



Together we  
can make  
breast cancer  
a preventable  
disease  
for the next  
generation

# Impact Report

The Impact of  
Genesis Breast  
Cancer Prevention,  
the only UK charity  
entirely dedicated to  
the prediction and  
prevention of breast  
cancer

 **genesis**  
preventing breast cancer

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*"I was inspired to become a volunteer for Genesis Breast Cancer Prevention because of their research into the actual prevention of breast cancer. As well as enabling me to give back something to society during my retirement years, my involvement here has given me the opportunity to find out more about the research carried out. I thoroughly enjoy working at the centre and as a result of my small contribution I have been made aware of the important role the staff here play in the lives of the people who come as patients".*

**Kathy Battersbury, Volunteer**

# Message From Our Chairman

**'Prevention is better than cure'** is the philosophy behind Genesis Breast Cancer Prevention.

Thankfully the cure rates for breast cancer have improved greatly over the years, but surely the next step is to prevent the disease from starting in the first place to avoid gruelling treatments and surgeries whenever possible. So how can breast cancer be prevented?

There is no simple single answer to that question, but the research team at The Genesis Prevention Centre is working on several strategies. Breast cancer seems to be caused by the interaction of the genes you are born with and certain factors in western diet and lifestyle. Lab research can help us understand the pathways that lead to breast cancer, and identify drugs to switch these pathways off. Early diagnosis and screening are also important keys to preventing the early stages of breast cancer from reaching its invasive potential. So our team is working on all those areas. This Impact Report outlines some of the ways in which our work has made a difference.

**In Gene Research:** Our team has been working with other groups to identify the genes behind breast cancer; not just the very high risk familial ones like BRCA1 and BRCA2 but now also a whole list of more intermediate-level predisposing genes. One of the benefits of this research is that we are now able to predict with much more accuracy which women are at risk of the disease. Early warning of susceptibility allows those women to take action before the disease starts, for example by regular screening. We are learning that breast cancer does not just strike randomly; most women who get the disease may have an underlying susceptibility in their genes.

**In Diet and Lifestyle Research:** Our team has published some of its research into the beneficial effects of an intermittent diet technique on weight loss, hormone levels and gene switching in the book *The 2-Day Diet*. The preliminary


data suggests that substantial reductions in breast cancer risk for some individuals could be achieved simply by changing to this healthier diet and lifestyle regime.

**In Drug Research:** Our team has been instrumental in the success of several clinical trials looking at drugs such as tamoxifen and raloxifene as prevention. A paper published in the *Lancet* in 2013 confirms that these drugs are effective, and will now become approved for prevention use. They will particularly benefit women who carry a high risk gene, and those who have had breast cancer once before and wish to prevent a reoccurrence; but this is only the start. Research is now underway on a second generation of prevention drugs with fewer side effects that might help a wider population.

**In Screening and Early Diagnosis:** Our team is currently investigating new methods of imaging the breast tissue in order to obtain earlier diagnosis of cancer and pre-cancer changes, such as 3D mammography, and breast density measurement.

**In Clinical Practice:** Our team has helped to develop strategies now in clinical practice such as methods for predicting risk, guidelines for referral and management of women with a family history, guidelines for women considering preventive surgery, and techniques for breast reconstruction surgery.

**Step by step we hope to reach our goal of preventing breast cancer. Thank you for your support.**



Lester Barr

Breast cancer is the most common cancer in the UK, despite it being a rare disease in men.

1 in 10 women and 1 in 1000 men will develop the disease in their lifetime.

Across the UK, 50,000 people annually are diagnosed with breast cancer.

Although survival rates are increasing, tragically 12,000 of these women do not survive.

In the last ten years, female incidence rates have increased by 3.6%.

Breast cancer rates have increased by 57% in the last 30 years.

If trends continue, it is predicted there will be 55,700 new cases per annum by 2024.

## The Facts

The biggest risk factor is age and women are now living longer.

Western diet and lifestyle also increases risk.

Currently only 2% of all cancer research funding is spent on prevention.

We agree with the 17th Century physician Thomas Adams who said,

*"Prevention is so much better than healing because it saves the labour of being sick".*



# Research Highlights

- The Genesis Research Teams, with their collaborators, have published 58 research papers in medical journals - more than in any other year.
- Over 50,000 women have been recruited to the Predicting the Risk of Cancer at Screening (PROCAS) Study, making this the largest study of its kind in the UK.
- Three women identified as at high risk on the PROCAS Study have had breast cancer detected on their extra mammogram (every 18 months rather than every three years). This means that for these three women, their cancer was detected potentially up to 18 months sooner than it would have been had they not joined the PROCAS study.
- Publication of *The 2-Day Diet* increases awareness of our vital work and sends a positive health message across the UK and the world through national and international media coverage.
- *The 2-Day Diet* is to be published in many countries over the next 12 months.
- *The 2-Day Diet Cookbook* was published in April 2013.



# Fundraising Highlights

- Genesis joins forces with Greater Manchester Police to launch Crime to Kind, offering secure parking for Manchester United matches, whilst raising funds for the charity.
- Fundraisers Jo Flitcroft, Hannah Reeves and Nicole Xodo travel the UK in an automated pink rickshaw raising awareness and over £15,000 for Genesis.
- Genesis raises the necessary funds (£101,000) to support our research into SNPs.
- The Genesis Ball 2012 is featured exclusively in OK! Magazine.
- Students from Wellington School take part in our Million Miles Challenge and raise £37,000.



# About Breast Cancer

There is not one single cause of breast cancer; rather it appears to be several different factors working together.

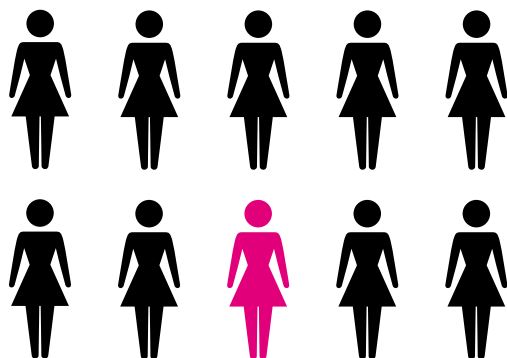
- Genes
- Lifestyle
- Environmental Factors
- Hormonal Factors (e.g. late first pregnancy)

The combination of all four factors could trigger a breast cancer.

Although there may never be a miracle cure or a simple vaccine that eliminates breast cancer; and there is no one single thing that women can do to prevent getting the disease, Genesis Breast Cancer Prevention's overall goal is to make breast cancer a preventable disease for the next generation of women by improving clinical practice.

We seed fund medical research projects into the **PREDICTION** and **PREVENTION** of breast cancer – without our original funding these research projects would not happen. Furthermore once the Genesis projects have been undertaken, they can often support large grant applications to organisations such as The National Institute of Health Research.

Our research strategy is twofold; firstly **PREDICTION** – finding methods of predicting a woman's personal risk of breast cancer; and secondly **PREVENTION** – researching ways of lowering their risk to prevent breast cancer in these women.



## Our Specific Aims

- To predict which women are most susceptible to breast cancer.
- To diagnose the disease early through better and earlier detection methods.
- To research and develop preventative procedures for the disease.
- To increase the uptake of breast screening in minority ethnic groups.

## Our Objectives

- To identify women as high, medium or low risk through gene, lifestyle and breast density testing.
- To undertake further research into high risk genes and gene fragments (SNPs).
- To offer diet and lifestyle interventions to those deemed high-risk.
- To increase the frequency of screening for high-risk women.
- To improve diagnosis and treatment of pre-cancer changes.
- To develop preventative drugs for appropriate patients.
- To provide more accurate breast screening tools.
- To raise awareness of the disease in minority ethnic communities.

1 in 10 women in the UK will develop breast cancer. Breast cancer in around 4-5% of all cases is due to inheritance of high risk gene faults, especially in the BRCA1 and BRCA2 genes.

It was previously thought that in the vast majority of patients (those without a family history), breast cancer could not be predicted and was **RANDOMLY TRIGGERED**.

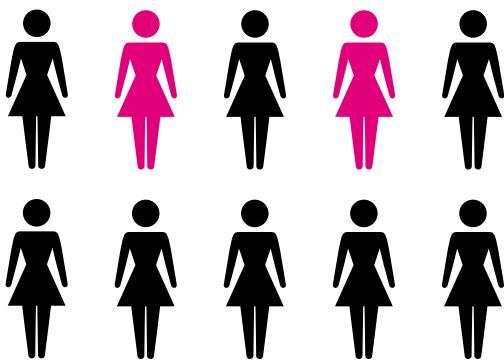
Our research now shows that breast cancer is **NOT RANDOM** and that women who develop the disease are **GENETICALLY PREDISPOSED**.

This combined with their **LIFESTYLE, ENVIRONMENTAL AND HORMONAL FACTORS** can trigger breast cancer.



## Prediction

Before we can **PREVENT** breast cancer we need to **PREDICT** which women are genetically predisposed and are more likely to develop the disease in the future unless someone intervenes. By **PREDICTING AND TARGETING** these high risk women, the main focus can be to **PREVENT** them from developing breast cancer.



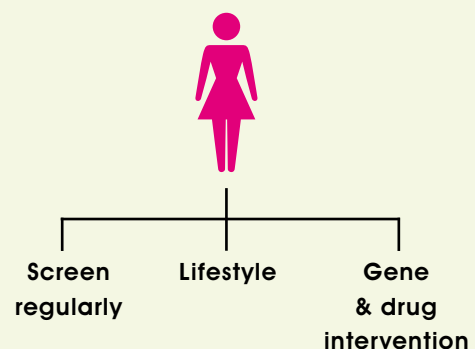
The current studies Genesis is funding (or part-funding) into **PREDICTION** are Predicting the Risk of Cancer at Screening (PROCAS) and Single Nucleotide Polymorphisms (SNPs).

## Prevention

Once we know which women are at a high risk of breast cancer, we can offer a number of strategies to reduce risk or even prevent the disease. These strategies include:-

- **Regular screening** for which we require improved technologies (over conventional mammography and MR scanning).
- **Lowering of lifestyle risk** by interventions that are acceptable and effective; such as dietary, exercise and hormone based interventions.
- **"Switching off" genetic factors** - through research into drugs, vaccines and antibodies, which interfere with biological pathways.

The current studies Genesis is funding or part-funding into **PREVENTION** are Tomosynthesis Trial (Screening), Tamoxifen-Prevention Study (Gene and Drug Intervention) and a number of Diet and Lifestyle Studies under the supervision of Dr. Michelle Harvie.



In many ways we are at a unique moment in history, as a result of 21st century genetic technological advances, which have opened the door to understanding how breast cancer might be **PREDICTED AND PREVENTED**.

Our overall purpose is to be able to predict within a group of 10 women which of them are the 1 or 2 who are most likely to develop breast cancer in the future and to intervene so their risk is decreased.

# Fundraising Update

**As always we must thank all of our wonderful supporters and volunteers in the community, from colleges, schools, sports clubs and businesses who have helped to raise such substantial sums over the past year.**

Due to the economic environment over the past few years, there has been little consistency in fundraising. It has therefore been necessary to review our fundraising strategy and focus on a variety of different areas to ensure that we would meet our financial targets and not be too reliant on one particular income stream.

Having reviewed the success of all the existing campaigns and initiatives, based on their ability to generate income and/ or raise awareness of Genesis, our multi-faceted strategy has seen development and progression in the following areas:-

## Highlights from 2011/12

- Since its launch, The Genesis Million Miles Challenge has been very successful and the feedback from our supporters has been positive. It appeals to all ages and to both the community and corporate sectors. The strap-line "Get Active, Have Fun and Help Prevent Breast Cancer" has been a good marketing tool as whilst it encourages fundraising, it also raises awareness of the importance of exercise and the link with breast cancer risk. Over the course of the year we have bought places in several sporting challenges and seen many of our supporters organise their own exercise based events.
- Genesis has been working closely with Greater Manchester Police, G4S security and several land owners on a new initiative. Crime to Kind has seen the police replace illegal car parks in Salford Quays with official car parks run by G4S on behalf of Genesis. The car parks provide secure parking during Manchester United matches, whilst raising vital funds for Genesis. The car parks have been operating since August 2012 and we expect that they will raise over £20,000 profit for the charity by the end of this football season.
- In 2012 Genesis established a Fundraising Board, which consists of a number of influential women who are using their expertise and experience to raise funds. The Board are currently focused on supporting our annual Genesis Ball. In 2012 the event was hosted by Genesis Patron, Sally Dynevor and featured exclusively in OK! Magazine.
- The Genesis Student Challenge has continued to grow and has had an enthusiastic response from schools in the North West. Students at participating schools are asked to form a committee and plan a fundraising and/or awareness event. The challenge gives the students experience in planning, budgeting, sales and PR, whilst Genesis provides support and helps the students to achieve their goals. In 2011 and 2012 The Student Challenge has resulted in a variety of events including a sponsored walk, a dance competition and Zumba sessions. Many students have also helped to raise awareness of the charity and breast cancer prevention through presentations to their fellow classmates.





- We have implemented a full re-brand as it was strongly felt that a fresh, new look and logo would move the charity forward in 2012/13. The rebrand was led by supporter and expert, Diana Harris who donated her time and expertise to ensure the project was a success..
- After a full review of our internal systems, we have invested in a new database. Installation and training began in July 2012. By investing in the database and staff training we aim to improve our professionalism and efficiency.
- Throughout 2011/12 we have received funding from a variety of Trusts and Foundations who have supported many of our different research projects including PROCAS, SNPs, Tamoxifen-Prevention, Tommy Trial and Diet & Lifestyle Research.

The overall success of our multi-faceted fundraising strategy is clearly illustrated by the funding we have secured for the SNPs Project (see page 10). Restricted income has been raised from:-

- Roberts Bakery - A corporate supporter
- A Bridge Drive - Community fundraisers Lady Joanna Gray, Rose Mahn and Susan Mannerswood
- The Hoover Foundation - A charitable foundation

## Fundraising Targets for 2013

- In February 2013, *The 2-Day Diet* was published by Vermillion, part of Random House. The immediate success of the book, the phenomenal publicity surrounding its publication and the interest from around the world has

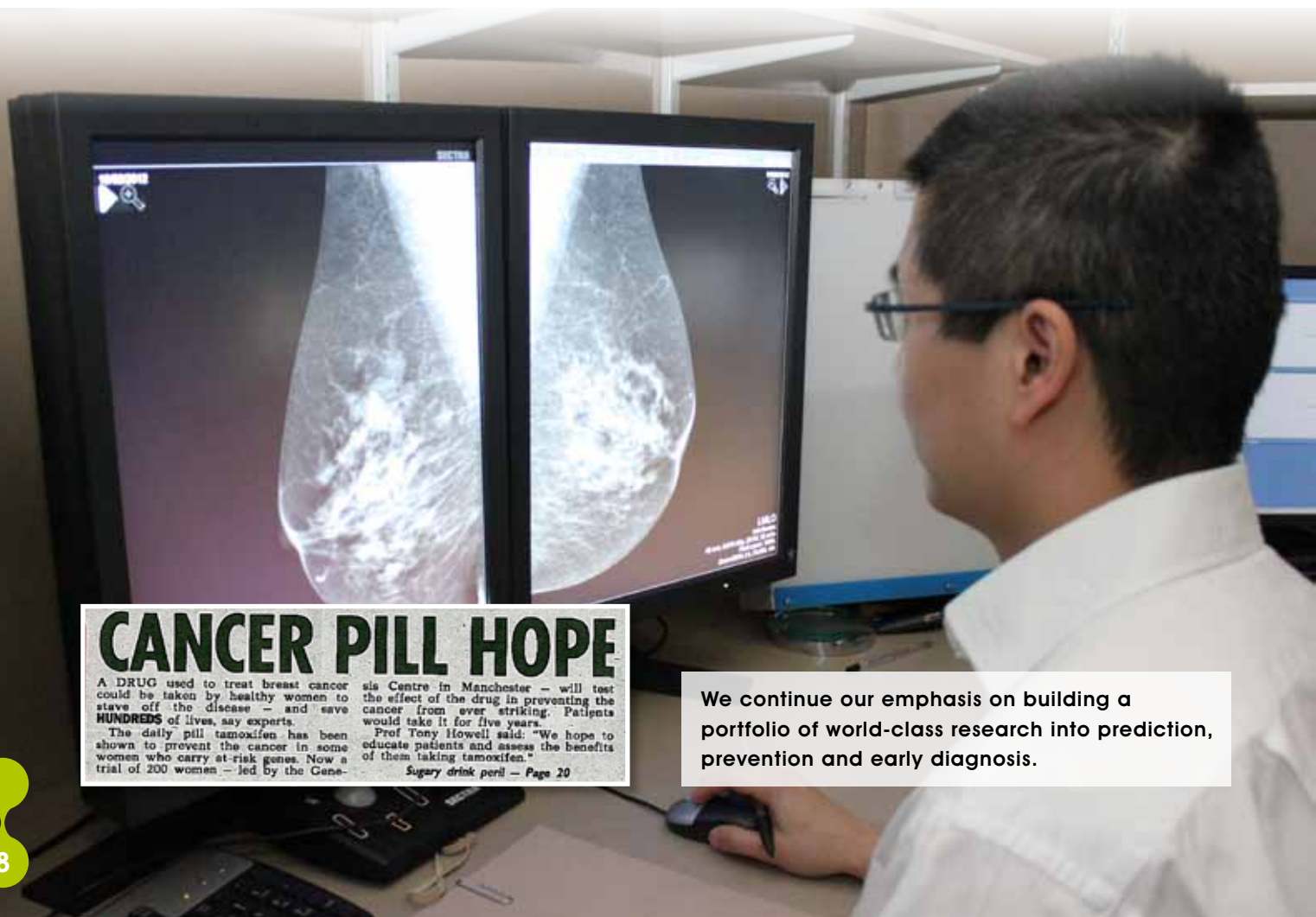
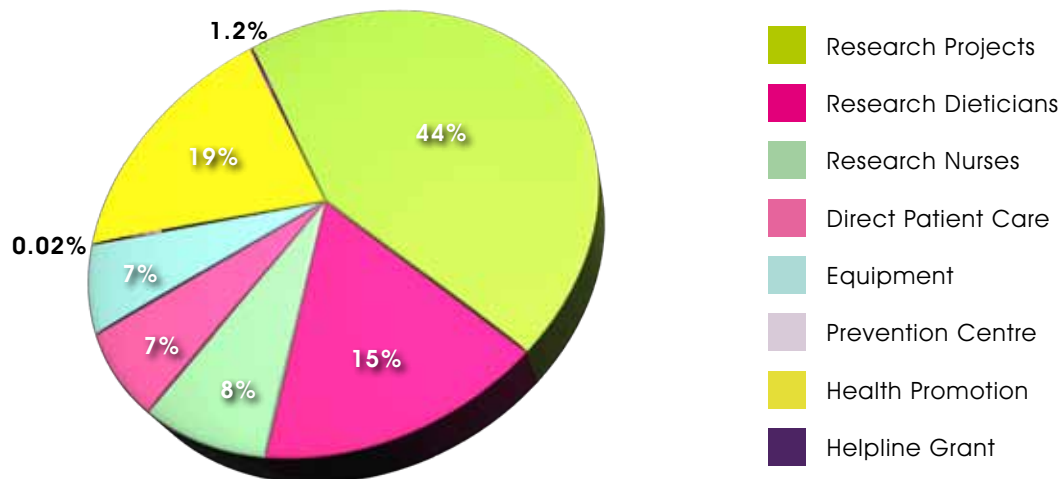
greatly increased the charity's profile and helped to raise awareness of a very important public health issue. We will continue to maximise on this opportunity throughout the year, working closely with Vermillion. *The 2-Day Diet Cookbook* was published in April 2013. All author proceeds from both books will go to Genesis Breast Cancer Prevention.

- Invest in a new website and content management system, which will incorporate our rebrand, be easier for visitors to navigate and encourage supporters to donate or register for events. Since the publication of *The 2-Day Diet* and associated publicity, the website has seen a 165% increase in unique visitors compared with the same period in 2012. It is apparent that we need to make the most of our increased profile and that our existing website does not meet the necessary requirements.
- Develop our Social Media Strategy to ensure that we maintain our profile after the publicity surrounding the book decreases.
- Continue to develop The Genesis Million Miles Challenge by investing in a variety of sporting events, which we know will appeal to our supporters. Our goal remains to raise £1 million through exercise based fundraising.
- Create and implement a new fundraising campaign encouraging supporters to organise tea parties, this can be an alternative to The Million Miles Challenge and will appeal to all types of supporters.



# Grants made in 2011/12

During the year under review, we have awarded the following grants.



## CANCER PILL HOPE

A DRUG used to treat breast cancer could be taken by healthy women to stave off the disease – and save HUNDREDS of lives, say experts.

The daily pill tamoxifen has been shown to prevent the cancer in some women who carry at-risk genes. Now a trial of 200 women – led by the Gene-

sis Centre in Manchester – will test the effect of the drug in preventing the cancer from ever striking. Patients would take it for five years.

Prof Tony Howell said: "We hope to educate patients and assess the benefits of them taking tamoxifen."

Sugary drink peril – Page 20

We continue our emphasis on building a portfolio of world-class research into prediction, prevention and early diagnosis.

# How Your Funds Are Spent

## Prediction Projects

### Our Aim:

- To predict which women are most susceptible to breast cancer.

### Our Objectives:

- To identify women as high, medium or low risk through gene, lifestyle and breast density testing.
- To undertake further research into high risk genes and gene fragments (SNPs).
- To increase the frequency of screening for high risk women.

### Predicting the Risk of Cancer at Screening (PROCAS)

The PROCAS study led by Professor Gareth Evans aims to determine whether it is feasible to accurately predict each woman's personal breast cancer risk when they attend routine breast screening. All women aged between 47 and 73 who attend routine breast screening mammograms as part of the NHS Breast Screening Programme in Greater Manchester are being invited over three years to join the study and it is expected that 55,000-60,000 women will agree to participate in this research. The study is being run from The Genesis Prevention Centre at University Hospital of South Manchester.

Data is being collected on the following breast cancer risk factors: mammographic breast density (the amount of dense tissue in the breast), lifestyle factors, reproductive factors and family history. Together these factors are used to give an overall risk score for each woman. In addition, 10,000 women are being invited to provide a saliva DNA sample which will be tested for genetic changes (single nucleotide polymorphisms [SNPs] thought to be associated with breast cancer risk).

PROCAS is the first study to investigate the use of these genetic tests on women who undergo routine screening. All women are given the choice of finding out their personal risk of breast cancer and so far 95% of women participating in the study have indicated a desire to know their risk at time of consent to the study. Any women who have chosen to know their risk and are high-risk are offered a consultation with an expert at The Nightingale Centre and Genesis Prevention Centre (Professor Howell

or Professor Evans). Women are given advice on ways of reducing their risk and if appropriate, may be offered more frequent screening and preventive measures. To date 315 high risk women have been seen, and 141 have been referred for more frequent screening (18-monthly screening, as opposed to three-yearly). Of these women, three have had breast cancer detected on their extra mammogram. This means that for these three women, their cancer was detected potentially up to 18 months sooner than it would have been had they not joined the PROCAS study.

If the PROCAS study can demonstrate that it is feasible to accurately predict and feedback breast cancer risk to women attending routine breast screening, then this process of personalised risk prediction could be incorporated into the screening process. In the longer term there may also be the potential for women's mammographic screening interval to be altered based on personal breast cancer risk (i.e. women at increased risk receiving more frequent screening).

As a result of PROCAS, University Hospital of South Manchester now has the largest number of participants recruited into a research study in the UK. Although recruitment started more slowly than expected, following feedback the PROCAS research team have now placed staff on the vans to explain the project in more detail to potential participants. They have also held many successful open days on Saturdays for women to donate their saliva samples. To date (May 2013), over 51,000 women have agreed to take part in PROCAS and over 7,180 saliva samples have been collected.

Genesis has also funded SNP research, which is being carried out within the PROCAS study. For the last 5-10 years the family history population has been the focus of prediction studies; however as the PROCAS study is being run within the national breast screening programme, we are now including women from the general population in our prediction research.

The study is funded by the National Institute for Health Research, with additional support from Genesis for special data capture software, the DNA kits to test women's saliva samples and the extraction of DNA from the samples.



# How Your Funds Are Spent continued...



## Angela's Story

Angela, 54, agreed to participate in the study as she thought she was fit and healthy and wanted to help others by taking part. After the researchers collected information on her family history, lifestyle, breast density and genetics through a questionnaire and mammogram, Angela was deemed high risk because of her lifestyle factors, reproductive factors, and the fact that her mother developed and recovered from breast cancer six years ago.

Due to her level of risk Angela was given the choice of having mammograms every 18 months rather than the standard three years. It was at her first 18-monthly mammogram that Angela's breast cancer was discovered. She had the lump removed, and after a course of radiotherapy she has an excellent prognosis. Angela says *"This trial is so important. It is literally saving lives, including mine. Regular screening is vital because it stops the cancer from spreading and allows you to have treatment before it's too late"*.

## SNPS Study

A SNP is a variation in your DNA building block (nucleotide) that is different for each person. Everyone has thousands of SNPs. Gene testing of women who have had breast cancer has identified that many carry specific SNPs that increase their risk of the disease. It may be that all women who develop breast cancer do so because they carry at least one of these SNPs. Thus, by combining a gene test to search for high risk genes and for lower risk SNPs, together with a study of bio-markers of risk such as mammographic breast density, it may be possible to predict within a group of 10 women who are at a higher risk of developing breast cancer unless someone intervenes.

**We asked Genesis researcher, Franchesca Gifford, a few questions about SNPs.**



## What are SNPs, and why are they so important?

A SNP is a Single Nucleotide Polymorphism- it is a variation of one of the four nucleotides (A, G, C or T) in the DNA sequence that differs between individuals.

Everyone has thousands of SNPs and it is this variation in our DNA that makes us all unique. SNPs can occur anywhere in genes and can contribute to various diseases.

## What are you investigating?

My project aims to find whether SNPs can change the density of breast tissue as seen on an X-ray (mammogram). Density is measured as the proportion of gland (tissue that makes milk) to fat and is a major risk factor for breast cancer.

## How will this help women in the next generation overcome breast cancer?

It may be possible to undertake a genetic test by giving a blood sample which would tell us the SNPs a woman has that can influence density, and therefore her personalised breast cancer risk. Knowing which women have a higher risk and which have a lower risk of developing breast cancer would allow tailored screening via mammography. It is hoped that this would lead to more cancers being detected at an earlier stage which improves the success of treatment.

## Upcoming Prediction Study

### The RNA Study

This two year study, led by Professor Gareth Evans, proposes a new strategy to identify high risk breast cancer genes, using tests on RNA instead of DNA to look for faults in the binders (introns) of the gene rather than the main reading area that makes the proteins (exons).

Breast cancer in around 4-5% of all cases is due to inheritance of high risk gene faults, especially in the BRCA1 and BRCA2 genes. These genes account for the vast majority of cases where breast and ovarian cancer occur in the same family.

However, the ability of current laboratory screening tests to identify ALL underlying genetic changes remains in doubt. Between 10-15% of families who are very high risk with either breast and ovarian cancer or male breast cancer, that would be predicted to almost definitely have a BRCA1 or BRCA2 mutation, do not have a genetic fault identified.

This leaves families in a quandary about whether to take decisive action such as risk reducing surgery. A particular problem is that some families may have 'missed' mutations in BRCA1 or BRCA2 because current techniques do not identify the causative mutation. Families with cancers caused by faulty BRCA genes are uniquely sensitive to drugs called PARP inhibitors. Knowing if a family has a mutation in BRCA1 or BRCA2 gives us the opportunity to offer access to these drugs.

Genes are divided into sections called exons and introns. Current genetic tests look at exons. However, we know from other genes that 2-5% of genetic faults occur in the

introns. It is not feasible to look at introns on most genes. However, there are tests that can identify the existence of a fault in the intron. DNA is contained in the nucleus or centre of the cell and RNA is produced to carry the genetic message from DNA out of the nucleus to communicate it to the rest of the cell. Tests that look at the RNA product from the DNA of a gene can identify when a fault deep in the binder (intron) exists.

We propose a new strategy to identify any missed mutations in BRCA1/2 using tests on RNA rather than DNA to look for deep mutations in the intron of the gene rather than in the exons and intron/exon boundaries.

Comprehensive analysis of RNA has never been carried out on BRCA1/2. Manchester has the largest recorded collection of families with BRCA1/2 mutations in the UK. This means we have access to RNA samples on 35 very high risk families with breast and ovarian or male breast cancer that should have a BRCA1/2 mutation but in whom none have been identified.

### Through this study -

- We will develop and carry out RNA analysis on these 35 families.
- We will carry out DNA testing of the entire genome, in those with no mutation, to find other high risk genes thus far unidentified. The analysis of their genes will be by a new technique called exome sequencing which we have successfully used in our laboratory, to identify new genes that are responsible for these cancers.
- We may identify a previously undiscovered BRCA1/2 mutation may make affected individuals eligible for new treatments with PARP inhibitors.

# How Your Funds Are Spent continued...

## Early Detection Project

### Our Aim:

- To diagnose the disease earlier through better and earlier detection methods.

### Our Objective:

- To provide more accurate breast screening tools.

This year Genesis has part-funded one project into the early detection of breast cancer.

### The Tomosynthesis (Tommy) Trial

Six NHS breast screening programme centres across the UK will be involved in this study and will recruit 9,000 participants over a 15-18 month period. Currently The Nightingale Centre and Genesis Prevention Centre is one of the largest recruiters for this trial.

Genesis is part-funding the rental of the tomosynthesis machine. Digital breast tomosynthesis is a newly developed three-dimensional (3D) X-ray technique that may help to improve the accuracy of the standard 2D mammography.

It is performed by taking multiple low dose X-ray images of the breast, which can reduce the chance of a lump being obscured by overlapping breast tissue. These multiple images are then developed by a computer to reconstruct a 3D image of breast tissue. This will reduce the number of cancers missed at screening and the number of women who have unnecessary tests. This research will also identify if tomosynthesis should replace or be used in addition to digital mammography as a screening tool.

The Tommy Trial has now recruited over 2,000 women from our centre and many more in the five other centres. Initial feedback is very positive from staff and this trial could potentially change practice over the next few years.



## Prevention Project

### Our Aim:

- To research and develop preventative procedures for the disease.

### Our Objectives:

- To develop preventative drugs for appropriate patients.

### The Tamoxifen Prevention (TAM-Prev) Study

Tamoxifen is a drug currently used for preventing recurrence of breast cancer. However when given for five years to women at increased risk of the disease it can prevent around 40% of breast cancers. Tamoxifen is currently licensed in the US for prevention but not in the UK.

TAM-Prev is a three-year study with two major aims. One aim is to determine the proportion of eligible women between the ages of 33 and 46 years who wish to take tamoxifen. The second aim is to predict the women most likely to benefit from treatment, so that in the future we can target preventive interventions and ensure that women are not needlessly tolerating side effects if they are unlikely to benefit from the intervention. The only women to benefit from tamoxifen are those who have a reduction in glandular/dense tissue on their mammograms at one year compared to the baseline mammogram. Economic analyses of the costs and benefits to the NHS of tamoxifen prevention for all moderate and high risk premenopausal women will also be carried out.

For many women deciding whether to take tamoxifen for prevention can be difficult, so as part of the study a specially designed decision aid is issued to all women who are considering joining the study. The decision aid is a forty page document which includes a detailed outline of the study, the potential risks and benefits of taking tamoxifen, and explains how the drug works. It also gives potential participants information on expected side-effects, how to deal with them, and a contact number should they wish to speak to a member of the TAM-Prev team.

Dr Donnelly is the psychology research fellow for the study. She explains *"The decision aid is given in addition to the more traditional participant*

*information sheets and aims to give depth of information in an easy to read and accessible format in order to aid women in making an informed choice when considering whether or not to join the study."*

During the first six months of the study, 30 women were interviewed (15 who joined the study and 15 who declined) so that feedback could be collected on the decision aid and the information it contained. On the basis of that feedback the decision aid was redesigned, so that the 'new look' decision aid is more reflective of women's information preferences.

After one year on tamoxifen, women are given feedback about changes to biomarkers including mammographic changes, which may provide an indication about whether tamoxifen is working for them. Women are then given the opportunity to continue with tamoxifen for an additional 4 years, or to stop. Dr Donnelly is conducting interviews with fifteen women who have continued taking tamoxifen and fifteen who have stopped taking tamoxifen, to explore the motivations around this. To date (22nd May 2013) 59 women have reached the one-year time point, and 48 have chosen to continue taking tamoxifen.

Uptake data from the study has been collated and is being written up for publication. Of the 1,279 eligible women; 136 (11%) joined the study. The highest uptake (15%) was seen in women in their forties at high risk who did not carry a BRCA1 or BRCA2 mutation. The publication will provide details of uptake to tamoxifen, specifying how uptake differs amongst women of different ages, levels of risk and circumstances (i.e. whether they have had children or not). In addition it will explore, in greater depth, women's motivations for taking tamoxifen. This will help provide a better understanding of women's attitudes towards tamoxifen use and will be of particular relevance if the new NICE guidelines, due to be issued in July 2013, recommend tamoxifen for breast cancer prevention in pre-menopausal women at increased risk of breast cancer.

The research team plan to build on this research in a number of ways. Plans are currently being put in place for two major studies:



# How Your Funds Are Spent continued...

1. A study looking at giving women better support when deciding to join a drug prevention study and whilst on the study. Support would be given using a variety of eHealth assistive technologies. The research team hope to use assistive eHealth technologies to address the issues raised in the TAM-Prev study.
2. A study aiming to determine whether it is possible to predict who is likely to benefit from raloxifene for breast cancer prevention. Raloxifene is used for breast cancer prevention in post-menopausal women in the US, though it is not yet licensed for prevention in the UK. It is however licensed for treatment of osteoporosis and is expected to be recommended for use in breast cancer prevention when the new NICE guidelines are issued in July 2013. Raloxifene is known to reduce breast cancer risk. However, like tamoxifen it will only be of benefit to a proportion of women at increased risk of breast cancer. Therefore if it is possible to predict who will benefit, treatment can be targeted appropriately.

The TAM-Prev study is being funded under the NIHR Research for Patient Benefit (RfPB) programme for approximately £250,000. Additional support is being provided by Genesis, who has funded all drug costs and some staff support.

## Charlotte's Story

Charlotte's mother died of breast cancer at the age of 44. Charlotte, 35, explains "My mother's death had a huge impact on me and I was conscious I had an increased risk of developing the disease."

Charlotte has been identified as high risk and was the first woman to join the Tamoxifen-Prevention (TAM-Prev) study and take tamoxifen as a preventative measure against breast cancer.

Charlotte says 'I want to do all I can to minimise my risk of getting the disease. I can do more exercise, watch my weight and be breast aware, but being part of this clinical trial means I am doing everything I can to protect my health.' After one year of tamoxifen Charlotte's mammograms indicated that tamoxifen was working and she elected to continue to complete the full five years of treatment.



## Diet and Lifestyle Research

### Our Aim

- To research and develop preventative procedures for the disease.

### Our Objective

- To offer diet and lifestyle interventions to those deemed high-risk.
- To introduce lifestyle change to prevent the disease.

Currently, across the UK there are rising trends of obesity, sedentary lifestyle and alcohol rates. In England alone, 65% of women are overweight and 25% obese (3 stone heavier than the ideal). Being overweight increases the risk of developing breast cancer as well as several other chronic diseases including cardiovascular disease, diabetes, dementia and eleven other types of cancer. Recent expert reports estimate that 40% of breast cancer cases may be preventable through weight control, exercise and reduced alcohol intake.

Our award winning Genesis research dietician, Dr Michelle Harvie, has attracted press from around the world with her ground-breaking intermittent diets and novel interventions for women with breast cancer and women deemed high risk. We asked her a few questions....

### Q. How are diet and lifestyle related to breast cancer?

The links between diet and the development and progression of breast cancer were first suggested as far back as 100 years ago. Current evidence suggests that being overweight, inactive and habitually having a high alcohol intake may all contribute to breast cancer. The precise amount of breast cancer due to these factors is debated but are said to account for between 17-40% of all breast cases in the UK today.

### Q. What have been the key findings of your work so far?

We were one of the first groups to demonstrate that weight loss can reduce the risk of breast cancer. A collaborative study with the Iowa Women's health study cohort (33,000 women) suggested modest weight loss (5% i.e. 10 pounds of weight) reduced risk by 25-40%. Weight loss is notoriously difficult to achieve and maintain. We have been developing and testing novel intermittent diets for weight loss and breast cancer prevention since 2006. The initial

randomised evaluation of intermittent energy restriction (IER) versus the normal approach of daily dieting showed intermittent dieting led to greater reductions in the hormone insulin, which promotes cancer, compared to standard daily dieting (25% greater reduction five days after the intermittent diet with a further 25% reduction during the 2 restricted days). Our recent intermittent energy and carbohydrate restricted diet appears to be easier to follow than daily dieting and offers beneficial effects in lowering insulin and other cancer causing hormones.

We have also been examining exactly how low calorie diets and weight loss may help protect from developing breast cancer. Understanding the underlying mechanism is important as it will help reinforce the message for women who struggle to comprehend the links, and also helps our understanding. If we understand the mechanism it also gives us the opportunity in the future to develop and test drugs which mimic the powerful effects of diet.

Our recent Genesis funded project examined the effects of a month of the 2 day intermittent diet on the genes within the breast cells of healthy women who were at high risk of breast cancer. This trial has shown changes in breast gene expression in 300 genes.

Our 2004 publication highlighted the problem of weight gain after diagnosis of breast cancer whilst our subsequent surveys indicate the lack of weight control services for patients. In 2008 we undertook a Genesis funded pilot trial to assess weight control interventions amongst early breast cancer patients called Breast - Activity & Healthy Eating after Diagnosis study (B-AHEAD). In 2008 we were awarded a £260,000 Research for Patient Benefit grant to compare three ways to deliver weight control advice in the NHS; a supervised diet and exercise class, home based programme or written advice only.

### Q. What projects are you currently working on?

We are working with Professor Gareth Evans and Professor Tony Howell to start introducing lifestyle programmes for the prevention of breast cancer (see below) into the Breast Screening Programme. We are also working with service users to develop what support would be required by the women. This is likely to include peer support as well as healthcare professional input.



# How Your Funds Are Spent continued...

## 'Healthy Lifestyle Promotion at Screening' Programme

The current approach to weight reduction and lifestyle change for disease prevention is not systematic or even particularly effective to cope with this epidemic. The costs are increasing for the NHS as the number of patients with obesity linked conditions escalates. The NHS Breast Screening Programme (NHS BSP) allows early diagnosis and improved breast cancer survival but does not currently incorporate disease prevention.

From three of our previous studies we have also found that many overweight women, of breast-screening age, have previously unidentified high risk profiles for heart disease and diabetes.

Recent cancer expert reports, widely covered in the media, have estimated that 40% of breast cancer cases could be prevented through

- Weight control
- Change in sedentary behaviour
- Reduced alcohol intake

This is supported by Dr Harvie and others who have confirmed that a 5% weight loss reduces postmenopausal breast cancer risk by 25%. Changing people's behaviour can be difficult and costly but we have shown in several studies that telephone support seems useful and potentially very

cost effective. We have also demonstrated in past studies that telephone support is as effective as centre visits and superior to standard written advice for achieving weight loss and lifestyle change.

The NHS BSP service reaches approximately 70% of the female population in the UK, every three years from the age 47 to 73. These women who attend screening have already shown a motivation to be health aware and are more likely to want to change their behaviour.

This one year pilot study assesses if we can introduce lifestyle changes for women at high risk of developing breast cancer in order to reduce their risk and prevent the disease. Additionally, participants will be screened for diabetes and CVD to investigate the feasibility of efficiently screening for these diseases in women in the screening programme.

This randomised pilot study, led by Dr Harvie, will test a tailored lifestyle programme to a group receiving standard NHS care and will involve overweight women from the BSP who have been identified from other Genesis projects as being at an increased risk of breast cancer (three times the population risk).

- An intervention group will receive their personal disease risk for breast cancer, CVD and diabetes, three months of personalised phone, mail and web supported 'Healthy Lifestyle Promotion at Screening' programme and a subsequent three months of web and peer support.
- A comparison group will receive disease risk information and standard written lifestyle advice.

We will evaluate the uptake and retention of women to the study, the feasibility of targeting women in the BSP for lifestyle intervention and the effects of the programme including reduction in obesity, change in diet and exercise behaviours and potential reduction in breast cancer risk using insulin, a breast cancer risk marker.

## Intermittent Diets

Following the success of Dr Harvie's diet book, *The Genesis Breast Cancer Prevention Diet*, a new diet book, *The 2-Day Diet* was published in February 2013 focusing on the results of her more recent research into intermittent dieting. This shows that restricting

*"The research into breast cancer prevention is vital and so much has improved over the last few years.*

*I volunteer for Genesis as it is a cause close to my own heart, because both my mother and I have had breast cancer. Over the years I have been very aware of the improvements in the prevention of breast cancer. More research is needed so one day it really will be prevented".*

**Chris Simmons,**  
Ex-patient and volunteer

carbohydrates for just two days per week may be a better dietary approach than a standard, daily calorie-restricted diet for preventing breast cancer and many other diseases. In April 2013 *The 2-Day Diet Cookbook* was published, offering a large selection of recipes for restricted and unrestricted days. All author proceeds from both books will go to Genesis Breast Cancer Prevention.

Dr. Harvie originally tested an intermittent diet that was very simple and restricted. It only allowed 650 calories per day from milk, vegetables and fruit and predictably our dieters found it difficult to maintain this diet long term. Following on from this previous research, Genesis Breast Cancer Prevention funded a new study looking at a simpler, low carbohydrate, high protein version of *The 2-Day Diet*, which Dr Harvie had devised to allow a greater choice of food and to ensure our dieters were not hungry on their restricted days.

*"Weight loss and reduced insulin levels are required for breast cancer prevention, but [these levels] are difficult to achieve and maintain with conventional dietary approaches,"* said Michelle Harvie,

This new improved *2-Day Diet*, which maximises loss of fat, but minimises loss of muscle, is more effective and easier to follow than a standard daily diet. It is the latest most powerful version of our intermittent diet research. It is also better than a daily diet for weight loss, reducing body fat and reducing levels of the hormone insulin, which is linked to breast cancer risk and other diseases. The results of this novel study were presented at The San Antonio Breast Cancer Symposium in December 2011 and were published in *The British Journal of Nutrition* in 2013.

Over the last few years a lot of progress has been made with diet and lifestyle studies for the prevention of breast cancer. Our researchers are now more confident in stating which diet will help women the most to not only lose weight but also to decrease their risk. We are also aware that our diet and lifestyle programmes can help prevent other cancers (i.e. bowel, womb, kidney) and other diseases (cardiovascular disease, diabetes and dementia).

### Case Study

Jane Whyatt, now aged 48, was concerned about her risk of breast cancer after three of her maternal aunts and one of her paternal aunts were diagnosed with the disease. Referred by her GP, Jane had a detailed consultation, including a family history assessment with a cancer genetics expert, at The Nightingale Centre and Genesis Prevention Centre.

She was told she had a lifetime risk of one in six, compared to the lifetime risk of the general population of one in ten. Her family history gave her a risk of one in seven but as she doesn't have any children her risk increased further to one in six. This meant she would need a mammogram every year until she was 50 and would then be screened every three years as part of the NHS Breast Screening Programme.

Jane was understandably upset by the news and agreed to participate in a cancer prevention trial as she felt *"I'd be more closely monitored but I was also really happy to be involved in something from which other people might benefit"*. She had put some weight on over a relatively short time (her heaviest was 11 stone) and had wanted to lose the weight as well as reduce her risk of breast cancer.

After four months on *The 2-Day Diet* Jane lost more than a stone in weight and lost four inches off her waist. Though Jane's insulin levels were in the normal range (5.6 micro units per millilitre) by the end of the trial they had dropped dramatically by 52% (to 2.7). Many of us have dangerously high levels of insulin in our bodies, and this excess is increasingly believed to be at the root of many weight-related diseases, such as type 2 diabetes, heart disease, some cancers and possibly dementia.

For Jane this drop in insulin meant her lifetime risk of breast cancer – despite her family history – was brought in line with rest of the population at one in ten. She has continued with the principles of the diet and kept the weight off over the last three years, keeping her lifetime risk of developing breast cancer lower than before.

# How your funds are spent continued...

## Awareness

### Our Aim

- To increase the uptake of breast screening in minority ethnic groups.

### Our Objective

- To raise awareness of the disease in minority ethnic communities.
- Recent research from The University Hospital of Leicester has identified that South Asian women have the same incidence of developing breast cancer as White British women. Cancer incidence for South Asian women has been increasing as they are exposed to the lifestyle and environment in the UK.
- In the non-Asian population, three quarters of women invited attend screening. Among members of the South Asian population this dropped to under two thirds, and for members of the Muslim population was just over half.
- As many women are not attending their mammograms they are more likely to be diagnosed with late stage breast cancer and therefore have poorer survival rates.
- 43% of black and ethnic minority (BME) women have never examined their breasts for lumps compared to 11% of the population. For 56 % of these women they said they were unsure what they were looking for in self-examination.
- South Asians are the largest minority ethnic group in the UK, representing 2.7% of the total population.
- The north west of the UK has a higher than average percentage of Pakistani, Bangladeshi and other Asian communities.

In 2010 we hosted an Asian Women's Health Awareness (AWHA) conference, jointly organised by Professor Anil Jain, Consultant Radiologist and Mr. Lester Barr, Breast Surgeon and Chairman of Genesis Breast Cancer Prevention. It highlighted the need to develop effective programmes to raise breast awareness in South Asian women.

Since 2010, Professor Anil Jain has hosted a Cross Cultural Communication Skills Training Workshop every quarter for health care professionals and members of the South Asian women's community.

We are looking at a number of ways to increase awareness about breast cancer and the importance of attending breast screening among South Asian Women and medical professionals across the North West. South Asian women are less likely to be breast aware or attend screening than the national average. One of the Genesis staff is also on secondment to Professor Jain to help with his Cross Cultural Communication Workshops.

### Shazia's Story

Shazia, 42 was diagnosed with breast cancer in 2011. Married with two children her family and friends rallied around her for support throughout her treatment. Born in the UK, Shazia's parents are from Pakistan and she understands firsthand the issues in the Asian community surrounding breast cancer. Shazia says, 'A lot of Asian women are also very private people so having breast cancer is taboo'. She is getting involved in the AWAH project as she believes there are obstacles facing the South Asian community such as language and education that can be overcome. "We need to raise more awareness amongst the Asian community through screening programmes and education. Women need to feel comfortable with getting support."

*"Genesis Breast Cancer Prevention has unique aims - it is the only charity that targets breast cancer prevention. Although research has led to great improvements in breast cancer survival, breast cancer is still too common, affecting one in ten women. Genesis supports or 'pump-primes' novel research ideas, allowing original, scientifically and medically sound ideas to be tested, with the ultimate aim of reducing the number of people affected by breast cancer".*

**Cliona Kirwan, Consultant Breast Surgeon  
& Senior Clinical Research Scientist  
and Genesis Medical Advisory  
Board Member**



# Research Vision

A major focus of our research grants in recent years has been to investigate the lifestyle and environmental factors that can predispose women to breast cancer and the genetic links from mutations and from SNPs. In the year ahead we are also looking forward to seeing progress in the area of improved early diagnosis; through improved technology (such as the TOMMY trial) and through improved prediction and breast screening strategies (the PROCAS study).

Our plans for the next five years are now beginning to take shape. We hope to invest in several areas of research into breast cancer prediction, prevention and early diagnosis by supporting key projects in the following areas:

- 1. Better prediction of risk.** Under the leadership of Professor Gareth Evans, we hope to improve our ability to predict which women within the general population are at risk of breast cancer. This will allow these women to have early warning, and allow us to offer protection through improved early screening and preventative interventions.
- 2. Screening for breast cancer.** Under the leadership of our Radiology Team, we are conducting clinical trials of new methods of breast screening. We hope this will convert into improved clinical practice over the next five years. We are also supporting projects into improving breast screening and breast awareness within minority ethnic communities.
- 3. Diet and lifestyle.** Under the leadership of Dr Michelle Harvie, we are running several projects related to diet and lifestyle and their influence in reducing breast cancer risk. Dr Harvie's current research is focused on the effectiveness of a two day low carbohydrate, restricted diet and the effects on weight loss and breast cancer risk. Research is also being undertaken looking at the effect of the diet on genes within the breast cells of high risk women.
- 4. Breast cancer prevention drugs.** Under the leadership of Professor Tony Howell, we are supporting projects within both premenopausal woman and postmenopausal women to assess whether or not breast cancer risk can be reduced through drugs that modify hormonal balance.

In addition Professor Howell is looking in the laboratory at other potential drugs that could lower risk.

- 5. Early breast cancer changes.** Professor Nigel Bundred is investigating the condition of ductal carcinoma in situ (DCIS). This is a pre-cancer condition that, if left untreated, can progress to breast cancer. His work should allow us to diagnose this condition at an early stage, and treat it more effectively, thus allowing us to prevent breast cancer in women who otherwise would have developed the disease. He is supported in this work by a clinical research team, and by Consultant Surgeon and Clinical Scientist, Cliona Kirwan.
- 6. Breast surgery.** Under the leadership of our Breast Surgery Team, we are developing new methods of breast reconstruction in women who require mastectomy either as a risk-reducing procedure or because breast cancer has already developed. We hope this will improve the quality of life of many women.

Over the past five years much of our research has concentrated on women who have a strong family history of breast cancer. In the next five years our emphasis is now changing towards the general population and predicting a woman's individual breast cancer risk. There is gathering excitement around the world that prevention of breast cancer could be an achievable goal. The world class scientists and investigators in Manchester that Genesis is supporting will be an important part of achieving this dream.

## Thank you to our supporters

We would like to thank all our fundraisers and volunteers for their help this year. Our ground breaking research into the prediction and prevention of breast cancer could not take place without your loyal and continuous support. Together we can create a future free from breast cancer.

# The Figures - 2011/12

During the course of the past financial year we have worked hard to maintain major fundraising initiatives whilst being constantly conscious of our budgetary constraints.

Our fundraising team continues to work tirelessly in its mission to generate both the income that the charity needs to continue its research, as well as its task of raising awareness of breast cancer prevention and health education.

We are focusing on funding and supporting research into breast cancer prediction, prevention, early diagnosis and screening, having already made many grants towards research projects.

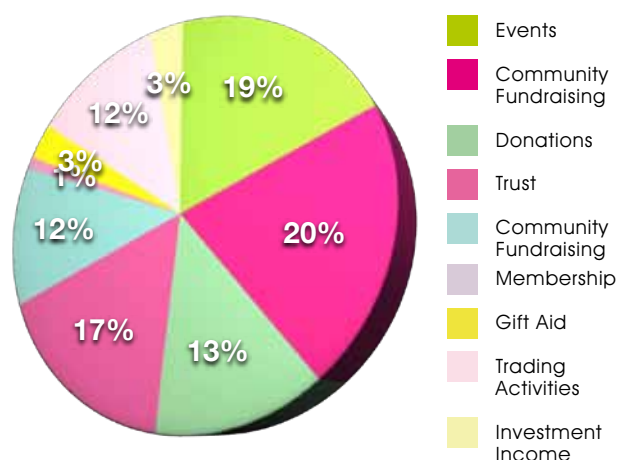
Applications for our research grants are on the increase and we continue to work alongside our

Scientific Advisory Board who consider applications and make recommendations to the Board of Trustees.

The downturn in the economy over the last few years saw our income drop significantly. During this time we dipped into our reserves, so that we could continue to fund all our research studies. By following this policy we have been able to award research grants of nearly £0.5 million more than our net charity income over the last four years. Due to this, and the economic climate in general, the Trustees felt it was sensible during this period to reduce the number of new research grants into the prediction and prevention of breast cancer as we had a commitment to our existing studies. However, last year our income significantly increased and Genesis is yet again funding many new innovative research projects, so we can prevent breast cancer for the next generation.

## Funds raised in 2011/12

Events	£112,695
Community Fundraising	£123,695
Donations	£76,865
Trusts	£101,171
Company Fundraising	£73,025
Membership	£7,041
Gift Aid	£19,517
Trading Activities	£69,681
Investment Income	£17,300
<b>Total Income</b>	<b>£600,741</b>



## How our funds are spent

Charitable expenditure	
Grants Awarded	£297,891
Cost of Health Promotion	£60,207
Other expenditure	
Cost of Trading	£38,310
Governance	£6,050
Administration & Finance	£33,512
Cost of Fundraising	£154,678
<b>Total expenditure</b>	<b>£590,648</b>

Already in this financial year (2012-13) we have committed to £211,147.20 of new multi-year grants towards research into genes, diet and lifestyle as well as equipment. This does not include our ongoing commitments that we make every year towards researchers salaries and ongoing large scale research projects.

For further information on our research please visit [www.genesisuk.org](http://www.genesisuk.org)





The only UK charity entirely  
dedicated to the prediction and  
prevention of breast cancer.

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