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Article:

Molassiotis, A, Dawkins, B orcid.org/0000-0002-7038-1975, Longo, R orcid.org/0000-0002-9379-1627 et al. (5 more authors) (2020) Economic evaluation alongside a randomised controlled trial to assess the effectiveness and cost-effectiveness of acupuncture in the management of chemotherapy-induced peripheral neuropathy. *Acupuncture in Medicine*. ISSN 0964-5284

<https://doi.org/10.1177/0964528420920285>

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Economic evaluation alongside a randomised controlled trial to assess the effectiveness and cost-effectiveness of acupuncture in the management of chemotherapy-induced peripheral neuropathy

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ABSTRACT

Objective: to assess the cost-effectiveness of acupuncture in the management of chemotherapy-induced peripheral neuropathy (CIPN) in Hong Kong.

Methods: A within trial cost-utility analysis with the primary endpoint for the economic evaluation being the Quality Adjusted Life Year (QALY) and associated Incremental Cost Effectiveness Ratio (ICER) over 14 weeks of treatment. A secondary cost-effectiveness analysis was undertaken with the endpoint being change in pain as measured on the Brief Pain Inventory (BPI).

Results: Eighty-seven patients were randomised to acupuncture or usual care. Acupuncture resulted in significant improvements in pain intensity (8 and 14 week mean changes compared to usual care of -1.8 and -1.8, respectively), pain interference (8 and 14 week mean changes compared to usual care of -1.5 and -0.9, respectively) and indicators of quality of life and neurotoxicity-related symptoms. However, in the economic evaluation there was little difference in QALYs between the two arms (mean change 0.209 and 0.200 in the acupuncture and usual care arms, respectively). Also, costs yielded deterministic ICERs of HK \$616,965.62, HK \$824,083.44 and HK \$540,727.56 per QALY gained from the health care provider perspective, the societal perspective and the patient perspective, respectively. These costs are significantly higher than the cost-effectiveness threshold of HK \$180,450 that was used for the base case analysis.

Conclusion: While acupuncture can improve symptoms and quality of life indicators related to CIPN, it is unlikely to be a cost-effective treatment for CIPN-related pain in health care systems with limited resources.

Trial registration number: NCT02553863 (ClinicalTrials.gov)

Key words: acupuncture, cost-effectiveness, peripheral neuropathy, chemotherapy

INTRODUCTION

Acupuncture as an intervention to manage a broad range of conditions has shown promising and positive results over the years, from the management of low back pain¹ to functional dyspepsia², migraine³, nausea/vomiting⁴ and others, although negative and inconclusive evidence does exist for other conditions⁴. Economic evaluations increasingly underpin decisions in health care about allocation of resources and as such they should be incorporated in all trials of new interventions. However, the cost-effectiveness of acupuncture has received little attention in the literature, with a small number of evaluations showing that at times it can be cost-effective and at times it is not. Systematic reviews support the cost-effectiveness of acupuncture for chronic pain⁵, dysmenorrhoea, allergic rhinitis, osteoarthritis and headache⁶. On the other hand, several studies showed that acupuncture was not cost-effective, including in the management of irritable bowel syndrome⁷, chronic low back pain (unless comorbid depression was included)⁸ and allergic rhinitis⁹.

Chemotherapy-induced peripheral neuropathy (CIPN) is a derangement in structure and function of peripheral motor, sensory and autonomic neurons, causing peripheral neuropathic signs and symptoms¹⁰. The prevalence of CIPN is reported to be 10-20% among patients during treatment and it may be as high as 100%, depending on the chemotherapy drug, dose-intensity, cumulative dose and other, as of yet unidentified, risk factors^{11,12}. CIPN has significant implications for patients' quality of life¹³ alongside an impact on use of health care resources, with those experiencing CIPN having more frequent outpatient visits and medication use, the cost of which has been estimated to be \$17,000 (USD) more in cancer patients with CIPN than those without CIPN¹⁴. The management of CIPN is difficult with a limited number of treatment options available. Some small-scale studies have provided initial evidence of effect, particularly in terms of decreasing neuropathic pain, as reviewed by Franconi¹⁵. We have recently completed the first fully-powered randomised trial in the management of CIPN¹⁶. Within this trial, we also assessed the cost-effectiveness of using acupuncture alongside usual care, versus usual care only, to allow for more informed health care decisions to be made in the future. Our trial included 87 patients randomised to acupuncture or usual care for 8 weeks¹⁶. The primary outcome for the trial was pain intensity or pain interference over the past week and secondary outcomes included patient-reported outcome measures with assessments taking place at baseline, at the end of treatment and 14 weeks after the beginning of treatment. At the end of the intervention, there were significant improvements in the acupuncture arm both in terms of primary and secondary outcomes. At 14 weeks there were still significant improvements in pain interference, neurotoxicity-related symptoms and functional aspects of quality of life ($p < 0.05$) and at 20 weeks improvements were sustained with regards to physical and functional well-being ($p < 0.05$). In this article, we examine the cost-effectiveness of acupuncture in the management of CIPN with respect to cost per

quality-adjusted life year (QALY) and cost per unit reduction in pain intensity and pain interference, compared to usual care, over 14 weeks from randomisation.

METHODS

The parent trial was an assessor-blinded randomised controlled trial of acupuncture for 8 weeks compared to a waitlist control arm receiving standard care, with the latter group receiving acupuncture at the end of the trial. Adult patients who had received neurotoxic chemotherapy and were reporting numbness/tingling in the hands/feet and having signs of neuropathy according to their medical practitioner, were eligible to participate. The primary outcome was 'worst pain' using the Brief Pain Inventory (BPI)¹⁷. Other outcomes include the BPI pain interference item and the Functional Assessment of Cancer Therapy (FACT/GOG-Ntx)¹⁸.

Measurement and valuation of outcomes

To determine the intervention's cost-effectiveness, we assessed the impact of the intervention on quality of life and reduction in pain over 14 weeks.

Quality of life was measured using the 27-item general assessment of quality of life sub-scale (FACT-G) of the FACT/GOG-Ntx¹⁸. The FACT-G questionnaire was completed by patients at home at baseline, at the end of the 8 weeks of treatment and at 14 weeks post randomisation. Patient responses to the FACT-G questionnaire were converted to utility values using a mapping algorithm to convert to the EQ-5D scale and utility values relevant to the Chinese population¹⁹. The equation used was as follows:

$$\text{EQ-5D utility index} = 0.238 + (0.014 \times \text{GP}) + (0.006 \times \text{GE}) + (0.008 \times \text{GF})$$

where, GP is physical, GE is emotional and GF is functional well-being.

The utility values represent patients' quality of life and were multiplied by duration (t) in each health state to generate quality adjusted life years (QALYs)²⁰. An area under the curve (AUC) approach was adopted to estimate QALYs with a linear transition assumed between adjacent time points, as follows:

$$QALY = \left(\left(\frac{Utility_{Baseline} + Utility_8}{2} \right) * t \right) + \left(\left(\frac{Utility_8 + Utility_{14}}{2} \right) * t \right)$$

where, $Utility_{Baseline}$, $Utility_8$ and $Utility_{14}$ are the utility scores at baseline, week 8 and week 14, respectively.

The secondary outcome measure was reduction in pain, represented by the 'worst pain during the past week' measured on the Brief Pain Inventory (BPI), which was completed by the patients at each time point. Reduction in pain was calculated at 8 and 14 weeks (with respect to baseline) for the two dimensions of the BPI

questionnaire: pain severity and pain interference. The pain severity subscale was calculated as the mean of four pain items (questions 3 to 6) and the pain interference subscale was calculated as the mean of the seven interference items (questions 9a to 9g).

Measurement and evaluation of resource use

Costs related to the intervention and wider healthcare utilisation

Healthcare resource use was estimated from the perspective of the healthcare provider and was collected for the trial period of 14 weeks from randomisation. This included primary care, such as GP, nurse and home visits, as well as secondary care, such as outpatient visits and other hospital admissions. Additionally, resource use and cost data from a patient perspective were obtained to enable analyses from patient and societal perspectives. The healthcare provider perspective included the costs of providing medical treatments. The patient perspective included costs of healthcare treatment and services, medications (paid for by patient), travel costs, food and drink costs and other expenses related to treatment that were paid for out of pocket. The societal perspective included all costs for healthcare, patient perspective costs and also costs associated with productivity loss from time out of work due to illness.

Resource use was captured using a bespoke questionnaire that patients completed at 14 weeks post randomisation. To determine the costs associated with the intervention and wider healthcare utilisation, unit costs were assigned to healthcare resource use using charge values from the Hospital Authority of Hong Kong²¹, and price year 2017. Charges are made up of two parts, namely the part paid by the patient and the part paid by the insurer. The sum of these two charges was used as the total cost of the relevant healthcare service. Costs were assigned on a per unit basis, with unit values taken from the resource use data collected within the trial. All recorded use of healthcare services that occurred within the trial period were costed irrespective of whether their use was directly associated with the treatment of cancer or the associated neuropathy. Unit costs for the main resource use items are presented in Table 1. Patients' use of healthcare resources and total costs were calculated for the intention-to-treat (ITT) population.

Cost-effectiveness analysis

Primary analysis

The primary analysis was a cost-utility analysis in which an incremental cost per QALY gained, due to acupuncture compared to usual care, was calculated over 14 weeks. As the intervention is intended to limit the side-effects of the chemotherapy, the benefits are not expected to continue after treatment has ceased and consequently this short time-horizon is appropriate for the research question being explored. For the main analysis, a healthcare provider perspective was adopted; a patient perspective and a societal perspective were also adopted for subsequent analyses. As the

timeframe of the trial was less than a year, discounting of the costs and benefits was not required.

The incremental cost per QALY gained as a result of the use of acupuncture compared to usual care was calculated by dividing the mean difference in cost of the two trial arms by the mean difference in QALYs to produce an incremental cost-effectiveness ratio, as follows:

$$ICER = (Cost_A - Cost_B) / (QALY_A - QALY_B)$$

The ICER represents the additional cost per QALY gained for the intervention compared to the best alternative (in this case usual care) ²².

After considering that, first, a single ICER threshold value for decision making is not officially available in Hong Kong and, second, the gross domestic product per capita threshold is no longer recommended by World Health Organisation²³, the cost-effectiveness threshold was set at \$23,105 based on a research paper by Woods et al.²⁴ on country-level cost-effectiveness thresholds. The paper indicates a threshold range for Hong Kong of \$17,409–\$28,801; hence the midpoint was selected as the reference threshold. This threshold range was converted to Hong Kong dollars using an exchange rate of 1 US dollar = 7.81 Hong Kong dollars to give HK \$135,964–\$224,936. The mid-point of HK \$180,450 was used as the cost-effectiveness threshold for the base case analysis. In line with current best practice for economic evaluations, we did not adjust the cost-effectiveness threshold with respect to inflation^{22,25}. Alternative thresholds were explored in the uncertainty analysis.

Secondary analysis

In the secondary cost-effectiveness analysis, the incremental cost was compared to the change in BPI scores, in the two pain subscales, between baseline and 8 weeks as well as baseline and 14 weeks, as a result of the use of acupuncture compared to usual care.

Missing data

Where patients indicated they had used a particular health care service but had not recorded the number of times it had been used, the mean of visits to that health service was imputed. For the BPI, only 25 patients responded “YES” to the first question (“Throughout our lives, most of us have had pain from time to time. Have you had pain other than these everyday kinds of pain today?”) and were prompted to answer the remaining items. Hence, in the original dataset, only these 25 subjects had a BPI score while the others showed missing values. It was agreed that those who responded “NO” to the first question should have a BPI score of ‘0’, so the missing values were imputed with zeros.

Multiple imputation was employed to account for missing EQ-5D data. This approach is recommended for economic analyses conducted alongside clinical trials as it reflects the uncertainty inherent in replacing missing data²⁶. The imputation was performed in

Stata Version 14 using predictive mean matching to perform multiple imputation by chained equations. Predictive mean matching was used due to the non-normal distribution of EQ-5D scores. This technique ensures that only plausible values of the missing variable are imputed as the imputed value is drawn from another individual whose predicted value is close to the predicted value of the individual with the missing observation²⁷.

Sensitivity analyses

Alternate scenarios were explored in the sensitivity analyses to test the robustness of the results of the main trial analysis. The effect of not imputing missing quality of life data was explored with an analysis including only complete cases. Additionally, sensitivity analyses were performed to explore the uncertainty around the costs by adding and subtracting 20% of the costs and outcomes and assessing the subsequent impact on the ICERs. The value of 20% is essentially arbitrary but was considered likely to represent any uncertainty that might exist in the values. The increase and decrease in costs by 20% was explored both from the health care provider perspective and the societal perspective.

Further sensitivity analyses were conducted to explore the effect of assumptions made in the base case analysis related to patient perspective costs. In the base case analysis, it was assumed that the costs reported for prescription medications were related only to the trial period, not for the whole time the medication was taken. The effect of this was explored in a sensitivity analysis in which it was assumed that the reported cost was for the whole time the medication was taken and the relevant cost for the trial period was calculated as the total cost divided by the number of days taken to estimate a cost per day, which was multiplied by 98 (98 days = 14 weeks = the length of the trial). In the base case analysis it was also assumed that the treatment cost was paid by the patient out-of-pocket. The effect of this was explored in a sensitivity analysis in which it was assumed that the treatment was paid for by an insurer/ public provider instead of by the patient.

Additional sensitivity analysis was also performed to explore the robustness of the secondary analysis results. The secondary analysis was based on changes in BPI (the primary outcome of the main trial analysis). As only a small number of patients had the primary outcome, the effect of acupuncture on other neurotoxic symptoms was also explored in a sensitivity analysis which instead used the outcome of neurotoxicity from the subscale of FACT/GOG.

Uncertainty analysis

The level of sampling uncertainty around the ICER was determined using a non-parametric bootstrap to generate 10,000 estimates of incremental costs and benefits. The bootstrapped estimates were plotted on the cost-effectiveness plane to illustrate the uncertainty surrounding the cost-effectiveness estimates²⁸. Net monetary benefit was calculated for each of the bootstrapped estimates as:

$$NMB = (\lambda \times QALYs) - costs$$

where, λ is the value a decision maker would be willing to pay per incremental QALY gained, i.e. the cost-effectiveness threshold.

The expected net monetary benefit was used to estimate the probability that acupuncture is cost-effective given a range of threshold values ($\lambda = \text{£}0$ to $\lambda = \text{£}100,000$) plotted on the cost-effectiveness acceptability curve (CEAC)²⁹. The cost-effectiveness frontier (CEF) was also plotted to show the intervention that provides the highest net benefit for a given threshold.

Ethical approval

Ethical approval was granted by the Human Research Ethics Review Committee of the Hong Kong Polytechnic University (HSEARS20141011004) on 29 October 2014 and the study hospital (CREC ref. 2014.529-T) on 18 November 2014. All participants signed a consent form. The trial was also prospectively registered with ClinicalTrials.gov (NCT02553863).

RESULTS

Sample

The first patient was recruited in November 2015, recruitment was completed in March 2017 and last patient follow-up was completed in May 2017. Among the 87 participants, the acupuncture arm had a higher share of male patients (62.5%), while in the usual care arm there was a higher share of female patients (55.6%). The mean age was 56.3 (SD=7.35) years in the acupuncture arm and 58 (SD=7.98) in the usual care arm.

Resource use and costs

Resource use and costs incurred by patients in each arm are presented in Table 2. Average total healthcare costs were HK \$8,849 and HK \$3,286, for the acupuncture and usual care arms of the trial, respectively, meaning that patients receiving the intervention, on average, showed higher total cost associated with the use of health care services (primarily due to the cost of acupuncture). Also, based on the control arm costs above (over 14 weeks), if costs remain constant, patients with CIPN cost the healthcare system HK \$12,205 (US \$1,565) annually.

Outcomes

Mean QALYs gained from baseline to 14 weeks were 0.209 and 0.200 for acupuncture and usual care, respectively (presented in table 3). In the usual care arm, the change from baseline regarding pain severity increased 0.5 points from baseline to 8 weeks and increased 1 point from baseline to 14 weeks, while for the acupuncture arm these decreased by 1.3 and 0.8 points, respectively. Pain interference increased by 0.5 points from baseline to week 8 and increased by 0.8 points from baseline to week 14, whereas in the acupuncture group pain interference decreased by 1 and 0.1 points, respectively. Mean BPI scores are presented in supplemental table 1.

Cost-effectiveness analysis

Primary analysis

The cost-effectiveness results estimated from the healthcare provider perspective, the societal perspective and the patient perspective are each presented in table 3. The QALYs and costs yielded deterministic ICERs of HK \$616,965.62, HK \$824,083.44 and HK \$540,727.56 per QALY for the health care provider perspective, the societal perspective and the patient perspective, respectively.

The healthcare provider perspective was taken as the base case analysis which was used to perform uncertainty analysis around the cost-effectiveness estimates. Bootstrapped uncertainty analysis produced a cloud of points predominantly in the north-east quadrant and entirely above the threshold, with a mean simulation ICER of HK \$598,289.19 (figure 1). The CEAC in figure 2 suggests that acupuncture had a 6% probability of being cost-effective at the HK \$180,450 threshold.

Secondary analysis

Regarding BPI changes over time compared to baseline, the cost-effectiveness results estimated for the two subscales (pain severity and pain interference) and over two time periods (8 and 14 weeks) are shown in table 4. The assumption was made that the costs incurred were evenly spread across the trial period, therefore a proportion was used for the cost-effectiveness analysis over 8 weeks. The results show that acupuncture is most cost-effective at reducing pain severity from baseline to 8 weeks.

Sensitivity analysis

The cost-effectiveness results for each scenario explored in the sensitivity analyses are presented in table 5. In each case, the results of the sensitivity analysis, for both the healthcare provider perspective and the societal perspective, support the results of the base case analysis and indicate that, compared to a cost-effectiveness threshold value of HK \$180,450, acupuncture alongside usual care for the management of CIPN is not a cost-effective use of health care resources.

For patient perspective costs, alternative assumptions around the costs of prescription medication had little impact on the ICER estimates. However, the cost of acupuncture appeared to be a key driver of the difference in patient costs between the control and intervention arms of the trial. When it was assumed that treatment (acupuncture) is paid for by an insurer or public provider, there was no significant difference in patient out of pocket costs between the two arms ($p=0.87$).

Sensitivity analysis exploring the impact of considering other neurotoxic symptoms is also shown in table 5. As in the analysis of BPI, estimates of cost-effectiveness are presented for the periods from baseline to 14 weeks and from baseline to 8 weeks. Costs incurred were assumed to be evenly spread across the trial period and therefore a proportion of the 14 week costs were used for the cost-effectiveness analysis over 8 weeks. The results confirm the robustness of the secondary analysis with BPI mean scores showing that acupuncture is most cost-effective at reducing symptoms of neurotoxicity from baseline to 8 weeks.

DISCUSSION

This is the first health economic analysis of acupuncture for the management of CIPN. While the trial showed acupuncture to be an effective treatment of CIPN in relation to pain and other neuropathic symptoms and quality of life indicators, the results of the economic evaluation indicated that the probability of acupuncture being cost-effective is only 6%. The cost of acupuncture appeared to be a key driver of the difference in patient costs between the control and intervention arms of the trial, a finding consistent with other studies in which acupuncture was effective but not necessarily cost-effective⁹. On the other hand, there was little difference in the QALYs gained between the two arms despite benefits in terms of pain reduction. On this point, it is worth considering that the EQ-5D is a generic measure of quality of life and may not be sensitive enough to pick up more nuanced changes in quality of life. Also, QALYs were estimated using a mapped algorithm for EQ-5D. Although this has been validated for the Chinese/Hong Kong population, this could be a source of bias. The sensitivity analyses conducted supported the results of the base case analysis and indicate that, compared to a cost-effectiveness threshold value of HK \$180,450, acupuncture alongside usual care for the management of CIPN is not a cost-effective use of resources. However, pain in this sample was mild (mean 1.2 and 2.1 and SD 0.3 and 0.4 in the control and intervention groups, respectively) and this may be a reason for the small clinical changes observed, reflected in a non-cost effective outcome in this evaluation. The low levels of pain experienced by patients recruited in this study poses a limitation to the analysis as healthcare resource use may consequently have been lower than in other similar patient groups. Also, as pain was not severe in our sample, this study does not answer the question of cost-effectiveness with acupuncture when there is severe pain with functional impairment.

The results of the secondary cost-effectiveness analysis suggested that acupuncture reduces pain severity and pain interference at both 8 and 14 weeks but that it is most cost-effective at reducing pain severity between baseline and 8 weeks. As the key

issue is the actual cost of acupuncture, this indicates that for patients with health insurance that will cover the cost of the treatment, the patient can potentially obtain the benefits of the treatment with little additional out-of-pocket costs. However, this may raise an equity issue for those patients who do not have appropriate health insurance as their out-of-pocket costs to obtain this treatment may be much higher. Access to acupuncture treatment may also be an issue, particularly in rural areas, as patients may be willing to pay for such an effective service but it may be unavailable. In addition, given that the cost of acupuncture is a key driver of the difference in cost between groups, and that the cost of acupuncture varies across different countries, the cost-effectiveness of acupuncture for CIPN will vary by country and context.

It is important to note that the treatment comparator used in an acupuncture trial can be fundamental as to whether the acupuncture will be cost-effective or not. In our case, the treatment comparator was usual care, which in reality involved very little supportive care and primarily painkillers, if there was any pain, or vitamin B. If the comparator had been another treatment, the results may have been different. Also, more widespread use of acupuncture in a clinical setting may decrease the costs of treating CIPN patients. Furthermore, this economic conclusion is tentative as we have not assessed long-term costs beyond 14 weeks, and if symptoms have not reverted to baseline beyond the 14-week assessment it is possible that function may have improved and cost-effectiveness may become more likely. The effect of acupuncture including pain reduction and possibly functional improvement (i.e. avoidance of falls and their associated healthcare costs) may well last beyond the study period, and these are important considerations in evaluating treatment effects in the future.

Lastly, a further important consideration is that cost-effectiveness is determined by the cost-effectiveness threshold and there is no pre-defined cost-effectiveness threshold for Hong Kong. We used the threshold reported by Woods et al.²⁵ as it provided a plausible estimate of health opportunity cost in Hong Kong. However it should be noted that further research would be of use to estimate appropriate cost-effectiveness thresholds for Hong Kong given the unique healthcare landscape and in order to account for decision making from different perspectives (e.g. healthcare provider, department of health, insurer etc.)³⁰. The choice of threshold will impact the results and it may be helpful for decision makers to use the CEAC to explore potential cost-effectiveness thresholds relevant to their specific decision making context.

Conclusion

This economic evaluation indicated that acupuncture alongside usual care for the management of CIPN, while effective for the management of pain and other neuropathic symptoms and improving quality of life, is unlikely to be a cost-effective use of healthcare resources when compared with a cost-effectiveness threshold based on opportunity costs elsewhere in the system.

Acknowledgements

This study was supported by a grant from the Health and Medical Research Fund (HMRF) of the Hong Kong Government (project ref. 12131801).

Conflict of Interest:

Authors declare no conflict of interest.

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Table 1 Unit costs of health care services

Resource item	Patient charge (HK\$)	Insurance charge (HK\$)	Source	Details
GP surgery visit	\$50	\$445	Hospital Authority	General clinic
GP home visit	\$80	\$445	Hospital Authority	General clinic
District nurse surgery visit	\$80	\$535	Hospital Authority	Community nursing service
District nurse home visit	\$80	\$535	Hospital Authority	Community nursing service
Oncology specialist visit	\$135 first visit, \$80 subsequent visits	\$1190	Hospital Authority	Specialist clinic
Hospital oncology clinic	\$96	\$895	Hospital Authority	Clinical oncology clinic
Psychologist	\$60	\$1730	Hospital Authority	Psychiatric day hospital
Physiotherapist	\$55	\$1730	Hospital Authority	Rehabilitation day hospital
Occupational health visit	\$55	\$1730	Hospital Authority	Rehabilitation day hospital
Dermatologist	\$135 first visit, \$80 subsequent visits	\$1190	Hospital Authority	Specialist clinic
Traditional Chinese medicine practitioner	\$50	\$445	Hospital Authority	General clinic
Other hospital departments: internal medication, blood taking	\$19	\$100	Hospital Authority	Hospital attendance for injection or dressing
Notes:				
1. Data was collected on contacts with healthcare services by telephone or email (reported below) but no costs are included in the analysis for these services as they are not charged for.				

Table 2 Resource use and costs

Healthcare	Resource use Mean (SD)		Patient cost Mean (SD)		Hospital cost Mean (SD)	
	Usual care	Acupunct ure	Usual care	Acupunctur e	Usual care	Acupunct ure
GP	0.49 (0.86)	0.98 (1.92)	24.42 (0.86)	48.86 (96.14)	217.33 (0)	434.89 (855.64)
GP (home)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
District nurse	0 (0)	0 (0)	0 (0)	0 (0)	0 (1.37)	0 (0)
District nurse (home)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Oncology hotline ¹	0 (0)	0.14 (0.51)	0 (0)	0 (0)	0 (0)	0 (0)
Oncology specialist	0.12 (0.39)	0.5 (1.21)	14.42 (0)	52.5 (115.76)	138.37 (4.05)	595 (1440.4)
Oncology specialist (home)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hospital oncology unit	1.51 (3.59)	1.5 (4.28)	145.12 (0.39)	144 (410.7)	1352.91 (0.15)	1342.5 (3828.92)
Psychologist/Psychiat rist	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Psychologist/Psychiat rist (home)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Physiotherapist	0.21 (1.37)	0.32 (1.07)	11.51 (0)	17.5 (59.04)	362.09 (42.78)	550.45 (1857.01)
Physiotherapist (home)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Other	2.02 (4.05)	2.56 (6.25)	98.84 (3.59)	102.98 (208.9)	98.84 (0)	102.98 (208.9)
Treatment (acupuncture) ²	-	-	0 (0)	4697.73 (589.24)	-	-
Prescription medication ³	-	-	1028.74 (0)	1194.32 (3132.55)	-	-
Non-prescription medication ³	-	-	789.35 (46.79)	959.82 (2794.78)	-	-
Travel ⁴	-	-	471.4 (345.1)	401 (518.84)	-	-
Food and drink ⁵	-	-	1631.98 (75.49)	952.5 (1236.83)	-	-
Other expenses ⁵	-	-	3702.14 (203.39)	4223.64 (15236.42)	-	-
Productivity loss (days) ⁶	50 (0)	55.11 (45.65)	15852.27 (380.73)	17789.77 (24003.07)	-	-

Notes:

¹ Oncology hotline is a free service;

² The treatment cost is assumed to fall to patients if implemented in practice (outside of trial setting);

³ These were reported as patient costs, no itemised prescription data was available;

⁴ The sum of out of pocket costs for taxis, public transport, fuel, additional miles and parking;

⁵ Cost data reported only;

⁶ Calculated using a human capital approach based on days out of work and associated income

Table 3 Cost-effectiveness analysis

Treatment group	Cost (HK\$) Mean (SD)	Incremental cost	QALYs Mean (SD)	Incremental QALYs	ICER (HK\$)/ QALY)
Health care provider perspective					
Usual care	\$3,286.16 (6009.04)		0.200 (0.022)		
Acupuncture	\$8,849.25 (6182.91)	\$5,563.09	0.209 (0.021)	0.009	\$616,965.62
Societal perspective					
Usual care	\$12,384.40 (19230.74)		0.200 (0.022)		
Acupuncture	\$19,815.03 (22955.75)	\$7,430.63	0.209 (0.029)	0.009	\$824,083.44
Patient perspective					
Usual care	\$7,919.19 (17636.65)		0.200 (0.022)		
Acupuncture	\$12,794.84 (17793.87)	\$4,875.65	0.209 (0.029)	0.009	\$540,727.56

QALY = Quality Adjusted Life Year. ICER = Incremental Cost Effectiveness Ratio.
 HK: Hong Kong

Table 4 Cost-effectiveness at reducing pain

Treatment group	Cost (HK\$) Mean	Incremental cost	Mean change in BPI score from baseline	Incremental change in BPI	ICER (HK\$/unit reduction BPI score)
14w change in pain severity					
Usual care	\$3,286.16		1.0		
Acupuncture	\$8,849.25	\$5,563.09	-0.8	-1.8	\$3,090.60
14w change in pain interference					
Usual care	\$3,286.16		0.8		
Acupuncture	\$8,849.25	\$5,563.09	-0.1	-0.9	\$6,181.21
8w change in pain severity					
Usual care	\$1,877.80		0.5		
Acupuncture	\$5,056.71	\$3,178.91	-1.3	-1.8	\$1,766.06
8w change in pain interference					
Usual care	\$1,877.80		0.5		
Acupuncture	\$5,056.71	\$3,178.91	-1	-1.5	\$2,119.27

BPI: Brief Pain Inventory; w: week; HK: Hong Kong

Table 5: Sensitivity analysis – cost-effectiveness results

Treatment Group	Cost (HK\$) Mean (SD)	Incremental cost	QALY Mean (SD)	Incremental QALY	ICER (HK\$/QALY)
Health care provider perspective: complete case analysis					
Usual care n=39	3597.82 (6230.45)		0.1997 (0.03)		
Acupuncture n=42	9134.93 (6169.93)	5537.11	0.2087 (0.022)	0.0089	618,280.5
Health care provider perspective: 20% increase in costs					
Usual care n=43	3943.40 (7210.85)		0.2003 (0.029)		
Acupuncture n=44	10619.1 (7419.49)	6675.70	0.2093 (0.022)	0.0090	740,359.50
Health care provider perspective: 20% decrease in costs					
Usual care n=43	2628.93 (4807.24)		0.2003 (0.029)		
Acupuncture n=44	7079.40 (4946.33)	4450.47	0.2093 (0.022)	0.0090	493,573.03
Societal perspective: 20% increase in costs					
Usual care n=43	14861.28 (23076.89)		0.2003 (0.029)		
Acupuncture n=44	23778.03 (27546.9)	8916.75	0.2093 (0.022)	0.0090	988,899.94
Societal perspective: 20% decrease in costs					
Usual care n=43	9907.52 (15384.59)		0.2003 (0.029)		
Acupuncture n=44	15852.02 (18364.6)	5944.50	0.2093 (0.022)	0.0090	659,266.75
Patient perspective: Prescription medication cost for whole duration prescribed					
Usual care n=43	7909.76 (17626.42)		0.2003 (0.029)		
Acupuncture n=44	12718.82 (17820.43)	4809.05	0.2093 (0.022)	0.0090	533,341.81
Patient perspective: Treatment (acupuncture) paid for by insurer or public provider					
Usual care n=43	7919.19 (17636.65)		0.2003 (0.029)		
Acupuncture n=44	8097.11 (17738.34)	177.93	0.2093 (0.022)	0.0090	19,732.82
14w change in FACT/GOG NtxS (from baseline)					
Usual care	\$3,286.16		0.96		
Acupuncture	\$8,849.25	\$5,563.09	3.23	2.27	\$2,446.73
8w change in FACT/GOG NtxS (from baseline)					
Usual care	\$1,877.80		1.73		
Acupuncture	\$5,056.71	\$3,178.91	4.90	3.16	\$1,005.98

HK: Hong Kong; w: week. QALY = Quality Adjusted Life Year. ICER = Incremental Cost Effectiveness Ratio.