

Has your name, address or telephone number changed?

If your name or address is different from that on the newsletter envelope, please detach and return this reply slip in an envelope addressed to:

Breakthrough Generations Study Team
FREEPOST NAT 21013
The Institute of Cancer Research
Sutton SM2 5BR
 (stamp not needed).

BLOCK CAPITALS PLEASE

First Name(s) _____

Surname(s) _____

Address _____

Postcode _____

Telephone Number _____

Date of birth _____

Day _____ Month _____ Year _____

Study number _____

(the 6 digit number next to your address on the envelope containing this newsletter)

Information from Breakthrough Breast Cancer

Breakthrough Breast Cancer, who are funding the Generations Study, are a charity committed to fighting breast cancer through research, campaigning and education. If you would like to receive information about Breakthrough Breast Cancer, please complete the other side of this slip and return it to the address below, or visit www.breakthrough.org.uk to complete a form online.

Please note that you will be giving your details to Breakthrough Breast Cancer, not to the Generations Study Team.

SEND TO:
Breakthrough Breast Cancer
FREEPOST LON 8816
London
WC1V 7BR

BREAKTHROUGH GENERATIONS STUDY

Newsletter No.4 WINTER 2009/10

New staff working on the study: Nicholas Orr



The newsletter gives us the opportunity to introduce members of the team working on the Generations Study. Dr Nicholas Orr is our latest recruit. He is an expert in the analysis of genetic causes of cancer, and will be responsible for much of the laboratory and statistical work needed to use the blood samples that you have contributed to investigate genetics.

Nick grew up in the Northern Irish countryside and studied molecular biology and genetics at Queen's University, Belfast. In 2005, he moved to Washington DC where he worked at the US National Cancer Institute and learned about cancer genetics. He says, "Living in the USA

was a long-time ambition of mine. DC is a great city – my wife and I had an amazing time in the US, but eventually decided to move back to the UK to be close to family and friends."

"It is very exciting to be able to join the Generations Study team. A lot of time and effort has clearly gone into the study over the past 5 years, both by the study team and the participants. Almost everybody knows someone who has been affected by breast cancer and I'm confident that this study will have a positive impact on our understanding of its causes, and of ways to help prevent future cases of the disease."

Oversight of the Study

Because the Breakthrough Generations Study is so large and is seen as so important by both Breakthrough Breast Cancer and The Institute of Cancer Research, a committee has been established, including senior individuals from Breakthrough and The Institute, as well as independent scientists and women taking part in the study, to oversee the progress of the study.

The committee is intended to ensure that the questionnaires and blood samples are used to maximum advantage to find the causes of breast cancer. The current membership is:- Mr Jeremy Hughes, the Chief Executive of Breakthrough, Mr Jonathan Kipling, the Secretary of The Institute, Professors Keith Willison and David Phillips, senior scientists at The Institute, Professor Robin Weiss and Mrs Jan Brooks, Trustees of Breakthrough, Mrs Amanda Jones and Miss Eve Smith, participants in the study, and two vacancies to be filled by independent scientists.

Amanda Jones joined the study because of her strong commitment to helping breast cancer research. Amanda's daughter, Rebecca, died of breast cancer at the age of 33. "When I lost my beautiful daughter to breast cancer I wanted to do everything I could to help further research into this disease. It is tremendous to think that by joining the Breakthrough Generations Study I could help scientists discover more about the causes of breast cancer."

Eve Smith says, "I realise how vital and how fundamental it is to understand the causes of breast cancer. It matters to every woman, whether or not she has had a diagnosis, and to her family and friends. How can we hope even to start to prevent or cure breast cancer unless we understand it? I am so pleased that Breakthrough had the vision to fund this study, and I'm so proud to be part of the group of women who have joined it."

More about the Oversight Committee can be found on the study website www.breakthroughgenerations.org.uk

BREAKTHROUGH
CANCER

ICR
 The Institute
 of Cancer Research

This study is supported by the commitment and funding provided by the sponsors of the study:- Breakthrough Breast Cancer (www.breakthrough.org.uk) and The Institute of Cancer Research (www.icr.ac.uk).

Finally,

Thank you, as ever, for your continuing support of the Generations Study. We are grateful to all of you whose participation makes the study possible. We will send you a Newsletter again in a year's time.

With best wishes, **The Breakthrough Generations Study Team**

GENERATIONS

Newsletter No.4 WINTER 2009/10

The Newsletter of
 breakthrough
 generations
 The UK study of the causes of breast cancer

WELCOME

Dear study member,

Another year has gone by, and we are very pleased to be writing to you again with this, our fourth newsletter to members of the Breakthrough Generations Study. This edition of the newsletter is a special one; we have passed an important milestone with the 100,000th woman joining the study. This is therefore an appropriate moment to summarize where we are and what we plan to do next.

This newsletter includes a report on the progress of the study to date, its funding for the next five years, and the ways in which we plan to use the information you have been sending us to investigate the causes of breast cancer and other cancers. We also include an item on three participants in the study.

Research into the causes of cancer is increasingly an international affair – some problems are too difficult, and need too many study participants, for any one research group to solve them alone, and for other problems even when one research group can give some answers, the combined strength of several groups from different countries can add more. We therefore describe in this newsletter, the ways in which we will be able to collaborate in future as part of the worldwide scientific effort to find the causes of breast cancer.

Our thanks to you again for your contribution to the study. We wish you a good year to come, and look forward to writing to you again in a year's time.

With best wishes,

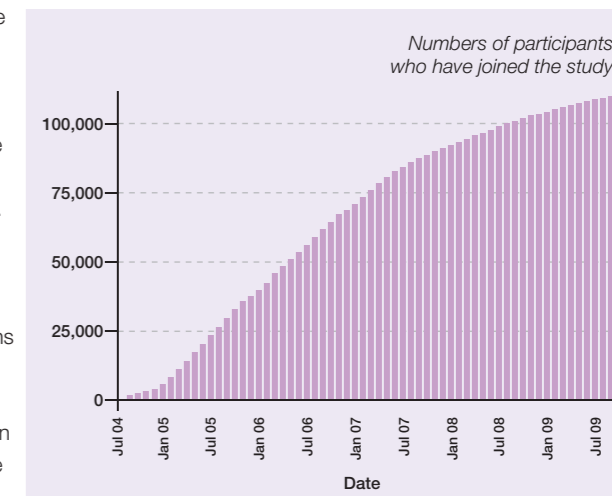
Professor Anthony Swerdlow

Professor Alan Ashworth

Progress of the study

100,000 women have joined

You may remember that when we launched the Generations Study publicly in September 2004, our first aim was to recruit more than 100,000 women to the study. We are pleased to tell you that we have now reached this milestone. The study now includes 109,000 members and is still growing. We will continue to recruit more study members for several months yet, so if you still have the study questionnaire or blood pack and have not yet sent them back, then it is not too late and we would be very pleased to hear from you.



Three participants in the study



Amanda Jones (left) and Charlotte Wright (right) with Sarah Brown at 10 Downing Street

Among those who have recently joined the Generations Study is the Prime Minister's wife, Sarah Brown. In March, she invited two other women taking part in the study, Amanda Jones from Surrey and Charlotte Wright from Staffordshire, as well as the study scientists, to 10 Downing Street to discuss the study and what it will be

doing. Sarah Brown said: "When Breakthrough told me about the Generations Study and asked me to sign up, I was delighted to do so. Like the other 100,000 women taking part in this study, I hope our small effort can help scientists find the causes of breast cancer and work towards better prevention and treatment for the future."

The funding of the study for the next 5 years

We are delighted to be able to tell you that Breakthrough have awarded us funding for the next 5 years of the study. This followed a review by independent scientific experts from this country and abroad who examined in great detail the quality and potential of the study. They reported to Breakthrough that the study has been conducted to the highest international standards, it will have an important impact on breast cancer research, and the recruitment has been achieved more quickly than anticipated.

We are very grateful to Breakthrough and the Institute of Cancer Research and all their fundraisers and donors for their support, without which the study would be impossible.

The next steps

As each of you reach 2½ years since you joined the study, we have been sending you a brief questionnaire asking about changes of address and any illnesses since you joined. The questionnaire is very short (3 sides of paper) and has now been sent to more than half the study members.

We are very grateful to all of you for sending it back; with a little reminder to those who forgot, we have had answers back from 99% of you. Of course, we would like to achieve 100% – the higher the response rate, the more valid the study's results will be – so if you have not yet returned yours we would be grateful if you would do so.

The next step in the study will be when you reach about five years from joining. At that time, we will be writing to ask if you would complete a questionnaire about changes in your lifestyle and your health since you joined the study, and to give a blood sample as before. This is important because, as you may remember, the causes of breast cancer are believed to relate to behaviours, and exposures

throughout life; we therefore need to continue to gather information from study members from time to time if we are to find how these changing factors are involved in causing cancer, and hence what could be done to prevent the disease.

The blood sample is similarly needed because women's hormone levels change over time (for instance at pregnancy and at the menopause, but also at other times), and these changes, too, are likely to be important to the causation of breast cancer and other female cancers. We hope therefore that you will be willing to assist us when we write to you – the Generations Study is already a unique enterprise to find the causes of breast cancer, and we would like, with your help, to improve it further.

Exercise ...and the risk of breast cancer

It has become clear from research in recent years, particularly by Professor Leslie Bernstein of Los Angeles, a member of the Breakthrough Generations Study Scientific Advisory Panel, that exercise can reduce the risk of breast cancer, and indeed can also reduce the risk of certain other cancers.

The evidence of a reduction of risk is strong for breast cancer occurring after the menopause and less certain for breast cancer occurring before the menopause. Of course, exercise tends to reduce weight, but its beneficial effects seem to go beyond those simply due to weight loss; the full reasons are unclear, but exercise seems to be good for us. You might feel, however, that if you are to act on this information, you need to know what type of

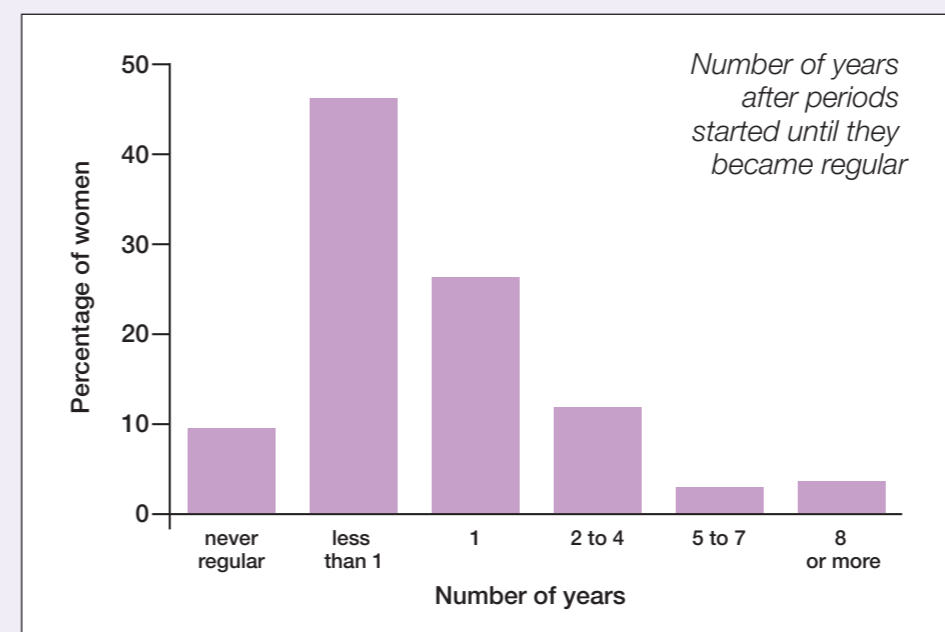
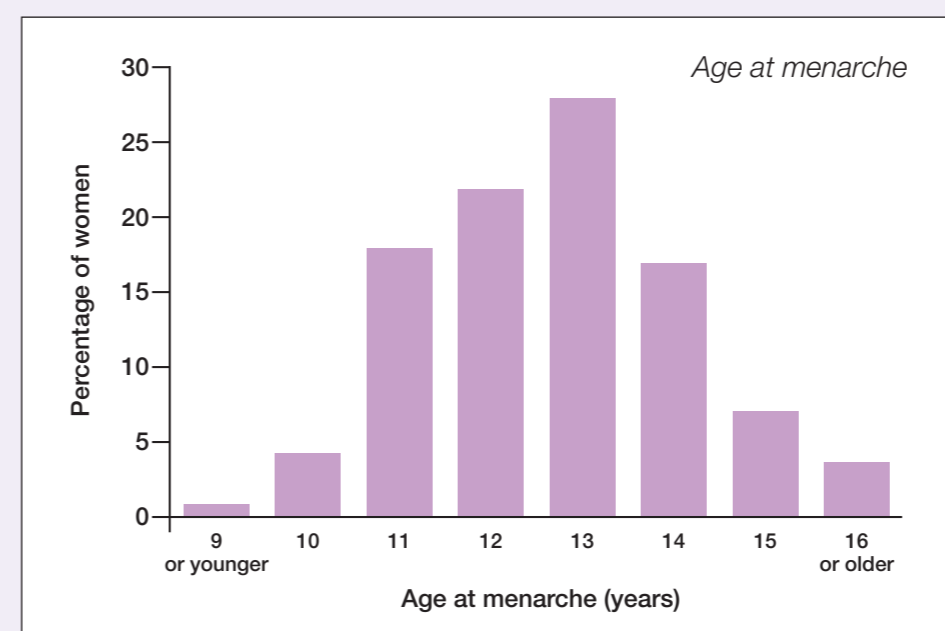
exercise, how much and how often, is needed, what the effect is of exercise at different ages, and whether the value of exercise depends on your genes – whether it has a greater preventive effect for women with some types of genes than others. The answers to all of these questions are not yet clear, and with your help this is one of the issues we are investigating in the Generations Study. Hence in the first questionnaire we sent to you there were many questions about your patterns of exercise, and in the questionnaire we will send you when you have been in the study for five years, there will be more – this is a particularly important factor to investigate because it could potentially provide practical measures that many women could take to reduce their cancer risks.

Menarche ...and the risk of breast cancer

It has been known for several decades that the risk of breast cancer relates to the age at which a woman has her first period – her age at menarche.

Women with a younger age at menarche have somewhat greater risk, although this is only one of many factors that increase or decrease risk, and is not one to be concerned about. We therefore asked in the study questionnaire about your age at first period, both in order to be able to analyse breast cancer risks in relation to this factor but also to enable us to address the question, 'what determines the age at which a woman's periods start?' Interestingly, the age at menarche of successive generations of women in the UK has been getting younger for more than 100 years – in the first half of the nineteenth century it generally ranged from ages 14 to 15½ years, whereas among Generations Study members it is about 12½ years. As shown in the diagram opposite, 23% of Generations Study members had a first period at ages under 12, 50% at ages 12 or 13, and 27% at older ages.

Breast cancer risk may also relate to the length of time between the first period and the start of regular cycles – another factor we asked you about in the questionnaire. The diagram opposite therefore shows this: for 46% of study members, the time from first period to regular cycles was less than a year, for 26% it was one year, for 19% it was more than one year, and for 9% regular periods had never started. Over the next few years we will be working to find out why these differences between women occur, and how in detail they relate to breast cancer risk.



If you have not yet returned your questionnaire, or your blood sample

If you have not yet returned your questionnaire or blood sample but would still like to participate in the study, it is not too late.

If you have not replied because you have a specific query, please contact us with your question and we will try to help.

Telephone **0208 722 4469** or write to:
Breakthrough Generations Study Team
FREEPOST NAT 21013
The Institute of Cancer Research
Sutton
SM2 5BR
 (stamp not needed)

Similarly, if you have lost the questionnaire or blood pack and need another one, please get in touch and we will be happy to send you what you need.

RESEARCH

The international scientific effort to find the causes of breast cancer, and how the Generations Study can contribute to this

Although the Generations Study is unique in several ways, clearly it is not the only study in the world trying to find the causes of breast cancer. Many of the problems in discovering cancer causation are too difficult for any one group to solve alone, and need information from larger numbers of study participants than any one study can include. There are some questions that the Generations Study can answer and other studies cannot, and some that they can answer and we cannot, but where there is the prospect of more powerful analyses by joining together, we hope that you will see why this is of benefit. We will not, of course, reveal to scientists anywhere else any private information about you, but sharing statistical data that do not identify individuals is important to enable progress.

The need for collaboration particularly applies to investigations of risks in particular sub-groups of women, such as when grouped according to their genes, and to investigation of the causes of different sub-types

of cancer. For instance, about three-quarters of breast cancers are sensitive to female sex hormones called oestrogens ("oestrogen-receptor positive" cancers), but around a quarter are not ("oestrogen-receptor negative"). Not only does treatment differ between these two types of cancer (because the oestrogen-receptor positive tumours tend to respond to hormonal treatments such as tamoxifen while the oestrogen-receptor negative tumours tend not to), but their causes may well be different too.

We have therefore joined the Cohort Consortium run by the United States National Cancer Institute, which brings together cohort studies from around the world to produce "poolings" of information on causes of cancer, and also joined the international Breast Cancer Association Consortium, which pools information on the genetic causes of breast cancer. Collaborative analyses take time, and the Generations cohort is as yet very 'young', but we will keep you informed on progress.

If you are interested, you can find more information about the Cohort Consortium at www.epi.grants.cancer.gov/Consortia/cohort.html, which also gives links to descriptions of the cohorts taking part in this research effort, and more about the Breast Cancer Association Consortium at www.srl.cam.ac.uk/consortia/bcac/

You can download copies of this newsletter, and other information, from our website:
www.breakthroughgenerations.org.uk

You can download copies of this newsletter, and other information, from our website:
www.breakthroughgenerations.org.uk

Information for Breakthrough Breast Cancer - Reply slip

BLOCK CAPITALS PLEASE

Title _____

First Name(s) _____

Surname(s) _____

Address _____

Postcode _____

If you are happy to receive emails or telephone calls from Breakthrough Breast Cancer, please provide your email address and/or telephone number:

Email _____

Telephone number _____

- I would like to receive information about Breakthrough Breast Cancer.
- If you already receive information from Breakthrough Breast Cancer, please tick this box. This will help Breakthrough to send you appropriate information about their activities.