



# Impact report

2013/14

“Together we can  
prevent breast cancer  
for future generations”



Most cancer research in the UK, Europe and the USA is concentrated on 'finding the cure'. Genesis Breast Cancer Prevention is different because it believes that 'prevention is better than cure' and so concentrates its efforts on trying to prevent cancer from ever starting. Breast cancer is caused by a mixture of genetic, environmental and western lifestyle factors.



# Chairman's report 2014



Our research grants fund various projects investigating the genetic causes of breast cancer, environmental factors, diet, lifestyle, methods of screening for breast cancer, cancer prevention drugs, and better surgery. Our plan is to enable top-quality research into breast cancer prevention through carefully targeted grants to top class investigators. We support their best ideas, provide seed funding for promising avenues of research, encourage them to work collaboratively with other groups in joint research projects, and provide support for some of the most important studies into breast cancer prevention currently being undertaken anywhere in the world.

Over the last 3 years we have published an annual Research Overview describing where our research has led us, and these documents are available to download from our website. They are rather technical in nature, and so we have also produced this 'Impact Report' which describes our research in more understandable lay terms, and this too can be accessed through our website.

## Breast Density

Our research focuses on breast density. Breast density has turned out to be a strong risk factor for breast cancer. Density is measured as the proportion of gland (tissue that makes milk) to fat within the breast, and this varies greatly from one individual to another. Women with denser breasts at breast screening age have a higher risk of breast cancer – in fact, women with more than 75% dense breasts have a five times stronger risk of developing breast cancer. Two factors influence breast density – environmental and genetic factors. Some researchers consider breast density to be second only to genetic predisposition in terms of breast cancer risk. It may not be that the density directly leads to breast cancer, but rather that the increased density reflects damaging changes occurring within the breast from other things which are harmful to the breast. An added dimension to the problem is that breast screening and mammography is much less accurate in dense breast tissue, when of course these are the very women at higher risk of breast cancer who need the most accurate scanning tools.

## Tomosynthesis

3D Mammography (Tomosynthesis) is an exciting new technology which allows us to see the breast tissue in three dimensions. It has come about as a result of the development of digital mammography, similar to digital photography used in modern cameras and phones. This has opened up new ways of computer processing of the images. In tomosynthesis, several low dose x-rays are taken of the breast at slightly different angles, and these are then formed into a 3-dimensional image consisting of a stack of thin slices. Traditional mammograms can be difficult to interpret in dense breast tissue, and cancers can be difficult or impossible to see. These problems are more marked in younger women who have relatively more dense glandular tissue in their breasts. One of our main goals is to detect breast cancers when they are very small, as that gives the woman the best chance of a good long term outcome. We have been sponsoring a study that uses tomosynthesis for screening women in their forties who are at increased risk of breast cancer. These are generally women who have one or more close relatives who have developed the disease, usually at an early age, and who are being screened through a family history clinic with yearly mammograms. Our study is designed to see whether the use of tomosynthesis in addition to standard mammography reduces the 'false alarm' rate, and whether it allows us to pick up cancers at an earlier stage. The study is being conducted initially at two sites (The Nightingale Centre and Genesis Prevention Centre in Manchester and King's College Hospital in London).

## SNPs

We are also researching the genetic factors that might lead to breast density. SNPs are small variations in DNA some of which can increase the risk of breast cancer, and it looks as if a proportion of those SNPs are linked to increased levels of breast density. We have identified a group of women with high breast density who have now had DNA samples taken for 'exome sequencing'. This will allow us to look for genetic variants that contribute to high breast density in these women who are at most risk of developing breast cancer.

## Outcomes

A very practical reason for our interest in breast density is that it could allow us to reach one of our very specific goals; namely to allow early PREDICTION of who is at risk of breast cancer. By combining a gene test to search for high risk genes and for lower risk SNPs, together with a study of an individual's mammographic breast density, and perhaps an analysis of certain lifestyle factors, it may be possible to predict women at high risk, and equally, women who are at a very low risk of breast cancer. Mammographic screening could be tailored to an individual, therefore increasing the efficacy. This means that some women may need to be screened less often as they have a lower risk of breast cancer and some women may need to be screened more often due to a higher risk, perhaps with 3D techniques or other scans. This tailored screening could increase the detection rate in the early stages of cancer for those at higher risk, leading to a better outcome for the patient.

Another practical outcome of our research into breast density could be in developing drugs that reduce breast density and hence reduce breast cancer risk. A good example is the drug Tamoxifen, which seems to do both in some individuals. One current study is trying to predict whether the risk-reducing effect of Tamoxifen is working in a particular individual by assessing the degree of lowered breast density at one year of treatment. This simple technique could help us evaluate other potential risk-lowering drugs in the future. And not just drugs – it could help evaluate the effect of diet and lifestyle interventions, another key element of Genesis funded research.

As you can see, this depth and breadth of research into breast density supported by Genesis funding represents a really exciting time for Genesis. An understanding of breast density provides an opportunity for prediction, early diagnosis and even prevention of breast cancer. It will remain the focus of much of our collaborative work in the year ahead, for which we need your continuing support.



# Who we are

## Our vision

“To create a breast cancer free future for the next generation through preventative testing, screening, lifestyle changes and drugs where needed.”

## Your support

“We receive no statutory or government funding so are here today thanks to your generosity.”

Genesis Breast Cancer Prevention leads ground-breaking research into the prediction and prevention of breast cancer. Our research will one day bring about a world where breast cancer is preventable and thousands of lives are saved from ever experiencing this terrible disease.

Our home is The Nightingale and Genesis Prevention Centre, a £14million state of the art research and screening centre, based at University Hospital South Manchester (UHSM). Much of our work is conducted here and in partnership with several other research facilities in the UK.

Our research is carried out and overseen by several prominent individuals in the breast cancer field, including:

- Prof Tony Howell
- Prof Gareth Evans
- Dr Michelle Harvie
- Dr Anthony Maxwell
- Prof Nigel Bundred

Between them they have carried out various research studies that are contributing to international recommendations for breast cancer prevention as well as continuing to identify key factors in predicting breast cancer.

The Genesis Prevention Centre is a world class facility leading the way in breast cancer early diagnosis and prevention research. Genesis collaborates nationally and internationally with the very best experts in the field.

In the past year we have recruited over 4,000 women on our studies and have given them the opportunity to find out more about their own risk as well as how their involvement could help so many women in the future.

Established in 1996 Genesis is governed by a board of 9 Trustees who bring with them a wealth of knowledge in many areas of cancer research, finance and 3rd sector management. Day to day, the charity is run by a team of 10 dedicated and enthusiastic staff members who are supported by a fantastic team of 65 volunteers. Without these individuals, we would not be able to raise the funds and administer the necessary grants that go towards the vital breast cancer research that our researchers carry out.

Genesis receives no statutory or government funding and therefore relies on the generous donations of our supporters to carry out our essential research.

Thank you to all who have supported us and to those who will continue to do so in the future.



Genesis Breast Cancer Prevention supports those affected by breast cancer through essential research that will one day create a breast cancer free future for all. Our work relies on the cooperation of patients and high-risk individuals who understand that by providing information about their lives now, they can save the lives of others in the future.

Our 4 research pillars are Gene Research, Early Detection and Screening, Preventative Drugs and Diet and Lifestyle and they all rely on participation from our patients. Whether it be filling in a questionnaire to providing a saliva sample, the involvement of these women means that Genesis' research can continue.

Our highly qualified researchers provide all participants with the vital information relating to their study as well as a listening ear whenever a patient has any questions as we carry out our studies. We would not be able to help as many people as we do without the commitment of our researchers and for this we are truly grateful.

#### About Breast Cancer

Breast cancer is the most common cancer in the UK; it accounts for 15% of all cancer diagnoses. Across the UK, 130 individuals are diagnosed with breast cancer every day; tragically 32 of them will lose their fight against the disease. If trends continue, we can expect a 12% increase in diagnoses in just 10 years' time.

There is no one single cause of breast cancer; rather it appears to be several different factors working together:

- Genes
- Lifestyle
- Environment

The combination of all three factors can 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 the disease, Genesis Breast Cancer Prevention's vision is to make breast cancer a preventable disease for the next generation.

## We Research

Our main purpose is to fund research into the prediction, early detection and prevention of breast cancer. Our research provides patients with the opportunity to be part of a future free of breast cancer. Our years of experience, along with working with innovative and exceptional individuals, means we are continuing to take vital steps towards preventing the disease.

## We Educate

Our information on risk factors, and ways to reduce them, can all be found online, in our leaflets and from our team over the phone or in person. We also work closely with the Asian community to raise awareness and provide support to those affected by the disease.

## We Communicate

Here at Genesis we feel that every woman should be aware of the risks that contribute to a breast cancer diagnosis and also the support that is available to them if they are worried about their personal risk. Our centre is home to the UK's largest family history clinic and we work closely with them to ensure all our patients know what research trials and information are available to them.

# Research overview

Research is essential, and research into prevention even more so. How can we protect future generations from ever experiencing this dreadful disease if we do not invest in the research that could prevent it developing at all?

Awareness raising is also a key area of importance to us. It's no use having a genetic test available to women with a high risk of developing the disease if an individual isn't aware that they may carry a mutated gene.

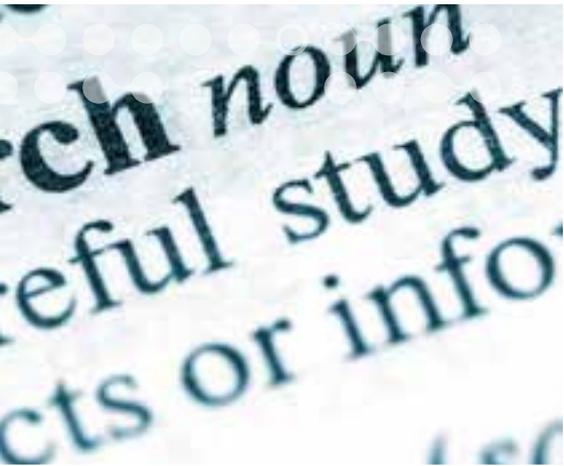
Likewise, our research into diet and lifestyle aims to increase an individual's knowledge of their own weight and fitness levels and how these can be improved to lower one's risk of developing breast cancer and many other diseases associated with a poor diet and unhealthy lifestyle.

Gene Research	Early Detection & Screening	Preventative Drugs	Diet and Lifestyle
 <p>Examining how changes and mutations in genes can affect someone's risk of developing breast cancer.</p>	 <p>Identifying new &amp; unique screening methods to ensure early &amp; accurate diagnoses.</p>	 <p>Investigating drugs that can be used as a preventative measure to reduce an individual's risk of developing breast cancer.</p>	 <p>Research into lifestyle factors that contribute to risk and how diet and exercise can reduce this.</p>

## Research Achievements in the last year

- Over 56,044 women have been recruited to The PROCAS Study and Genesis has agreed to continue to fund recruitment to the study until April 2015.
- Genesis has funded a new three year study, FH Tomo which will use Digital Breast Tomosynthesis (DBT) on younger high risk women. This study will also be undertaken at Kings College Hospital, London.
- Publication of The 2-Day Diet, Cookbook and Quick & Easy edition continues to increase awareness of our vital work and send a positive health message across the UK and the world. To date over 290,000 copies have sold in the UK and the diet has been published in over 16 countries.
- Proceeds from The 2-Day Diet have enabled Genesis to fund a new dietician and a dietetic assistant to support Dr Michelle Harvie's research.
- Scientific Director, Professor Tony Howell and a Genesis case study appeared on Newsnight to discuss Angelina Jolie's risk reducing surgery and the prevention of breast cancer, helping to raise awareness of an inherited risk of breast cancer.
- We have demonstrated that hormone altering tablets such as Tamoxifen, Raloxifene and Aromatase inhibitors are effective in lowering breast cancer risk in selected women, a policy now adopted in NICE guidelines.
- Our research paper on the "Angelina Effect" on relevant referrals for genetic testing was one of the most accessed journals of the year and appeared in countless media stories.

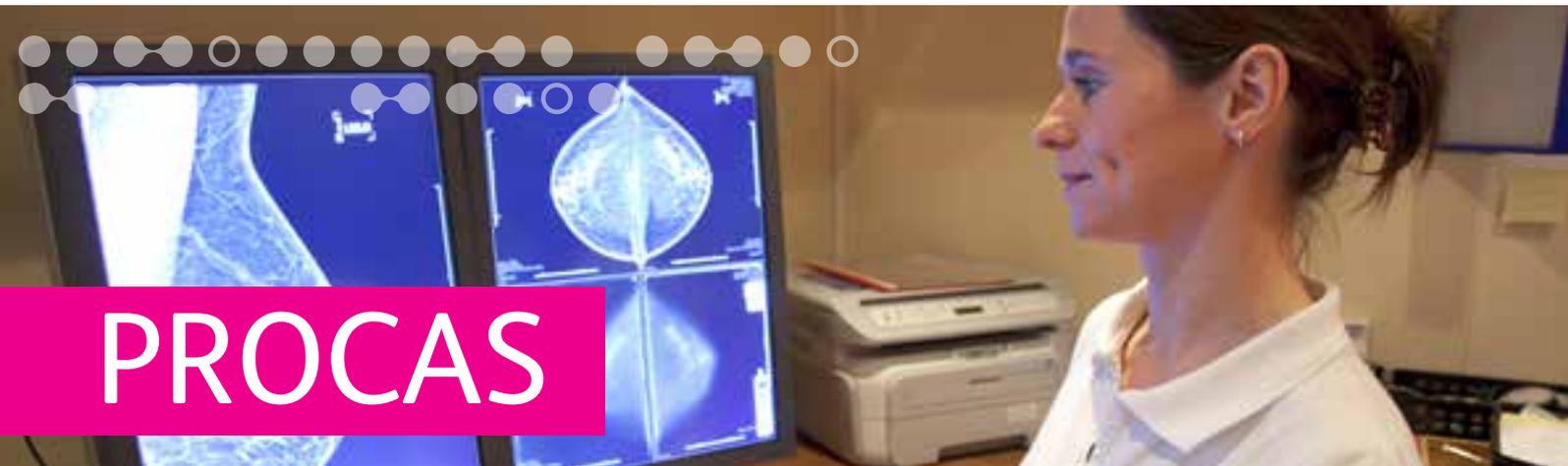




“Only 3.6% of all cancer research funding is spent on prevention”.



All of our research is dependent on participation from patients who attend The Nightingale and Genesis Prevention Centre. Without their willingness to join us in our aims to predict and prevent breast cancer, we would not be where we are today. From everyone here at Genesis, thank you to all those who have joined us in our studies and who will be joining us in the future.



Genesis are pleased to include PROCAS as one of our research projects. This study could one day see the NHS Breast Screening Programme changing to include these vital tests that will produce a tailored and personal experience for every woman.

I believe PROCAS is an essential study to prevent breast cancer. It was so easy to take part. For my friends and I, as we reach breast screening age, we are more and more aware of the risk of developing breast cancer. Knowing you are at low risk is reassuring. Knowing you are at high risk means you can try to reduce your chance of developing this devastating disease. We all have people in our lives who have sadly developed breast cancer; this study will prevent future women from having to go through the trauma of treatment and save many women's lives.

**Linda, PROCAS Participant**

#### What is PROCAS?

The PROCAS (Predicting Risk Of breast Cancer At Screening) study aims to provide women who attend the NHS Breast Screening Programme (NHS BSP) a risk score that predicts the chances of them developing breast cancer in the next 10 years.

#### How long has it been running?

The study started in 2010 at The Nightingale and Genesis Prevention Centre and will continue to recruit patients until April 2015 thanks to additional funding from Genesis Breast Cancer Prevention.

#### The study so far

Presently, only women referred to a Family History Clinic or a Genetic Clinic (through self-referral) have access to information about their risk of breast cancer. Although family history plays a large part in determining breast cancer risk, there are other risk factors which contribute to risk such as lifestyle and environmental factors. Awareness raising of these risk factors is required to ensure no-one misses key information about their own personal risk.

Since 2010, The Nightingale and Genesis Prevention Centre have been running the PROCAS Study. This study aims to predict breast cancer risk for women who attend the routine NHS BSP in Greater Manchester. We also aim to evaluate the feasibility of introducing personalised breast cancer risk estimation into the NHS Breast Screening Programme (accessed by 70% of women aged 47-70 years).

PROCAS works by collecting information from participating women through a questionnaire, a mammogram and in 18% of cases, a DNA sample. Breast cancer is caused by the interplay of genes, lifestyle and environmental factors. For these reasons, the PROCAS questionnaire, given to every woman taking part, poses questions regarding: Age; Weight; Height; Age at first period; Age at first pregnancy; Age at menopause; Family history (mother, sisters, aunts); Exercise; Alcohol intake and Ethnicity.

All these factors are fed into a risk assessment tool and a risk score is produced. This, combined with the analysis of a woman's mammogram, predicts a woman's chances of developing breast cancer in the next 10 years.

A standard mammogram is taken to check for any signs of breast cancer. Breast density is a key part of this study and this is best analysed from the mammograms produced. Higher breast density increases a woman's chances of developing breast cancer.

The 10,000 DNA samples being analysed will look at SNPs (small gene fragments) which are associated with increased breast cancer risk. These results will be combined with the questionnaire and mammogram to give 10,000 women a more accurate result. The increased accuracy of this result, and the cost involved in obtaining it will be evaluated to see if it is a feasible addition to the NHS Breast Screening Programme.

#### Next steps

The next critical stage of the PROCAS study is informing all the participants of their risk score (a study we are funding in 2014/15). All women deemed high risk have been invited to an appointment with one of the key Professors on the study (Prof Tony Howell or Prof Gareth Evans). At these appointments the professor and patient will discuss various preventative measures – increased screening frequency, preventative drugs, diet and lifestyle interventions or preventative surgery.



# RNA Study

4-5 % of all breast cancer cases are due to the inheritance of high risk gene faults, especially in the BRCA1 and BRCA2 genes. These are the most common high risk genes for breast cancer identified thus far as they account for the vast majority of cases where breast and ovarian cancer occur in the same family.

### The Project

The RNA Study will analyse different sections of the breast cell which are not currently investigated for BRCA1 and BRCA2 mutations. BRCA1 & 2 mutations can be found in the exons of a cell. If no mutation is found there, mutations must be looked at in the introns of the gene. Genes are divided into sections called exons and introns.

### Exons

Exons are like the chapters of a book. BRCA1 has 24 chapters (exons) and BRCA2 has 27 chapters. Current genetic tests are like looking at the print of this book.

#### These tests look for -

- Spelling mistakes in the genetic code of the chapters.
- Mistakes in the immediate code at either end of a chapter (in a book this would be the 1-2 pages containing the headings for new chapters).
- Whole chapters that have been deleted from the book.

### Introns

We know from other genes that 2-5 % of genetic faults occur in the binder of the book. These binder areas are called introns and are usually vastly bigger than the exons. It is not feasible to look at introns on most genes.

### RNA Analysis

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 but has proved successful in other research studies.

Our Family History Clinic has the largest recorded collection of families with BRCA1/2 mutations in the UK. This means we have access to RNA samples on 33 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.

Between 10-15 % of families (men and women) who are predicted to carry the BRCA1/2 mutation due to their very high risk with either breast and ovarian cancer (male or female), actually do not carry any mutation. These are the families who will be helping us with this study by allowing us to investigate other parts of their breast cells.

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 contributing mutation.

### Methodology

33 blood samples will be analysed to check for any mutations in their RNA. In order to check for these mutations, cell lines (duplicates of the blood cells) will be created to ensure there is an infinite number of samples available from each individual. From this, the RNA in each cell is transformed into cDNA (complementary DNA) which then allows the DNA software to analyse it for mutations.

By looking at different parts of the gene, and hopefully finding mutations here, individuals can take the necessary steps to prevent a diagnosis of breast cancer which would have otherwise occurred without discovering these mutations.

### Research Aims

- To identify BRCA1/2 mutations unrecognised in usual techniques as contributing in breast or ovarian cancer.
- To undertake gene identification by exome sequencing.

RNA testing is essential as it will determine whether deep intronic mutations in BRCA1/2 are responsible for causing breast cancer in these high risk families. If not sequencing of the whole genome can be performed to try and identify new high risk breast cancer genes.

**Helen Byers, Research Assistant**



# SNPs

## SNPs (Single Nucleotide Polymorphisms)

Breast density is a strong risk factor for breast cancer. The density of breast tissue can be calculated using a standard mammogram. Density is measured as the proportion of gland (tissue that makes milk) to fat. Women with denser breasts at breast screening age have a five times higher risk of developing breast cancer.

Two factors influence breast density – hormonal and genetic factors. If we can understand the genetic basis (the SNPs) of breast density, it will help identify those women at high risk of breast cancer and develop new strategies to reduce their risk and prevent the disease through more frequent screening, preventative drugs or diet and lifestyle interventions.

We have access to samples from 10,000 women who have undergone mammography as part of the National Breast Screening Programme and 1500 women with a family history of breast cancer. Women who are part of the SNPs study have come to us through the PROCAS study (Predicting the Risk of Cancer At Screening).

We studied these samples as well as mammograms in order to determine their breast density. Further more, we undertook whole exome sequencing in individuals with very high mammographic density (>90%) to identify rare variants that cause high mammographic density.

### The Experiments

- **Find common SNPs with small effects:** Seventeen SNPs known to increase breast cancer risk were sequenced for women who agreed to give a DNA sample. These have been linked to breast tissue density in some other studies and we wanted to look for the same links in these women. We have completed the statistical analysis of these breast cancer SNPs and association with breast tissue density in the first 5,000 women recruited and found some positive results. We have found one SNP thought to be associated with breast density. This has now been written as a paper and submitted to the American Journal of Breast Cancer Research.
- **Find common SNPs with small effects:** The sequencing of more SNPs (involved in breast development) to see whether they have any links with breast density is complete. 30 SNPs in 1,700 women were genotyped. The statistical analysis of whether these SNPs are linked to breast density showed no links.

- **Find rare SNPs with larger effects:** For the next part of the project we wanted to find rare SNPs with larger effects. We identified 10 women with the highest breast density in the whole PROCAS study (50,000 women) and obtained consent to take a blood sample. These 10 blood samples have been subjected to exome sequencing, a technique to sequence specific parts of the genome. This will allow us to see whether there are any very rare genetic variants that contribute to an extremely high breast density in these women who are at most risk of developing breast cancer. Each had around 15,000 SNPs, and shared around 10,000. The exome sequencing is complete, and the statistical analysis of the results is showing some positive results around genes linked to extracellular matrix (a supportive structure for cells) and genes known to regulate contraction and tension in the cells.
- **Analyse the “gene signature” of the breast tissue:** In order to understand which genes are turned on or off, or turned on to a different degree, in tissues of different

densities, it is vital to look at breast tissue samples. PROCAS does not have the approval to do this, so we have entered in to collaboration with Prof. Charles Streuli at the University of Manchester, who, in partnership with the Biobank, has collected around 30 breast tissue samples from patients undergoing cancer surgery or elective mastectomy. Work is currently underway to process these samples and compare the “gene signatures” (the genes turned on and off) of the different tissues to assess whether the genes are turned on or off in different patterns in tissues of different density. Unfortunately, this is proving difficult as many of the samples are of a poor quality.

- **Further SNP Research:** We have found one breast cancer susceptibility gene which is associated with mammographic density. It has a role in DNA repair and dysfunction can lead to cancer. We need to prove this is in the breast cell. We also need to show how this changes density.



9,800 women aged 49 and below are diagnosed with breast cancer every year (19.8% of all diagnoses). Diagnoses in these young women are often extremely difficult as their breast tissue is still quite dense and therefore conventional mammograms can often miss key indicators or misinterpret some images which can result in further tests and added anxiety.

Traditional mammograms can be difficult to interpret because normal breast tissue can overlap other normal breast tissue, and this can cause appearances that look like a cancer. This usually results in the need for further tests. Also, normal breast tissue can obscure cancers and make them difficult or impossible to see. These problems are more marked in younger women who have relatively more dense glandular tissue in their breasts.

### The Solution

Tomosynthesis is an exciting new technology which allows us to see breast tissue in three dimensions. It has come about as a result of the development of digital mammography, similar to digital photography used in modern cameras and phones. This has opened up new ways of computer processing of the images. In tomosynthesis, several low dose x-rays are taken of the breast at slightly different angles, and these are then formed into a 3-dimensional image consisting of a stack of thin slices.

Conventional mammography takes a 2D image that may not detect cancer, which can go undiagnosed, or if the image is not very clear, will require the patient to come back for further testing, causing undue stress and anxiety.

The lead applicant for this research project is Dr Anthony James Maxwell, who brings with him a wealth of knowledge and experience and is the ideal candidate to be leading this revolutionary research. His thirteen years as a Consultant Radiologist at Royal Bolton Hospital followed by his current role as Consultant Breast Radiologist and Honorary Senior Lecturer in Imaging at University Hospital of South Manchester have allowed him to be actively involved in how mammograms are conducted and how the information they gather can be improved.

### Methodology

There will be two groups of women followed over two years. The first group will receive DBT and a conventional mammogram at their first appointment and just a conventional mammogram at their second appointment. For the second group they will receive a conventional mammogram at their first appointment and then DBT and another conventional mammogram at the second appointment. This will allow the team to assess the number of women who are called back after their first appointment dependent on the form of screening they received. A reduction in the number who are called back due to the higher accuracy of DBT will mean that this method can be rolled out into routine clinical practice. This study is a great example of how better screening can improve the prognosis for many women and Genesis are very excited about the upcoming results.

The team have considered the implications around the increased levels of radiation that this group of women will receive and due to the low levels of both a standard mammogram and DBT in the first instance, feel that there is no additional risk to any individual. Having both screenings done in one appointment still falls under the national dose reference limit and therefore should not endanger any of the patients.



# Tam-Prev

Tamoxifen is a drug used for preventing recurrence of breast cancer. When given for five years to women at increased risk of breast cancer it can prevent around 40% of breast cancers. Tamoxifen is readily available in the USA, but is still not being regularly prescribed in the UK.

The TamPrev study was designed to assess the number of women in the Genesis Family History Clinic who wished to take Tamoxifen to prevent breast cancer and to assess the women likely to benefit from treatment. Of 1279 eligible women approached we found that 136 (10.6%) wished to take Tamoxifen in order to prevent breast cancer. We were able to confirm that approximately half of the women had a marked reduction in the density (whiteness) of the breast indicating responsiveness to Tamoxifen. Importantly we were also able to demonstrate that automatic measures of density showed reduction and may be the method of choice in the future to let women know that Tamoxifen is working.\*

**Professor Anthony Howell,**  
Research Director at Genesis  
Breast Cancer Prevention

### The Study

Tam-Prev was a three-year study aiming to recruit 130-150 premenopausal women aged 33-46 years at moderate or high risk of breast cancer who attend the Family History Clinic at The Nightingale and Genesis Prevention Centre. We were able to determine uptake to Tamoxifen for the prevention of breast cancer amongst pre-menopausal women at increased risk in our Family History Clinic and found that this varied according to women's ages and breast cancer risk. In addition, through in-depth interviews, we identified the motivations and barriers to taking Tamoxifen for prevention.

### Our findings

It is widely known that very few women choose to take Tamoxifen for the prevention of breast cancer, despite the fact that its efficacy is well known and accepted; there has been very little in-depth research to fully explore the reasons for low uptake to Tamoxifen for prevention. As part of the TAM-prev study, semi-structured interviews were carried out with women who chose to take Tamoxifen and women who chose not to take Tamoxifen. By completing these interviews with both groups of women, four key themes fundamental to their decision to take Tamoxifen were identified: perceived impact of side effects; the impact of others' experience on beliefs about Tamoxifen; Tamoxifen as a 'cancer drug'; and Tamoxifen as a daily reminder of cancer risk. These results are important because they help us to understand women's feelings and beliefs about taking drugs for prevention which in turn will help us to improve our clinical care of women at increased risk of breast cancer.

### NICE Guidelines

In July 2013 NICE recommended that Tamoxifen and Raloxifene be offered to pre and post-menopausal women respectively, who are at increased risk of breast cancer. Although NICE made these recommendations, Tamoxifen and Raloxifene are not commonly prescribed for prevention. This research is important because it has enabled us to better understand women's motivations for, and barriers to, taking Tamoxifen for prevention. This in turn will help healthcare professionals when they are discussing preventive drugs with patients.

### Decision Aid

As part of the study we developed a Decision Aid to help women decide whether or not to take Tamoxifen for prevention. During our interviews with participants, we asked them for feedback on the Decision Aid and revised it in line with these suggestions. This enabled us to improve our patient literature and gain a better insight into how best to communicate information about drug prevention to this group of patients. We have now developed Decision Aids (for both Tamoxifen and Raloxifene) for general use within our Family History Clinic and other Family History Clinics regionally.

### Next Steps

Once we have completed further research, we will be able to identify the biomarkers that are indicative of Tamoxifen effectiveness. We plan to run a similar trial with Raloxifene; so this study was the first step towards our longer term aim of being able to predict those who are likely to benefit from Tamoxifen or Raloxifene and target prevention these women. This would mean that those unlikely to benefit would not be taking the drugs long term and so avoid unnecessary side effects. This in turn would make drug prevention of breast cancer a more cost effective option for the NHS.



# The 2-Day Diet

At Genesis, we fund Dr. Michelle Harvie, the UK's only dietitian looking at the link between diet and breast cancer prevention. Our researchers have developed a novel effective 2-Day Diet for weight loss which involves 2 days of low carb, low calorie diet and 5 days of a healthy Mediterranean diet.

Our clinical trials have found The 2-Day Diet is better than daily diets for weight loss and for lowering levels of the hormone insulin which promotes cancer. Information about the 2-Day Diet and our research has been published in the book "The 2-Day Diet". Our research suggests that women could achieve and maintain weight loss and therefore reductions in breast cancer risk simply by changing to this healthier diet and lifestyle plan

We are running several projects related to diet, lifestyle, and their influence in reducing breast cancer risk. These are:

- **Intermittent Diet (2-Day Diet) Research**
  - How effective is The 2-Day Diet vs a daily calorie controlled diet for weight loss?
  - What is the effect of The 2-Day Diet on genes within the breast cells of high risk women?
  - Can the 2-Day Diet help to diminish harmful fat stores in the liver and pancreas?
- **PROCAS Lifestyle Study**
  - Can we engage women in the NHS breast screening programme with a web based diet and exercise weight loss programme?
- **B-AHEAD-2 - Breast - Activity and Healthy Eating After Diagnosis**
  - During chemotherapy how effective is the 2-day diet vs a daily calorie controlled diet for breast cancer patients receiving chemotherapy?

## Let's take a closer look at the PROCAS Lifestyle Study

Genesis researchers have estimated risk of breast cancer for 55,000 women in the breast screening programme in the PROCAS study. Around one percent of women are at high risk (30% or greater lifetime risk), nine percent

are at moderately increased risk (between 20 and 30% lifetime risk) seventy percent are at average risk (between 4 and 20% lifetime risk) and 20% below average risk (lifetime risk less than 4%). PROCAS lifestyle is a follow up study to testing the following research questions:

- Can we engage overweight women from all of these risk categories to a diet and exercise weight loss programme?
- Does level of breast cancer risk influence uptake and adherence to the programme?
- Do women in the breast screening programme have increased risks and/or concerns about their risk of other cancers, diabetes, heart disease, stroke and dementia?
- Can we support weight loss with our novel web based 2-Day Diet and exercise weight loss programme?

## Background

Currently 65% of women in the UK are overweight and 25% of these are obese. Losing five percent of your weight or more and keeping it off can reduce your risk of developing breast cancer by 25 - 40%. This weight loss will halve your risk of diabetes and reduce your chance of stroke and heart disease by 30%.

The problems of obesity and unhealthy lifestyle and the cost to the NHS has had much media coverage, and has been highlighted as a priority by the government. However, the NHS has few effective services to tackle these trends in obesity and unhealthy lifestyle, and there is a need for new approaches.

We are testing whether we can target women in the NHS Breast Screening Programme (NHSBSP) with lifestyle prevention of breast cancer and other diseases. Changing people's behaviour can be difficult to achieve and costly for the NHS.

We have shown that telephone support seems useful and potentially very cost effective. We now wish to see whether a web based programme which gives feedback to women can support women to achieve weight loss and behaviour change.

## Current Situation

Our expert recently estimated that we could prevent 30% of breast cancer cases through lifestyle changes:

- Weight control
- Increasing activity
- Reduced alcohol intake

The NHSBSP service reaches approximately 70% of women in the UK aged 47 to 73 years. The NHSBSP allows early diagnosis and improved breast cancer survival but does not currently tackle breast cancer prevention.

## What happens on the study?

This study, led by Dr Harvie, will involve 120 overweight women from the breast screening programme who will receive their personal disease risk for breast cancer, heart disease, stroke and diabetes and dementia, three months of personalised phone, mail and web supported PROCAS lifestyle programme followed by three months of web support.

## The Future

The data from this study is essential to support a future large scale clinical trial which will test the effectiveness, health care costs, and potential reduction in risk of breast cancer and other diseases of this tailored lifestyle programme. This proposal has the support of Diabetes UK and the British Heart Foundation. We believe this project supports our vision of preventing breast cancer for future generations.

# Did you know?

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 in the UK 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 women each year do not survive.

In the last 40 years, there has been a 44% increase in diagnoses.

The UK incidence rate is the sixth highest in Europe.

If we could stop breast cancer tomorrow, by 2024, 534,218 women would never suffer from the disease.

Our volunteers donate around 3,500 hours of time every year.

The 2-Day Diet book raised over 20% of our income for 2013/14.

Currently only 3.6% 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 for it saves the labour of being sick.”



# Fundraising highlights

As always we must thank our wonderful supporters in the community, companies, colleges, schools and sports clubs who have helped to raise such substantial sums in 2013/2014. There have been so many fantastic fundraising efforts and achievements – from our annual ball, to numerous corporate and community events. The commitment from our supporters and volunteers continues to amaze us all and we would like to take this opportunity to thank each and every single one of you. Below are some key highlights.

## Individuals and Communities

Many of our supporters fundraise for Genesis because they have been directly affected by breast cancer and believe in our vision of a breast cancer free future for the next generation. It is impossible to thank each and every one of them, but below we have highlighted key individuals and groups who have really made a difference in 2013 and 2014.

- Family and friends of late supporter, Tracy Thornley, held a thrilling firewalk and raised £12,500 in Tracy's memory.
- We thank Claire Whittaker who, with the help of Mary Wilson, organised a beautiful Bluebell Walk in ancient woodlands near Hungerford, raising around £3000. Claire also organised another wonderful ball for her family and friends. Since December 2012, Claire has helped to raise over £25,000.
- The spectacular musical show 'Showcase' chose Genesis to be their charity of the year in 2014 and raised an amazing £5,000.
- Sue and Tony Showman organised a bonfire fundraising party and raised over £7,000.
- Sam Morris held her fifth annual 'Pink & Sparkle Ladies Night'. An amazing £1,852 was raised for Genesis at this sell out event.
- Well done to Marion Meakin who arranged an evening jam-packed with amazing entertainment at the Parrswood Pub in Didsbury and raised over £2,700.
- Supporter Bernie O'Brien held a wonderful ladies night at the Vao Restaurant in Sale, raising £3,000.
- After selecting Genesis to be their Charity of the Year, Bramhall Golf Club Lady Captain Robi Burling has held a number of fundraising events and raised over £5,000.

- Lady Grey, Roz Mahon and friends have raised over £23,000 for Genesis through their annual bridge drive.
- The Didsbury Village WI also chose Genesis to be their charity of the year and raised a fantastic £1,782.
- We would also like to thank the following individuals:-  
Annie, Rosie and David McNamara, Betty and Peter Byrne, Clare Stuart, Di and Kevin Boyer, Di Collins, Diana Harris, Emma Neville and family, Emma Sabin & family, Janine Kay, Linda Kelly, Melanie Yeomans, Merv Valentine, Paul Wolfgang Webster, Peter Richardson, Ralph Manners Wood, Sally Harrison QC, Sandra Frais, Sue and Tony Showman, Tracy Capal, Wendy Verber.

## Companies working with Genesis

We are extremely fortunate to have so many dedicated and active corporate supporters. Organisations across the UK play a crucial role in fundraising and raising awareness of our cause.

Throughout 2013 and 2014 staff from a wide range of companies united to fundraise. Activities ranged from sponsoring our Christmas Concert, competing in teams in the Great Manchester Run, holding cake sales and even painting company lorries pink! We would particularly like to thank the following organisations:-

52 Alderley Road, Barclays Bank, Beaverbrook The Jewellers, BOC, Britannia Bradshaw Removals, Bupa, CHEP, Clarke Nicklin Chartered Accountants, Croma Restaurant, Gorvins Solicitors, Innov8 Development Solutions, Jon Richard, Manchester Airport, Omnium Resource Management, Roberts Bakery, Royal Bank of Scotland, RRG Group, Siemens, Southbeach Swimwear, St John's Street Buildings, Suttons & Robertson, The Association of Manchester Electrical Traders, The Confederation of Passenger Transport, The Talbot Validus Group, UK Healthcare, Ward Hadaway LLP.



### The Genesis Million Miles Challenge

Our Million Miles Challenge encourages you to raise money through sporting challenges. So far the challenge has raised over £350,000 and we would like 2015 to be a year packed with events to get the heart pumping!

2013 and 2014 saw many of you get involved in a variety of ways from golf events to mammoth walks, gruelling bike challenges to marathons, epic treks along the Great Wall of China to terrifying skydives - no task was too small! We would particularly like to thank the following people:-

- A huge well done to Manchester Grammar School pupil, Ben Sciama who organised and hosted MGS Genesis Golf Day in September raising £31,000
- The Milk Maid Marchers from Sandbach, Cheshire walked 34 miles along the Sandstone Trail in May 2014. The ladies also hosted family fun nights, coffee mornings, a donation in lieu of fortieth birthday presents and a charity luncheon, raising a grand total of £2,800 over the year.
- Sally Harrison and nine friends cycled three mountains in the French Alps over three consecutive days and raised over £5,000.
- Stuart Dale completed an epic Great Wall of China trek in memory of Tracy Thornley, who was not only a valued colleague and dear friend to Stuart, but also a dedicated supporter of Genesis. Through a fantastic fundraising effort he raised £3,145, more than trebling his original target figure.
- We would like to thank Iain Kelly who completed a series of fundraising events for Genesis throughout 2014 including a charity race night and a 100 day alcohol ban! Iain chose to support Genesis with his good friend Emma Sabin who has experienced breast cancer. Their fundraising reached a whopping £7,500.
- Dawn Comber, her husband Ian and their nine year old son, Michael took on the mammoth task of a 180 kilometre walk across the Alps and have raised over £2,000
- Over 150 supporters took part in the Genesis Peaks Cycle Challenge, completing 11, 35 or 49 miles by bike and together raising over £5,000.
- In May 2014, Martyn Hague embarked on an epic year of fundraising and has completed the Great Manchester Run, cycled 500 miles from Barcelona to Nice, travelled by zip wire and much more and to date has raised over £6,500.

### The Genesis Student Challenge

Amazing things happen when students work together! Young people from schools, colleges and universities across the region have played an important role in fundraising for Genesis for a number of years now and we have seen thousands of pounds being raised in so many inventive and imaginative ways.

We are so proud of everyone who participated in the Student Challenge in 2014 - the results have been truly remarkable, thanks must go to:-

Manchester Enterprise Academy, Hulme Hall Grammar School, Altrincham Grammar for Boys, Cheadle & Marple Sixth Form College, Manchester High School for Girls, Altrincham Grammar School for Girls and Burnage Media Arts College.

### The 2-Day Diet

Following its publication in February 2013, we have been delighted with the success of Dr Michelle Harvie and Professor Anthony Howell's The 2-Day Diet.

Since the publication of the original book, a Cookbook and a Quick and Easy Edition of the original diet are now on sale. All three books bring together our latest intermittent diet research, which has been shown to be more effective and easier to follow than a standard daily diet.

Published by Vermillion, part of the Random House Group, all author proceeds from The 2-Day Diet are donated to Genesis. Over the course of this financial year the book has been published in over 16 countries including South Korea, Brazil, Taiwan, the USA and across Europe.

The success of The 2-Day Diet clearly shows the international impact of the work carried out by our amazing research team and the book helps to promote a very important public health message to a much wider audience. Since January 2013 the books have raised over £210,000.

### Crime to Kind

This exciting collaboration between Greater Manchester Police, G4S and Genesis involved operating two car parks in Salford Quays on land owned by Transloyd and Ask Developments. The car parks, which were previously run illegally, are open on Manchester United match days and provide secure parking to football fans. Over £71,000 has been raised from this initiative since it started in August 2012.

### The Genesis Annual Ball

The success of our annual ball continues to grow and each year our guests have been wowed by our unique and exciting themes. In 2013 the Genesis Skyball invited guests to enjoy dinner beneath Concorde whilst enjoying a celebrity cabaret. In 2014 The Genesis Wonderland Ball transported guests into a magical land inspired by the Mad Hatter's Tea Party and Charlie and the Chocolate Factory. Since 2011 our annual balls have raised over £200,000.

### Volunteering Highlights

Volunteers have always contributed to the success of the charity and they continue to play a vital role in our success. Our volunteers run both the Coffee Bar and Welcome Desk in The Nightingale and Genesis Prevention Centre, providing an essential service to patients and staff. Whilst our gardening volunteers ensure that the internal courtyards and outdoor spaces look welcoming and tidy.

The economic value of our 69 volunteers, as suggested by [www.volunteernorthwest.co.uk](http://www.volunteernorthwest.co.uk), is currently £62,394 per annum. This figure includes the volunteers based at the centre, along with those volunteers who regularly help out at bucket collections, stalls and fundraising events. In fact, the value of our volunteers is immeasurable.

Our volunteers have also held tea parties, attended ladies lunches, donated prizes for raffles and tombolas, supported million miles events, helped with the Student Challenge, organised and helped to run the first Genesis Craft Fair, and run fundraising events in the local area.





### Trusts

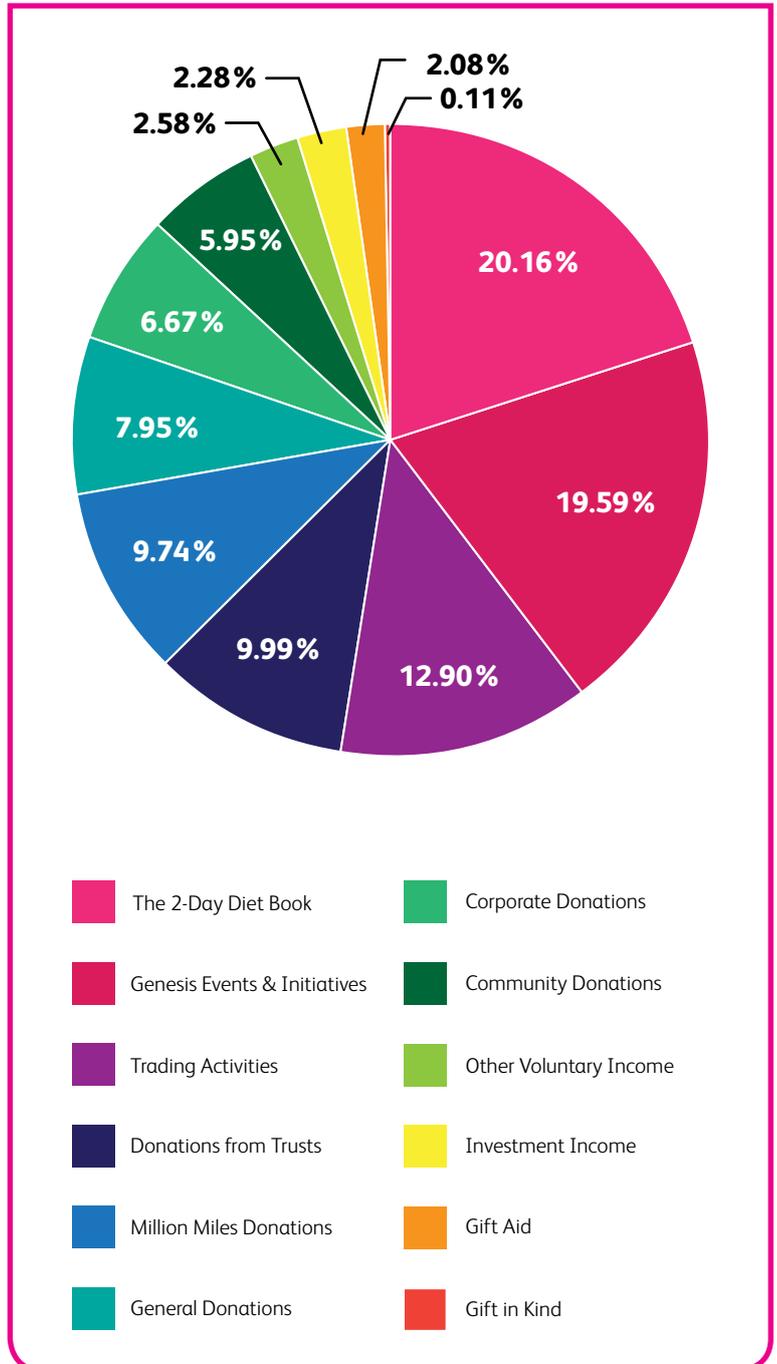
**Many thanks to all the Charitable Trusts and Foundations who have supported us over the last year:**

Arihant Charitable Trust; Bolton and District HSF (UK Healthcare); Brian Wilson Charitable Trust; Cancer Care Facility; Douglas Heath Eves Charitable Trust; Froggnal Trust; Gladys Wightwick Charitable Trust; Hull and East Riding Breast Friends; J & P Rose Charity Trust; Mazars Charitable Trust; Mills And Reeve Charitable Trust; Mrs E K Harding Charitable Foundation; Paycare Charity Trust; Pink Ribbon Foundation; Rosetrees Trust; Sapta Rishi Charitable Trust; Sir Samuel Scott of Yews Trust; Swinton Charitable Trust Ltd; The AMR Sciana Charitable Trust; The Annandale Charitable Trust; The Blueberry Charitable Trust; The Culra Charitable Trust; The Fanny Rapaport Charitable Trust; The Highcliffe Trust; The Hoover Foundation; The Hospital Saturday Fund; The John Mason Family Trust; The Kay Williams Charitable Foundation; The Manchester Guardian Society Charitable Trust; The Maurice & Pearl Esterkin Charitable Trust; The Maurits Mulder Canter Charity; The Michael and Anna Wix Charitable Trust; The Michael Goldstone Charitable Trust; The Oakdale Trust; The Poynton Foundation; The Rest-Harrow Trust; The Roger Vere Foundation; The Ronald Cruickshanks Foundation; The Rothera Family Charitable Trust; The Salter Family Charitable Trust; The Steinberg Family Charitable Trust; The Souter Charitable Trust; The Violet Mauray Charitable Trust; The Zochonis Charitable Trust; Vernacare; Yorkshire Building Society Charitable Foundation.

# The Figures 2013/14

We have worked hard to maintain major income generation initiatives whilst being conscious of our budgetary constraints. During the course of the year the Genesis team and our dedicated supporters have raised funds of £660,769.

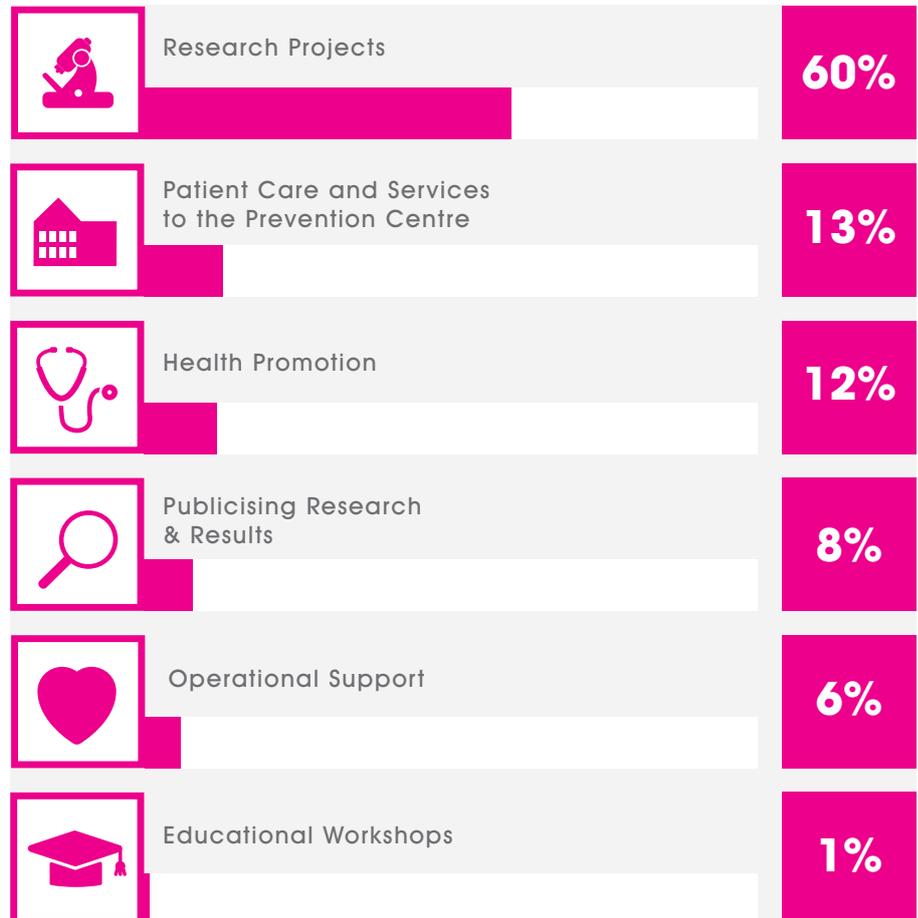
Incoming resources	£
The 2-Day Diet Book	133,224
Genesis Events & Initiatives	129,433
Trading Activities	85,244
Donations from Trusts	66,034
Million Miles Donations	64,411
General Donations	52,537
Corporate Donations	44,060
Community Donations	39,321
Other Voluntary Income	16,970
Investment Income	15,075
Gift Aid	13,698
Gift in Kind	763
<b>Total Income</b>	<b>660,769</b>



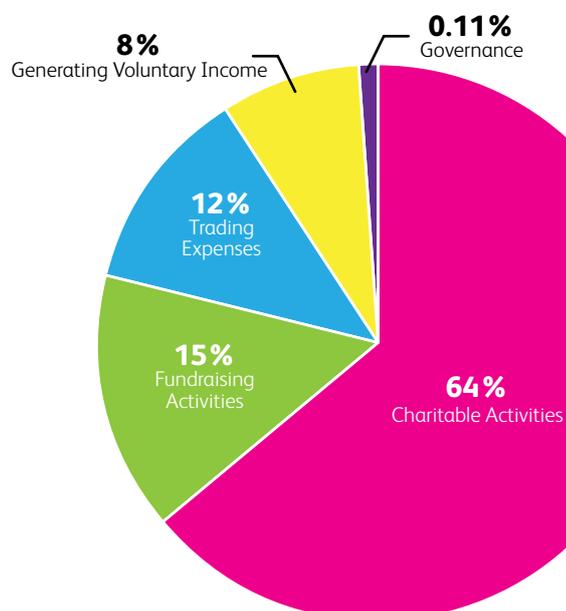
As always we must thank the wonderful supporters in the communities, colleges, schools and sports clubs who have helped to raise such substantial sums.

# How our funds are spent

During the year under review, we have spent £452,588 on Charitable Activities. Whilst this is less than last financial year, there are several important multi-year projects in the pipeline for 2015 & 2016. Furthermore in January 2014 we agreed to fund an additional Research Dietitian and Dietetic Assistant for a 12 month period to support our Diet and Lifestyle Team.



How we spend our funds	£
Charitable Activities	452,588
Fundraising Activities	106,979
Trading Expenses	54,267
Generating Voluntary Income	84,005
Governance	7,500
<b>Total Expenditure</b>	<b>705,339</b>



*Thank you*

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The Nightingale Centre and Genesis Prevention Centre,  
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