

Welcome

Dear study member,

We are pleased to be writing to you at an important milestone for the Breakthrough Generations Study. It is now 10 years since the first woman joined the study, in June 2003. Since then over 113,000 more women have joined, and the study has started to produce the research findings about breast cancer and its causes and prevention that it will continue to do for at least the next 40 years.

We have therefore devoted most of this newsletter to a look back over the last 10 years by those who have worked on the study and those who have participated in and contributed to it, and a consideration of where we have reached and what we hope to achieve in future.

We have also included in the newsletter, some information from the study of breast cancer in men that we have been conducting, with Breakthrough funding, in parallel to the Generations Study in women.

At this 10th anniversary, we would like to send our personal thanks to all of you, the participants who have made the Study possible, as well as to Breakthrough Breast Cancer and the Institute of Cancer Research for funding and supporting it, to those who have contributed to Breakthrough's fundraising, and to the study staff here at the Institute.

We look forward to writing to you again about the progress of the study, over the next 10 years and beyond.

With best wishes,



Professor Anthony Swerdlow



Professor Alan Ashworth

Ten years of the Generations Study: Carol Battey – the first woman to join

One of the earliest questions I asked when I developed breast cancer (almost 23 years ago now) was "Why?". I was a young mother and considered myself fit and healthy, therefore my diagnosis didn't seem to make a lot of sense. For that reason, I didn't think twice about joining the Generations Study.

Some types of breast cancer have a stronger family link than others. In my case no-one else in my family had had breast cancer (as far as I knew), but I still wanted to protect my daughters' future health as much as I could, so giving a blood sample and filling in a health questionnaire every few years seemed a small price to pay to help future generations find answers.

I have always been fascinated by human biology, and trained to become a nurse and midwife straight from college. The friends I made during my training have remained close. We have all had our share of ups and downs, but true friendship transcends everything.

A cancer diagnosis is scary, and sometimes I think the fear that accompanies the diagnosis is far worse than the condition itself. Knowledge takes away some of the fear and that is why it is so important to look for answers. It takes experts to do this, and of course lots of women willing to become involved. It's amazing to think there are now over 113,000 women taking part in the study, and comforting to know that some of the top scientists from around the world are working so hard to find answers.



At one time, I didn't think I would see my daughters grow up into such beautiful and talented young women. My youngest daughter was too young at the time to understand what was going on, but she still seemed to sense that I needed extra cuddles and vice versa, so if anything my breast cancer diagnosis brought us closer.

If there is one piece of advice I could give any woman with breast cancer, it's to never feel that they have to 'go it alone'.

Six years ago I decided to start studying for a science degree in Nutrition. I would be lying if I said it had been easy, but I have just completed my final round of clinic consultations, so in the next few months I hope to hear that I have qualified and can practice as a Nutritional Therapist. Knowledge gained through my studies has helped in all kinds of ways: I have managed to keep my weight under control, and manage bouts of stress and 'emotional eating'. I have learnt since having breast cancer that nothing in life is as black and white as it first seems. What appears to be bad luck can open up new opportunities that lead down paths you might otherwise not venture!

All the women taking part in the Generations study should feel proud of their involvement in shaping the future.

Ten years of working on the Breakthrough Generations Study: the Study Staff

When we sent out the first questionnaires for the pilot phase of the Generations Study in June 2003, there were only three people working on the study, and even they only spent part of their time on it. By the time we started preparing for the formal launch, however, we had to bring together a larger team, and now it has grown so that there are 25 staff who work for most or all of their time on the study.

Dawn Thomas joined us in 2004, to recruit and supervise the team who communicate with study participants. She and her team prepared carefully for the launch day, but none of us could have expected what actually occurred. More than 15,000 of you contacted us by phone or email in the first 24 hours, and even with all the staff here answering the phones nonstop we were rapidly overwhelmed. We had hoped that the study would be popular, but still the large wave of calls was beyond what we could have hoped for – it was

an extraordinary moment. Since then, Dawn and her team have always been busy, and there is a constant stream of calls and letters and emails from you, the participants, for them to respond to, but never again have there been 15,000 in a day!

We have included below the reflections of Dawn, and of Jean Hoare who has also worked here since the study was launched, on the last 10 years of working on the Generations Study.



DAWN THOMAS

After nine stressful years in retail management, the decision to return to “office work” by joining the Generations Study was somewhat daunting. I was therefore a little apprehensive when I started work at the Institute of Cancer Research in May 2004, but also excited by the prospects of the

study and of working at a cancer research institute, helping to put procedures in place and recruiting a good admin team.

The response of participants on the launch day was astonishing, far beyond my expectations, but thanks to hard work from a great team, we managed, over time, to pull it all together.

It is hard to believe it all started 10 years ago! The time has flown by. My teenagers have grown into young adults, the portacabins we used to work in have been replaced by nice office space, and we have learned and therefore gained a much improved knowledge and understanding of cancer research. I guess the only downside is that we are all now 10 years older! But thanks to the contributions of you, the participants, many of whom we have spoken to over the years, and the Study scientists and admin team, we have made enormous progress.

I am proud to be part of such a great unit, most of whom have been with us working together for many years, and of the achievements of the Study so far. I am excited for what the future holds and continuing to contribute (even if only in a small way) to further research findings.

Here's to the next 10 years!



JEAN HOARE

I joined the study a few weeks after Dawn, in June 2004, having previously worked as a Registrar of Births, Deaths and Marriages. I had never worked in medical research before so was not sure of what to expect, but I must say that I have thoroughly enjoyed the varied work as the study developed and working as part of the team.

Our aim to recruit 100,000 ladies seemed a huge challenge. We set ourselves smaller achievable targets of 10,000s, and celebrated reaching each with a glass of bubbly which I must say made it all the more enjoyable!

A large part of my job is contacting participants by phone and I am sure many ladies reading this will recall conversations with me gently reminding them of the importance of sending back their questionnaires that were sitting in their ‘to do’ pile.

My family are very proud of the work I am doing for the study, particularly my son who works for the NHS as a clinical scientist and knows the importance of this kind of research.

Over the years the team and I have become good friends and we have developed a really good working relationship. We have had a lot of fun along the way as well as working hard to make the study a success. I am looking forward to continuing working on the study over the coming years.

Ten years of the Generations Study:



Jan Brooks MBE – study member and Trustee of Breakthrough Breast Cancer

Ten years ago I was very excited to be invited to be the Breakthrough patient representative for a proposed new study into the causes of breast cancer, named the Generations Study. I had been involved with Breakthrough as a fundraiser since it started in 1992, having myself experienced breast cancer the previous year.

The idea of “generations” of mothers and daughters joining appealed to me, as I have a daughter who I was concerned about in the future and I could see that this idea would appeal to many women. My daughter is now a doctor and has always taken a special interest in breast cancer and Breakthrough’s research.

The first stage in the formation of the Study was to obtain ethics approval, and for this I joined Professors Swerdlow and Ashworth at The Medical Society of London, to be able to answer from a patient’s perspective any questions the ethics committee had about the proposals. Happily the study was quickly given ethics approval and there was born the Generations Study, the largest of its kind in the world and giving hope to millions of women. From a patient’s

perspective I think the study has given enormous hope to many women, especially in regard to future generations. For mothers to be able to involve their daughters, sisters and in the future grandchildren is truly wonderful and I personally would like to thank the scientists and investigators for all the work they do to enable us to get a step nearer to controlling breast cancer and finding out the causes.

I have continued my involvement in the study during the past 10 years and now sit on the Study Oversight Body as a Breakthrough Trustee representative. It has been an enormous privilege to have been closely involved with the study and to see at first hand the dedication and enthusiasm of the scientists working on it.

We are grateful for 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).

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CANCER**
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Ten years of the Generations Study: what have we found?

As you know, the Generations Study is a very long-term enterprise and we are still in the early stages of it. Nevertheless, in the last 3 or 4 years we have received enough information from participants to start the process of scientific research using the material you have sent.

You can find a complete list of the research papers that the study has produced at www.breakthroughgenerations.org.uk/about_the_study/study_publications.html. Several of the papers have examined the factors that determine the age at which a woman reaches menarche (first menstrual period) and menopause, because these are important influences on a woman’s breast cancer risk. This research found several genes and other genetic changes that considerably increase the risk of a woman having an early menopause, and also several lifestyle factors that are associated with menopause age – menopause occurred younger in smokers, but drinking alcohol, being heavier and gaining weight as an adult were factors associated with a later menopause. We found that more recently born members of the Generations Study had their menarche at younger ages than their mothers’ or grandmothers’ generations, and that overweight and lack of exercise were among the factors leading to a younger menarche.

These findings add to our knowledge of the complex mechanisms that lead from everyday events and behaviours to reproductive and hormone-related changes that affect a woman’s eventual risk of breast cancer. We have also been investigating hormones more directly.

A woman’s sex hormone levels after the menopause relate to her breast cancer risk. Women with higher levels have greater risk of developing breast cancer, and women who are overweight have greater hormone levels. We used the blood samples from study members who have sent us two samples 5 years apart, to look at whether hormone levels after the menopause change if a woman increases, or decreases her weight. We found that hormone levels do indeed decrease if you lose weight and increase if you put on weight.

The last 10 years have been a time of exceptional progress in research to find the genes that can cause breast cancer. When the Generations Study started several genes were known that are uncommon and result in high breast cancer risk in a small number of families, but little was known about factors that are common in the general population and result in smaller risks to more women (these are known as ‘SNPs’, pronounced Snips). Ten years ago, no SNPs were known that affect breast cancer risk, but now there are 76. You will be pleased to know that blood samples from the Generations Study have contributed to finding 53 of them.

If you are interested to read the scientific papers from the study, abstracts can be found via the Study website, which also gives the references if you want to read the papers in their entirety (although we must confess that sometimes they are a little technical).

Study progress

There are currently more than 113,000 women who have joined the Generations Study.

The great majority of you have been study members for long enough to have sent back your first follow-up questionnaire, and more than half have also received the second follow-up questionnaire: if you have received it but have not yet sent it back, can we take this opportunity to give you a gentle reminder.

For those who joined the very earliest, 10 years ago, we have recently sent out the third questionnaire: this one is different, however, in that you can all complete it online if you wish to. If you

have already sent us your email address, or if you do so now by registering on the study website (bgs.icr.ac.uk), then when your questionnaire is due, we will email to let you know that you can login and complete it. It is, we think, quicker and easier to complete online than on paper, because the online system doesn't show you further detail if your initial reply to a question indicates that it doesn't apply to you. So, if you are computer-literate, please give it a try; you will also save us costs, which we can then spend on other aspects of the study.

Ten years of the Generations Study: Where are we going next?

When we set up the Breakthrough Generations Study, we knew that it would be a very long term effort: the causation of breast cancer is a consequence of factors acting over many decades of a woman's life, not a single event, and therefore to find the causes the study would need information from women over a long time too.

For this reason, the questionnaires we have sent you have asked about events in your life all the way through from your birth to (if you have reached that age) your menopause and later. Similarly, for the same reason we have sent you follow-up questionnaires every few years, because factors such as your weight, diet, drinking and smoking can change over time, and likewise whether you have children, and have reached menopause can change.

It is known that factors acting in childhood, before puberty, affect a woman's breast cancer risk, and there is evidence that even factors before birth may matter. Much later in life, factors after menopause – notably weight and use of HRT – can affect risk too. We will therefore continue to use the information you have sent us to analyse which factors cause breast cancer, and how this disease can be prevented, and also will send you further questionnaires from time to time, to update the information we can analyse.

With regard to results to come from the study, it is of course the nature of research that we can't be sure what we will find – if we knew the answers, we wouldn't need to ask the questions. Nevertheless, we would expect that in the next five years or so there will be a great deal more progress in finding the genetic factors that affect breast cancer risk, using your blood samples. We also expect to find out more about how hormone levels throughout life affect breast cancer risks, and how behaviours, especially those that a woman could choose to alter, can act. This is an exciting point in the progress of the study. We will let you know, via our website and in these newsletters, as the results are published.

Breast cancer in men

You may remember that in a newsletter several years ago we told you that we were starting, with funding from Breakthrough Breast Cancer, a study of the causes of breast cancer in men.

Because breast cancer is much less common in men than in women, the study could not be done in the same way as the Generations Study. Instead we have been gaining information from men across England and Wales who have developed breast cancer, and from other men who have not as a comparison.

After five years of the study, over 1,000 men with breast cancer have joined, and we have been successful in finding for the first time common genetic changes

that increase the risk of breast cancer in men. It turns out that these genetic changes also affect women's risks too, but interestingly their effect on the difference in risk between women is much smaller than the effect on differences between men. We are now examining various other factors that affect women's breast cancer risk – overweight and drinking alcohol, for instance – to see if they affect men's risk too. More about the study can be found at www.breakthroughgenerations.org.uk

Online Newsletters

In order to save costs, we intend in future to send newsletters electronically to those of you for whom we hold an email address, unless you contact us to say you don't want this. We will still continue to send newsletters by mail to those for whom we don't have an email address, and also would be happy to do so for anyone who has an email address but would prefer a paper copy. If you receive a newsletter electronically but would prefer the paper version, please let us know.

Finally

Thank you again for your continuing support of the Generations Study. We are very grateful for the contributions from all of you, which make the study possible.

With best wishes,
The Breakthrough Generations Study Team

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)

Title	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)



For more information about Breakthrough Breast Cancer

Breakthrough Breast Cancer, who fund the Generations Study, is a charity dedicated to saving lives through improving early diagnosis, developing new treatments and preventing all types of breast cancer.

If you would like to know more about Breakthrough, please complete the other side of this slip and return it to the address below, or visit www.breakthrough.org.uk

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

Breakthrough Breast Cancer
FREEPOST LON 8816
London
WC1V 7BR



Please send me information on Breakthrough Breast Cancer

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First name(s)

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Breakthrough may contact you, by the means specified above, to keep you updated about their work and opportunities to support. If, at a later date you would prefer not to be contacted, please call Breakthrough on 08080 100 200.