

To Sign Up Your Daughters or Mother

If you would like us to send an information pack to your mother and/or your daughter(s), please complete the details below and return this slip in an envelope (no stamp needed) to:

Breakthrough Generations Study Team
FREEPOST NAT 21013
Institute of Cancer Research
Sutton
SM2 5BR

Your details (BLOCK CAPITALS PLEASE)

Your name

Your date of birth / /

Your study number

(Six-digit number next to your address on envelope containing this newsletter)

Your mother/daughter's details (Block capitals please)

Full name
 Relationship to you
 Date of birth / /
 Address

 Post code

Full name
 Relationship to you
 Date of birth / /
 Address

 Post code

Full name
 Relationship to you
 Date of birth / /
 Address

 Post code



Professor Montserrat García-Closas

Professor García-Closas joined the Generations Study team in September 2010. She was born in Spain and trained as a doctor before studying and working at Harvard University in the US for six years. She then worked at the US National Cancer Institute, but she and her family have now decided to return to Europe.

"The Generations Study was a key factor in my decision to move to the Institute of Cancer Research and Breakthrough Research Centre. I am particularly interested in investigating the causes of different subtypes of breast cancer and the causes of cancers occurring in younger women.

The study already has enormous research potential, and will increase in value as more data are gathered across many years of follow-up. This requires highly motivated and committed participants, which has been demonstrated by the high participation rates in the study to date.

My ultimate aim is to discover new causes of cancer and develop strategies to prevent it. Because breast cancer is an extremely varied disease, one of my first goals in the study is to obtain detailed information on the type of cancers that occur in study participants. I will be using information from the questionnaires and blood samples, as well as obtaining samples of cancers from hospitals.

Understanding what causes cancer will improve our ability to predict who is at high risk of developing it. This knowledge will help with the development of strategies to prevent the occurrence of this devastating disease, or to detect it in its early stages so that more successful treatment options can be considered."



Jacquie Leonard

For Jacquie Leonard, Community Programme Manager for Marks & Spencer, what started as part of her job turned into something much more personal.

Jacquie was asked to tour the research facility where the Generations Study is undertaken, on behalf of her employer, Marks & Spencer, a major funder of the Generations Study and long-time supporter of Breakthrough Breast Cancer.

"I was struck by how amazing it was. The study is so unique and wide-ranging. I was also inspired by the fact that even though it is a long-term study, some results will come out while it's going on."

These reasons, as well as the fact that the study has the potential to help to prevent all types of cancer, inspired Jacquie to sign up to be a participant. "I lost my very best friend to cancer at 31 and had a form of advanced pre-cancer myself. With a busy life it's often easier to give money, but I felt it was time to do more

than that. Before finding out about the Generations Study I never knew what that was. This gave me an opportunity to give something back."

Jacquie also asked her 18-year-old daughter, Alessandra, if she wanted to participate in the study, when she realised the importance of genetic factors to breast cancer risk. "We went to get our blood taken together and spent the rest of the morning filling out our questionnaires. We made the time to do it."

If like Jacquie, you have a daughter aged 16 or older who may be interested in signing up for the study, please submit the tear off card on the left hand side of this page, or if you are a daughter whose mother hasn't joined the study but might like to, please do the same.

Online communications

If there are enough members who would like to complete questionnaires online, we hope to offer online questionnaires in future, as an alternative to the paper version. There is potential to save mailing costs, which could then be used for other aspects of the research, and also to reduce use of natural resources. If you would be interested to complete future questionnaires online, or to receive future newsletters via the internet, please register at 'bgs.icr.ac.uk'.

We do appreciate however, that there are many of you who would prefer to communicate by post, in which case you don't need to do anything and we will continue to write to you.

Thank you

As always, thank you for your continued support of the Generations Study. We are grateful to all of you who make the study possible.

With best wishes,
The Breakthrough Generations Study Team

Issue No.5 Summer 2011

Welcome

Dear study member,

As we do each year, we are writing to let you know about the progress of the Breakthrough Generations Study, of which you are a member. The study has advanced very well over the last year and now includes more than 111,000 participants. Ninety thousand of you have reached 2½ years within the study and have sent back your first follow-up questionnaire, and 10,000, who have been in the study since its earliest days, have returned your second follow-up.

We are beginning to produce the first research papers from the study, two of which have been published in the past few months. One of these has shown genetic factors that increase the risk of early menopause, an important issue for women deciding when to start a family. The other paper identified a wide range of factors that affect the age at which a girl starts her periods, a factor related to breast cancer risk.

The scientific team working on the study is also expanding. We are very pleased to announce that Professor Montserrat García-Closas has recently joined us from the US National Cancer Institute. Her work here will particularly focus on how the causes of breast cancer differ between different types of the cancer.

On a personal note, one of us has recently moved jobs: Professor Ashworth has been appointed Chief Executive of the Institute of Cancer Research. He will, however, continue to work on the study, as well as leading the Institute forward.

Our thanks to you all again for your contributions to the study; without your help it would not be possible. We wish you well in the coming year and look forward to writing to you about progress in a year's time.

With best wishes,

Professor Anthony Swerdlow

Professor Alan Ashworth



Mary Behannah and her daughter Claire Hunn, study participants from Cornwall, at No.10 Downing Street

A year after Sarah Brown joined the Generations Study, she invited the study team and several participants, who were selected at random, to 10 Downing Street to celebrate its progress. Sarah Brown said that she was honoured to meet the study participants, who had

Study participants attend special events

travelled from every part of the country to be there. The study participants and staff who attended were fascinated to visit Number 10 and everyone greatly enjoyed the evening.

In a similar event, Breakthrough Breast Cancer in Scotland welcomed over 50

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Mothers and daughters joining the study

One of the special features of the Generations Study is that many of you have joined with other members of your family, often mothers or daughters. The information and blood samples from mother-daughter pairs are already proving a valuable resource for our research. Mothers and daughters not only share genes, they also often have similar lifestyles and environments. Mothers may also know more about their daughter's birth and early childhood than the daughter herself may know.

We are keen to increase the number of mother-daughter pairs in the study so that we can investigate further the extent to which family risks are due to shared genes and to what extent they are due to similar lifestyles or environments. For

example, we have found that mothers and daughters tend to reach menopause at similar ages, but that this is more due to genetic similarities than to similar environments and behaviours.

So, if you have a daughter(s) aged 16 or over who might like to join the study, or if your mother might like to join, we would be very pleased to hear from you. Please complete the tear-off form on this newsletter and return it to the Freepost address. We will then send your mother or daughter an information pack and invitation (as we sent you when you joined). It will, of course, be entirely their choice whether they join the study.

Thank you.

Study progress and the next steps

The number of women taking part in the Generations Study has now reached 111,000. Over 90,000 have been study members for more than 2½ years, and have been sent and returned the first follow-up questionnaire. Thank you to all who have sent it back. The remainder of you will be mailed as you reach 2½ years from joining.

We have also started sending out the second follow-up questionnaire, to those who have been in the study longest, and will be sending these out to many more of you over the next year, depending on

when you joined. For those study members who were mailed for this follow-up earliest, we asked for a blood sample at this stage of the study. Recently, however, we have had to discontinue sending the blood packs for the present, because of the downturn in the economy and resulting financial constraints. We would still be grateful to receive blood samples back from those of you who did receive the blood packs, and we plan to ask the rest of you for blood samples in the future, if and when funds are available.

A step towards predicting early menopause

Initial research from the Breakthrough Generations Study could lead to a test to predict a woman's reproductive lifespan.

The first findings from the Generations Study were published recently, and will have particular relevance for women considering when to start a family.

menopause occurred later. The four genes each affected the risk of early menopause, and in combination they had a larger impact.

The research tested four genes that are associated with the menopause. Blood samples, which were anonymised, were analysed from women from the Study who had experienced early menopause, and compared with blood samples from a group of women in the study whose

Dr Anna Murray, who worked on the analyses said, "It is estimated that a woman's ability to conceive decreases on average ten years before she starts the menopause. Therefore, those who are destined to have an early menopause and delay childbearing

until their 30s are more likely to have problems conceiving."

The research could help women determine whether they have a genetic predisposition to early menopause, and therefore whether they are at raised risk of an early end to their reproductive life. They could then make informed family planning decisions on the basis of this knowledge.

Hum Molec Genet 2011; **20**:186-92

Menopause and breast cancer risk

The age at which a woman enters the menopause has long been established as a risk factor for breast cancer, with risk gradually increasing with an increased age of menopause.

On average, breast cancer risk increases with older age at menopause. This is true both for natural menopause and for artificial menopause – for instance menopause resulting from surgical operations or radiotherapy. For this reason we included several questions in the questionnaire about whether your periods have stopped, and the reasons for this. We are now using the Generations Study samples and questionnaires to investigate the reasons why a woman's menopause occurs when it does.

It is known that cigarette smoking causes menopause to occur earlier, and that there is a resemblance between mothers and daughters in their age at menopause. Apart from this, however, there is a great deal yet to be understood, and we are therefore investigating both the causes of age at menopause, and its effect on long-term breast cancer risk.



Study participants attend special events

CONTINUED FROM PAGE ONE

Generations Study participants to the Scottish launch of Breast Cancer Awareness Month at Edinburgh Castle. Professor Swerdlow talked about the progress of the study and Deputy First Minister, Nicola Sturgeon, spoke about breast cancer in Scotland.

Breakthrough Breast Cancer plans to host similar participant events at different places around the UK in the future. If you would like to be invited to such an event, if there is one in your area, please contact Breakthrough's supporter care team at 08080 100 200 or 'supportercare@breakthrough.org.uk'. Please note that you will be giving your details to Breakthrough Breast Cancer, not to the Generations Study research team. Please also note that we cannot promise that there will be an event in your area, nor that if there is one, you will be invited. Breakthrough will choose at random among those who live nearby and have expressed an interest.

Risk factors vary by type of breast cancer

Different types of breast cancer require different types of treatment. Now researchers are discovering that these different types of breast cancer may also have different causes.

Although breast cancer is often spoken about as a single disease, there are actually many different types of it which need different treatments. For instance, breast cancers vary in whether the cells respond to female hormones such as oestrogen. Types that respond to oestrogen (called "oestrogen receptor positive") respond to different treatments from those that are not oestrogen responsive ("oestrogen receptor negative"). Breast cancers can also be

subdivided by their appearance under the microscope, and in other ways.

Knowledge about these differences has been important in recent advances in treating breast cancer, and there has been growing research into the extent to which these different types of breast cancer may also have different causes, and hence how women can reduce their risks. This question will be the main focus of research of Professor Montserrat

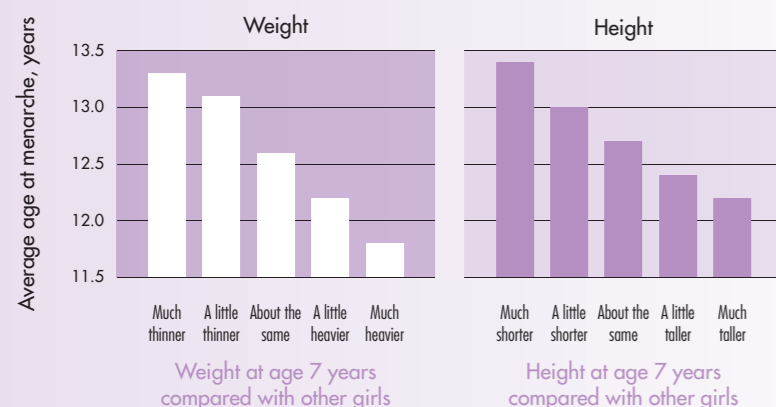
García-Closas, who recently joined the Generations Study team (see page 4).

In order to investigate these important aspects of breast cancer causation, we need to obtain samples of breast cancer tissue and examine them in the laboratory. It is for this reason that we asked in the questionnaire for permission from those of you who have suffered breast cancer to obtain a small sample of the cancer from your hospital.

Study data used to find factors behind age at puberty

Research using data from the study has shown a wide range of factors – some beginning before a child is born – are related to the age at which a girl starts her periods.

Age at menarche of women in the study according to their childhood body size



Br J Cancer 2010;103:1760-4

Age at menarche (when periods begin) has long been established as a risk factor for breast cancer. Risk of the disease gradually increases with a younger age at menarche. The average age at menarche has been getting younger in the UK for more than a century, which may be part of the reason why breast cancer has become more common.

Using data from the first 81,000 participants in the study, results published by the study team show that girls who were heavier and exercised less were more likely to reach their menarche at a younger age. Danielle Morris, who worked on the analysis, said "A girl who takes more exercise is likely to start her periods later in life. We know exercising regularly as an adult can help reduce the risk of developing breast cancer. This study shows that exercising as a child could also potentially have an effect on breast cancer risk later in life."

Other factors that were found to relate to early periods were: having a low birth weight, not being breast fed as a baby, and being tall. Danielle continued, "This research shows that there are factors that relate to age at first period – an important breast cancer risk factor – that begin very young, probably even before a child is born. Such factors, some beginning in the womb, may affect risk of developing breast cancer decades later."



For more about Breakthrough Breast Cancer

Breakthrough Breast Cancer, who fund the Generations Study, is a charity committed to fighting breast cancer on three fronts – research, campaigning, and education.

If you would like to receive information about Breakthrough Breast Cancer please call 08080 100 200 or go to 'breakthrough.org.uk'. Please note that you will be giving your details to Breakthrough Breast Cancer, not the Generations Study research team.

In addition to Breakthrough Breast Cancer, this study is also supported by The Institute of Cancer Research. icr.ac.uk



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 (no stamp needed) addressed to:

Breakthrough Generations Study Team
FREEPOST NAT 21013
Institute of Cancer Research
Sutton
SM2 5BR

(BLOCK CAPITALS PLEASE)

First name(s)

Surname(s)

Address

Postcode

Telephone number

Your date of birth (Day) / (Month) / (Year)

Your study number

(Six-digit number next to your address on envelope containing this newsletter)