendar year 2013, requests will be reviewed at the November meeting. For calendar year 2014, requests will be reviewed at the July meeting. Review of requests in no way obligates the State Treasurer to make changes to benefits.

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Comparison of Health Care Expenditures Among Insured Users and Nonusers of Complementary and Alternative Medicine in Washington State: A Cost Minimization Analysis

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Abstract

Objectives: The purpose of this analysis was to compare health care expenditures between insured patients with back pain, fibromyalgia syndrome, or menopause symptoms who used complementary and alternative medical (CAM) providers for some of their care to a matched group of patients who did not use any CAM care. Insurance coverage was equivalent for both conventional and CAM providers.
Design: Insurance claims data for 2000–2003 from Washington State, which mandates coverage of CAM providers, were analyzed. CAM-using patients were matched to CAM-nonusing patients based on age group, gender, index medical condition, overall disease burden, and prior-year expenditures.
Results: Both unadjusted tests and linear regression models indicated that CAM users had lower average expenditures than nonusers. (Unadjusted: \$3,797 versus \$4,153, $p = 0.0001$; β from linear regression -\$367 for CAM users.) CAM users had higher outpatient expenditures that which were offset by lower inpatient and imaging expenditures. The largest difference was seen in the patients with the heaviest disease burdens among whom CAM users averaged \$1,420 less than nonusers, $p < 0.0001$, which more than offset slightly higher average expenditures of \$158 among CAM users with lower disease burdens.
Conclusions: This analysis indicates that among insured patients with back pain, fibromyalgia, and menopause symptoms, after minimizing selection bias by matching patients who use CAM providers to those who do not, those who use CAM will have lower insurance expenditures than those who do not use CAM.

Introduction

THE USE OF COMPLEMENTARY AND ALTERNATIVE medicine (CAM) has grown in recent decades,[1,2] and as a result insurance coverage for various types of CAM providers has become more prevalent.[1,3–5] But due to concern over ever-increasing health care costs, increasing emphasis is being given to cost-effectiveness of care. Patients desire choices in sources of health care, but if CAM providers are to be added to insurance coverage, their care must be cost effective.

One researcher noted that CAM therapies may be good candidates not only for cost-effective care but even cost savings, because "they avoid high technology, offer inexpensive remedies, and harness the power of *vis medicatrix naturae* (the body's natural ability to heal itself)"[6]. However, several difficulties have hindered the assessment of CAM's cost effectiveness. One of the biggest challenges in evaluating the effect of CAM use on health care costs is the selection bias inherent in patients' self-selection into CAM using and non-CAM using groups.[7] Researchers have consistently reported that CAM users have poorer health status, more visits to conventional providers, and/or higher rates of hospitalization than nonusers.[8–14] Thus, it has been difficult to find or create comparable groups of CAM users and nonusers for which costs can be compared.

In the early 1990s, a Swiss group conducted a randomized clinical trial offering free insurance coverage of CAM providers to half of a group of insured individuals. They

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reported that covering CAM care did not lead to an increase in costs for the insurance company because CAM utilization comprised only a tiny percentage of overall expenditures.[15] Given the increase in CAM use since the early 1990s in the United States,[12] the cost of CAM coverage today might be larger than that found in the Swiss study. However, data from Washington State, which mandates private insurance coverage of all licensed CAM providers,[16] found a similar tiny percentage of expenditures devoted to CAM care based on data from 2002.[17] The Washington State data reflect self-selection of patients into CAM-using and nonusing groups and thus may reflect a more "real-world" experience for insurance companies than the Swiss randomized study.

Another difficulty in performing economic analyses of CAM use occurs because many CAM providers are not covered by insurance, and patients pay for their services out of pocket. As a result, data on CAM utilization and expenditures are not available in administrative databases and must be collected through primary data collection,[6] which may be subject to recall bias and response bias. Washington State provides a unique environment in which to perform an economic analysis of CAM use because of the state-mandated insurance coverage referenced above. As a result, administrative claims data from Washington State include data on CAM utilization and expenditure that are consistent with data for conventional care.

A final difficulty in performing a cost–benefit evaluation of CAM involves measuring outcomes of care. Data on outcomes of care are not available in the administrative claims databases often used to provide data on expenditures. With CAM care, a further difficulty lies in how to quantify what Hollinghurst refers to as "the wider benefits of CAM," some of which may appear over long periods of time or be based more on a patient's sense of well-being than a measurable clinical outcome.[7,18] To avoid these problems in measuring outcomes, this analysis takes a cost-minimization approach,[6] analyzing which of two approaches to care is associated with lower overall expenditures, assuming comparable health outcomes between the two approaches.

The purpose of this article is to compare insurance expenditures for matched groups of CAM users and nonusers with selected health conditions, to evaluate whether use of CAM for some care is associated with higher or lower overall health care expenditures.

Materials and Methods

Population

This research was approved by the institutional review boards of the University of Washington and Boise State University. The study sample was constructed using 2000–2003 enrollment and claims data from two large insurance companies in Washington State that offer a variety of product types. The analysis was restricted to insured individuals covered by the law requiring coverage of CAM providers, which excluded enrollees funded through Medicare, Medicaid, or other state or federal programs. The data acquisition process, data cleaning, and the creation of analytic variables have been previously described.[19] The analyses presented here were limited to adults aged 18–64 who had at least 2 continuous years of coverage and at least one visit that contained a diagnosis for one of the index conditions defined below.

Index conditions. Three health conditions were chosen for study: back pain, fibromyalgia syndrome (FMS), and menopause symptoms. These index conditions were selected because a substantial proportion of associated patients use CAM for at least part of their care.[17,20,21] FMS was defined as at least one visit containing ICD-9 code 729.1. Low back pain and menopause symptoms were defined using the Johns Hopkins Adjusted Clinical Group (ACG) software, Version 8,[22] which groups ICD-9 codes per visit into expanded diagnosis clusters (EDC). Low back pain was defined as EDC MUS14 (Low Back Pain) and menopause symptoms was defined as EDC FRE11 (Menopausal Symptoms).

Time frame. Two (2) time periods of interest were created. The "study year" for each patient started on the day of the first visit for an index condition and continued for 365 days; and the "prior year" for each patient was defined as the 365 days preceding the first visit for the index condition. All data were derived from calendar years 2000–2003.

Patients included in the analysis had at least one provider visit containing an ICD-9 code/EDC for an index condition during the study year and no visits containing an ICD-9 code/EDC for the index condition during the prior year.

Provider types. CAM providers were defined as chiropractors, licensed massage therapists, acupuncturists, and naturopathic physicians. Conventional providers were defined as physicians (including osteopaths and specialists), advanced registered nurse practitioners, and physician assistants.

Dependent variables. Dependent variables were total allowed expenditures in the study year, outpatient expenditures, expenditures related to the index condition, and expenditures related to imaging procedures (back pain patients only). Data for each visit included the dollar amount the insurance company allowed for that visit. These amounts were totaled over the study year to create total allowed expenditures. For some analyses, these totals are broken out into allowed expenditures for CAM visits versus allowed expenditures for conventional visits. Imaging expenditures were divided into expenditures for plain radiographs and expenditures for all other types of imaging (e.g., magnetic resonance imaging [MRI], computed tomography). Imaging expenditures were further divided into those that occurred within 28 days of the initial diagnosis (called "early" imaging) and those that occurred more than 28 days after initial diagnosis. This division was based on the Healthcare Effectiveness Data and Information Set recommendation that no imaging should be performed within the first 28 days after an initial diagnosis of back pain.[23]

Independent variables. Age, gender, and zip code were included in the claims information along with ICD-9 diagnosis codes, dates and types of visits, and providers seen. County population was calculated based on 2000 census data and then categorized as <100,000; 100,000–400,000; and >400,000.

CAM users were defined as patients with at least one visit to a CAM provider for the index condition during the study year. Most also had at least one visit to a conventional provider for the index condition. CAM nonusers were those with no visits to a CAM provider for any reason during the study year and at least one visit to a conventional provider for the index condition during the study year.

Overall disease burden for each patient was constructed using the Resource Utilization Band (RUB) index created by the Johns Hopkins ACG software described above. RUBs estimate the overall disease burden and expected resource use for each individual, and are created by grouping individuals with similar levels of expected resource use based on the ACG index. Lower RUBs included individuals with less expected resource use and higher RUBs included those with greater expected resource use. Throughout the Results and Tables, the term "Low disease burden" refers to patients in RUBs 1 and 2; "Moderate disease burden" refers to patients in RUB 3; and "High disease burden" refers to patients in RUBs 4 and 5. For the regression analysis, disease burden was dichotomized into high versus moderate or low.

Matching. Because patients were not randomly assigned to use CAM but rather self-selected into CAM users and nonusers, we used a matching process to create groups that were as comparable as possible, using a frequency matching process. That is, each CAM user was placed into a stratum based on index condition, gender, 10-year age group, total allowed expenditures during the prior year (matched within $1,000 up to $9,999; all expenditures $10,000 or above were grouped), and disease burden categorized as high, medium, or low during the study year. The number of CAM users in each stratum was determined and half that number of CAM nonusers in each stratum was randomly identified, resulting in a 2:1 match. The 2:1 matching process was necessary because there were too few CAM nonusers in many strata to create a 1:1 match. There were 1330 potential strata, of which 770 contained at least one CAM user. In 256 strata there were an odd number of CAM users, creating the need for a de facto 3:1 match for these individuals. In addition, there were 125 CAM users who could not be matched due to too few controls in the stratum. All CAM users were included in the analysis, including the total of 381 (1.4%) described above who could not be placed in a 2:1 match. Characteristics of unmatched CAM users are described in the Results section.

Statistical analysis. Independent samples t tests were used for unadjusted comparisons of expenditures (total, outpatient, and expenditures related to index condition) between CAM users and nonusers, also to compare mean age. Chi-square tests were used to compare distributions of gender, disease burden, county population, and insurance companies between CAM users and nonusers.

Linear regression analysis was used to perform adjusted comparisons of total expenditures between CAM users and nonusers after adjustment for age, gender, disease burden, county population, and insurance company. Disease burden was dichotomized as high disease burden versus low or moderate disease burden, and an interaction term between CAM use status and disease burden was included in the model. Beta estimates for the interaction terms were calculated using the lincom function in Stata (Stata Corp., College Station, TX).[24] Models were constructed for all patients combined and then separately for those with each index condition.

Although expenditure data are highly skewed, leading to a violation of the requirement for constant variance and for normally distributed residuals from the model, the large sample size available here ensures that estimates will be accurate, based on the Central Limit Theorem (CLT).[25] However, it was not apparent whether the groups with FMS ($n = 5508$) or menopause ($n = 6566$) were large enough for the CLT to apply for the two models created from these smaller samples. Two (2) simulation analyses were performed to determine this, one analysis for the FMS group and the other for the menopause group. In each case, 1000 bootstrap samples were created from the original sample and regression analyses were performed. If the CLT is applicable, 95% of the β estimates from these 1000 models should fall in the 95% confidence interval based on the entire group. Results of the analysis showed that for the FMS group, 97.2% of the β estimates fell into the 95% confidence interval, and for the menopause group, 96.8% of the β estimates fell into the 95% confidence interval. Based on these results, we were confident that the linear regression models would give us accurate estimates in spite of the skewed nature of the dependent variable. To ensure accurate inference, "robust" standard errors were used.[26] Stata version 10 was used for all analyses.[27]

Results

A total of 26,466 CAM users were identified for this analysis: 18,343 with back pain, 3722 with FMS, and 4401 with menopause. These were matched to 13,025 CAM nonusers on a 2:1 basis. There were 381 (1.4%) CAM users who were not matched in this process; 125 due to having no matching controls available and the remaining 256 due to having an odd number of CAM users in some strata. All CAM users were included in the analysis. Those who were unmatched were younger (mean 42.4 versus 45.2 years, $p < 0.0001$); had higher average total expenditures in the study year ($5,902 versus $3,766, $p < 0.0001$), and had heavier disease burdens in the study year (46% in highest category versus 33% among matched CAM users, $p < 0.0001$). To the extent the inclusion of these unmatched CAM users may lead to bias, it will make CAM users look more expensive than the matched controls. However, because the unmatched CAM users are only 1.4% of all CAM users, any bias will be small. For example, as stated above, the mean total expenditure was $3766 for matched CAM users. When the 381 unmatched CAM users were included, mean expenditure for all CAM users was $3,797.

Table 1 displays the comparison of the CAM users and nonusers. The groups did not differ on average age, average allowed expenditures in the prior year, percent female, or disease burden in the study year; that is, as expected, users and nonusers did not differ on any of the matching criteria. CAM users and nonusers were not matched on county population or insurance company, and CAM users were less likely to live in urban counties than nonusers, also more likely to be from insurance company B.

Table 2 displays the results of unadjusted t-tests which showed that CAM users had lower overall average

TABLE 1. COMPARISON OF COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) USERS AND NONUSERS[a] MATCHED ON AGE GROUP, GENDER, ALLOWED EXPENDITURES IN PRIOR YEAR, AND DISEASE BURDEN IN STUDY YEAR

	CAM users (n = *26,466*)	*CAM nonusers* (n = *13,025*)	p-*value*
Average age (SD)	45.2 (10.5)	45.4 (10.6)	0.14
Average allowed expenditures in prior year (SD)	$2,494 (6351)	$2,454 (6114)	0.55
Percent female	66.6%	66.7%	0.80
Disease burden in study year			
Low	8.3%	8.1%	0.72
Moderate	58.3	58.7	
High	33.4	33.2	
County population			
<100,000	11.9	8.4	<0.001
100,000–400,000	15.2	11.0	
>400,000	72.9	80.6	
Insurance company			
A	90.8	92.6	<0.001
B	9.2	7.4	

[a]CAM users, those with at least one visit to a CAM provider related to index condition during study year; nonusers, no visit to a CAM provider for any reason during study year.
SD, standard deviation.

expenditures than nonusers in the study year ($3,797 versus $4,153, $p = 0.0001$). The distribution of expenditures for outpatient, inpatient, and other expenditures differed between the two groups; CAM users had higher average outpatient expenditures ($1,848 versus $1,502, $p < 0.0001$) but lower inpatient expenses and lower expenses for other types of claims not linked to a specific provider visit such as imaging and lab claims (Fig. 1). Among CAM users, expenditures for conventional outpatient care were lower than among CAM nonusers ($1,219 versus $1,502, $p < 0.0001$), but this was offset by CAM expenditures, which averaged $630 per user.

TABLE 2. COMPARISON OF EXPENDITURES BETWEEN COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) USERS AND NONUSERS IN STUDY YEAR

	CAM users (n = *26,466*)	*CAM nonusers* (n = *13,025*)	p *value*
Average allowed expenditures in study year:	Mean (SD)	Mean (SD)	
Total	$3,797 (7623)	$4,153 (9505)	0.0001
Outpatient: Total	$1,848 (2370)	$1,502 (3027)	<0.0001
Conventional	$1,219 (2214)	$1,502 (3027)	<0.0001
CAM	$630 (746)	0	
Total related to index condition	$588 (1280)	$554 (1947)	0.04
Outpatient related to index condition	445 (594)	231 (438)	<0.0001

SD, standard deviation.

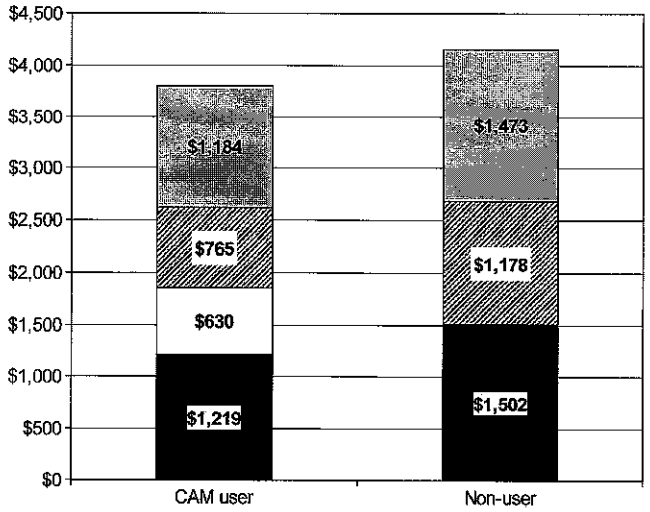

FIG. 1. Average annual allowed expenditures by complementary and alternative medicine (CAM) use status. Solid black, outpatient expenditures from conventional providers; solid white, outpatient expenditures from CAM providers; gray stripe, inpatient expenditures; solid gray, other expenditures not related to a provider visit, such as imaging and lab work.

When analyses were restricted to visits related to the index condition, total average expenditures were slightly higher among CAM users ($588 versus $554, $p = 0.04$), while average outpatient expenditures related to the index condition were much higher among CAM users ($445 versus $231, $p < 0.0001$) (Table 2). The expenditure patterns were similar within each condition (Table 3).

The linear regression analysis revealed a significant interaction between CAM use and disease burden. Among those in the low or moderate disease burden category, CAM users were predicted to have mean total expenditures $160 higher than nonusers. However, among those with high disease burden, predicted mean expenditures for CAM users were $1,421 lower than for nonusers (β: $6,726 for nonusers compared to $5,305 for CAM users, $p < 0.001$) (Table 4). When a model was fit excluding the interaction term, the β coefficient for CAM use was -$367 (standard error = $90, $p < 0.001$), confirming that overall, after adjustment, CAM users as a group have lower average total expenditures than nonusers. Similar results were seen in regression models restricted to each index condition.

The next set of analysis was aimed at identifying where the differences in expenditures between CAM users and nonusers occurred. Expenditures were analyzed by gender, and results showed that among males, CAM users had significantly lower expenditures than nonusers ($2,863 versus $3,634, $p < 0.0001$), while among females average expenditures did not differ significantly between CAM users and nonusers ($4,266 versus $4,412, $p = 0.19$). CAM users were less likely to be hospitalized (5.2% versus 7.5%, $p < 0.001$), and among those with menopause symptoms, CAM users were less likely to get a hysterectomy within 1 year of diagnosis (1.3% versus 2.9%, $p < 0.001$). Next we looked at the contribution of imaging to expenditures among back pain patients. CAM users were more likely than nonusers to have some type of imaging done (42.6% versus 38.3%, $p < 0.001$) and were also more likely to

TABLE 3. EXPENDITURES BY DISEASE CONDITION AND CAM USE STATUS

	Back pain		*FMS*		*Menopause*	
	User	*Nonuser*	*User*	*Nonuser*	*User*	*Nonuser*
N	18,343	9074	3722	1786	4401	2165
Mean allowed expenditures in study year						
Total	$3,410***	$3,739	$4,830*	$5,449	$4,535	$4,818
Outpatient	$1,637***	$1,312	$2,374***	$1,840	$2,285**	$2,019
Total related to index condition	$677	$660	$554***	$412	$249**	$223
Outpatient related to index condition	$511***	$259	$407***	$170	$207**	$166

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
FMS, fibromyalgia syndrome.

have imaging done "early" (within 28 days of diagnosis): 12.5% versus 9.8%, $p < 0.001$. However, overall expenditures related to imaging were higher among nonusers, averaging (standard deviation) $197 ($485) compared to $140 ($388) among CAM users ($p < 0.0001$). This apparently contradictory finding is explained in that CAM users are more likely than nonusers to have plain radiographs (39% versus 28%, $p < 0.001$), and CAM users are less likely to have the other, more expensive types of imaging such as MRIs (11.4% versus 19.4%, $p < 0.001$).

Because CAM users were more likely to be covered by Company B and less likely to live in urban counties than nonusers, analyses were then performed to ensure that the differences in imaging were not due to differences in coverage between companies or differences in access to imaging between rural and urban residents. There was no significant difference in the percentage of back pain patients from Company A versus Company B who had MRI or other "high tech" imaging (all imaging other than plain x-ray). Rates were 14.0% for Company A and 14.7% for Company B ($p = 0.35$). Looking at the issue of access to high-tech imaging in rural areas, Table 5 shows that use of high-tech imaging was substantially lower for CAM users than nonusers for all three categories of county size. Furthermore, for nonusers, rates of high-tech imaging were very similar in the smallest counties (18%) and most urban counties (19%), indicating that lack of access in more rural areas does not explain the difference between CAM users and nonusers.

Discussion

The results of this analysis indicated that among patients with back pain, FMS, or menopause symptoms, those who used CAM providers for at least part of their care had slightly lower overall average expenditures than matched patients who saw conventional providers exclusively. The largest difference was seen among the patients with the heaviest disease burden, who tend to be the most expensive patients. Among patients with the lightest disease burden, CAM users tended to be slightly more expensive than nonusers. The majority of patients fall into the low and moderate disease categories, so this is not an inconsequential finding. However, the size of the cost saving among those with heavy disease burdens more than compensated for this; both the unadjusted results and the regression model omitting the interaction term showed that overall, CAM users had lower mean expenditures than nonusers. In fact, given the expected $356 lower expenditure for each CAM user, we

TABLE 4. RESULTS OF LINEAR REGRESSION MODEL[a]

	All conditions (n = 39,491)		*Back pain (n = 27,417)*		*FMS (n = 5508)*		*Menopause (n = 6566)*	
	β	*SE*	*β*	*SE*	*β*	*SE*	*β*	*SE*
Interaction of CAM use and disease burden:								
Low disease burden, CAM nonuser	Reference category							
Low disease burden, CAM user	$160***	$37	$93*	$41	$392***	$114	$322**	$108
High disease burden, CAM nonuser	$6,726***	$230	$6526***	$267	$7,973***	$747	$6468***	$476
High disease burden, CAM user	$5305***	$129	$5,196***	$164	$5,849***	$302	$5,335***	$287
Other covariates in the model:								
Age	$28***	$4	$31***	$4	$11	$17	$22	$19
Sex	$478***	$88	$452***	$87	$615	$333	–	–
County pop 100k–400k[b]	$166	$150	$267	$168	$-98	$469	$-45	$408
County pop >400k[b]	$239*	$121	$294*	$127	$96	$418	$127	$349
Insurance co.	$716***	$167	$771***	$204	$1,068*	$530	$416	$337
Constant	$-1,223	$280	$-1,362	$312	$-651	$1,001	$433	$952

[a]Outcome = total allowed expenditures in study year.
[b]Compared to counties with population <100k.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
CAM, complementary and alternative medicine; FMS, fibromyalgia syndrome; SE, standard error.

TABLE 5. PERCENT OF BACK PAIN PATIENTS RECEIVING MAGNETIC RESONANCE IMAGING OR OTHER "HIGH-TECH" IMAGING BY COUNTY POPULATION AMONG COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) USERS AND NONUSERS

County population	*CAM nonusers*	*CAM users*	*Total*
<100k	18%	9%	11%
100–400k	21	10	13
>400k	19	12	15
Total	19	11	14

would expect an overall $9.4 million lower expenditure in a group of 26,466 CAM patients with these medical conditions compared to a similar group of CAM nonusers of equal size. CAM users actually had higher outpatient expenditures and more outpatient visits than nonusers, but this was offset by lower inpatient and other expenditures (such as high-tech imaging) among CAM users.

Both Nelson et al.[28] and Legorreta[29] et al. compared insured back pain patients with chiropractic insurance coverage to those without chiropractic insurance coverage and found that those with chiropractic coverage had lower average back pain episode-related costs as well as lower rates of both MR and radiographic imaging. Our findings extend these analyses in finding that among those with chiropractic insurance coverage, those who actually use this benefit have lower costs than those who do not. Our findings also confirm the findings of Sarnat[30] that use of CAM-oriented primary care providers was associated with lower costs than conventional primary care providers.

This analysis has several limitations. First, although CAM users and nonusers were matched as closely as possible, the results may reflect differences between the groups that were unaccounted for in the matching process. Demographic information available in claims data is quite limited and does not include potentially important factors such as income, education, or race. Earlier regression analyses with these data used zip code–level income, education, and race to attempt to adjust for these factors, but none were significant. This likely indicates that the zip code–level aggregation was not sensitive enough to model the effects of these variables in this instance (unpublished data). Due to the correlation between health status and income, matching by disease burden provided limited matching on income.

A second limitation is that claims data are collected primarily for billing reasons and as such may not reflect all diagnosis codes with ideal accuracy. Third, cost minimization assumes that health outcomes are equivalent between groups. We did not have appropriate data available to test this assumption. Finally, we do not know how CAM-using patients would have behaved if insurance coverage was not available for these visits; if they had substituted conventional care in place of CAM care, costs to the insurance company would likely have been higher, while if they had paid out-of-pocket for CAM care, costs to the insurance company would have been lower.

Conclusions

The conclusion of this analysis is that in a large group of insured individuals, patients who use CAM providers for some of their care have lower expenditures as a group than a matched group of patients who do not use CAM, and the difference in expenditures is related in large part to less inpatient care and less use of high-tech imaging.

Acknowledgments

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Disclosure Statement

No competing financial interests exist.

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Acupuncture for chronic pain: individual patient data meta-analysis

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Abstract

Background—Although acupuncture is widely used for chronic pain, there remains considerable controversy as to its value. We aimed to determine the effect size of acupuncture for four chronic pain conditions: back and neck pain, osteoarthritis, chronic headache, and shoulder pain.

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Ethics statement
An ethics statement was not required for this work.

Conflicts of Interest
The authors declare that they have no competing interests.

Authors' contributions
The study was conceived by AV, GL, CW, and KL. AV was responsible for the overall study design with input from AC for the statistical analysis; AM for the systematic review; GL and HM with respect to acupuncture analyses; NV, CW, NF, KS and KL with respect to clinical trial methodology and meta-analysis. Statistical analyses were conducted by AV, AC and AM. The first draft of the manuscript was written by AV and AM. All authors gave comments on early drafts and approved the final version of the manuscript. AV 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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Methods—We conducted a systematic review to identify randomized trials of acupuncture for chronic pain where allocation concealment was determined unambiguously to be adequate. Individual patient data meta-analyses were conducted using data from 29 of 31 eligible trials, with a total of 17,922 patients analyzed.

Results—In the primary analysis including all eligible trials, acupuncture was superior to both sham and no acupuncture control for each pain condition (all $p<0.001$). After exclusion of an outlying set of trials that strongly favored acupuncture, the effect sizes were similar across pain conditions. Patients receiving acupuncture had less pain, with scores 0.23 (95% C.I. 0.13, 0.33), 0.16 (95% C.I. 0.07, 0.25) and 0.15 (95% C.I. 0.07, 0.24) standard deviations lower than sham controls for back and neck pain, osteoarthritis, and chronic headache respectively; the effect sizes in comparison to no acupuncture controls were 0.55 (95% C.I. 0.51, 0.58), 0.57 (95% C.I. 0.50, 0.64) and 0.42 (95% C.I. 0.37, 0.46). These results were robust to a variety of sensitivity analyses, including those related to publication bias.

Conclusions—Acupuncture is effective for the treatment of chronic pain and is therefore a reasonable referral option. Significant differences between true and sham acupuncture indicate that acupuncture is more than a placebo. However, these differences are relatively modest, suggesting that factors in addition to the specific effects of needling are important contributors to the therapeutic effects of acupuncture.

Introduction

Acupuncture is the insertion and stimulation of needles at specific points on the body to facilitate recovery of health. Although initially developed as part of traditional Chinese medicine, some contemporary acupuncturists, particularly those with medical qualifications, understand acupuncture in physiologic terms, without reference to pre-modern concepts[1].

An estimated 3 million American adults receive acupuncture treatment each year[2], and chronic pain is the most common presentation[3]. Acupuncture is known to have physiologic effects relevant to analgesia[4, 5], but there is no accepted mechanism by which it could have persisting effects on chronic pain. This lack of biological plausibility, and its provenance in theories lying outside of biomedicine, makes acupuncture a highly controversial therapy.

A large number of randomized trials of acupuncture for chronic pain have been conducted. Most have been of low methodologic quality and, accordingly, meta-analyses based on these trials are of questionable interpretability and value[6]. Here we present an individual patient data meta-analysis of randomized trials of acupuncture for chronic pain, where only high quality trials were eligible for inclusion. Individual patient data meta-analysis is superior to the use of summary data in meta-analysis as it enhances data quality, enables different forms of outcome to be combined, and allows use of statistical techniques of increased precision.

Methods

The full protocol of the meta-analysis has been published.[6] In brief, the study was conducted in three phases: identification of eligible trials; collection, checking and harmonization of raw data; individual patient data meta-analysis.

Data Sources and Searches

To identify papers, we searched MEDLINE, the Cochrane Collaboration Central Register of Controlled Trials and the citation lists of systematic reviews (full search strategy in Appendix). There were no language restrictions. The initial search, current to November 2008, was used to identify studies for the individual patient data meta-analysis; a second search was conducted in December 2010 for summary data to use in a sensitivity analysis.

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Study Selection

Two reviewers applied inclusion criteria for potentially eligible papers separately, with disagreements about study inclusion resolved by consensus. Randomized trials were eligible for analysis if they included at least one group receiving acupuncture needling and one group receiving either sham (placebo) acupuncture or no acupuncture control. Trials must have accrued patients with one of four indications - non-specific back or neck pain, shoulder pain, chronic headache or osteoarthritis - with the additional criterion that the current episode of pain must be of at least four weeks duration for musculoskeletal disorders. There was no restriction on the type of outcome measure, although we specified that the primary endpoint must be measured more than four weeks after the initial acupuncture treatment.

It has been demonstrated that unconcealed allocation is the most important source of bias in randomized trials[7] and, as such, we included only those trials where allocation concealment was determined unambiguously to be adequate (further detail in the review protocol[6]). Where necessary, we contacted authors for further information concerning the exact logistics of the randomization process. Trials were excluded if there was any ambiguity about allocation concealment.

Data Extraction and Quality Assessment

The principal investigator of eligible studies was contacted and asked to provide raw data from the trial. To ensure data accuracy, all results reported in the trial publication, including baseline characteristics and outcome data, were then replicated.

Reviewers assessed the quality of blinding for eligible trials with sham acupuncture control. Trials were graded as having a low likelihood of bias if either the adequacy of blinding was checked by direct questioning of patients (e.g. by use of a credibility questionnaire) and no important differences were found between groups, or the blinding method (e.g. the Streitberger sham device[8]) had previously been validated as able to maintain blinding. Trials with a high likelihood of bias from unblinding were excluded from the meta-analysis of acupuncture versus sham; a sensitivity analysis included only trials with a low risk of bias.

Data Synthesis and Analysis

Each trial was reanalyzed by analysis of covariance with the standardized principal endpoint (scores divided by pooled standard deviation) as the dependent variable, with the baseline measure of the principal endpoint and variables used to stratify randomization as covariates. This approach has been shown to have the greatest statistical power for trials with baseline and follow-up measures.[9, 10] The effect size for acupuncture from each trial was then entered into a meta-analysis using the *metan* command in Stata 11 (Stata Corp., College Station, TX): the meta-analytic statistics were created by weighting each coefficient by the reciprocal of the variance, summing and dividing by the sum of the weights. Meta-analyses were conducted separately for comparisons of acupuncture with sham and no acupuncture control, and within each pain type. We pre-specified that the hypothesis test would be based on the fixed effects analysis as this constitutes a valid test of the null hypothesis of no treatment effect.

Results

Systematic review

We identified 82 trials (see figure 1 for flowchart) of which 31 were eligible (Table 1 and Appendix online). Four of the studies were organized as part of the German Acupuncture Trials (GERAC) initiative[11–14], 4 were part of the Acupuncture Randomized Trials (ART) group[15–18]; 4 were Acupuncture in Routine Care (ARC) studies[19–22]; 3 were UK National

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Health Service acupuncture trials[23–25]. Eleven studies were sham controlled, 10 had no acupuncture control and 10 were three-armed studies including both sham and no acupuncture control. The second search for subsequently published studies identified an additional four eligible studies[26–29], with a total of 1,619 patients.

An important source of clinical heterogeneity between studies concerns the control groups. In the sham controlled trials, the type of sham included acupuncture needles inserted superficially[13], sham acupuncture devices with needles that retract into the handle rather than penetrate the skin[30] and non-needle approaches such as deactivated electrical stimulation[31] or detuned laser[32]. Moreover, co-interventions varied, with no additional treatment other than analgesics in some trials[15], whereas in other trials, both acupuncture and sham groups received a course of additional treatment, such as exercise led by physical therapists[25]. Similarly, the no acupuncture control groups varied between usual care, such as a trial in which control group patients were merely advised to "avoid acupuncture"[23]; attention control, such as group education sessions[33]; and guidelined care, where patients were given advice as to specific drugs and doses[13].

Data extraction and quality assessment

Usable raw data were obtained from 29 of the 31 eligible trials, including a total of 17,922 patients from the US, UK, Germany, Spain and Sweden. For one trial, the study database had become corrupted[34]; in another case, the statisticians involved in the trial failed to respond to repeated enquiries despite approval for data sharing being obtained from the principal investigator[35].

The 29 trials comprised 18 comparisons with 14,597 patients of acupuncture with no acupuncture group and 20 comparisons with 5,230 patients of acupuncture and sham acupuncture. Patients in all trials had access to analgesics and other standard treatments for pain. Four sham-controlled trials were determined to have an intermediate likelihood of bias from unblinding[13, 32, 36, 37]; the 16 remaining sham-controlled trials were graded as having a low risk of bias from unblinding. On average, drop-out rates were low (weighted mean 10%). Drop-out rates were only above 25% for four trials: Molsberger 2002[35] and 2010[27] (33% and 27%, but raw data not received and neither trial included in main analysis); Carlsson 2001[37] (46%, trial excluded in a sensitivity analysis for blinding) and Berman 2004[33] (31%). This had a high drop-out rate amongst no acupuncture controls (43%); drop-out rates were close to 25% in the acupuncture and sham groups. The Kerr trial had a large difference in drop-out rates between groups (acupuncture 13%, control 33%) but was excluded in the sensitivity analysis for blinding[36].

Meta-analysis

Forest plots for acupuncture against sham acupuncture and against no acupuncture control are shown separately for each of the four pain conditions in figures 2 and 3. Meta-analytic statistics are shown in table 2. Acupuncture was statistically superior to control for all analyses ($p<0.001$). Effect sizes are larger for the comparison between acupuncture and no acupuncture control than for the comparison between acupuncture and sham: 0.37, 0.26 and 0.15 in comparison with sham versus 0.55, 0.57 and 0.42 in comparison with no acupuncture control for musculoskeletal pain, osteoarthritis and chronic headache respectively.

For five of the seven analyses, the test for heterogeneity was statistically significant. In the case of comparisons with sham acupuncture, the trials by Vas et al are clear outliers. For example, the effect size of the Vas trial for neck pain is about 5 times greater than meta-analytic estimate. One effect of excluding these trials in a sensitivity analysis (table 3) is that there is no significant heterogeneity in the comparisons between acupuncture and sham.

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Moreover, the effect size for acupuncture becomes relatively similar for the different pain conditions: 0.23, 0.16 and 0.15 against sham, and 0.55, 0.57 and 0.42 against no acupuncture control for back and neck pain, osteoarthritis, and chronic headache respectively (fixed effects; results similar for the random effects analysis).

To give an example of what these effect sizes mean in real terms, baseline pain score on a 0 – 100 scale for a typical trial might be 60. Given a standard deviation of 25, follow-up scores might be 43 in a no acupuncture group, 35 in sham acupuncture and 30 in patients receiving true acupuncture. If response were defined in terms of a pain reduction of 50% or more, response rates would be approximately 30%, 42.5% and 50%, respectively.

The comparisons with no acupuncture control show evidence of heterogeneity. This appears largely explicable in terms of differences between the control groups used. In the case of osteoarthritis, the largest effect is for Witt 2005[17], where patients in the waiting list control received only rescue pain medication, and the smallest for Foster 2007[25], which involved a program of exercise and advice led by physical therapists. For the musculoskeletal analyses, heterogeneity is driven by two very large trials[19, 20] (n=2565 and n=3118) for back and neck pain. If only back pain is considered (table 3), heterogeneity is dramatically reduced and is again driven by one trial, Brinkhaus 2006[15], with waiting list control. In the headache meta-analysis, Diener 2006[13] had much smaller differences between groups. This trial involved providing drug therapy according to national guidelines in the no acupuncture group, including initiation of beta-blockers as migraine prophylaxis. There was disagreement within the collaboration about whether this constituted active control. Excluding this trial reduced evidence of heterogeneity (p=0.04) but had little effect on the effect size (0.42 to 0.45).

Table 3 shows several pre-specified sensitivity analyses. Neither restricting the sham control trials to those with low likelihood of unblinding nor adjustment for missing data had any substantive effect on our main estimates. Inclusion of summary data from trials for which raw data were not obtained (2 trials) or which were published recently (4 trials) also had little impact on either the primary analysis (table 3) or the analysis with the outlying Vas trials excluded (data not shown).

To estimate the potential impact of publication bias, we entered all trials in to a single analysis and compared the effect sizes from small and large studies[38]. We saw some evidence that small studies had larger effect sizes for the comparison with sham (p=0.023) but not no acupuncture control (p=0.7). However, these analyses are influenced by the outlying Vas trials, which were smaller than average, and by indication, as the shoulder pain trials were small and had large effect sizes. Tests for asymmetry were non-significant when we excluded Vas and shoulder pain studies (n=15; p=0.065) and when small studies were also excluded(n<100, n=12; p=0.3). Nonetheless, we repeated our meta-analyses excluding trials with a sample size less than 100. This had essentially no effect on our results. As a further test of publication bias, we considered the possible effect on our analysis if we had failed to include high-quality, unpublished studies. Only if there were 47 unpublished trials with n=100 showing an advantage to sham of 0.25 standard deviations would the difference between acupuncture and sham lose significance.

A final sensitivity analysis examined the effect of pooling different endpoints measured at different periods of follow-up. We repeated our analyses including only pain endpoints measured at 2 – 3 months after randomization. There was no material effect on results: effect sizes increased by 0.05 to 0.09 SD for musculoskeletal and osteoarthritis trials and were stable otherwise.

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As an exploratory analysis, we compared sham to no acupuncture control. In a meta-analysis of 9 trials[11–13, 15–18, 25, 33], the effect size for sham was 0.33 (95% C.I. 0.27, 0.40) and 0.38 (95% C.I. 0.20, 0.56) for fixed and random effects models respectively ($p<0.001$ for tests of both effect and heterogeneity).

Comment

Overview of findings

In an analysis of patient-level data from 29 high quality randomized trials, including 17,922 patients, we found statistically significant differences between both acupuncture versus sham and acupuncture versus no acupuncture control for all pain types studied. After excluding an outlying set of studies, meta-analytic effect sizes were similar across pain conditions.

The effect size for individual trials comparing acupuncture to no acupuncture control did vary, an effect that appears at least partly explicable in terms of the type of control used. As might be expected, acupuncture had a smaller benefit in patients who received a program of ancillary care – such as physical therapist led exercise[25] – than in patients who continued on usual care. Nonetheless, the average effect, as expressed in the meta-analytic estimate of approximately 0.5 standard deviations, is of clear clinical relevance whether considered either as a standardized difference[39] or when converted back to a pain scale. The difference between acupuncture and sham is of lesser magnitude, 0.15 to 0.23 standard deviations.

Limitations

Neither study quality nor sample size appear to be a problem for this meta-analysis, on the grounds that only high quality studies were eligible and the total sample size is large. Moreover, we saw no evidence that publication bias, or failure to identify published eligible studies, could affect our conclusions.

As the comparisons between acupuncture and no acupuncture cannot be blinded, both performance and response bias are possible. Similarly, while we considered the risk of bias of unblinding low in most studies comparing acupuncture and sham acupuncture, providers obviously were aware of the treatment provided and, as such, a certain degree of bias of our effect estimate for specific effects cannot be entirely ruled out. However, it should be kept in mind that this problem applies to almost all studies on non-drug interventions. We would argue that the risk of bias in the comparison between acupuncture and sham acupuncture is low compared to other non-drug treatments for chronic pain, such as cognitive therapies, exercise or manipulation, which are rarely subject to placebo control.

Another possible critique is that the meta-analyses combined different endpoints, such as pain and function, measured at different times. However, results did not change when we restricted the analysis to pain endpoints measured at a specific follow-up time, 2 – 3 months after randomization.

Comparison with other studies

Many prior systematic reviews of acupuncture for chronic pain have had liberal eligibility criteria, accordingly included trials of low methodologic quality, and then came to the circular conclusion that weaknesses in the data did not allow conclusions to be drawn[40, 41]. Other reviews have not included meta-analyses, apparently due to variation in study endpoints[42, 43]. We have avoided both problems by including only high quality trials and obtaining raw data for individual patient data meta-analysis. Some more recent systematic reviews have published meta-analyses[44–46 47] and reported findings that are broadly

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comparable to ours with clear differences between acupuncture and no treatment control and smaller differences between true and sham acupuncture. Our findings have greater precision: all prior reviews have analyzed summary data, an approach of reduced statistical precision when compared to individual patient data meta-analysis [6, 48]. In particular, we have demonstrated a robust difference between acupuncture and sham control that can be distinguished from bias. This is a novel finding that moves beyond the prior literature.

Interpretation

We believe that our findings are both clinically and scientifically important. They suggest that the total effects of acupuncture, as experienced by the patient in routine clinical practice, are clinically relevant, but that an important part of these total effects is not due to issues considered to be crucial by most acupuncturists, such as the correct location of points and depth of needling. Several lines of argument suggest that acupuncture (whether real or sham) is associated with more potent placebo or context effects than other interventions[49–52]. Yet many clinicians would feel uncomfortable in providing or referring patients to acupuncture if it were merely a potent placebo. Similarly, it is questionable whether national or private health insurance should reimburse therapies that do not have specific effects. Our finding that acupuncture has effects over and above sham acupuncture is therefore of major importance for clinical practice. Even though on average these effects are small, the clinical decision made by doctors and patients is not between true and sham acupuncture, but between a referral to an acupuncturist or avoiding such a referral. The total effects of acupuncture, as experienced by the patient in routine practice, include both the specific effects associated with correct needle insertion according to acupuncture theory, non-specific physiologic effects of needling, and non-specific psychological (placebo) effects related to the patient's belief that treatment will be effective.

Conclusion

We found acupuncture to be superior to both no acupuncture control and sham acupuncture for the treatment of chronic pain. Although the data indicate that acupuncture is more than a placebo, the differences between true and sham acupuncture are relatively modest, suggesting that factors in addition to the specific effects of needling are important contributors to therapeutic effects. Our results from individual patient data meta-analyses of nearly 18,000 randomized patients on high quality trials provide the most robust evidence to date that acupuncture is a reasonable referral option for patients with chronic pain.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

The Acupuncture Trialists' Collaboration includes physicians, clinical trialists, biostatisticians, practicing acupuncturists and others. The list of collaborators is as follows.

Claire Allen is the consumer representative ('patient advocate'). Mrs Allen is the Deputy Administrator at the Cochrane Collaboration Secretariat.

Mac Beckner, MIS, is Vice President of the Information Technology and Data Management Center at the Samueli Institute.

Brian Berman, MD, is Professor of Family & Community Medicine at the University of Maryland School of Medicine and Director of the Center for Integrative Medicine.

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Angel M. Cronin, MS, is a biostatistician at the Dana-Farber Cancer Institute.

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Albrecht Molsberger, MD, PhD, Prof. is an orthopedic surgeon, a practicing acupuncturist and the president of the German acupuncture research group.

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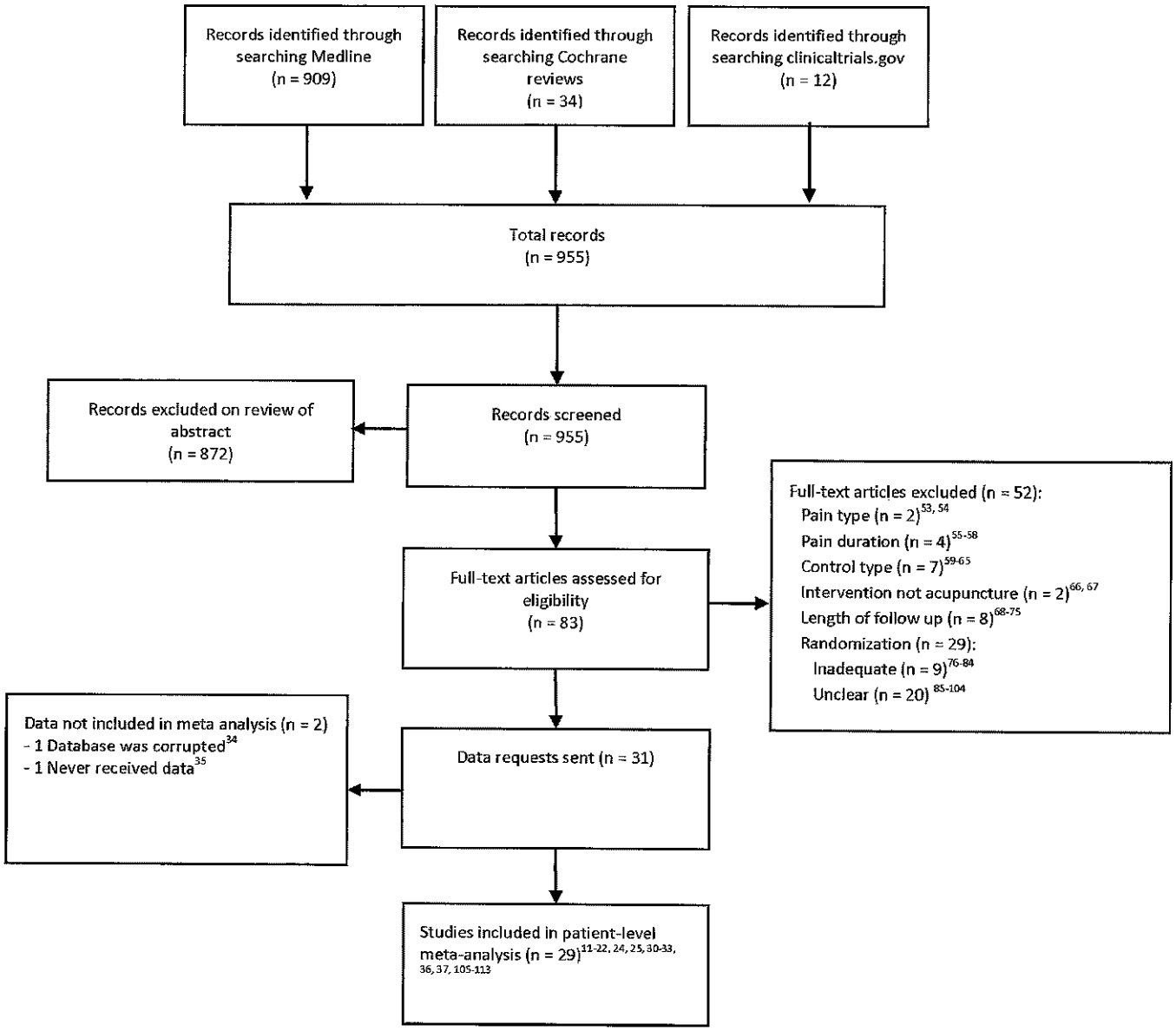

Figure 1.
PRISMA Flow Diagram

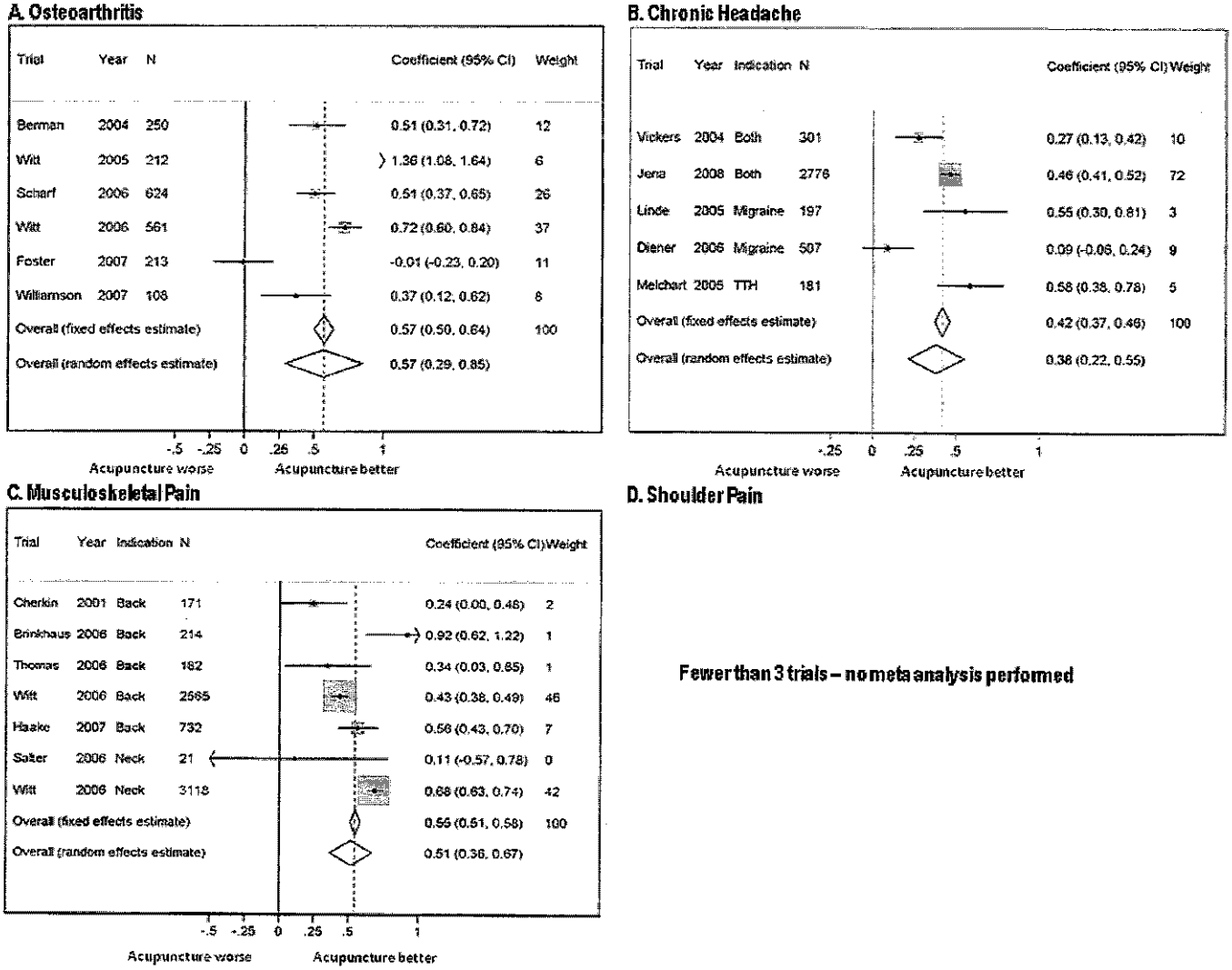

Figure 2.
Forest plots for the comparison of acupuncture with no acupuncture control.

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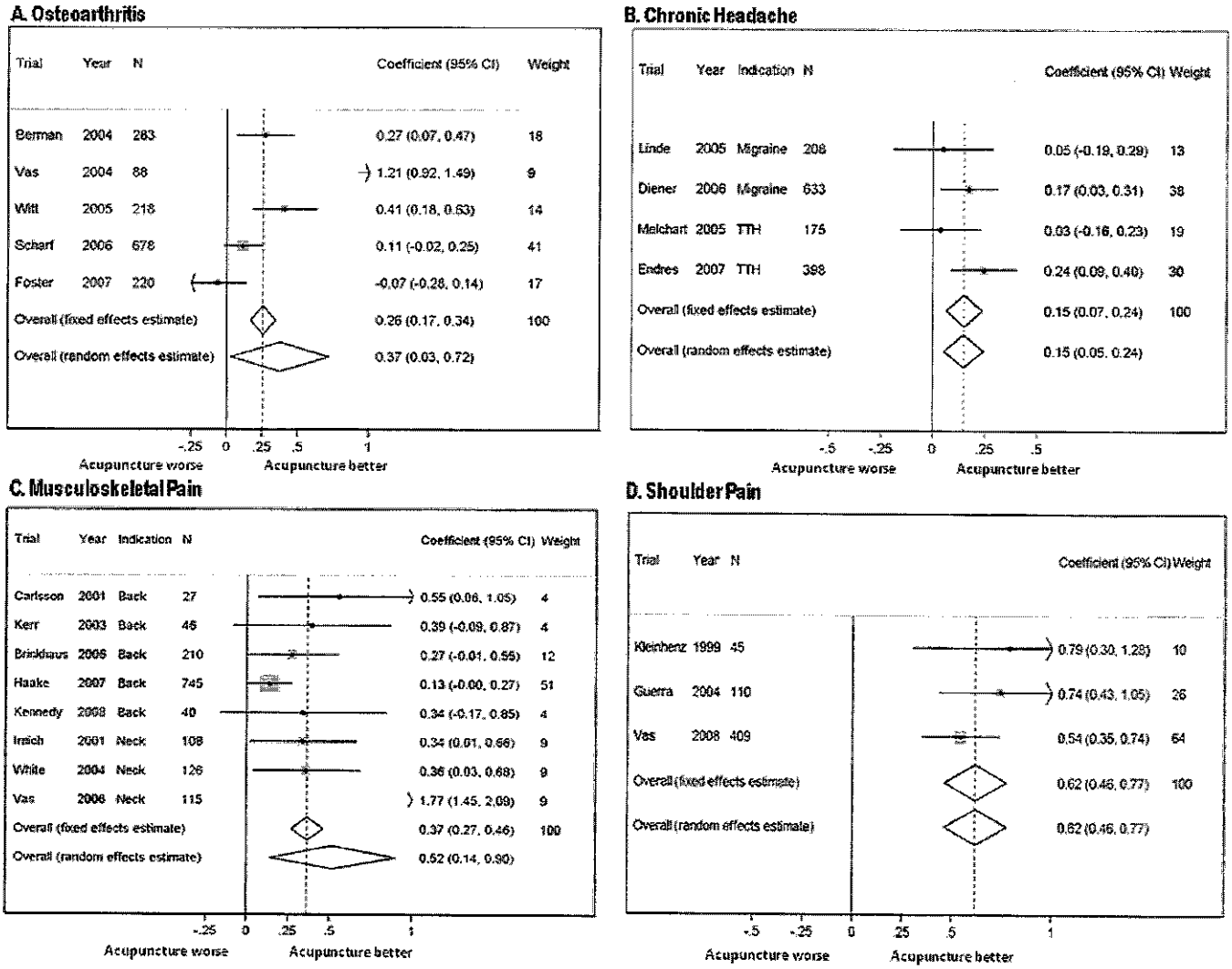

Figure 3.
Forest plots for the comparison of true and sham acupuncture.

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Table 1

Characteristics of included studies (Trial level information is provided in the Appendix)

The table includes the 31 trials identified in the initial search plus the four recently identified trials for which summary data were used.

Indication n=35	Pain Type	Control group	Primary Outcome Measure	Time point
Chronic headache n=7	Migraine n=2[13, 18] Tension-type headache n=3[14, 16, 34] Both n=2[21, 53]	Sham n=4[13, 14, 16, 18] No acupuncture control n=6 Ancillary care * n=1[34] Usual care ^ n=4[16, 18, 21, 53] Guidelined care# n=1[13]	Severity score n=2[34, 53] Days with headache n=1[14] Migraine days n=3[13, 16, 21] Days with moderate to severe pain n=1[18]	1 month n=1[34] 3 months n=3[16, 18, 21] 6 months n=2[13, 14] 12 months n=1[53]
Non-specific Musculoskeletal Pain (back and neck) n=15	Back n=10[12, 15, 19, 24, 28, 35–37, 54, 55] Neck n=5[20, 31, 32, 56, 57]	Sham n=10[12, 15, 28, 31, 32, 35–37, 54, 57] No acupuncture control n=9 Ancillary care * n=1[35] Usual care ^ n=6[15, 19, 20, 24, 28, 56] Non specific advice§ n=1[55] Guidelined care# n=1[12]	VAS n=7[15, 31, 32, 35–37, 57] Roland Morris Disability Questionnaire n=3[28, 54, 55] Neck Pain and Disability n=1[20] Hannover Functional Questionnaire n=1[19] Northwick Park Neck Pain Questionnaire n=1[56] Von Korff pain score n=1[12] SF36 Bodily pain n=1[24]	1 month n=4[31, 32, 36, 57] 2 months n=3[15, 28, 55] 3 months n=5[19, 20, 26, 29, 35, 54, 56] 6 months n=2[12, 37] 24 months n=1[24]
Osteoarthritis n=9		Sham n=6[11, 17, 25, 26, 33, 58] No acupuncture control n=8 Ancillary care * n=2[11, 25, 26] Usual care ^ n=4[17, 22, 29] Non specific advice§ n=2[33, 59]	Oxford Knee Score questionnaire n=1[59] Western Ontario and McMaster Universities Arthritis Index (WOMAC) n=2[17, 22] WOMAC pain subscore n=6[11, 25, 26, 29, 33, 58]	2 months n=2[17, 59] 3 months n=4[22, 26, 29, 58] 6 months n=3[11, 25, 33]
Shoulder pain n=4		Sham n=4[27, 30, 60, 61] No acupuncture control n=1 Usual care ^ n=1[27]	Constant-Murley-score n=2[30, 61] VAS n=2[27, 60]	1 month n=2[30, 61] 6 months n=2[27, 60]

*Ancillary care: Program of care received by both acupuncture and non acupuncture groups (e.g. trial comparing physiotherapy plus acupuncture to physiotherapy alone)

^Usual care: Protocol did not specify treatments received in control group (e.g. trials with 'waiting list control')

§Non specific advice: Patients in control group receive general advice and support ('attention control').

#Guidelined care: Patients in control group received care according to national guidelines

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Table 2

Primary analyses

Effect sizes are standardized differences.

	Acupuncture vs. Sham acupuncture				Acupuncture vs. no acupuncture control			
	N	Fixed effects (95%CI)	Random effects (95%CI)	P value for overall effect	N	Fixed effects (95%CI)	Random effects (95%CI)	P value for overall effect
Non-specific musculoskeletal pain (back and neck)	8	0.37 (0.27, 0.46) Heterogeneity: p<0.001	0.52 (0.14, 0.90)	p<0.001	7	0.55(0.51, 0.58) Heterogeneity: p<0.001	0.51 (0.36, 0.67)	p<0.001
Osteoarthritis	5	0.26 (0.17, 0.34) Heterogeneity p<0.001	0.37 (0.03, 0.72)	p<0.001	6	0.57 (0.50, 0.64) Heterogeneity: p<0.001	0.57 (0.29, 0.85)	p<0.001
Chronic headache	4	0.15 (0.07, 0.24) Heterogeneity: p=0.3	0.15 (0.05, 0.24)	p<0.001	5	0.42 (0.37, 0.46) Heterogeneity: p<0.001	0.38 (0.22, 0.55)	p<0.001
Shoulder pain	3	0.62 (0.46, 0.77) Heterogeneity: p=0.4	0.62 (0.46, 0.77)	p<0.001	0	No trials		

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Table 3

Sensitivity analyses

Effect sizes are standardized differences.

	Indication	Acupuncture vs. Sham acupuncture				Acupuncture vs. no acupuncture control			
		N	Fixed effects (95%CI)	Random effects (95%CI)	P value for overall effect	N	Fixed effects (95%CI)	Random effects (95%CI)	P value for overall effect
Exclusion of Vas trials	Non-specific musculoskeletal pain	7	0.23 (0.13, 0.33) Heterogeneity: p=0.5	0.23 (0.13, 0.33)	p<0.001	Not applicable			
	Osteoarthritis	4	0.16 (0.07, 0.25) Heterogeneity: p=0.15	0.17 (0.00, 0.35)	p<0.001				
	Shoulder pain	Fewer than 3 trials							
Separate pain types	Back pain	5	0.20 (0.09, 0.31) Heterogeneity: p=0.4	0.20 (0.09, 0.32)	p<0.001	5	0.46 (0.40, 0.51) Heterogeneity: p=0.004	0.49 (0.33, 0.64)	p<0.001
	Neck Pain	3	0.83 (0.64, 1.01) Heterogeneity: p<0.001	0.82 (−0.11, 1.75)	p<0.001	No trials			
Inclusion of trials for which raw data not obtained	Non-specific musculoskeletal pain	10	0.30 (.21, 0.38) Heterogeneity: p<0.001	0.48 (0.14, 0.81)	p<0.001	9	0.55 (0.51, 0.58) Heterogeneity: p<0.001	0.57 (0.42, 0.71)	p<0.001
	Osteoarthritis	6	0.22 (0.14, 0.30) Heterogeneity p<0.001	0.31 (0.02, 0.60)	p<0.001	8	0.58 (0.51, 0.64) Heterogeneity: p<0.001	0.57 (0.33, 0.80)	p<0.001
	Chronic headache	No trials				6	0.42 (0.38, 0.47) Heterogeneity: p<0.001	0.41 (0.25, 0.56)	p<0.001
	Shoulder pain	4	0.57 (0.44, 0.69) Heterogeneity: p= 0.4	0.57 (0.44, 0.69)	<0.001	1	Fewer than 3 trials		
Only trials with low likelihood of bias for blinding	Non-specific musculoskeletal pain	5	0.36 (0.25,0.46) Heterogeneity: p<0.001	0.57 (0.00, 1.14)	p<0.001	Not applicable			
	Osteoarthritis	As for table 2: all trials have a low likelihood of bias for blinding							
	Chronic headache	3	0.14 (0.03, 0.25) Heterogeneity: p=0.18	0.12 (−0.02, 0.27)	p=0.013				
	Shoulder pain	As for table 2: all trials have a low likelihood of bias for blinding							
Multiple imputation for missing data	Non-specific musculoskeletal pain	8	0.36 (0.27, 0.46) Heterogeneity: p<0.001	0.52 (0.15, 0.88)	p<0.001	7	0.55 (0.51, 0.58) Heterogeneity: p<0.001	0.51 (0.36, 0.66)	p<0.001
	Osteoarthritis	5	0.25 (0.16, 0.33) Heterogeneity: p<0.001	0.37 (0.03, 0.71)	p<0.001	6	0.57 (0.50, 0.64) Heterogeneity: p<0.001	0.57 (0.29, 0.85)	p<0.001
	Chronic headache	4	0.16 (0.07, 0.25) Heterogeneity: p=0.4	0.16 (0.07, 0.25)	p<0.001	5	0.42 (0.38, 0.46) Heterogeneity: p<0.001	0.38 (0.22, 0.55)	p<0.001
	Shoulder pain	3	0.62 (0.46, 0. 78)	0.62 (0.46, 0.78)	p<0.001	No trials			

Indication		Acupuncture vs. Sham acupuncture				Acupuncture vs. no acupuncture control			
	N	Fixed effects (95%CI)	Random effects (95%CI)	P value for overall effect	N	Fixed effects (95%CI)	Random effects (95%CI)	P value for overall effect
		Heterogeneity: p=0.4						

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