ASCEND: A Study of Cardiovascular Events in Diabetes

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ASCEND: The Research Question

ASCEND: A Study of Cardiovascular Events in Diabetes

• For people with diabetes who have not yet had a heart attack or stroke:
  – Is low-dose aspirin beneficial?
  – Are omega-3 fish oils beneficial?
  – Are these treatments safe?
The Study Design:

2x2 factorial design randomised trial of aspirin vs placebo and omega-3 FA vs placebo

<table>
<thead>
<tr>
<th>Omega-3 Fatty acids (FA) capsules</th>
<th>Aspirin tablets</th>
<th>Placebo tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>3750 Aspirin + Omega-3 FA</td>
<td>3750 Omega-3 FA</td>
<td></td>
</tr>
<tr>
<td>3750 Aspirin</td>
<td>3750 Neither</td>
<td></td>
</tr>
<tr>
<td>7500 Aspirin</td>
<td>7500 Placebo</td>
<td></td>
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<tr>
<td>7500 Placebo</td>
<td>7500 Placebo</td>
<td></td>
</tr>
</tbody>
</table>
The Problem
The Solution

- Streamlined
- Cost effective
- Simple eligibility criteria
- Mail-based trial design
No study clinics required
The Funding

• British Heart Foundation special project grant £2.7 million

• Bayer/Abbott: study drug and funding for packaging
Trial coordination

• Sponsor: University of Oxford
• Steering Committee
• Independent Data Monitoring Committee
The Next Problem

• Identification of potentially eligible study participants
  – Central databases
    • Hospital-based registers
    • Regional registers (eg retinopathy screening)
  – Other approaches
    • Invited direct from GP
    • Self-nominate/friends & family
Central recruitment: invitations sent to potentially eligible patients

- Patients mailed
  - Invitation letter (from lead clinician)
  - Information leaflet
  - Screening questionnaire
  - Consent form

- 24 hour telephone service to deal with any questions about the study
INVITATION TO JOIN A LARGE MEDICAL RESEARCH PROJECT

A randomised study of aspirin and of natural oils for the primary prevention of cardiovascular events in diabetes

You are being invited to take part in a research study. Before you decide whether to participate, it is important for you to understand why the research is being done and what is involved. Please take time to read the following information carefully and discuss it with friends or relatives if you wish. You are entirely free to decide whether or not to take part in this trial. If you choose not to take part, the standard of care you are given by your own doctors will not be affected.

If there is anything that is not clear, or if you would like more information, please telephone the ASCEND Freephone number (0800 585323) and speak to a study nurse or doctor. The study is to be conducted mainly by mail, so no extra clinic visits will be required.

Co-ordinated by:
Clinical Trials Centre, University of Oxford
Website: www.clintrials.ox.ac.uk/ASCEND
Each participant will have a 50% chance of receiving the omega-3 containing capsules and a 50% chance of receiving olive oil capsules. The type of study treatment being taken will not generally be known by you or your doctor. This information will be known only by certain staff at the coordinating centre in Oxford, but it would be made available to your doctor if this were medically necessary. This design helps ensure that reliable information will be obtained about the effects of these potentially important treatments.

**What you have to do to join the study**

If you might like to participate in this study you should complete the brief Screening Questionnaire on the back of the letter, sign the Agreement to Participate and return them both in the enclosed Freepost envelope. We will use your answers on the questionnaire to check that you are suitable for the study. If you are suitable, then we will send a box of conveniently packaged study treatments, and ask you to start taking one tablet and one capsule each day by mouth for the next 2 months. We shall also inform your general practitioner of your involvement in the study and check that this is happy with you continuing.

Within a few weeks of receiving this first pack of study treatment, you will also be sent an optional blood taking kit. It is convenient for you to do so, you would be asked to attend your local surgery to have a small blood sample taken (about 2 teaspoons full). Measurements of your height, weight and blood pressure would also be recorded at the surgery and this information, along with the sample, would then be mailed to the ASCEND coordinating centre.

**Long-term commitment to the study**

Towards the end of the 2 months you will be sent a second study questionnaire. This will allow you to indicate whether or not you would be willing to continue taking the study treatments long-term. Participation in the study does require a commitment to take the study treatments regularly for at least 5 years and to complete questionnaires regularly.

If you do not think that you would be willing or able to do this then it would be better not to join in the first place.

If you decide to continue you would then be sent further supplies of the study treatments and asked to take one tablet (which would be active or dummy aspirin) and one capsule (containing one or other naturally-occurring oil) every day for the next 5 years. Further questionnaires would be sent out at 6-monthly intervals. We would ask you to tell us about your current medication and any changes to your health since your last questionnaire. Additional supplies of study treatment would be sent to you 6-monthly if you were willing to continue taking it. If you do stop during the first 2 months then no further enquiries will be made of you. But, if you decide to continue, we would like to remain in contact with you for the next several years – even if you stop taking the study treatment during this period. Throughout the study, your own doctors would remain fully responsible for all your other medical care as usual.

However, if you develop any unexpected symptoms which you believe may be due to study treatment you should contact a study doctor on the 24-hour Freephone service: 0800 585 5323.

**What are the side-effects and risks of taking part?**

A low dose of aspirin is being used in this study in order to reduce any stomach upset or other gastrointestinal problems. Some minor bleeding (e.g. after having blood taken) and bruising may be experienced by some people, but serious bleeding is likely to be rare. We shall monitor whether aspirin causes an unacceptable level of bleeding during the study. Bleeding risks with aspirin may be somewhat greater among those who are taking warfarin (Marvin, Nicoulaudine, Sarithrene). So, if you are taking warfarin you would not be suitable to join the study, and if you are prescribed it later we recommend stopping the study aspirin/placebo tablets. People who join the study would be asked to avoid taking aspirin-containing painkillers, and to take an alternative (such as paracetamol) whenever pain relief is necessary. All other prescribed treatments can be taken as usual. There are no other lifestyle or dietary restrictions required.

Choose not to take part, the standard of care you are given by your own doctors will not be affected.

If there is anything that is not clear, or if you would like more information, please telephone the ASCEND Freephone number (0800 585 5323) and speak to a study nurse or doctor. The study is to be conducted mainly by mail, so no extra clinic visits will be required.

Co-ordinated by:
Clinical Trials Groups, University of Oxford

Co-ordinating Centre: Oxford Centre for Studies in Inflammatory Bowel Disease

Website: www.clinicaltrials.oxford.ac.uk
Each participant is given a treatment that involves taking a capsule containing omega-3 fatty acid capsules. The doses of the naturally occurring oils being tested in ASCEND are not known to cause any particular problems, although some people may experience gastrointestinal (“tummy”) disturbances. If you did experience any symptoms that you thought were related to either of the study treatments, medical advice is available at all times through the 24-hour Freephone service: 0800 585 523.

What are the possible benefits of taking part?

We hope that both the study treatments may help you. However, this cannot be guaranteed. The information we get from this study may help us to treat future patients with diabetes better and may help to prevent many thousands of heart attacks and strokes.

What if new information becomes available?

Sometimes during the course of a research project, relevant new information becomes available about the treatment that is being studied. If this happens we will tell you and your general practitioner about it and you can discuss whether you want to continue in the study. A study doctor is available through the 24-hour Freephone service if either you or your GP need to discuss any new information.

What happens at the end of the study?

When the research study finishes, we will inform you and your GP of the study result. You will then be able to decide whether or not you should take either omega-3 fatty acids. After the study finishes we will no longer continue to provide study medication for you. But, if the study results suggest you would benefit, your GP will be able to prescribe the treatments. We will also publish the study results in a professional medical journal as soon as possible after the study finishes. You would not be identified individually in any published report.

What the study hopes to answer

The main purpose of the ASCEND study, is to find out whether long-term treatment with aspirin in people with diabetes who are not already known to have heart or circulation problems produces benefits by preventing heart attacks and strokes which outweigh the possible risks of bleeding. ASCEND will also help establish whether oils rich in omega-3 fatty acids are of any importance in reducing the chances of having a heart attack in people with diabetes who have not yet got circulatory problems.

Why have I been chosen?

ASCEND will involve about ten thousand men and women from around the UK, who like you they are being invited to take part because they have diabetes. This invitation has been sent from either your own GP or a Specialist at your local hospital because they think you might be suitable for the study. It is up to you to decide whether or not to take part in this study. If you do decide to take part, you would, of course, be free to withdraw from the study at any time without necessarily giving any reason (and without adversely affecting the medical care you can expect from your own doctors). In particular, at the end of the first 2 months, when you finish your first box of treatment, you will have the chance to withdraw if you have any second thoughts or problems with study treatment.

What taking part in ASCEND involves

Everyone taking part will have agreed to do so voluntarily, knowing that it may involve them in taking study treatment for at least 5 years. The daily study treatments (which would be sent to you by mail) will be small white tablets and a single red capsule taken from a blister pack. The white tablets will contain either active aspirin (100mg) or a similar looking inactive substance called a “placebo”. Whether or not a participant receives active or placebo tablets will be determined randomly (like tossing a coin). Each participant will have a 50% chance of receiving active aspirin, and a 50% chance of receiving placebo (“tummy”) tablets. The red capsules will each contain 1 gram of naturally occurring oil, either mainly omega-3 fatty acids or mainly olive oil.

Co-ordinated by:
Centre for Inflammation Research, University of Edinburgh
Lidouston Dene, Western General Hospital
100 Grange Road
Edinburgh EH4 2XU
Website: www.cfir.ed.ac.uk
Email: info@cfir.ed.ac.uk
Each participant.

The doses of the real known to cause an experience gastro-intestinal symptoms that you will.

If you might like to

Screening Our

Participate and

use your arrow

to select which

at the end of the text.

within 24 hours and

Once you have

received all the

information, you

will be contacted

by the study team

to arrange a

review.

What if something goes wrong?

In the unlikely event of you being harmed as a result of taking part in the ASCEND study, the University of Oxford provides insurance cover and you would retain the same rights of care as any other patient treated in the National Health Service.

Will my taking part in this study be kept confidential?

The coordinating centre would seek information from participants' own doctors and from central registries about any serious illnesses (such as heart attacks, strokes, cancer etc) that occur. All such information would be used, in confidence, only for medical research purposes and for routine regulatory and audit purposes.

Study organisation

The ASCEND study has been designed, and is coordinated, by Oxford University's Clinical Trials Service Unit. It involves the collaboration of many doctors and nurses around the country. The study design has been reviewed and agreed by Independent Research Ethics Committees, which include people from outside the medical profession. The British Heart Foundation has provided a grant to conduct the research study, and packaged study treatment has been provided free by Bayer (makers of the aspirin) and Solvay (who are providing the natural oils). An independent Data Monitoring Committee will review various outcomes among participants during the study, and will inform the organisation if any important new information has emerged that needs to be provided to participants and their doctors.

Any questions about the study should be directed to the coordinating centre in Oxford either by telephone (24-hour Freephone service: 0800 5853523) or by mail to: ASCEND Study, CTSU, Harman Building, Radcliffe Infirmary, Woodstock Road, Oxford, OX2 6HE.
The Pennine Acute Hospitals
NHS Trust

ASCEND: A Study of Cardiovascular Events in Diabetes

Mr Thomas White
24 Raspberry Road
Gardentown
G34 3AR

26 January 2010

ASCEND: Invitation to Join a Large Medical Research Project

We are writing to invite you to participate in the ASCEND research study of the prevention of heart attacks and strokes in people with diabetes. At the Diabetes Centre at The Royal Oldham Hospital, we are working with Oxford University's Clinical Trial Service Unit to help identify suitable people for this nationwide study. So, we are writing (having first informed your GP, Dr Rosalyn Gardner) to all those people on our local diabetes register who are aged over 40 and may be suitable, in order to find out whether they might be interested in taking part. The purpose of the study is to assess whether aspirin and/or naturally-occurring vit C are useful for preventing heart attacks and strokes in people with diabetes who have not had circulatory problems.

Please read the enclosed information leaflet entitled "ASCEND: Invitation to Join a Large Medical Research Project". It is then up to you whether or not you would like to take part. If you would like to, then please complete the attached questionnaire. Based on your answers, the study coordinators will write to you whether or not you would be suitable.

If you have any questions regarding this study you may telephone the study co-ordinators (Professor Jane Armitage or Dr Louisa Bowman) on Freephone 0800 555 323. Alternatively, you may wish to discuss matters with your GP or diabetes nurse before deciding whether to join. If you do not want to take part this will have no effect on your usual medical care. If you want to join the study then please complete the questionnaire and sign the Agreement to Participate. We hope you will decide to take part in ASCEND. If you do not want to participate then please indicate this on the questionnaire on the back of this letter so that you do not get approached again. In either case, please return the questionnaire in the Freepost envelope provided.

Thank you very much

[Signature]

Dr Deepak Bhatnagar
Consultant/Senior Lecturer in Diabetes & Metabolism
Royal Oldham Hospital

Dr Biswa Mishra
Consultant Diabetologist and Endocrinologist
Royal Oldham Hospital
ASCEND: Screening Questionnaire

INSTRUCTIONS FOR COMPLETION:
Please complete the questionnaire in BLOCK CAPITALS using blue or black ink.
Please place a cross in the appropriate box, e.g. Yes ☑ No ☐
(If you make a mistake, fill the entire box and mark the correct box, e.g. Yes ☑ No ☐)
OR write clearly in the appropriate boxes, e.g. 26/01/2007

1. Contact Details
Please write your name and contact details clearly in the boxes provided.
Title: Mr ☐ Mrs ☐ Ms ☐ Miss ☐ Other ☐
First name(s): ☐
Surname: ☐
Address: ☐
Home telephone number (inc. code): ☐
Daytime telephone number (inc. code): ☐
Postcode: ☐

2. Personal Details
Date of birth: ☐ 19 ☐ Sex: Male ☐ Female ☐

3. Joining ASCEND
Please read the enclosed leaflet (ASCEND: Invitation to join a large medical research project), and indicate whether you are interested in taking part in ASCEND: Yes ☑ No ☐
If you answered YES, then please complete ALL the remaining sections of this questionnaire, sign and date the form, and return it in the FREEPOST envelope provided.
If you answered NO, then return the questionnaire in the FREEPOST envelope provided (but do not complete the remaining sections).

4. GP Details
Please give your GP’s surname and initials, as well as the address of the GP practice.
GP surname: ☐
GP initials: ☐
Address: ☐
Postcode: ☐

5. Medical History
5.1 Has a doctor ever told you that you had any of the following?
   a) Diabetes, Type 1 or Type 2 (i.e. “sugar” diabetes) Yes ☑ No ☐
   b) Heart attack Yes ☑ No ☐
   c) Angina (chest pain from the heart) Yes ☑ No ☐
   d) Stroke or ministroke (sometimes called TIA) Yes ☑ No ☐
   e) Coronary artery bypass operation (CABG or “cabbage”) Yes ☑ No ☐
   f) Coronary angioplasty (“balloon”, “stent” insertion or PTCA) Yes ☑ No ☐
   g) Other arterial surgery or angioplasty (e.g. leg bypass) Yes ☑ No ☐
      (Do not include angiogram)
      If Yes, please specify:
   h) Liver disease (active or chronic, or cirrhosis) Yes ☑ No ☐
      If Yes, please specify:
   i) Cancer within the last 5 years (e.g. skin, breast, lung, bowel etc) Yes ☑ No ☐
      If Yes, please give the type of cancer:
   j) Other serious illness Yes ☑ No ☐
      If Yes, please specify:

5.2 In the last 6 months have you been in hospital with, or has a doctor said you have:
   a) Active peptic (stomach or duodenal) ulcer? Yes ☑ No ☐
   b) Bleeding from the stomach or bowel? Yes ☑ No ☐

6. Current Medication
As a participant in ASCEND, you would be asked not to use NON-STUDY aspirin, medications containing aspirin or blood thinning drugs on a regular basis (i.e. more than one day per week) unless this becomes necessary.

6.1 Do you currently take any of the following regularly?
   a) Aspirin (e.g. Anadine, Caprin, Disprin, Ibramarin, PostMI) Yes ☑ No ☐
   b) Warfarin (Marevan), Acenocoumarol (Nicoumalone, Synthrom) or Phenindione Yes ☑ No ☐

6.2 Are you known to be allergic to aspirin or omega-3 fatty acid (fish oil) supplements? Yes ☑ No ☐

6.3 Are you willing to avoid medications containing aspirin (apart from ASCEND study treatment) during the course of the study? (N.B. you could use paracetamol instead for pain relief) Yes ☑ No ☐
Pre-randomisation run-in phase

- GP informed that patient has entered run-in; option to withdraw
- Blood kit mailed during run-in period
- Randomisation form mailed after 6 weeks
Baseline blood samples (optional)

- 22,900 blood and urine kits sent out
- 13,000 participants returned samples
- 11,500 from randomised participants (74%)
- HbA1C, TC, HDL c, Apo A1, Apo B, urinary albumin/creatinine measured on fresh samples
- Urine, plasma, red cells and genetic material stored long-term
Need help completing this form? Please call Freefone 0800 585323

7. Current Medication

7.1 Please list your current medication as prescribed by your doctor (names only, doses not required). Please do not list any medication (e.g. aspirin) you have stopped to enter ASCEND.

7.2 Please list any other treatments you take regularly (i.e. more than twice a week), for example, pain killers, vitamins, supplements, over-the-counter tablets or capsules.

8. Alternative Contact

It would be very helpful for us if you could provide the details of a relative, friend or neighbour living at a different address who we could contact if for any reason we were unable to get hold of you. Please indicate their relationship to you and write their contact details clearly in the boxes provided.

Relationship: [ ] Relative [ ] Friend [ ] Neighbour [ ] Other

Title: [ ] Mr [ ] Mrs [ ] Ms [ ] Miss [ ] Other

First name(s): 

Surname: 

Address: 

Postcode:

Telephone number (incl. code):

9. Continuing in ASCEND

Thank you for completing the questionnaire. If you are happy to continue taking the ASCEND tablets and capsules for the next 5 years, then please SIGN and DATE the form below using blue or black ink, and return it in the FREEPOST envelope provided. Within about 2 weeks of us receiving your questionnaire, if eligible, you will receive a new box of ASCEND medication and will be asked to take one tablet and one capsule daily.

I am happy to take part in ASCEND: [ ]

(Please use blue or black ink)

Signature: 

PRINTED name: 

Today's date: [ ] [ ] [ ] [ ] [ ]

Please check that you have answered every question, signed and dated the form. Return the completed questionnaire in the FREEPOST envelope provided (no stamps needed) to:

FREEPOST envelope

If you have any questions about the study, please contact the coordinating centre in Oxford on FREEPHONE 0800 585323 (preferably during office hours 9 am - 5 pm, Monday to Friday).

Thank you very much

ASCEND Document Ref. A796-0673

Dear Mr Stigwood,

ASCEND: A Study of Cardiovascular Events in Diabetes

It is now about 2 months since you provisionally agreed to take part in ASCEND and received a box of study treatment. We would now like to know whether you are happy to continue into the long-term part of the ASCEND study. You may remember that the purpose of the study is to assess whether aspirin and/or naturally-occurring oils are useful for preventing heart attacks and strokes in people with diabetes who do not already have diagnosed circulatory problems.

On the back of this letter is a brief questionnaire which we would like you to complete and sign. Then please return it in the enclosed Freepost envelope. If you have any questions regarding the study you may telephone us or one of the other ASCEND staff on Freefone 0800 585323. Alternatively, you may wish to discuss matters with your GP or diabetes nurse before deciding whether to continue.

We hope you will decide to continue in ASCEND. If you do, then we shall send a new pack of study treatment as soon as we have received this completed form back from you. Subsequently, you will be sent a brief questionnaire to complete every six months and new supplies of study treatment. Alternatively, if you do not want to participate then please indicate this on the form and return it in the Freepost envelope provided.

Yours sincerely

[Signature]

Dr Jane Armitage

[Signature]

Dr Louise Bowman

On behalf of Dr Jane Armitage

Study Coordinators

Enc. FREEPOST envelope

ASCE0D-PeccmniQd O13 3, 291098

Thank you very much
ASCEND: Randomisation Questionnaire

INSTRUCTIONS FOR COMPLETION
Please complete the questionnaire in BLOCK CAPITALS using blue or black ink. If you make a mistake, fill the entire box and mark the correct box, e.g. Yes [X] No [ ] OR write clearly in the appropriate boxes, e.g. 2007

1. Contact and GP Details
Please check that the contact details for you and your GP are correct. If not, then please call Freephone 0800 5855323 and provide the correct information. Please quote the reference number from the covering letter on the front of this questionnaire.

Your details:
Mr Maurice Stigwood
13 Hopkins Road
Hogford
Hogwoodshire
HGB 5PG
09484 33993 (day); 09484 33993 (home)

GP details:
Dr GP Jones
55 Swanston Road
Hogford
Hogwoodshire
HGB 5PG

2. Continuing in ASCEND
Are you willing to continue taking study tablets and capsules in ASCEND for the next 5 years? Yes [ ] No [ ]
If you answered YES, then please complete ALL the remaining sections of this questionnaire, sign and date the form, and return it in the FREEPOST envelope provided.
If you answered NO, then return the questionnaire in the FREEPOST envelope provided (but do not complete the remaining sections).

3. About Your ASCEND Medication
Please indicate how regularly you have taken your ASCEND medication since you received it:

<table>
<thead>
<tr>
<th>White Tablets</th>
<th>Brown Capsules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every day</td>
<td>approx or placebo</td>
</tr>
<tr>
<td>Most days</td>
<td>(one or other natural oil)</td>
</tr>
<tr>
<td>Only occasionally</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td></td>
</tr>
</tbody>
</table>

Please cross ONE box only in EACH column.

4. About Your Diabetes
4.1 What year was your diabetes diagnosed? [ ]
4.2 Do you inject INSULIN for your diabetes? Yes [ ] No [ ]
4.3 If Yes, did you start insulin within one year of having diabetes? Yes [ ] No [ ]
4.4 Are you known to have diabetes changes at the back of the eye? Yes [ ] No [ ]
4.5 If Yes, have you had laser treatment to the eye for this? Yes [ ] No [ ]
4.6 Do you take treatment for high blood pressure or hypertension? Yes [ ] No [ ]

5. Confirming Your Medical History
5.1 Has a doctor ever told you that you had any of the following?
   a. Heart attack [ ]
   b. Angina (chest pain from the heart) [ ]
   c. Stroke or ministroke (sometimes called TIA) [ ]
   d. Coronary artery bypass operation (CABG or "cabbage") [ ]
   e. Coronary angioplasty ("balloon", "stent" insertion or PTCA) [ ]
   f. Other arterial surgery or angioplasty (e.g. leg bypass) [ ]
   (Do not include angiogram)
   If Yes, please specify:

5.2 In the last 6 months have you been in hospital with, or has a doctor said you have:
   a. Active peptic (stomach or duodenal) ulcer? Yes [ ] No [ ]
   b. Bleeding from the stomach or bowel? Yes [ ] No [ ]

6. About You
6.1 Please give your date of birth: [ ]
6.2 Which best describes your ethnic origin?
   White [ ]
   Indian, Pakistani or Bangladeshi [ ]
   Black: African/Caribbean [ ]
   Other [ ]
   Please cross ONE box only.

6.3 Please provide your weight in light indoor clothes without shoes (round to nearest whole number):
   lbs [ ]
6.4 Please provide your standing height without shoes (round to nearest whole number):
   feet [ ]
6.5 Do you smoke cigarettes regularly (i.e. on most days)? Yes [ ] No [ ]
   If Yes, give approximate number smoked per day: [ ]
6.6 If No, have you ever smoked regularly? Yes [ ] No [ ]
   If Yes, give the age you stopped: [ ]

[ ]

ASCEND Randomisation Questionnaire (v3.0.0.19/2019)
## ASCEND: recruitment completed July 2011

<table>
<thead>
<tr>
<th></th>
<th>Centrally-held Register</th>
<th>GP practices</th>
<th>Others *</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invitations sent</td>
<td>300,188</td>
<td>120,875</td>
<td>2223</td>
<td>423,286</td>
</tr>
<tr>
<td>Patients enter Run-in</td>
<td>16,104</td>
<td>9,741</td>
<td>635</td>
<td>26,480</td>
</tr>
<tr>
<td>Patients randomised</td>
<td>9013</td>
<td>6037</td>
<td>430</td>
<td>15,480</td>
</tr>
<tr>
<td></td>
<td>(3.0%)</td>
<td>(5.0%)</td>
<td>(19%)</td>
<td>(3.7%)</td>
</tr>
</tbody>
</table>

* HPS follow up/Self/friends/Hospital referral
Follow-up by mail

- Follow-up questionnaires sent 6 monthly:
  - serious adverse events
  - significant bleeding episodes
  - study treatment compliance
  - non-study treatments of interest

- Treatment packs mailed at appropriate intervals

- Central registries (death, cancer, MI, cardiac interventions, hospital admissions)

- 24 hour freefone telephone service
ASCEND: Follow-up Questionnaire

INSTRUCTIONS FOR COMPLETION
Please complete the questionnaire in BLOCK CAPITALS using blue or black ink.
Please place a cross in the appropriate box, e.g. Yes ☑ No ☐
(if you make a mistake, fill the entire box and mark the correct box, e.g. Yes ☑ No ☐)
OR write clearly in the appropriate boxes, e.g. 20 04 2004

1. Contact and GP Details
Please check that these contact details are still correct. If not, then please telephone 0800 585323 and provide the correct information. Please quote the reference number from the covering letter on the front of this questionnaire.

Your details:
Mr Thomas White
24 Raspberry Road
Gardentown
Gardeshsire
GA3 5TR
01234-987654

Alternative contact:
Dr SC Black
The Surgery
23 Strawberry Street
Gardentown
Gardeshsire
GA3 5TR
01234-9876321

2. ASCEND Medication
2.1. Please indicate how regularly you have taken your ASCEND medication during the last 6 months:
Every day ☐ Most days ☐ Only occasionally ☐ Never ☐

Please cross ONE box only in each column

2.2. Are you willing to continue taking the white (aspirin/placebo) ASCEND tablets?
Yes ☐ No ☐
If No, please tell us why:

2.3. Are you willing to continue taking the brown (one or other natural oil) ASCEND capsules?
Yes ☐ No ☐
If No, please tell us why:

3. Other Current Medication
3.1. Do you currently take any of the following regularly (i.e. more than one day per week)?
(a) Warfarin (Marvarin), Aenocoumarol (Nicoumalone, Synthrom) or Phenindione
Yes ☐ No ☐
(b) Aspirin, prescribed or over-the-counter (e.g. Anadin, Caprin, Disprin, Imazin, PostMi). Do not include your ASCEND study tablets.
Yes ☐ No ☐
(c) Clopidogrel (Plavix)
Yes ☐ No ☐
(d) Dipryridamole (Persantin, Persantin Retard or Assistanin Retard)
Yes ☐ No ☐

4. Medical Events
4.1. Since completing your last questionnaire on ___[date]___ have you had ANY of the following?
(If Yes, please give the date and the name and town of the hospital you attended). Please note there is extra space overlaid to list second occurrences of any of the medical events listed below.

(a) Heart attack
Name and town of hospital attended:

(b) Admission to hospital with angina or any chest pains
Name and town of hospital attended:

(c) Stroke
Name and town of hospital attended:

(d) Ministroke (sometimes called TIA)
Name and town of hospital attended:

(e) Coronary artery bypass operation (CABG or “cabbage”)
Name and town of hospital attended:

(f) Coronary angioplasty (“balloon,” “stent” insertion or PTCA)
Name and town of hospital attended:

(g) Other arterial surgery or angioplasty (e.g. leg bypass)
Name and town of hospital attended:

(h) Cancer (e.g. skin, breast, lung, bowel etc)
Type of cancer:
Name and town of hospital attended:

(i) Bleeding for which you saw a doctor (e.g. serious nose bleed, bleeding in the eye)
Site in body of bleeding:
Were you admitted to hospital?
Name and town of hospital attended:
5. Other Serious Illnesses or Hospital Admissions

5.1 Since completing your last questionnaire on have you had ANY other serious illness or admission to hospital (e.g. pneumonia, day surgery, laser treatment to the eye)? Please give details of the illness or surgery, the date, and the name and town of the hospital you attended. (Please note you can also record second occurrences of any of the medical events listed in Section 4.)

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<th>Details of illness or admission:</th>
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<td>Date:</td>
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</tbody>
</table>

6. Personal Details

6.1 Please give your date of birth:

Thank you for completing the questionnaire. Please SIGN and DATE the form below using blue or black ink.

Signature: ____________________________

PRINTED name: ____________________________

Today's date: ____________________________

Please check that you have answered every question, and signed and dated the form. Return the completed form in the Freepost envelope provided (no stamps needed to):

ASCEND, FREEPOST NAT13900, Harkness Building, Radcliffe Infirmary, OXFORD, OX2 6BR

If you have any questions about the study, please contact the coordinating centre in Oxford on FREEPHONE: 0800 585323 (preferably during office hours 9 am – 5 pm, Monday to Friday).

Thank you for your continued participation in ASCEND.

ASCEND: A Study of Cardiovascular Events IN Diabetes

Dear Mr White,

Thank you for your continued participation in ASCEND and your commitment to research into diabetes. On the back of this letter is a simple questionnaire similar to earlier ones you have returned. We would be grateful if you would complete and return it promptly in the Freepost envelope enclosed. We cannot emphasise enough how important it is that we receive this information regularly from each of the participants in ASCEND. We shall be sending you a new supply of study treatment automatically when it is required.

Please let us know if you have any questions or need help completing the questionnaire, by telephoning Freefone: 0800 585323.

Thank you for your continued support of ASCEND, and for being prepared to complete regular questionnaires. We are grateful for your help with finding ways of preventing the complications of diabetes.

Yours sincerely,

[Signatures]

Dr Jane Armitage

Dr Louise Bowman

Study Coordinators

On behalf of [local collaborator]
HIMALAYA

The newsletter of the ASCEND Study

Winter 2010 – Number 8

Welcome to the eighth edition of HIMALAYA – the newsletter of the ASCEND study. Thank you very much for your interest and participation in the ASCEND study so far. If you have not received HIMALAYA before, we hope this newsletter will educate and entertain you, and tell you more about the study that you are playing such a vital role in. If you have, then read on and find out what we have been up to since the last issue. The picture opposite shows Mt. Manaslu, located in the Manasnu Himal, part of the Nepalese Himalayas, which means “Mountain of the Spirit”, and it is the eighth highest mountain in the world.

WE HAVE REACHED 12,000 PARTICIPANTS!

People from all over the UK are participating in ASCEND. We collect data on everyone who participates and here are some of the characteristics of the people taking part:
- 62% are men and 38% are women;
- 53% of participants have type 2 diabetes;
- average age is about 62 years;
- participants have had diabetes for an average of 10 years before entering the study;
- about 1 in 3 participants take insulin.

HOW DO I GET THE TABLETS OUT OF THE PACKS?

We realize that some of you have difficulty getting the study treatments out of the packaging. Our packaging has to meet “The Medicines (Child Safety) Regulations 2003” which require medicinal products containing aspirin to be packaged in child-resistant containers. The packaging technology is currently under review due to the problems encountered and we will let you know if there are any changes.

1. First remove the aspirin capsule by applying moderate pressure to the arm of the outer pack.
2. Then peel back the foil and remove the brown capsule.
3. Continue to peel away the foil until the tablet is revealed.
4. Finally, it should now be possible to take out the white tablet.

WHERE CAN PEOPLE FIND OUT MORE?

They can:
- visit the ASCEND website: www.ctsu.ox.ac.uk/ascend
- call a member of the study team: (Freephone) 0800 585333
- send an email to ascend@ctsu.ox.ac.uk
- visit www.ctsu.ox.ac.uk/ascend

THE ASCEND TEAM

In each issue of HIMALAYA, we hope to introduce you to different members of the ASCEND team. This time we would like to introduce you to the faces behind the voices you hear on your calls. Your calls are received by Angela and Edna, who are the team who take calls and transfer them to the research assistant. They have been responsible for answering many thousands of telephone calls over the years, reminding your doctors and nurses when you have needed advice from a study doctor or nurse or administrator. We could call them the “gateway to ASCEND” without whom the support network would not function either.

ASPIRIN AND CANCER

You might have read or heard the recent news stories about the effect of aspirin on cancer. This is indeed interesting news, but is yet to be fully understood. The published studies have not been able to weigh the relative benefits and harms of aspirin on cancer prevention. In particular, the recent publications have raised concerns about the use of aspirin in patients with diabetes. It is not clear whether taking aspirin on a daily basis prevents cancer but it is important to note that the study was not done in patients with diabetes, and there is no evidence that aspirin can prevent cancer. The use of aspirin for cancer prevention is subject to ongoing research and we await the results of future trials to further clarify the benefits and harms of aspirin in relation to cancer.

YOU KNOW IF THE TABLETS ARE HAVING AN EFFECT?

Problems with their consumption. It is important that you are not taking the study treatments incorrectly, e.g., if you are taking aspirin with food. We have found that the study treatments are required to be consumed with food and drinks. We are not aware of any studies demonstrating that aspirin can prevent cancer. However, we believe that the benefits of aspirin in reducing cardiovascular risk outweigh the concerns. It is important that you take the study treatments correctly and report any problems you experience to your study doctor.

ascend@ctsu.ox.ac.uk
www.ctsu.ox.ac.uk/ascend
Summary of experience in ASCEND

• Successful recruitment of 15000 trial participants by mail using centrally-held and GP databases

• Streamlined trial design, simple CRFs completed by participants – no study clinics

• Follow-up is on-going, results anticipated 2017

• Results relevant to 350 million people worldwide with diabetes
The evolution of diabetes