

Title: Protocol for economic evaluation alongside the IMPLEMENT cluster randomised controlled trial

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Abstract

Background. The recent development and publication of evidence-based clinical practice guidelines (CPGs) for acute low-back pain (LBP) has resulted in evidence-based recommendations that, if implemented, have the potential to improve the quality and safety of care for acute LBP. While a strategy has been specified for dissemination of the CPG for acute LBP in Australia, there is no accompanying plan for active implementation. Evidence regarding the cost-effectiveness of active implementation of CPGs for acute LBP is sparse. The IMPLEMENT study will consider the incremental benefits and costs of progressing beyond development and dissemination to implementation.

Methods/design. Cost-effectiveness and cost-utility analyses alongside the IMPLEMENT cluster randomised controlled trial (C-RCT) from a societal perspective to quantify the additional costs (savings) and health gains associated with a targeted implementation strategy as compared with access to the CPG via dissemination only.

Discussion. The protocol provided here registers our intent to conduct an economic evaluation alongside the IMPLEMENT study, facilitates peer-review of proposed methods and provides a transparent statement of planned analyses.

Trial registration. Australian New Zealand Clinical Trials Registry ACTRN012606000098538

Background

The IMPLEMENT Study

The recent development and publication of evidence-based clinical practice guidelines (CPGs) for acute low-back pain (LBP) has resulted in evidence-based recommendations that, if implemented, have the potential to improve the quality and safety of care for acute LBP [1]. While a strategy has been specified for dissemination of the CPG for acute LBP in Australia, there is as yet no accompanying plan for active implementation. The IMPLEMENT study will consider the incremental benefits and costs of progressing beyond development and dissemination to implementation and has the following objectives:

1. To develop a targeted strategy for implementing CPG for acute LBP into Australian general practice,
2. To test the effectiveness of the strategy for implementing the CPG for acute LBP, with respect to both general practitioners' practice and patient outcomes by conducting a cluster randomised controlled trial (C-RCT), and
3. To determine the cost effectiveness of the developed strategy as compared to current practice.

The purpose of the present paper is to describe methods for the cost effectiveness analysis alongside the C-RCT. Detailed descriptions of methods for development of the targeted implementation strategy and design of the C-RCT in the IMPLEMENT study are given elsewhere [2].

Economics of Implementation

It is now well established that development and dissemination of CPGs will not necessarily produce improvements in clinical practice [3]. Clinical practice has proved remarkably resilient to recommendations for practice change embedded in a CPG even where the gap between current and best practice care equates to a clinically significant difference in patient outcomes [3]. Where development and dissemination of a CPG requires substantial investment and where further expenditure on implementation might be required to effect any change in practice [4], there is a clear imperative to understand the cost effectiveness of competing strategies for practice change.

Despite this imperative, a recent review of 63 economic evaluations and cost analyses conducted alongside rigorous experimental studies of guideline implementation strategies and published between 1966 and 1998 concluded that the available economic evidence was lacking in methodological rigour and often drew conclusions that 'must clearly be treated with suspicion' (p116) [4]. A significant number of cost effectiveness analyses of guideline implementation strategies have been published in the subsequent period from 1998 to present [5-9]. Of these, just one study directly considered the effectiveness and efficiency of strategies for the implementation of a CPG for non-specific LBP. Hoeijenbos et al [9] conducted a cost-utility analysis alongside a C-RCT comparing active implementation plus standard dissemination of the Royal Dutch Physiotherapy Association guideline for non-specific LBP against standard dissemination alone in a sample of 113 physiotherapists and 483 patients drawn from 68 practices [10]. The active implementation strategy in the Dutch trial consisted of an initial training session with presentation and discussion of the guideline plus 'special skills' practice, and a follow-up session four weeks later to discuss experience or problems identified while practicing according to the guideline. Standard dissemination consisted of mail distribution of the guideline together with self-evaluation forms to assess whether current management was consistent with the guideline, additional materials including forms designed to facilitate peer-to-peer discussion and a copy of the Quebec Back Pain Disability Scale. Physiotherapists in both arms of the trial may also have been aware of discussion around the development of the guideline in local professional journals.

Hoeijenbos et al [9] calculated the incremental treatment cost of active implementation over standard dissemination at 366 euros per physiotherapist for roll-out of the active implementation strategy to 50% of the 12,687 physiotherapists working in primary care in the Netherlands. Total healthcare utilisation reported at 6 week follow-up was significantly lower for patients in the intervention arm (mean=€125, SD=€91) than for patients in the control group (mean=€145, SD=€95, $p=0.026$). Given treatment of a sufficient number of patients per physiotherapist, the incremental treatment cost associated with active implementation might well be recovered through savings in healthcare utilisation in the initial 6 weeks of follow-up. However, the observed savings in healthcare utilisation in the initial 6 weeks of follow-up could

not be attributed to the intervention because randomisation of physiotherapists per practice failed to insure against pre-existing between-group differences in patient characteristics. EQ5D health-related quality of life scores for the intervention group at baseline (mean=0.6730, SD=0.2042) were significantly higher than for the control group (mean=0.6134, SD=0.2661, $p=0.006$), with much of this difference attributable to a difference on the self-care dimension of the EQ5D in favour of the intervention group. Hoeijenbos et al [9] conclude that “it is very likely that the extended implementation strategy incurs extra costs without producing health gains, hence it is very likely to be not cost-effective” (p93). While controlling for observed differences in quality of life at baseline would be unlikely to alter this conclusion, it is possible that between-group differences at baseline were also present in one or more *unobserved* patient characteristics.

While the principles of economic evaluation for health care interventions are now well-established, the literature provides relatively few examples of well-executed economic evaluations of implementation strategies and the characteristics of CPGs raise several issues in the estimation and interpretation of cost effectiveness [11, 12]. The first such issue concerns the breadth of the evaluated intervention. Vale et al [4] suggest that strategies for implementation of a CPG should typically be considered as just one component of a broader strategy to promote best-practice care that would also include development and dissemination of the CPG. Vale et al [4] argue that, unless development and dissemination have themselves been demonstrated to be cost-effective as compared to current practice or where perspective or relevance justifies exclusion of development and dissemination, costs and benefits arising from a combined strategy of development plus dissemination plus implementation should be compared against costs and benefits arising from ‘no intervention’. There may, however, be many circumstances where development and dissemination of the CPG have already been undertaken and where their costs and benefits have already been reflected in current practice. In such circumstances, practice patterns in the absence of development and dissemination may not be observable. Moreover, the costs and effects associated with development and dissemination of the CPG cannot easily be ‘undone’ and therefore have little bearing on the subsequent policy decision as to implementation.

Recall that the costs of guideline development might be substantial and that development and dissemination alone might have relatively little impact on practice patterns [4]. Comparing a combined strategy of development plus dissemination plus implementation versus 'no intervention' would therefore be expected to yield very different results than would a comparison between the combined strategy and development plus dissemination. Each comparison may, however, be of assistance to policy makers in a particular policy context. Where development and dissemination have already taken place, the incremental costs and effects associated with implementation are likely to be of greatest interest. Where development and dissemination have not yet taken place, the incremental costs and benefits associated with the combined strategy of development plus dissemination plus implementation as compared to 'no intervention' will be of greatest use to policy-makers (together with incremental costs/effects of adding dissemination to development and of adding implementation to development plus dissemination).

The second issue concerns the potential for repeated or wider use of various components of the evaluated intervention. The information embedded in a CPG and an implementation strategy is 'non-rival' such that a single use does not diminish the quantity or quality of information available for subsequent use. The development of a CPG therefore amounts to a one-time investment in intellectual property that may find a repeated or wider use in other populations, for subsequent cohorts of practitioners, or in other contexts. Likewise, an implementation strategy may find repeated or wider use in other populations/contexts, for subsequent cohorts, or perhaps even for implementation of another CPG in another disease-area. Drummond et al [13] note the importance of identifying capital outlays (such as expenditure associated with development of a CPG or implementation strategy) that should be amortized over the lifetime of the asset. The question then arises: what is the lifetime of a CPG or implementation strategy? For non-rival assets bearing repeated and wider use over a sufficiently long life-time, the cost of a single use approaches zero. It may, however, be appropriate to include the entire cost of development if the usefulness of the CPG or implementation strategy is restricted to the disease-area, institutional context, practitioner group or patient population under study or if the usefulness of the CPG or implementation strategy has an expiration date contingent upon the current technology or the existing evidence-base.

Protocol for Economic Evaluation

A number of recent findings suggest that cost-effectiveness studies in the public domain may represent a biased sample of the population of economic evaluations [14, 15]. It is possible that this finding reflects a publication bias, whereby journal editors with a preference for clearly 'positive' or 'negative' results are responsible for a lack of 'intermediate' incremental cost-effectiveness ratios (ICERs) in the public domain. However, it seems more likely (and more consistent with the available data) that sponsors may be suppressing the publication of intermediate or negative results or that analysts are 'gaming' modelled evaluations and 'mining' trial data to meet a target cost effectiveness ratio [15]. Bell et al [14] suggest that registering all economic evaluations prior to their commencement may provide one means of limiting publication bias and/or the suppression of unfavourable results. However, closer scrutiny of methods employed by analysts may be required to provide a disincentive for 'gaming' or 'mining' analyses to meet a target cost effectiveness ratio. In the past, close scrutiny has been frustrated by a failure to publish a sufficiently detailed description of methods and analyses to permit critical appraisal.

Published trial protocols typically include a section headed 'economic analyses' whenever such analyses are planned but the description of the proposed economic evaluation alongside the trial is often insufficiently detailed to achieve the purpose of a protocol. Without detail, it is not possible to distinguish planned analyses from post-hoc 'mining' or 'gaming' and analysts can freely substitute between outcomes (eg. lower the 'response' required to be classified as a 'responder'), extend the time-horizon (eg. project differences at trial-end out to full life-expectancy) and/or revise the unit cost attached to particular categories of resource use (eg. value volunteer time at the marginal overtime wage rate instead of at zero in the base case) [13]. Each of these variations might produce a considerable improvement in the base-case ICER but it would not be possible to distinguish such variations from planned analyses based on the scant detail contained in many trial protocols. Publication and peer-review of detailed study protocols for modelled and trial-based cost-effectiveness analyses is therefore proposed to overcome publication bias, permit closer scrutiny of methods and to provide a strong disincentive for post-hoc 'gaming' and 'mining'.

The impact of moves to improve transparency and rigour in the conduct of modelled and trial-based evaluations will likely vary depending on the extent of available evidence (multiple studies replicating findings regarding the cost-effectiveness of an intervention), the extent of discretion exercised by sponsors and vested interest over research methods and dissemination of findings, the complexity of the disease-process under study, and the extent to which evidence-gaps necessitate a reliance on assumption and/or lower-level evidence when modelling the relative cost-effectiveness of an intervention and its comparator [14]. For implementation science, where few studies have included economic analyses and uncertainty surrounds many key parameters [16], the publication and peer-review of detailed protocols for economic analyses might be expected to yield a comparatively greater improvement in transparency and rigour than for disease-areas and interventions with an already well-developed evidence-base. The methods specified below provide a protocol for cost effectiveness analysis alongside the IMPLEMENT study [ACTRN012606000098538], with the aim of facilitating early peer-review of proposed methods and to provide a transparent statement of planned analyses.

Methods

The IMPLEMENT study is a C-RCT, with the clusters being a sample of 92 general practices of one or more GPs drawn from a sampling frame of 1000 general practices within the state of Victoria, Australia. Participating practices will be randomised to either a control group or an intervention group. Enrolling an average of 25 patients per practice will yield 2300 patients for inclusion in intention-to-treat analyses. A detailed description of the design of the C-RCT and of proposed methods for sample selection, randomisation and analysis of clinical outcomes are provided elsewhere [2].

Cost-effectiveness and cost-utility analyses will be conducted alongside the C-RCT to quantify the additional costs (savings) and health gains associated with the implementation strategy as compared with dissemination alone from a societal perspective. Specific secondary aims will be (a) to determine whether the incremental costs of the implementation strategy are outweighed by incremental cost savings associated with any change in practice (ie, whether implementing CPG for acute LBP is cost-

saving as compared with dissemination alone) and (b) to determine whether the implementation strategy dominates dissemination alone (ie, less costly but of at least equivalent effect). The time horizon for inclusion of relevant costs and consequences is set at three months, consistent with the final scheduled follow-up of patients from the C-RCT. That is to say, the economic evaluation is explicitly 'within-trial' and any subsequent extrapolation beyond the trial-period will be treated as a separate research task.

The perspective of the economic evaluation proposed here is determined by the policy context. The proposed economic evaluation will take a societal perspective in identifying, measuring and valuing all costs and consequences associated with (i) development of the implementation strategy, (ii) delivery of the implementation strategy, and (iii) any subsequent changes in practice and subsequent health effects. Note, however, that the development and dissemination of the CPG for acute LBP have already taken place in Australia with the result that their associated costs and effects are common and invariant to both intervention and control groups. The incremental costs and effects associated with implementation are therefore likely to be of greatest interest to policy makers and the proposed study will not explicitly calculate costs associated with development and dissemination of the CPG.

Description of the comparator intervention

In 2003, the National Health and Medical Research Council (NHMRC) of Australia endorsed a CPG for acute LBP [1]. There is a strategy in place to disseminate the CPG for acute LBP. This strategy comprises development of user-friendly material for the target audiences (clinicians and consumers), a range of methods to access the information, publicising the availability of the materials, endorsement by professional and lay associations and approval by the NHMRC. All documents are available electronically via the NHMRC website [1]. In addition, the summary (user-friendly) version of the review for clinicians, which includes the consumer information sheets, was distributed by post to approximately 40,000 general practitioners and other clinicians across Australia. While the comparator intervention closely approximates the 'existing practice' described above, a printed copy of the guideline and a written reminder of how to access the electronic version of the CPG will be sent to control group practices after randomisation.

Description of the evaluated intervention

In addition to access via the existing dissemination strategy, the intervention group will receive active implementation of the CPG for acute LBP. The GPs randomised to the intervention arm will receive an implementation strategy specifically designed to address the barriers and enablers for implementation of the CPG. The intervention will concentrate on delivering the CPG's key messages, namely that diagnostic x-rays are rarely necessary in the management of acute LBP and that remaining active reduces pain and disability. The intervention will consist of a series of facilitated face-to-face small group workshops. These workshops will involve a combination of didactic lectures and small group interaction that will utilise multiple behavioural change techniques including small group discussion and reflection, persuasive communication, modelling, rehearsal, scripting and action planning. These specific techniques have been chosen because they are considered the best available approach to address the barriers and enablers to the CPG's implementation [17]. The delivery of the intervention will be co-ordinated by a project officer and delivered by members of the research team and external facilitators.

Identification of health outcomes

The program logic of the evaluated intervention and the symptomatology of acute LBP suggest that specific dimensions of health-related quality of life (HRQoL) such as pain-related disability, physical function and physical pain are most relevant in capturing variation in health outcomes. However, it is possible that a differential effect might arise between the evaluated intervention and the comparator with respect to dimensions of health-related quality of life other than physical disability or physical pain. The outcome measures specified below will therefore provide broad coverage of HRQoL.

Measurement of health outcomes

The measures chosen to assess patient outcome are commonly used in trials of interventions for acute LBP and provide broad coverage of HRQoL including those dimensions of health-related quality of life that are most likely to be relevant in identifying an effect attributable to the intervention.

(i) The Roland Morris Disability Questionnaire (RDQ): The RDQ is among the most widely used and well-validated measures of LBP specific disability. The RDQ has high validity and reliability for use over the telephone and is recommended for inclusion in core sets of measures used in LBP [18]. It has 24 items, each scored as a yes or no. The RDQ measures 24 activity limitations due to back pain. The RDQ score is calculated by adding up the number of items with positive responses, the scores therefore ranging from 0 (no disability) to 24 (maximum disability).

(ii) Usual pain: An 11-point scale (0=no pain to 10=worst pain ever) has acceptable reliability and validity for self reported assessment of pain [19].

(iii) Assessment of Quality of Life (AQoL): The AQoL can be used as either a psychometric instrument, yielding a descriptive measure of health-related quality of life (HRQoL), or a multi-attribute utility (MAU) instrument, yielding a preference-based measure of HRQoL. The AQoL descriptive system includes 5 latent dimensions with each latent dimension reflected in three manifest items: illness (prescribed medicines, medication and aids, and medical treatment), independent living (self-care, household tasks, and mobility), social relationships (relationships with others, social isolation and family role), physical senses (seeing, hearing and communication) and psychological well-being (sleep, anxiety and depression). Only four of the five dimensions and 12 of the 15 items contribute to the AQoL's preference-based measure of HRQoL, with the illness dimension and associated items excluded because they were deemed indicative of an underlying health condition rather than the impact of that health condition on HRQoL [20]. The AQoL preference-based measure of HRQoL ranges from -0.04 to 1.00 where unity designates full health, zero designates death, negative scores designate states worse than death and the lower bound of -0.04 designates the AQoL's 'all worst health state'. The validity and reliability of the AQoL Version 1.0 for the measurement of preference-based HRQoL has been demonstrated in the Australian general population [20, 21]. The effect of mode of administration (mail versus telephone administration) on mean AQoL scores was neither clinically nor statistically significant [20].

Follow-up of patient level outcomes for the IMPLEMENT study is scheduled for seven days and three months after their initial GP consultation for acute non-specific LBP. Table 1 provides a schedule of patient-level outcome measures for the cost-effectiveness and cost-utility analyses. Due to the method chosen to recruit patients to the trial, it is not possible to obtain baseline observations for outcome measures. It is expected that the majority of any treatment effect would be observed within the initial week of treatment and that between-group differences will have stabilised by three month follow-up. The patient-level outcome measures specified above will therefore be administered at seven days and three months post their initial GP consultation for acute non-specific LBP. Intervention effects for the cost-effectiveness analyses will be taken from the main analysis of RDQ and usual pain measures at seven day and three month follow-up, controlling for a pre-specified set of potential confounders [2].

Valuation of health outcomes

While the patient level outcomes described above are expected to capture all relevant dimensions of health outcome, there are a number of advantages in expressing the results of cost-effectiveness analyses in cost per quality adjusted life year (QALY) terms. Between-group differences in preference-based HRQoL weights derived from the AQoL will be combined with the period of time over which such differences persist to calculate effectiveness in QALY terms. Intervention effects with respect to AQoL scores will be estimated using methods specified for the main analysis of patient level clinical outcome measures, controlling for the same set of pre-specified set of potential confounders [2]. In the absence of detailed information as to the form of the time-trend in HRQoL for the target condition, patients in both groups will be assumed to track a linear path from their AQoL score at seven days to their AQoL score at three months and the incremental QALY gain calculated as the difference between curves for treatment and control groups. For the within-trial analysis proposed here, groups will be assumed equivalent prior to the seven day follow-up and post the three month follow-up.

Identification of resource use

In line with the societal perspective adopted for the proposed analysis, our estimate of incremental costs will reflect all resource use associated with (i) development of the implementation strategy, (ii) delivery of

the implementation strategy, and (iii) any subsequent changes in practice and subsequent health effects. All research and evaluation costs will be excluded from the cost-analysis. Two questions arise in specifying the minimum dataset for the cost-analysis. First, can any cost items be excluded from the base-case analysis without biasing our estimate of incremental costs? And, second, for which of these included costs should we directly collect data from either GPs or patients? In addressing these questions, we may be able to exclude some cost items based on *a priori* considerations. For example, Drummond et al [13] note that some costs may simply confirm a result that would be obtained by consideration of a narrower range of costs.

Sometimes the consideration of patients' costs merely confirms a result that might be obtained from, say, consideration of only operating costs within the health sector. Therefore, if consideration of patients' costs requires extra effort and the choice of program is very unlikely to be changed, it may not be worthwhile to complicate the analysis unnecessarily (p54).

Volunteer carer time and patients' waiting time and travel time to attend x-ray appointments and follow-up GP consults may fall into this category. Or, at any rate, can be conservatively estimated given health status data, the number of ordinary x-rays by patient and the number of GP consults per patient. The scope of the within-trial cost-analysis proposed here is also constrained by the design of the IMPLEMENT C-RCT, with observation on relevant costs and consequences limited to three months from each patient's initial GP consultation. Scheduled observations on resource use for the cost-effectiveness and cost-utility analyses are listed in Table 1.

Any costs associated with development and dissemination of the CPG under existing practice are assumed to arise in equal magnitude for intervention and control groups and are excluded from further consideration. Note, however, that the cost of sending written reminders to control group practices detailing how to access the CPG is specific to the control group and will be included in the cost analysis.

Costs items associated with development of the implementation strategy include the cost of recruiting informants to inform development of the intervention, the cost of time spent in focus groups for informants and facilitators, the opportunity cost of interview and meeting rooms, the cost of time and equipment for analysis of focus group data, the cost of time in reviewing and interpreting findings from focus groups, and the cost of consultation with the GP advisory committee. Drummond et al [13] note the importance of identifying capital outlays that should be amortized over the lifetime of the asset. Certainly the development of the implementation strategy amounts to a one-time investment in intellectual property that may find a repeated or broader use. Given repeated use of intellectual property, it would be inappropriate to apportion the entire cost of development to a single use. That said, it would also be inappropriate to disregard the investment in intellectual property and the full cost must be estimated before it can be amortized. The question then arises: what is the lifetime of intellectual property? Intellectual property is frequently non-rival such that a single-use does not diminish the quantity of the asset for subsequent use. However, in this case the implementation strategy is likely to be specific to LBP CPG, specific to the institutional context of Australia, specific to general practice, likely to have limited value in repeated use for the current cohort of practitioners and may have an expiration date contingent upon the current technology or the existing evidence-base. The cost of developing the implementation strategy will therefore be amortized under the assumption that the strategy will eventually be delivered to the entire cohort of Australian GPs with current Medicare provider numbers but will bear no repeated or wider use.

Cost items associated with delivery of the implementation strategy include administrative costs associated with coordinating small group workshops, production of materials for workshops, the opportunity cost of venue use, the opportunity cost of travel time and attendance at workshops for GPs, opportunity cost of pre- and post-workshop reflection for GPs, and labour costs associated with preparation/delivery/facilitation of workshops.

Cost items associated with change in clinical practice include direct and indirect health care costs such as use of x-rays, over-the-counter or prescription analgesics and allied health or GP consults and the time of volunteer or paid carers. Practice change is also expected to impact on direct and indirect costs outside the health sector including waiting time and travel time to attend treatment, productivity gains due to a change in specific disability and time lost from work associated with treatment.

Measurement of resource use

In measuring resource use associated with (i) development of the implementation strategy, (ii) delivery of the implementation strategy, and (iii) any subsequent changes in practice and subsequent health effects; data will be collected from the research team, from the enrolled practitioners and from the enrolled patients. Scheduled observations on resource use for the cost-effectiveness and cost-utility analyses are listed in Table 1.

Resource use associated with the development of the implementation strategy will be costed based on financial and administrative records and a detailed description of the development process obtained from the project manager and project officers. This will require recall over a relatively short period of time as to proportion of an equivalent full-time salary that project staff spent in development of the implementation strategy (as opposed to activities associated with research and evaluation such as administration/design of the C-RCT). Administrative and financial records will provide data as to the number of informants, total person hours spent in focus groups and interviews for informants and facilitators, use and location of interview and meeting rooms, total person time for data analysis and interpretation of findings, and total person hours for advisory committee members.

Resource use associated with the delivery of the implementation strategy will be estimated from administrative and financial records detailing resource use associated with the production of materials, total person hours spent in organising and facilitating workshops, total hours GP attendance, venue location and total hours venue hire, and practice location for attending GPs. Time spent by GPs in pre-

and post-workshop reflection or self-education will be estimated based on a description of the intervention (rather than self-report) and varied in sensitivity analysis.

Resource use associated with a change in clinical practice and subsequent health effects will be based on patient self-report. While GPs may be in a position to report the percentage of LBP patients referred for x-ray, patients' use of allied health care and their use of over-the-counter analgesic cannot be obtained from enrolled practitioners. It is well-known that patient self-report becomes increasingly unreliable as the period of recall increases. "For example, one study found that 10% of patients failed to report that they had been hospitalized when they were interviewed approximately five months after discharge. Even if subjects remember that they have seen a physician or have gone to a hospital, they often will not know what services they received" [22]. For longer periods of recall, memory aids such as patient diaries have proven useful in improving the reliability of self-report data. In the present study, the period of recall is just the period since baseline at each follow-up (seven days and three months). The use of patient diaries is not possible for the seven days prior to the post-consultation follow-up. Moreover, there is good reason to believe that recall with respect to use of allied health consults and over-the-counter medication is likely to be relatively accurate because these items are typically paid as out-of-pocket costs rather than bulk-billed to Medicare or reimbursed directly from private insurance. It therefore seems sufficient to present a short questionnaire to patients at each follow-up with the breadth and form of questions based on health-related actions items from the ABS National Health Survey (ABS 4801.0, 1995). This short questionnaire will also ask patients to nominate a category describing their usual main activity and to estimate the amount of time they spent away from their usual main activity due to illness or to attend treatment; providing the raw data for estimating productivity gains/losses and travel/waiting time. A list of items to be included in the questionnaire is given in Table 2. While self-report for professional and volunteer home care has not been requested in the questionnaire due to reliability concerns, total hours of carer time will be conservatively estimated based on measures of LBP-related disability.

Valuation of resource use

Unit costs for health service resource use will be as per the Manual of Resource Items for use in submissions to the Commonwealth of Australia's Pharmaceutical Benefits Advisory Committee (PBAC) [23]. Resource use of marketed goods and services outside the health sector and not included in the Manual will be valued at market prices. Unmarketed goods and services such as travel time and the time of volunteer carers will be valued as described below. Intervention effects with respect to total cost will be estimated using methods specified for the main analysis of patient level clinical outcome measures, controlling for the same set of pre-specified set of potential confounders [2].

Travel time

The cost of travel time is just the value of the next best alternative use of that time (eg. paid work, voluntary work, leisure). Litman [24] summarised a number of findings with respect to the cost of travel, concluding that personal travel time is usually estimated at one-quarter to one-half of prevailing wage rates and that travel time costs tend to increase in line with income, implying a lower cost of travel time for children and for people who are retired or unemployed. Attempts to quantify personal travel costs are therefore complicated by variation in the mode as well as the qualitative characteristics and distance of travel. Pisarki [25] and the US Center for Urban Transportation Research [26] reported wide disparities in the travel time, trip length and average speed for different modes of public and private transport. Results from these studies suggest that public transport, ride-sharing and walking often entail more travel time but at a lower average speed than self-drive trips. Under favourable conditions, time spent ride-sharing or on public transport entails a lower per-minute cost than self-drive trips because passengers can relax or perform productive work. However, the per-minute cost of time spent ride-sharing or on public transport might entail a higher per minute cost than self-drive trips if buses or trains are crowded, late or unreliable [24]. Using stated preference techniques, a number of studies have estimated travel time costs for major Australian cities [27, 28]. These estimates should provide a relatively good approximation of travel time costs in Melbourne but are unlikely to reflect travel time costs in rural and regional Victoria. A similar stated preference survey estimated travel time costs in 2000 AUDs for longer

distance travel in rural and regional Australia at \$12/hour for commuters and \$6/hour for non-commuters [29, 30].

Time of volunteer carers

In the absence of market prices, unmarketed goods and services such as travel time and the time of volunteer carers are most appropriately costed using opportunity cost prices. If individuals make no distinction between paid and unpaid work when making the leisure/work trade-off, then prevailing wage rates provide a good approximation of the cost of volunteer time. Note, however, that there might be significant utility attached to caring for a partner or a parent such that individuals would gladly give up their leisure time. If individuals reduce their leisure time (rather than paid work) in order to volunteer, then the cost of volunteer time might be better approximated by the value of the marginal unit of leisure time.

Drummond et al [13] suggest a value for lost leisure time *of zero in the base case* but concede that arguments could also be made for valuing lost leisure time at the average wage rate or at average overtime rates. Because the law of diminishing marginal utility applies to both volunteer time and leisure time, the first unit of volunteer time will carry a relatively low opportunity cost but the tenth unit of volunteer time might carry an opportunity cost as high as average overtime rates. For the proposed study, the value of volunteer carer time will be proxied by the average ordinary hourly wage rate for health and community services taken from the ABS Labour Price Index for the year of study completion [29].

Productivity gains and losses

Production losses are most frequently valued via the human capital approach; whereby the actual gross earnings of those in paid employment are used to estimate the value of time absent from work due to treatment or illness [13]. Note, however, that a significant minority of enrolled patients are expected to be retirees or engaged in home duties as their major activity such that the human capital approach would underestimate the value of lost production. To avoid bias and certain unpalatable equity implications of the human capital approach, a proxy (eg, average wage rates, cost of services such as childcare or cleaning services that would be required to replace role of homemaker) is frequently used to value the unpaid work of

retirees, homemakers and the unemployed. For example, the Bureau of Transport Economics (BTE) [30] estimated the value of lost production in household and community sectors using the ABS Time Use Survey [31] and average earnings by age-group. The proposed study will adopt a similar approach, deriving the cost of a week out of role as the product of the average ordinary hourly wage rate taken from the ABS Labour Price Index for the year of study completion [29] and the average number of hours per week spent on unpaid work in household and community sectors by age-group taken from the ABS Time Use Survey [31].

Due to the relatively short duration for an episode of acute non-specific LBP and the relatively short duration of follow-up, the difference between human capital and friction cost [13] estimates of productivity gains/losses in the present study is expected to be negligible. The friction cost approach would censor productivity losses that accrue beyond the minimum period of time required for the replacement of effective labour. While Hoeijenbos et al [9] employed a friction cost approach to the estimation of productivity gains/losses in their study of guideline implementation for non-specific LBP, productivity losses were not censored until 22 weeks of absence under the assumption that recruitment and training could not routinely be accomplished within a shorter time-frame. For this reason, the proposed study will not censor productivity losses that arise within the study period.

Adjustment for differential timing

All costs will be inflated to current AUD for the year of study completion. While costs and benefits associated with delivery of the implementation strategy and any subsequent within-trial changes in practice are expected to accrue within a 12 month period, costs associated with development of the implementation strategy are expected to accrue up to 24 months prior to costs associated with delivery of the implementation strategy and any subsequent within-trial changes in practice. All costs and benefits will be converted to present values using an annual discount rate of 5% in the base-case, and annual rates of 3% and 7% in sensitivity analysis.

Incremental analysis

Results from the economic evaluation will be expressed as: (i) additional costs (savings) per point difference in RDQ at seven days and three months, (ii) additional costs (savings) per point difference in usual pain at seven days and three months, and (iii) additional costs (savings) per QALY gained.

Uncertainty

Cost-effectiveness acceptability curves (CEACs) will be used to quantify and visualise sampling and parameter uncertainty associated with the decision to replace the comparator with the evaluated intervention (rather than that associated with individual inputs or model structure or characteristics of the target population). The CEAC is derived from the joint density or joint distribution of incremental costs (ΔC) and incremental effects (ΔE) for the intervention of interest against a comparator, and represents the proportion of the density where the intervention is cost-effective for a range of willingness to pay thresholds (λ). The CEAC plots the relative frequency, or probability, that an intervention is cost-effective, compared to its comparator for varying threshold values of the cost-effectiveness ratio. The joint density will be obtained via non-parametric bootstrapping from the distribution of observed cost/effect pairs.

Because the base-case analysis will include all cost items listed above, a separate CEAC will be calculated using best estimate and upper/lower bound estimates for travel time, time of volunteer carers, productivity gains and for other uncertain parameters such as the discount rate. Sensitivity analysis on the CEAC will also adjust estimates of incremental costs and incremental benefits for practice characteristics and patient characteristics to consider the external validity of study findings.

Conclusion

Publication and peer-review of detailed protocols for economic evaluation is advisable for much the same reasons as has been advocated elsewhere for the registration of trial protocols [32]. Publication bias and the 'mining' or 'gaming' of analyses are no less a problem for economic analyses than they are for experimental and observational studies of efficacy and effectiveness [14, 15]. The protocol provided here

registers our intent to conduct an economic evaluation alongside the IMPLEMENT study, allows peer-review of proposed methods and provides a transparent statement of planned analyses.

Ethical review

Ethical approval for this trial was obtained from the Monash University Standing Committee on Ethics in Research involving Humans (2006/047).

List of abbreviations used

ABS: Australian Bureau of Statistics

AQoL: Assessment of Quality of Life

AUD: Australian Dollar

BTE: Bureau of Transport Economics

CEAC: Cost-effectiveness acceptability curve

CPG: clinical practice guideline

C-RCT: cluster randomised controlled trial

GP: general practitioner

HRQoL: health-related quality of life

ICERs: incremental cost-effectiveness ratios

LBP: low-back pain

MAU: multi-attribute utility

NHMRC: National Health and Medical Research Council

PBAC: Pharmaceutical Benefits Advisory Committee

QALY: quality-adjusted life year

RDQ: Roland Morris Disability Questionnaire

SD: standard deviation

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

DM participated in the design of the trial-based economic evaluation and drafted the protocol. SF, JM, DO'C and SG participated in the design of the trial-based economic evaluation and suggested edits and revisions to the protocol. All authors read and approved the final manuscript.

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Table 1: Schedule of measures for economic evaluation

Outcome	Data collection	Timing	Source	Level
RDQ	Telephone interview	7 days and 3 months after consultation	Patient	Patient
Usual pain	Telephone interview	7 days and 3 months after consultation	Patient	Patient
AQoL	Telephone interview	7 days and 3 months after consultation	Patient	Patient
X-ray referral	Data abstraction	3 months	GP case notes	Patient
Any imaging referral	Data abstraction	3 months	GP case notes	Patient
Health Service Utilisation	Telephone interview	7 days and 3 months after consultation	Patient	Patient
Direct costs of developing intervention	Data abstraction Interview	On completion of development	Admin records Project officers	Intervention
Direct costs of delivering intervention	Data abstraction Interview	On completion of delivery to all GPs	Admin records Project officers	Intervention

Table 2: Patient self-report of health service utilisation

INSTRUCTIONS: Thinking about your use of health services over the last (7 days/3 months)...

- Have you received an x-ray in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, how many times have you attended radiology for an x-ray in the last (7 days/last 3 months)?*
- Have you been hospitalised in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, how many times have you been hospitalised in the last (7 days/last 3 months)?*
- Have you visited casualty/emergency in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, how many times have you visited casualty/emergency in the last (7 days/last 3 months)?*
- Have you visited an outpatient or day clinic in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, how many times have you visited an outpatient or day clinic in the last (7 days/3 months)?*
- Have you visited any GP in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, how many times have you visited a GP in the last (7 days/3 months)?*
- Have you visited a medical/surgical specialist in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, how many times have you visited a specialist in the last (7 days/3 months)?*
- Have you visited any physiotherapist in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, how many times have you consulted a physiotherapist in the last (7 days/3 months)?*
- Have you visited any osteopath in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, how many times have you visited an osteopath in the last (7 days/3 months)?*
- Have you visited any chiropractor in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, how many times have you visited a chiropractor in the last (7 days/3 months)?*
- Have you visited any other health provider (OHP1) in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, how many times have you visited OHP1 in the last (7 days/3 months)?*
- Have you visited any other health provider (OHP2) in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, how many times have you visited OHP2 in the last (7 days/3 months)?*
- Have you used any prescription or over-the-counter medications in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, how many different medications have you used in the last (7 days/3 months)?*
- Have you used any prescription or over-the-counter pain relievers in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, on how many days have you taken pain relievers in the last (7 days/3 months)?*
- Have you used any prescription or over-the-counter sleeping medications in the last (7 days/3 months)? *(YES/NO/NOT SURE)*
- If yes, on how many days have you taken sleeping medications in the last (7 days/3 months)?*

INSTRUCTIONS: Thinking about your usual main activity over the last (7 days/3 months)...

What is your usual main activity? *Full-time student*
Part-time student
Employed
Unemployed
Not applicable

How many hours would you usually spend on your main activity in a week? *0 hours*
1-15 hours

16-24 hours
25-34 hours
40 hours
41-48 hours
49 hrs or more

Have you spent time away from your usual main activity due to illness or to attend treatment in the last (7 days/3 months)? *(YES/NO/NOT SURE)*

If yes, how many full days away from usual main activity due to illness in the last (7 days/3 months)?

And how many hours away from usual main activity to attend treatment in the last (7 days/3 months)?

Additional files provided with this submission:

Additional file 1: ethics_letter_of_approval.pdf, 13K

<http://www.implementationscience.com/imedia/6867897431750858/supp1.pdf>

Additional file 2: nhmrc_success_letter.pdf, 123K

<http://www.implementationscience.com/imedia/4148945011750858/supp2.pdf>