The cost-effectiveness of recommended adjunctive interventions for knee osteoarthritis: Results from a computer simulation model

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ARTICLE INFO

Keywords:
Knee osteoarthritis
Cost-effectiveness analysis
Simulation modelling
Adjunctive interventions

ABSTRACT

Objective: To estimate the potential lifetime health gains, healthcare costs, and cost-effectiveness of recommended adjunctive treatments for knee osteoarthritis delivered in addition to established core treatments, relative to core treatment only, from the perspective of the New Zealand (NZ) healthcare sector.

Design: Recommended adjunctive knee osteoarthritis treatments were identified in clinical practice guidelines. Evidence of effectiveness was sourced from existing systematic reviews and meta-analyses. Treatment costs were calculated by applying local reference prices to estimated resource use. We used a validated computer simulation model of the impacts of knee osteoarthritis to estimate the cost-effectiveness of each adjunctive treatment at willingness-to-pay thresholds of one (primary), two, and three times per-capita GDP ($NZ2 300).

Results: Data were collected on nine recommended adjunctive treatments: aquatic-based exercise, heat therapy, massage therapy, walking cane, cognitive behavioural therapy (CBT), topical non-steroidal anti-inflammatory drugs (NSAIDs), oral NSAIDs, intra-articular corticosteroids, and duloxetine. Relative to core treatments only, walking cane and heat therapy were cost-saving and provided greater QALYs; aquatic exercise and intra-articular corticosteroids were also cost-effective at all WTP thresholds. Topical NSAIDs and CBT were cost-effective only at higher WTP thresholds, while duloxetine, massage therapy, and oral NSAIDs were not cost-effective at any relevant threshold. Results were generally robust to varying modelling assumptions, although topical and oral NSAIDs and CBT became cost-effective in some scenarios.

Conclusions: Delivering high-value, low-cost adjunctive interventions for knee osteoarthritis, alongside recommended core treatment, could deliver substantial health gains at low cost to the health system.

1. Introduction

Clinical practice guidelines for the management of knee osteoarthritis (OA) consistently recommend patient education and self-management, exercise therapy, and weight management as core first-line treatments [1–4]. These interventions are effective, low to moderate cost, and have minimal risk of adverse events, making them high-value care options. A range of adjunctive treatment options are also recommended for patients whose symptoms are not optimally alleviated by these first-line treatments and where adjunctive treatments may provide a further therapeutic window for core first-line treatments to be delivered. However, there is less consensus regarding these second-line or adjunctive treatments, as evidenced by variability in recommendations between guidelines, and little guidance is available as to how they should be prioritised.

Given limited resources and increasing demand for healthcare, the prioritisation of potential alternative treatments should be informed, at least in part, by their cost-effectiveness. For a fixed healthcare budget, prioritisation of the most cost-effective treatments provides the greatest possible health gains to the population. To allow meaningful comparison across different health conditions and treatment options, estimation of cost-effectiveness should be based on cost-utility analysis, comparing the quality-adjusted life years (QALYs) gained in the target population with the incremental costs of the intervention [5]. Given the chronic nature of OA, cost-effectiveness analysis (CEA) should consider a long time horizon, preferably over the lifetime of those receiving treatment.

There is limited or no published cost-effectiveness data for many recommended treatments for OA [4,6,7]. In the absence of primary data on cost-effectiveness, computer simulation modelling can be used to combine available data on treatment effectiveness and adverse events, preferably from randomised controlled trials, with other sources of data.
on patient trajectories and the healthcare resources required for different treatments, to estimate treatment cost-effectiveness [8–10]. Even where trial-based cost-effectiveness data are available, simulation modelling can extend the analysis beyond the typically limited trial follow-up period and can provide results tailored to a specific policy context (e.g. by adjusting for differing target populations, resource availability, competing treatment pathways, or treatment costs). Simulation modelling is increasingly being used to model the economic impact and cost-effectiveness of interventions across many health conditions [11], including OA [12–15].

The aim of this study was to use a previously validated computer simulation model [12] to estimate the potential lifetime incremental health gains, costs, and cost-effectiveness of recommended adjunctive treatments for knee OA, delivered in addition to recommended core treatments, compared with core treatments only, in the context of the New Zealand (NZ) healthcare system.

2. Methods

2.1. Simulation model

We used the NZ-MOA model, a validated state-transition micro-simulation model of the disease course, healthcare costs, and health-related quality of life (HRQoL) impacts of knee OA [12]. The model has previously been used to estimate the lifetime health losses attributable to knee OA [12], the future healthcare costs and demand for joint replacement surgery associated with increasing OA prevalence due to the aging population and increasing obesity rates [16], and the lifetime cost-effectiveness of physical therapy interventions for knee OA [17].

In brief, the model simulates the disease course of knee OA, including radiographic disease incidence and progression (defined by Kellgren-Lawrence [K-L] grade), fluctuation (with gradual progression) of disease symptoms and HRQoL losses, and treatment pathways and their costs and effects. Model input data are drawn from large-scale national population datasets [18,19] and published intervention effectiveness results. By running the same simulated cohort through different hypothetical treatment pathways, the incremental QALYs and costs of treatments can be estimated. Details of the model structure and input parameters have been provided previously [12].

To estimate costs and QALYs at the whole health system level, we defined a cohort representative of the entire 2013 NZ adult population aged 35–99 years, based on the 2013 NZ Census [18], and modelled outcomes over the remaining lifetime of the cohort. Individuals with knee pain together with radiographic knee OA (either at model baseline or developing incident knee OA during the simulated life course) were assumed to follow a treatment pathway consisting of (1) core first-line treatments (patient education, land-based exercise therapy, weight loss if overweight or obese); (2) one of the recommended adjunctive interventions, if symptoms persisted after receiving core first-line treatments; and (3) total knee replacement surgery, if symptoms continued to worsen and K-L grade progressed to grade 3 or higher. The comparison treatment pathway, through which the same cohort was run to estimate the incremental effects of each adjunctive treatment, consisted of items (1) and (3) only. The pair of treatment pathways was repeated for each recommended adjunctive treatment (see Fig. A1, Appendix A).

The impact of uncertainty in input parameters was assessed by probabilistic sensitivity analysis (PSA). PSA involves drawing multiple sets of random input parameter values from the estimated distribution of true parameter values, and re-running the model with each set of input values to derive measures of uncertainty in the resulting model outputs [20,21]. We used, for each adjunctive treatment, 1000 sets of input values from the estimated parameter distributions for treatment effects, costs, and rates of withdrawal from treatment and of serious adverse events. For each set of parameter values, we ran the model for a cohort of 100 000 individuals.

2.2. Data sources

We included treatments recommended as either ‘optional adjunctive management’ or ‘advanced pharmacological attempts’ in the clinical algorithm of the Royal Australian College of General Practitioners’ (RACGP) Guideline for the management of knee and hip osteoarthritis, 2nd edition [1]. This was the most recently updated clinical practice guideline at the time of project conception, included a comprehensive systematic review evidence supplement, and has strong relevance to the NZ healthcare system. We selected interventions from the algorithm as this is the resource most widely used by clinicians [22]. We searched the original studies cited in the systematic review conducted to inform the Guideline to obtain model input data. All identified studies and the data collected from them are reported in Appendix C.

We extracted all reported data on treatment effects measured by the generic SF-12 and SF-36 HRQoL instruments. These were combined following the Cochrane Collaboration guidelines for meta-analyses [23], to estimate the treatment effect (and uncertainty) on each health domain described by the instruments. For treatments for which SF-12 or SF-36 estimates were not available, effects reported using the WOMAC osteoarthritis index were extracted and transformed into the required model input parameters using the relationship between WOMAC and SF-12/SF-36 effects derived from all included studies that reported on both measures (Table A2, Appendix A; Table C2, Appendix C). The NZ-MOA model reduces the SF-12/SF-36 domains to the six dimensions of the SF-6D [12], from which utility values were calculated using widely-used UK population values [24].

Rates of treatment withdrawal due to minor adverse events or poor adherence were extracted from the Guideline systematic review, and assumed to be constant over time. Rates of serious adverse events resulting in hospitalisation or death were obtained from published systematic reviews. The HRQoL impacts of these events were sourced from published literature [25–27]. Costs of treatment for serious adverse events were derived from NZ public health system cost weights [28].

Costs were considered from the perspective of the NZ healthcare system. The healthcare resources required to deliver each treatment were estimated from the original study reports and valued using NZ-specific reference prices (in 2013 NZD; see Table A4, Appendix A) [29–31]. Where treatments were only shown to be effective during the period of utilization, we assumed continual utilization (and thus constant treatment cost) to maintain treatment effect. Where there was evidence that effects persisted beyond the period during which the treatment was applied, we spread treatment costs over the longest period for which there was evidence of effectiveness (e.g., if a 12-week course of treatment was shown to still be effective at 6-month follow-up, we assumed the 12-week treatment cost would be applied twice in every year to maintain treatment effect).

Input parameter distributions for the PSA were chosen based on published recommendations [20]. Treatment effect estimates were drawn from a multivariate normal distribution with mean and variance given by the point estimates and covariance matrix of the effect estimates from the meta-analysis for each intervention. Cost input values were drawn from a gamma distribution, with parameters calculated from the mean and variance of costs across all included studies for each intervention. Rates of withdrawal from treatment were drawn from a beta distribution, with parameters calculated from reported withdrawals in the RACGP systematic review. Serious adverse event rates were drawn from a log-normal distribution for the relative risk of serious adverse events (per person-year on the treatment), from the relevant systematic reviews.
Future costs and QALYs were discounted at a rate of 3.5% per annum, as recommended by the NZ Pharmaceutical Management Agency (PHARMAC) for CEA in NZ [32].

2.3. Outcome measures

The primary outcomes were the lifetime change in population QALYs and healthcare costs, cost-effectiveness ratios, and net monetary benefits (NMB) of each recommended adjunctive intervention. The NMB is a measure of the overall cost-effectiveness of a healthcare intervention, defined as the value of the QALY gains, at a given monetary value (willingness-to-pay [WTP]) per QALY, minus the net cost of the intervention. A positive NMB indicates a ‘cost-effective’ treatment at the given WTP threshold.

QALY gains, costs, and NMBs were calculated for each intervention provided in addition to core treatments, relative to the comparator of core treatments only. Incremental cost-effectiveness ratios (ICERs) were calculated sequentially, for each intervention in order of increasing net costs. Interventions that were dominated (having higher costs and lower QALYs than another intervention) or extendedly-dominated (higher costs and lower QALYs than a combination of other interventions) were excluded from ICER calculations (i.e. each intervention was compared to the next-most-expensive non-dominated alternative) [33].

We considered cost-effectiveness, for the calculation of NMBs and interpretation of ICERs, at policy-relevant thresholds of one, two, and three-times gross domestic product (GDP) per capita [34]; one times GDP per capita (NZ $52 300 ≈ US $42 900 in 2013) was our primary cost-effectiveness threshold.

QALYs, costs, and NMBs were calculated for each PSA model run, and reported as point estimates (mean effect across the 1000 runs) and 90% uncertainty intervals (5th and 95th percentiles of effect estimates). Cost-effectiveness acceptability curves (CEACs) were calculated for each intervention to assess uncertainty in the findings. The 1000 effect estimates for each intervention were also plotted on a cost-effectiveness plane to visually examine uncertainty in estimated outcomes.

2.4. Sensitivity analyses

To evaluate the sensitivity of our results to modelling assumptions, we undertook one-way sensitivity analyses of key model inputs and assumptions. First, we varied the discount rate applied to future costs and QALYs to 0% and to 5% per annum, as recommended by PHARMAC [32].

As no NZ-specific SF-6D utility value set is available, our primary analyses used a UK population value set [24], the most widely-used SF-6D value set internationally. As these values may not represent local health preferences, we considered as alternatives an Australian population SF-6D value set [35] and mapping of WOMAC pain outcomes to NZ-specific EQ-5D-3L utility values [36,37].

For pharmacological interventions for which no evidence on serious adverse events was available (topical non-steroidal anti-inflammatory drugs (NSAIDs), intra-articular corticosteroids, and duloxetine), we conducted sensitivity analyses assuming the ratio of serious adverse events to all withdrawals due to adverse events would be the same as for oral NSAIDs; for oral NSAIDs, we conducted sensitivity analysis assuming no increased risk of serious adverse events. For oral NSAIDs only, we also conducted an additional sensitivity analysis assuming the baseline risk, but varying the impact of serious adverse events by ±50% to reflect uncertainty in these impacts. Serious adverse event scenarios were not considered for non-pharmacological interventions.

Lastly, we assessed sensitivity to treatment cost estimates by varying the assumptions on treatment dosage, frequency, and duration used to derive these costs. Detailed descriptions of all one-way sensitivity analysis assumptions and parameters used are provided in Table A6 in Appendix A.

3. Results

3.1. Recommended treatments

Nine ‘optional adjunctive management’ options and two ‘advanced pharmacological attempts’ were recommended in the RACGP Guideline algorithm: aquatic-based exercise, heat therapy, massage therapy, manual therapy (manipulation and mobilisation), assistive walking devices (walking cane), cognitive behavioural therapy (CBT), transcutaneous electrical nerve stimulation (TENS), NSAIDs (oral and topical formulations); and intra-articular corticosteroids and duloxetine. For intra-articular corticosteroids, oral and topical NSAIDs, and heat therapy, no suitable SF-12 or SF-36 data were available, so effectiveness input data were derived from WOMAC effect estimates. As no suitable outcomes data were reported in studies identified by the Guideline for manual therapy or TENS, these two treatments were excluded from further analyses. Three further ‘conditionally recommended’ options – stationary cycling, yoga, and combination weight management and exercise programmes – were not considered separately in our analysis as they were assumed to be included in the core treatments (land-based exercise, weight management) provided to all OA patients in the model. The GRADE ratings reported for quality of evidence ranged from ‘Very low’ (intra-articular corticosteroids, heat therapy) to ‘Moderate’ (oral and topical NSAIDs, duloxetine).

3.2. Model input parameters

All adjunctive interventions had positive treatment effects as measured by SF-6D utility values (Table 1). The costs of treatment varied widely. Most treatments had annual rates of patient withdrawal or discontinuation of between 14% and 25%, although these estimates had wide uncertainty intervals for several interventions due to limited data.

Evidence of serious adverse events was found only for oral NSAIDs. These were associated with increased risk of vascular events (absolute relative risk 2.4 events per 1000 patients per year, including 1.4 fatal events), heart failure (2.8), and upper gastrointestinal complications (3.2) [38].

### Table 1

| Adjunctive intervention                   | Incremental utility gain | Treatment cost (NZD) | Withdrawal from treatment |
|------------------------------------------|--------------------------|----------------------|----------------------------|
| Walking cane                             | 0.035                    | $150 (97–214)*       | 18% (1–44)                |
| (0.017–0.052)                            |                          |                      |                            |
| Aquatic exercise                         | 0.023                    | $458 (251–725)       | 19% (16–21)               |
| (0.015–0.031)                            |                          |                      |                            |
| Duloxetine                               | 0.019                    | $2 151               | 41% (34–49)               |
| (0.011–0.027)                            |                          |                      |                            |
| Oral NSAIDs                              | 0.018                    | $59 (34–97)          | 24% (22–25)               |
| (0.014–0.023)                            |                          |                      |                            |
| Topical NSAIDs                           | 0.018                    | $881 (354–1 642)     | 25% (22–28)               |
| (0.012–0.024)                            |                          |                      |                            |
| Massage therapy                          | 0.015                    | $4 680               | 14% (5–25)                |
| (–0.005 to 0.035)                        |                          |                      |                            |
| Intra-articular corticosteroids and       | 0.014                    | $366 (327–443)       | 2% (0–6)                  |
| duloxetine                               | (0.004–0.024)            |                      |                            |
| Heat therapy                             | 0.013                    | $50 (19–96)          | 20% (4–43)                |
| (–0.001 to 0.028)                        |                          |                      |                            |
| CBT                                      | 0.006                    | $400 (52–1 097)      | 4% (2–8)                  |
| (–0.015 to 0.026)                        |                          |                      |                            |

Cells report mean (90% uncertainty interval) of parameter input value. For utility gain, the full effect is assumed to occur in the first year of treatment, and to be maintained thereafter for as long as the patient remains on the treatment. For costs, the reported annual cost is applied in each year on the treatment, and to be maintained thereafter for as long as the patient remains on the treatment. With the exception of walking cane modelled as a one-off cost only. Treatment withdrawals are assumed to be constant at the reported annual rate.

CBT: Cognitive behavioural therapy; NSAIDs: Non-steroidal anti-inflammatory drugs; NZD: New Zealand dollars.

* One-off cost only.
3.3. Lifetime incremental health gains, costs, and cost-effectiveness

Walking cane and heat therapy dominated core treatments only (i.e., higher population QALYs and lower costs, the latter due to improvements in symptoms necessitating slightly reduced rates of progression to joint replacement surgery). Oral NSAIDs resulted in reduced lifetime QALYs due to rare but serious, and occasionally fatal, adverse events. All other interventions resulted in positive lifetime health gains at increased costs due to rare but serious, and occasionally fatal, adverse events. All other interventions were not cost-effective relative to core treatments only due to the impact of adverse events on lifetime QALYs. Heat therapy was highly cost-effective (ICER $4064 compared to oral NSAIDs), aquatic exercise was marginally cost-effective compared to heat therapy, but extendedly-dominated by intra-articular corticosteroids, and intra-articular corticosteroids were cost-effective relative to heat therapy (ICER $39,251). All other interventions were dominated by heat therapy or intra-articular corticosteroids.

The CEACs for all interventions are presented in Fig. 1. Among the non-pharmacological treatments (Fig. 1A), walking cane, aquatic exercise, and heat therapy had probabilities of cost-effectiveness compared to core treatments only above 80% at all relevant WTP levels. CBT reached probability of cost-effectiveness of around 50% at a WTP of 2x GDP/
capita and higher, while massage therapy had low probability of being cost-effective at all relevant WTP levels.

Among the pharmacological therapies (Fig. 1B), intra-articular corticosteroids had a high probability of being cost-effective (>80%) at all relevant WTP levels, and topical NSAIDs at the 2x GDP/capita WTP level and above. Oral NSAIDs and duloxetine had low probability of being cost-effective (<25%) at all WTP levels.

The cost-effectiveness plane showing results from all PSA model runs is shown in Fig. B1 in Appendix B. Uncertainty in lifetime treatment effectiveness was highest for massage therapy (not shown), CBT, intra-articular corticosteroids, walking cane, and heat therapy. Incremental treatment costs were reasonably precisely estimated with the exceptions of massage therapy and CBT. Treatment effects and costs for oral NSAIDs were precisely estimated, but estimates of lifetime population outcomes were affected by uncertainty about the risk of serious adverse events.

3.4. Sensitivity analyses

One-way sensitivity analysis results are shown in the Tornado plot in Fig. 2. Walking cane and heat therapy were highly cost-effective in all scenarios. Intra-articular corticosteroids and aquatic exercise were also cost-effective in all scenarios, and below the 1x GDP/capita level in all but the high-cost scenario for corticosteroids and the WOMAC-derived utility scenario for aquatic exercise.

The findings for topical NSAIDs and CBT were the most sensitive to input parameter assumptions. Topical NSAIDs were more highly cost-effective (ICER < 1x GDP/capita) with the Australian SF-6D value set or the low-cost scenario, but was dominated by core treatments only when assuming serious adverse event risk proportional to that for oral NSAIDs. Estimates for CBT were highly sensitive to input assumptions on utility instrument and costs, due to the small and uncertain treatment effect parameters.

Duloxetine and massage were not cost-effective at any threshold below 3x GDP/capita in any scenarios. Oral NSAIDs (not shown in Fig. 2) resulted in positive QALY gains and dominated core treatments only using the Australian SF-6D value set or assuming no risk of serious adverse events, but had negative QALY gains and were not cost-effective in all other scenarios. Varying the discount rate made little difference to the cost-effectiveness of any interventions.

4. Discussion

In this CEA of recommended adjunctive and advanced pharmacologic treatments for knee OA informed by Australian guidelines, we found several such interventions – walking cane, heat therapy, aquatic exercise, and intra-articular corticosteroids – to be cost-effective from the health sector perspective, compared to recommended core treatments only, at the population level. Other recommended interventions were found to be not cost-effective, due to high costs (massage, topical NSAIDs, duloxetine), small and uncertain treatment effect (CBT), or risk of serious adverse events (oral NSAIDs).

Several high-quality clinical practice guidelines for the management of knee OA have been published recently [1–4]. While these have been generally consistent in their core recommendations – education, support for physical activity and exercise, dietary weight management if appropriate – variation in recommendations for additional, adjunctive, or
second-line treatments can make interpretation and application of the guidelines difficult for end-users. For healthcare policy-makers, funders, and providers, economic evaluation can help to inform decision-making, particularly for interventions with ‘conditional’ or mixed recommendations. We found wide variation across recommended adjunctive interventions in their cost-effectiveness from the health system perspective, which may inform health policy, funding, or clinical decision-making when choosing between these interventions.

For example, walking cane (either conditionally or strongly recommended in all recent guidelines [1–4]) and heat therapy (mixed recommendations) are both low-cost, easily accessible self-management options with minimal risk of serious harms; our modelling suggests they should be considered as potential high-value adjunctive options (despite the low quality of available evidence). Although both the RACGP and ACR guideline panels made commentaries about the low quality of evidence for massage therapy and its potential high cost for consumers, they reached different recommendations: conditionally recommended in the RACGP guideline, but conditionally recommended against in the ACR guideline. Similarly, intra-articular corticosteroids were conditionally recommended in the RACGP guidelines, but strongly recommended in the ACR guideline. The differences in final recommendations may suggest variance in contextual interpretation of the evidence by the guideline panels and slightly different development methods (e.g. the ACR panel also considered systematic reviews of observational studies in some circumstances). In our analysis, massage was not found to be cost-effective due to high costs, while intra-articular corticosteroids were cost-effective.

CBT is conditionally recommended by most guidelines, but was not found to be cost-effective and had extremely wide uncertainty intervals due to limited primary data in OA. Certain people may respond better to CBT than do others [39], suggesting that it remains important to tailor care at the individual level to achieve cost-effectiveness. Oral NSAIDs are recommended for pharmacologic pain relief ahead of options such as paracetamol or opioid analgesics [1,2], and strongly recommended by the most recent ACR guideline [3], but were not found to be cost-effective in this analysis due to rates and consequences of serious adverse events. They may be assessed more favourably in individual patients at low risk of cardiovascular and gastrointestinal events, with active monitoring for potential adverse events and when co-prescribed with a proton-pump inhibitor or the use of a COX-2 inhibitor. Our sensitivity analyses indicated that oral NSAIDs would be both effective and cost-effective at lower adverse event risk levels.

Strengths of this study include the use of a validated computer simulation model, bringing together comprehensive national-level population data, up-to-date clinical practice guideline recommendations, and the best available treatment effect evidence from systematic reviews and meta-analyses, to provide relevant, rigorous, and timely information on treatment cost-effectiveness. This is the first study to do this for a range of recommended pharmacologic and non-pharmacologic treatments under a consistent modelling structure, with a long (lifetime) time horizon to reflect the chronic nature of OA progression.

The study has limitations relating to the availability and quality of input data. The most recent available population data at the time of model development were from the 2013 NZ Census; updating the model to incorporate more recent data remains an area for future research. Despite the use of systematic review evidence to inform treatment input data, evidence for several treatments was still based on only limited data, often of low quality [1]. For four recommended interventions (intra-articular corticosteroids, oral and topical NSAIDs, and heat therapy), only WOMAC outcomes were available, so mapping was required to estimate SF-12/SF-36 effects to inform modelling. Estimates of health gains for these interventions should therefore be treated with some caution; however, with the partial exception of oral NSAIDs (due to the impact of health losses associated with serious adverse events), the results were robust to variations in the derivation of health utility values, giving us confidence in these findings. For a further two interventions (manual therapy and TENS), no suitable input data using the most widely-used disease-specific (WOMAC) or generic (SF-12/SF-36) HRQoL instruments were found, and cost-effectiveness could not be estimated.

Cost-effectiveness estimates were limited by a lack of primary data collection as well as contextual variation in reference prices and healthcare resources, although allowing for relatively wide uncertainty in resource use and costs did not change our conclusions for most treatments. Variation in medicine pricing structures, however, was not considered in our analyses. In NZ, PHARMAC subsidises and negotiates prices for selected medicines; oral NSAIDs and intra-articular corticosteroids are subsidised medicines, whereas topical NSAIDs and duloxetine are not. If these were to be subsidised, the unit prices may be substantially lower than assumed in this study, which for topical NSAIDs in particular may result in a meaningful improvement in estimated cost-effectiveness (i.e. to become cost-effective at the policy-relevant one times GDP per capita threshold).

Due to a lack of suitable input data, our modelling did not allow for downstream cost savings resulting from reduced consumption of other healthcare (other than eventual need for TKR), which may underestimate the true cost-effectiveness of these treatments. A small number of previous studies have shown that the cost savings from provision of effective early interventions for OA may be substantial [17,31,40]. We also considered only health sector costs, so our results are likely to understate the cost-effectiveness of these treatments from the broader societal perspective.

Generalisability of cost-effectiveness between countries is limited by several factors, including disease epidemiology, clinical practice patterns, policy and resourcing variability, relative prices, and population health preferences. [41] While our results should therefore be interpreted only in the context of the NZ healthcare system, we believe they are likely to be broadly generalisable to other publicly-funded healthcare systems in high-income countries. In particular, several of the treatments found to be cost-effective – walking cane, heat therapy, topical NSAIDs (in some analyses) – require limited healthcare workforce resources and readily-available equipment, consumables, or medications, so are likely to be similarly cost-effective in varying healthcare settings. We used widely-accepted UK population SF-6D utility values; using Australian population values instead improved the estimated cost-effectiveness of most treatments.

Cost-effectiveness findings may also differ according to the guidelines used to provide input data. While all recent guidelines used up-to-date systematic reviews to inform recommendations, differences in search strategies, inclusion criteria, and thresholds for quality of included evidence may change the data used to derive model inputs and therefore the cost-effectiveness of some treatments. Differences between guideline panels in interpretation of the evidence also affects which treatments were recommended and would therefore be included in our modelling. Replicating this analysis across different clinical practice guidelines and meta-synthesising the results remains an important area for further research.

There is limited prior research on the cost-effectiveness of adjunctive treatments for knee OA. A systematic review conducted in 2010 [6] and a National Institute for Health and Care Excellence (NICE) clinical guideline and literature review in 2014 [4] each found only one cost-effectiveness study of any interventions considered here (of aquatic exercise and oral NSAIDs, respectively) [40,42]. More recent studies have looked at the cost-effectiveness of different oral NSAID options [43] and manual therapy [44]. No prior studies have compared guideline-recommended treatment options under a common model structure and with consistent methods for identification, extraction, and derivation of data on treatment effectiveness and costs.

The dearth of cost-effectiveness evidence for adjunctive OA interventions limits the ability of funders, policy-makers, clinicians, and patients to make informed decisions on the optimal allocation of healthcare spending for the management of OA. We urge researchers conducting clinical trials of OA interventions to collect and report
patient-reported generic HRQoL outcome measures, preferably with preference-based health utility values, and comprehensive healthcare resource use data to inform economic evaluations. Where feasible and appropriate, trial-based CEA should be considered.

5. Conclusion

Delivering high-value, low-cost adjunctive treatments for knee OA, such as walking cane, heat therapy, aquatic-based exercise, and corticosteroid injections, alongside recommended core long-term management, has the potential to be cost-effective, or even cost-saving, in the NZ healthcare system. However, more high-quality RCTs, particularly with the collection of health utility and healthcare resource use data, are needed to provide a stronger evidence base for many recommended interventions.

Author contributions

JHA led conception and design of the study. All authors contributed to the acquisition and interpretation of data. RW led the data analysis and modelling and drafted the manuscript. All authors critically revised the manuscript for important intellectual content and approved the final version to be submitted.

Role of the funding source

This study was funded by the Health Research Council of New Zealand (Project grant 15/263). The funding agency played no role in study design, conduct, interpretation, reporting, or the decision to submit for publication.

Declaration of competing interest

AMB was on the development group for the RACGP Guideline. The other authors declare no relevant competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eclarot.2020.100123.

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