1. EXECUTIVE SUMMARY IN_plain English: Provide a brief summary of the project outlining the broad aims, background, key questions, research design/approach, the participants in the study and what they will be asked to do, and the importance or relevance of the project. [This description must be in everyday language, free from jargon, technical terms or discipline-specific phrases. (No more than 300 words).]

Chronic knee pain is a common joint disease, particularly affecting people over the age of 50. The disease leads to pain, functional limitations and is a significant financial burden to the community. Effective interventions that reduce knee pain and result in increased function need to be identified. Acupuncture is one of the most popular therapies for treating chronic joint pain utilised by patients. Although acupuncture has been traditionally given with needles, the use of laser acupuncture has increased significantly because of patient preference and minimal adverse effects. The purpose of the present study is to identify the effectiveness of laser acupuncture and compare it with that of needle acupuncture in treating chronic knee pain.

This will be a randomised clinical trial of a 10-week acupuncture program with a 12-month follow-up. Two hundred and eighty people over the age of 50 suffering from chronic knee pain will be recruited and undergo telephone screening. A standard Zelen methodology will be used whereby participants are initially enrolled into a longitudinal study. Following enrolment into the study, participants will be covertly randomised into one of four groups: (1) a no treatment control group, (2) laser acupuncture, (3) placebo laser acupuncture and (4) needle acupuncture. The participants in the no treatment control group are not informed about the other treatment groups. The reason for using this Zelen methodology is to minimise group expectations and patient-therapist interactions that can potentially bias the outcomes. All participants will be required to have a recent (last 12 months) and appropriate xray of their knee at baseline (if they do not have one, a new xray will be organised) and to complete a set of questionnaires about their pain, function, quality of life, physical activity levels and psychological status at baseline, 12 weeks and 12 months after baseline. These will take approximately 45-60 minutes to complete. Participants will also keep a monthly diary to record medication use and other interventions, adverse events to allow collection of the cost effectiveness of the interventions. Those randomised into the laser acupuncture, placebo laser acupuncture and needle acupuncture will have 8-12 treatment visits over 10 weeks all performed by medical practitioners who are qualified acupuncturists.

1.2 AIMS OF AND JUSTIFICATION FOR THE RESEARCH: State the aims and significance of the project. Where relevant, state the specific hypothesis to be tested. Also provide a brief description of current research/literature review, a justification as to why this research should proceed and an explanation of any expected benefits to the community. [No more than 500 words]

Chronic knee pain is a common and disabling condition affecting approximately 50% of patients over 50-years of age. It is most commonly due to OA and this problem results in significant health care costs, loss of functional
independence and a reduction in the overall quality-of-life for affected individuals. The Australian Government has recognised this by making arthritis and related disorders a priority health area. Acupuncture is a popular form of complementary and alternative medicine (CAM) for treating pain and dysfunction associated with musculoskeletal conditions. Published meta-analyses have demonstrated the effectiveness of needle acupuncture as a CAM treatment modality for knee OA. (3, 4) By contrast to needle acupuncture, laser acupuncture, is relatively poorly studied. International guidelines have concluded that needle acupuncture has positive treatment benefits in knee OA but have also highlighted significant methodological factors that make objective evaluation of the results difficult. (5-8) The principal methodological criticisms of acupuncture studies relate to:

1. Placebo effects in clinical trial ‘control’ subjects – the difficulty in having a true placebo control group given pre-existing subject expectations, particularly where the treatment itself is multidimensional (involving therapist-patient interaction as well as a treatment intervention) has been the subject of numerous reviews. (7, 9-11) Studies of dental analgesia suggest a pain placebo effect in the order of 27% using laser acupuncture. (12) For this reason, a Zelen epidemiological design with true blinding of the control (no treatment) arm is often recommended as the best means of minimising this form of bias or confounding.

2. Sham acupuncture needle effects - The difficulty in having a sham or placebo treatment comparison is problematic. With needle acupuncture, various sham needles have been designed that withdraw the needle into the sheath with little or no skin penetration. (4, 13, 14) These still produce some local irritation and may stimulate similar neurophysiological mechanisms to needles penetrating more deeply. This is a particular issue in chronic regional pain syndromes where neural sensitisation is well recognised.

Laser acupuncture is a relatively poorly studied CAM treatment modality. This modality is increasingly preferred by acupuncturists, given the minimal side effects and ease of use in patients. (15-17) A recent RCT study of laser acupuncture in chronic neck pain found a statistically significant reduction in pain. (18) The proposed study builds on that experience and examines the effect of laser and needle acupuncture on chronic knee pain. Only two trials to date have studied laser acupuncture in the management of knee pain, the first of these tested different laser dose regimes (19) and the second was a small underpowered RCT that found no significant difference in treatment arms. (20) No study has compared needle and laser acupuncture in a head-to-head trial for any musculoskeletal condition.

AIMS and STUDY HYPOTHESES
The primary hypotheses of the RCT are that:
H1: Laser acupuncture will result in significantly greater improvements in pain, physical function and health-related quality of life than sham laser acupuncture in individuals with knee pain
H2: Laser acupuncture will result in significantly greater improvements in pain, physical function and health-related quality of life than no treatment in individuals with knee pain
H3: Laser acupuncture will be equal or superior to needle acupuncture in measures of pain, physical function and health-related quality of life in individuals with knee pain

The secondary hypotheses of the RCT are that:
H4: Improvements in pain, function and health-related quality of life at the conclusion of a 10-week acupuncture program will be sustained at 12-months post-treatment.
H5: A laser acupuncture program will be more cost-effective than placebo laser acupuncture when total knee pain-related costs are compared and related to the effects of the active intervention.
H5: In both laser and needle acupuncture arms, psychosocial measures will differentiate treatment responders and non-responders.

References:
1.3 **METHOD** Provide an outline of the proposed method, including details of the recruitment strategy and data collection techniques, the tasks participants will be asked to do, the estimated time commitment involved, and how data will be analysed. [No more than 500 words]

This will be a randomised, double-blind, controlled trial of a 10-week acupuncture program with a 12-month follow-up. Control and treatment arms are allocated via a standard Zelen design in order to minimise control group expectations and patient-therapist interaction potentially confounding the treatment outcomes. The treatment arm is randomised into laser, sham laser or needle acupuncture. (21-23) Zelen trials are a standard epidemiological technique involving a randomized consent design in a multidimensional treatment trial where the knowledge of the intervention itself may influence the study outcome (Hawthorne effect) in the control group. A researcher will conduct telephone screening of volunteers. Participants will be informed of the trial and sent a plain language statement and consent form. All participants will then complete a baseline assessment using the outcome measures described below. These include a series of questionnaire based assessments which can be completed at home and will take approximately 45-60 minutes. These will be posted back to the researchers via a reply paid envelope. Participants will also be required to have a standardised knee radiograph (24) to assess radiographic degree of any osteoarthritis. X-rays will be taken and will enable the analysis of the differential effect of acupuncture on varying degrees of knee osteoarthritis. If participants already have an appropriate recent knee xray (within 12 months), they will not be required to have another one. Those requiring a knee xray will be sent to a radiology centre that is most convenient to them. This will take approximately 30 mins. Using the Zelen RCT methodology, subjects will be randomised to treatment or no treatment (control) arms. The control subjects will continue as a natural history observational cohort for the 12-month duration of the study. The subjects randomised into treatment arms will be randomised into one of three treatment groups: (i) laser acupuncture; (ii) placebo/sham laser acupuncture; (iii) needle acupuncture. Randomisation will be by random permuted blocks of size from 6 to 12 and will be stratified by gender and treatment centre (cluster randomised). The randomisation schedule will be prepared by the study biostatistician (AF). He will be the only person with access to the schedule and laser machine code numbers, which will be kept in a locked location. The patient code numbers for the randomized treatment arms will be entered into the trial laser machines by an independent biomedical engineer. After the completion of the intervention period for the acupuncture groups, all participants will be re-assessed. Follow up will occur at the conclusion of the treatment phase (at 12 weeks) and then at 12-months to monitor long term outcome. The control group will also complete the same outcome assessments at the same time points. The questionnaires will be sent to the participants who can complete them at home (approx 45-60 mins) and return them to the researchers via reply paid envelopes. All measures have been selected based on those recommended for clinical trials of knee pain. (25,26)

Outcomes: The questionnaire outcomes chosen have well established reliability and validity. Pain severity and physical function will be evaluated using visual analogue scales and the Knee Osteoarthritis Outcome Scale (KOOS). Expectation of treatment benefit and self-perceived change in pain and function following treatment will also be measured using 5-point Likert scales. Health related quality of life will be measured using the Assessment of Quality of Life (AQL) instrument. The AQL will also be used for the cost effectiveness analysis. The SF-36 will also be collected as a generic measure of quality of life. Physical activity levels will be measured by the Physical Activity Scale for the Elderly. Psychological measures include the Arthritis Self Efficacy Scale, the Hospital Anxiety and Depression Scale, the Centre for Epidemiologic Studies Depression Scale and the Revised Health Hardiness Inventory Scale. Use of health care: Participants will record visits to health care providers (e.g. general practitioner, medical specialist, other health care professionals), prescription and over the counter medication, professional home care and hospitalization in a monthly log-book, which will be sent back in a reply paid envelope. This data are used for the health economic evaluation.

Interventions: Participants will be treated by general practitioners (MBBS) who are Fellows of the Australian Medical Acupuncture College, a process requiring 3 years of supervised post graduate training in acupuncture followed by a formal accreditation process. Medical acupuncturists have been selected for this study in order to minimise potential confounders related to different qualifications and variable clinical experience and expertise. The acupuncturists will undergo training by one of the investigators (IR) to ensure compliance with the trial protocols and this will be followed up by face to face visits during the study. Treatments will be pragmatic in nature occurring once or twice weekly (at the practitioner’s discretion) for ten weeks, with a minimum of 8 and maximum of 12 treatments using standardised and defined acupuncture treatment points. These treatment sessions will take approx 20 mins. Participants will not pay for treatment and the treating acupuncturists will be reimbursed for their time on a per patient basis. The treating acupuncturists will be based in metropolitan Melbourne as well as the major Victorian country centres.

Data analysis: Treatment groups will be statistically examined for comparability at baseline. The main dependent variables will be the changes in pain and function over 12 months (calculated as reassessment minus baseline). To test hypotheses 1 and 2, the groups will be compared using an intention to treat analysis of the difference between time points with 95% confidence intervals and Mann-Whitney U or independent t-tests. Analysis of covariance will be applied after adjusting for baseline outcome values and other characteristics imbalanced at baseline if required. To evaluate the influence
of loss to follow up, data will be analysed by best case and worst case to ensure that missing data do not alter the results. Proportional odds models will compare improvement between the treatment, sham and control groups based on perceived ratings of change.

Cost effectiveness: The primary economic evaluation will take the form of a cost effectiveness study with a range of outcome measures including the incremental cost per extra person with a clinically significant improvement in pain, per extra person perceived to be recovered, and per extra quality adjusted life years (QALYs) (using the AQoL over 12 months). The inclusion of time/productivity gains is controversial and the cost effectiveness ratios will be calculated with and without these “indirect costs”. A social perspective on costs will be taken and will include resource use incurred both by health services and by the patient irrespective of the source of payment. Direct health care costs will be calculated from the logbook. Standard methods of economic evaluation alongside a clinical trial will be used to evaluate the differences in resource use and health outcomes over 12 weeks and 12 months. The inclusion of productivity gains is controversial and the cost effectiveness ratios will be calculated with and without these “indirect costs” based on reported labour outcomes. The statistical analysis of costs data will be similar to outcome data although adjustments for over-dispersion may be necessary. Confidence intervals for incremental cost effectiveness can be calculated directly using non-parametric bootstrapping. An increasingly common presentation of uncertainty around cost effectiveness is to calculate a cost effectiveness acceptability curve based on the net benefits of an intervention for a range of hypothetical money values of outcomes. This will be done using individual cost and outcome data or, if adjustments for imbalance at baseline are necessary, using regression analysis.

References:

1.4 USE OF INDEPENDENT CONTRACTORS
Will parts of this project be carried out by independent contractors? (e.g. interviewing, questionnaire design and analysis, sample testing, etc)

☐ YES  ☐ NO

If YES, confirm that the independent contractor will be engaged on the basis of relevant qualifications and experience and will receive from the Responsible Researcher, a copy of the approved ethics protocol and be made aware of their responsibilities arising from it. [The responsibility for effective oversight and proper conduct of the project remains with the Responsible Researcher]

Knee Xrays will be performed through MIA Victoria, an independent radiology service who have over 50 locations across metropolitan and rural Victoria. The participants will be directed to the service closest to where they live. Standard knee xrays will be performed by qualified radiographers and reported on by qualified radiologists. A copy of the radiologist report will be provided to the participants who will be advised to contact their own general practitioner if they wish to discuss the results of the report. Approval from the Department of Health and Human Services for x-rays will be obtained. The Principal Researcher will provide the radiology department with a copy of the ethics protocol and inform the radiologist of their responsibilities. Radiological information will be used to establish the presence or absence of knee osteoarthritis and if present, to grade its severity.

Eight General Medical practitioners who are Fellows of the Australian Medical Acupuncture College and currently registered with the Medical Board of Victoria will perform the laser, placebo laser and needle acupuncture treatments in their own treatment rooms. They are located in the Melbourne metropolitan region and major regional centres. Fellows of the Australian Medical Acupuncture College have a standardised University-delivered acupuncture training course, formal accreditation by examination, a minimum period of supervised clinical experience, have current medical insurance and are registered as medical acupuncturists by the Medical Board of Victoria. They will be overseen by the Associate Investigators in this project, Dr Marie Pirotta and Dr Ian Relf who are both General Practitioners and affiliated with the Department of General Practice, University of Melbourne. Furthermore, Dr Ian Relf is the Past-President of the Australian Medical Acupuncture College. All GPs will be provided with
1.5 MONITORING

(a) How will researchers monitor the conduct of the project to ensure that it complies with the protocols set out in this application, the University’s human ethics guidelines and the National Statement on Ethical Conduct in Human Research? [Address, in particular, cases where several people are involved in recruiting, interviewing or administering procedures, or when the research is being carried out at some distance from the Principal Researcher (i.e., interstate or overseas)]

The principal researcher, A/Prof Paul McCrory, will be responsible for monitoring the project and ensuring that all procedures comply with the guidelines outlined here and relevant ethics guidelines. All researchers and participants will be informed of the study protocols.

Dr Ian Reif and Dr Marie Pirotta will oversee the general medical practitioners who are delivering the acupuncture treatments. Dr Reif will educate the acupuncturists in the protocol, make site visits to the clinics to ensure that the reception staff and the medical practitioners understand the logistics of the study and will be in regular contact with the medical practitioners to ensure compliance with the protocol and to deal with any issues that may arise. Dr Pirotta will liaise with the Department of General Practice and oversee the research assistant based there who will be in regular contact with the treatment sites. The study protocol will also be assessed by the inspections of the treating GP patient notes (which are supplied in this submission).

(b) For student research projects how will the student be supervised to ensure they comply with the protocols? If the student is working overseas, provide additional details of any local supervision arrangements.

2. PARTICIPANT DETAILS

2.1 DOES THE RESEARCH SPECIFICALLY TARGET: [Tick as many as applicable]

- a. students or staff of this University
- b. adults (over the age of 18 years and competent to give consent)
- c. children/legal minors (anyone under the age of 18 years)
- d. the elderly
- e. people from non-English speaking backgrounds
- f. pensioners or welfare recipients
- g. anyone intellectually or mentally impaired who cannot provide consent
- h. anyone who has a physical disability
- i. patients or clients of professionals
- j. anyone who is a prisoner or parolee
- k. a ward of the state
- l. any other person whose capacity to give informed consent may be compromised
- m. Aboriginal and/or Torres Strait Islander people and/or communities
- n. other collectives where a leader or council of elders may need to give consent

2.2 NUMBER, AGE RANGE AND SOURCE OF PARTICIPANTS

Provide number, age range and source of participants.

Two hundred and eighty subjects, all aged over 50 years will be recruited through the media including State and local newspapers and through advertisements in doctors waiting rooms, senior clubs, country women’s associations, rural GP networks and from our database of participants from previous studies who have agreed to be contacted for future research.

2.3 JUSTIFICATION OF PARTICIPANT NUMBERS [The quality and validity of research is an essential condition of its ethical acceptability (refer National Statement)]. Where applicable, provide a justification of sample size (including details of statistical power of the sample, where appropriate), explaining how this sample size will allow the aims of the study to be achieved.

Our primary endpoints will be knee pain measured on a VAS and WOMAC physical function score. Sample size calculations are done using a post-baseline comparison which gives the largest number of subjects for the primary hypotheses. The minimum clinically important difference to be detected in trials is a change in pain of 1.8 cm (on VAS) (62) and a change of 6 normalised physical function WOMAC units. (72) Applying power calculations to detect these differences in pain scores from baseline to post treatment comparison, gives 44 subjects per test group. For the functional assessment using the WOMAC scale...
assuming a common between-subject standard deviation of 3 cm for pain and 12 units for WOMAC physical function, 63 subjects per group are required to achieve 80% power at a two-sided 5% significance level. Including the 12-month follow-up in a repeated measures analysis, assuming a conservative correlation of 0.8 between all post-baseline measurements and a uniform treatment effect, the power of the study is 92% for pain and 89% for physical function. To allow for loss to follow-up and Zelen design, we plan to recruit 70 subjects per group giving a total of 280 subjects.

2.4 PARTICIPANT RECRUITMENT
(a) Please indicate the method of recruitment by ticking the appropriate boxes. Tick all that apply.

- Mail out - see below
- Advertisement - see below
- Contact details obtained from public documents (eg. phone book)
- Participants from a previous study
- Recruitment carried out by third party (eg. employer, doctor) – see below
- Contact details obtained from private sources (eg. employee list, membership database) – see below
- Snowball (participants suggest other potential participants)
- Recruitment carried out by researcher/s
- Personal contacts
- Other (Please explain in no more than 50 words):

- If using a mail out or email who will be distributing it?

- If using an advertisement:
  - explain where will it be placed?[e.g. on waiting room wall, in newspaper, in newsletter]
  - have you attached a copy?
    - Yes ☒ No ☐ ☐ NA ☐ If “No” please explain (no more than 50 words):

- If recruitment is to be conducted by a third party, (eg employer, doctor) have you attached an approval letter?
  - requesting their assistance?[yes, no or not applicable]
    - Yes ☒ No ☐ ☐ NA ☐ If “No” please explain (no more than 50 words):
  - confirming their willingness to assist?
    - Yes ☒ No ☐ ☐ NA ☐ If “No” please explain (no more than 50 words):
  - that has been drafted for the third party to send to potential participants?
    - Yes ☒ No ☐ ☐ NA ☐ If “No” please explain (no more than 50 words):

- If contact details are to be obtained from private sources, have you attached an approval letter?
  - Yes ☒ No ☐ ☐ NA ☐ If “No” please explain (no more than 50 words):

(b) Describe how, by whom, where potential participants are to be identified or selected for this research.

Potential participants will respond to advertising and will be requested to contact the research assistant using a special telephone contact 1800 number

(c) Describe how, by whom, where potential participants are to be approached or invited to take part in this research.

Once potential participants respond to an advertisement they will contact the research assistant via telephone. The research assistant will then outline the study and ascertain their eligibility. If the person is eligible and interested in participating, they will be sent a plain language statement and consent form via post and will then return the consent form via reply paid postage to the researchers.

2.5 DEPENDENT RELATIONSHIPS
[The issue of research involving persons in dependent or unequal relationships (e.g. teacher/student, doctor/patient, student/lecturer, client/counsellor, warder/prisoner, and employer/employee) is discussed in Sections 2 and 4.3 of the National Statement. Such a relationship may compromise a participant’s ability to give consent which is free from any form of pressure (real or implied)]. Are any of the participants in a dependent relationship with any of the researchers, particularly those involved in recruiting for or conducting the project?
☐ YES  ☒ NO  (If YES, explain the dependent relationship and the steps to be taken by the researchers to ensure that participation is purely voluntary and not influenced by the relationship in any way.

2.6 PAYMENT OR INCENTIVES OFFERED TO PARTICIPANTS

Do you propose to pay, reimburse or reward participants?

☐ YES  ☐ NO  (If YES, how, how much and for what purpose? Please justify the approach)

2.7 DECEPTION OR CONCEALMENT

[Limited disclosure, deception and active concealment are discussed in Section 2.3 of the National Statement. Essentially the practice is not considered ethical unless there are compelling reasons given for its use] Will the true purpose of the research, or the collection of data itself, be concealed from participants or will participants in any way be deceived?

☒ YES  ☐ NO

If you answered YES, provide a clear justification. [You will also need to provide participants with details of the deception in a debriefing (refer 3.4) and give them the opportunity to withdraw their data if they wish to do so.]

This study will utilize a Zelen methodology which is a standard epidemiological technique and is the recommended approach for multidimensional studies where therapist-patient interactions and pre-existing patient expectations can potentially result in outcome bias. This technique involves initially enrolling participants in a longitudinal cohort study and then subsequently randomizing the participants into the treatment groups. The 'control group' are then unaware of the treatments being compared. Those who are randomized into the treatment groups are then given another plain language statement and consent form detailing the treatments and offering them the choice to be involved. If they do not wish to be involved, they will continue in a longitudinal cohort. At the conclusion of the 12 month study, those in the control group will be re-approached with a separate consent form requesting that their data be used to compare with the outcomes in the treatment groups.

Thus, the use of a Zelen methodology will be concealed from participants but all interventions that participants will be asked to performed will be fully disclosed.

The other aspect of the study is that we are using a placebo/sham laser acupuncture condition. Participants who are being offered the opportunity to be involved in the laser acupuncture aspect of the study will be informed in the plain language statement that they have a 50% chance of receiving inactive laser that will be made to look like real laser. At the conclusion of the study when participants are unblinded, the researcher will provide debriefing.

3. RISK AND RISK MANAGEMENT

3.1 STUDY PROFILE –DOES THE RESEARCH INVOLVE THE FOLLOWING:

[Tick as many as apply. Provide details in methodology –section 1.5 and attach information where indicated]

• use of questionnaires designed by the researcher (attach a copy)
• use of standard survey instruments (attach a copy)
• use of on-line surveys (attach printout of screen information)
• use of interviews (attach the list of interview questions)
• use of focus groups (attach the list of focus group topics/questions)
• observation of participants without their knowledge
• covert observation
• audio-taping interviewees or events
• video-taping interviewees or events
• access to personal and/or confidential data (including student, patient or client data) without the participant’s specific consent
• administration of any stimuli, tasks, investigations or procedures which may be experienced by participants as physically or mentally painful, stressful or unpleasant during or after the research process
• performance of any acts which might diminish the self-esteem of participants or cause them to experience embarrassment, regret or depression
• research about participants involved in illegal activities
• research conducted in an overseas setting

YES  NO
3.2 POTENTIAL RISKS TO PARTICIPANTS
Identify, as far as possible, all potential risks to participants (e.g. physical, psychological, social, legal or economic etc.), associated with the project and the setting (e.g. overseas) in which the project is conducted. It may be useful to consider the study profile above and your response to participant details in section 2

Ionizing radiation from knee x-rays: These are essential to the project to enable diagnosis of any knee joint osteoarthritis and to grade the disease severity. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisievert (mSv) each year. The additional effective dose participants will receive from entering this trial is approximately 0.02 mSv. At this dose level, no harmful effects of radiation have been demonstrated as any effect is too small to measure. Studies suggest any risk is minimal. We have approval from the Radiation Advisory Committee (Dept Hum Service) to perform these x-rays in other studies of knee osteoarthritis. If participants have had a knee xray within 12 months, they will not be required to have another one as part of this study.

Risk from needle acupuncture: Adverse events with acupuncture are rare, and are usually avoidable with adequate training and care during acupuncture treatments. General complications relate to direct needle puncture of underlying skin structures and organs. There have been no deaths in medical practice from medical acupuncture in Australia in 37 years of established medical acupuncture practice. The minor significant adverse events have been well studied and occur at approximately 14 per 10,000 treatments in skilled hands. Adverse effects reported from peripheral treatments such as used in this study include: Bleeding (occurs in 3%), drowsiness (occurs in 1%), local pain (occurs in 1%), syncope, infection, retained needle, erythema. To reduce the risk of adverse events, acupuncture is generally regarded as contraindicated in patients with severe bleeding disorders (needle acupuncture), pregnancy, cardiac pacemaker (acupuncture with electrical stimulation), and patients at risk from bacteraemia such as asplenic or neutropenic patients (indwelling needle acupuncture). The doctors in the trial have long term experience in treating these adverse events if they arise. Needle insertion will be done using standard needle insertion techniques and with careful anatomical precision regarding avoidance of important structures and organs. Needles used in the trial will be standard single use disposable needles with standard needle safety and sterile techniques. Patients will be lying down for treatment to minimize risk of fainting.

Risk from laser acupuncture: Very few side effects have been reported from laser acupuncture. If a patient is allergic to light then they may get a rash or blister for a few days. Rarely the underlying condition or pain may feel aggravated for a few days presumably as the healing response is more active after treatment. The patients will be treated with 10 milli-Watt laser acupuncture as per routine clinical practice. No general long-term detrimental effects of laser acupuncture have ever been recorded in 25 years of usage in Australia or overseas.

Risk from placebo laser acupuncture: If a patient is allergic to light then they may get a rash or blister for a few days. It is also possible that patients in the placebo arm of the trial who experience a treatment benefit may experience psychological issues when informed of their randomisation status.

The participants may experience some psychological distress while completing the psychological questionnaires relating to depression and mood.

3.3 MANAGING POTENTIAL RISKS
Describe what measures you have in place to minimize these potential risks to participants and to ensure that support is available if needed. (Depending on risks, participants may need additional support (e.g. external counseling) during or after the study)

To minimise the risks from needle and laser acupuncture, we will be excluding people who have contraindications to receiving this treatment such as bleeding disorders. The treatments are being performed by qualified experienced acupuncturists who are medical doctors with postgraduate acupuncture training so they are well qualified to deal with any medical emergencies. The acupuncturist will discuss verbally the nature and risks of the intervention prior to the treatment itself. The needle procedures will be performed under aseptic conditions using standardised techniques. The participants are asked in the PLS to discuss with the acupuncturist any side effects they experience.

To minimise any feelings of psychological discomfort following unblinding of the participants who received placebo/sham laser acupuncture, the researcher will discuss the mechanisms of pain, the natural history of knee pain etc to help the participant understand why they may have reported improvement despite receiving a placebo treatment.

If the questionnaire results indicate very severe depression in an individual, the participant will be contacted and advised to speak to their usual general practitioner about their feelings.

3.4 DEBRIEFING (if applicable)
What debriefing will participants receive following the study and when? (Attach a copy of any written material or statement to be used in such a debriefing, if applicable). [Participants may need to talk about the experience of being involved in the study with the researchers, as well as learn more about the aims of the research]

Research participants will receive a written report, outlining the overall study results, at its conclusion. They will also be given the opportunity to discuss with researcher any aspects of the study or any issues that they may have.

3.5 BENEFITS COMPARED TO POTENTIAL RISKS
Outline the benefits of the study to the community (and participants, if applicable), relative to the potential risks to participants

The results of this study will help determine the efficacy and cost effectiveness of acupuncture in the treatment of chronic knee pain. This will help to identify interventions that may reduce the symptoms, and subsequently the personal and economic burden of the condition. The risks associated with the study are small and thus are outweighed by the benefits. Another benefit for those participants who receive the needle or laser acupuncture is that they may receive significant reduction in symptoms.

3.6 MANAGING ADVERSE / UNEXPECTED OUTCOMES
Describe what measures you have in place in the event that participants experience adverse effects arising from their involvement in the project (e.g. adverse drug reaction, revelation of illegal activity, or unexpected distress due to questioning)

The following measures will be in place in the event of adverse effects experienced by the participants:

1. General medical practitioners who are qualified and experienced in providing acupuncture will be delivering the treatments and thus are well qualified to deal with any adverse effects that may arise. The interventions are performed according to standardised treatment protocols designed to minimise adverse effects.

2. The research team consists of specialist physicians, general practitioners, physiotherapists and a psychologist who are experienced in the conduct of clinical trials, the delivery of acupuncture treatment and in management of chronic knee pain.

3.7 POTENTIAL RISKS TO RESEARCHERS
Will there be any significant risks to researchers associated with the project and the setting (e.g. overseas) in which the project is conducted. (e.g. personal safety, health, emotional well being)? [Refer to the University’s Environmental Health & Safety Manual for more information]

☐ YES ☒ NO (If YES, how will such risks be addressed)

4. INFORMATION FOR PARTICIPANTS AND INFORMED CONSENT

Before research is undertaken, the informed and voluntary consent of participants (and other properly interested parties) is generally required (refer Section 2 of the National Statement for more details). Information needs to be provided to participants at their level of comprehension about the purpose, methods, demands, risks, inconveniences, discomforts and possible outcomes of the research. Such information is often provided in a written Plain Language Statement. Each participant’s consent needs to be clearly established (e.g. by using a signed Consent Form, returning an anonymous survey or recording an agreement for interview).

4.1 PROVIDING INFORMATION FOR PARTICIPANTS

(a) Will you be providing participants with information in a written Plain Language Statement?

☒ YES ☐ NO (If NO, provide details of the protocol you will use to explain the research project to participants and invite their participation?)

(b) Will arrangements be made to ensure that participants who have difficulty understanding English can comprehend the information provided about the research project?

☐ YES ☒ NO (If YES, what arrangements have been made? If NO, give reasons. The questionnaires to be used require that participants can understand English and the use of interpreters would invalidate the results.)
4.2 PLAIN LANGUAGE STATEMENT (IF APPLICABLE)

CONFIRM THAT THE PLAIN LANGUAGE STATEMENT WILL:

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[**Re 10 – it is possible for data to be subject to subpoena, freedom of information request or mandated reporting by some professions. Depending on the research proposal you may need to specifically state these limitations]

PLEASE ATTACH A COPY OF THE PLAIN LANGUAGE STATEMENT TO YOUR APPLICATION

4.3 OBTAINING CONSENT

(a) How will each participant's consent be established?

By signing and returning a Consent Form – see 4.4
By returning an anonymous survey
Via a verbal agreement
Via a recorded agreement for interview

(b) If participants are unable to give informed consent, explain who will consent on their behalf and how such consent will be obtained.

4.4 CONSENT FORM (IF APPLICABLE)

CONFIRM THAT THE CONSENT FORM WILL:

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1. be printed on University of Melbourne letterhead
2. include the title of the project and names of researchers
3. state that the project is for research purposes
4. state that involvement in the project is voluntary and that participants are free to withdraw at any time, and free to withdraw any unprocessed identifiable data previously supplied
5. outline particular requirements of participants including, for example, whether interviews are to be audio and/or video-taped
6. include arrangements to protect the confidentiality of data
7. include advice that there are legal limitations to data confidentiality (see below)**
8. (if the sample size is small) confirm that this may have implications for protecting the identity of the participants
9. (once signed and returned) be retained by the researcher

[**Re 7 – it is possible for data to be subject to subpoena, freedom of information request or mandated reporting by some professions. Depending on the research proposal you may need to specifically state and explain these limitations]

PLEASE ATTACH A COPY OF THE CONSENT FORM TO YOUR APPLICATION

5. PRIVACY AND CONFIDENTIALITY

Privacy can be described as "...a complex concept that stems from a core idea that individuals have a sphere of life from which they should be able to exclude any intrusion." A major application of the concept of privacy is information privacy: the interest of a person in controlling access to and use of any information personal to that person. 'Confidentiality', a narrower more specific term than 'privacy' refers to the legal and ethical obligation that arises from a relationship in which a person receives information from or about another.

At the Commonwealth level, the collection, storage, use and disclosure of personal information by Commonwealth agencies is regulated by the Privacy Act 1988. Sections 95 and 95A of the Act are of particular relevance to researchers. There is regulation at State and Territory level in the form of legislation related to privacy generally or the administration of agencies, or administrative codes of practice. In Victoria, the Health Records Act 2001 regulates health information handled by the Victorian public sector and private sector, while the Information Privacy Act 2000 regulates the collection and handling of non-health-related personal information. The National Statement states that an HREC must be satisfied that a research proposal conforms to all relevant Commonwealth, State or Territory privacy legislation or codes of practice.

5.1 ACCESSING PERSONAL INFORMATION

[Personal Information’ includes names, addresses, or information/opinion about an individual whose identity is apparent, or can reasonably be ascertained, from the information/opinion. It also includes Health Information (e.g. health opinions, organ donation or genetic information) and Sensitive Information (e.g. political views, sexual preferences, criminal records)]

Is there a requirement for the researchers to obtain Personal Information (either identifiable or potentially identifiable) about individuals without their consent? YES NO

a) from Commonwealth departments or agencies?
   □ YES □ NO
b) from State departments or agencies?
   □ YES □ NO
c) from Other Third Parties, such as non-government organisations?
   □ YES □ NO

If you answered YES to (a), (b) or (c), you will need to complete Module P and attach it to this application

5.2 REPORTING PROJECT OUTCOMES

(a) Will the project outcomes be made public at the end of the project?
   □ YES □ NO (If YES, give details of how the results will be made public (eg in journal articles book, conference paper, the media, working paper or other). If NO, explain why not. The study outcomes will be reported in a journal article and presented at conferences.

(b) Will a report of the project outcomes be made available to participants at the end of the project?
   □ YES □ NO (If Yes, give details of the type of report and how it will be made available. If No, explain why not. A summary of the study outcomes will be sent to participants if requested.
5.3 WILL THE RESEARCH INVOLVE:

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- complete anonymity of participants (i.e., researchers will not know the identity of participants as participants are part of a random sample and are required to return responses with no form of personal identification)?
  - YES ☐ NO ☒

- de-identified samples or data (i.e., an irreversible process whereby identifiers are removed from data and replaced by a code, with no record retained of how the code relates to the identifiers. It is then impossible to identify the individual to whom the sample of information relates)?
  - YES ☐ NO ☒

- potentially identifiable samples or data (i.e., a reversible process in which the identifiers are removed and replaced by a code. Those handling the data subsequently do so using the code. If necessary, it is possible to link the code to the original identifiers and identify the individual to whom the sample or information relates)?
  - YES ☐ NO ☒

- participants having the option of being identified in any publication arising from the research?
  - YES ☐ NO ☒

- participants being referred to by pseudonym in any publication arising from the research?
  - YES ☐ NO ☒

- any other method of protecting the privacy of participants? Please describe:

Note that where the sample size is very small, it may be impossible to guarantee anonymity/confidentiality of participant identity. Participants involved in such projects need to be clearly advised of this limitation in the Plain Language Statement.
6. DATA STORAGE, SECURITY AND DISPOSAL

6.1 DATA STORAGE

Does data storage comply with the University policy? [University of Melbourne Policy on the Management of Research Data and Records is available at: http://www.unimelb.edu.au/records/research.html]

☐ YES ☐ NO (If NO, please explain.)

6.2 DATA SECURITY

(a) Will the Principal Researcher be responsible for security of data collected?

☐ YES ☐ NO (If NO, please provide further details. You may also use this space to explain any differences between arrangements in the field, and on return to campus.)

(b) Will data be kept in locked facilities in the Department through which the project is being conducted?

☐ YES ☐ NO (If NO, please explain how and where data will be held, including any arrangements for data security during fieldwork.)

The medical practitioners delivering the acupuncture treatments will record details of their treatments. These will be stored in locked cupboards at the practitioners practice in accordance with the privacy Act and government regulatory guidelines on the storage of medical records.

(c) Which of the following methods will be used to ensure confidentiality of data? (select all options that are relevant)

• data and codes and all identifying information to be kept in separate locked filing cabinets ☒
• access to computer files to be available by password only ☒
• access by named researcher(s) only ☒
• other (please describe) ☐

(d) Will others besides the researchers associated with this project have access to the raw data?

☐ YES ☒ NO (If YES, please explain who and for what purpose? What is their connection to the project?)

6.3 DATA RETENTION AND DISPOSAL

[Research data and records should be maintained for as long as they are of continuing value to the researcher and as long as recordkeeping requirements such as patent requirements, legislative and other regulatory requirements exist. The minimum retention period for research data and records is five years after publication, or public release, of the work of the research as stated in the University of Melbourne Code of Conduct for Research. If the project involves clinical trial(s), the data should be kept for a minimum of 15 years (refer to Section 3.3 of the National Statement for further details)]

Specify how long materials (e.g. files, audiotapes, questionnaires, videotapes, photographs) collected during the study will be retained after the study and how they will ultimately be disposed of.

Study data will be maintained for 15 years after publication of results. All paper records will be shredded and electronic files will be deleted by the principal researcher.

7. POTENTIAL CONFLICT OF INTEREST

7.1 POTENTIAL CONFLICT OF INTEREST

Is there any affiliation or financial interest for researchers in this research or its outcomes or any circumstances which might represent a perceived, potential or actual conflict of interest?

☐ YES ☒ NO (If YES, give brief details?)
7.2 COMPLIANCE WITH THE CODE OF CONDUCT FOR RESEARCH

[University researchers must disclose and manage Conflict of Interest in accord with the provisions of the University’s Code of Conduct for Research. See http://www.unimelb.edu.au/ExecServ/Statutes/r171r8.html ]

Is the Conflict of Interest noted above in section 7.1 being managed in accordance with the Code of Conduct?

☐ YES ☐ NO ☑ Not Applicable

8. DECLARATION BY RESEARCHERS

The information contained herein is, to the best of our knowledge and belief, accurate.

We have read the University’s current human ethics guidelines, and accept responsibility for the conduct of the procedures set out in the attached application in accordance with the guidelines, the University’s Code of Conduct for Research and any other condition laid down by the University of Melbourne’s Human Research Ethics Committee or its Sub-Committees. We have attempted to identify all risks related to the research that may arise in conducting this research and acknowledge our obligations and the rights of the participants. We have the appropriate qualifications, experience and facilities to conduct the research set out in the attached application and to deal with any emergencies and contingencies related to the research that may arise.

If approval is granted, the project will be undertaken in strict accordance with the approved protocol and relevant laws, regulations and guidelines.

We, the researcher(s) agree:
• To only start this research project after obtaining final approval from the Human Research Ethics Committee (HREC);
• To only carry out this research project where adequate funding is available to enable the project to be carried out according to good research practice and in an ethical manner;
• To provide additional information as requested by the HREC;
• To provide progress reports to the HREC as requested, including annual and final reports;
• To maintain the confidentiality of all data collected from or about project participants, and maintain security procedures for the protection of privacy;
• To notify the HREC in writing immediately if any change to the project is proposed and await approval before proceeding with the proposed change;
• To notify the HREC in writing immediately if any adverse event occurs after the approval of the HREC has been obtained;
• To agree to an audit if requested by the HREC;
• To only use data and any tissue samples collected for the study for which approval has been given;

We have read the National Statement on Ethical Conduct in Human Research and agree to comply with its provisions.

All researchers associated with this project must sign

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<th>Researchers’ Name (please PRINT)</th>
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<td>A/Prof Paul McCrory</td>
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<td>Prof Kim Bennell</td>
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<td>Dr Rana Hinman</td>
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<td>Prof Prasuna Reddy</td>
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<td>A/Prof Kay Crossley</td>
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<td>Mr Ben Metcalf</td>
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<td>Dr Marie Pirotta</td>
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<td>A/Prof Andrew Forbes</td>
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<td>Prof Philip Conaghan</td>
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<td>Dr Roberta Chow</td>
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<td>A/Prof Anthony Harris</td>
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9. DECLARATION BY DEPARTMENTAL HUMAN ETHICS ADVISORY GROUP (HEAG)

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☐ TECHNICAL REVIEW COMPLETED ☐ ETHICAL REVIEW COMPLETED

The HEAG has reviewed this project and considers the methodological/technical and ethical aspects of the proposal to be appropriate to the tasks proposed and recommends approval of the project. The HEAG considers that the researcher(s) has/have the necessary qualifications, experience and facilities to conduct the research set out in the attached application, and to deal with any emergencies and contingencies that may arise. [Note: If the HEAG Chair is also a principal researcher for this project, the declaration should be signed by another authorised member of the HEAG]

Comments/Provisos:

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10. DECLARATION BY HEAD OF DEPARTMENT

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☐ TECHNICAL REVIEW COMPLETED ☐ ETHICAL REVIEW COMPLETED

I have reviewed this project and consider the methodological, technical and ethical aspects of the proposal to be appropriate to the tasks proposed and recommend approval of the project. I consider that the researcher(s) has/have the necessary qualifications, experience and facilities to conduct the research set out in the attached application, and to deal with any emergencies and contingencies that may arise. [Note: If the Head of Department is also a principal researcher for this project, the declaration should be signed by another authorised member of the Department]

This project has the approval and support of this Department/School/Centre.

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11. WHEN COMPLETE

When this form has been completed and finalised it should be attached to the coversheet section of the application completed in Themis Research and then submitted to the nominated Human Ethics Advisory Group for review.