eFORM VERSION

Version 4.1 18-Jul-2015

PROTOCOL

Protocol No: 017036

Title: Open placebo administration for wound healing

GENERAL

Prior to completing your application:

- Read the Guiding Principles for conducting research with human participants.
- Go through the Applicants' Reference Manual.
- Check if an exemption applies (see Guiding Principles section 6.1 and Applicants' Reference Manual Section 3.8).
- Check if the matter needs to be referred to a Health and Disability Ethics Committee (HDEC) (see Guiding Principles section 3.1 and 6.1 and Applicants' Reference Manual Section 4.5).

For creating and submitting your application refer to the Human Ethics Module Quick Guide.

All documentation to support your application is on the UAHPEC web page.

For any queries please log a call with the Staff Service Centre at ext. 86000 or staffservice@auckland.ac.nz and it will be referred to the relevant team in the Research Office or ITS.

Please Note: Internet Explorer should not be used when working in InfoEd as many functions are not compatible with this browser. We recommend using the following browsers: Google Chrome, Mozilla Firefox, or Safari (for Mac).

SECTION A: PERSONNEL

***Are you a Student?**

Yes ☐ No ☑

PI: Petrie, Keith J*

Department: Psychological Medicine*

1. List all personnel, including co-investigators and ethics advisors, by selecting their name from the UNIVERSITY PERSONNEL page and add their Role from the dropdown list. ?☐
2. If you are a student, you must add your own name to allow access after closing the form.
3. To change the Principal Investigator, tick the 'PI' checkbox to the left of the relevant person's name.

Note: A student cannot be a PI. See Applicants' Reference Manual Section 5.0 that states: "For Doctoral, Masters and Honours research, applications should be submitted by the primary supervisor who will be the Principal Investigator (PI)".

UNIVERSITY PERSONNEL

(Add)

Petrie, Keith J

PI	N/A	N/A	*Role
☑	23-Feb-2016		PI

Broadbent, Elizabeth A

PI	N/A	N/A	*Role
☐			Co-Inv

Jarrett, Paul

PI	N/A	N/A	*Role
☐			Co-Inv

Any University of Auckland personnel and other personnel that cannot be found in the lookup list should be added here.

If you are a student, please add your University of Auckland ID

Full Name (and ID)	Institution / Department	Project Role	Email address	
Ashwin Mathur	Psychological Medicine	Researcher	red.ash.mathur@gmail.com	

*Is this a Research Project or Coursework Application? ?

Research

SECTION B: RESEARCH PROCEDURES

B:1 Title.
Open placebo administration for wound healing

***B:2 Aims/objectives of the project.** ?❐
Aim: The aim of the study is to establish if wound healing is faster for participants taking open-label placebo pills (i.e. known by the participant to be pharmacologically inert) than participants taking no treatment for their wound healing.
Hypothesis: Photographs of a 4 mm diameter punch biopsy wound in the inner arm will show a greater area of re-epithelialisation at 7 days and 10 days after wounding for participants using daily open placebo treatment than participants using no treatment.

Please note: all acronyms must be written out in full the first time they appear in the application, recruiting materials, Participant Information Sheet (PIS) and Consent Form (CF).

***B:3 Summary of the project.** ?❐
Placebo treatment can be effective for subjective complaints (Miller, Colloca, & Kaptchuk, 2009) and also results in physiological changes (Finniss et al., 2010), suggesting that it may be an effective treatment option for some people. However, it is currently unethical to prescribe placebo treatment, as this typically requires deception of patients, undermining the principle of informed consent. This study aims to establish whether open placebo treatment (i.e. placebo administration without deception, where participants are aware that they are taking placebos) is effective for wound healing, which would allow patients to benefit from harnessing placebo effects with full informed consent.

Wound healing rates can be affected by psychosocial factors such as stress (Walburn et al., 2009), and psychosocial interventions can improve wound healing rates (Broadbent et al., 2012; Koschwanez et al., 2013). This means that a psychologically-based treatment such as placebo may affect wound healing rates through mechanisms such as expectation of improvement or conditioned physiological effects from ingesting medication (Benedetti & Amanzio, 2013). Kaptchuk et al. (2010) demonstrated that open placebo treatment was effective for improving symptoms and functioning for participants with Irritable Bowel Syndrome, setting a precedent for the use of open placebo treatment to improve participant outcomes. Given these results, it is worth investigating whether open placebo is effective in improving wound healing rates in healthy participants.

***B:4 Project duration (in months).** ?❐
12

Note: The start date is when the proposal is approved

***B:5 Describe the study design.** ?❐
Overview
This study is a randomized controlled trial (RCT) comparing open placebo treatment with no-treatment controls. All participants will meet with a specialist dematologist who will use a script to explain the study and the efficacy and evidence for the placebo effect, setting up the expectation for greater wound healing from placebo treatment. They will then receive a punch biopsy wound to the inner arm. Participants will be then randomized to either the open placebo group, who will receive pharmacologically inert pills to take twice daily for two weeks, or to a no treatment control group. Healing rates will be measured and blindly rated as the area of re-epithelialisation of the wound at 7 days and 10 days after the punch biopsy.
Design methodology
Participants interested in completing the research will initially be contacted by e-mail or telephone with the participant information sheet and a summary of the research aims and design to ascertain interest and availability.
In the experimental session the study information will be provided to all participants and informed consent obtained. Following informed consent and baseline measures, participants will be taken to another room at the University Research Clinic where a small punch biopsy procedure will be carried out by Dr Paul Jarret, specialist dermatologist. Using a script developed for the study, Dr Jarrett will again briefly explain the study and provide a rationale for placebo treatment may be beneficial for wound healing. The dermatologist will provide an additional consent form specifically related to receiving the wound prior to carrying out the procedure. The procedure involves creating a 4 mm punch biopsy wound 7 cm superior to the medial epicondyle of the inner upper arm (the participant chooses which arm), delivered under local anaesthetic and covered with a hydrocolloid dressing until the first photograph session 7 days later.
Participants will then be randomised to either the open placebo or the control group using a randomization procedure completed by a co-investigator not involved in the experiment, and group allocation will be provided in sealed opaque sequentially numbered envelopes. Participants in the open placebo condition will be provided

with two weeks' worth of placebo pills by Dr Jarrett, along with instructions for how to take the pills.
Two brief follow up sessions will be scheduled at 7 days and 10 days following the wounding session. These sessions will both involve the Master student Ash Mathur taking a photograph of the wound site using a digital camera with macro lens, and administration of a brief follow up questionnaire. Healing will be determined by blind ratings of wound photographs to determine healing and plotting the area of re-epithelialisation using ImageJ software.
Measures
Wound healing will be measured from photographs, rated as healed or not and also operationalised as the percentage of the wound area re-epithelialised out of the whole wound area. Two separate measures will be taken at 7 days and 10 days after wounding. Photographs will be taken with the same camera under similar conditions, using a standard spot size next to the wound for calibration, and judgment of re-epithelialisation will be carried out by a researcher blind to participant or group. Histological analyses of the skin samples will also be taken to correlate immune markers with baseline sleep and stress, and subsequent wound healing rate.
Additional measures will be from a brief baseline questionnaire, including demographic information (age, sex, ethnicity), health behaviours (smoking, alcohol use, activity level, caffeine intake, sleep amount and quality), stress, body mass index, and medication usage (currently and prior frequency).
Additional items will also ask about placebo adherence, and expectation that the placebo pills will be beneficial. Items on health behaviours, medication usage, placebo adherence, and expectation will be administered at baseline and at the final follow up session at 10 days.

***B:6 List all the methods used for obtaining information.**

***Interviews** ?☐
Yes ☐ No☑

***Focus groups** ?☐
Yes ☐ No☑

***Questionnaires** Please attach the questionnaire(s) in the 'Attachment' section at the end of the form. ?☐
Yes ☑ No☐

***Observations**
Yes ☐ No☑

***Other**
Yes ☑ No☐

*Explain:
Wound healing will be measured by taking photographs of the punch biopsy site at 7 days and 10 days following wounding and measuring the area of re-epithelialisation. The photographs will be taken by the researchers and measurement of re-epithelialisation completed by a researcher blind to group.

***B:7 Does the research involve processes that involve EEG, ECG, MRI, TMS, FMRI, EMG, radiation, invasive or surface recordings?** ?☐
Yes ☐ No☑

***B:8 Does the research involve processes that are potentially disadvantageous to a person or group (for example, the collection of information which may expose the person/group to discrimination)?**
Yes ☐ No☑

***B:9 Who will carry out the research procedures?**
Initial contact, questionnaire administration, and all follow up sessions for participants after wounding will be carried out by Ashwin Mathur, Masters candidate. The punch biopsy procedure and briefing about the placebo effect will be carried out by a dermatologist, Dr Paul Jarrett.

If necessary, please provide more details of the role(s) of each member of the research team. If the research procedures will be carried out by a third party other than the researcher or co-investigators, please attach a copy of the confidentiality agreement to the "Attachment" section at the end of this form.

* B:10a Where will the research procedures take place? ?☐
Please use a maximum of 100 characters (including spaces)
Clinical Research Centre, FMHS

If permission is required to conduct the study at a specific location, please attach an appropriate PIS and Consent form, or a support letter, in the "Attachment" section at the end of the form.

***B:10b Will the research be conducted overseas?**
Yes ☐ No☑

***B:11a Is the questionnaire web-based?** ?☐
Yes ☐ No☑

***B:11b Is it an anonymous questionnaire?** ?☐
Yes ☐ No☑

***B:12 How much time will participants need to give to the research?** ?☐
1 hour

***B:13 Will information on the participants be obtained from third parties?** ?☐
Yes ☐ No☑

***B:14 Will any identifiable information on the participants be given to third parties?** ?☐
Yes ☐ No☑

***B:15 Does the research involve evaluation of the University of Auckland services or organisational practices where information of a personal nature may be collected and where participants may be identified?**
Yes ☐ No☑

***B:16 Does the research involve a conflict of interest or the appearance of a conflict of interest for the researcher?** ?☐
Yes ☐ No☑

***B:17 Does the research involve matters of commercial sensitivity?**
Yes ☐ No☑

***B:18 Has the study design or the use of the data been influenced by an organisation outside the University of Auckland?** ?☐
Yes ☐ No☑

***B:19 Are you intending to conduct the research in the University of Auckland class time?** ?☐
Yes ☐ No☑

***B:20 Does the research involve deception of the participants, including concealment or covert observations?** ?☐
Yes ☐ No☑

***B:21 Is there any koha, compensation or reimbursement of expenses to be made to participants?** ?☐
Yes ☑ No☐

*Explain the level of payment and indicate in the PIS:
$20 Westfield gift voucher participants who withdraw will still receive the voucher

***B:22a Is this an intervention study?** ?☐
Yes ☑ No☐

*Explain and indicate this on the PIS:
Yes we have described this on PIS

***B:22b Does this research involve potentially hazardous substances?** ?☐
Yes ☐ No☑

SECTION C: PARTICIPANTS

*C:1 Who are the participants in the research? ?☐

*Adults
Yes ☑ No ☐

*Own colleagues
Yes ☐ No ☑

*Own students
Yes ☐ No ☑

*Persons whose capacity to give informed consent (other than children) is compromised
Yes ☐ No ☑

*Persons who are in a dependent situation, such as people with a disability, residents of a hospital, nursing home or prison, or patients highly dependent on medical care
Yes ☐ No ☑

*Persons aged less than 16 years old where parental consent is NOT being sought
Yes ☐ No ☑

*Persons aged less than 16 years old where parental consent is sought
Yes ☐ No ☑

*Other
Yes ☐ No ☑

*C:2 How many organisations and departments within the organisations will participate in your project?
Department of Psychological Medicine and Department of Medicine

If you have letters of support, please attach these in the 'Attachment' section at the end of the form.

*C:3 How many individual participants (research participants) will participate in your project?
68 participants will be required to achieve a power of 80% (i.e. 1-β = 0.8), given an expected effect size of d = 0.7 based on a meta-analysis of wound healing studies (Robinson et al., unpublished manuscript) and α = .05. However, to increase power to detect a potentially smaller effect size and to control for possible attrition at follow-up, the researchers will aim to recruit at least 100 participants.

*C:4 How will you identify potential participants and by which method are participants invited to take part in the research? ?☐
Participants will be recruited through an advertisement flyer promoted through social media, the University of Auckland's junk email address book, in public areas at the university's campuses, or from emails sent by course coordinators to the university's students. Interested participants will contact the experimenter and screened with a generic checklist detailing the inclusion and exclusion criteria by phone. If they meet criteria, they will then be invited to participate in the study.

Using a direct approach to recruit potential participants is not recommended.

Please attach the advertisement, media release, or notice, etc. and the letter of permission from the agency supplying them (if applicable) in the 'Attachment' section at the end of the form.

*C:5 Who will make the initial approach to potential participants? ?☐
Researcher(s)

*C:6 Will access to participants be gained with consent of any organisation? ?☐
Yes ☐ No ☑

*C:7 Is there any special relationship between participants and researchers? ?☐
Yes ☐ No ☑

*C:8 Does the research involve the University of Auckland staff or students where information of a personal nature may be collected and where participants may be identified?
Yes ☐ No ☑

*C:9 Does the research involve participants who are being asked to comment on employers?
Yes ☐ No ☑

*C:10 Are there any potential participants who will be excluded?
Yes ☑ No ☐

*Explain and state the criteria for excluding participants:
Participants will be non-smokers, aged between 18 and 65. They must be able to understand and write in English. Participants will be excluded if they have medical conditions that would affect wound healing (e.g. eczema, psoriasis, anemia, diabetes, etc.), regular use of other treatments affecting wound healing (e.g. anticoagulants, non-steroidal anti-inflammatories), or any surgery or tattoos within the last 30 days.

SECTION D: INFORMATION AND CONSENT

***D:1 By whom and how will information about the research be given to participants?** ?☐

Initial information will be provided in the Participant Information Sheet, and then expanded in more detail in consultation with the participant at the experimental session with the researcher. This includes information on the study procedure, the effectiveness of placebo treatment, and the punch biopsy procedure.
Detailed information of the punch biopsy procedure will be provided by the dermatologist prior to and during the punch biopsy procedure and a separate consent form completed for the biopsy.

***D:2a Will the participants have difficulty giving informed consent on their own behalf?** ?☐

Yes ☐ No☑

***D:3a If a questionnaire is used, will the participants have difficulty completing the questionnaire on their own behalf?** ?☐

Yes ☐ No☑

***D:4 Does the research involve participants giving oral consent rather than written consent?** ?☐

Yes ☐ No☑

***D:5 Does the research use previously collected information or biological samples for which there was no explicit consent?**

Yes ☐ No☑

***D:6 Is access to the Consent Forms restricted to the Principal Investigator and/or the researcher?** ?☐

Yes

***D:7 Will Consent Forms be stored by the Principal Investigator, in a secure manner?** ?☐

Yes

***D:8 Are Consent Forms stored separately from data and kept for six years?** ?☐

Yes

SECTION E: STORAGE AND USE OF RESULTS

*E:1 Will the participants be audio-recorded, video-recorded, or recorded by any other electronic means such as Digital Voice Recorders? ?☐
Yes ☐ No☑

*E:3 For the questionnaire, is any coding scheme used to identify the respondent? ?☐
Yes ☑ No☐

*Explain:
Questionnaires will be labelled with the participant number rather than their name.

*E:4a Explain how and how long the data (including audio-recordings, video-recordings and electronic data) will be stored. ?☐
Six years. Questionnaires will be kept in a locked University filing cabinet in the department of psychological medicine. Electronic data will be stored on the PI's University computer.

*E:4b Explain how data will be used. (For example, in a thesis/dissertation, publications, and/or conference presentations etc.) ?☐
Individuals' data will be pooled with those of other participants and subjected to statistical analyses. Confidentiality will be maintained at all times. The results of analyses will be used for a thesis and may be published in peer reviewed scientific journals and/or presented at conferences.

*E:4c Explain how data will be destroyed. ?☐
Documents will be shredded using commercial confidential document destruction. Electronic records will be deleted.

*E:5 Describe any arrangements to make results available to participants. ?☐
Participants will be asked if they wish to receive a copy of the study results. This may be emailed or posted to participants.

*E:6a Are you going to identify the research participants in any publication or report about the research?
Yes ☐ No☑

*E:6b Is there any possibility that individuals or groups could be identified in the final publication or report? ?☐
Yes ☐ No☑

SECTION F: TREATY OF WAITANGI

*F:1 Does the proposed research have impact on Māori persons as Māori? ?☐

Yes ☐ No ☑

SECTION G: OTHER CULTURAL ISSUES

*G:1 Are there any aspects of the research that might raise any specific cultural issues? ?☐

Yes ☐ No ☑

SECTION H: RISKS & BENEFITS

***H:1 What are the possible benefits to research participants of taking part in the research?** ?☐

There are likely to be no direct benefits for participants. Participants may gain more knowledge about the placebo effect and the process of wound healing.

***H:2 Is the research likely to place the researcher at risk of harm?**

Yes ☐ No☑

***H:3 Is the research likely to cause any possible harm to the participants, such as physical pain beyond mild discomfort, embarrassment, psychological or spiritual harm?** ?☐

Yes ☑ No☐

*Clearly identify/explain these risks in the PIS and CF:

Brief, physical discomfort may be experienced when the local anaesthetic is injected using a needle and syringe when taking punch biopsies. There may also be minor discomfort at the wound site as the local anaesthesia wears-off after the procedure.

There is a very small risk of infection at the wound site. To minimize infection, the wound will be created using standard, sterile procedure, and the wound will be initially covered by a hydrocolloid dressing, which is sterile and provides an impermeable film to protect against bacteria. Any infection will be reported to the study Dermatologist for treatment. Similar studies were carried out in 2010 and 2015 by Broadbent and colleagues in which there were no infections

***H:4 Does the research involve collection of information about illegal behaviour(s) which could place the research or participants at risk of criminal or civil liability or be damaging to their financial standing, employability, professional or personal relationships?**

Yes ☐ No☑

***H:5 Is the research likely to give rise to incidental findings?** ?☐

Yes ☐ No☑

SECTION I: HUMAN REMAINS, TISSUE AND BODY FLUIDS

***I:1 Does the research involve use of human blood, body fluids, or tissue samples?** ?☐

Yes ☑ No ☐

Explain this in the PIS. Please attach a copy of the information to be given to the Transplant Coordinator (if necessary) in the 'Attachment' section at the end of the form, and state the information that the Transplant Coordinator will provide to those giving consent.

***I:2 Are these sample obtained from persons involved in research or will the tissue be obtained from a tissue bank?**

A 4mm cylindrical core of skin tissue will be taken from the upper arm of participants.

***I:3 Is the tissue imported or taken in New Zealand?**

Taken in New Zealand

***I:4 Describe how the sample / specimen is taken.** ?☐

The biopsy will taken from participants' chosen inside upper arm by a specialist dermatologist. This wound is sufficiently small to not require a suture. Biopsying will follow an established protocol from previous work. Briefly, the skin will be cleansed and locally anesthetized (e.g. lignocaine). A full-thickness 4mm circular wound will be created using a sterile, disposable biopsy punch. The tissue will be stored in paraffin and transported back to the University of Auckland for histological processing and analyses. The wound will be photographed, and a hydrocolloid occlusive dressing will be applied. This will take approximately 10 minutes to complete.

***I:5a Is blood being collected?**

Yes ☐ No ☑

***I:6a Will the sample / specimens be retained for possible future use?**

Yes ☐ No ☑

***I:7a Will material remain after the research process?**

Yes ☐ No ☑

SECTION J: CLINICAL TRIALS

*J:1 Is this project a Clinical Trial? ?
Yes ☑ No ☐

Include the declaration of the trial in the PIS under 'Compensation' and answer the remaining questions in this section.

*J:2 Is this project initiated by a pharmaceutical company or any other company involved in health research, including a manufacturer or distributor of the medicine or item in respect of which the research is carried out?
Yes ☐ No ☑

*J:3 Are there other New Zealand or International Centres involved?
Yes ☐ No ☑

*J:4 Is there a clear statement about indemnity?
Yes ☑ No ☐

*Explain:
In PIS

Please attach a copy of the indemnity in the 'Attachment' section at the end of the form.

*J:5 Is Standing Committee on Therapeutic Trials (SCOTT) approval required?
Yes ☐ No ☑

*J:6 Is National Radiation Laboratory (NRL) approval required?
Yes ☐ No ☑

*J:7 Is Ethics Committee on Assisted Reproductive Technology (ECART) approval required?
Yes ☐ No ☑

SECTION K: FUNDING

*K:1 Have you applied for, or received funding for this project? ?
Yes ☑ No ☐

* K:2 From which funding institution? ?
Funding Provider:
Departmental graduate fund

* K:3a Is this a UniServices project? ?
(Please note: for all UniServices contracts, a nominal one-off fee will be charged to the contract for the UAHPEC review of this application).
Yes ☐ No ☑

*K:4 Contract reference number:
NA

Please attach the UniServices/commercial contracts associated with the study in the 'Attachment' section at the end of the form.

*K:5 Do you see any conflict of interest between the interests of the researcher, the participants or the funding body? ?
Yes ☐ No ☑

SECTION L: ETHICAL SUMMARY

***L:1 Have you made any other related applications?**

Yes ☐ No ☑

***L:2 Is there any relevant information from past applications or interaction with UAHPEC?**

Yes ☐ No ☑

***L:3 Please provide a summary of all the ethical issues arising from this project and explain how they are to be resolved:** ?☐

Participation is voluntary. Written informed consent will be obtained from all participants. Participants will have the right to withdraw from the study at any time during the experiment. Data will be kept confidential to the researchers. No reports will publish any material that could identify participants. There are no conflicts of interest.

There is a very small risk of infection at the wound site. To minimize infection, the wound will be created using standard, sterile procedure, and the wound will be initially covered by a hydrocolloid dressing, which is sterile and provides an impermeable film to protect against bacteria. Any infection will be reported to the dermatologist for treatment.

UAHPEC expects applicants to identify the ethical issues in the project and explain in the documentation how they have been resolved. The application will not be considered if this is not answered adequately. A 'Not applicable' response is not acceptable.

SECTION M: ETHICS ADVISOR REVIEW

***M:1 Will this Application be reviewed by an Ethics Advisor after you submit it?**

Yes ☐ No ☑

***M:2 Has an Ethics Advisor been consulted in the preparation of this Application?**

Yes ☐ No ☑

ATTACHMENTS

Files of the following formats can be uploaded: .doc, .docx, .xls, .xlsx, .pdf, .gif and .jpg

Document title	Upload	
Questionnaires		
PIS and consent		
Flyer		

SECTION N: APPLICATION CHECKLIST

Please tick below to confirm that you have considered whether the following documents are required for your application and that you have attached them in the attachments section where necessary:

N:1 Participant Information Sheet ☑
(see Applicants' Reference Manual Sections 6.3 and 6.4 for explanation and sample)

N:2 Consent Form ☑
(see Applicants' Reference Manual Section 6.5 for explanation and sample)

N:3 Advertisement ☑

N:4 Questionnaire ☑

N:5 List of Interview Questions ☐

N:6 Confidentiality Agreement ☐
(see Applicants' Reference Manual Sections 6.8 for explanation and sample.)

N:7 Observation Schedule ☐

N:8 Any other supporting documents (for example: approval from Course Coordinator, debriefing sheet) ☐

FEEDBACK/COMMENTS

If you wish to provide feedback on the usability of this e-form, please do so here.

Please do not use this section to make any comments related to the application itself, as the comments made here will not be included in the application.

WHEN YOU ARE FINISHED AND HAVE ANSWERED ALL QUESTIONS, TICK THE 'COMPLETE' BOX AT THE TOP OF THE FORM.

The University of Auckland
Research Office
Level 10, Building 620, 49 Symonds Street, Auckland

Appendix 1

EForm Name: HE Application Form - v4.1

Page:

ATTACHMENTS

Section:

Files of the following formats can be uploaded: .doc, .docx, .xls, .xlsx, .pdf, .gif and .jpg

Question: Upload

File Name: Open Placebo (AM) - Questionnaires.docx

DATE			
ID			

THE UNIVERSITY OF AUCKLAND
FACULTY OF MEDICAL AND HEALTH SCIENCES

Baseline Questionnaire

This questionnaire is designed to gather some background information on your demographics, as well as your health and medication use, and your perceptions of this experiment. All of the information you give us is in confidence to the researchers and will be used only for the purposes of the study.

For all these questions there are no right or wrong answers - an answer is correct if it is true for you. We are most interested in your own opinion. Please choose the response that best fits with your circumstances.

Thank you for your help with this study!

Background Information

Please answer the following questions by filling in the blanks or circling the answer that best correspond to you:

Gender:	Age:
Height (cm):	Weight (kg):

1. What ethic group do you belong to? Circle the numbers that apply to you

New Zealand European	1
Maori	2
Samoan	3
Cook Island Maori	4
Tongan	5
Niuean	6
Chinese	7
Indian	8
Other (such as Dutch, Japanese, Tokelauan, etc.)	9
Please specify:	

1. At what level did you complete your formal education? (circle number)

Primary school	1
Secondary school (up to Year 10)	2
Secondary school (including Year 11)	3
Secondary school (including Years 12 & 13)	4
Technical or Trade Certificate	5
University or Polytechnic Diploma	6
University degree	7

Health-related behaviours

1. Do you currently smoke?

	Yes. On an average day, I smoke _____ cigarettes.
	No, not any more. I quit smoking _____ago.
	No, I have never smoked.

2. During the past three months how often have you drunk alcohol, on average?

	Not at all			1-3 times a month
	Less than once a month			3-6 times a week
	1-3 times a month			Every day

3. On days when you did drink alcohol in the last three months, how many drinks did you have on an average day?

	0 drinks			3-4 drinks
	1 drink			5-6 drinks
	2 drinks			7-11 drinks
				12 or more drinks

4. During the past three months how often have you drunk caffeine, on average?

	Not at all			1-3 times a month
	Less than once a month			3-6 times a week
	1-3 times a month			Every day

5. On days when you did drink caffeine in the last three months, how many caffeinated beverages did you have on an average day?

	0 drinks			3-4 drinks
	1 drink			5-6 drinks
	2 drinks			7-11 drinks
				12 or more drinks

6. During your average week, how many times do you engage in 30 minutes or more of physical activity (e.g. going for a walk, going to the gym, riding a bike, swimming)?

	Never			Four times
	Once			Five time
	Twice			Six times
	Three times			Every day

7. During the past week, how would you rate your diet?

	Very poor
	Poor
	Fair
	Good
	Very good

Current Sleep

The following questions relate to your usual sleep habits during the past seven days only. Your answers should indicate the most accurate reply for the majority of days and nights in the past week.

1. During the past week, what time have you usually gone to bed at night?

BED TIME _____

2. During the past week, how long (in minutes) has it usually taken you to fall asleep each night?

NUMBER OF MINUTES _____

3. During the past week, what time have you usually gotten up in the morning?

GETTING UP TIME _____

4. During the past week, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)

HOURS OF SLEEP PER NIGHT _____

5. During the past week, how would you rate your sleep quality overall?

	Very good
	Fairly good
	Fairly bad
	Very bad

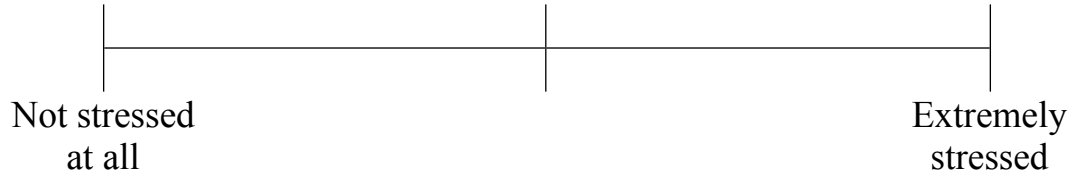
PSS

The questions in this scale ask you about your feelings and thoughts **during the last week**. In each case, you will be asked to indicate by circling *how often* you felt or thought a certain way.

0 = Never 1 = Almost Never 2 = Sometimes 3 = Fairly Often 4 = Very Often

In the last week, how often have you been upset because of something that happened unexpectedly?	**0 1 2 3 4**
In the last week, how often have you felt that you were unable to control the important things in your life?	**0 1 2 3 4**
In the last week, how often have you felt nervous and "stressed"?	**0 1 2 3 4**
In the last week, how often have you felt confident about your ability to handle your personal problems?	**0 1 2 3 4**
In the last week, how often have you felt that things were going your way?	**0 1 2 3 4**
In the last week, how often have you found that you could not cope with all the things that you had to do?	**0 1 2 3 4**
In the last week, how often have you been able to control irritations in your life?	**0 1 2 3 4**
In the last week, how often have you felt that you were on top of things?	**0 1 2 3 4**
In the last week, how often have you been angered because of things that were outside of your control?	**0 1 2 3 4**
In the last week, how often have you felt difficulties were piling up so high that you could not overcome them?	**0 1 2 3 4**

Please rate how stressed you have felt over the last seven days on the scale below by putting an X on the appropriate place on the line.



Medications

The following questions relate to your medication usage, currently and in the past.

1. How frequently have you taken pills of any type within the last 3 months?

Every 1-3 days____ Every 4-7 days____ Every 2-3 weeks____ Never_____

2. Please list all medications that you **currently** take or are likely to take over the next two weeks.

Medication (Name of medication)	**Dosage** (Best knowledge if unsure, e.g. 'two pills')	**Frequency** (How often, e.g. twice daily)	**Reason** (Condition or purpose for medicine, e.g. allergies)

3. Please list all medications that you have taken **within the last year.**

Medication (Name of medication)	**Dosage** (Best knowledge if unsure, e.g. 'two pills')	**Frequency** (How often, e.g. twice daily)	**Reason** (Condition or purpose for medicine, e.g. allergies)

Experiment-related questions

These questions are related to your understanding and response to the experiment procedure for this study.

1. How well did you understand the information you were just read about the placebo response and wound healing?

Did not understand____	Understood a little____	Understood most____	Understood fully_____

2. If you are randomised to take placebos, how helpful do you expect placebos to be to help your wound heal faster?

Not at all helpful____	A little helpful____	Somewhat helpful____	Very helpful_____

3. If you are randomised to NOT take placebos, how disappointed do you expect to feel that you are not taking the placebo medication?

Not at all disappointed____	A little disappointed____	Somewhat disappointed____	Very disappointed____

Thank you for your participation in this study!

DATE			
ID			

THE UNIVERSITY OF AUCKLAND
FACULTY OF MEDICAL AND HEALTH SCIENCES

Follow Up Questionnaire

This questionnaire is designed to gather information on your health and medication use, and your perceptions of this experiment, since you completed the first questionnaire. All of the information you give us is in confidence to the researchers and will be used only for the purposes of the study.

For all these questions there are no right or wrong answers - an answer is correct if it is true for you. We are most interested in your own opinion. Please choose the response that best fits with your circumstances.

Thank you for your help with this study!

Health-related behaviours

1. Have you smoked during the last seven days?

	Yes. On an average day, I have smoked _____ cigarettes.
	No, I have not smoked in the last week.

2. During the <u>past week</u>, how many days have you drunk alcohol?

	Not at all			3-4 times
	1-2 times			5-7 times

3. <u>On days when you did drink</u> alcohol in the last week, how many drinks did you have on an average day?

	0 drinks			3-4 drinks
	1 drink			5-6 drinks
	2 drinks			7-11 drinks
				12 or more drinks

4. During the <u>past week,</u> how many days have you drunk caffeine?

	Not at all			3-4 times
	1-2 times			5-7 times

5. <u>On days when you did drink</u> caffeine in the last week, how many caffeinated beverages did you have on an average day?

	0 drinks			3-4 drinks
	1 drink			5-6 drinks
	2 drinks			7-11 drinks
				12 or more drinks

6. During <u>the last week</u>, how many times have you engaged in <u>30 minutes</u> or more of physical activity (e.g. going for a walk, going to the gym, riding a bike, swimming)?

	Never			Four times
	Once			Five time
	Twice			Six times
	Three times			Every day

7. During the past week, how would you rate your diet?

	Very poor
	Poor
	Fair
	Good
	Very good

Current Sleep

The following questions relate to your usual sleep habits during the past seven days only. Your answers should indicate the most accurate reply for the majority of days and nights in the past week.

6. During the past week, what time have you usually gone to bed at night?

BED TIME _____

7. During the past week, how long (in minutes) has it usually taken you to fall asleep each night?

NUMBER OF MINUTES _____

8. During the past week, what time have you usually gotten up in the morning?

GETTING UP TIME _____

9. During the past week, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)

HOURS OF SLEEP PER NIGHT _____

10. During the past week, how would you rate your sleep quality overall?

	Very good
	Fairly good
	Fairly bad
	Very bad

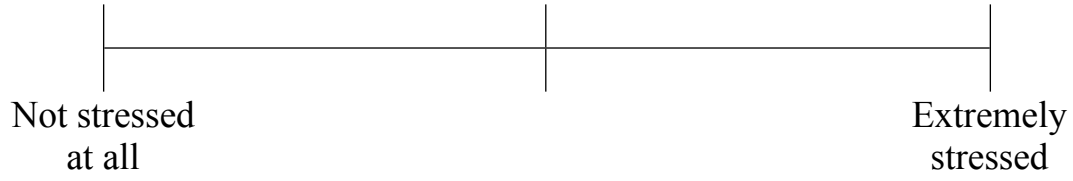
PSS

The questions in this scale ask you about your feelings and thoughts **during the last week**. In each case, you will be asked to indicate by circling *how often* you felt or thought a certain way.

0 = Never 1 = Almost Never 2 = Sometimes 3 = Fairly Often 4 = Very Often

In the last week, how often have you been upset because of something that happened unexpectedly?	**0 1 2 3 4**
In the last week, how often have you felt that you were unable to control the important things in your life?	**0 1 2 3 4**
In the last week, how often have you felt nervous and "stressed"?	**0 1 2 3 4**
In the last week, how often have you felt confident about your ability to handle your personal problems?	**0 1 2 3 4**
In the last week, how often have you felt that things were going your way?	**0 1 2 3 4**
In the last week, how often have you found that you could not cope with all the things that you had to do?	**0 1 2 3 4**
In the last week, how often have you been able to control irritations in your life?	**0 1 2 3 4**
In the last week, how often have you felt that you were on top of things?	**0 1 2 3 4**
In the last week, how often have you been angered because of things that were outside of your control?	**0 1 2 3 4**
In the last week, how often have you felt difficulties were piling up so high that you could not overcome them?	**0 1 2 3 4**

Please rate how stressed you have felt over the last seven days on the scale below by putting an X on the appropriate place on the line.



Medications

Please list all medications that you have taken **during the last week**.

Medication (Name of medication)	**Dosage** (Best knowledge if unsure, e.g. 'two pills')	**Frequency** (How often, e.g. twice daily)	**Reason** (Condition or purpose for medicine, e.g. allergies)

Experiment-related questions

These questions are related to your understanding and response to the experiment procedure for this study.

1. If you were randomised to take placebos, how helpful do you think the placebos have been to help your wound heal faster?

Not at all helpful____	A little helpful____	Somewhat helpful____	Very helpful_____

2. If you were randomised to take placebos, how many times did you miss out on taking the doses? Count morning and evening as separate doses (2 doses per day).

Missed 5+ doses____	Missed 3-4 doses____	Missed 1-2 doses____	Completed all doses_____

3. If you were randomised to NOT take placebos, how disappointed have you felt that you are not taking the placebo medication?

Not at all disappointed____	A little disappointed____	Somewhat disappointed____	Very disappointed____

Thank you for your participation in this study!

Appendix 2

EForm Name: HE Application Form - v4.1

Page:

ATTACHMENTS

Section:

Files of the following formats can be uploaded: .doc, .docx, .xls, .xlsx, .pdf, .gif and .jpg

Question: Upload

File Name: Open Placebo (AM) - PIS and CF.docx

Placebo and wound healing

Supervisor: Professor Keith Petrie
Co-supervisor: Dr Paul Jarrett & Assoc Prof Liz Broadbent

Researcher: Ashwin Mathur

January 2016

THE UNIVERSITY OF AUCKLAND
FACULTY OF MEDICAL AND HEALTH SCIENCES
Department of Psychological Medicine
Faculty of Medical and Health Sciences
Level 12, Support Building
Auckland City Hospital
Park Road, Grafton
Auckland, New Zealand
Jniversity of Auckland Private Bag 92019
Auckland 1142, New Zealand

Participant Information Sheet

Dear Participant

You are invited to take part in a study exploring the effect of a placebo intervention on healing.

This project is being carried out by Ashwin Mathur, a Masters candidate in the Department of Psychological Medicine at the University of Auckland, Dr Paul Jarrett (Consultant dermatologist, Middlemore Hospital), Associate Professor Elizabeth Broadbent and Professor Keith Petrie (Department of Psychological Medicine, University of Auckland), who will be supervising the project.

It is important that you read this document carefully so that you can make an informed decision about whether you would like to participate.

Purpose of the study: Previous research has found that placebo treatment - that is a pill containing no medicine (sugar pill) - is powerful and has measurable effects for many physical conditions. The aim of the study is to investigate the effects of placebo treatment on skin healing after a 4mm punch biopsy wound and whether taking placebo pills after the biopsy makes a difference to healing.

Your rights as a participant: Participation in the study is *entirely voluntary*. If you choose to participate, you can change your mind at any time without giving a reason and without any negative consequences. You can withdraw from the study at any time and withdraw any data traceable to you until you have finished the study. Whether or not you participate in this study will not affect your relationship with the researchers. You will be given a copy of this document to keep.

Procedure:
If you chose to participate in this research you will be contacted by the researcher and a time will be arranged to meet to undertake the research. At this session you will be asked to complete baseline measures that will ask you about your physical

health, sleep, stress level, and medication usage. You will then have a small punch biopsy taken in your inner arm by specialist dermatologist Dr Paul Jarrett. To take the biopsy the dermatologist will mark a 4mm area on your upper inner arm. He will give you a local anaesthetic and will take the biopsy using a sterile, disposable biopsy punch. The wound will be dressed with a clear hydrocolloid (waterproof plastic) dressing. The skin sample will then be transported to the lab for analysis. You will then be randomised to one of two groups: either to take placebo medication after the biopsy, or to let the wound heal without placebo treatment.

Seven and ten days after the biopsy is taken you will meet the researcher again to photograph the wound and complete another brief questionnaire.

Eligiblity: We are recruiting participants who are aged 18 years or over and speak English. You must be a non-smoker. You must be able to understand English. You will not be eligible for this research if you have any current medical conditions that may affect wound healing (e.g. inflammatory skin disease like eczema or psoriasis; chronic illness like diabetes or anemia; or immunological-related health problems) or you are taking medication that may impact immunity or wound healing (e.g. anticoagulants, or painkillers more than once a week). If you are allergic to local anaesthetic you will not be able to take part in this research.

A total of 1 hour will be required for this study. You will receive a $20 Westfield voucher to thank you for your participation

Risks and discomforts: The procedures outlined in this protocol are minimally invasive and have been performed in other research settings. The biopsy procedure may cause slight discomfort when the local anaesthetic is injected using a needle and syringe. There may also be minor discomfort at the wound site as the local anaesthesia wears-off after the procedure. There is a very small risk of infection at the wound site. The wound will be initially covered by a hydrocolloid dressing, which is sterile and provides an impermeable film to protect against bacteria.

Compensation

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Accident Compensation Act 2001. ACC cover is not automatic, and your case will need to be assessed by ACC according to the provisions of the Accident Compensation Act 2001. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors, such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses, and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

If you have any questions about ACC, contact your nearest ACC office or the investigator.
You are also advised to check whether participation in this study would affect any indemnity cover you have or are considering, such as medical insurance, life insurance and superannuation.

Data storage: All data will be stored in electronic format by the researcher. Consent forms will be stored in a locked filing cabinet in the researcher's office at the University, and will be kept for a period of six years. The sample of your skin will be stored at the University of Auckland for analysis. You may request your skin sample be returned to you after analysis.

Confidentiality: All personal information will remain strictly confidential and no material that could personally identify you will be used in any report on this study. Participant names will only appear on the consent form, which will be coded with a participant identification number so that your identity is kept confidential on all questionnaires, essays and physiological data files. After completion of the study, all confidential data, including computer data files, will be kept for a minimum period of six years to allow for publication and re-analysis, after which time it will be securely and confidentially disposed of. Research publications and presentations from the study will not contain any information that could personally identify you.

Results: A summary of the results of this study will be sent to you if you wish. As it takes some time to analyse the results of studies, it may be more than a year after your participation that you receive this information.

We appreciate the time you have taken to read this invitation. If you have any questions please contact:

Ashwin Mathur
Masters student, Department of Psychological Medicine,
The University of Auckland
Private Bag 92019, Auckland 1142
Email: amat079@aucklanduni.ac.nz

Alternative contacts:
Dr Keith Petrie, Department of Psychological Medicine,
The University of Auckland
Private Bag 92019, Auckland 1142
Email: kj.petrie@auckland.ac.nz
Phone: +64 9 923-6564

For ethical concerns, contact:
The Chair of the University of Auckland Human Participants Ethics Committee,

Office of the Vice Chancellor, Research Office,
Alfred Nathan House, The University of Auckland,
Private Bag 92019, Auckland 1142.
ext. 83711; ro-ethics@auckland.ac.nz

Head of Department:
Associate Professor Sally Merry, Department of Psychological Medicine,
The University of Auckland
Email: s.merry@auckland.ac.nz

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE ON __/__/20__ for 3 years, Reference Number

CODE				
DATE				

WRITTEN CONSENT FORM
THIS FORM WILL BE HELD FOR A PERIOD OF SIX YEARS
Project title: Open Placebo and wound healing

Names of researchers: Dr Keith Petrie (supervisor), Dr Paul Jarrett (co-supervisor) and Ashwin Mathur (Masters candidate)

Department of Psychological Medicine
Faculty of Medical and Health Sciences
Level 12, Support Building
Auckland City Hospital
Park Road, Grafton
Auckland, New Zealand
The University of Auckland Private Bag 92019
Auckland 1142, New Zealand

I have read and understood the Participant Information Sheet, have understood the nature of the research, and know why I have been selected. I have had an opportunity to ask questions and have had them answered to my satisfaction.

Consent forms will be held for six years in accordance to university policy

- I agree to take part in this research.
- I understand that taking part in this research is voluntary (my choice).
- I understand that participation will take a total of 1 hour
- I understand that I am able to withdraw from the study at any time without giving a reason, and to withdraw any data traceable to me until I have finished the study.
- I understand that the overall results may be published in a scientific journal but will not include any information that could identify me.
- I am aware that as a result of taking part in this study I will be given a $20 Westfield voucher
- I understand that the research data will be stored for 6 years after which they will be destroyed.
- I understand that the biopsy procedures will be performed by a medcial specialist and registered dermatologist (Dr Paul Jarrett) and may cause slight discomfort

Name:……

Signature:…….…… Date:…….

I wish to receive a copy of the results of this research Yes / No

Email/postal address……

……

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE ON __/__/20__ for 3 years, Reference Number

Appendix 3

EForm Name: HE Application Form - v4.1

Page:

ATTACHMENTS

Section:

Files of the following formats can be uploaded: .doc, .docx, .xls, .xlsx, .pdf, .gif and .jpg

Question: Upload

File Name: PLACEBOS AND WOUND HEALING flyer.docx

THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

MEDICAL AND HEALTH SCIENCES

PLACEBOS AND WOUND HEALING

VOLUNTEERS WANTED

We are looking for volunteers for a study looking at the benefits of taking placebos (pills with no active ingredients) on wound healing.

Help in our research and you will receive $20 Westfield voucher

If you are a non-smoker aged between 18 and 55, do not have any inflammatory skin diseases or immunological-related health problems and are fluent in English, please contact us to assess your eligibility in this study.

Interested?

Contact: Ash Mathur (Masters candidate) Department of Psychological Medicine Faculty of Medical and Health Sciences The University of Auckland, 85 Park Road, Grafton

Email: red.ash.mathur@gmail.com **Phone or text**: +64 21 207 3878

Approved by the University of Auckland Human Participants Ethics Committee on //2014 for 3 years. Reference number